

Supplementary Information

Supplement Table S17

Casual effects of MR Analysis between DN and causal GM (P<1.00E-05)							
Exposure	Outcome	Method	NSNP	β	95%CI		P
	Class						
DN	<i>Gammaproteobacteria</i>	IVW	16	0.019101	-0.013464	0.051667	0.250292
	<i>Verrucomicrobiae</i>	IVW	15	0.035929	-0.002094	0.073952	0.064014
	Family						
DN	<i>Verrucomicrobiaceae</i>	IVW	15	0.035861	-0.002162	0.073884	0.06452
	Genus						
	<i>Butyricoccus</i>	IVW	16	-8.23E-04	-0.033451	0.031804	0.960556
	<i>Eubacteriumcoprostanoligenesgroup</i>	IVW	16	-0.006155	-0.043457	0.031148	0.746405
	<i>Howardella</i>	IVW	12	0.019079	-0.051494	0.089651	0.596206
DN	<i>Lachnoclostridium</i>	IVW	16	-0.011066	-0.047813	0.02568	0.555023
	<i>Olsenella</i>	IVW	12	-0.004858	-0.08008	0.070364	0.899275
	<i>Oxalobacter</i>	IVW	12	0.019993	-0.044556	0.084541	0.543804
	<i>RuminococcaceaeUCG002</i>	IVW	16	0.028739	-0.002835	0.060313	0.074417
	<i>Tyzzarella3</i>	IVW	13	0.021698	-0.037667	0.081063	0.473758
	Order						
DN	<i>Rhodospirillales</i>	IVW	15	0.057802	0.012913	0.102692	0.01161
	<i>Verrucomicrobiales</i>	IVW	15	0.035671	-0.002382	0.073724	0.066163
	Phylum						
DN	<i>Bacteroidetes</i>	IVW	16	0.009145	-0.021315	0.039606	0.556225
	<i>Proteobacteria</i>	IVW	16	0.040189	0.008524	0.071855	0.01286

Supplement Table S18

Results of sensitivity analysis DN on causal GM (IVW: P<0.05)						
Exposure	Outcome	IVW_Q	IVW_Q_P	Egger_intercept	Pleiotropy_P	MR-PRESSO
	Order					
DN	<i>Rhodospirillales</i>	10.87189	0.6960694	0.006074415	0.5784344	0.4486667
	Phylum					
DN	<i>Proteobacteria</i>	16.1341	0.3731958	0.000513166	0.9486579	0.7693333

