Supplementary Tables.

Tables	**Description**
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Table S2	The instruments of gut microbiome taxa.
Table S3	The instruments of gut bacterial pathways.
Table S4	The instruments of MAFLD.
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Supplementary Figures.

Figures	**Description**
Figure S1	The methodologies of mediation selection.
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Figure S3	Forestplot of bidirectional causal effects between bacterial pathways and MAFLD ($p < 0.05$).
Figure S4	Sensitivity analyses of meta-analysis.

Table S1. STROBE-MR checklist.[1 2]

Item No.	Section	Checklist item	Page No.	Relevant text from manuscript
1	**TITLE and ABSTRACT**	Indicate Mendelian randomization (MR) as the study's design in the title and/or the abstract if that is a main purpose of the study	1	Title. Integrative Analysis of Causal Links between Gut Microbiome and Metabolic Dysfunction-Associated Fatty Liver Disease: Focusing on Species and Novel Mediators.
	INTRODUCTION			
2	**Background**	Explain the scientific background and rationale for the reported study. What is the exposure? Is a potential causal relationship between exposure and outcome plausible? Justify why MR is a helpful method to address the study question	3	thus, Mendelian randomization (MR) analysis is essential as it is capable of determining causal ties.
3	**Objectives**	State specific objectives clearly, including pre-specified causal hypotheses (if any). State that MR is a method that, under specific assumptions, intends to estimate causal effects	4	Through these approaches, we aimed to enhance our understanding of gut microbiota - MAFLD interplay and pave the way for potential mechanism studies regarding the metabolic mediators.
	METHODS			

4	**Study design and data sources**		Present key elements of the study design early in the article. Consider including a table listing sources of data for all phases of the study. For each data source contributing to the analysis, describe the following:	4-5	Figure 1 presents an overview of the analytical framework employed in this study. Data Source: 2.2 Data source utilized in the MR analysis.
		a)	Setting: Describe the study design and the underlying population, if possible. Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, when available.		Figure1 presents an overview of the analytical framework employed in this study.
		b)	Participants: Give the eligibility criteria, and the sources and methods of selection of participants. Report the sample size, and whether any power or sample size calculations were carried out prior to the main analysis	4-5	Figure 1 presents an overview of the analytical framework employed in this study. Data Source: 2.2 Data source utilized in the MR analysis.
		c)	Describe measurement, quality control and selection of genetic variants	5	Methods2.3Bidirectional de novo UVMR analysis between the gut microbiome and MAFLD. In this research, we selected SNPs as instrumental variables (IVs) for the gut microbiota with a threshold of 1×10^{-5} and excluded SNPs in linkage disequilibrium (LD, $R^2 < 0.001$) within a 10,000 kilobase pairs window. For SNPs not directly available from GWAS results, suitable proxy SNPs were selected.
		d)	For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for	4	2.2 Data source utilized in the MR analysis.

			diseases		
		e)	Provide details of ethics committee approval and participant informed consent, if relevant		The datasets utilized in the present study were exclusively sourced from publicly accessible repositories, and consequently, ethical approval was not deemed necessary.
5	**Assumptions**		Explicitly state the three core IV assumptions for the main analysis (relevance, independence and exclusion restriction) as well assumptions for any additional or sensitivity analysis		These assumptions include the reliability and strength of the relationship between the IVs and the exposure, the absence of any confounding associations between the IVs and potential confounders, and the premise that the IVs exert their influence on the outcome exclusively through the exposure.
6	**Statistical methods: main analysis**		Describe statistical methods and statistics used	5	Methods 2.3 Bidirectional de novo UVMR analysis between the gut microbiome and MAFLD.
		a)	Describe how quantitative variables were handled in the analyses (i.e., scale, units, model)		Not Applicable
		b)	Describe how genetic variants were handled in the analyses and, if applicable, how their weights were selected	5	Methods 2.3 Bidirectional de novo UVMR analysis between the gut microbiome and MAFLD. The inverse–variance weighted (IVW) method was adopted as the primary approach for estimating causal effects, MR Egger, Weighted median, Simple mode, and

					Weighted mode were utilized as four supplementary methods
		c)	Describe the MR estimator (e.g. two-stage least squares, Wald ratio) and related statistics. Detail the included covariates and, in case of two-sample MR, whether the same covariate set was used for adjustment in the two samples	5	Methods 2.3 Bidirectional de novo UVMR analysis between the gut microbiome and MAFLD. The inverse–variance weighted (IVW) method was adopted as the primary approach for estimating causal effects, MR Egger, Weighted median, Simple mode, and Weighted mode were utilized as four supplementary methods. In univariate MR, we did not introduce any additional3 covariates for analysis.
		d)	Explain how missing data were addressed	5	For SNPs not directly available from GWAS results, suitable proxy SNPs were selected.
		e)	If applicable, indicate how multiple testing was addressed	NA	
7	**Assessment of assumptions**		Describe any methods or prior knowledge used to assess the assumptions or justify their validity	6	Methods 2.7 Sensitivity analysis.
8	**Sensitivity analyses and additional analyses**		Describe any sensitivity analyses or additional analyses performed (e.g. comparison of effect estimates from different approaches, independent replication, bias analytic techniques, validation of instruments, simulations)	6	Methods 2.7 Sensitivity analysis. To quantify the heterogeneity of selected SNPs in MR analysis, we used the Cochran's Q

					statistic and MR-Egger regression test to assess pleiotropic effects. The p-values exceeding 0.05 indicate the absence of heterogeneity and horizontal pleiotropy.
9	**Software and pre-registration**				
		a)	Name statistical software and package(s), including version and settings used	6	Methods 2.7 Sensitivity analysis. In R software (version 4.2.2), the following packages were used for statistical calculations: "TwoSampleMR" (version 0.5.7) for MR analyses, "meta" (version 7.0.0) and "metafor" (version 4.6.0) for meta-analyses, "MRInstruments" (version 0.3.2) for handling MR instruments.
		b)	State whether the study protocol and details were pre-registered (as well as when and where)		NA
	RESULTS				
10	**Descriptive data**				
		a)	Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow		NA

			diagram.	
		b)	Report summary statistics for phenotypic exposure(s), outcome(s), and other relevant variables (e.g. means, SDs, proportions).	Supplementary Tables 2,3,4
		c)	If the data sources include meta-analyses of previous studies, provide the assessments of heterogeneity across these studies.	NA
		d)	For two-sample MR: i. Provide justification of the similarity of the genetic variant-exposure associations between the exposure and outcome samples ii. Provide information on the number of individuals who overlap between the exposure and outcome studies	i. The overall harmonized data for each exposure-outcome pair have been packed and could be made available on request. Supplementary Figure 2. MR scatter plots ii. There was no overlap between the exposure and outcome samples in our study.
11	**Main results**			
		a)	Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale	The overall harmonized data for each exposure-outcome pair have been packed and could be made available on request.
		b)	Report MR estimates of the relationship between exposure and outcome, and the measures of uncertainty from the MR analysis, on an interpretable scale, such as odds ratio or	Figure 2, Figure 4 Supplementary Tables 5, 6, 8, 10, 12

			relative risk per SD difference	Supplementary Figure 2
		c)	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
		d)	Consider plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure)	Supplementary Figure 2. MR scatter plots
12	**Assessment of assumptions**			
		a)	Report the assessment of the validity of the assumptions	Sensitivity analyses, including the Q statistics from the inverse-variance weighted (IVW) test and the MR-Egger regression, revealed no significant heterogeneity or horizontal pleiotropy, thus substantiating the robustness of our findings. Supplementary Table 9
		b)	Report any additional statistics (e.g., assessments of heterogeneity across genetic variants, such as I^2, Q statistic or E-value)	Sensitivity analyses, including the Q statistics from the inverse-variance weighted (IVW) test and the MR-Egger regression, revealed no significant heterogeneity or horizontal pleiotropy, thus substantiating the robustness of our findings.

				Supplementary Table 9
13	**Sensitivity analyses and additional analyses**			
		a)	Report any sensitivity analyses to assess the robustness of the main results to violations of the assumptions	Sensitivity analyses, including the Q statistics from the inverse-variance weighted (IVW) test and the MR-Egger regression, revealed no significant heterogeneity or horizontal pleiotropy, thus substantiating the robustness of our findings. Supplementary Table 9
		b)	Report results from other sensitivity analyses or additional analyses	NA
		c)	Report any assessment of direction of causal relationship (e.g., bidirectional MR)	We conducted bidirectional MR analysis.
		d)	When relevant, report and compare with estimates from non-MR analyses	NA
		e)	Consider additional plots to visualize results (e.g., leave-one-out analyses)	The overall leave-one-out analyses plots have been packed and could be made available on request.

	DISCUSSION				
14	**Key results**		Summarize key results with reference to study objectives	9	Discussion paragraph #1
15	**Limitations**		Discuss limitations of the study, taking into account the validity of the IV assumptions, other sources of potential bias, and imprecision. Discuss both direction and magnitude of any potential bias and any efforts to address them	11	Limitations: The first is related to the sample sizes and the representativeness of the cohorts used. While our study combined data from multiple sources to increase statistical power, the generalizability of our findings to broader populations may still be somewhat restricted.
16	**Interpretation**				
		a)	Meaning: Give a cautious overall interpretation of results in the context of their limitations and in comparison with other studies	10-11	Disscussion paragraph #2, #3, #4
		b)	Mechanism: Discuss underlying biological mechanisms that could drive a potential causal relationship between the investigated exposure and the outcome, and whether the gene-environment equivalence assumption is reasonable. Use causal language carefully, clarifying that IV estimates may provide causal effects only under certain assumptions	10-11	Disscussion paragraph #2, #3, #4
		c)	Clinical relevance: Discuss whether the results have clinical or public policy relevance, and to what extent they inform effect sizes of possible interventions		NA

17	**Generalizability**	Discuss the generalizability of the study results (a) to other populations, (b) across other exposure periods/timings, and (c) across other levels of exposure	11	Disscussion paragraph #5
	OTHER INFORMATION			
18	**Funding**	Describe sources of funding and the role of funders in the present study and, if applicable, sources of funding for the databases and original study or studies on which the present study is based		Funding is declared on Title Page
19	**Data and data sharing**	Provide the data used to perform all analyses or report where and how the data can be accessed, and reference these sources in the article. Provide the statistical code needed to reproduce the results in the article, or report whether the code is publicly accessible and if so, where	12	Data Availability
20	**Conflicts of Interest**	All authors should declare all potential conflicts of interest		Conflict of Interest is declared separately

1. Skrivankova VW, Richmond RC, Woolf BAR, Yarmolinsky J, Davies NM, Swanson SA, et al. Strengthening the Reporting of Observational Studies in Epidemiology using Mendelian Randomization (STROBE-MR) Statement. JAMA. 2021;under review.

2. Skrivankova VW, Richmond RC, Woolf BAR, Davies NM, Swanson SA, VanderWeele TJ, et al. Strengthening the Reporting of Observational Studies in Epidemiology

using Mendelian Randomisation (STROBE-MR): Explanation and Elaboration. BMJ. 2021;375:n2233.

Table S2. The instruments of gut microbiome taxa.

Exposure	**Data Source**	**SNP**	***p*-value**	**CHR**	**BP**	**A1**	**A2**	**EAF**	**Beta**	**SE**	**Samplesize**
g.Parabacteroides	the Dutch Microbiome Project	rs16848174	8.25E-06	3	175195490	G	C	0.0675263	0.148535474	0.033314822	7,738
	the Dutch Microbiome Project	rs113638576	6.60E-06	5	176756088	T	C	0.131189111	-0.115998551	0.025742543	7,738
	the Dutch Microbiome Project	rs6910508	4.23E-06	6	166531345	A	G	0.324371437	0.081977493	0.017821767	7,738
	the Dutch Microbiome Project	rs17706792	3.60E-06	7	104500549	G	A	0.283512435	0.088051847	0.019004852	7,738
	the Dutch Microbiome Project	rs9409512	5.50E-06	9	97061771	A	G	0.40045728	0.077649702	0.01708573	7,738
	the Dutch Microbiome Project	rs9663125	5.65E-06	10	29866909	T	G	0.434981906	0.076438723	0.016840767	7,738
	the Dutch Microbiome Project	rs315588	8.42E-06	10	36487049	T	C	0.18382123	0.097286545	0.02184119	7,738
	the Dutch Microbiome Project	rs56238206	2.48E-06	11	13918589	A	G	0.144300953	0.113252279	0.024044282	7,738
	the Dutch	rs541877	6.33E-06	11	1023575	G	A	0.20969223	0.092849386	0.020564211	7,738

	Microbiome Project				29						
	the Dutch Microbiome Project	rs11603389	6.68E-06	11	130448209	G	C	0.096048997	0.128010964	0.028424304	7,738
	the Dutch Microbiome Project	rs366171	1.06E-06	16	66906450	T	A	0.39114927	-0.083644199	0.017141208	7,738
	the Dutch Microbiome Project	rs17639446	4.88E-06	17	48273903	C	A	0.121318438	-0.12867189	0.028157536	7,738
	the Dutch Microbiome Project	rs11083824	5.90E-06	19	46910130	G	C	0.650560431	0.081391582	0.017967127	7,738
	the Dutch Microbiome Project	rs10854303	2.95E-06	21	29126637	G	A	0.809309849	-0.101857303	0.021791205	7,738
g.Roseburia	the Dutch Microbiome Project	rs13019272	3.86E-06	2	160658863	A	G	0.51578673	0.074402055	0.016108597	7,738
	the Dutch Microbiome Project	rs73106151	5.68E-06	3	71229328	G	A	0.061284047	-0.152218322	0.033542161	7,738
	the Dutch Microbiome Project	rs61217796	6.67E-06	4	160643088	G	A	0.119450675	-0.114004963	0.025311511	7,738
	the Dutch Microbiome Project	rs12653554	8.74E-06	5	118255998	A	T	0.07162534	0.141552168	0.031837047	7,738
	the Dutch Microbiome Project	rs11748902	7.10E-06	5	167709235	G	C	0.051524122	0.166532692	0.037084295	7,738
	the Dutch	rs7819696	9.42E-07	8	5634933	T	C	0.16588337	0.109168977	0.022263926	7,738

	Microbiome Project				4						
	the Dutch Microbiome Project	rs11789010	2.12E-07	9	80129910	C	T	0.241159686	-0.099102409	0.019099335	7,738
	the Dutch Microbiome Project	rs1258842	4.90E-06	11	134167225	T	A	0.375940083	-0.076657352	0.016778073	7,738
	the Dutch Microbiome Project	rs57070158	6.82E-06	13	29048828	C	A	0.120797284	-0.112350531	0.024971392	7,738
	the Dutch Microbiome Project	rs7985034	1.55E-06	13	110370464	C	T	0.239139137	-0.095472521	0.019869936	7,738
	the Dutch Microbiome Project	rs2210174	4.37E-06	14	83600010	T	C	0.628314387	-0.078342581	0.017057719	7,738
	the Dutch Microbiome Project	rs66973779	5.71E-06	15	89340942	A	G	0.313273569	0.083770955	0.018465195	7,738
	the Dutch Microbiome Project	rs7404803	6.37E-07	16	15530454	C	T	0.889107856	-0.128686353	0.025842916	7,738
	the Dutch Microbiome Project	rs72963797	6.41E-06	18	73896030	A	G	0.114502937	-0.116120369	0.025734484	7,738
s.Parabacteroides_merdae	the Dutch Microbiome Project	rs12116657	4.09E-06	1	63034646	C	A	0.186048737	-0.111274952	0.024153615	7,738
	the Dutch Microbiome Project	rs7631540	7.12E-06	3	113830519	T	C	0.454161742	0.082540202	0.018382322	7,738
	the Dutch	rs1508792	1.70E-06	5	9810914	C	G	0.578673036	-0.087603868	0.018301736	7,738

	Microbiome Project				8						
	the Dutch Microbiome Project	rs702101	6.28E-06	5	171276393	A	G	0.623602242	0.089625047	0.019843616	7,738
	the Dutch Microbiome Project	rs66722558	1.07E-06	6	132090239	T	G	0.054051173	0.199748402	0.040947341	7,738
	the Dutch Microbiome Project	rs4237122	4.25E-06	9	133313115	A	G	0.10518815	0.14155731	0.030780303	7,738
	the Dutch Microbiome Project	rs10733815	1.78E-06	10	67316008	A	G	0.776162385	0.109024761	0.022822261	7,738
	the Dutch Microbiome Project	rs2005874	3.27E-07	19	46810991	T	C	0.085652806	0.171143673	0.033510796	7,738
	the Dutch Microbiome Project	rs148330790	1.81E-06	22	24326693	A	G	0.095061459	0.218191842	0.045711926	7,738
s.Bacteroides_salyersiae	the Dutch Microbiome Project	rs17111728	4.10E-06	1	55691384	C	T	0.071126761	0.333599915	0.072423032	7,738
	the Dutch Microbiome Project	rs76194327	8.79E-06	3	116352196	A	T	0.06423916	0.379902913	0.085469245	7,738
	the Dutch Microbiome Project	rs16845299	7.17E-07	4	71520630	T	C	0.262022922	0.266973648	0.053860106	7,738
	the Dutch Microbiome Project	rs3776996	1.17E-06	5	153797049	A	G	0.171478873	0.241028451	0.049579237	7,738
	the Dutch	rs1265300	4.20E-06	6	4456400	G	A	0.503446562	-0.177503242	0.038578945	7,738

	Microbiome Project										
	the Dutch Microbiome Project	rs412657	5.88E-06	6	32211085	G	T	0.404577465	-0.175940569	0.038833315	7,738
	the Dutch Microbiome Project	rs12534702	8.55E-06	7	36769290	T	C	0.344150787	0.177921834	0.039973815	7,738
	the Dutch Microbiome Project	rs117662076	4.86E-06	10	120769498	A	G	0.055194698	0.403549701	0.088290157	7,738
	the Dutch Microbiome Project	rs12896430	4.79E-06	14	21431376	A	G	0.687717481	-0.192311544	0.042047905	7,738
	the Dutch Microbiome Project	rs9960494	6.76E-06	18	51206632	C	G	0.337761668	-0.190905006	0.042413961	7,738
s.Lachnospiraceae_bacterium_8_1_57FAA	the Dutch Microbiome Project	rs752704	4.56E-06	1	47011372	C	T	0.47108307	-0.148743321	0.032448944	7,738
	the Dutch Microbiome Project	rs4970837	5.40E-06	1	109822008	T	G	0.651374198	-0.156474456	0.034400027	7,738
	the Dutch Microbiome Project	rs11581135	5.08E-06	1	203341531	A	C	0.381589039	-0.161678515	0.035443976	7,738
	the Dutch Microbiome Project	rs11127034	6.20E-06	2	86648492	C	G	0.662287376	0.152524424	0.03374792	7,738
	the Dutch Microbiome Project	rs140741191	4.69E-06	6	34301848	C	T	0.050340199	-0.347811994	0.075970628	7,738
	the Dutch	rs16899159	8.85E-06	6	6788715	A	C	0.36524917	-0.149746912	0.033700394	7,738

	Microbiome Project				6						
	the Dutch Microbiome Project	rs78404253	3.88E-06	7	12732484	A	G	0.089540422	0.283488944	0.061391285	7,738
	the Dutch Microbiome Project	rs4559153	2.26E-06	7	46213818	T	C	0.266561514	0.175284534	0.037070835	7,738
	the Dutch Microbiome Project	rs3750889	1.08E-06	8	132002334	T	C	0.593716624	-0.15847885	0.03250163	7,738
	the Dutch Microbiome Project	rs61854800	3.34E-06	10	70008028	T	C	0.117059442	0.236180023	0.050806457	7,738
	the Dutch Microbiome Project	rs76588436	5.53E-06	10	130572914	A	T	0.066107915	0.30976155	0.068174112	7,738
	the Dutch Microbiome Project	rs61895387	2.41E-06	11	102268603	T	A	0.074851034	-0.315749856	0.066960948	7,738
	the Dutch Microbiome Project	rs11223731	6.90E-07	11	134100499	A	G	0.243694975	-0.186069837	0.037482351	7,738
	the Dutch Microbiome Project	rs1346173	5.94E-06	12	108635460	A	G	0.658018391	0.156595213	0.034581011	7,738
	the Dutch Microbiome Project	rs28521978	6.88E-06	14	33633609	A	G	0.289056927	0.163099567	0.036266311	7,738
	the Dutch Microbiome Project	rs8089654	4.50E-06	18	12734224	G	T	0.863953321	0.228585765	0.049837178	7,738
	the Dutch	rs12986007	5.78E-06	19	4976821	T	G	0.07593761	-0.296424813	0.065375876	7,738

