Supplementary Materials for

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Figure S1. Leave-one-out analysis of inverse-variance weighted (IVW) estimates between genetically determined gut microbiota traits ($p < 1 \times 10^{-5}$) and Type 2 diabetes (T2D), as well as coronary artery disease (CAD).

Figure S2. Leave-one-out analysis of inverse-variance weighted (IVW) estimates between genetically determined type 2 diabetes (T2D) traits ($P < 5\times 10^{-8}$), as well as coronary artery disease (CAD) traits ($P < 5\times10^{-8}$), and gut microbiota.

Figure S3. Leave-one-out analysis of inverse-variance weighted (IVW) estimates between genetically determined metabolites traits ($p < 1 \times 10^{-5}$) and Type 2 diabetes (T2D), as well as coronary artery disease (CAD).

Additional information 1. Harmonized data**.**

Additional information 2. Results of MR analysis.

Table S1. Description of Type 2 diabetes, Coronary artery disease, gut microbiota and metabolite.

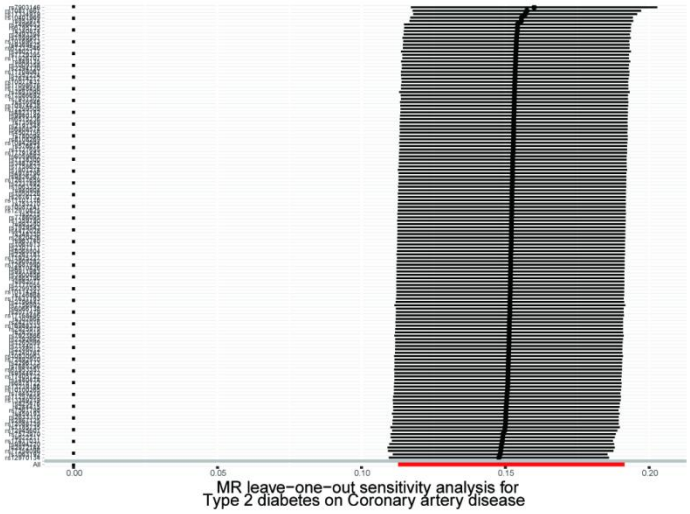
Traits	Consortium	First author	Sample size	Populations	Journal	Year	Download link
Type 2 diabetes	NA	Xue A	655,666 (61,714 cases / 1,178 controls)	European ancestry	Nat Commun.	2018	https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST006867/
Coronary artery disease	NA	Nikpay M	141,217 (42,096 cases / 361 controls)	European ancestry	Nat Genet.	2015	https://gwas.mrcieu.ac.uk/datasets/ebi-a-GCST003116/
Gut microbiota	MiBioGen[a]	Kurilshikov	18,340	predominantly European ancestry	Nat Genet.	2020	https://mibiogen.gcc.rug.nl/
Metabolites	FHS	Rhee	2076	European ancestry	Cell Metab.	2013	https://www.cell.com/cell-metabolism/fulltext/S1550-4131(13)00257-X?_returnURL=https%3A%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS15504131300257X%3Fshowall%3Dtrue#secsectitle0110

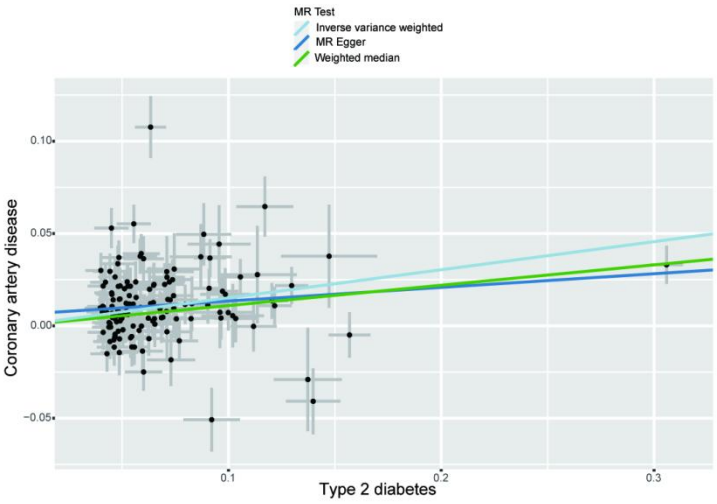
[a] MiBioGen consortium curated and analyzed genome-wide genotypes and 16S fecal microbiome data from 18,340 individuals (24 cohorts). Twenty cohorts included samples of single ancestry, namely European (16 cohorts; n= 13,266), Middle Eastern (1 cohort; n= 481), East Asian (1 cohort; n= 811), American Hispanic/Latin (1 cohort; n= 1,097) and African American (1 cohort; n= 114), whereas four cohorts included samples from multiple ancestries (n = 2,571).

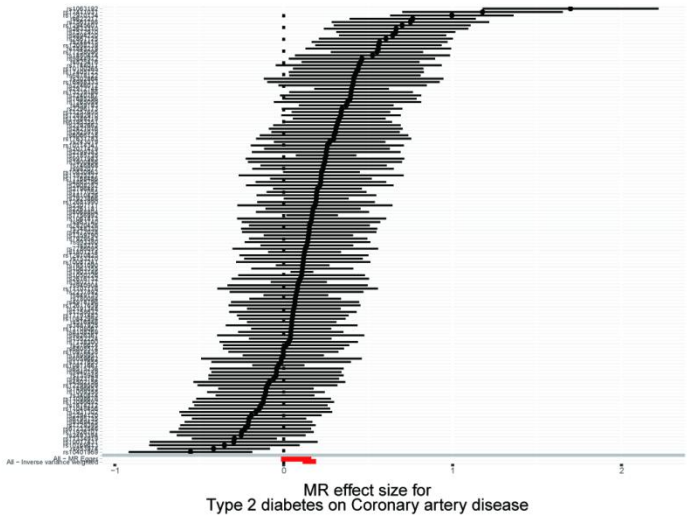
Table S2. Results of a bidirectional Mendelian randomization analysis of type 2 diabetes ($P<5\times10^{-8}$) and coronary artery disease ($P<5\times10^{-8}$).

Exposure	Outcome	Method	NSNP	Beta	P	Directional pleiotropy		Cochrane's Q-statistic(P)	Steiger P	IVW MRE
						Egger intercept(P)	MRPRESSO RSSobs(P)			
CAD	T2D	MR Egger	29	-0.005 (-0.219,0.210)	9.67E-01	0.007 (0.495)	148.952 (<0.001)	131.446 (2.44E-15)	6.17E-152	0.104
		Weighted median	29	0.062 (-0.011,0.135)	9.67E-02					
		IVW	29	0.066 (-0.014,0.145)	1.04E-01					
T2D	CAD	MR Egger	134	0.074 (-0.015,0.163)	1.07E-01	0.006 (0.058)	308.837 (<0.001)	303.207 (2.59E-15)	0	3.51E-14
		Weighted median	134	0.110 (0.057,0.163)	4.50E-05					
		IVW	134	0.152 (0.113,0.191)	3.51E-14					

T2D, Type 2 diabetes; CAD, Coronary artery disease; IVW, inverse variance weighted; NSNPs, number of single nucleotide polymorphisms; beta, mendelian randomization effect estimate; se, standard error of mendelian randomization effect estimate; OR(95%-CI), odds ratio and 95% confidence interval of odds ratio estimate; IVW MRE, Inverse variance weighted (multiplicative random effects)







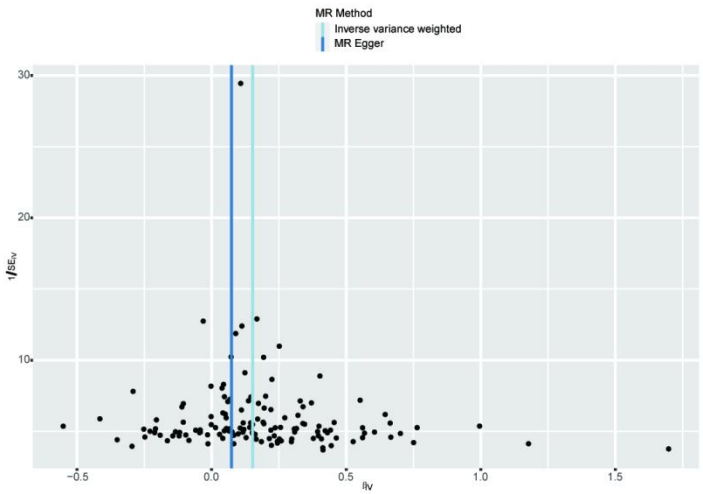


Table S3. MR Results of metabolites on T2D.

Exposure	Outcome	Method	NSNP	Beta (95%CI)	P	Directional pleiotropy		Cochrane's Q-statistic(P)	Steiger P
						Egger intercept(P)	MRPRESSO RSSobs(P)		
SM 14_0	T2D	MR Egger	68	-0.006(-0.041,0.029)	0.735	-0.007(0.152)	73.772(0.37)	71.865(0.32)	0
		Weighted median	68	-0.03(-0.044,-0.016)	<0.001				
		IVW	68	-0.031(-0.041,-0.02)	<0.001				
salicylurate	T2D	MR Egger	56	-0.022(-0.056,0.011)	0.197	0(0.925)	49.032(0.78)	47.374(0.758)	0
		Weighted median	56	-0.021(-0.038,-0.005)	0.012				
		IVW	56	-0.024(-0.035,-0.013)	<0.001				
proline	T2D	MR Egger	24	-0.067(-0.139,0.006)	0.084	0.012(0.364)	29.089(0.276)	27.085(0.252)	8.21E-216
		Weighted median	24	-0.051(-0.072,-0.031)	<0.001				
		IVW	24	-0.034(-0.05,-0.017)	<0.001				
LPC 18_2	T2D	MR Egger	41	-0.1(-0.189,-0.011)	0.034	0.014(0.153)	56.839(0.074)	54.044(0.068)	1.60E-228
		Weighted median	41	-0.059(-0.082,-0.037)	<0.001				
		IVW	41	-0.035(-0.052,-0.018)	<0.001				
citrulline	T2D	MR Egger	14	-0.143(-0.213,-0.072)	0.002	0.036(0.024)	18.286(0.327)	15.727(0.264)	2.19E-67
		Weighted median	14	-0.072(-0.112,-0.033)	<0.001				
		IVW	14	-0.057(-0.087,-0.027)	<0.001				
glycerol	T2D	MR Egger	38	-0.022(-0.065,0.022)	0.343	-0.001(0.882)	24.241(0.976)	22.807(0.968)	1.03E-255
		Weighted median	38	-0.022(-0.042,-0.003)	0.022				
		IVW	38	-0.025(-0.039,-0.011)	<0.001				
ornithine	T2D	MR Egger	72	-0.048(-0.091,-0.005)	0.031	0.007(0.186)	63.115(0.823)	61.124(0.792)	0
		Weighted median	72	-0.025(-0.042,-0.009)	0.002				
		IVW	72	-0.02(-0.031,-0.009)	0.001				
taurocholate	T2D	MR Egger	58	0.049(0.019,0.078)	0.002	-0.017(0.022)	33.341(0.996)	31.997(0.997)	0
		Weighted median	58	0.025(0.012,0.038)	<0.001				
		IVW	58	0.015(0.006,0.025)	0.002				
adenosine monophosphate	T2D	MR Egger	24	-0.034(-0.095,0.026)	0.280	0.001(0.84)	11.649(0.996)	9.267(0.995)	5.99E-139
		Weighted median	24	-0.039(-0.062,-0.016)	0.001				
		IVW	24	-0.028(-0.046,-0.01)	0.002				