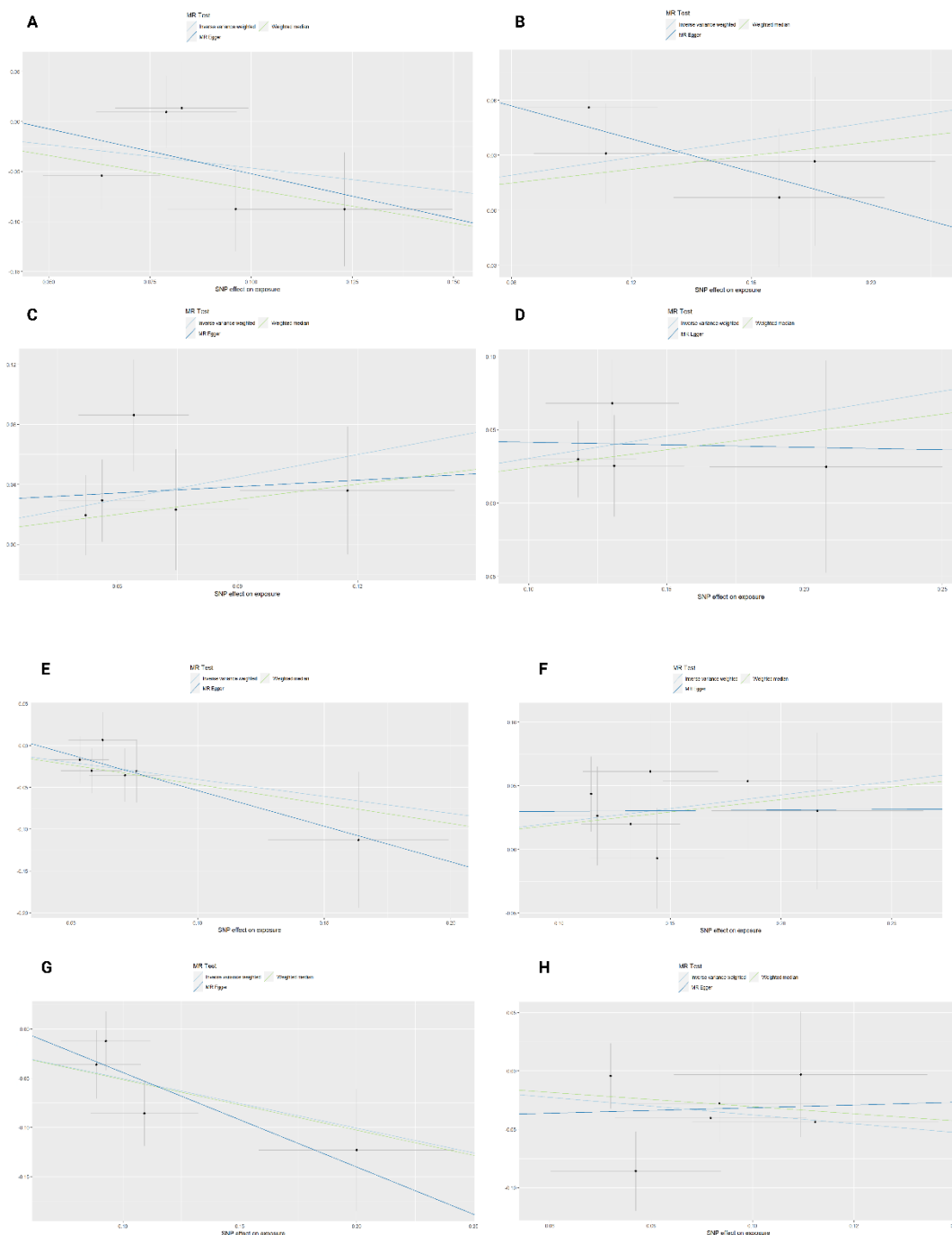
Supplement Table S19

