

**Non-alcoholic fatty liver disease and gestational diabetes mellitus : A
bidirectional two-sample Mendelian randomization study**

Supplementary online information		
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Table S1 Characteristics of instrumental variables of NAFLD and <i>F</i> statistics							
SNP	Effect allele	Other allele	EAF	Beta	SE	<i>P</i>	<i>F</i>
rs17321515	G	A	0.476097	-0.15409	0.020931	1.81E-13	54.20
rs182611493	G	A	0.012616	0.453817	0.067899	2.33E-11	44.67
rs2642442	T	C	0.316965	0.13769	0.022383	7.67E-10	37.84
rs3747207	A	G	0.214703	0.369714	0.022649	6.74E-60	266.46
rs429358	C	T	0.156247	-0.19922	0.029761	2.17E-11	44.81
NAFLD, nonalcoholic fatty liver disease; SNP, single-nucleotide polymorphism; EAF, effect allele frequency; SE, standard error.							

Table S2 Characteristics of instrumental variables of GDM and <i>F</i> statistics							
SNP	Effect allele	Other allele	EAF	Beta	SE	<i>P</i>	<i>F</i>
rs34872471	C	T	0.202724	0.161767	0.017049	2.35E-21	90.03
rs7123869	C	T	0.020088	0.295913	0.045894	1.14E-10	41.57
rs7722200	C	T	0.31561	-0.14408	0.015255	3.56E-21	89.20
rs7756992	G	A	0.332859	0.102687	0.014676	2.62E-12	48.96
rs9275373	A	G	0.120313	0.158059	0.020838	3.32E-14	57.53
GDM, gestational diabetes mellitus; SNP, single-nucleotide polymorphism; EAF, effect allele frequency; SE, standard error.							

Table S3 Mendelian randomization results of the causal effects of potential shared influencing factors on NAFLD

Trait	SNPs	IVW		MR-Egger		WM		MR-PRESSO			$P_{\text{pleiotropy}}$	$P_{\text{heterogeneity}} (I^2)$
		OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	SNPs	OR (95%CI)	P		
BMI	436	1.93 (1.52-2.44)	< 0.001	2.26 (1.22-4.19)	0.009	2.06 (1.41-3.01)	< 0.001	436	1.93 (1.52-2.44)	< 0.001	0.580	<0.001 (19.61%)
WHR	27	2.87 (1.50-5.50)	0.002	9.93 (0.45-217.2)	0.157	3.28 (1.49-7.25)	0.003	27	2.87 (1.50-5.50)	0.002	0.427	0.061(31.57%)
TG	239	1.52 (1.25-1.86)	< 0.001	1.30 (0.97-1.75)	0.081	1.47 (1.10-1.96)	0.009	239	1.52 (1.25-1.86)	< 0.001	0.158	<0.001 (31.84%)
LDL-C	136	0.98 (0.77-1.25)	0.893	0.80 (0.57-1.14)	0.225	0.93 (0.66-1.32)	0.691	136	0.98 (0.77-1.25)	0.893	0.127	0.004 (26.16%)
HDL-C	272	0.70 (0.57-0.85)	< 0.001	0.72 (0.53-0.97)	0.032	0.73 (0.52-1.04)	0.080	272	0.70 (0.57-0.85)	< 0.001	0.805	0.007 (18.16%)
Apo A-1	230	0.71 (0.58-0.87)	< 0.001	0.67 (0.49-0.93)	0.017	0.69 (0.50-0.96)	0.027	230	0.71 (0.58-0.87)	< 0.001	0.670	0.002 (23.08%)
Apo B	151	1.03 (0.84-1.27)	0.764	0.81 (0.62-1.06)	0.132	0.79 (0.58-1.07)	0.131	151	1.03 (0.84-1.27)	0.764	0.008	<0.001 (29.15%)
HOMA-B	11	0.88 (0.32-2.43)	0.801	2.20 (0.07-67.5)	0.663	1.31 (0.33-5.24)	0.698	11	0.88 (0.32-2.43)	0.801	0.594	0.370 (7.71%)
HOMA-IR	6	1.67 (0.42-6.65)	0.467	5.81 (0.05-636.6)	0.504	0.87 (0.12-6.38)	0.895	6	1.67 (0.42-6.65)	0.467	0.613	0.440 (0.00%)
TV	98	2.34 (1.21-4.50)	0.011	1.40 (0.05-37.91)	0.843	2.44 (0.95-6.29)	0.065	98	2.34 (1.21-4.50)	0.011	0.756	0.300 (6.54%)
Computer	70	0.84 (0.41-1.70)	0.622	1.49 (0.03-74.3)	0.842	1.03 (0.37-2.88)	0.957	70	0.84 (0.41-1.70)	0.622	0.769	0.339 (5.86%)
Driving	6	2.87 (0.26-31.3)	0.388	0.00 (0.00-20804)	0.327	4.47 (0.22-89.0)	0.326	6	2.87 (0.26-31.3)	0.388	0.292	0.500 (0%)