cystathionine	T2D	MR Egger	21	-0.131(-0.209,-0.053)	0.004	0.028(0.017)	20.203(0.605)	18.002(0.587)	2.42E-98
		Weighted median	21	-0.045(-0.073,-0.017)	0.001				
		IVW	21	-0.03(-0.049,-0.011)	0.002				
serotonin	T2D	MR Egger	25	-0.192(-0.461,0.077)	0.174	0.033(0.258)	38.98(0.062)	35.716(0.058)	1.41E-117
		Weighted median	25	-0.015(-0.044,0.014)	0.314				
		IVW	25	-0.034(-0.057,-0.01)	0.005				
asparagine	T2D	MR Egger	46	-0.006(-0.056,0.045)	0.829	-0.003(0.654)	42.776(0.708)	34.805(0.864)	0
		Weighted median	46	-0.016(-0.034,0.003)	0.094				
		IVW	46	-0.017(-0.03,-0.004)	0.013				
adenosine	T2D	MR Egger	8	-0.162(-0.359,0.036)	0.159	0.025(0.266)	4.843(0.826)	3.708(0.813)	3.04E-34
		Weighted median	8	-0.043(-0.085,0)	0.048				
		IVW	8	-0.04(-0.074,-0.007)	0.019				
TAG 58_8	T2D	MR Egger	37	0.053(-0.039,0.146)	0.264	-0.015(0.123)	44.58(0.239)	42.146(0.222)	5.71E-241
		Weighted median	37	-0.029(-0.051,-0.006)	0.012				
		IVW	37	-0.02(-0.036,-0.003)	0.019				
PC 36_1	T2D	MR Egger	22	0.041(-0.18,0.262)	0.719	-0.003(0.868)	21.319(0.671)	16.577(0.736)	2.33E-145
		Weighted median	22	0.014(-0.01,0.039)	0.252				
		IVW	22	0.022(0.003,0.041)	0.022				
suberic acid	T2D	MR Egger	4	0.109(-0.455,0.672)	0.742	-0.018(0.848)	1.096(0.902)	0.465(0.927)	4.80E-18
		Weighted median	4	0.04(-0.009,0.089)	0.113				
		IVW	4	0.046(0.006,0.086)	0.023				

MR, mendelian randomization; T2D, Type 2 diabetes; IVW, inverse variance weighted; NSNPs, number of single nucleotide polymorphisms; beta, mendelian randomization effect estimate; CI, confidence interval; RSSobs, residual sums of squares of observations; SM, sphingomyelin; LPC lysophosphatidylcholine; TAG, triacylglycerol; PC, phosphatidylcholine.

Table S4. MR Results of metabolites on CAD.

Exposure	Outcome	Method	NSNP	Beta (95%CI)	P	Directional pleiotropy		Cochrane's Q-statistic(P)	Steiger P
						Egger intercept(P)	MRPRESSO RSSobs(P)		
3_hydroxyphenylacetic acid	CAD	MR Egger	18	-0.095(-0.206,0.016)	0.114	0.025(0.047)	19.849(0.477)	17.117(0.446)	1.82E-82
		Weighted median	18	0.021(-0.015,0.056)	0.252				
		IVW	18	0.024(-0.001,0.049)	0.057				
lysine	CAD	MR Egger	12	-0.083(-0.182,0.015)	0.129	0.009(0.524)	7.878(0.851)	6.756(0.818)	1.17E-51
		Weighted median	12	-0.063(-0.097,-0.028)	<0.001				
		IVW	12	-0.051(-0.078,-0.025)	<0.001				
alpha_ketoglutarate	CAD	MR Egger	42	-0.003(-0.047,0.04)	0.878	-0.007(0.248)	33.428(0.873)	31.813(0.848)	1.41E-249
		Weighted median	42	-0.042(-0.064,-0.02)	<0.001				
		IVW	42	-0.027(-0.043,-0.011)	0.001				
LPC 18_2	CAD	MR Egger	44	0.085(0.01,0.16)	0.032	-0.013(0.138)	48.301(0.354)	46.235(0.34)	1.02E-248
		Weighted median	44	0.016(-0.009,0.041)	0.218				
		IVW	44	0.029(0.011,0.047)	0.002				
CE 18_2	CAD	MR Egger	15	0.035(-0.058,0.127)	0.476	0.002(0.869)	9.655(0.89)	8.478(0.863)	6.46E-70
		Weighted median	15	0.049(0.012,0.087)	0.010				
		IVW	15	0.042(0.014,0.07)	0.003				
guanosine diphosphate	CAD	MR Egger	47	-0.019(-0.091,0.052)	0.595	0(0.982)	32.725(0.964)	31.292(0.952)	0
		Weighted median	47	-0.036(-0.055,-0.017)	<0.001				
		IVW	47	-0.02(-0.034,-0.006)	0.004				
proline	CAD	MR Egger	39	-0.008(-0.059,0.043)	0.760	-0.004(0.604)	39.739(0.476)	37.746(0.481)	0
		Weighted median	39	-0.023(-0.044,-0.002)	0.031				
		IVW	39	-0.021(-0.036,-0.007)	0.004				
carnitine	CAD	MR Egger	71	-0.064(-0.096,-0.033)	<0.001	0.015(0.001)	56.262(0.927)	54.978(0.906)	NA
		Weighted median	71	-0.016(-0.03,-0.003)	0.019				
		IVW	71	-0.014(-0.024,-0.004)	0.005				

hypoxanthine	CAD	MR Egger	21	0.064(0.001,0.126)	0.061	-0.008(0.263)	9.564(0.988)	8.698(0.986)	4.43E-102
		Weighted median	21	0.037(0.009,0.065)	0.009				
		IVW	21	0.029(0.008,0.05)	0.007				
salicylurate	CAD	MR Egger	59	0.001(-0.016,0.018)	0.942	0.005(0.087)	36.548(0.992)	34.661(0.994)	0
		Weighted median	59	0.005(-0.011,0.022)	0.533				
		IVW	59	0.013(0.003,0.023)	0.008				
aspartate	CAD	MR Egger	17	0.034(-0.008,0.075)	0.130	-0.003(0.621)	8.855(0.973)	6.47(0.982)	5.29E-89
		Weighted median	17	0.031(0.006,0.055)	0.015				
		IVW	17	0.024(0.006,0.043)	0.010				
anthranilic acid	CAD	MR Egger	46	0.038(-0.005,0.081)	0.092	-0.004(0.409)	45.065(0.599)	42.363(0.584)	2.86E-289
		Weighted median	46	0.01(-0.013,0.032)	0.403				
		IVW	46	0.021(0.005,0.037)	0.011				
UDP glucose; UDP galactose	CAD	MR Egger	50	-0.025(-0.105,0.055)	0.544	0.002(0.854)	26.901(0.999)	25.866(0.997)	0
		Weighted median	50	-0.021(-0.04,-0.002)	0.033				
		IVW	50	-0.018(-0.032,-0.003)	0.015				
allantoin	CAD	MR Egger	32	-0.054(-0.1,-0.008)	0.028	0.012(0.126)	18.482(0.977)	17.4(0.976)	1.22E-185
		Weighted median	32	-0.031(-0.053,-0.009)	0.006				
		IVW	32	-0.019(-0.035,-0.003)	0.017				
quinolinic acid	CAD	MR Egger	72	-0.043(-0.074,-0.012)	0.009	0.008(0.048)	53.779(0.956)	51.442(0.961)	0
		Weighted median	72	-0.026(-0.041,-0.01)	0.001				
		IVW	72	-0.013(-0.024,-0.002)	0.020				
asparagine	CAD	MR Egger	49	0.047(-0.003,0.098)	0.071	-0.008(0.228)	20.766(1)	19.63(1)	0
		Weighted median	49	0.009(-0.011,0.03)	0.362				
		IVW	49	0.017(0.003,0.032)	0.021				

MR, mendelian randomization; CAD, coronary artery disease ; IVW, inverse variance weighted; NSNPs, number of single nucleotide polymorphisms; beta, mendelian randomization effect estimate; CI, confidence interval; RSSobs, residual sums of squares of observations; LPC lysophosphatidylcholine; CE, cholesterol ester.

Table 3. Particulars of SNPs used in MR analyses of gut microbiota.

Exposure traits	SNPs	EA	OA	Beta	Se	samplesize	P	R^2	F-statistic
Type 2 diabetes ($P<5\times10^{-8}$)	rs1127655	T	C	-0.0438	0.0079	62892	2.47E-08	0.000	30.739
	rs12088739	G	A	-0.0884	0.013	62892	9.79E-12	0.001	46.240
	rs2493394	G	A	0.073	0.0113	62892	1.15E-10	0.001	41.734
	rs348330	A	G	-0.0487	0.0081	62892	1.86E-09	0.001	36.148
	rs2820426	G	A	0.0521	0.0073	62892	1.30E-12	0.001	50.937
	rs2296173	G	A	0.065	0.0087	62892	7.66E-14	0.001	55.820
	rs340874	C	T	0.0626	0.0073	62892	8.41E-18	0.001	73.536
	rs7572970	G	A	0.059	0.0087	62892	1.39E-11	0.001	45.990
	rs1009358	C	T	-0.0545	0.008	62892	9.81E-12	0.001	46.410
	rs2972144	G	A	0.0913	0.0075	62892	2.55E-34	0.002	148.190
	rs243019	C	T	0.0566	0.0071	62892	2.29E-15	0.001	63.550
	rs780094	C	T	0.0692	0.0074	62892	5.16E-21	0.001	87.448
	rs10169613	T	C	-0.0429	0.0078	62892	3.57E-08	0.000	30.250
	rs12617659	T	C	-0.0685	0.0103	62892	2.83E-11	0.001	44.229
	rs17334919	T	C	-0.1398	0.0128	62892	6.69E-28	0.002	119.287
	rs2867125	C	T	0.0601	0.0096	62892	4.33E-10	0.001	39.193
	rs13389219	T	C	-0.0722	0.0074	62892	2.11E-22	0.002	95.194
	rs7561798	G	A	0.04	0.0072	62892	2.79E-08	0.000	30.864
	rs3887925	T	C	0.0474	0.0079	62892	2.47E-09	0.001	36.000
	rs9844972	C	G	0.0956	0.0148	62892	1.03E-10	0.001	41.725
	rs6808574	C	T	0.0552	0.0076	62892	4.39E-13	0.001	52.753
	rs11708067	G	A	-0.0965	0.0086	62892	5.93E-29	0.002	125.909
	rs9826367	G	A	-0.0439	0.0079	62892	2.77E-08	0.000	30.880
	rs2292662	T	C	-0.0629	0.0111	62892	1.24E-08	0.001	32.111
	rs6795735	T	C	-0.0558	0.0073	62892	1.63E-14	0.001	58.428
	rs7651090	G	A	0.1204	0.0076	62892	3.85E-57	0.004	250.972
	rs11926707	C	T	0.0463	0.0082	62892	1.69E-08	0.001	31.881
	rs1899951	T	C	-0.1118	0.0109	62892	1.64E-24	0.002	105.204
	rs11925227	A	G	-0.0534	0.0095	62892	2.25E-08	0.001	31.596
	rs4472028	C	T	-0.0453	0.0071	62892	2.08E-10	0.001	40.708