	Microbiome Project				4						
o.Haloplasmatales	the FR02 cohort	rs111906523	6.6E-06	1	59377477	T	C	0.263494	-0.0620179	0.0137632	5,959
	the FR02 cohort	rs12722982	3.2E-06	1	65865561	T	G	0.147247	0.0806774	0.0173118	5,959
	the FR02 cohort	rs72692745	8.8E-06	1	151655397	A	G	0.0651479	0.109634	0.0246618	5,959
	the FR02 cohort	rs7570971	9.4E-11	2	135080336	A	C	0.42247	-0.0806449	0.0124527	5,959
	the FR02 cohort	rs72966145	3.8E-06	2	222594690	G	A	0.0182752	0.212489	0.0459892	5,959
	the FR02 cohort	rs150113830	7.5E-06	3	42851850	T	C	0.0129027	0.240706	0.0537248	5,959
	the FR02 cohort	rs13099974	4.9E-08	3	152069496	G	T	0.232505	-0.0795141	0.0145768	5,959
	the FR02 cohort	rs114719527	9.2E-06	3	187281615	A	G	0.0310263	0.157878	0.035606	5,959
	the FR02 cohort	rs6843920	8.3E-06	4	87778196	A	G	0.471462	0.0543307	0.0121884	5,959
	the FR02 cohort	rs7730299	3.5E-06	5	36460005	T	G	0.350227	0.0583301	0.0125785	5,959
	the FR02 cohort	rs73790046	2.4E-06	6	1690213	A	G	0.0533107	0.127899	0.0271176	5,959

					83						
	the FR02 cohort	rs11763364	8.7E-07	7	79263	A	T	0.466794	-0.0608604	0.0123734	5,959
	the FR02 cohort	rs79020676	9.6E-06	7	137801508	C	T	0.0492839	0.124765	0.0281956	5,959
	the FR02 cohort	rs12703112	7.3E-06	7	151068149	A	G	0.142845	-0.0786674	0.0175438	5,959
	the FR02 cohort	rs117975365	3.2E-06	11	110328655	A	G	0.0150445	0.233786	0.0501915	5,959
	the FR02 cohort	rs182749893	9.1E-06	12	131629694	C	T	0.0141061	-0.231613	0.0522063	5,959
	the FR02 cohort	rs1175397	9.6E-06	13	44918011	A	G	0.0860206	0.0970104	0.0219154	5,959
	the FR02 cohort	rs150481959	8.1E-06	15	101154903	A	C	0.0113714	0.260867	0.0584666	5,959
	the FR02 cohort	rs7211768	8.3E-06	17	16665186	T	A	0.321429	0.0587315	0.0131761	5,959
	the FR02 cohort	rs148796276	7E-06	17	31682961	G	A	0.0410832	0.138038	0.030716	5,959
	the FR02 cohort	rs117629222	5.6E-06	18	76357836	T	C	0.0218941	0.190808	0.042023	5,959
	the FR02 cohort	rs150493675	1.9E-06	19	31159060	T	C	0.034933	0.158546	0.0333182	5,959

	the FR02 cohort	rs408302	8.3E-06	21	29828186	T	C	0.383454	-0.0553498	0.0124154	5,959
f.Brevibacillaceae	the FR02 cohort	rs147736660	4.9E-06	1	50009317	A	G	0.0209555	0.0636726	0.0139353	5,959
	the FR02 cohort	rs6739491	6.8E-06	2	19338483	G	T	0.0153509	0.0721473	0.0160291	5,959
	the FR02 cohort	rs6716079	5.1E-06	2	66585327	T	C	0.042951	-0.0442771	0.00970867	5,959
	the FR02 cohort	rs77127114	3.4E-06	2	102331084	A	T	0.0163034	0.0727416	0.0156588	5,959
	the FR02 cohort	rs4988235	9.6E-09	2	135851076	G	A	0.414723	-0.0231996	0.00404391	5,959
	the FR02 cohort	rs146219913	7E-06	2	239978432	T	C	0.0154778	0.0720868	0.0160437	5,959
	the FR02 cohort	rs111977341	2.4E-06	4	136102358	C	T	0.0310872	0.0531281	0.0112614	5,959
	the FR02 cohort	rs1390623	9.1E-06	5	7149250	A	G	0.0892587	-0.0306676	0.00690999	5,959
	the FR02 cohort	rs118082134	2.9E-06	6	168566364	A	G	0.0168577	0.0716149	0.0153154	5,959
	the FR02 cohort	rs10813878	5.7E-06	9	32859236	C	T	0.455599	-0.0180266	0.00397383	5,959
	the FR02 cohort	rs7035425	5.7E-06	9	8325826	T	G	0.459539	-0.0178883	0.00394153	5,959

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	the FR02 cohort	rs78619477	1.7E-06	10	83683845	G	C	0.0368929	0.0495261	0.010343	5,959
	the FR02 cohort	rs1502242	9.2E-06	11	13604072	A	C	0.0813078	0.0321902	0.00725783	5,959
	the FR02 cohort	rs73217238	5.8E-06	12	119318932	C	T	0.180278	0.0233949	0.00516107	5,959
	the FR02 cohort	rs77519307	6.3E-06	17	7423770	A	C	0.029313	0.052605	0.0116485	5,959
	the FR02 cohort	rs189828013	5E-06	17	36154429	C	T	0.0178908	0.0676205	0.0148164	5,959
	the FR02 cohort	rs9612804	7E-07	22	24891561	G	T	0.147344	0.0280192	0.0056475	5,959
g.Bacillus U	the FR02 cohort	rs4255347	9.1E-06	1	38420129	C	T	0.0443038	-0.0683033	0.0153913	5,959
	the FR02 cohort	rs41285010	8.6E-07	1	56708615	G	A	0.0315913	0.08974	0.0182341	5,959
	the FR02 cohort	rs35908994	1.8E-06	1	218166595	A	C	0.0402582	0.077261	0.0161797	5,959
	the FR02 cohort	rs74743869	9.1E-06	2	76709783	T	C	0.0886872	0.0506938	0.0114258	5,959
	the FR02 cohort	rs11687684	1.8E-06	2	107190307	T	C	0.197868	0.0379068	0.00794536	5,959

	the FR02 cohort	rs10188368	7.6E-06	2	144737103	A	G	0.124894	0.0432598	0.00966314	5,959
	the FR02 cohort	rs78775534	1.4E-06	2	191671352	G	A	0.0439161	0.0752356	0.0156059	5,959
	the FR02 cohort	rs10201907	9.1E-09	2	223053094	T	C	0.0279179	0.111219	0.0193523	5,959
	the FR02 cohort	rs12630499	8.4E-06	3	121617882	T	C	0.14763	-0.0404499	0.00908118	5,959
	the FR02 cohort	rs13140008	5.3E-06	4	81003695	A	G	0.0539451	0.0657781	0.0144521	5,959
	the FR02 cohort	rs71597328	6.6E-08	5	175381094	A	G	0.0570757	0.0740244	0.0137066	5,959
	the FR02 cohort	rs55728141	8.1E-06	7	4809274	A	C	0.0858782	0.0511359	0.0114573	5,959
	the FR02 cohort	rs500907	9.7E-06	7	16553570	A	G	0.34574	-0.0298278	0.00674385	5,959
	the FR02 cohort	rs12350649	1.9E-06	9	27174172	T	A	0.114639	-0.0469452	0.00985272	5,959
	the FR02 cohort	rs73655567	2.4E-06	9	116984909	A	C	0.0433755	0.073489	0.0155792	5,959
	the FR02 cohort	rs11822329	5.8E-06	11	9354758	T	C	0.237434	0.0342529	0.00755375	5,959
	the FR02 cohort	rs7297939	8.3E-07	12	42700483	A	G	0.314001	0.0337675	0.00685091	5,959

	the FR02 cohort	rs2269322	1.4E-07	14	102983436	T	C	0.397393	0.034321	0.0065262	5,959
	the FR02 cohort	rs74172688	9.6E-06	19	5086062	A	G	0.113279	-0.0451738	0.0102062	5,959
g.CAG-145	the FR02 cohort	rs12074319	3.5E-06	1	10770486	C	T	0.0149317	0.126398	0.027256	5,959
	the FR02 cohort	rs10931443	4.3E-10	2	153054957	A	G	0.4361	0.0411734	0.00659452	5,959
	the FR02 cohort	rs13025431	3.8E-06	2	153154209	A	G	0.168014	0.0408933	0.00884377	5,959
	the FR02 cohort	rs73203290	4.1E-06	3	106540146	T	A	0.325444	-0.0329054	0.00714317	5,959
	the FR02 cohort	rs113106320	4E-06	6	161328361	G	A	0.0170847	0.117179	0.0254124	5,959
	the FR02 cohort	rs156926	3.4E-06	7	132487165	T	G	0.102151	0.0504456	0.0108539	5,959
	the FR02 cohort	rs62553714	3.7E-06	9	29342796	C	T	0.120988	-0.0467362	0.0101009	5,959
	the FR02 cohort	rs12902139	9.2E-06	15	59416952	G	A	0.467343	-0.029252	0.00659568	5,959
	the FR02 cohort	rs2073142	4.3E-06	20	57590880	C	T	0.362568	-0.0321878	0.00700624	5,959
	the FR02 cohort	rs739110	6.6E-06	22	4725686	A	C	0.432625	0.0300664	0.00667151	5,959

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g.CAG-449	the FR02 cohort	rs116381583	6.7E-06	1	63410031	T	C	0.0260672	0.145898	0.0324091	5,959
	the FR02 cohort	rs111396089	8.8E-06	1	203518098	T	G	0.118967	0.0724211	0.0162898	5,959
	the FR02 cohort	rs79827100	3.2E-06	2	19509829	T	G	0.0513814	0.107963	0.0231847	5,959
	the FR02 cohort	rs874272	7.7E-06	2	101253611	C	T	0.1047	0.075793	0.0169392	5,959
	the FR02 cohort	rs1530023	3.5E-06	2	215501544	A	C	0.183471	0.0618585	0.0133361	5,959
	the FR02 cohort	rs114554860	5.3E-06	2	216316437	A	G	0.0152511	0.190276	0.0418038	5,959
	the FR02 cohort	rs111738579	3.5E-06	3	11760913	A	T	0.0235104	0.158066	0.034076	5,959
	the FR02 cohort	rs778937	1E-06	4	62376628	G	C	0.211137	-0.0608686	0.0124586	5,959
	the FR02 cohort	rs74618463	3.3E-06	4	79830310	T	C	0.0141082	0.200073	0.0430425	5,959
	the FR02 cohort	rs35408398	6.9E-06	4	117498306	A	T	0.0225855	0.156984	0.0349153	5,959
	the FR02 cohort	rs72728657	6E-06	4	1427975	T	C	0.0142472	0.195197	0.0431084	5,959

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	the FR02 cohort	rs138363248	3E-06	4	162515596	T	C	0.021816	0.163425	0.0350042	5,959
	the FR02 cohort	rs150951511	3E-06	5	122526725	C	T	0.0297489	0.140952	0.0301747	5,959
	the FR02 cohort	rs12153949	5.3E-06	6	46466075	T	C	0.278535	-0.0533673	0.0117207	5,959
	the FR02 cohort	rs4961334	9.8E-06	8	141179037	G	C	0.136943	-0.0665759	0.0150602	5,959
	the FR02 cohort	rs17441162	9.9E-06	9	129326169	A	G	0.0132489	0.19651	0.04447	5,959
	the FR02 cohort	rs4750718	4.4E-06	10	128735317	A	G	0.232507	0.0570997	0.0124325	5,959
	the FR02 cohort	rs118040875	2.3E-06	11	4625075	T	G	0.024066	0.157668	0.0333677	5,959
	the FR02 cohort	rs961746	8.3E-06	11	20139419	A	G	0.433007	0.0484905	0.0108809	5,959
	the FR02 cohort	rs139688932	2.2E-08	11	28690045	A	C	0.0233165	0.191506	0.0342385	5,959
	the FR02 cohort	rs9550215	4.5E-06	13	112805591	A	G	0.36545	-0.0493376	0.0107534	5,959
	the FR02 cohort	rs76014583	8.1E-06	15	57026112	T	C	0.0105272	0.225732	0.0505802	5,959

	the FR02 cohort	rs17808031	7.2E-06	18	58336864	A	G	0.0617845	0.0952642	0.0212269	5,959
g.CAG-552	the FR02 cohort	rs7531221	6.5E-06	1	1517993	G	A	0.380346	-0.0769419	0.0170657	5,959
	the FR02 cohort	rs7520853	6.5E-06	1	178057159	C	T	0.282151	0.0820368	0.0181888	5,959
	the FR02 cohort	rs823165	6.3E-06	1	231633700	A	T	0.378362	-0.0748667	0.0165783	5,959
	the FR02 cohort	rs62158858	4.2E-06	2	136303082	A	G	0.047173	0.174603	0.0379318	5,959
	the FR02 cohort	rs77709254	7.3E-06	3	188629034	T	G	0.00994773	0.367184	0.0818913	5,959
	the FR02 cohort	rs10515114	7.7E-06	5	71718007	G	A	0.0658537	0.146351	0.0327231	5,959
	the FR02 cohort	rs2518210	7.4E-06	6	101907892	A	G	0.0109225	0.347936	0.0776237	5,959
	the FR02 cohort	rs4556017	5.3E-06	7	100989509	C	T	0.178173	0.0961711	0.0211244	5,959
	the FR02 cohort	rs4725984	3.3E-06	7	150971426	T	C	0.308791	0.0810388	0.0174319	5,959
	the FR02 cohort	rs35515607	2.6E-10	9	3018435	C	A	0.363683	-0.106747	0.016886	5,959
	the FR02 cohort	rs62572809	1.7E-06	9	80572325	A	G	0.0724747	-0.148944	0.0310931	5,959

	the FR02 cohort	rs2231409	3.2E-06	9	132887754	A	G	0.0204511	0.263614	0.0566243	5,959
	the FR02 cohort	rs2796566	7.5E-06	10	42853071	G	T	0.255085	0.0830046	0.0185345	5,959
	the FR02 cohort	rs71460754	2.9E-06	12	126976503	T	C	0.0600272	0.158994	0.0339875	5,959
	the FR02 cohort	rs6486512	5.2E-06	12	130001956	T	C	0.430991	0.0743985	0.0163342	5,959
	the FR02 cohort	rs74780291	7.9E-06	14	35344296	A	G	0.046623	0.172387	0.0385769	5,959
	the FR02 cohort	rs12882898	5.9E-06	14	61062783	T	C	0.112122	0.11634	0.0256749	5,959
	the FR02 cohort	rs1673061	5.7E-06	16	20642462	A	G	0.0822976	0.13397	0.0295206	5,959
	the FR02 cohort	rs11671426	9.5E-06	19	47794651	A	G	0.0319024	0.203928	0.0460417	5,959
	the FR02 cohort	rs2327592	9.8E-07	20	12030940	G	A	0.072732	0.154564	0.0315733	5,959
	the FR02 cohort	rs149099762	7.1E-06	21	46155810	T	C	0.0282624	-0.219921	0.0489676	5,959
g.CAG-884	the FR02 cohort	rs79457354	7.8E-06	1	3745644	A	G	0.0159106	0.234772	0.0525006	5,959
	the FR02 cohort	rs4854491	3.3E-06	2	6869155	C	T	0.29889	-0.065017	0.0139776	5,959

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	the FR02 cohort	rs139654497	2.8E-06	3	95611253	A	T	0.0114175	0.289504	0.0618073	5,959
	the FR02 cohort	rs74873861	3E-06	3	110696189	C	G	0.0360323	0.165303	0.0354111	5,959
	the FR02 cohort	rs147833749	4.9E-06	4	95308187	T	C	0.0122792	0.272125	0.0595397	5,959
	the FR02 cohort	rs149643665	1.3E-06	5	3138489	T	C	0.0130471	0.279161	0.0575896	5,959
	the FR02 cohort	rs2400705	1E-06	5	148811455	A	G	0.187436	-0.0827502	0.0169425	5,959
	the FR02 cohort	rs1015465	8.9E-07	6	30118563	C	T	0.0390166	0.162722	0.0331164	5,959
	the FR02 cohort	rs9453677	7.4E-06	6	66289769	C	A	0.183737	0.0747969	0.016691	5,959
	the FR02 cohort	rs7801158	3.6E-06	7	64773248	T	C	0.369082	-0.0624261	0.0134785	5,959
	the FR02 cohort	rs881358	1.4E-07	7	106571913	T	C	0.267978	-0.0771078	0.0146513	5,959
	the FR02 cohort	rs11142878	7.6E-06	9	71550576	T	C	0.0156224	0.235041	0.0525207	5,959
	the FR02 cohort	rs2583258	5.3E-06	12	104048953	T	C	0.10005	-0.0982251	0.0215685	5,959

	the FR02 cohort	rs142169167	7.2E-06	14	47675891	T	C	0.0994924	0.097332	0.0216829	5,959
	the FR02 cohort	rs710274	7.7E-06	14	97027576	A	G	0.304461	0.0640658	0.0143216	5,959
	the FR02 cohort	rs76012754	3.3E-06	16	20151540	A	C	0.0247019	0.195669	0.0420947	5,959
	the FR02 cohort	rs117574388	3.1E-06	17	20960653	A	G	0.0470578	0.143834	0.0308596	5,959
	the FR02 cohort	rs143543844	2.9E-07	22	42634424	A	G	0.0126284	0.300573	0.0586024	5,959
g.Demequina	the FR02 cohort	rs72652672	8.5E-06	1	29571984	A	G	0.0946246	0.0354638	0.0079669	5,959
	the FR02 cohort	rs114523689	4E-08	1	172586633	G	A	0.0311974	-0.0736704	0.0134152	5,959
	the FR02 cohort	rs12407592	2.4E-07	1	211486674	C	T	0.278331	0.0266857	0.0051625	5,959
	the FR02 cohort	rs1378751	9.5E-06	2	137747119	T	C	0.202343	-0.0260768	0.00588729	5,959
	the FR02 cohort	rs7605169	2.6E-06	2	211720911	T	C	0.470089	-0.0219276	0.00466603	5,959
	the FR02 cohort	rs112429089	9.4E-06	3	6080369	T	C	0.186448	0.0263855	0.00595555	5,959
	the FR02 cohort	rs772811	9.8E-06	3	1490957	T	C	0.0343019	-0.057019	0.0128939	5,959