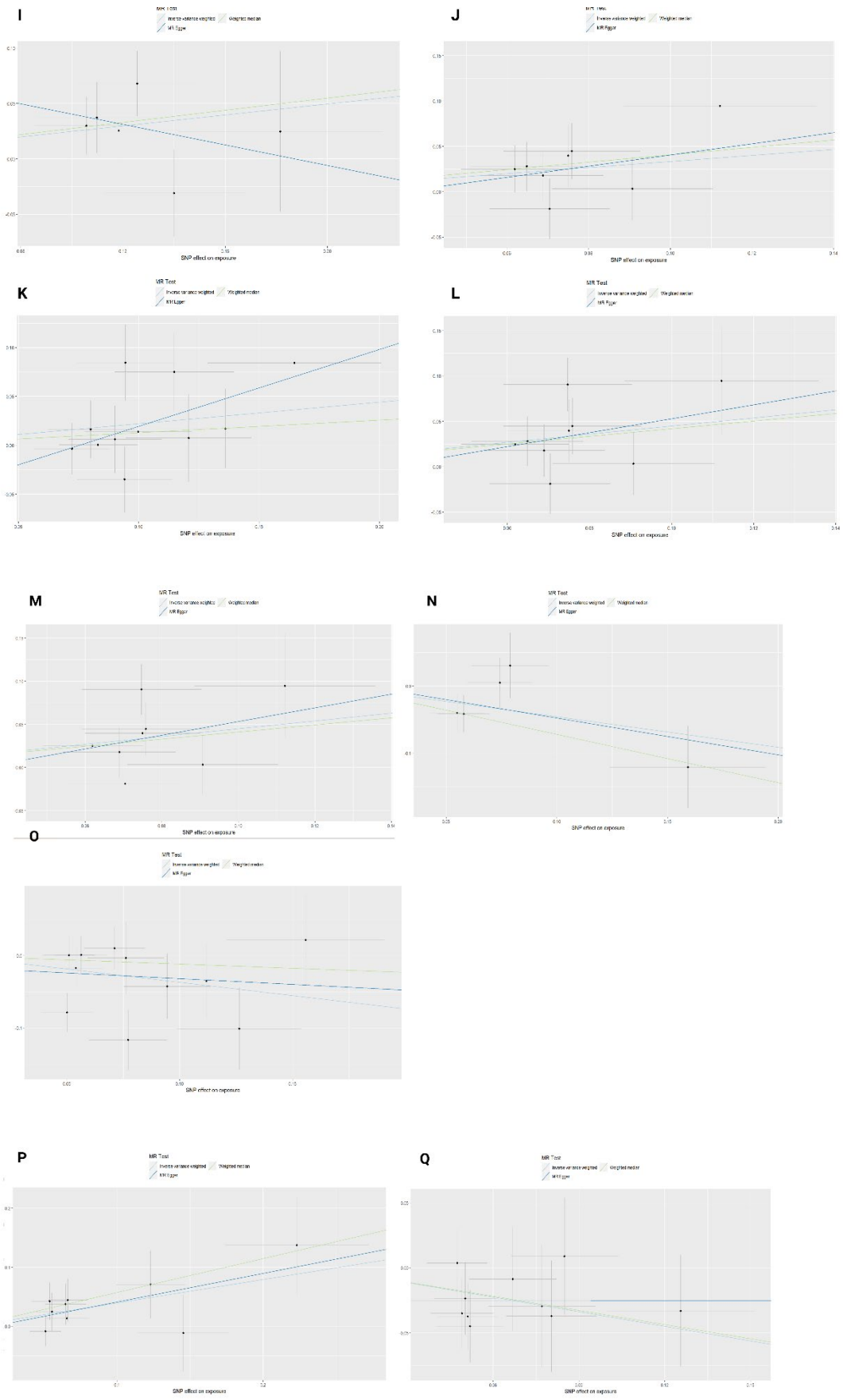
Characterization of Exposure and Outcome