rs1496653	G	A	-0.0769	0.0088	62892	2.57E-18	0.001	76.364
rs7674212	T	G	-0.0465	0.0075	62892	6.18E-10	0.001	38.440
rs993380	G	A	-0.0507	0.0081	62892	4.59E-10	0.001	39.178
rs11098676	C	T	0.054	0.0096	62892	2.03E-08	0.001	31.641
rs1801214	T	C	0.0903	0.0074	62892	5.52E-34	0.002	148.906
rs17086692	T	G	-0.0467	0.0084	62892	2.48E-08	0.000	30.908
rs7685296	T	C	-0.0511	0.0081	62892	2.32E-10	0.001	39.799
rs735949	C	T	-0.0711	0.0106	62892	1.95E-11	0.001	44.991
rs459193	G	A	0.0711	0.0083	62892	8.81E-18	0.001	73.381
rs3900856	A	G	0.1136	0.0185	62892	7.35E-10	0.001	37.706
rs6878122	A	G	-0.0564	0.0079	62892	1.19E-12	0.001	50.969
rs7729395	T	C	0.1373	0.016	62892	1.10E-17	0.001	73.638
rs1061813	A	G	-0.0429	0.0073	62892	3.37E-09	0.001	34.536
rs4865796	A	G	0.053	0.0078	62892	1.33E-11	0.001	46.170
rs2307111	C	T	-0.0407	0.0074	62892	3.03E-08	0.000	30.250
rs10077431	A	C	-0.0487	0.0089	62892	4.75E-08	0.000	29.942
rs853974	C	T	-0.0601	0.0088	62892	7.86E-12	0.001	46.643
rs746868	G	C	0.0519	0.0081	62892	1.40E-10	0.001	41.055
rs9369425	A	G	-0.0546	0.0085	62892	1.13E-10	0.001	41.262
rs72892910	T	G	0.0648	0.0099	62892	6.43E-11	0.001	42.843
rs7756992	G	A	0.1297	0.0078	62892	6.00E-62	0.004	276.497
rs622217	C	T	-0.0485	0.0077	62892	3.13E-10	0.001	39.674
rs1063355	G	T	0.0709	0.0079	62892	3.72E-19	0.001	80.545
rs1265099	G	A	0.0452	0.0074	62892	9.95E-10	0.001	37.309
rs2071479	T	C	0.1473	0.0226	62892	6.62E-11	0.001	42.480
rs2246012	C	T	0.0527	0.0094	62892	2.43E-08	0.000	31.432
rs1050226	G	A	-0.0491	0.0074	62892	3.34E-11	0.001	44.025
rs17168486	T	C	0.0742	0.0094	62892	2.18E-15	0.001	62.309
rs2908282	A	G	0.0552	0.0094	62892	4.25E-09	0.001	34.484
rs2191348	T	G	0.0652	0.0073	62892	3.44E-19	0.001	79.772
rs7786095	G	A	-0.0743	0.0129	62892	9.64E-09	0.001	33.174
rs13239186	T	C	0.0539	0.0085	62892	2.70E-10	0.001	40.211

rs13234269	A	T	-0.0583	0.0078	62892	6.98E-14	0.001	55.866
rs2299383	T	C	0.0412	0.0073	62892	1.49E-08	0.001	31.853
rs849135	A	G	-0.0999	0.0072	62892	1.04E-43	0.003	192.516
rs10100265	C	A	-0.0491	0.0079	62892	6.29E-10	0.001	38.629
rs2294120	G	A	-0.0443	0.0079	62892	1.62E-08	0.000	31.445
rs7845219	C	T	-0.0422	0.0072	62892	4.54E-09	0.001	34.353
rs12681990	C	T	0.0634	0.0096	62892	3.62E-11	0.001	43.615
rs10087241	A	G	-0.0475	0.008	62892	2.80E-09	0.001	35.254
rs3802177	A	G	-0.1217	0.008	62892	2.32E-52	0.004	231.420
rs516946	C	T	0.0824	0.0085	62892	3.16E-22	0.001	93.976
rs17411031	G	C	-0.045	0.0081	62892	3.04E-08	0.000	30.864
rs10974438	C	A	0.0591	0.0075	62892	3.01E-15	0.001	62.094
rs17791483	G	A	-0.102	0.0147	62892	3.42E-12	0.001	48.147
rs10811661	C	T	-0.1569	0.0098	62892	4.13E-58	0.004	256.327
rs2796441	A	G	-0.0715	0.0073	62892	1.96E-22	0.002	95.933
rs1758632	G	C	0.0491	0.0081	62892	1.36E-09	0.001	36.745
rs10114341	C	T	-0.0409	0.0072	62892	1.15E-08	0.001	32.269
rs1063192	A	G	0.0634	0.0073	62892	3.30E-18	0.001	75.428
rs2633310	T	G	-0.0443	0.0079	62892	2.37E-08	0.000	31.445
rs4918796	C	T	0.0623	0.0086	62892	4.01E-13	0.001	52.478
rs7923866	T	C	-0.0972	0.0074	62892	9.34E-40	0.003	172.532
rs2421016	T	C	-0.0458	0.0071	62892	1.48E-10	0.001	41.612
rs753270	C	T	0.0528	0.0079	62892	2.70E-11	0.001	44.670
rs11257655	T	C	0.0737	0.0087	62892	1.97E-17	0.001	71.762
rs7903146	T	C	0.3059	0.0077	62892	1.00E-200	0.024	1578.256
rs11591741	C	G	-0.0475	0.0078	62892	1.23E-09	0.001	37.085
rs2616132	A	G	0.0455	0.0078	62892	6.58E-09	0.001	34.028
rs7929543	C	A	0.0828	0.0138	62892	2.20E-09	0.001	36.000
rs7931302	A	C	-0.0461	0.008	62892	7.65E-09	0.001	33.206
rs67232546	T	C	0.0596	0.0096	62892	4.66E-10	0.001	38.543
rs10830963	G	C	0.0909	0.008	62892	5.85E-30	0.002	129.106
rs1552224	C	A	-0.1034	0.0101	62892	8.64E-25	0.002	104.809

rs2237892	T	C	-0.096	0.0157	62892	8.75E-10	0.001	37.389
rs5215	T	C	-0.0678	0.0073	62892	2.09E-20	0.001	86.261
rs10842994	T	C	-0.0755	0.0091	62892	1.02E-16	0.001	68.835
rs2261181	T	C	0.0985	0.0118	62892	9.18E-17	0.001	69.680
rs11107116	T	G	0.0467	0.0085	62892	3.75E-08	0.000	30.185
rs11048456	T	C	-0.0488	0.0082	62892	2.97E-09	0.001	35.417
rs940904	A	G	0.0499	0.0083	62892	2.08E-09	0.001	36.145
rs1480474	G	A	0.0411	0.0073	62892	1.68E-08	0.001	31.698
rs12299509	G	A	0.0467	0.0073	62892	2.09E-10	0.001	40.925
rs825476	T	C	0.0524	0.0073	62892	6.80E-13	0.001	51.525
rs7138300	T	C	-0.0443	0.0072	62892	5.65E-10	0.001	37.857
rs61953351	T	G	-0.07	0.0091	62892	1.98E-14	0.001	59.172
rs963740	T	A	-0.0479	0.0086	62892	2.23E-08	0.000	31.022
rs576674	A	G	-0.0654	0.0097	62892	1.79E-11	0.001	45.458
rs1359790	A	G	-0.0796	0.008	62892	2.80E-23	0.002	99.003
rs7144011	T	G	0.0482	0.0085	62892	1.64E-08	0.001	32.156
rs12910825	G	A	0.0517	0.0074	62892	2.16E-12	0.001	48.811
rs982077	G	A	-0.0453	0.0072	62892	2.58E-10	0.001	39.585
rs7177055	A	G	0.0647	0.0079	62892	2.75E-16	0.001	67.074
rs4502156	C	T	-0.0411	0.0073	62892	1.66E-08	0.001	31.698
rs244415	A	G	-0.0467	0.0079	62892	3.88E-09	0.001	34.945
rs7185735	G	A	0.1056	0.0073	62892	1.59E-47	0.003	209.258
rs77258096	A	C	-0.1171	0.0134	62892	1.78E-18	0.001	76.367
rs2925979	C	T	-0.0534	0.0078	62892	9.06E-12	0.001	46.870
rs9940149	A	G	-0.058	0.0095	62892	9.29E-10	0.001	37.274
rs17631783	T	C	-0.0487	0.0089	62892	3.95E-08	0.000	29.942
rs17405722	A	G	0.087	0.0146	62892	2.28E-09	0.001	35.509
rs302864	A	G	0.071	0.0127	62892	2.46E-08	0.000	31.254
rs9911983	T	C	0.0397	0.0073	62892	4.82E-08	0.000	29.576
rs8068804	A	G	0.0587	0.0078	62892	4.41E-14	0.001	56.635
rs12945601	C	T	-0.048	0.008	62892	1.72E-09	0.001	36.000
rs9894220	G	A	-0.0585	0.0079	62892	1.52E-13	0.001	54.835

	rs12970134	A	G	0.0555	0.008	62892	5.31E-12	0.001	48.129
	rs7240767	C	T	0.0451	0.0081	62892	2.16E-08	0.000	31.002
	rs8108269	G	T	0.0644	0.0079	62892	3.11E-16	0.001	66.453
	rs10401969	C	T	0.0921	0.0133	62892	4.13E-12	0.001	47.953
	rs6515236	C	A	-0.0504	0.0091	62892	3.34E-08	0.000	30.675
	rs6059662	G	A	0.0446	0.0079	62892	1.51E-08	0.001	31.872
	rs6066138	A	G	-0.049	0.0082	62892	1.93E-09	0.001	35.708
	rs4810426	T	C	0.0726	0.013	62892	2.15E-08	0.000	31.188
	rs16988333	G	A	-0.0745	0.013	62892	9.17E-09	0.001	32.842
	rs4823182	G	A	0.0482	0.0077	62892	3.36E-10	0.001	39.184
coronary artery disease ($P<5\times10^{-8}$)	rs67180937	G	T	0.078807	0.0110551	42457	1.01E-12	0.001	50.816
	rs6689306	G	A	-0.056012	0.0094061	42457	2.60E-09	0.001	35.460
	rs7528419	G	A	-0.11453	0.011482	42457	1.97E-23	0.002	99.495
	rs11206510	C	T	-0.074519	0.0133438	42457	2.34E-08	0.001	31.187
	rs9970807	T	C	-0.12575	0.016695	42457	5.00E-14	0.001	56.734
	rs7568458	A	T	0.059618	0.0095093	42457	3.62E-10	0.001	39.306
	rs115654617	A	C	0.137846	0.0158314	42457	3.12E-18	0.002	75.814
	rs17678683	G	T	0.098786	0.0166548	42457	3.00E-09	0.001	35.181
	rs16986953	A	G	0.08516	0.0150265	42457	1.45E-08	0.001	32.119
	rs515135	C	T	0.067499	0.0121924	42457	3.09E-08	0.001	30.649
	rs1199338	C	A	0.073596	0.0124987	42457	3.90E-09	0.001	34.672
	rs4593108	G	C	-0.07083	0.0115558	42457	8.82E-10	0.001	37.569
	rs17087335	T	G	0.060764	0.0111159	42457	4.59E-08	0.001	29.882
	rs72689147	T	G	-0.068558	0.0117905	42457	6.07E-09	0.001	33.811
	rs56336142	C	T	-0.066813	0.0118763	42457	1.85E-08	0.001	31.649
	rs12202017	G	A	-0.066813	0.0099612	42457	1.98E-11	0.001	44.988
	rs55730499	T	C	0.316641	0.0242403	42457	5.39E-39	0.004	170.631
	rs186696265	T	C	0.550351	0.0481949	42457	3.35E-30	0.003	130.400
	rs9349379	G	A	0.131836	0.0096527	42457	1.81E-42	0.004	186.539
	rs3918226	T	C	0.133315	0.0221275	42457	1.69E-09	0.001	36.299
	rs2107595	A	G	0.073415	0.0112951	42457	8.05E-11	0.001	42.246
	rs11556924	T	C	-0.072569	0.0110605	42457	5.34E-11	0.001	43.048