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	the FR02 cohort	rs111701541	5.2E-06	5	167175054	C	T	0.0339286	-0.0578256	0.0126853	5,959
	the FR02 cohort	rs2180025	8E-06	6	161737548	G	A	0.495133	-0.0204974	0.00459066	5,959
	the FR02 cohort	rs2280919	7.8E-06	8	123539539	G	A	0.487947	0.020581	0.00460354	5,959
	the FR02 cohort	rs2256862	8.9E-06	9	101048862	A	G	0.419235	0.0208573	0.00469416	5,959
	the FR02 cohort	rs11223695	9.6E-07	11	134112179	T	C	0.18259	-0.0296275	0.00604656	5,959
	the FR02 cohort	rs7216027	4.3E-06	17	78660257	A	G	0.445711	0.0211947	0.00460906	5,959
	the FR02 cohort	rs541713	4.1E-07	18	4332080	G	A	0.153245	-0.0329883	0.0065139	5,959
	the FR02 cohort	rs151012844	9.9E-06	19	46940009	G	A	0.0161426	-0.0809428	0.0183174	5,959
	the FR02 cohort	rs112783565	7.9E-06	21	26902378	G	A	0.0107744	0.100767	0.0225576	5,959
	the FR02 cohort	rs73369545	8.8E-06	21	42043692	A	G	0.0733525	-0.0393736	0.00885758	5,959
g.Halarcobacter	the FR02 cohort	rs78213796	4.1E-06	2	64915276	G	A	0.0186561	0.113156	0.0245736	5,959

	the FR02 cohort	rs4399689	2.1E-06	2	173165838	T	A	0.118936	0.0485399	0.0102405	5,959
	the FR02 cohort	rs115056000	3.4E-06	3	72359526	A	G	0.207914	0.0381646	0.00821312	5,959
	the FR02 cohort	rs6831073	4.2E-06	4	110200685	A	G	0.206772	-0.0385484	0.00837619	5,959
	the FR02 cohort	rs17536666	1.5E-06	5	1844201	C	T	0.091371	-0.0561867	0.011662	5,959
	the FR02 cohort	rs2243293	4.2E-06	5	132684107	G	A	0.434168	-0.0310526	0.00674888	5,959
	the FR02 cohort	rs4565291	7.6E-06	6	22143830	G	A	0.430452	-0.0300526	0.00671549	5,959
	the FR02 cohort	rs28637876	8.2E-06	7	75628640	A	G	0.0522766	0.0659689	0.0147948	5,959
	the FR02 cohort	rs150202331	2E-08	7	82185403	C	G	0.029059	-0.111428	0.0198548	5,959
	the FR02 cohort	rs10226194	3E-06	7	157926147	G	A	0.447613	0.0315365	0.00675324	5,959
	the FR02 cohort	rs16899163	4E-07	8	123977120	G	A	0.253658	-0.0393723	0.00776783	5,959
	the FR02 cohort	rs2091579	5E-06	10	13798679	T	C	0.265204	0.0354503	0.00776956	5,959
	the FR02 cohort	rs596117	1.6E-06	11	9693361	A	G	0.167759	0.0423219	0.00881617	5,959

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	the FR02 cohort	rs72775804	7.6E-07	16	15892382	T	C	0.0176797	-0.124786	0.025239	5,959
g.Olsenella C	the FR02 cohort	rs17375005	5.6E-07	1	60825286	C	A	0.0391099	-0.101641	0.0203064	5,959
	the FR02 cohort	rs544038	1.3E-09	1	89243780	C	T	0.0144611	0.20173	0.033259	5,959
	the FR02 cohort	rs78977847	2.9E-06	1	187096833	G	C	0.0187805	0.137218	0.0293351	5,959
	the FR02 cohort	rs692260	9.7E-06	7	129534330	C	T	0.368955	0.0364625	0.00824424	5,959
	the FR02 cohort	rs13251886	2.8E-06	8	13673659	T	A	0.0888496	-0.0657449	0.0140256	5,959
	the FR02 cohort	rs78269913	3.4E-06	9	7701869	G	A	0.0462035	0.0880942	0.0189764	5,959
	the FR02 cohort	rs148907664	4.5E-06	9	78696349	G	A	0.013849	-0.156927	0.0342257	5,959
	the FR02 cohort	rs11225975	2.2E-06	11	103690715	A	G	0.141598	0.0540954	0.0114373	5,959
	the FR02 cohort	rs680276	1.5E-06	11	128835058	C	T	0.434028	-0.0397643	0.0082604	5,959
	the FR02 cohort	rs143498649	2.6E-06	13	28521837	T	C	0.0156618	0.149729	0.0318524	5,959

	the FR02 cohort	rs6497169	2.1E-06	15	94108029	G	A	0.467714	0.03802	0.00801272	5,959
	the FR02 cohort	rs75617675	7.9E-06	15	100811755	A	G	0.141559	-0.0512568	0.0114713	5,959
	the FR02 cohort	rs1991027	2.9E-06	16	82916897	G	A	0.160955	0.0511537	0.0109343	5,959
	the FR02 cohort	rs117510332	6E-06	16	84405778	A	G	0.0737422	-0.0685682	0.0151489	5,959
g.Turicibacter	the FR02 cohort	rs12127678	2.9E-06	1	65848169	A	T	0.147376	0.0943716	0.0201866	5,959
	the FR02 cohort	rs72692745	9.3E-06	1	151655397	A	G	0.0651479	0.12755	0.0287742	5,959
	the FR02 cohort	rs114379109	7.9E-06	2	67843764	T	C	0.092238	-0.109083	0.0244169	5,959
	the FR02 cohort	rs7570971	1.6E-10	2	135080336	A	C	0.42247	-0.0929224	0.0145294	5,959
	the FR02 cohort	rs72966145	2.9E-06	2	222594690	G	A	0.0182752	0.250925	0.0536587	5,959
	the FR02 cohort	rs13099974	2.5E-07	3	152069496	G	T	0.232505	-0.0877121	0.0170076	5,959
	the FR02 cohort	rs114719527	8.9E-06	3	187281615	A	G	0.0310263	0.184561	0.0415434	5,959

	the FR02 cohort	rs7730299	5.8E-06	5	36460005	T	G	0.350227	0.0665636	0.0146776	5,959
	the FR02 cohort	rs73790046	1.8E-06	6	169021383	A	G	0.0533107	0.150939	0.0316411	5,959
	the FR02 cohort	rs11763364	9.2E-07	7	79263	A	T	0.466794	-0.0708472	0.0144378	5,959
	the FR02 cohort	rs12703112	5.2E-06	7	151068149	A	G	0.142845	-0.0932397	0.0204706	5,959
	the FR02 cohort	rs142693368	4.8E-06	8	107643192	C	A	0.0167593	0.254256	0.0556165	5,959
	the FR02 cohort	rs117975365	4E-06	11	110328655	A	G	0.0150445	0.270237	0.0585696	5,959
	the FR02 cohort	rs2686386	8.2E-06	12	121201854	C	T	0.12384	0.0972486	0.0218081	5,959
	the FR02 cohort	rs182749893	7.8E-06	12	131629694	C	T	0.0141061	-0.272379	0.0609181	5,959
	the FR02 cohort	rs1175397	7.7E-06	13	44918011	A	G	0.0860206	0.114366	0.025573	5,959
	the FR02 cohort	rs66692590	5.4E-06	15	97122976	A	C	0.157401	0.0913067	0.0200662	5,959
	the FR02 cohort	rs7211768	8.8E-06	17	16665186	T	A	0.321429	0.0683471	0.0153749	5,959
	the FR02 cohort	rs148796276	2.4E-06	17	3168296	G	A	0.0410832	0.169144	0.0358419	5,959

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	the FR02 cohort	rs150493675	2.2E-06	19	31159060	T	C	0.034933	0.184187	0.0388799	5,959
g.UNC496MF	the FR02 cohort	rs72679176	2.1E-06	1	102622427	G	C	0.0114826	-0.100507	0.0211778	5,959
	the FR02 cohort	rs2859246	8.1E-08	1	172656528	T	C	0.470935	-0.0246499	0.00459504	5,959
	the FR02 cohort	rs114698862	7.7E-08	3	7353116	G	A	0.0631402	-0.0501221	0.00932633	5,959
	the FR02 cohort	rs181581167	9.3E-06	4	171989056	G	A	0.0834486	-0.036741	0.00828673	5,959
	the FR02 cohort	rs189353830	4.1E-06	6	80689645	A	G	0.0434051	0.0511509	0.0111033	5,959
	the FR02 cohort	rs794860	8.2E-06	6	118693643	C	G	0.0454393	0.0481593	0.0107971	5,959
	the FR02 cohort	rs34708501	6.8E-06	7	5448458	C	A	0.493704	0.021163	0.00470324	5,959
	the FR02 cohort	rs2465153	2.2E-06	7	91554313	G	A	0.246845	0.025014	0.00528849	5,959
	the FR02 cohort	rs8192856	4E-06	7	139991120	T	A	0.0670973	-0.0421359	0.00913326	5,959
	the FR02 cohort	rs62495394	1.1E-06	8	15006362	G	A	0.0414777	-0.0548959	0.0112642	5,959
	the FR02 cohort	rs13255030	3.2E-06	8	3181381	G	A	0.349521	0.0221479	0.00475292	5,959

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	the FR02 cohort	rs2842124	4.8E-07	10	50246241	G	T	0.187395	0.0289328	0.00574796	5,959
	the FR02 cohort	rs56295230	4.7E-06	11	6275800	G	A	0.109992	0.0332505	0.0072611	5,959
	the FR02 cohort	rs146721298	4.3E-07	12	114750495	G	C	0.0235492	0.0750267	0.0148432	5,959
	the FR02 cohort	rs56160072	3.2E-06	17	71750106	A	G	0.0335267	-0.0589414	0.0126549	5,959
	the FR02 cohort	rs387455	1.8E-06	20	14865247	G	A	0.319575	0.0230825	0.00483943	5,959
	the FR02 cohort	rs1847329	8.8E-06	20	49352479	C	G	0.236027	0.0232263	0.0052264	5,959
s.Bifidobacterium	the FR02 cohort	rs3940549	3.2E-32	2	135381057	G	A	0.421891	0.179917	0.0152246	5,959
	the FR02 cohort	rs34934741	7E-06	2	173886890	G	C	0.0265599	-0.20999	0.046731	5,959
	the FR02 cohort	rs7369560	5.4E-06	2	211640274	C	T	0.0450924	0.163228	0.035878	5,959
	the FR02 cohort	rs12497495	1.6E-06	3	71820588	C	G	0.259365	-0.0844585	0.0176034	5,959
	the FR02 cohort	rs76830965	3.7E-06	3	159919889	A	C	0.0836569	-0.125818	0.0271832	5,959

	the FR02 cohort	rs71323798	1.2E-06	3	197312881	G	A	0.0604517	-0.152987	0.0314536	5,959
	the FR02 cohort	rs464850	8.5E-06	5	179228116	C	T	0.122001	-0.100882	0.0226594	5,959
	the FR02 cohort	rs6900690	7E-06	6	125901886	G	A	0.435399	-0.0675703	0.0150387	5,959
	the FR02 cohort	rs2158787	8.3E-06	8	1432886	T	C	0.0893939	0.11584	0.0259949	5,959
	the FR02 cohort	rs72650093	4.7E-06	8	55623253	T	C	0.0136203	-0.294329	0.0642817	5,959
	the FR02 cohort	rs76648959	1.6E-07	8	70752304	A	G	0.0373665	-0.204228	0.039002	5,959
	the FR02 cohort	rs1890115	5.3E-06	9	82551078	T	G	0.147355	-0.0956388	0.021002	5,959
	the FR02 cohort	rs1805488	4.1E-06	12	13584780	C	T	0.084035	0.124482	0.0270383	5,959
	the FR02 cohort	rs3809260	5.7E-06	12	101697239	G	T	0.422378	0.06789	0.0149671	5,959
	the FR02 cohort	rs74023499	6.5E-06	15	74395407	T	A	0.0306826	-0.194651	0.0431546	5,959
	the FR02 cohort	rs116980236	3.2E-06	20	36827927	G	A	0.0637829	-0.142455	0.0306045	5,959
s.CAG-884	the FR02 cohort	rs4854491	6E-06	2	6869155	C	T	0.29889	-0.0575848	0.0127222	5,959

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	the FR02 cohort	rs139654497	2.4E-06	3	95611253	A	T	0.0114175	0.26551	0.0562554	5,959
	the FR02 cohort	rs74873861	3.5E-06	3	110696189	C	G	0.0360323	0.149538	0.0322303	5,959
	the FR02 cohort	rs185065427	8.8E-06	4	6351544	T	C	0.0319807	0.151102	0.0339876	5,959
	the FR02 cohort	rs147833749	9E-06	4	95308187	T	C	0.0122792	0.24065	0.0541912	5,959
	the FR02 cohort	rs149643665	1.1E-06	5	3138489	T	C	0.0130471	0.254995	0.0524167	5,959
	the FR02 cohort	rs2400705	5.1E-07	5	148811455	A	G	0.187436	-0.0774502	0.0154207	5,959
	the FR02 cohort	rs1015465	8.7E-07	6	30118563	C	T	0.0390166	0.148269	0.0301408	5,959
	the FR02 cohort	rs7801158	4.4E-06	7	64773248	T	C	0.369082	-0.0563334	0.0122678	5,959
	the FR02 cohort	rs881358	1E-07	7	106571913	T	C	0.267978	-0.070967	0.0133353	5,959
	the FR02 cohort	rs60994783	8.3E-06	10	126501679	T	C	0.197246	-0.0664996	0.0149229	5,959
	the FR02 cohort	rs2583258	5.7E-06	12	104048953	T	C	0.10005	-0.0890731	0.0196314	5,959
	the FR02 cohort	rs142169167	8.2E-06	14	4767589	T	C	0.0994924	0.0880409	0.0197353	5,959

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	the FR02 cohort	rs710274	7.3E-06	14	97027576	A	G	0.304461	0.0584675	0.0130352	5,959
	the FR02 cohort	rs11632141	9.5E-06	15	39338070	C	T	0.120941	0.0823729	0.0185989	5,959
	the FR02 cohort	rs8037071	9.4E-06	15	66803291	C	A	0.251148	-0.0613069	0.0138365	5,959
	the FR02 cohort	rs76012754	3.2E-06	16	20151540	A	C	0.0247019	0.178522	0.0383148	5,959
	the FR02 cohort	rs117574388	4.3E-06	17	20960653	A	G	0.0470578	0.129091	0.0280872	5,959
	the FR02 cohort	rs4289081	5.2E-06	18	64277657	T	C	0.482539	0.0545141	0.0119685	5,959
	the FR02 cohort	rs28576121	8.5E-06	19	20380913	A	G	0.147768	-0.0739361	0.0166089	5,959
	the FR02 cohort	rs143543844	2.5E-07	22	42634424	A	G	0.0126284	0.275216	0.0533387	5,959
s.DTU024 sp002411105	the FR02 cohort	rs80336408	3E-07	1	91785612	T	C	0.103952	0.0473096	0.00923858	5,959
	the FR02 cohort	rs61823204	4.1E-07	1	192996390	A	G	0.0394404	-0.07314	0.0144463	5,959
	the FR02 cohort	rs6705535	4.5E-06	2	5933290	A	G	0.388217	-0.0267326	0.00582634	5,959

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	the FR02 cohort	rs6801093	8.5E-06	3	64219741	A	C	0.014179	-0.106881	0.0240123	5,959
	the FR02 cohort	rs72795723	1.7E-06	5	129941056	G	A	0.0475298	-0.0636163	0.0132868	5,959
	the FR02 cohort	rs10044281	7.7E-06	5	175563349	G	A	0.120238	-0.0386016	0.00863	5,959
	the FR02 cohort	rs926856	8.8E-06	6	81803685	G	A	0.416315	0.0252189	0.00567387	5,959
	the FR02 cohort	rs73157388	1.6E-07	7	79720414	C	T	0.110378	0.0473347	0.00902401	5,959
	the FR02 cohort	rs57748809	4.4E-06	10	18226859	G	C	0.0391728	0.0668565	0.0145576	5,959
	the FR02 cohort	rs112663685	8.6E-06	10	96070484	A	G	0.0114952	-0.117873	0.0264941	5,959
	the FR02 cohort	rs12419984	2.4E-06	11	24055856	T	C	0.410943	0.0269302	0.00570751	5,959
	the FR02 cohort	rs10879832	1.1E-06	12	74752378	G	A	0.297777	-0.0299422	0.0061423	5,959
	the FR02 cohort	rs12425070	7.8E-06	12	94704236	A	G	0.0702358	0.0499106	0.0111617	5,959
	the FR02 cohort	rs9552628	2.8E-08	13	2226842	G	C	0.0420734	0.0784247	0.0141182	5,959

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	the FR02 cohort	rs9594422	1.8E-06	13	40519827	T	C	0.175021	-0.0353496	0.00741034	5,959
	the FR02 cohort	rs11074810	8.5E-06	16	26944253	A	T	0.296551	0.0276892	0.00622083	5,959
	the FR02 cohort	rs10403984	9.6E-07	19	28995032	C	T	0.220715	0.0330868	0.00675404	5,959
	the FR02 cohort	rs214831	6.6E-06	20	2340717	A	G	0.319013	0.0272376	0.00604313	5,959
s.Faecalicatena lactaris	the FR02 cohort	rs75934098	9.4E-06	1	18981462	C	T	0.045863	0.156704	0.035368	5,959
	the FR02 cohort	rs149036558	3.7E-06	1	73343172	C	T	0.0122854	0.311399	0.0673214	5,959
	the FR02 cohort	rs7596505	4.8E-06	2	68746090	G	A	0.101463	0.111679	0.024429	5,959
	the FR02 cohort	rs10186271	4.1E-06	2	118823675	A	G	0.235708	-0.0799744	0.0173656	5,959
	the FR02 cohort	rs140392762	6.4E-06	3	12881479	A	T	0.0278858	0.201972	0.0447606	5,959
	the FR02 cohort	rs11714653	8.9E-06	3	189015171	C	T	0.0554047	0.144472	0.0325279	5,959
	the FR02 cohort	rs62321488	8.8E-06	4	98345542	T	C	0.0398927	-0.169394	0.0381202	5,959

	the FR02 cohort	rs6894441	8.6E-06	5	127470112	G	A	0.4171	0.0672876	0.0151201	5,959
	the FR02 cohort	rs9374596	2E-06	6	116268127	G	A	0.10351	-0.115804	0.0243756	5,959
	the FR02 cohort	rs10243589	8.7E-06	7	30775414	T	C	0.208726	0.0803311	0.0180641	5,959
	the FR02 cohort	rs545971	8.9E-13	9	133267960	T	C	0.451418	0.105341	0.0147396	5,959
	the FR02 cohort	rs117998008	3.2E-06	11	133884585	T	C	0.0345149	-0.190928	0.0409797	5,959
	the FR02 cohort	rs113458344	2.7E-06	15	79789582	G	C	0.160693	0.0945163	0.020141	5,959
	the FR02 cohort	rs11652513	1.7E-06	17	9200736	T	C	0.261782	0.0841582	0.0175767	5,959
	the FR02 cohort	rs900966	7.4E-06	18	45718922	T	C	0.371264	-0.0690947	0.015421	5,959
	the FR02 cohort	rs36173890	8.8E-06	20	61238956	T	C	0.0170484	-0.254444	0.0572321	5,959
	the FR02 cohort	rs135736	3.2E-06	22	38282558	T	G	0.338283	-0.0752567	0.0161503	5,959
	the FR02 cohort	rs62220605	8.1E-06	22	49289224	A	G	0.0674387	-0.13086	0.0293187	5,959
s.Lactococcus	the FR02 cohort	rs79001423	8.8E-06	4	6625032	T	G	0.261223	-0.0529809	0.0119176	5,959