Abbreviations: NAFLD, nonalcoholic fatty liver disease; SNPs, single-nucleotide polymorphisms; IVW, Inverse Variance Weighted; WM, Weighted median; MR- PRESSO, Mendelian randomization pleiotropy residual sum and outlier; OR, odds ratio; BMI, body mass index; WHR, waist-to-hip ratio; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Apo A-1, apolipoprotein A-I; Apo B, apolipoprotein B; HOMA-B, homeostasis model assessment of beta-cell function; HOMA-IR, homeostasis model assessment of insulin resistance; TV, Time spent watching television; Computer, Time spent using computer; Driving, Time spent driving.

Table S4 Mendelian randomization results of the causal effects of potential shared influencing factors on GDM

Trait	SNPs	IVW		MR-Egger		WM		MR-PRESSO			<i>P</i> _{pleiotropy}	<i>P</i> _{heterogeneity (I²)}
		OR (95%CI)	<i>P</i>	OR (95%CI)	<i>P</i>	OR (95%CI)	<i>P</i>	SNPs	OR (95%CI)	<i>P</i>		
BMI	430	1.63 (1.46-1.82)	< 0.001	1.69 (1.26-2.25)	< 0.001	1.74 (1.46-2.07)	< 0.001	430	1.63 (1.46-1.82)	< 0.001	0.806	<0.001 (31.86%)
WHR	24	1.64 (1.23-2.38)	0.010	0.38 (0.03-4.08)	0.431	1.37 (0.90-2.10)	0.139	24	1.64 (1.23-2.38)	0.010	0.234	0.001 (53.13%)
TG	238	1.27 (1.16-1.39)	< 0.001	1.05 (0.93-1.19)	0.429	1.09 (0.97-1.24)	0.150	238	1.27 (1.16-1.39)	< 0.001	<0.001	<0.001 (35.48%)
LDL-C	135	0.95 (0.85-1.06)	0.369	0.99 (0.84-1.16)	0.904	0.91 (0.78-1.07)	0.271	135	0.95 (0.85-1.06)	0.369	0.503	<0.001 (32.75%)
HDL-C	274	0.77 (0.71-0.84)	< 0.001	0.84 (0.74-0.96)	0.014	0.83 (0.72-0.96)	0.017	274	0.77 (0.71-0.84)	< 0.001	0.058	<0.001 (32.22%)
Apo A-1	232	0.82 (0.75-0.90)	< 0.001	0.90 (0.78-1.03)	0.140	0.83 (0.72-0.95)	0.008	232	0.82 (0.75-0.90)	< 0.001	0.127	<0.001 (31.14%)
Apo B	151	1.03 (0.94-1.13)	0.488	1.04 (0.92-1.18)	0.509	1.08 (0.95-1.23)	0.226	151	1.03 (0.94-1.13)	0.488	0.831	<0.001 (30.54%)
HOMA-B	5	0.57 (0.24-1.38)	0.212	0.47 (0.00-246.2)	0.827	0.61 (0.24-1.58)	0.310	5	0.57 (0.24-1.38)	0.212	0.953	0.198 (33.47%)
HOMA-IR	6	0.65 (0.36-1.17)	0.151	0.72 (0.11-4.88)	0.750	0.75 (0.34-1.65)	0.475	6	0.65 (0.36-1.17)	0.151	0.918	0.723 (0.00%)
TV	98	1.57 (1.15-2.15)	0.005	2.43 (0.50-11.74)	0.272	1.51 (1.01-2.26)	0.045	98	1.57 (1.15-2.15)	0.005	0.581	0.022 (23.61%)
Computer	70	0.75 (0.54-1.05)	0.096	0.87 (0.14-5.54)	0.884	0.67 (0.43-1.04)	0.077	70	0.75 (0.54-1.05)	0.096	0.875	0.062 (21.53%)
Driving	6	1.30 (0.16-10.7)	0.809	0.00 (0.00-2036)	0.299	1.39 (0.25-7.66)	0.703	6	1.30 (0.16-10.7)	0.809	0.287	<0.001 (76.14%)