	rs2891168	G	A	0.193401	0.0091877	42457	2.29E-98	0.010	443.102
	rs2487928	A	G	0.062633	0.0095049	42457	4.41E-11	0.001	43.422
	rs1870634	G	T	0.075878	0.0097113	42457	5.55E-15	0.001	61.049
	rs11191416	G	T	-0.079249	0.0135252	42457	4.65E-09	0.001	34.332
	rs1412444	T	C	0.066812	0.0096809	42457	5.15E-12	0.001	47.630
	rs2128739	C	A	-0.065565	0.0100568	42457	7.05E-11	0.001	42.503
	rs10840293	A	G	0.054714	0.009619	42457	1.28E-08	0.001	32.355
	rs11065979	T	C	0.068556	0.0107672	42457	1.93E-10	0.001	40.540
	rs2681472	G	A	0.074114	0.0113331	42457	6.17E-11	0.001	42.766
	rs4773141	G	C	0.069732	0.0116482	42457	2.14E-09	0.001	35.838
	rs11617955	A	T	-0.088766	0.0161041	42457	3.55E-08	0.001	30.382
	rs11838776	A	G	0.068566	0.0107552	42457	1.83E-10	0.001	40.643
	rs10139550	G	C	0.05538	0.0097569	42457	1.38E-08	0.001	32.217
	rs4468572	C	T	0.077234	0.0095277	42457	4.44E-16	0.002	65.711
	rs56062135	T	C	-0.069743	0.0118937	42457	4.52E-09	0.001	34.385
	rs8042271	A	G	-0.096711	0.0175662	42457	3.68E-08	0.001	30.311
	rs7212798	C	T	0.079961	0.0142216	42457	1.88E-08	0.001	31.613
	rs663129	A	G	0.058163	0.0105173	42457	3.20E-08	0.001	30.583
	rs4420638	G	A	0.091906	0.0140977	42457	7.07E-11	0.001	42.500
	rs41290120	A	G	-0.181026	0.0281987	42457	1.37E-10	0.001	41.212
	rs56289821	A	G	-0.13361	0.0170415	42457	4.44E-15	0.001	61.470
	rs28451064	A	G	0.127571	0.015952	42457	1.33E-15	0.002	63.955
	rs180803	T	G	-0.180923	0.0283062	42457	1.64E-10	0.001	40.853
genus Lachnoclostridium id.11308 ($P<1\times10^{-5}$)	rs12566975	T	C	-0.0468097	0.0105787	14306	9.57194E-06	0.001	19.580
	rs1528479	A	G	0.0497799	0.0111919	14306	9.63984E-06	0.001	19.783
	rs615997	T	C	0.0511752	0.0106491	14306	2.0268E-06	0.002	23.094
	rs62285313	A	G	0.0864203	0.0181565	14306	1.58332E-06	0.002	22.655
	rs1031599	T	G	0.078627	0.0175644	14306	6.31379E-06	0.001	20.039
	rs3821998	C	A	-0.0864066	0.0192519	14306	6.72048E-06	0.001	20.144
	rs4738679	A	G	0.0520267	0.011404	14306	4.41754E-06	0.001	20.813
	rs1997204	C	T	0.108075	0.0242022	14306	5.97077E-06	0.001	19.941
	rs62028349	G	C	0.0469989	0.0105971	14306	9.17044E-06	0.001	19.670

	rs72829893	G	T	0.117472	0.0268103	14306	5.57763E-06	0.001	19.198
	rs78068103	A	G	0.0886199	0.0194248	14306	3.66522E-06	0.001	20.814
	rs2385421	A	G	0.0746186	0.0180734	14306	7.13724E-06	0.001	17.046
	rs789029	C	T	-0.0641288	0.0137974	14306	3.75327E-06	0.002	21.603
	rs6112314	A	C	-0.0561715	0.0108174	14306	2.43215E-07	0.002	26.964
genus Streptococcus id.1853 ($P<1\times10^{-5}$)	rs11720390	G	A	0.107024	0.0228121	14306	3.59484E-06	0.002	22.011
	rs6806351	T	C	-0.0633829	0.0136647	14306	4.93867E-06	0.002	21.515
	rs57646748	G	A	-0.0907696	0.0200344	14306	5.47545E-06	0.001	20.527
	rs10028567	C	T	-0.0921167	0.0191881	14306	7.30348E-06	0.002	23.047
	rs395407	C	G	0.0792781	0.0173697	14306	4.36506E-06	0.001	20.832
	rs77558518	A	G	-0.103999	0.0229714	14306	4.70858E-06	0.001	20.497
	rs11764382	A	G	-0.0695345	0.0143671	14306	1.28632E-06	0.002	23.424
	rs17708276	A	G	-0.0793955	0.0170628	14306	3.04096E-06	0.002	21.652
	rs10448310	A	G	-0.0517935	0.0111324	14306	3.30704E-06	0.002	21.646
	rs71481756	T	G	0.0931048	0.0207949	14306	6.51478E-06	0.001	20.046
	rs7916711	A	G	0.102891	0.0217362	14306	0.000002717	0.002	22.407
	rs1918540	A	G	-0.059639	0.0128148	14306	2.44068E-06	0.002	21.659
	rs11110281	T	C	-0.137519	0.0227398	14306	2.58315E-09	0.003	36.572
	rs2370083	G	T	-0.0816836	0.0185851	14306	9.75237E-06	0.001	19.317
	rs72739637	A	G	0.0959942	0.0193213	14306	1.03307E-06	0.002	24.684
	rs6563952	C	G	-0.0827344	0.0180035	14306	5.8213E-06	0.001	21.118
	rs4968759	A	G	-0.0515109	0.0112068	14306	3.7812E-06	0.001	21.127
	rs9903102	C	A	-0.0709483	0.0155275	14306	4.17994E-06	0.001	20.878
genus Actinomyces id.423 ($P<1\times10^{-5}$)	rs71315246	A	G	-0.0969809	0.021925	14306	9.82969E-06	0.001	19.566
	rs34583783	G	T	0.126596	0.0268461	14306	4.48528E-06	0.002	22.237
	rs4073240	G	A	0.0749687	0.0167368	14306	7.94273E-06	0.001	20.064
	rs35011108	A	G	0.232634	0.0512044	14306	6.33826E-06	0.001	20.641
	rs4146653	G	A	0.0985224	0.0214182	14306	4.49645E-06	0.001	21.159
	rs10787984	G	C	0.094316	0.0213513	14306	9.62299E-06	0.001	19.513
	rs7915461	C	T	-0.18776	0.0401636	14306	5.91984E-06	0.002	21.855
	rs2715439	T	C	-0.0746684	0.0164822	14306	6.27004E-06	0.001	20.523
family Streptococcaceae id.1850 ($P<1\times10^{-5}$)	rs77968078	G	A	-0.0993013	0.0224788	14306	7.93341E-06	0.001	19.515

	rs76717940	T	A	0.150606	0.0334079	14306	3.08937E-06	0.001	20.323
	rs6806351	T	C	-0.0619209	0.0135744	14306	6.93793E-06	0.001	20.808
	rs10028567	C	T	-0.0934027	0.0190343	14306	3.72495E-06	0.002	24.079
	rs57646748	G	A	-0.088021	0.019876	14306	7.88352E-06	0.001	19.612
	rs395407	C	G	0.0826855	0.0172536	14306	1.32559E-06	0.002	22.967
	rs77558518	A	G	-0.104239	0.022806	14306	3.72195E-06	0.001	20.891
	rs957755	T	G	-0.0642449	0.0142702	14306	7.41515E-06	0.001	20.268
	rs2952251	G	A	0.0639298	0.0126525	14306	3.72237E-07	0.002	25.530
	rs28718126	A	G	0.109069	0.0246868	14306	9.41044E-06	0.001	19.520
	rs7916711	A	G	0.0959639	0.021545	14306	6.32732E-06	0.001	19.839
	rs16950051	A	G	0.107008	0.0236973	14306	5.33814E-06	0.001	20.391
	rs11110281	T	C	-0.130554	0.0225943	14306	1.40136E-08	0.002	33.387
	rs2370083	G	T	-0.0842751	0.0184509	14306	4.25667E-06	0.001	20.862
	rs72739637	A	G	0.0927983	0.0192021	14306	1.82163E-06	0.002	23.355
	rs6563952	C	G	-0.0801931	0.0178576	14306	8.70583E-06	0.001	20.166
	rs35344081	G	A	0.0609349	0.0129703	14306	2.63846E-06	0.002	22.072
	rs9903102	C	A	-0.0693015	0.0154096	14306	4.91802E-06	0.001	20.226
	rs4968759	A	G	-0.0544035	0.0111271	14306	8.91887E-07	0.002	23.905
unknown genus id.2041 ($P<1\times10^{-5}$)	rs1032598	G	A	-0.0886426	0.0189039	14306	4.07587E-06	0.002	21.988
	rs16843660	A	G	0.234697	0.04907	14306	1.75344E-06	0.002	22.876
	rs11941716	A	G	0.101243	0.0224414	14306	9.0663E-06	0.001	20.353
	rs249459	A	G	0.0737341	0.0165018	14306	8.12307E-06	0.001	19.965
	rs553072	G	A	0.109193	0.0230198	14306	3.69097E-06	0.002	22.500
	rs1962916	G	A	-0.0737876	0.0162232	14306	6.13847E-06	0.001	20.687
	rs35703006	G	T	0.0926669	0.0190779	14306	9.00762E-07	0.002	23.593
	rs921383	G	A	0.0723153	0.0159706	14306	7.72894E-06	0.001	20.503
	rs2651663	A	G	-0.0762556	0.0168635	14306	5.64144E-06	0.001	20.448
	rs2336448	T	C	0.0773742	0.0160883	14306	1.42899E-06	0.002	23.130
	rs7187855	A	C	0.199941	0.0418308	14306	2.20602E-06	0.002	22.846
	rs6514318	T	C	0.128198	0.0281765	14306	5.37675E-06	0.001	20.701
genus Oxalobacter id.2978 ($P<1\times10^{-5}$)	rs4428215	G	A	0.130293	0.0242237	14306	7.51069E-08	0.002	28.931
	rs36057338	G	T	0.207847	0.0421439	14306	8.79812E-07	0.002	24.323