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	the FR02 cohort	rs146142280	5.1E-06	4	74910823	A	G	0.0177635	0.176521	0.0386912	5,959
	the FR02 cohort	rs144983228	5.5E-06	4	181113357	T	G	0.0336709	0.127133	0.0279671	5,959
	the FR02 cohort	rs112289399	1.8E-06	5	3883003	T	C	0.0133816	0.210313	0.0440737	5,959
	the FR02 cohort	rs11520695	1.6E-07	7	13403964	G	A	0.0585419	0.112105	0.0214098	5,959
	the FR02 cohort	rs35643205	4.6E-06	7	152930133	G	A	0.300155	-0.0501383	0.0109419	5,959
	the FR02 cohort	rs2804570	8.2E-06	10	29138461	T	C	0.14113	0.0649822	0.0145693	5,959
	the FR02 cohort	rs77246646	3.2E-06	14	65492684	A	G	0.0280785	0.142509	0.0305813	5,959
	the FR02 cohort	rs79214353	4.3E-06	16	13242693	T	G	0.05	0.106786	0.0232306	5,959
	the FR02 cohort	rs28567510	1.3E-06	16	66289573	A	G	0.309247	0.0529845	0.0109473	5,959
	the FR02 cohort	rs112437747	2.3E-08	17	27422521	T	C	0.0105936	0.277633	0.0497008	5,959
	the FR02 cohort	rs62070469	3.7E-06	17	80828781	T	A	0.0318487	-0.133836	0.0289381	5,959

	the FR02 cohort	rs12971669	5.2E-06	19	35239235	A	G	0.238484	0.0548441	0.0120393	5,959
s.Negativibacillus massiliensis	the FR02 cohort	rs2641348	5.5E-06	1	119895261	G	A	0.145746	-0.0514341	0.011319	5,959
	the FR02 cohort	rs1326749	8.5E-06	2	214909084	T	C	0.425568	-0.0359234	0.00807051	5,959
	the FR02 cohort	rs188774576	5.1E-06	3	1076956	T	C	0.0340084	0.100358	0.0220043	5,959
	the FR02 cohort	rs79831182	9.4E-06	3	59609283	A	C	0.0309383	0.100837	0.0227651	5,959
	the FR02 cohort	rs1497993	8.7E-06	3	111483889	A	G	0.0191013	0.130958	0.0294407	5,959
	the FR02 cohort	rs16851304	7.3E-06	3	141284407	A	G	0.107353	-0.0574071	0.012802	5,959
	the FR02 cohort	rs117450486	4.1E-08	6	105114266	G	A	0.0338094	0.121761	0.0221913	5,959
	the FR02 cohort	rs9384293	8.4E-06	6	155190646	C	T	0.0468056	0.0840887	0.018876	5,959
	the FR02 cohort	rs2763223	8.7E-06	6	168461894	A	C	0.371095	-0.0371594	0.00835648	5,959
	the FR02 cohort	rs28634441	4E-06	7	103897524	A	G	0.272965	0.0413209	0.0089593	5,959
	the FR02 cohort	rs4979255	5.3E-06	9	1077005	A	G	0.183923	0.0467896	0.01028	5,959

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	the FR02 cohort	rs17552264	6.6E-06	12	43974026	C	T	0.0248053	0.115801	0.0257054	5,959
	the FR02 cohort	rs1242927	1.9E-06	14	22608000	C	T	0.378808	-0.0387437	0.00812621	5,959
	the FR02 cohort	rs4898867	6.6E-06	14	55543679	C	T	0.253631	-0.0414088	0.00919063	5,959
	the FR02 cohort	rs74032121	2.7E-06	15	98945907	A	C	0.0221022	0.127099	0.027064	5,959
	the FR02 cohort	rs73279647	4.7E-06	20	44465891	A	G	0.0212228	-0.126962	0.0277252	5,959
	the FR02 cohort	rs36124608	9E-06	22	36564970	A	G	0.0751246	0.067738	0.0152539	5,959
	the FR02 cohort	rs5771271	3.7E-06	22	50245883	A	G	0.0929226	-0.0633948	0.0137061	5,959
s.Negativibacillus sp000435195	the FR02 cohort	rs12748888	3.6E-06	1	56593433	A	C	0.0349055	0.181136	0.0390994	5,959
	the FR02 cohort	rs583495	7.4E-06	1	218121531	G	A	0.423992	0.0666522	0.0148674	5,959
	the FR02 cohort	rs35947696	3.7E-06	2	42097279	A	T	0.333532	0.0713618	0.0154144	5,959
	the FR02 cohort	rs56369224	6.2E-10	2	1355713	T	A	0.419715	-0.0904894	0.0146325	5,959

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	the FR02 cohort	rs9860326	6E-06	3	35641612	G	C	0.268862	0.0729163	0.0161054	5,959
	the FR02 cohort	rs2405761	7.3E-06	3	162386811	G	A	0.219369	0.0767029	0.0171035	5,959
	the FR02 cohort	rs1825885	2.9E-06	4	120509894	A	G	0.405732	0.0679391	0.0145184	5,959
	the FR02 cohort	rs58133020	9E-06	4	132856089	T	C	0.116338	-0.0999801	0.0225202	5,959
	the FR02 cohort	rs16869764	1.3E-06	7	67999623	C	G	0.0750422	-0.131565	0.0271993	5,959
	the FR02 cohort	rs701323	9.3E-06	7	80985095	C	T	0.224815	0.0750352	0.0169266	5,959
	the FR02 cohort	rs73452757	6E-06	7	138210313	C	G	0.0921252	-0.112046	0.0247551	5,959
	the FR02 cohort	rs117617797	7.8E-06	8	11409725	C	G	0.0303211	0.188396	0.0421343	5,959
	the FR02 cohort	rs201459703	6E-06	9	40711772	G	A	0.00642832	0.414914	0.0916348	5,959
	the FR02 cohort	rs72826474	7.9E-07	10	119956956	A	C	0.0346977	0.191743	0.0388262	5,959
	the FR02 cohort	rs7928180	9.9E-06	11	3897802	A	G	0.445971	0.0630972	0.0142749	5,959

					8						
	the FR02 cohort	rs112886298	9.7E-06	12	7978184	A	G	0.276393	-0.0717846	0.0162282	5,959
	the FR02 cohort	rs4372602	6.3E-06	14	42725990	G	A	0.0780878	0.120471	0.0266745	5,959
	the FR02 cohort	rs12443734	4.2E-06	16	8407518	T	A	0.277579	0.0744321	0.0161749	5,959
	the FR02 cohort	rs139819082	8.7E-06	16	11563188	A	G	0.0274427	0.196725	0.0442332	5,959
	the FR02 cohort	rs78316167	2.6E-07	17	27474934	A	G	0.0142256	0.310666	0.0602916	5,959
	the FR02 cohort	rs150289681	6.7E-07	18	70391468	C	T	0.266735	-0.0806639	0.0162348	5,959
	the FR02 cohort	rs146489738	9.4E-06	19	43202261	A	T	0.10132	0.105287	0.0237622	5,959
	the FR02 cohort	rs77310311	6.9E-06	20	59099481	T	A	0.0160343	0.253052	0.0562597	5,959
s.Prevotella buccae	the FR02 cohort	rs36197101	8.9E-06	1	28020631	G	T	0.153519	0.0730201	0.0164412	5,959
	the FR02 cohort	rs75408989	6.7E-07	1	152185794	G	A	0.0103535	0.280128	0.0563496	5,959
	the FR02 cohort	rs11679697	3.3E-06	2	46257047	G	C	0.408909	0.0568342	0.0122249	5,959
	the FR02 cohort	rs13064335	8E-06	3	1236416	A	G	0.0756629	0.0986168	0.022084	5,959

	the FR02 cohort	rs139429107	7.3E-06	3	8622605	C	T	0.0169233	0.201199	0.0448675	5,959
	the FR02 cohort	rs113723748	6.2E-06	3	65586006	C	G	0.032651	0.148332	0.0328125	5,959
	the FR02 cohort	rs117340758	1.1E-06	6	94367468	C	T	0.0351131	0.154364	0.0316473	5,959
	the FR02 cohort	rs118016027	2.6E-07	6	114175811	A	T	0.0193342	0.216502	0.042052	5,959
	the FR02 cohort	rs12528718	9.2E-06	6	154990256	C	G	0.253262	-0.0613571	0.0138378	5,959
	the FR02 cohort	rs77493572	7.5E-06	7	16143491	A	G	0.0176263	0.198914	0.0444108	5,959
	the FR02 cohort	rs11769617	3.2E-06	7	149997801	A	G	0.0362773	0.144135	0.0309478	5,959
	the FR02 cohort	rs6981089	5.7E-06	8	65895118	G	A	0.212211	-0.0644998	0.0142168	5,959
	the FR02 cohort	rs4977443	3.8E-06	9	18802724	G	C	0.290694	-0.0591151	0.0127918	5,959
	the FR02 cohort	rs11789769	3E-06	9	96333322	T	C	0.0650662	0.112028	0.0239896	5,959
	the FR02 cohort	rs71501367	1.3E-06	10	80254771	C	A	0.350591	0.0590912	0.0122248	5,959
	the FR02 cohort	rs560195	6.6E-06	11	1142755	T	C	0.0928523	0.0901447	0.0199997	5,959

					29						
	the FR02 cohort	rs11535963	1.1E-06	12	18201586	T	C	0.27665	0.063215	0.0129644	5,959
	the FR02 cohort	rs7132624	3.9E-06	12	105082516	A	G	0.173576	0.0702467	0.0152209	5,959
	the FR02 cohort	rs117911018	5.1E-06	17	81115275	T	C	0.0683926	0.104753	0.022967	5,959
	the FR02 cohort	rs182865049	2E-06	19	5840206	T	C	0.0224094	0.187746	0.0395128	5,959

Abbreviations: *p*-value, *p*-value of causal estimation in the IVW method; CHR, Chromosome; BP, Base pair location; A1, Effect allele; A2, Other allele; EAF, Effect allele frequency; Beta,estimated causal effect coefficient; SE, standard error of coefficient estimate.

Table S3. The instruments of gut bacterial pathways that are causally associated with MAFLD.

Exposure	SNP	*P*-value	CHR	BP	A1	A2	EAF	Beta	SE	Samplesize
PWY.dTDP-L-rhamnose biosynthesis I	rs10779615	1.05E-06	1	214596434	G	C	0.508390981	-0.079847503	0.016354348	7,738
	rs145140903	9.87E-06	1	231364626	C	T	0.111675257	-0.115636358	0.026161833	7,738
	rs16856918	2.47E-06	2	217960513	A	G	0.055213892	0.171977137	0.036508811	7,738
	rs73171592	4.04E-06	3	171047195	C	G	0.077174271	0.143445673	0.031121056	7,738
	rs11745906	8.73E-07	5	83575190	C	T	0.281705766	-0.08740556	0.017771203	7,738
	rs3819331	4.76E-06	11	112099410	C	T	0.15925253	0.104197008	0.022774326	7,738
	rs2620868	2.87E-06	12	61370770	C	T	0.438607534	-0.075993151	0.016237223	7,738
	rs80343422	3.44E-07	13	110456322	G	A	0.076102403	-0.156490678	0.03069903	7,738
	rs72987936	9.63E-06	18	75120908	A	T	0.364515328	-0.075508	0.0170631	7,738

								051	14	
PWY.Gluconeogenesis I	rs75506401	3.82E-06	3	71038802	C	T	0.06877627	-0.150857473	0.032644937	7,738
	rs10866460	5.04E-07	4	59288104	T	C	0.393209206	-0.084693818	0.01685508	7,738
	rs77004407	1.09E-06	14	32115228	A	C	0.05316971	0.179299651	0.036777014	7,738
	rs117665320	8.66E-08	19	35175877	A	G	0.063170331	-0.193309861	0.03611377	7,738
PWY. L.histidine degradation I	rs12137024	3.53E-08	1	95409858	A	G	0.169299147	0.118929008	0.021573179	7,738
	rs13010502	9.37E-06	2	3524216	T	A	0.927338312	-0.139759259	0.031539837	7,738
	rs6783574	2.75E-06	3	30775466	G	T	0.389025495	0.078269732	0.016692188	7,738
	rs1501270	1.40E-06	4	105011169	A	C	0.253442601	0.090524496	0.018761085	7,738
	rs11948304	3.48E-06	5	14111048	A	G	0.271580173	0.084634651	0.018238304	7,738
	rs17613381	2.06E-06	6	32622130	T	C	0.394205447	-0.087743382	0.018482418	7,738
	rs76864278	6.20E-06	8	14672692	G	T	0.271007443	-0.083879	0.0185588	7,738

								13	86	
	rs2175835	4.33E-06	8	29275779	C	T	0.086797504	-0.145775975	0.031727303	7,738
	rs77982223	5.86E-06	9	133536170	G	C	0.105957211	0.120950677	0.026692217	7,738
	rs11818856	1.02E-06	10	14094653	C	G	0.549486268	-0.080725949	0.016514714	7,738
	rs1339631	8.51E-06	10	107789712	T	A	0.449921208	-0.07371266	0.016557053	7,738
	rs144371117	9.59E-06	14	80077900	A	G	0.061605219	-0.165830869	0.037465097	7,738
	rs3095927	8.78E-07	19	6810484	C	G	0.10545807	0.158715622	0.032277047	7,738
PWY. TCA cycle IV 2 oxoglutarate decarboxylase	rs857120	5.47E-06	1	57211399	C	T	0.088345486	0.208416068	0.045846417	7,738
	rs11582075	5.99E-06	1	83675735	T	C	0.2191973	-0.137143648	0.030296681	7,738
	rs12034038	9.31E-06	1	84041610	C	G	0.174619366	0.145687657	0.032866726	7,738
	rs27099	9.73E-06	5	14463639	T	A	0.208738524	-0.137509165	0.031088579	7,738
	rs10223540	9.36E-06	6	21206319	T	C	0.100899795	-0.185492	0.0418583	7,738

								521	36	
	rs36182340	2.00E-08	7	155118470	T	G	0.903211304	0.235877309	0.042032148	7,738
	rs72814612	3.04E-06	10	95941459	C	A	0.107887844	0.200657699	0.042982116	7,738
	rs6562993	6.42E-06	13	77914588	G	A	0.236848137	-0.133595514	0.029607635	7,738
	rs2518968	5.54E-07	15	91307410	G	C	0.539119347	0.134970662	0.026958981	7,738
PWY.Urea cycle	rs17530744	9.75E-06	4	22348934	C	G	0.217453226	-0.091977206	0.020796792	7,738
	rs1035394	4.15E-06	5	58013548	T	A	0.690264991	-0.081865475	0.017781999	7,738
	rs12113402	5.63E-06	7	97567997	T	C	0.279523393	0.08610756	0.018966557	7,738
	rs7825304	4.99E-06	8	15420526	T	A	0.465015086	0.074267814	0.016267503	7,738
	rs3131899	9.37E-06	9	97025979	T	C	0.366632856	0.076395815	0.017239967	7,738
	rs7906344	7.79E-06	10	14168048	A	G	0.629832726	-0.075559367	0.01690081	7,738
	rs17772715	9.67E-06	14	49342300	C	T	0.722258786	0.0798891	0.0180567	7,738

								29	99	
	rs11862432	9.80E-06	16	1111401	T	C	0.345883437	0.080828924	0.018280693	7,738
	rs79525129	5.95E-06	19	46806527	T	C	0.135182877	0.108940451	0.024058918	7,738
	rs2213429	8.16E-06	22	37217172	T	C	0.182427532	-0.096433587	0.021617181	7,738
PWY.5100.Pyruvate fermentation to acetate and lactate II	rs602386	5.98E-06	1	9405923	G	C	0.184480207	-0.097191906	0.021469522	7,738
	rs75331157	8.72E-06	1	63553371	G	C	0.057573016	0.159162112	0.035794008	7,738
	rs12128621	5.17E-07	1	214584517	A	T	0.504520092	-0.082513803	0.016436937	7,738
	rs7595525	7.72E-06	2	49254815	C	A	0.200692787	-0.091227284	0.020395392	7,738
	rs4533457	6.60E-06	2	67787348	G	T	0.813064885	0.094956263	0.021072157	7,738
	rs2624881	6.25E-06	4	177169430	C	T	0.087941607	0.128453645	0.028432242	7,738
	rs11249616	2.64E-06	5	178617695	A	G	0.219035673	-0.096062247	0.020451121	7,738
	rs3812328	6.25E-06	7	29517436	A	G	0.347247351	-0.077209	0.0170909	7,738

								93	66	
	rs80315336	7.68E-06	9	38310405	A	G	0.065459231	0.156288572	0.034933955	7,738
	rs117996720	5.33E-06	11	32460157	A	C	0.060832459	-0.167688265	0.036844384	7,738
	rs12280724	6.35E-06	11	116613423	T	G	0.076246839	-0.137533188	0.030465129	7,738
	rs9954361	7.72E-06	18	5327489	A	T	0.195491564	0.09619913	0.021507659	7,738
	rs1187244	1.08E-06	18	35322638	C	T	0.304887771	-0.086373566	0.017710028	7,738
	rs4816116	5.73E-06	20	959339	G	A	0.127912923	-0.113438738	0.025007883	7,738
PWY.5101 L isoleucine biosynthesis II	rs17793651	3.76E-06	2	143316345	T	C	0.052631901	-0.173606924	0.037544846	7,738
	rs57592260	9.37E-07	3	29318409	T	G	0.287596585	-0.089978529	0.018346585	7,738
	rs10015335	5.33E-06	4	13235866	A	T	0.338509355	-0.079337006	0.017431915	7,738
	rs67560429	8.88E-06	5	179636575	G	A	0.333712782	0.077666852	0.017482018	7,738
	rs12189770	9.66E-06	6	138668982	G	A	0.258697982	-0.091716	0.0207282	7,738

								801	16	
	rs4744061	3.69E-06	9	94337875	A	G	0.176990895	-0.09942086	0.021482045	7,738
	rs680138	6.71E-06	9	110882980	T	C	0.617860642	-0.076740704	0.01704343	7,738
	rs34025630	3.19E-06	11	11768444	T	C	0.182398618	-0.100746278	0.02162675	7,738
	rs2596115	7.96E-06	14	81124514	G	A	0.797058313	0.091277544	0.020437609	7,738
	rs116856824	5.33E-06	14	89369102	T	G	0.054696288	-0.171955251	0.037782033	7,738
	rs28513874	5.11E-07	15	80799378	G	A	0.371010044	-0.085261076	0.016976701	7,738
	rs4798876	3.57E-06	18	9868910	A	G	0.468011452	-0.077782452	0.016781005	7,738
	rs9304309	5.53E-06	18	41981339	G	A	0.252998591	0.087149226	0.019179947	7,738
PWY.6545.Pyrimidine deoxyribonucleotides de nov biosynthesis III	rs9681001	6.62E-06	3	129719723	T	C	0.162699993	-0.100324867	0.022267403	7,738
	rs62335957	9.36E-07	5	1651198	G	T	0.073881633	-0.152282017	0.031048939	7,738
	rs113333050	5.44E-06	7	136417370	T	C	0.070767894	-0.146765	0.0322777	7,738

								658	52	
	rs2381195	7.07E-06	9	5145887	C	T	0.47570457	0.07313656	0.01628338	7,738
	rs9630400	5.51E-06	14	71129209	G	C	0.326502516	-0.078674622	0.017311923	7,738
	rs1719290	4.17E-06	15	65132236	T	C	0.389748833	-0.076210894	0.016557582	7,738
	rs2620049	8.63E-06	17	71839114	A	G	0.084474379	-0.131349333	0.029523307	7,738
	rs144373948	1.34E-06	22	43888228	G	A	0.586091557	-0.07975012	0.01650056	7,738
PWY.7198.Pyrimidine deoxyribonucleotides de novo biosynthesis IV	rs12466926	1.77E-06	2	22219465	A	G	0.255776116	-0.099162278	0.02075126	7,738
	rs9310781	9.59E-06	3	25482147	G	C	0.24216239	-0.096291232	0.021754261	7,738
	rs6854439	9.79E-06	4	40203439	T	C	0.481756968	0.078926697	0.017849582	7,738
	rs4739729	1.51E-06	8	81149186	A	G	0.353331737	-0.09242853	0.019213999	7,738
	rs77945651	1.42E-06	12	24318151	C	A	0.055130402	0.19726825	0.040906512	7,738
	rs9508816	5.59E-06	13	31256569	T	A	0.734996592	-0.096216	0.0211863	7,738