Level	Name	Population	Reference or Website	Database
Exposure	Gut Microbiota	European	Kurilshikov A, Medina-Gomez C, Bacigalupe R, et al. Large-scale association analyses identify host factors influencing human gut microbiome composition.	MiBioGen Consortium
Outcome	DN	European	https://risteys.finregistry.fi/endpoints/DM_NEPHROPATHY	FinnGen
	T1DM	European	https://risteys.finregistry.fi/endpoints/T1D_WIDE	
	T2DM	European	https://risteys.finregistry.fi/endpoints/T2D_WIDE	
	T1DN	European	https://risteys.finregistry.fi/endpoints/E4_DM1REN	
	T2DN	European	https://risteys.finregistry.fi/endpoints/E4_DM2REN	

Supplement Figure S1

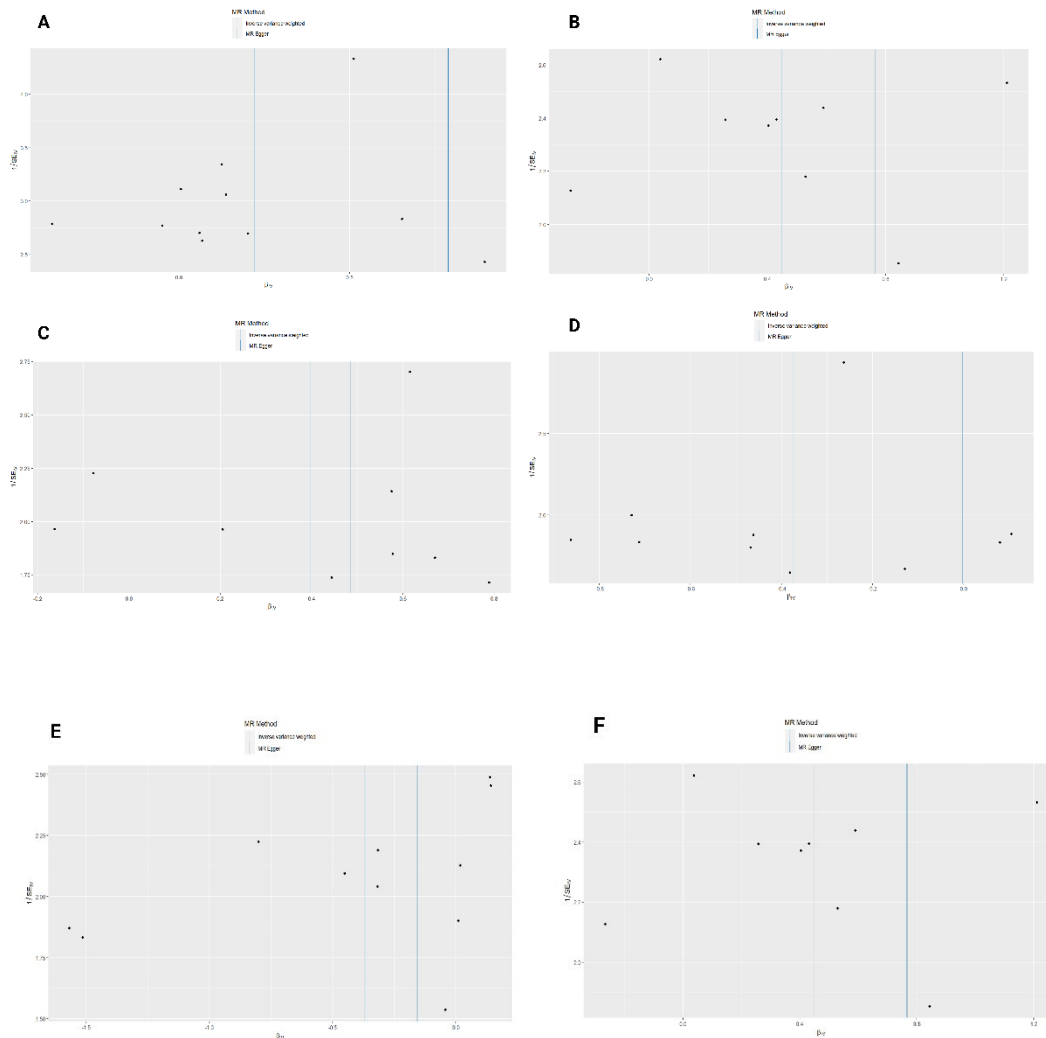
Scatter plots of significant and nominal significant from GM on DN.(A:genus.Eubacterium;B:genus.Howardella;C:genus.Lachnoclostridium;D:genus.Oxalobacter;E:genus.RuminococcaceaeUCG002;F:genus.Tyzzerella3;G:genus.unknowngenus;H:genus.unknowngenus;I:family.Oxalobacteraceae;J:family.Verrucomicrobiaceae;K:order.Rhodospirillales;L:order.Verrucomicrobiales;M:class.Actinobacteria;N:class.Gammaproteobacteria;O:class.Verrucomicrobiae;P:phylum.Bacteroidetes;Q:phylum.Proteobacteria)





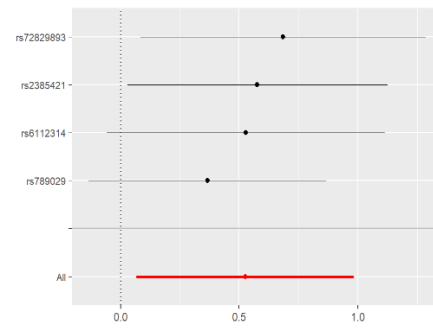
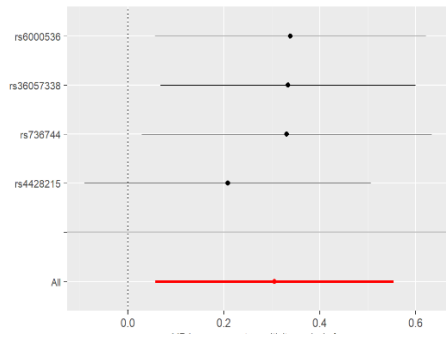
Supplement Figure S2

Funnel plots of significant and nominal significant from GM on DN. (A: order.Rhodospirillales;B: order.Verrucomicrobiales; C: phylum.Bacteroidetes;D: phylum.Proteobacteria;E: class. Actinobacteria; F:class.Verrucomicrobiae, SNP>8 can be drawn)