	rs1569853	T	C	-0.138078	0.0296981	14306	3.64502E-06	0.002	21.617
	rs6993398	G	A	0.127217	0.0278855	14306	7.12771E-06	0.001	20.813
	rs10464997	G	A	0.137691	0.0294804	14306	3.29754E-06	0.002	21.814
	rs12002250	A	C	0.217122	0.0466317	14306	1.41504E-06	0.002	21.679
	rs736744	T	C	-0.117882	0.0211262	14306	2.57472E-08	0.002	31.135
	rs3862635	C	T	-0.172142	0.0394026	14306	9.18692E-06	0.001	19.086
	rs11108500	A	G	-0.199099	0.0427327	14306	3.74283E-06	0.002	21.708
	rs111966731	T	C	0.213114	0.047162	14306	7.29861E-06	0.001	20.419
	rs6071435	T	A	-0.105512	0.021489	14306	1.07431E-06	0.002	24.109
	rs6000536	C	T	-0.130992	0.0253804	14306	2.06054E-07	0.002	26.637
genus Turicibacter id.2162 ($P<1\times10^{-5}$)	rs149744580	A	G	0.169883	0.0315478	14306	7.00971E-08	0.002	28.998
	rs4869133	G	A	0.131186	0.027197	14306	2.5537E-06	0.002	23.267
	rs2221441	G	C	0.0710364	0.015343	14306	3.45669E-06	0.001	21.436
	rs3734633	G	A	-0.120957	0.02683	14306	5.31912E-06	0.001	20.325
	rs55756211	T	C	-0.115115	0.0240708	14306	2.8053E-06	0.002	22.871
	rs2952020	A	G	0.0759019	0.0165764	14306	5.63313E-06	0.001	20.966
	rs61265175	G	C	-0.0858591	0.0185778	14306	4.13676E-06	0.001	21.359
	rs11054680	T	C	-0.104751	0.0226997	14306	2.30978E-06	0.001	21.295
	rs4247078	G	C	-0.0710377	0.0155221	14306	5.46072E-06	0.001	20.945
	rs11649454	G	C	0.0950891	0.0203433	14306	3.26625E-06	0.002	21.848
	rs7199484	G	A	-0.0731428	0.0160172	14306	5.7666E-06	0.001	20.853
	rs12603364	T	C	0.110861	0.0225598	14306	8.66603E-07	0.002	24.148
	rs11666533	C	T	-0.111689	0.0248436	14306	7.37106E-06	0.001	20.211
	rs2834977	T	C	-0.0959995	0.0208261	14306	3.95585E-06	0.001	21.248
genus Butyricicoccus id.2055 ($P<1\times10^{-5}$)	rs12034718	G	A	-0.0701199	0.0158213	14306	9.57679E-06	0.001	19.643
	rs10084203	G	A	-0.0549699	0.0123563	14306	8.58638E-06	0.001	19.791
	rs56221232	T	C	0.0828027	0.0167401	14306	7.61939E-07	0.002	24.467
	rs2017189	T	G	0.0506956	0.011024	14306	3.87258E-06	0.001	21.148
	rs62478070	T	G	0.224039	0.0494959	14306	5.93772E-06	0.001	20.488
	rs4962426	T	G	-0.0614216	0.0135979	14306	7.38482E-06	0.001	20.403
	rs7322368	C	T	-0.0815733	0.0183167	14306	5.51785E-06	0.001	19.834
	rs12585793	T	C	-0.262206	0.0564729	14306	5.79189E-06	0.002	21.558

	rs75238760	T	A	0.0619423	0.0139942	14306	6.79704E-06	0.001	19.592
unknown genus id.2071 ($P<1\times10^{-5}$)	rs4644504	T	C	-0.0969321	0.0216146	14306	5.81969E-06	0.001	20.111
	rs11809762	G	A	-0.0934634	0.0190198	14306	1.68287E-06	0.002	24.147
	rs11904514	A	G	0.109498	0.0249839	14306	7.89951E-06	0.001	19.208
	rs1809136	C	G	-0.0994594	0.0228638	14306	8.36989E-06	0.001	18.923
	rs16823675	C	T	-0.0767515	0.0149973	14306	2.33346E-07	0.002	26.191
	rs11684166	A	G	-0.0769635	0.0168349	14306	3.49116E-06	0.001	20.900
	rs10200320	T	C	-0.0641139	0.0142769	14306	5.6607E-06	0.001	20.167
	rs2898979	G	C	0.0901515	0.0202199	14306	7.67291E-06	0.001	19.879
	rs35740166	C	T	-0.112246	0.0226824	14306	8.39982E-07	0.002	24.489
	rs17086536	C	A	-0.100851	0.022432	14306	3.3638E-06	0.001	20.213
	rs34985298	G	A	-0.0623526	0.013772	14306	8.33758E-06	0.001	20.498
	rs1455639	A	G	-0.0760307	0.0169831	14306	7.83899E-06	0.001	20.042
	rs11195523	C	A	-0.0689278	0.0145351	14306	2.40121E-06	0.002	22.488
	rs2939766	A	G	-0.0591611	0.013042	14306	7.01148E-06	0.001	20.577
	rs76532867	T	C	0.112353	0.0242364	14306	2.55859E-06	0.001	21.490
	rs56975773	T	A	0.113282	0.0248859	14306	7.65491E-06	0.001	20.721
	rs12147596	C	T	-0.0719818	0.0141609	14306	2.86207E-07	0.002	25.838
	rs72700702	T	C	-0.091726	0.0189005	14306	1.59272E-06	0.002	23.553
	rs72707147	C	T	0.110109	0.0244644	14306	6.84022E-06	0.001	20.257
	rs6007642	C	T	-0.0791412	0.0177958	14306	9.95543E-06	0.001	19.777
family Clostridiales vadin BB60 group id.11286	rs7538034	T	G	-0.078598	0.0165982	14306	2.36706E-06	0.002	22.423
($P<1\times10^{-5}$)	rs6588624	A	G	0.0662317	0.0138147	14306	1.79287E-06	0.002	22.985
	rs13409132	A	G	-0.165419	0.0352154	14306	4.3723E-06	0.002	22.065
	rs2191834	T	G	-0.0746375	0.0159136	14306	2.50196E-06	0.002	21.998
	rs6755871	C	G	-0.0613825	0.0138976	14306	9.33061E-06	0.001	19.508
	rs989682	A	G	0.070194	0.0155364	14306	6.84715E-06	0.001	20.413
	rs10517600	G	T	-0.0626993	0.0139364	14306	6.82763E-06	0.001	20.241
	rs34088226	A	G	-0.117807	0.026924	14306	7.66214E-06	0.001	19.145
	rs7725895	A	G	-0.116224	0.0240367	14306	3.94357E-06	0.002	23.380
	rs66714985	A	C	0.116908	0.0252447	14306	4.85333E-06	0.001	21.446
	rs118104867	C	T	0.214464	0.0455098	14306	3.43598E-06	0.002	22.207

	rs10904722	C	T	-0.0672314	0.0147123	14306	5.04836E-06	0.001	20.883
	rs17121075	G	A	0.0769254	0.0172234	14306	7.91425E-06	0.001	19.948
	rs55682560	C	T	-0.131519	0.0261319	14306	4.97038E-07	0.002	25.330
	rs28691777	C	T	0.137134	0.0266996	14306	6.95697E-07	0.002	26.380
	rs7226487	A	G	-0.0643682	0.0138701	14306	3.58286E-06	0.002	21.537
	rs9979874	G	C	-0.0738925	0.0150911	14306	1.05271E-06	0.002	23.975
unknown genus id.1000000073 ($P<1\times10^{-5}$)	rs6588624	A	G	0.0662317	0.0138147	14306	1.79287E-06	0.002	22.985
	rs7538034	T	G	-0.078598	0.0165982	14306	2.36706E-06	0.002	22.423
	rs2191834	T	G	-0.0746375	0.0159136	14306	2.50196E-06	0.002	21.998
	rs13409132	A	G	-0.165419	0.0352154	14306	4.3723E-06	0.002	22.065
	rs6755871	C	G	-0.0613825	0.0138976	14306	9.33061E-06	0.001	19.508
	rs989682	A	G	0.070194	0.0155364	14306	6.84715E-06	0.001	20.413
	rs10517600	G	T	-0.0626993	0.0139364	14306	6.82763E-06	0.001	20.241
	rs7725895	A	G	-0.116224	0.0240367	14306	3.94357E-06	0.002	23.380
	rs34088226	A	G	-0.117807	0.026924	14306	7.66214E-06	0.001	19.145
	rs66714985	A	C	0.116908	0.0252447	14306	4.85333E-06	0.001	21.446
	rs118104867	C	T	0.214464	0.0455098	14306	3.43598E-06	0.002	22.207
	rs10904722	C	T	-0.0672314	0.0147123	14306	5.04836E-06	0.001	20.883
	rs17121075	G	A	0.0769254	0.0172234	14306	7.91425E-06	0.001	19.948
	rs55682560	C	T	-0.131519	0.0261319	14306	4.97038E-07	0.002	25.330
	rs28691777	C	T	0.137134	0.0266996	14306	6.95697E-07	0.002	26.380
	rs7226487	A	G	-0.0643682	0.0138701	14306	3.58286E-06	0.002	21.537
	rs9979874	G	C	-0.0738925	0.0150911	14306	1.05271E-06	0.002	23.975
genus Clostridium innocuum group id.14397 ($P<1\times10^{-5}$)	rs6577484	G	A	0.160425	0.0360857	14306	8.40601E-06	0.001	19.764
	rs1948423	T	A	-0.108859	0.023425	14306	3.49406E-06	0.002	21.596
	rs40656	C	T	0.142664	0.0311021	14306	8.61529E-06	0.001	21.040
	rs6890185	C	T	-0.113424	0.0233137	14306	1.12243E-06	0.002	23.669
	rs4869133	G	A	-0.180591	0.0409505	14306	7.24453E-06	0.001	19.448
	rs10074000	T	C	-0.102648	0.0227508	14306	6.99939E-06	0.001	20.357
	rs71564433	T	A	-0.126746	0.0274657	14306	7.8001E-06	0.001	21.295
	rs10506058	A	G	0.0997048	0.0221926	14306	8.92442E-06	0.001	20.184
	rs77845139	A	G	-0.114993	0.0257186	14306	8.40621E-06	0.001	19.992