								165	87	
	rs8046267	7.26E-06	16	57877231	G	C	0.142949344	-0.116058255	0.025871375	7,738
PWY.UDP N acetyl D glucosamine biosynthesis I	rs4846474	7.59E-06	1	218453434	T	C	0.495263759	0.079699228	0.017804539	7,738
	rs35804940	7.86E-06	4	157148271	A	C	0.315924696	-0.078751832	0.01762225	7,738
	rs11745387	6.71E-06	5	151059231	A	G	0.363027473	-0.076339441	0.016954552	7,738
	rs35130680	5.46E-06	6	115840180	T	C	0.088669973	-0.13596817	0.029908712	7,738
	rs208029	9.81E-07	8	17840987	G	T	0.800461511	0.100989149	0.020629007	7,738
	rs11014565	4.00E-06	10	25733319	A	G	0.824417425	-0.100301933	0.021751275	7,738
	rs61862985	5.60E-06	10	132905339	A	G	0.158244724	0.104003799	0.022903551	7,738
	rs74083978	3.29E-06	14	91621098	C	G	0.057902807	0.163554272	0.035158355	7,738
	rs145287082	7.80E-06	22	35756340	G	A	0.062630359	-0.158760177	0.035512743	7,738

Abbreviations: *p*-value, p-value of causal estimation in the IVW method; CHR, Chromosome; BP, Base pair location; A1, Effect allele; A2, Other allele; EAF, Effect allele frequency;

Beta,estimated causal effect coefficient; SE, standard error of coefficient estimate

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Table S4. The instruments of MAFLD.						
SNP	***p*-value**	**A1**	**A2**	**EAF**	**Beta**	**SE**
rs61811895	9.75E-06	T	T	0.053873	0.0949891	0.0214777
rs2642442	9.38E-06	T	C	0.761868	0.0776752	0.0175301
rs780093	4.09E-06	T	C	0.284041	0.0769064	0.0166949
rs73943422	5.89E-06	T	C	0.717989	-0.1126834	0.0248727
rs307569	9.87E-06	A	C	0.171768	0.1044349	0.0236277
rs710462	4.07E-06	T	G	0.415209	-0.0759048	0.0164732
rs77888509	2.62E-06	A	G	0.024047	-0.114621	0.0243933
rs1397844	1.79E-06	T	C	0.802311	-0.1010635	0.0211625
rs10504255	6.06E-06	A	G	0.784197	-0.0758459	0.0167641
rs28601761	2.20E-11	C	G	0.702217	0.1100328	0.0164425
rs79605669	7.38E-06	T	C	0.009369	0.2864204	0.0638977
rs138427591	7.58E-06	T	C	0.993442	0.327559	0.0731692
rs72637037	7.96E-06	A	G	0.081043	0.1677248	0.0375547
rs2933904	1.95E-06	A	G	0.73376	0.0804682	0.0169093
rs7144175	2.50E-06	C	G	0.166302	0.1146814	0.0243596
rs9922619	2.32E-06	T	G	0.279044	0.0766643	0.0162305
rs45467396	6.48E-06	A	G	0.991255	-0.2054911	0.0455635

rs56058005	8.69E-06	T	G	0.447689	0.0866335	0.0194789
rs8108364	1.33E-07	T	C	0.574641	-0.129307	0.024517
rs73001065	7.36E-18	C	G	0.031387	0.2810094	0.0326406
rs429358	1.14E-08	T	C	0.848844	0.1366152	0.0239288
rs2423387	5.30E-06	A	G	0.008745	-0.250578	0.0550414
rs6061763	6.23E-06	T	G	0.38476	-0.0935125	0.0206965
rs3747207	5.07E-48	A	G	0.256715	0.2886006	0.019822

Abbreviations: *p*-value, p-value of causal estimation in the IVW method; A1, Effect allele; A2, Other allele; EAF, Effect allele frequency; Beta,estimated causal effect coefficient; SE, standard error of coefficient estimate

Table S5. The additional MR methods on the causal effect between 25 gut microbiome taxa and MAFLD in the de novo analysis.								
Exposure	**Data source**	**Method**	**SNPs**	**Beta**	**SE**	***p*-value**	**OR**	**95% CI**
g.Parabacteroides	the Dutch Microbiome Project	MR Egger	13	-0.004	0.304	0.989	0.996	0.549-1.806
	the Dutch Microbiome Project	Weighted median	13	0.118	0.076	0.123	1.125	0.969-1.306
	the Dutch Microbiome Project	Simple mode	13	0.063	0.124	0.624	1.065	0.834-1.358
	the Dutch Microbiome Project	Weighted mode	13	0.083	0.125	0.521	1.086	0.85-1.389
g.Roseburia	the Dutch Microbiome Project	MR Egger	14	0.202	0.229	0.394	1.224	0.782-1.917
	the Dutch Microbiome Project	Weighted median	14	0.14	0.075	0.063	1.15	0.992-1.333
	the Dutch Microbiome Project	Simple mode	14	0.108	0.127	0.411	1.114	0.869-1.427
	the Dutch Microbiome Project	Weighted mode	14	0.115	0.111	0.321	1.122	0.902-1.395
s.Parabacteroides_merdae	the Dutch Microbiome Project	MR Egger	6	0.674	0.303	0.091	1.962	1.082-3.555
	the Dutch Microbiome Project	Weighted median	6	0.131	0.101	0.192	1.14	0.936-1.389
	the Dutch Microbiome Project	Simple mode	6	0.129	0.155	0.444	1.137	0.84-1.541
	the Dutch Microbiome Project	Weighted mode	6	0.125	0.159	0.466	1.133	0.831-1.546
s.Bacteroides_salyersiae	the Dutch Microbiome Project	MR Egger	7	0.12	0.133	0.408	1.128	0.869-1.463
	the Dutch Microbiome Project	Weighted median	7	0.079	0.045	0.078	1.082	0.991-1.182
	the Dutch Microbiome Project	Simple mode	7	0.112	0.077	0.195	1.118	0.962-1.3
	the Dutch Microbiome Project	Weighted mode	7	0.09	0.067	0.224	1.095	0.961-1.247
s.Lachnospiraceae_bacterium_8_1_57FAA	the Dutch Microbiome Project	MR Egger	16	0.005	0.109	0.963	1.005	0.811-1.246
	the Dutch Microbiome Project	Weighted median	16	-0.086	0.037	0.019	0.918	0.854-0.986

	the Dutch Microbiome Project	Simple mode	16	-0.129	0.082	0.138	0.879	0.749-1.033
	the Dutch Microbiome Project	Weighted mode	16	-0.127	0.072	0.097	0.88	0.765-1.014
o.Haloplasmatales	the FR02 Cohort	MR Egger	15	0.603	0.364	0.122	1.827	0.895-3.729
	the FR02 Cohort	Weighted median	15	0.234	0.18	0.195	1.263	0.887-1.799
	the FR02 Cohort	Simple mode	15	0.132	0.298	0.664	1.141	0.637-2.045
	the FR02 Cohort	Weighted mode	15	0.137	0.296	0.649	1.147	0.643-2.048
f.Brevibacillaceae	the FR02 Cohort	MR Egger	13	0.119	0.15	0.442	1.127	0.84-1.511
	the FR02 Cohort	Weighted median	13	0.095	0.091	0.299	1.099	0.919-1.315
	the FR02 Cohort	Simple mode	13	0.12	0.146	0.426	1.128	0.847-1.5
	the FR02 Cohort	Weighted mode	13	0.133	0.12	0.291	1.142	0.902-1.445
g.Bacillus U	the FR02 Cohort	MR Egger	13	0.856	0.505	0.118	2.353	0.875-6.327
	the FR02 Cohort	Weighted median	13	0.619	0.314	0.048	1.858	1.004-3.436
	the FR02 Cohort	Simple mode	13	0.54	0.462	0.265	1.716	0.694-4.245
	the FR02 Cohort	Weighted mode	13	0.515	0.466	0.291	1.673	0.672-4.168
g.CAG-145	the FR02 Cohort	MR Egger	7	2.22	1.099	0.099	9.211	1.068-79.465
	the FR02 Cohort	Weighted median	7	0.419	0.263	0.111	1.521	0.909-2.545
	the FR02 Cohort	Simple mode	7	0.282	0.477	0.576	1.326	0.521-3.374
	the FR02 Cohort	Weighted mode	7	0.287	0.45	0.547	1.332	0.551-3.219
g.CAG-449	the FR02 Cohort	MR Egger	17	-0.273	0.171	0.131	0.761	0.544-1.063
	the FR02 Cohort	Weighted median	17	-0.233	0.103	0.024	0.792	0.647-0.969
	the FR02 Cohort	Simple mode	17	-0.24	0.18	0.202	0.787	0.553-1.12
	the FR02 Cohort	Weighted mode	17	-0.254	0.173	0.163	0.776	0.553-1.09

g.CAG-552	the FR02 Cohort	MR Egger	18	0.097	0.142	0.505	1.102	0.834-1.457
	the FR02 Cohort	Weighted median	18	0.176	0.063	0.005	1.192	1.054-1.349
	the FR02 Cohort	Simple mode	18	0.206	0.095	0.045	1.229	1.02-1.481
	the FR02 Cohort	Weighted mode	18	0.204	0.1	0.056	1.227	1.009-1.491
g.CAG-884	the FR02 Cohort	MR Egger	16	0.018	0.18	0.923	1.018	0.716-1.447
	the FR02 Cohort	Weighted median	16	-0.094	0.095	0.318	0.91	0.756-1.095
	the FR02 Cohort	Simple mode	16	-0.078	0.171	0.655	0.925	0.661-1.294
	the FR02 Cohort	Weighted mode	16	-0.027	0.155	0.862	0.973	0.718-1.318
g.Demequina	the FR02 Cohort	MR Egger	13	0.087	0.155	0.585	1.091	0.805-1.478
	the FR02 Cohort	Weighted median	13	-0.072	0.091	0.428	0.93	0.778-1.112
	the FR02 Cohort	Simple mode	13	-0.03	0.158	0.852	0.97	0.712-1.322
	the FR02 Cohort	Weighted mode	13	-0.011	0.139	0.936	0.989	0.754-1.297
g.Halarcobacter	the FR02 Cohort	MR Egger	17	0.077	0.391	0.846	1.08	0.502-2.324
	the FR02 Cohort	Weighted median	17	-0.215	0.25	0.389	0.806	0.494-1.316
	the FR02 Cohort	Simple mode	17	-0.633	0.449	0.178	0.531	0.22-1.281
	the FR02 Cohort	Weighted mode	17	-0.068	0.389	0.864	0.934	0.436-2.003
g.Olsenella C	the FR02 Cohort	MR Egger	15	-0.215	0.4	0.6	0.807	0.368-1.766
	the FR02 Cohort	Weighted median	15	0.062	0.224	0.783	1.064	0.686-1.65
	the FR02 Cohort	Simple mode	15	0.022	0.45	0.963	1.022	0.423-2.466
	the FR02 Cohort	Weighted mode	15	-0.018	0.385	0.963	0.982	0.462-2.089
g.Turicibacter	the FR02 Cohort	MR Egger	16	0.016	0.162	0.922	1.016	0.74-1.397
	the FR02 Cohort	Weighted median	16	-0.196	0.088	0.025	0.822	0.692-0.976

	the FR02 Cohort	Simple mode	16	-0.344	0.18	0.076	0.709	0.498-1.009
	the FR02 Cohort	Weighted mode	16	-0.329	0.184	0.094	0.72	0.502-1.032
g.UNC496MF	the FR02 Cohort	MR Egger	13	0.266	0.336	0.446	1.304	0.675-2.52
	the FR02 Cohort	Weighted median	13	0.299	0.177	0.091	1.348	0.953-1.907
	the FR02 Cohort	Simple mode	13	0.305	0.288	0.311	1.356	0.771-2.385
	the FR02 Cohort	Weighted mode	13	0.302	0.264	0.276	1.353	0.806-2.271
s.Bifidobacterium	the FR02 Cohort	MR Egger	15	-0.065	0.176	0.719	0.937	0.663-1.324
	the FR02 Cohort	Weighted median	15	-0.177	0.101	0.078	0.838	0.688-1.02
	the FR02 Cohort	Simple mode	15	-0.158	0.174	0.38	0.854	0.607-1.201
	the FR02 Cohort	Weighted mode	15	-0.21	0.162	0.218	0.811	0.59-1.115
s.CAG-884 sp000433875	the FR02 Cohort	MR Egger	11	-0.063	0.192	0.749	0.939	0.644-1.367
	the FR02 Cohort	Weighted median	11	-0.132	0.133	0.321	0.876	0.674-1.138
	the FR02 Cohort	Simple mode	11	-0.304	0.207	0.172	0.738	0.492-1.106
	the FR02 Cohort	Weighted mode	11	-0.189	0.184	0.328	0.827	0.577-1.187
s.DTU024 sp002411105	the FR02 Cohort	MR Egger	15	0.283	0.351	0.435	1.327	0.667-2.639
	the FR02 Cohort	Weighted median	15	0.12	0.163	0.462	1.127	0.819-1.552
	the FR02 Cohort	Simple mode	15	0.078	0.275	0.782	1.081	0.63-1.853
	the FR02 Cohort	Weighted mode	15	0.072	0.255	0.782	1.075	0.652-1.773
s.Faecalicatena lactaris	the FR02 Cohort	MR Egger	15	0.051	0.14	0.72	1.053	0.8-1.385
	the FR02 Cohort	Weighted median	15	0.15	0.084	0.074	1.162	0.986-1.371
	the FR02 Cohort	Simple mode	15	0.172	0.14	0.241	1.187	0.902-1.563
	the FR02 Cohort	Weighted mode	15	0.163	0.125	0.211	1.178	0.922-1.504

s.Lactococcus lactis	the FR02 Cohort	MR Egger	13	0.358	0.26	0.196	1.43	0.859-2.382
	the FR02 Cohort	Weighted median	13	0.335	0.159	0.035	1.398	1.023-1.911
	the FR02 Cohort	Simple mode	13	0.377	0.265	0.18	1.458	0.868-2.45
	the FR02 Cohort	Weighted mode	13	0.372	0.24	0.147	1.451	0.906-2.324
s.Negativibacillus massiliensis	the FR02 Cohort	MR Egger	15	-0.422	0.156	0.018	0.656	0.483-0.89
	the FR02 Cohort	Weighted median	15	-0.177	0.121	0.145	0.838	0.66-1.063
	the FR02 Cohort	Simple mode	15	-0.378	0.212	0.096	0.685	0.452-1.038
	the FR02 Cohort	Weighted mode	15	-0.198	0.147	0.198	0.82	0.616-1.093
s.Negativibacillus sp000435195	the FR02 Cohort	MR Egger	13	-0.27	0.193	0.19	0.763	0.523-1.115
	the FR02 Cohort	Weighted median	13	-0.153	0.091	0.092	0.858	0.718-1.025
	the FR02 Cohort	Simple mode	13	-0.173	0.136	0.228	0.841	0.645-1.098
	the FR02 Cohort	Weighted mode	13	-0.18	0.133	0.202	0.835	0.643-1.085
s.Prevotella buccae	the FR02 Cohort	MR Egger	15	-0.979	0.441	0.045	0.376	0.158-0.892
	the FR02 Cohort	Weighted median	15	-0.488	0.264	0.064	0.614	0.366-1.03
	the FR02 Cohort	Simple mode	15	-0.466	0.438	0.305	0.628	0.266-1.48
	the FR02 Cohort	Weighted mode	15	-0.524	0.435	0.248	0.592	0.252-1.388

Abbreviations: Method, the method used in MR analysis; SNPs, number of SNPs; Beta,estimated causal effect coefficient; SE, standard error of coefficient estimate; *p*-value, *p*-value of causal estimation in the MR method; OR [95%CI], odds ratio and 95% confidence interval.

Table S6. The reverse MR analysis results between MAFLD and gut microbiome taxa.

Gut microbiome	**Source**	**Method**	**SNPs**	**SE**	***p*-value**	**OR[95%CI]**	**Heterogeneity**	**Pleiotropy**
c.Gammaproteobacteria	the Dutch Microbiome Project	IVW	13	0.047	0.005	0.875[0.798-0.96]	0.901	0.372
o.Pasteurellales	the Dutch Microbiome Project	IVW	15	0.074	0.043	0.861[0.744-0.996]	0.538	0.27
f.Pasteurellaceae	the Dutch Microbiome Project	IVW	15	0.074	0.043	0.861[0.744-0.996]	0.538	0.27
g.Barnesiella	the Dutch Microbiome Project	IVW	14	0.045	0.013	1.12[1.025-1.224]	0.609	0.619
g.Veillonella	the Dutch Microbiome Project	IVW	14	0.075	0.036	0.855[0.738-0.99]	0.855	0.272
g.Sutterella	the Dutch Microbiome Project	IVW	15	0.049	0.029	0.898[0.816-0.989]	0.551	0.533
s.Barnesiella intestinihominis	the Dutch Microbiome Project	IVW	14	0.045	0.012	1.121[1.025-1.225]	0.623	0.634
s.Sutterella wadsworthensis	the Dutch Microbiome Project	IVW	15	0.049	0.032	0.9[0.818-0.991]	0.546	0.499
s.Escherichia unclassified	the Dutch Microbiome Project	IVW	15	0.059	0.042	0.888[0.792-0.996]	0.215	0.428
s.Lachnospiraceae bacterium.1.1.57FAA	the Dutch Microbiome Project	IVW	13	0.12	0.036	0.778[0.615-0.983]	0.889	0.547
s.Johnsonella ignava	the FR02 cohort	IVW	23	0.018	0.002	0.944[0.911-0.979}	0.589	0.741
g.Klebsiella A	the FR02 cohort	IVW	23	0.024	0.003	0.932[0.889-0.977}	0.808	0.443
s.Faecalicatena lactaris	the FR02 cohort	IVW	23	0.041	0.013	0.904[0.835-0.979}	0.074	0.636
f.Enterococcaceae	the FR02 cohort	IVW	23	0.013	0.019	0.97[0.946-0.995}	0.488	0.336
g.Citrobacter A	the FR02 cohort	IVW	23	0.02	0.022	0.956[0.92-0.994}	0.907	0.552
s.Pseudomonas aeruginosa	the FR02 cohort	IVW	23	0.015	0.023	0.967[0.939-0.995}	0.909	0.568
g.Enterococcus	the FR02 cohort	IVW	23	0.014	0.024	0.968[0.941-0.996}	0.595	0.364
s.Negativibacillus massiliensis	the FR02 cohort	IVW	23	0.022	0.025	0.952[0.912-0.994}	0.861	0.567

s.CAG-269 sp001915995	the FR02 cohort	IVW	23	0.039	0.025	1.09[1.011-1.176}	0.218	0.697
s.Bacteroides A plebeius A	the FR02 cohort	IVW	23	0.051	0.027	1.119[1.013-1.237}	0.71	0.869
s.Bacteroides sp002160055	the FR02 cohort	IVW	23	0.035	0.031	1.079[1.007-1.156}	0.389	0.848
s.Bacteroides A plebeius	the FR02 cohort	IVW	23	0.049	0.031	1.11[1.01-1.221}	0.237	0.422
s.UBA1777 sp900319275	the FR02 cohort	IVW	23	0.016	0.035	0.968[0.939-0.998}	0.31	0.287
s.Enterococcus faecalis	the FR02 cohort	IVW	23	0.018	0.038	0.963[0.93-0.998}	0.406	0.859
s.RUG147 sp900315495	the FR02 cohort	IVW	23	0.014	0.041	0.972[0.945-0.999}	0.697	0.176
s.CAG-488 sp000434055	the FR02 cohort	IVW	23	0.033	0.042	0.935[0.876-0.998}	0.047	0.659
g.Corynebacterium	the FR02 cohort	IVW	23	0.009	0.044	0.982[0.965-1}	0.258	0.79
g.Rhodanobacter	the FR02 cohort	IVW	23	0.011	0.044	0.978[0.956-0.999}	0.217	0.522
o.Chromatiales	the FR02 cohort	IVW	23	0.008	0.047	0.984[0.968-1}	0.794	0.367

Abbreviations: Source, gut microbiome data from the Dutch Microbiome Project and the FR02 cohort; Method, the method used in MR analysis; SNPs, number of SNPs; SE, standard error of coefficient estimate; *p*-value, p-value of causal estimation in the MR method; OR[95%CI], odds ration and 95% confidence interval.