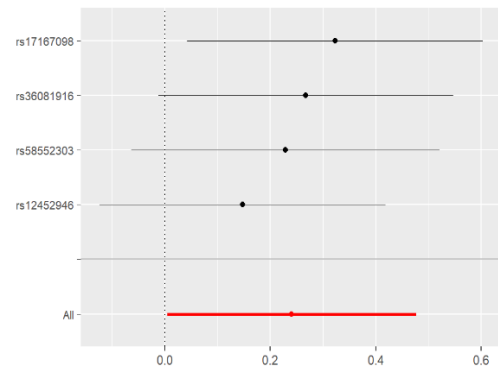
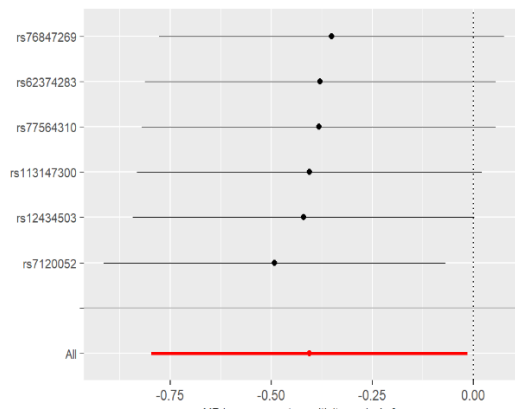
Supplement Figure S3

Leave-one-out plots of significant and nominal significant from GM on DN. (A: order.Rhodospirillales; B: order.Verrucomicrobiales; C: phylum.Bacteroidetes; D: phylum.Proteobacteria; E: class. Actinobacteria; F:class.Verrucomicrobiae; G:family.Verrucomicrobiaceae; H:genus.Tyzzerrlla3; I:genus.Oxalobacter J:genus.Lachnoclostridium; K:genus.RuminococcaceaeUCG002; L:genus.Howardella; M:genus. Eubacteriumcoprostanoligenesgroup; N:family.Oxalobacteraceae; O:class.Gammaproteobacteria)



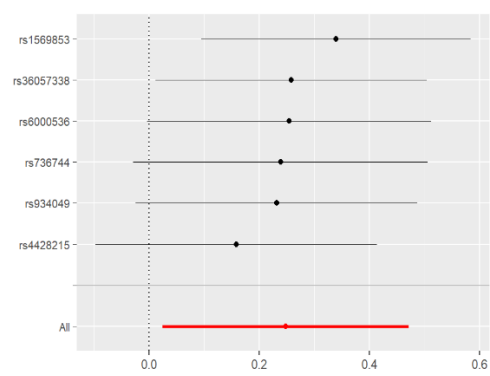
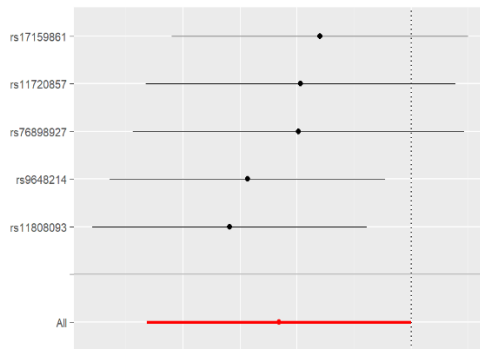
K