	rs61267978	T	C	0.14708	0.0320875	14306	5.58509E-06	0.001	21.010
	rs1942371	G	A	-0.157938	0.034187	14306	4.0634E-06	0.001	21.343
class Lentisphaeria id.2250 ($P<1\times10^{-5}$)	rs72640280	A	G	0.220207	0.0486196	14306	5.18036E-06	0.001	20.513
	rs73113483	T	A	-0.131217	0.0288713	14306	8.66343E-06	0.001	20.656
	rs2731834	G	C	-0.109438	0.023693	14306	4.24356E-06	0.001	21.335
	rs11770843	C	T	0.109431	0.0234879	14306	1.9073E-06	0.002	21.707
	rs62570196	C	T	-0.21635	0.0439866	14306	1.07924E-06	0.002	24.192
	rs2031282	A	G	0.122368	0.0270329	14306	4.38258E-06	0.001	20.490
	rs17114848	G	A	0.152377	0.0324332	14306	4.05864E-06	0.002	22.073
	rs1002941	A	G	-0.105025	0.0233484	14306	8.14836E-06	0.001	20.234
	rs77599476	A	G	0.230292	0.0480168	14306	1.86132E-06	0.002	23.002
	rs2825714	A	G	-0.13741	0.0289246	14306	1.72211E-06	0.002	22.568
order Victivallales id.2254 ($P<1\times10^{-5}$)	rs72640280	A	G	0.220207	0.0486196	14306	5.18036E-06	0.001	20.513
	rs73113483	T	A	-0.131217	0.0288713	14306	8.66343E-06	0.001	20.656
	rs2731834	G	C	-0.109438	0.023693	14306	4.24356E-06	0.001	21.335
	rs11770843	C	T	0.109431	0.0234879	14306	1.9073E-06	0.002	21.707
	rs62570196	C	T	-0.21635	0.0439866	14306	1.07924E-06	0.002	24.192
	rs2031282	A	G	0.122368	0.0270329	14306	4.38258E-06	0.001	20.490
	rs1002941	A	G	-0.105025	0.0233484	14306	8.14836E-06	0.001	20.234
	rs17114848	G	A	0.152377	0.0324332	14306	4.05864E-06	0.002	22.073
	rs77599476	A	G	0.230292	0.0480168	14306	1.86132E-06	0.002	23.002
	rs2825714	A	G	-0.13741	0.0289246	14306	1.72211E-06	0.002	22.568
genus Bifidobacterium id.436 ($P<1\times10^{-5}$)	rs12022129	A	G	-0.0619356	0.0138937	14306	7.9965E-06	0.001	19.872
	rs1961273	C	T	0.0674036	0.0132319	14306	3.50865E-07	0.002	25.949
	rs13020688	G	A	0.0562696	0.0122617	14306	4.07258E-06	0.001	21.059
	rs182549	T	C	-0.119703	0.0127294	14306	1.2782E-20	0.006	88.429
	rs62181700	G	A	-0.0624643	0.0131205	14306	2.17245E-06	0.002	22.665
	rs4567981	T	A	0.0562084	0.0117923	14306	1.92832E-06	0.002	22.720
	rs55888705	A	G	0.0546319	0.0121139	14306	6.67022E-06	0.001	20.339
	rs4957061	T	C	0.0534239	0.0117431	14306	5.77936E-06	0.001	20.697
	rs73797465	T	G	-0.0953566	0.0209236	14306	4.38157E-06	0.001	20.770
	rs76671854	C	G	-0.0846055	0.0184003	14306	3.95667E-06	0.001	21.142

rs857444	C	T	0.0558234	0.0121219	14306	0.000003571	0.001	21.208
rs2686790	C	T	-0.070741	0.0157926	14306	7.49894E-06	0.001	20.065
rs2491158	A	G	-0.0712624	0.015983	14306	8.04711E-06	0.001	19.879
rs10841473	G	C	-0.0624207	0.0129438	14306	1.6452E-06	0.002	23.256
rs7322849	T	C	0.112428	0.0201813	14306	1.08368E-08	0.002	31.035
rs540489	T	G	-0.0637641	0.0138746	14306	5.19457E-06	0.001	21.121
rs75344046	C	T	0.232354	0.0505979	14306	4.86351E-06	0.001	21.088
rs5746486	T	C	-0.0536216	0.0120801	14306	8.99953E-06	0.001	19.703

SNPs, single nucleotide polymorphisms; EA, effect allele; OA, other allele; Beta, effect estimate; SE, standard error; $R^2 = (beta^2) / (se^2 \times N + beta^2)$; $F = beta^2 / se^2$.

Table S6. MR Power calculation for detecting significant (P < 0.05) causal effect of gut microbiota on the risk of T2D/CAD, and T2D/CAD on the risk of gut microbiota.

Expoure	Outcome	NSNPs	R^2	Power	
				beta=0.1	beta=0.2
T2D	genus Butyrivibrio id.1993	124	0.143	1.00	1.00
	genus Catenibacterium id.2153	114	0.134	1.00	1.00
	genus Olsenella id.822	124	0.143	1.00	1.00
	family Oxalobacteraceae id.2966	125	0.143	1.00	1.00
	genus Erysipelotrichaceae UCG003 id.11384	14	0.013	0.82	1.00
	genus Veillonella id.2198	36	0.053	1.00	1.00
	genus Butyricicoccus id.2055	36	0.053	1.00	1.00
	family Christensenellaceae id.1866	10	0.011	0.58	0.99
	genus Ruminococcaceae UCG004 id.11362	36	0.053	1.00	1.00
	genus Haemophilus id.3698	36	0.053	1.00	1.00
	class Gammaproteobacteria id.3303	36	0.053	1.00	1.00
	family Prevotellaceae id.960	36	0.053	1.00	1.00
	genus Coprococcus1 id.11301	36	0.053	1.00	1.00
	genus Lachnospiraceae UCG008 id.11328	35	0.052	1.00	1.00
CAD	genus Family XIII UCG001 id.11294	36	0.053	1.00	1.00
	genus Methanobrevibacter id.123	34	0.048	1.00	1.00
	genus Lachnospiraceae UCG010 id.11330	36	0.053	1.00	1.00
	class Methanobacteria id.119	34	0.048	1.00	1.00
	family Methanobacteriaceae id.121	34	0.048	1.00	1.00
	order Methanobacteriales id.120	34	0.048	1.00	1.00
	family Lachnospiraceae id.1987	36	0.053	1.00	1.00
	family Pasteurellaceae id.3689	36	0.053	1.00	1.00
	order Pasteurellales id.3688	36	0.053	1.00	1.00
	genus Prevotella9 id.11183	36	0.053	1.00	1.00
Outcome	**Expoure**	**NSNPs**	**R^2**	**Power**	
				beta=0.1	**beta=0.2**
CAD	genus Oxalobacter id.2978	11	0.018	0.36	0.91
	genus Turicibacter id.2162	10	0.016	0.33	0.87
	genus Butyricicoccus id.2055	8	0.120	0.26	0.76
	unknown genus id.2071	16	0.240	0.46	0.97
	family Clostridiales vadin BB60 group id.11286	15	0.260	0.49	0.98
	unknown genus id.1000000073	15	0.230	0.45	0.96
	genus Clostridium innocuum group id.14397	9	0.130	0.28	0.79
	class Lentisphaeria id.2250	8	0.120	0.26	0.76
	order Victivallales id.2254	8	0.120	0.26	0.76
	genus Bifidobacterium id.436	14	0.260	0.49	0.98
	genus Lachnoclostridium id.11308	8	0.012	0.26	0.76
	genus Streptococcus id.1853	11	0.018	0.36	0.91
T2D	genus Actinomyces id.423	5	0.007	0.17	0.53
	family Streptococcaceae id.1850	13	0.020	0.40	0.93
	unknown genus id.2041	6	0.009	0.21	0.64

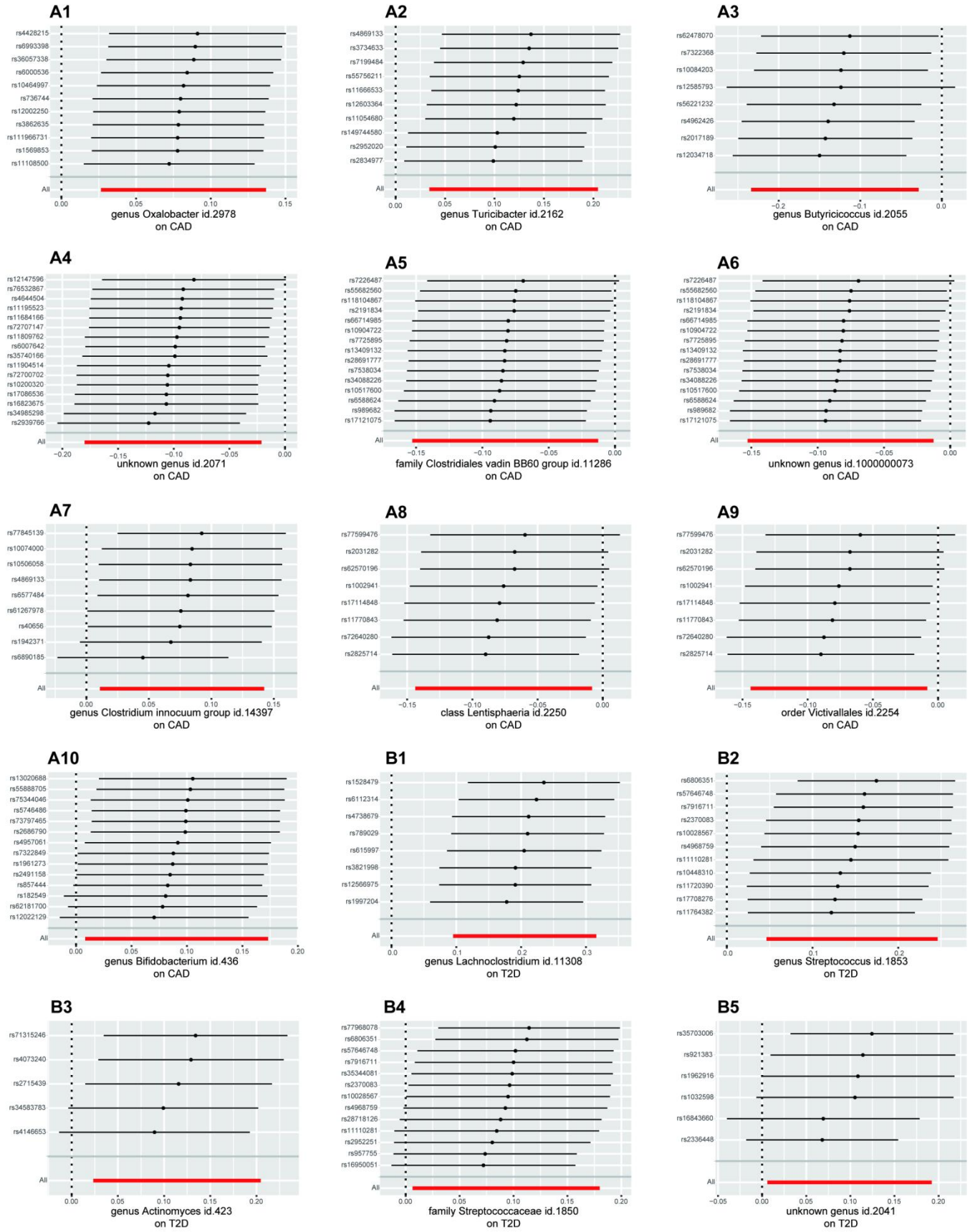
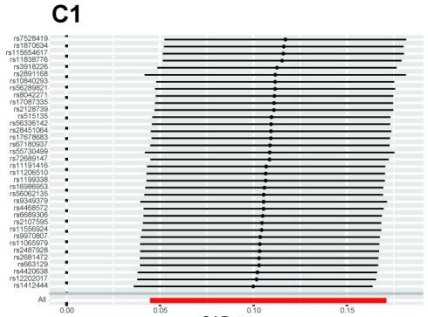


Figure S1. Leave-one-out analysis of inverse-variance weighted (IVW) estimates between genetically determined gut microbiota traits ($p < 1 \times 10^{-5}$) and Type 2 diabetes (T2D), as well as coronary artery disease (CAD).