Table S7. Characteristics of studies included in the meta-analysis

PMID	Author. Year	Exposure			Outcome					Gut Micobiome	SNPs	Main method	F-statistics	*OR* (95% *CI*)
		Source	Ancestry	Sample size	Source	Ancestry	Sample size	Cases	Controls					
37476494	Lilong Zhang.2023	MiBioGen consortium	European	18,340	GWAS summary by Anstee et al.,	European	19,264	1,483	17,781	Anaerotruncus	13	IVW	-	0.595(0.378-0.937)
										Intestinimonas Genus	17	IVW	-	0.726(0.550-0.958)
										Lachnoclostridium Genus	13	IVW	-	0.523(0.297-0.920)
										Lachnospiraceae NC2004 group	9	IVW	-	0.676(0.505-0.904)
										Olsenella	11	IVW	-	0.770(0.623-0.953)
										Peptococcus	12	IVW	-	0.817(0.66

														9-0.998)
										Ruminococcus 1 Genus	10	IVW	-	1.833(1.142-2.940)
38106475	Qilong Zhai.2023	MiBioGen consortium	European	18,340	FinnGen R9 Consortium	European	377,277	2,275	375,002	Enterobacteriaceae Family	10	IVW	30.7	1.43(1.02-2.00)
										Enterobacteriales Order	10	IVW	30.2	1.43(1.02-2.00)
										Lachnospiraceae UCG 004	9	IVW	27.9	1.52(1.06-2.19)
										Prevotella 9	11	IVW	48.1	1.28(1.01-1.63)
37543433	Yu Li.2023	MiBioGen consortium	European	18,340	GWAS summary by N. Ghodsian et al.,	European	778,614	8,434	770,180	Actinomycetaceae Family	4	IVW	21.32	1.25(1.02-1.53)
										Actinomycetal	4	IVW	21.32	1.25(1.02-

es Order				1.53)
Christensenellaceae Genus	8	IVW	20.48	0.64(0.30-1.37)
Coriobacteriaceae Family	17	IVW	20.27	1.22(1.01-1.48)
Coriobacteriales Order	17	IVW	20.27	1.22(1.01-1.48)
Coriobacteriia Class	17	IVW	20.27	1.22(1.01-1.48)
Intestinibacter Genus	14	IVW	20.75	0.85(0.73–0.99)
Lactobacillaceae Family	8	IVW	20.9	0.83(0.72–0.95)
Oxalobacteraceae Family	14	IVW	20.96	1.10(1.01–1.21)
Ruminococcaceae UCG 005	14	IVW	21.14	1.18(1.01–1.38)

										Genus				
39085775	Chen Ouyang. 2024	MiBioGen consortium	European	18,340	UK Biobank	European	377,988	4,761	373,227	Christensenellaceae Family	12	IVW	-	0.755(0.601-0.949)
										Defluviitaleaceae UCG 011 Genus	10	IVW	-	0.824(0.698-0.973)
										Eryspelotrichaceae UCG 003 Genus	17	IVW	-	0.833(0.698-0.994)
										Haemophilus Genus	14	IVW	-	0.851(0.741-0.977)
										Oxalobacter Genus	12	IVW	-	1.172(1.044-1.315)
										Oxalobacteraceae Family	15	IVW	-	1.129(1.007-1.266)
										Prevotella 9	19	IVW	-	1.174(1.02

38518048	Xiangyi Dai.2024	MiBioGen consortium	European	18,340	FinnGen R8 Consortium	European	342,99	1,908	340,591					5-1.344)
										Ruminococcus 2 Genus	15	IVW	-	0.738(0.613-0.888)
										Sutterella Genus	12	IVW	-	1.29(1.004-1.657)
										Deltaproteobacteria Class	12	IVW	>10	1.65(1.162-2.349)
										Desulfovibrionaceae Family	9	IVW	>10	1.73(1.164-2.571)
										Desulfovibrionales Order	11	IVW	>10	1.62(1.127-2.339)
										Enterobacteriaceae Family	7	IVW	>10	0.57(0.369-0.889)
										Enterobacteriales Order	7	IVW	>10	0.57(0.369-0.889)
										Hungatella	5	IVW	>10	1.37(1.030

										Genus				-1.813)
										Mollicutes Class	12	IVW	>10	1.37(1.028-1.838)
										Senegalimassilia Genus	5	IVW	>10	0.66(0.445-0.969)
										Tenericutes Phylum	12	IVW	>10	1.37(1.028-1.838)
38192292	Wanhui Dai.2023	MiBioGen consortium	European	18,340	Discovery: the Anstee Cohort Replication: the FinnGen Consortium	European	Discovery: 342,499 Replication: 218,792	Discovery:1,483 Replication: 894	Discovery: 17,781 Replication: 217,898				-	
					the Anstee Cohort	European	342,499	1,483	17,781	Intestinimonas Genus	17	IVW	-	0.694(0.533-0.903)
					the FinnGen Consortium	European	218,792	894	217,898	Intestinimonas Genus	17	IVW	-	1.030(0.709-1.498)

					the Anstee Cohort	European	342,499	1,483	17,781	Lachnoclostridium Genus	12	IVW	-	0.420(0.245-0.719)
					the FinnGen Consortium	European	218,792	894	217,898	Lachnoclostridium Genus	12	IVW	-	0.531(0.304-0.928)
					the Anstee Cohort	European	342,499	1,483	17,781	Ruminococcus 1 Genus	11	IVW	-	1.852(1.179-2.908)
					the FinnGen Consortium	European	218,792	894	217,898	Ruminococcus 1 Genus	11	IVW	-	1.214(0.740-1.992)
					the Anstee Cohort	European	342,499	1,483	17,781	Senegalimassilia Genus	6	IVW	-	0.596(0.363-0.978)
					the FinnGen Consortium	European	218,792	894	217,898	Senegalimassilia Genus	6	IVW	-	0.524(0.293-0.939)
38260910	Tongtong Pan.2024	MiBioGen consortium	European	18,340	GWAS summary by N. Ghodsian et al.,	European	778,614	8,434	770,180	Actinomycetaceae Family	4	IVW	-	1.25(1.02-1.53)
										Actinomycetal	4	IVW	-	1.25(1.02-

es Order				1.53)
Christensenellaceae R7 Group Genus	8	IVW	-	0.74(0.59-0.92)
Intestinibacter Genus	14	IVW	-	0.85(0.73-0.99)
Lactobacillaceae Family	7	IVW	-	0.83(0.71-0.97)
NB1n Order	12	IVW	-	1.11(1.00-1.23)
Oxalobacteraceae Family	14	IVW	-	1.10(1.01-1.21)
Ruminococcaceae Genus	14	IVW	-	1.18(1.01-1.38)

Abbreviations: SNPs, number of SNPs; F-statistics, F statistics; *OR* [95% *CI*], odds ratio and 95% confidence interval; *P*-value, the *P*-value of causal estimation in the IVW method.

Table S8. The gut microbiome associated with MAFLD combining the de novo and meta-analysis.

Gut microbiota	**Reasons**	**OR**
o.Actinomycetales	Meta-analysis	1.14
f.Actinomycetaceae	Meta-analysis	1.25
f.Oxalobacteraceae	Meta-analysis	1.10
g.Bifidobacterium	Meta-analysis / the FR02 cohort	1.11
g.Defluviitaleaceae UCG 011	Meta-analysis	0.82
g.Hungatella	Meta-analysis	1.33
g.Intestinibacter	Meta-analysis	0.87
g.Intestinimonas	Meta-analysis	0.77
g.Lachnoclostridium	Meta-analysis	0.49
g.Lachnospiraceae	Meta-analysis	1.31
g.Oxalobacter	Meta-analysis	1.10
g.Ruminococcaceae	Meta-analysis	1.18
g.Roseburia	Meta-analysis / the Dutch Microbiome Project	1.12
g.Senegalimassilia	Meta-analysis	0.60
o.Haloplasmatales	the FR02 cohort	0.86
f.Brevibacillaceae	the FR02 cohort	1.80
g.Bacillus U	the FR02 cohort	1.39
g.CAG-145	the FR02 cohort	1.66

g.CAG-449	the FR02 cohort	0.81
g.CAG-552	the FR02 cohort	1.13
g.CAG-884	the FR02 cohort	0.87
g.Demequina	the FR02 cohort	0.70
g.Halarcobacter	the FR02 cohort	1.43
g.UNC496MF	the FR02 cohort	0.66
s.CAG-884 sp000433875	the FR02 cohort	0.87
s.DTU024 sp002411105	the FR02 cohort	1.40
s.Faecalicatena lactaris	the FR02 cohort	0.84
s.Lactococcus lactis	the FR02 cohort	0.82
s.Negativibacillus massiliensis	the FR02 cohort	1.31
s.Negativibacillus sp000435195	the FR02 cohort	1.15
s.Prevotella buccae	the FR02 cohort	0.84
s.Parabacteroides merdae	the Dutch Microbiome Project	1.19
s.Bacteroides salyersiae	the Dutch Microbiome Project	1.08
s.Lachnospiraceae.bacterium.8.1.57FAA	the Dutch Microbiome Project	0.95

Abbreviation: Reasons, the reasons for the gut microbiota that are associatedn with MAFLD: positive results from meta-analysis, positive results from de novo MR of the Dutch Microbiome Project, and positive results from de novo MR of the FR02 Cohort. After the diagonal stripe, the texts show the original source of the initial positive results prior to the meta-analysis.

Table S9. The IVW MR analysis on the causal effect between 53 blood metabolites and MAFLD.							
Exposure	**Category**	**SNPs**	**Beta**	**SE**	***p*-value**	**OR**	**95% CI**
X-24337 levels	Unknown	27	-0.107	0.034	0.002	0.899	0.84-0.961
1-palmitoyl-2-oleoyl-gpc (16:0/18:1) levels	Lipid	17	-0.156	0.052	0.003	0.856	0.773-0.947
Sphingadienine levels	Lipid	10	-0.157	0.053	0.003	0.855	0.771-0.948
Pregnenetriol sulfate levels	Lipid	28	0.126	0.043	0.003	1.134	1.043-1.234
Ximenoylcarnitine (C26:1) levels	Lipid	24	0.115	0.04	0.004	1.122	1.037-1.213
X-24344 levels	Unknown	10	-0.166	0.059	0.005	0.847	0.754-0.952
1-palmitoyl-2-linoleoyl-GPI (16:0/18:2) levels	Lipid	20	0.111	0.04	0.005	1.118	1.033-1.209
Branched-chain, straight-chain, or cyclopropyl 10:1 fatty acid (1) levels	Partially Characterized Molecules	12	-0.2	0.072	0.006	0.819	0.711-0.944
Deoxycholate levels	Lipid	19	-0.164	0.062	0.008	0.849	0.752-0.959
Dihydroorotate levels	Nucleotide	26	0.084	0.032	0.01	1.088	1.021-1.159
X-16397 levels	Unknown	10	-0.165	0.064	0.01	0.848	0.748-0.962
Imidazole lactate levels	Amino Acid	21	-0.062	0.024	0.011	0.94	0.897-0.986
Dopamine 3-o-sulfate levels	Amino Acid	19	0.143	0.057	0.012	1.154	1.032-1.291
Bilirubin degradation product, C17H18N2O4 (1) levels	Partially Characterized Molecules	19	0.081	0.033	0.014	1.084	1.016-1.156
X-21285 levels	Unknown	20	-0.105	0.043	0.015	0.9	0.827-0.979
X-18913 levels	Unknown	17	0.12	0.05	0.016	1.128	1.023-1.243

Glutamine levels	Amino Acid	20	-0.134	0.056	0.016	0.875	0.785-0.976
X-25422 levels	Unknown	20	0.102	0.043	0.017	1.108	1.018-1.204
Adenosine 5'-diphosphate (ADP) to mannose ratio	Ratio	16	0.128	0.054	0.017	1.137	1.023-1.264
Gamma-glutamylalanine levels	Peptide	11	0.149	0.062	0.017	1.16	1.027-1.311
1-stearoyl-2-oleoyl-GPI (18:0/18:1) levels	Lipid	19	0.094	0.04	0.017	1.099	1.017-1.188
Phenyllactate (PLA) levels in elite athletes	Amino Acid	24	-0.103	0.044	0.019	0.902	0.828-0.983
Mannose levels	Carbohydrate	19	-0.122	0.052	0.02	0.885	0.799-0.981
Threonine levels	Amino Acid	25	-0.12	0.052	0.021	0.887	0.802-0.982
5alpha-pregnan-3beta,20alpha-diol monosulfate (2) levels	Lipid	24	-0.087	0.038	0.021	0.916	0.851-0.987
X-24565 levels	Unknown	18	-0.095	0.042	0.022	0.909	0.838-0.986
Arabitol/xylitol levels	Carbohydrate	18	0.13	0.057	0.022	1.139	1.019-1.273
Perfluorooctanoate (PFOA) levels	Xenobiotics	17	-0.136	0.06	0.023	0.872	0.776-0.981
4-cholesten-3-one levels	Lipid	20	-0.106	0.048	0.026	0.899	0.819-0.987
Vanillactate levels	Amino Acid	20	0.117	0.052	0.026	1.124	1.014-1.245
1-stearoyl-2-linoleoyl-GPI (18:0/18:2) levels	Lipid	25	0.105	0.047	0.026	1.111	1.012-1.219
9-hydroxystearate levels	Lipid	21	-0.109	0.049	0.026	0.897	0.814-0.987
1-(1-enyl-palmitoyl)-2-palmitoleoyl-GPC (P-16:0/16:1) levels	Lipid	31	-0.072	0.032	0.027	0.931	0.874-0.992
Ursodeoxycholate levels	Lipid	17	-0.127	0.057	0.027	0.881	0.787-0.986
Alpha-ketoglutaramate levels	Amino Acid	14	-0.114	0.052	0.027	0.892	0.806-0.987
Isovalerylcarnitine (C5) levels	Amino Acid	17	-0.095	0.044	0.029	0.909	0.834-0.99

Bilirubin (E,Z or Z,E) levels	Cofactors and Vitamins	16	0.063	0.029	0.03	1.065	1.006-1.128
Sphingomyelin (d18:0/20:0, d16:0/22:0) levels	Lipid	29	0.097	0.045	0.032	1.101	1.009-1.203
Formiminoglutamate levels	Amino Acid	18	0.143	0.067	0.033	1.154	1.011-1.317
(R)-3-hydroxybutyrylcarnitine levels	Lipid	18	-0.111	0.052	0.034	0.895	0.808-0.992
Xanthurenate levels	Amino Acid	21	0.093	0.044	0.035	1.098	1.007-1.197
Adenosine 3',5'-cyclic monophosphate (camp) levels	Nucleotide	25	0.082	0.039	0.035	1.086	1.006-1.173
X-07765 levels	Unknown	13	-0.112	0.054	0.036	0.894	0.805-0.993
Trans-urocanate levels	Amino Acid	17	-0.078	0.038	0.039	0.925	0.858-0.996
3-(3-hydroxyphenyl)propionate sulfate levels	Xenobiotics	17	0.099	0.048	0.04	1.104	1.005-1.212
Adenosine 5'-diphosphate (ADP) to aspartate ratio	Ratio	23	0.072	0.035	0.041	1.074	1.003-1.151
1-linoleoyl-2-arachidonoyl-GPC (18:2/20:4n6) levels	Lipid	21	-0.141	0.069	0.042	0.868	0.758-0.995
Anthranilate levels	Amino Acid	21	0.087	0.043	0.043	1.091	1.003-1.186
Nisinate (24:6n3) levels	Lipid	17	-0.079	0.039	0.043	0.924	0.857-0.998
Mannonate levels	Xenobiotics	13	-0.167	0.083	0.044	0.846	0.719-0.996
N-acetylmethionine levels	Amino Acid	9	0.142	0.071	0.046	1.152	1.003-1.324
Pimeloylcarnitine/3-methyladipoylcarnitine (C7-DC) levels	Lipid	22	-0.078	0.039	0.048	0.925	0.857-0.999
Phenylpyruvate levels	Lipid	25	-0.087	0.044	0.048	0.916	0.84-0.999

Abbreviations: Category, the category of blood metabolites; SNPs, number of SNPs; Beta,estimated causal effect coefficient; SE, standard error of coefficient estimate; *p*-value, p-value of causal estimation in the IVW method; OR, odds ratio; 95%CI, 95% confidence interval.

Table S10. The sensitivity analysis results of MR analysis of 53 blood metabolites on MAFLD.

Exposure	**Outcome**	**Heterogeneity**	**Horizontal pleiotropy**
Xanthurenate levels	MAFLD	0.733	0.567
Imidazole lactate levels	MAFLD	0.506	0.071
Phenyllactate (PLA) levels in elite athletes	MAFLD	0.275	0.126
Isovalerylcarnitine (C5) levels	MAFLD	0.71	0.27
Gamma-glutamylalanine levels	MAFLD	0.52	0.263
5alpha-pregnan-3beta,20alpha-diol monosulfate (2) levels	MAFLD	0.44	0.566
4-cholesten-3-one levels	MAFLD	0.186	0.958
Alpha-ketoglutaramate levels	MAFLD	0.495	0.239
Formiminoglutamate levels	MAFLD	0.096	0.352
(R)-3-hydroxybutyrylcarnitine levels	MAFLD	0.614	0.875
Mannonate levels	MAFLD	0.001	0.183
3-(3-hydroxyphenyl)propionate sulfate levels	MAFLD	0.405	0.654
9-hydroxystearate levels	MAFLD	0.564	0.198
Vanillactate levels	MAFLD	0.376	0.561

Arabitol/xylitol levels	MAFLD	0.364	0.741
Dopamine 3-o-sulfate levels	MAFLD	0.269	0.701
1-stearoyl-2-linoleoyl-GPI (18:0/18:2) levels	MAFLD	0.012	0.691
1-(1-enyl-palmitoyl)-2-palmitoleoyl-GPC (P-16:0/16:1) levels	MAFLD	0.248	0.791
1-linoleoyl-2-arachidonoyl-GPC (18:2/20:4n6) levels	MAFLD	<0.001	0.541
1-stearoyl-2-oleoyl-GPI (18:0/18:1) levels	MAFLD	0.474	0.336
Pimeloylcarnitine/3-methyladipoylcarnitine (C7-DC) levels	MAFLD	0.458	0.931
Sphingadienine levels	MAFLD	0.437	0.346
Nisinate (24:6n3) levels	MAFLD	0.623	0.885
Sphingomyelin (d18:0/20:0, d16:0/22:0) levels	MAFLD	0.003	0.432
Ximenoylcarnitine (C26:1) levels	MAFLD	0.055	0.493
Perfluorooctanoate (PFOA) levels	MAFLD	0.346	0.929
Pregnenetriol sulfate levels	MAFLD	0.581	0.197
Branched-chain, straight-chain, or cyclopropyl 10:1 fatty acid (1) levels	MAFLD	0.318	0.391
N-acetylmethionine levels	MAFLD	0.904	0.627
Ursodeoxycholate levels	MAFLD	0.086	0.908
Anthranilate levels	MAFLD	0.364	0.421
1-palmitoyl-2-linoleoyl-GPI (16:0/18:2) levels	MAFLD	0.665	0.13
1-palmitoyl-2-oleoyl-gpc (16:0/18:1) levels	MAFLD	0.803	0.637
Adenosine 3',5'-cyclic monophosphate (camp) levels	MAFLD	0.884	0.586
Phenylpyruvate levels	MAFLD	0.802	0.582
Deoxycholate levels	MAFLD	0.041	0.811

Trans-urocanate levels	MAFLD	0.91	0.449
Glutamine levels	MAFLD	0.019	0.617
Threonine levels	MAFLD	0.033	0.926
Mannose levels	MAFLD	0.045	0.89
Dihydroorotate levels	MAFLD	0.821	0.986
X-07765 levels	MAFLD	0.467	0.403
X-16397 levels	MAFLD	0.92	0.397
X-18913 levels	MAFLD	0.47	0.977
X-21285 levels	MAFLD	0.819	0.891
X-24344 levels	MAFLD	0.482	0.869
X-24337 levels	MAFLD	0.72	0.144
X-24565 levels	MAFLD	0.309	0.555
X-25422 levels	MAFLD	0.318	0.744
Bilirubin (E,Z or Z,E) levels	MAFLD	0.92	0.749
Bilirubin degradation product, C17H18N2O4 (1) levels	MAFLD	0.262	0.602
Adenosine 5'-diphosphate (ADP) to mannose ratio	MAFLD	0.042	0.867
Adenosine 5'-diphosphate (ADP) to aspartate ratio	MAFLD	0.571	0.69

Abbreviations:*p*-value of heterogeneity analysis; Pleiotropy, *p*-value of horizontal pleiotropy analysis.