L

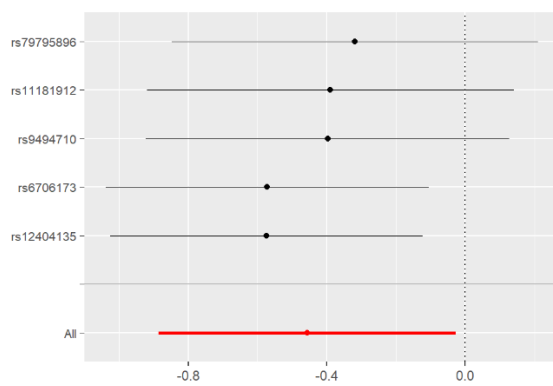


M

N



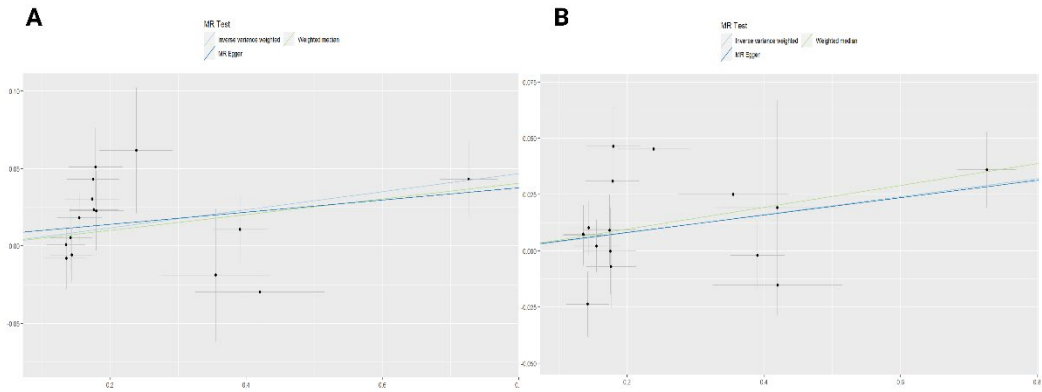
O



Supplement Figure S4

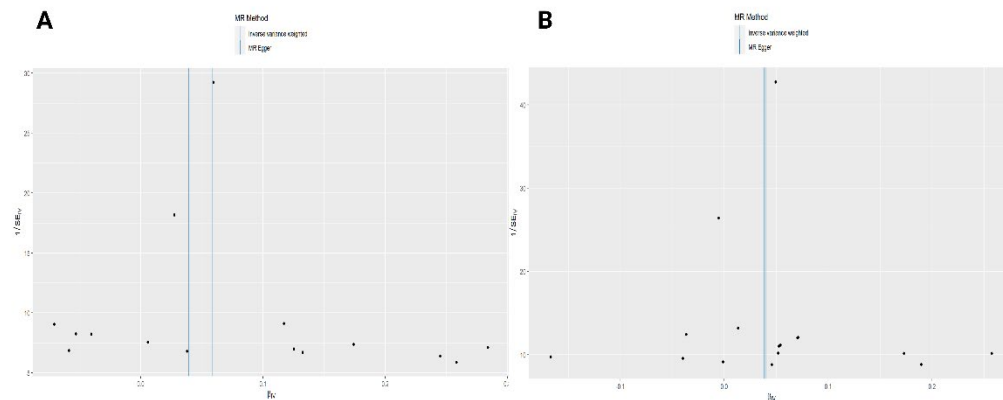
Scatter plots of reverse MR analysis between DN and causal GM

(A:order.Rhodospirillales; B:phylum.Proteobacteria, IVW: $P < 0.05$).



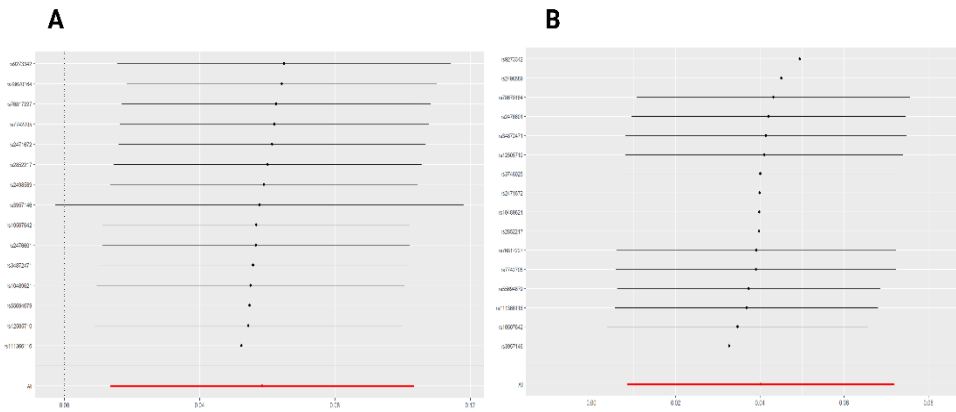
Supplement Figure S5

Funnel plots of reverse MR analysis between DN and causal GM
(A:order.Rhodospirillales; B:phylum.Proteobacteria, IVW: $P < 0.05$).