Black dots indicate the IVW estimates (raw beta) after leaving a SNP in the calculation. The red dots indicate the pooled IVW estimates (raw beta). The horizontal line indicates the range of 95% confidence intervals.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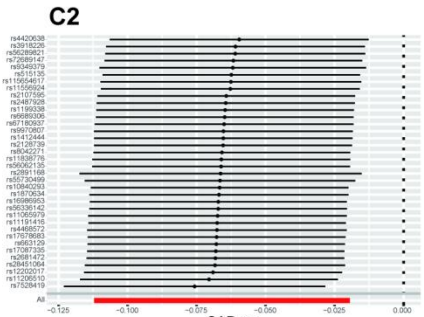
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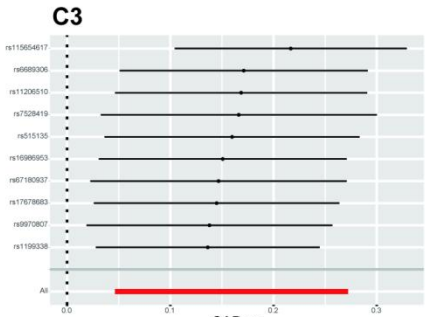
C3
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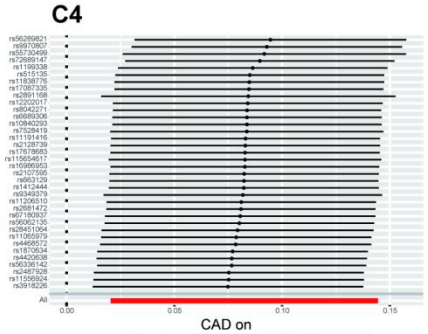
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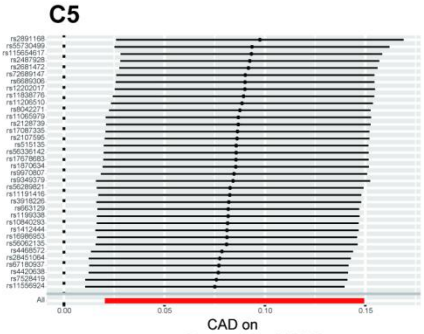
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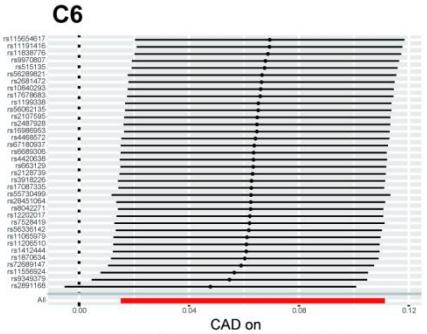
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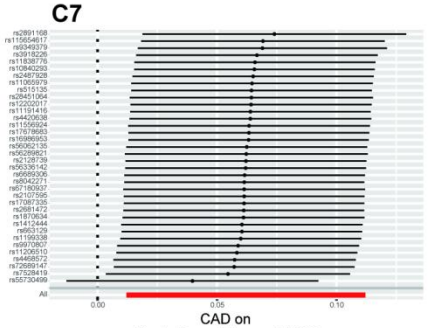
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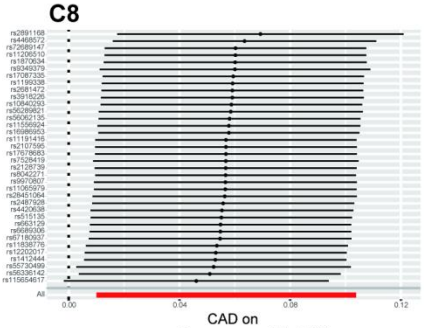
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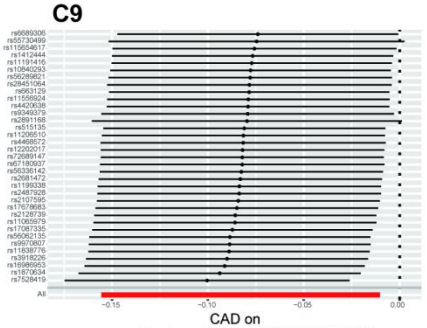
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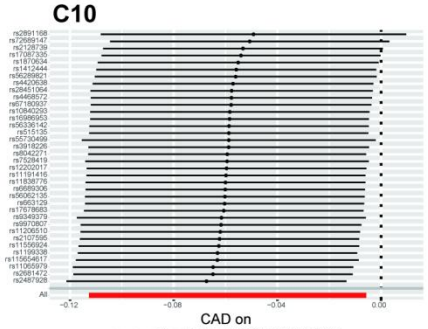
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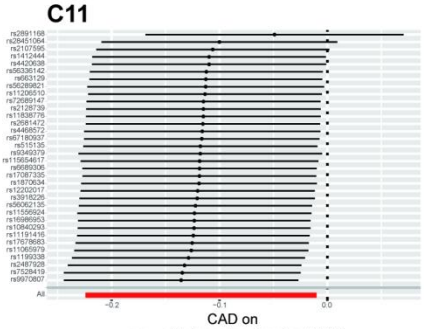
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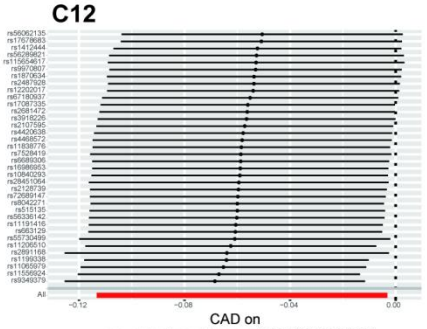
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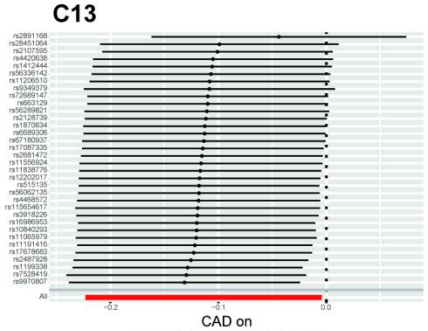
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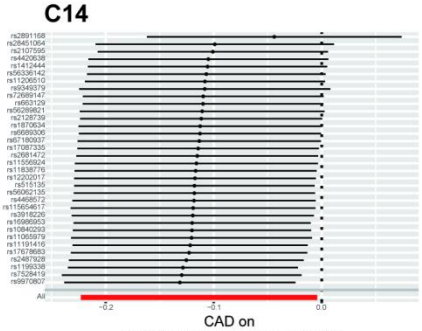
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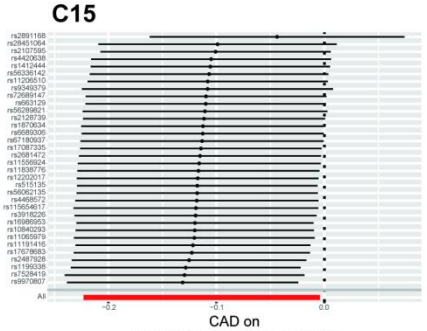
C15
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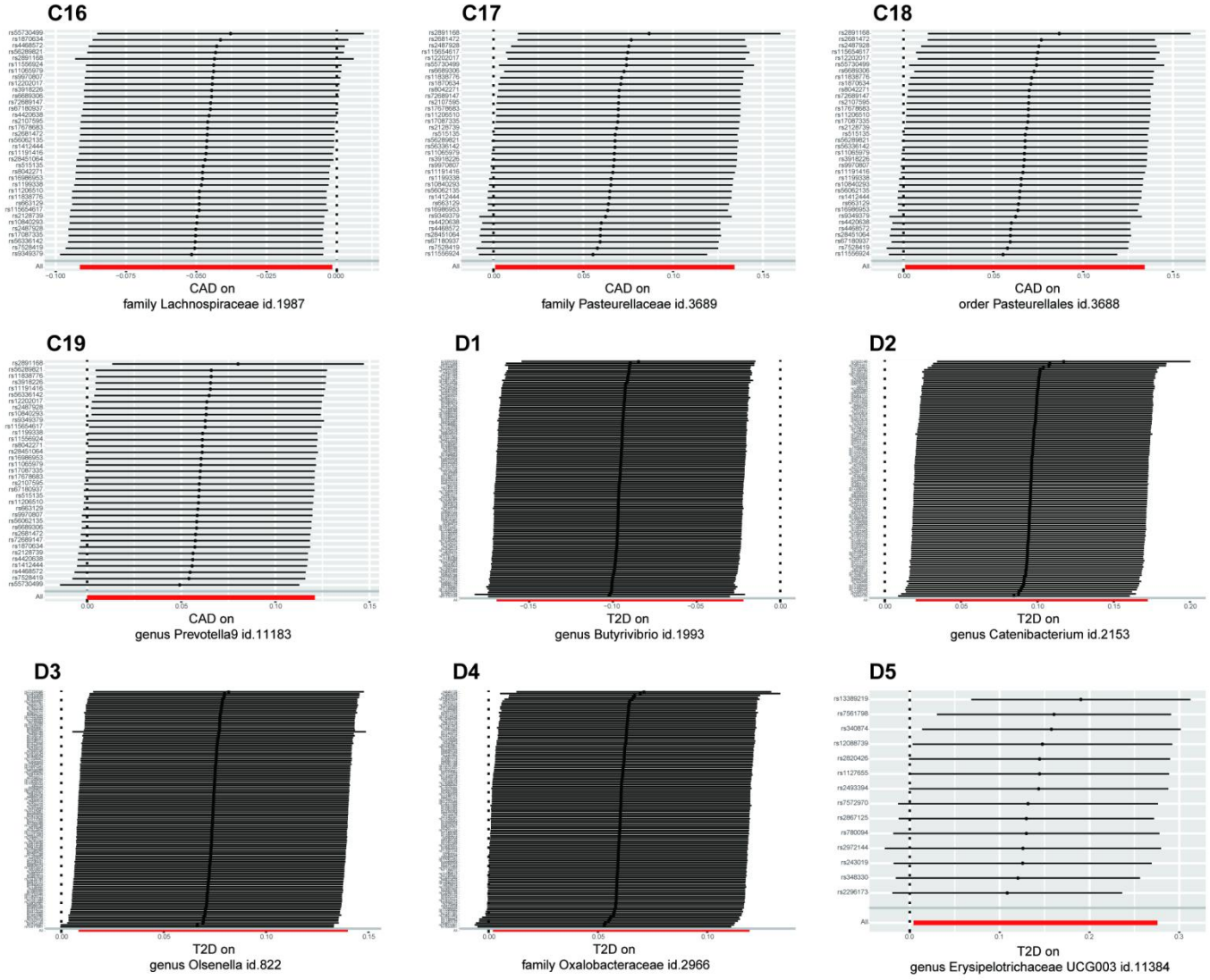
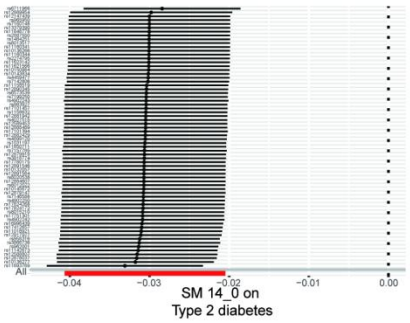


Figure S2. Leave-one-out analysis of inverse-variance weighted (IVW) estimates between genetically determined type 2 diabetes (T2D) traits ($P < 5\times10^{-8}$), as well as coronary artery disease (CAD) traits ($P < 5\times10^{-8}$), and gut microbiota.