Table S11. The MR analysis to estimate the causal effect of gut microbiome taxa on the blood metabolites.

Exposure: gut microbiome	**Outcome: blood metabolites**	**SNPs**	**SE**	***p*-value**	**Beta (95%CI)**
g.Roseburia	Xanthurenate	14	0.055	0.029	-0.119(-0.227,-0.011)
s.Parabacteroides merdae	Branched-chain, straight-chain,or cyclopropyl 10:1 fatty acid (1)	7	0.064	0.037	0.134(0.009,0.259)
s.Parabacteroides merdae	X-07765	7	0.081	0.026	0.181(0.022,0.34)
s.Bacteroides salyersiae	3-(3-hydroxyphenyl)propionate sulfate	8	0.037	0.012	0.094(0.021,0.167)
s.Bacteroides salyersiae	Anthranilate	8	0.037	0.039	0.076(0.003,0.149)
s.Bacteroides salyersiae	X-07765	8	0.031	0.03	-0.068(-0.129,-0.007)
s.Bacteroides salyersiae	X-18913	8	0.031	0.018	0.073(0.012,0.134)
s.Lachnospiraceae.bacterium.8.1.57FAA	Alpha-ketoglutaramate	16	0.024	0.023	-0.055(-0.102,-0.008)
s.Lachnospiraceae.bacterium.8.1.57FAA	Phenylpyruvate	16	0.025	0.032	0.053(0.004,0.102)
g.Bacillus U	Threonine	19	0.118	0.032	-0.253(-0.484,-0.022)
g.Bifidobacterium	Deoxycholate	16	0.058	0.003	-0.174(-0.288,-0.06)
g.Bifidobacterium	Trans-urocanate	16	0.048	0.019	-0.113(-0.207,-0.019)
f.Brevibacillaceae	Deoxycholate	17	0.252	0.044	0.507(0.013,1.001)
g.CAG-145	Nisinate (24:6n3)	10	0.198	0.014	-0.486(-0.874,-0.098)
g.CAG-145	Dihydroorotate	10	0.151	0.002	-0.480(-0.776,-0.184)
g.CAG-449	Formiminoglutamate	23	0.066	0.022	0.152(0.023,0.281)
g.CAG-449	X-24337	23	0.073	0.04	0.149(0.006,0.292)

g.CAG-552	Dopamine 3-o-sulfate	20	0.045	0.002	0.137(0.049,0.225)
g.CAG-552	1-linoleoyl-2-arachidonoyl-GPC (18:2/20:4n6)	20	0.045	0.031	0.096(0.008,0.184)
g.CAG-552	X-24565	20	0.064	0.03	0.139(0.014,0.264)
s.CAG-884 sp000433875	1-(1-enyl-palmitoyl)-2-palmitoleoyl-GPC (P-16:0/16:1)	21	0.053	0.015	-0.130(-0.234,-0.026)
s.CAG-884 sp000433875	X-24337	21	0.055	0.015	0.134(0.026,0.242)
s.CAG-884 sp000433875	Bilirubin (E,Z or Z,E)	21	0.064	0.009	-0.167(-0.292,-0.042)
s.CAG-884 sp000433875	Bilirubin degradation product, C17H18N2O4 (1)	21	0.057	0.018	-0.136(-0.248,-0.024)
g.CAG-884	1-(1-enyl-palmitoyl)-2-palmitoleoyl-GPC (P-16:0/16:1)	17	0.052	0.036	-0.110(-0.212,-0.008)
g.CAG-884	Bilirubin (E,Z or Z,E)	17	0.053	0.006	-0.147(-0.251,-0.043)
g.CAG-884	Bilirubin degradation product, C17H18N2O4 (1)	17	0.051	0.015	-0.124(-0.224,-0.024)
g.Demequina	4-cholesten-3-one	17	0.221	0.018	0.524(0.091,0.957)
g.Demequina	Dopamine 3-o-sulfate	17	0.169	0.039	-0.350(-0.681,-0.019)
g.Demequina	Anthranilate	17	0.201	0.038	0.416(0.022,0.81)
s.Faecalicatena lactaris	5alpha-pregnan-3beta,20alpha-diol monosulfate (2)	17	0.055	0.004	0.157(0.049,0.265)
s.Faecalicatena lactaris	Mannose	17	0.053	0.041	0.108(0.004,0.212)
g.Halarcobacter	Trans-urocanate	14	0.145	0.024	-0.326(-0.61,-0.042)
o.Haloplasmatales	Alpha-ketoglutaramate	21	0.066	0.043	-0.133(-0.262,-0.004)
o.Haloplasmatales	N-acetylmethionine	21	0.059	0.029	0.129(0.013,0.245)
s.Lactococcus lactis	Adenosine 5'-diphosphate (ADP) to aspartate ratio	12	0.117	0.007	-0.315(-0.544,-0.086)

s.Negativibacillus massiliensis	Ursodeoxycholate	18	0.117	0.035	-0.247(-0.476,-0.018)
s.Negativibacillus sp000435195	Isovalerylcarnitine (C5)	20	0.051	0.008	0.135(0.035,0.235)
s.Prevotella buccae	Sphingomyelin (d18:0/20:0, d16:0/22:0)	17	0.068	0.032	0.146(0.013,0.279)
s.Prevotella buccae	Mannose	17	0.075	0.047	-0.150(-0.297,-0.003)
g.UNC496MF	Mannonate	16	0.16	0.031	0.344(0.030,0.658)

Abbreviations: SNPs, number of SNPs; SE, standard error of coefficient estimate; *p*-value, the *p*-value of causal estimation in the IVW method; Beta (95%CI), estimated causal effect coefficient and 95% confidence interval.

Table S12. The MVMR analysis results of gut microbiome, blood metabolites and MAFLD.

Exposure	**Mediator**	**β1(95%CI)**	**p1**	**β2(95%CI)**	**p2**	**βA(95%CI)**	**pA**
Roseburia genus	Xanthurenate	-0.119(-0.011,-0.227)	0.029	0.101(0.008,0.194)	0.033	0.155(0.057,0.253)	0.002
Parabacteroides merdae species	Branched-chain, straight-chain, or cyclopropyl 10:1 fatty acid (1)	0.134(0.259,0.009)	0.037	-0.203(-0.398,-0.007)	0.042	0.162(-0.022,0.346)	0.084
	X-07765	0.181(0.34,0.022)	0.026	-0.054(-0.168,0.061)	0.361	0.171(0.03,0.312)	0.017
Bacteroides salyersiae species	3-(3-hydroxyphenyl) propionate sulfate	0.094(0.167,0.021)	0.012	0.044(-0.075,0.163)	0.474	0.074(0.019,0.129)	0.008
	Anthranilate	0.076(0.149,0.003)	0.039	0.076(-0.026,0.178)	0.145	0.072(0.011,0.132)	0.02
	X-07765	-0.068(-0.007,-0.129)	0.03	-0.079(-0.187,0.029)	0.153	0.058(-0.001,0.117)	0.053
	X-18913	0.073(0.134,0.012)	0.018	0.049(-0.092,0.19)	0.497	0.073(0.013,0.133)	0.017
Lachnospiraceae.bacterium.8.1.57FAA species	Alpha-ketoglutaramate	-0.055(-0.008,-0.102)	0.023	-0.106(-0.223,0.01)	0.074	-0.075(-0.128,-0.021)	0.006
	Phenylpyruvate	0.053(0.004,0.102)	0.032	-0.107(-0.203,-0.108)	0.029	-0.056(-0.107,-0.005)	0.032
Bacillus U genus	Threonine	-0.253(-0.484,-0.022)	0.032	-0.128(-0.220,-0.036)	0.007	0.095(-0.207,0.397)	0.539
Bifidobacterium genus	Deoxycholate	-0.174(-0.288,-0.06)	0.003	-0.164(-0.264,-0.064)	0.001	0.053(-0.049,0.155)	0.312
	Trans-urocanate	-0.113(-0.207,-0.019)	0.019	-0.076(-0.131,-0.021)	0.006	0.107(0.011,0.203)	0.027
Brevibacillaceae family	Deoxycholate	0.507(0.013,1.001)	0.044	-0.165(-0.275,-0.055	0.003	0.658(0.135,1.181)	0.014

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CAG-145 genus	Nisinate (24:6n3)	-0.486(-0.874,-0.098)	0.014	-0.088(-0.164,-0.012)	0.024	-0.307(-0.662,0.048)	0.090
	Dihydroorotate	-0.48(-0.776,-0.184)	0.002	0.085(0.022,0.148)	0.007	-0.367(-0.714,-0.02)	0.038
CAG-449 genus	Formiminoglutamate	0.152(0.023,0.281)	0.022	0.127(0.015,0.239)	0.025	-0.19(-0.345,-0.035)	0.016
	X-24337	0.149(0.006,0.292)	0.04	-0.103(-0.16,-0.046)	3.99E-04	-0.171(-0.296,-0.046)	0.008
CAG-552 genus	Dopamine 3-o-sulfate	0.137(0.049,0.225)	0.002	0.167(0.051,0.283)	0.005	0.021(-0.081,0.123)	0.691
	1-linoleoyl-2-arachidonoyl-GPC (18:2/20:4n6)	0.096(0.008,0.184)	0.031	-0.125(-0.245,-0.005)	0.041	0.057(-0.102,0.216)	0.486
	X-24565	0.139(0.014,0.264)	0.03	-0.075(-0.157,0.007)	0.072	0.053(-0.049,0.155)	0.312
CAG-884 sp000433875 species	1-(1-enyl-palmitoyl)-2-palmitoleoyl-GPC (P-16:0/16:1)	-0.13(-0.234,-0.026)	0.015	-0.079(-0.138,-0.02)	0.01	-0.137(-0.268,-0.006)	0.040
	X-24337	0.134(0.026,0.242)	0.015	-0.11(-0.171,-0.049)	3.89E-04	-0.103(-0.219,0.013)	0.082
	Bilirubin (E,Z or Z,E)	-0.167(-0.292,-0.042)	0.009	0.065(0.02,0.11)	0.005	-0.113(-0.219,-0.007)	0.039
	Bilirubin degradation product, C17H18N2O4 (1)	-0.136(-0.248,-0.024)	0.018	0.079(0.02,0.138)	0.008	-0.106(-0.237,0.025)	0.113
CAG-884 genus	1-(1-enyl-palmitoyl)-2-palmitoleoyl-GPC (P-16:0/16:1)	-0.11(-0.212,-0.008)	0.036	-0.076(-0.137,-0.015)	0.015	-0.092(-0.221,0.037)	0.165
	Bilirubin (E,Z or Z,E)	-0.147(-0.251,-0.043)	0.006	0.061(0.012,0.11)	0.013	-0.082(-0.19,0.026)	0.135
	Bilirubin degradation	-0.124(-0.224,-0.024)	0.015	0.075(0.014,0.136)	0.017	-0.073(-0.204,0.058)	0.277

	product, C17H18N2O4 (1)						
Demequina genus	4-cholesten-3-one	0.524(0.091,0.957)	0.018	-0.104(-0.194,-0.014)	0.025	-0.244(-0.618,0.13)	0.200
	Dopamine 3-o-sulfate	-0.35(-0.681,-0.019)	0.039	0.151(0.033,0.269)	0.013	-0.231(-0.598,0.136)	0.216
	Anthranilate	0.416(0.022,0.81)	0.038	0.069(-0.019,0.157)	0.121	-0.225(-0.582,0.132)	0.217
Faecalicatena lactaris species	5alpha-pregnan-3beta,20alpha-diol monosulfate (2)	0.157(0.049,0.265)	0.004	-0.091(-0.173,-0.009)	0.029	0.013(-0.114,0.14)	0.848
	Mannose	0.108(0.004,0.212)	0.041	-0.142(-0.242,-0.042)	0.005	0.007(-0.13,0.144)	0.915
Halarcobacter genus	Trans-urocanate	-0.326(-0.61,-0.042)	0.024	-0.085(-0.14,-0.03)	0.002	0.191(-0.005,0.387)	0.057
Haloplasmatales order	Alpha-ketoglutaramate	-0.133(-0.262,-0.004)	0.043	-0.119(-0.207,-0.031)	0.008	-0.109(-0.232,0.014)	0.085
	N-acetylmethionine	0.129(0.013,0.245)	0.029	0.125(0.021,0.229)	0.019	-0.1(-0.21,0.01)	0.075
Lactococcus lactis species	Adenosine 5'-diphosphate (ADP) to aspartate ratio	-0.315(-0.544,-0.086)	0.007	0.072(0.007,0.137)	0.030	-0.191(-0.365,-0.017)	0.032
Negativibacillus massiliensis species	Ursodeoxycholate	-0.247(-0.476,-0.018)	0.035	-0.13(-0.246,-0.014)	0.028	0.158(-0.109,0.425)	0.245
Negativibacillus sp000435195 species	Isovalerylcarnitine (C5)	0.135(0.035,0.235)	0.008	-0.091(-0.164,-0.018)	0.014	0.125(0.027,0.223)	0.012
Prevotella buccae species	Sphingomyelin (d18:0/20:0, d16:0/22:0)	0.146(0.013,0.279)	0.032	0.089(0.001,0.177)	0.047	-0.092(-0.294,0.11)	0.368
	Mannose	-0.15(-0.297,-0.003)	0.047	-0.126(-0.222,-0.03)	0.011	-0.139(-0.311,0.033)	0.116

UNC496MF genus	Mannonate	0.344(0.03,0.658)	0.031	-0.173(-0.308,-0.038)	0.012	0.085(-0.415,0.585)	0.740

Abbreviations: β1, the effect of gut microbial taxonomy on the blood metabolites; p1, the *p*-value of gut microbial taxonomy on the blood metabolites; β2, the effect of the blood metabolite on MAFLD after adjustment for gut microbial taxonomy; p2, the *p*-value of the blood metabolite on MAFLD after adjustment for gut microbial taxonomy; βA, direct effect of the gut microbial taxonomy on MAFLD; pA, the *p*-value of the gut microbial taxonomy on MAFLD.

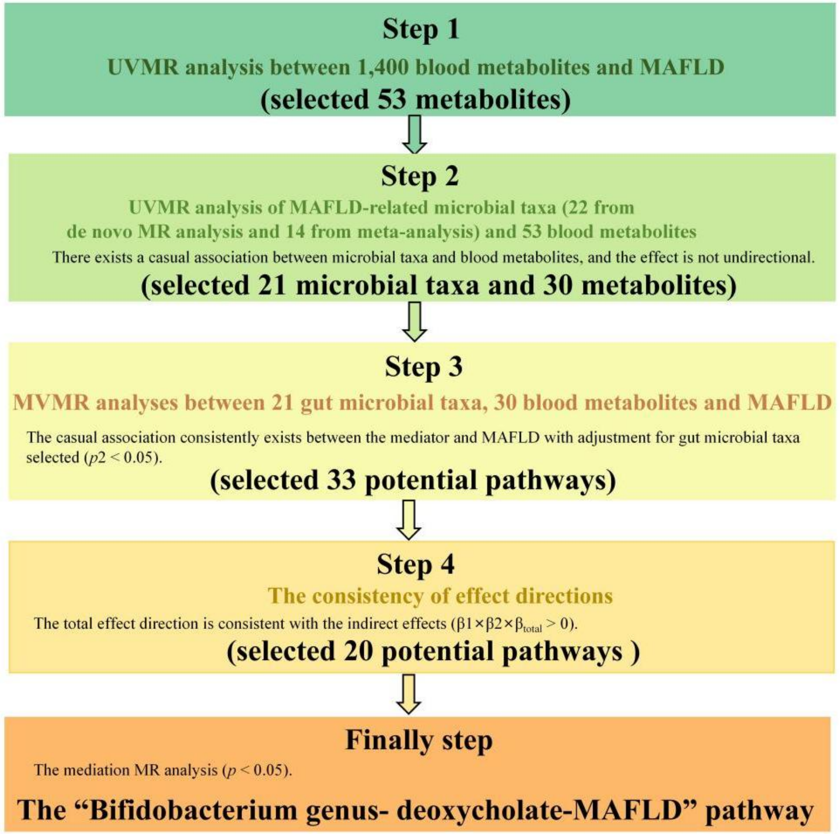
Table S13. The mediation MR analysis between gut microbiome, blood metabolites and MAFLD.									
Exposure	**Mediation**	**Outcome**	**Mediation Effect**	**Direct Effect**	**SE**	***p*-value**	**95% CI Lower**	**95% CI Upper**	**Mediation Effect Proportion**
s.Lachnospiraceae.bacterium.8.1.57FAA	Phenylpyruvate	MAFLD	-0.005	-0.051	0.004	0.254	-0.013	0.003	-
g.Bacillus U	Threonine	MAFLD	0.03	0.297	0.031	0.321	-0.03	0.09	-
g.Bifidobacterium	Deoxycholate	MAFLD	0.028	0.101	0.014	0.046	0	0.056	22.06%
g.Bifidobacterium	Trans-urocanate	MAFLD	0.009	0.12	0.006	0.154	-0.003	0.021	-
g.CAG-145	Nisinate (24:6n3)	MAFLD	0.038	0.469	0.469	0.691	-0.15	0.227	-
g.CAG-449	X-24337	MAFLD	-0.016	-0.199	0.011	0.163	-0.038	0.006	-
g.CAG-552	Dopamine 3-o-sulfate	MAFLD	0.02	0.104	0.01	0.056	0	0.04	-
s.CAG-884 sp000433875	X-24337	MAFLD	-0.014	-0.123	0.008	0.082	-0.03	0.002	-
s.CAG-884 sp000433875	Bilirubin (E,Z or Z,E)	MAFLD	-0.011	-0.127	0.011	0.327	-0.032	-0.032	-
s.CAG-884 sp000433875	Bilirubin degradation product, C17H18N2O4 (1)	MAFLD	-0.01	-0.128	0.007	0.143	-0.023	0.003	-
g.CAG-884	Bilirubin (E,Z or Z,E)	MAFLD	-0.009	-0.132	0.008	0.248	-0.025	0.006	-
g.CAG-884	Bilirubin	MAFLD	-0.01	-0.131	0.007	0.143	-0.023	0.003	-

	degradation product, C17H18N2O4 (1)								
g.Demequina	4-cholesten-3-one	MAFLD	-0.056	-0.301	0.116	0.631	-0.284	0.172	-
g.Demequina	Dopamine 3-o-sulfate	MAFLD	-0.05	-0.307	0.06	0.403	-0.167	0.067	-
s.Faecalicatena lactaris	5alpha-pregnan-3beta,20alpha-diol monosulfate (2)	MAFLD	-0.014	0.348	0.009	0.136	-0.032	0.004	-
s.Faecalicatena lactaris	Mannose	MAFLD	-0.013	0.348	0.009	0.125	-0.03	0.004	-
g.Halarcobacter	Trans-urocanate	MAFLD	0.026	0.331	0.047	0.589	-0.067	0.118	-
s.Lactococcus lactis	Adenosine 5'-diphosphate (ADP) to aspartate ratio	MAFLD	-0.023	-0.178	0.037	0.539	-0.095	0.05	-
s.Negativibacillus massiliensis	Ursodeoxycholate	MAFLD	0.031	0.239	0.03	0.293	-0.027	0.09	-
g.UNC496MF	Mannonate	MAFLD	-0.057	-0.354	0.057	0.311	-0.168	0.054	-

Abbreviations: *p*-value, the *p*-value of mediation MR analysis.