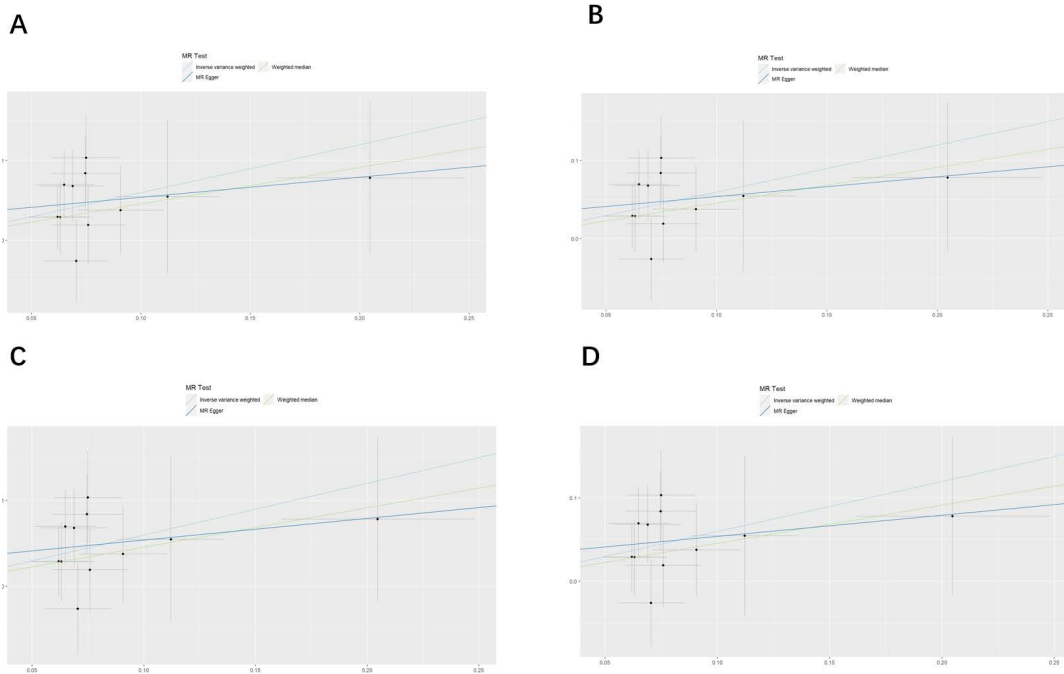
Supplement Figure S6

Leave-one-out plots of reverse MR analysis between DN and causal GM
(A:order.Rhodospirillales; B:phylum.Proteobacteria, IVW: $P < 0.05$).



Supplement Figure S7

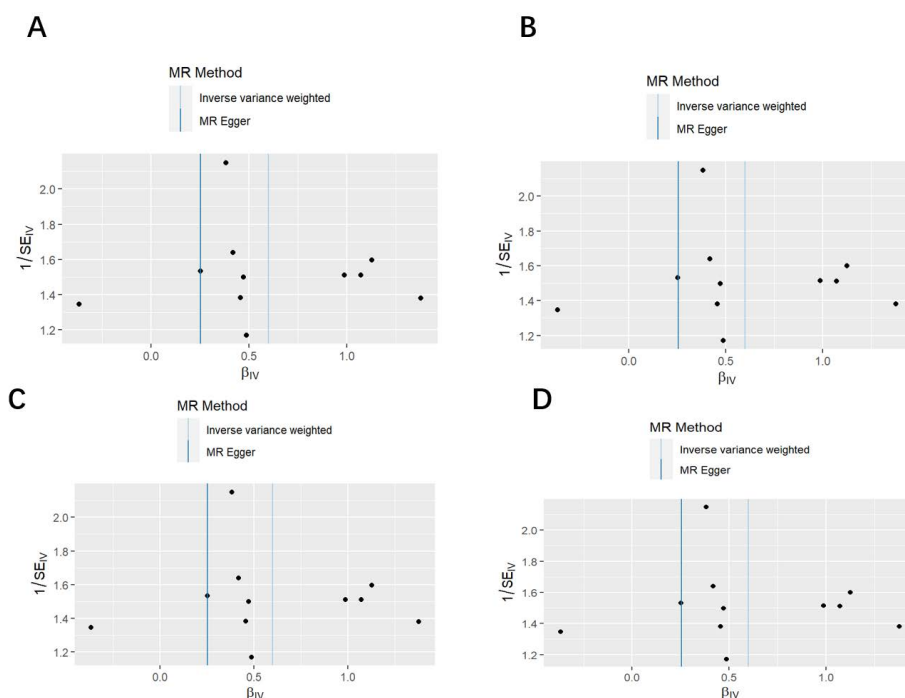
Scatter plots of MR analysis between T2DN and 19 causal GM. (A: family.Verrucomicrobiaceae;B:order.Rhodospirillales;C:order.Verrucomicrobiales; D:class.Verrucomicrobiaea, IVW: P<0.05)