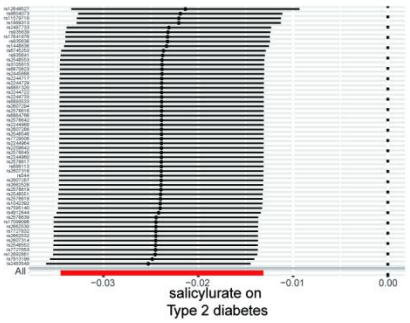
Black dots indicate the IVW estimates (raw beta) after leaving a SNP in the calculation. The red dots indicate the pooled IVW estimates (raw beta). The horizontal line indicates the range of 95% confidence intervals.

E1



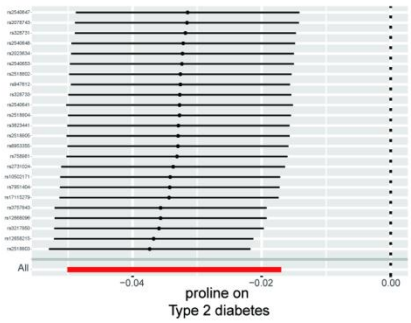
SM 14_0 on
Type 2 diabetes

E2



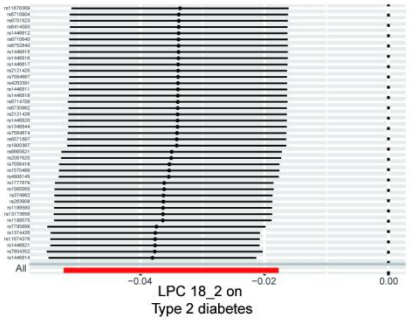
salicylurate on
Type 2 diabetes

E3



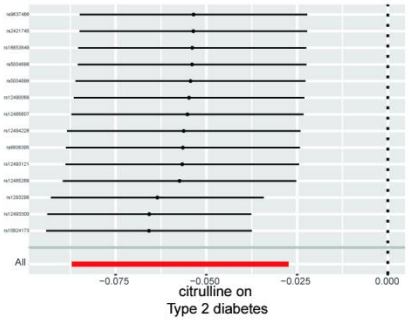
proline on
Type 2 diabetes

E4



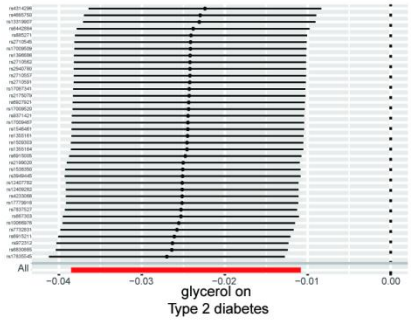
LPC 18_2 on
Type 2 diabetes

E5



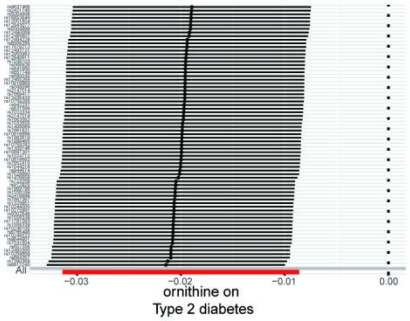
citrulline on
Type 2 diabetes

E6



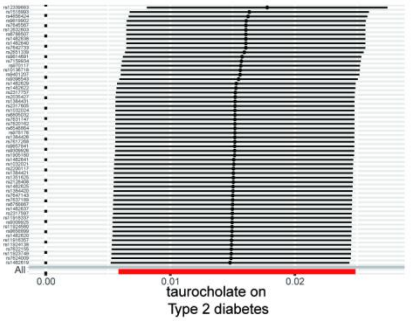
glycerol on
Type 2 diabetes

E7



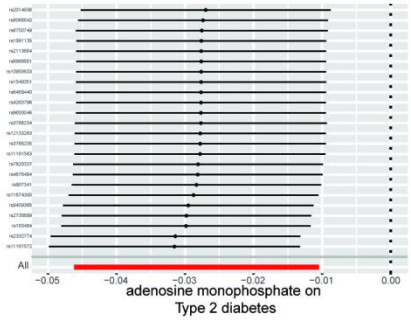
ornithine on
Type 2 diabetes

E8



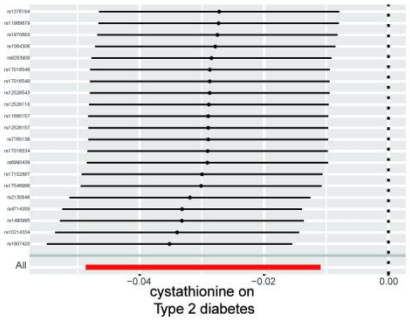
taurocholate on
Type 2 diabetes

E9



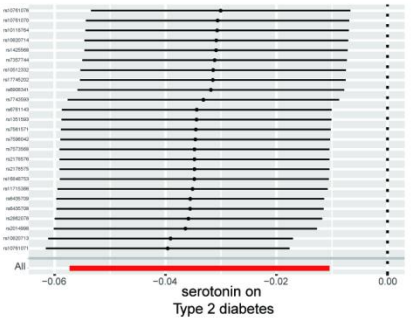
adenosine monophosphate on
Type 2 diabetes

E10



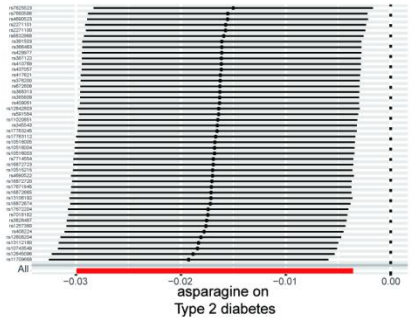
cystathionine on
Type 2 diabetes

E11



serotonin on
Type 2 diabetes

E12



asparagine on
Type 2 diabetes

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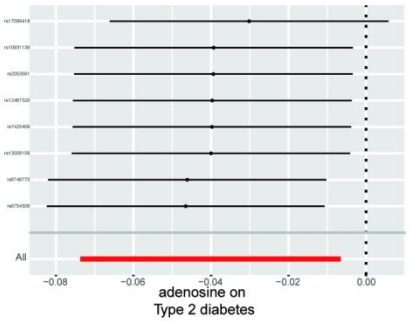
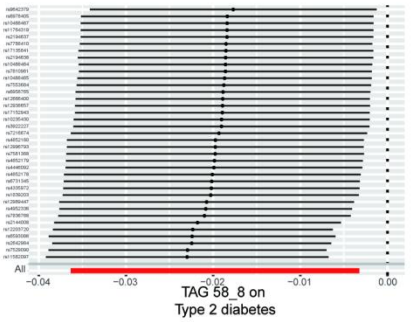


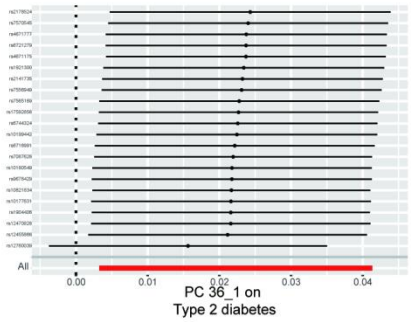
adenosine on
Type 2 diabetes

E14



TAG 58_8 on
Type 2 diabetes

E15



PC 36_1 on
Type 2 diabetes

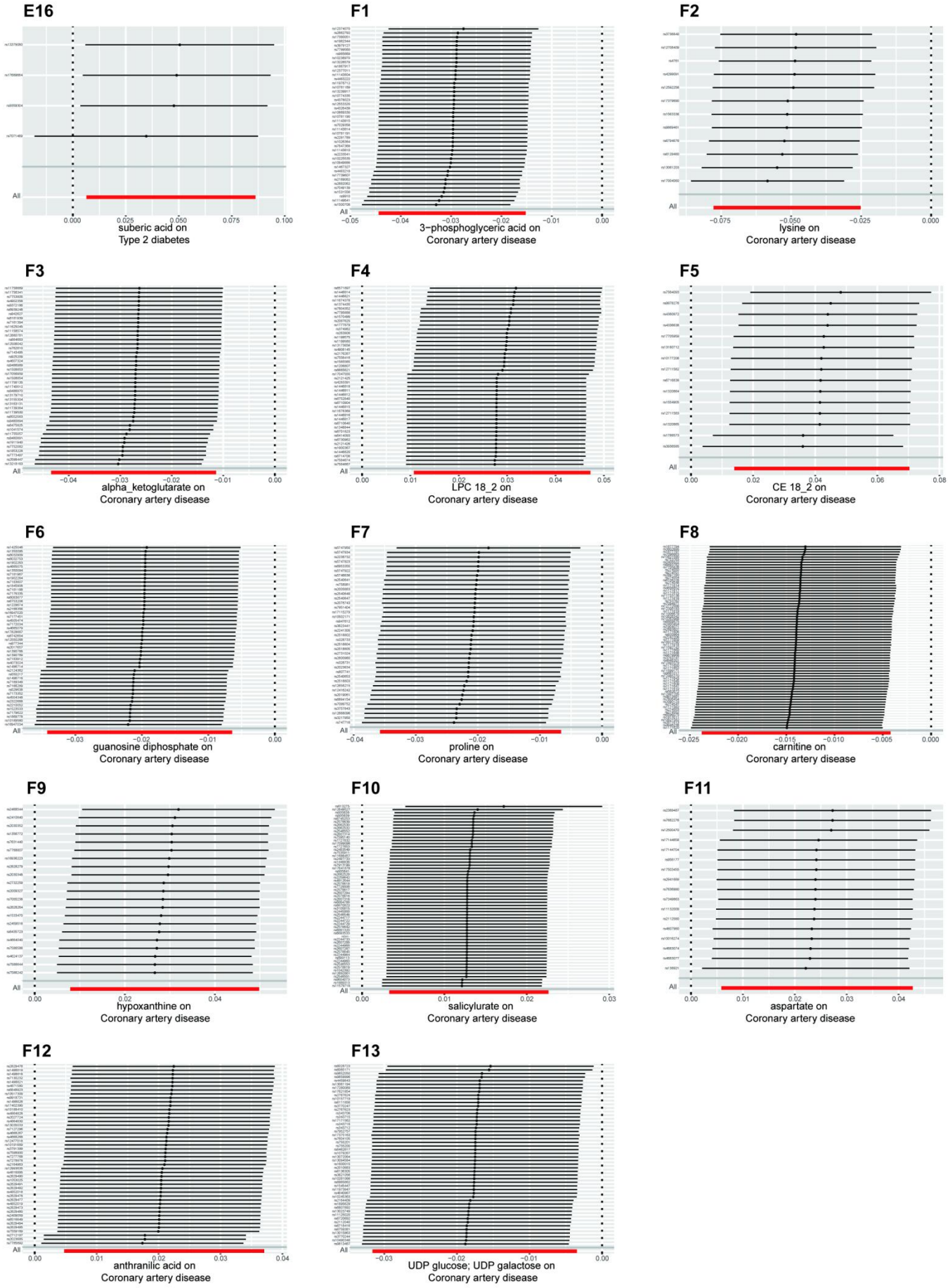


Figure S3. Leave-one-out analysis of inverse-variance weighted (IVW) estimates between genetically determined metabolites traits ($p < 1 \times 10^{-5}$) and Type 2 diabetes (T2D), as well as coronary artery disease (CAD).
Black dots indicate the IVW estimates (raw beta) after leaving a SNP in the calculation. The red dots indicate the pooled IVW estimates (raw beta). The horizontal line indicates the range of 95% confidence intervals.