Table S14. The reverse MR analysis between the potential mediation pathway.							
Exposure	**Outcome**	**SNPs**	**Beta**	**SE**	***p*-value**	**OR**	**95% CI**
“Bifidobacterium genus-Deoxycholate levels-MAFLD” pathway							
Deoxycholate levels	g.Bifidobacterium	27	0.001	0.027	0.981	1.001	[0.950-1.054]
MAFLD	Deoxycholate levels	23	-0.027	0.085	0.751	0.973	[0.824-1.150]
MAFLD	g.Bifidobacterium	23	-0.019	0.041	0.636	0.981	[0.905-1.063]

Abbreviations: SNPs, number of SNPs; Beta,estimated causal effect coefficient; SE, standard error of coefficient estimate; *p*-value, *p*-value of causal estimation in the IVW method; OR, odds ratio; 95%CI, 95% confidence interval.



Step 1

UVMR analysis between 1,400 blood metabolites and MAFLD

(selected 53 metabolites)

Step 2

UVMR analysis of MAFLD-related microbial taxa (22 from de novo MR analysis and 14 from meta-analysis) and 53 blood metabolites

There exists a casual association between microbial taxa and blood metabolites, and the effect is not undirectional.

(selected 21 microbial taxa and 30 metabolites)

Step 3

MVMR analyses between 21 gut microbial taxa, 30 blood metabolites and MAFLD

The casual association consistently exists between the mediator and MAFLD with adjustment for gut microbial taxa selected ($p2 < 0.05$).

(selected 33 potential pathways)

Step 4

The consistency of effect directions

The total effect direction is consistent with the indirect effects ($\beta1 \times \beta2 \times \beta_{total} > 0$).

(selected 20 potential pathways)

Finally step

The mediation MR analysis ($p < 0.05$).

The “Bifidobacterium genus- deoxycholate-MAFLD” pathway

Figure S1. The methodologies of mediation selection.

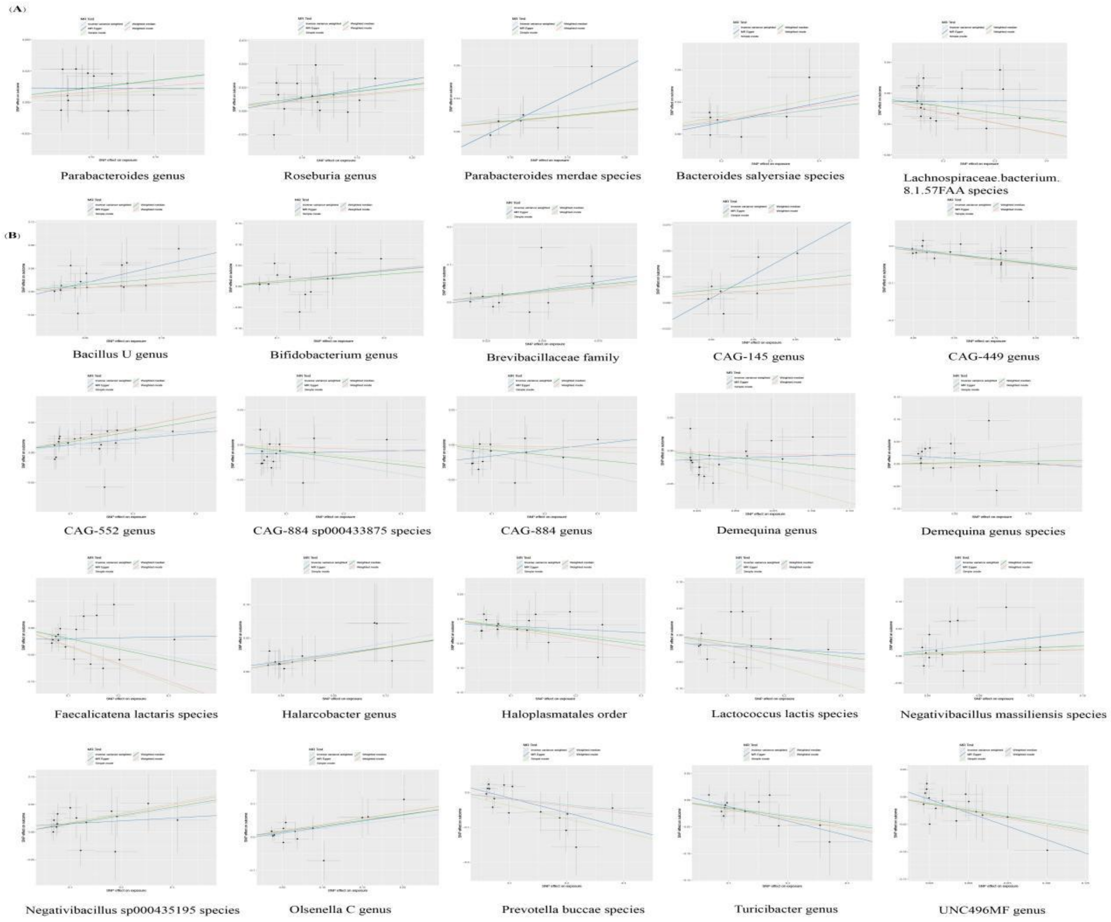
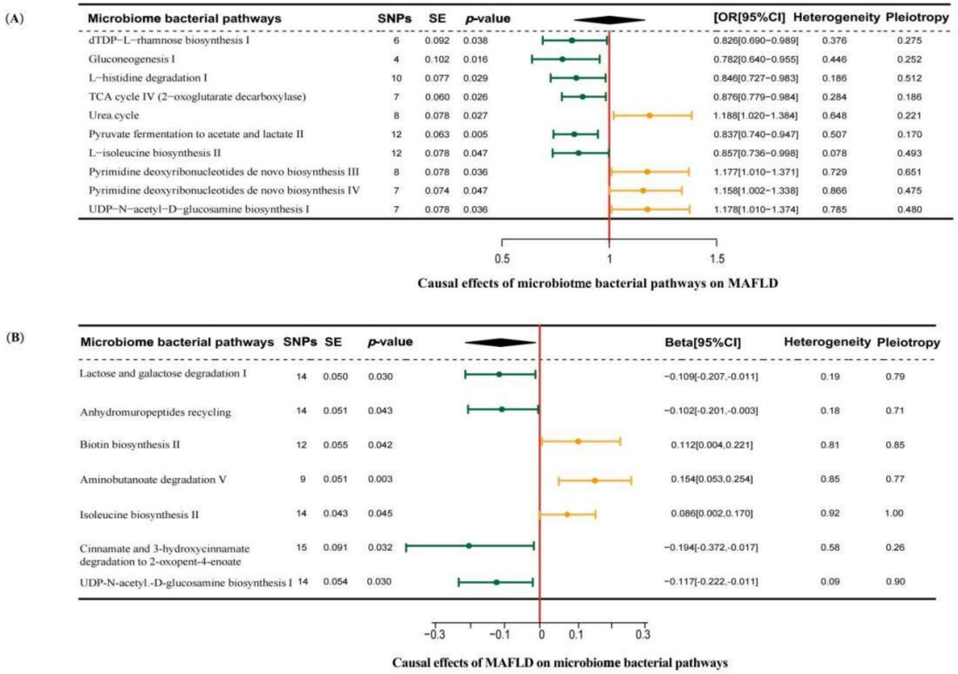


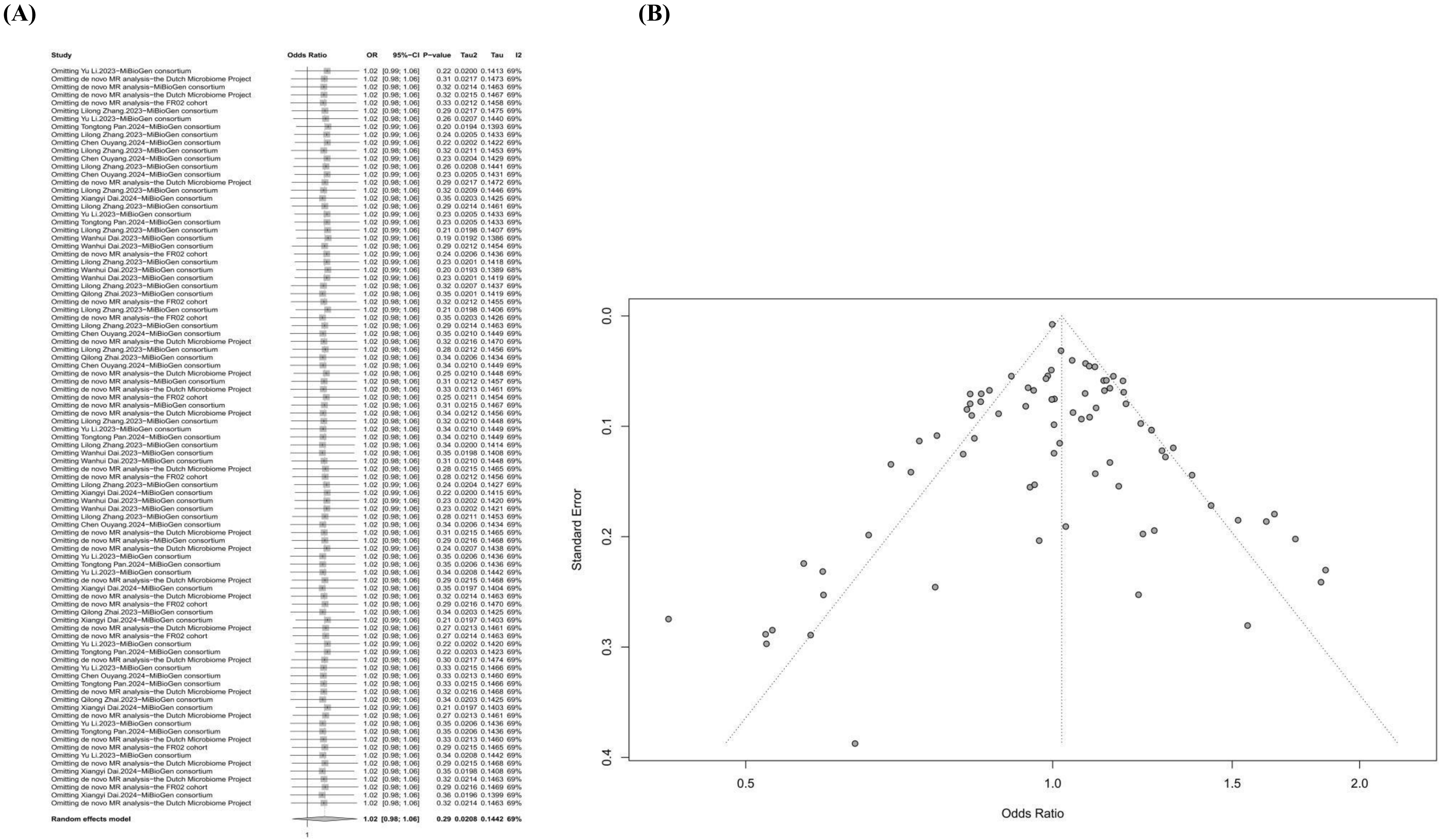
Figure S2. MR scatter plots of the forward de novo MR analysis. (A) Scatterplot of SNP potential effects of gut microbiome taxa (the Dutch Microbiome Project) on MAFLD; (B) Scatterplot of SNP potential effects of gut microbiome taxa (the FR02 cohort) on MAFLD.



Microbiome bacterial pathways	SNPs	SE	*p*-value	[OR[95%CI]	Heterogeneity	Pleiotropy
dTDP−L−rhamnose biosynthesis I	6	0.092	0.038	0.826[0.690−0.989]	0.376	0.275
Gluconeogenesis I	4	0.102	0.016	0.782[0.640−0.955]	0.446	0.252
L−histidine degradation I	10	0.077	0.029	0.846[0.727−0.983]	0.186	0.512
TCA cycle IV (2−oxoglutarate decarboxylase)	7	0.060	0.026	0.876[0.779−0.984]	0.284	0.186
Urea.cycle	8	0.078	0.027	1.188[1.020−1.384]	0.648	0.221
Pyruvate fermentation to acetate and lactate II	12	0.063	0.005	0.837[0.740−0.947]	0.507	0.170
L−isoleucine biosynthesis II	12	0.078	0.047	0.857[0.736−0.998]	0.078	0.493
Pyrimidine deoxyribonucleotides de novo biosynthesis III	8	0.078	0.036	1.177[1.010−1.371]	0.729	0.651
Pyrimidine deoxyribonucleotides de novo biosynthesis IV	7	0.074	0.047	1.158[1.002−1.338]	0.866	0.475
UDP−N−acetyl−D−glucosamine biosynthesis I	7	0.078	0.036	1.178[1.010−1.374]	0.785	0.480

Microbiome bacterial pathways	SNPs	SE	*p*-value	Beta[95%CI]	Heterogeneity	Pleiotropy
Lactose and galactose degradation I	14	0.050	0.030	−0.109[-0.207,-0.011]	0.19	0.79
Anhydromuropeptides recycling	14	0.051	0.043	−0.102[-0.201,-0.003]	0.18	0.71
Biotin biosynthesis II	12	0.055	0.042	0.112[0.004,0.221]	0.81	0.85
Aminobutanoate degradation V	9	0.051	0.003	0.154[0.053,0.254]	0.85	0.77
Isoleucine biosynthesis II	14	0.043	0.045	0.086[0.002,0.170]	0.92	1.00
Cinnamate and 3-hydroxycinnamate degradation to 2-oxopent-4-enoate	15	0.091	0.032	−0.194[-0.372,-0.017]	0.58	0.26
UDP-N-acetyl.-D-glucosamine biosynthesis I	14	0.054	0.030	−0.117[-0.222,-0.011]	0.09	0.90

Figure S3. Forestplot of bidirectional causal effects between bacterial pathways and MAFLD (*p* < 0.05). (A) Causal effects of microbiome bacterial pathways on MAFLD; (B) Causal effects of MAFLD on microbiome bacterial pathways. SNPs, number of SNPs; SE, standard error of coefficient estimate; *p*-value, *p*-value of causal estimation in the IVW method; OR [95%CI], odds ratio and 95% confidence interval; Heterogeneity, *p*-value of heterogeneity analysis; Pleiotropy, *p*-value of horizontal pleiotropy analysis.



Study	OR	95%-CI	P-value	Tau2	Tau	I2
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.22	0.0200	0.1413	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.31	0.0217	0.1473	69%
Omitting de novo MR analysis-MiBioGen consortium	1.02	[0.98; 1.06]	0.32	0.0214	0.1463	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.32	0.0215	0.1467	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.33	0.0212	0.1458	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.29	0.0217	0.1475	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.26	0.0207	0.1440	69%
Omitting Tongtong Pan.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.20	0.0194	0.1393	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.24	0.0205	0.1433	69%
Omitting Chen Ouyang.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.22	0.0202	0.1422	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.32	0.0211	0.1453	69%
Omitting Chen Ouyang.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0204	0.1429	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.26	0.0208	0.1441	69%
Omitting Chen Ouyang.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0205	0.1431	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.29	0.0217	0.1472	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.32	0.0209	0.1446	69%
Omitting Xiangyi Dai.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0203	0.1425	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.29	0.0214	0.1461	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0205	0.1433	69%
Omitting Tongtong Pan.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0205	0.1433	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.21	0.0198	0.1407	69%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.19	0.0192	0.1386	69%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.29	0.0212	0.1454	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.99; 1.06]	0.24	0.0206	0.1436	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0201	0.1418	69%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.20	0.0193	0.1389	68%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0201	0.1419	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.32	0.0207	0.1437	69%
Omitting Qilong Zhai.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0201	0.1419	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.32	0.0212	0.1455	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.21	0.0198	0.1406	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.35	0.0203	0.1426	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.29	0.0214	0.1463	69%
Omitting Chen Ouyang.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0210	0.1449	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.32	0.0216	0.1470	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.28	0.0212	0.1456	69%
Omitting Qilong Zhai.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0206	0.1434	69%
Omitting Chen Ouyang.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0210	0.1449	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.25	0.0210	0.1448	69%
Omitting de novo MR analysis-MiBioGen consortium	1.02	[0.98; 1.06]	0.31	0.0212	0.1457	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.33	0.0213	0.1461	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.25	0.0211	0.1454	69%
Omitting de novo MR analysis-MiBioGen consortium	1.02	[0.98; 1.06]	0.31	0.0215	0.1467	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.34	0.0212	0.1456	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.32	0.0210	0.1448	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0210	0.1449	69%
Omitting Tongtong Pan.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0210	0.1449	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0200	0.1414	69%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0198	0.1408	69%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.31	0.0210	0.1448	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.28	0.0215	0.1465	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.28	0.0212	0.1456	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.24	0.0204	0.1427	69%
Omitting Xiangyi Dai.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.22	0.0200	0.1415	69%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0202	0.1420	69%
Omitting Wanhui Dai.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.23	0.0202	0.1421	69%
Omitting Lilong Zhang.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.28	0.0211	0.1453	69%
Omitting Chen Ouyang.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0206	0.1434	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.31	0.0215	0.1465	69%
Omitting de novo MR analysis-MiBioGen consortium	1.02	[0.98; 1.06]	0.29	0.0216	0.1468	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.99; 1.06]	0.24	0.0207	0.1438	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0206	0.1436	69%
Omitting Tongtong Pan.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0206	0.1436	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0208	0.1442	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.29	0.0215	0.1468	69%
Omitting Xiangyi Dai.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0197	0.1404	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.32	0.0214	0.1463	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.29	0.0216	0.1470	69%
Omitting Qilong Zhai.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0203	0.1425	69%
Omitting Xiangyi Dai.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.21	0.0197	0.1403	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.27	0.0213	0.1461	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.27	0.0214	0.1463	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.99; 1.06]	0.22	0.0202	0.1420	69%
Omitting Tongtong Pan.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.22	0.0203	0.1423	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.30	0.0217	0.1474	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.33	0.0215	0.1466	69%
Omitting Chen Ouyang.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.33	0.0213	0.1460	69%
Omitting Tongtong Pan.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.33	0.0215	0.1466	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.32	0.0216	0.1468	69%
Omitting Qilong Zhai.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0203	0.1425	69%
Omitting Xiangyi Dai.2024-MiBioGen consortium	1.02	[0.99; 1.06]	0.21	0.0197	0.1403	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.27	0.0213	0.1461	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0206	0.1436	69%
Omitting Tongtong Pan.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0206	0.1436	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.33	0.0213	0.1460	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.29	0.0215	0.1465	69%
Omitting Yu Li.2023-MiBioGen consortium	1.02	[0.98; 1.06]	0.34	0.0208	0.1442	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.29	0.0215	0.1468	69%
Omitting Xiangyi Dai.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.35	0.0198	0.1408	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.32	0.0214	0.1463	69%
Omitting de novo MR analysis-the FR02 cohort	1.02	[0.98; 1.06]	0.29	0.0216	0.1469	69%
Omitting Xiangyi Dai.2024-MiBioGen consortium	1.02	[0.98; 1.06]	0.36	0.0196	0.1399	69%
Omitting de novo MR analysis-the Dutch Microbiome Project	1.02	[0.98; 1.06]	0.32	0.0214	0.1463	69%
Random effects model	**1.02**	**[0.98; 1.06]**	**0.29**	**0.0208**	**0.1442**	**69%**

Figure S4. Sensitivity analyses of meta-analysis. (A) The leave-one-out analysis; (B) The funnel plot.