Supplement Figure S8

Funnel plots of MR analysis between T2DN and 19 causal GM.

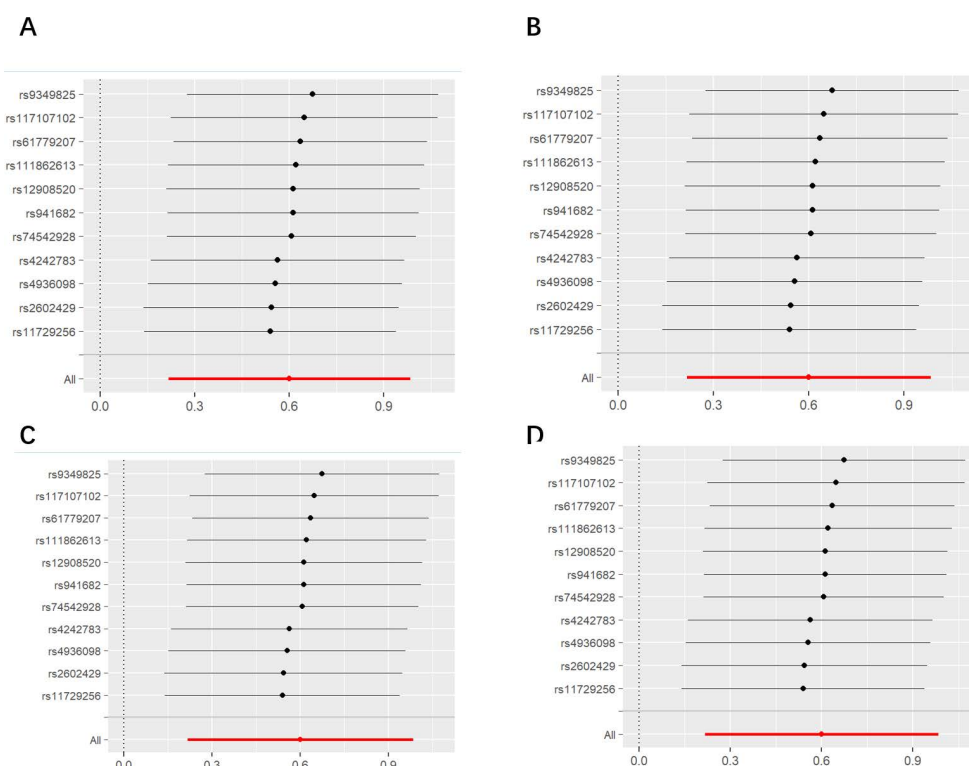
(A: family. Verrucomicrobiaceae;
 B:order.Rhodospirillales;C:order.Verrucomicrobiales;
 D:class.Verrucomicrobiaea, IVW: P<0.05)



Supplement Figure S9

Leave-one-out plots of MR analysis between T2DN and 19 causal GM.

(A: family. Verrucomicrobiaceae;
 B:order.Rhodospirillales;C:order.Verrucomicrobiales;
 D:class.Verrucomicrobiaea, IVW: P<0.05)



Supplement Figure S10

MR analysis between T1DN and Genus. Eubacterium.

A: Scatter plots of MR analysis

B: Funnel plots of MR analysis

C: Leave-one-out plots of MR analysis