Abbreviations: GDM, gestational diabetes mellitus; SNPs, single-nucleotide polymorphisms; IVW, Inverse Variance Weighted; WM, Weighted median; MR- PRESSO, Mendelian randomization pleiotropy residual sum and outlier; OR, odds ratio; BMI, body mass index; WHR, waist-to-hip ratio; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Apo A-1, apolipoprotein A-I; Apo B, apolipoprotein B; HOMA-B, homeostasis model assessment of beta-cell function; HOMA-IR, homeostasis model assessment of insulin resistance; TV, Time spent watching television; Computer, Time spent using computer; Driving, Time spent driving.

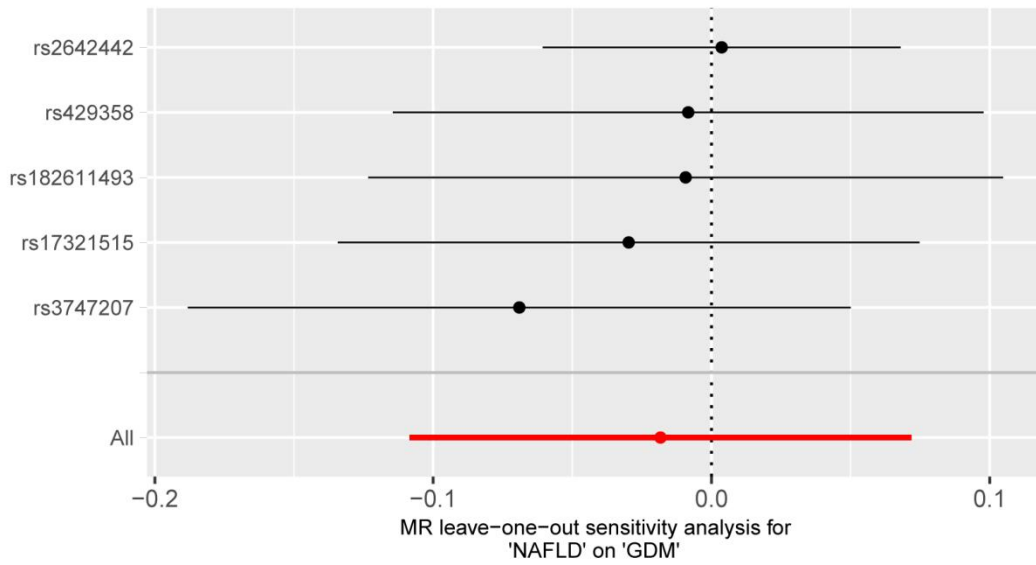


Fig S1. The result of leave-one-out sensitivity analysis of the causal effect of NAFLD on GDM

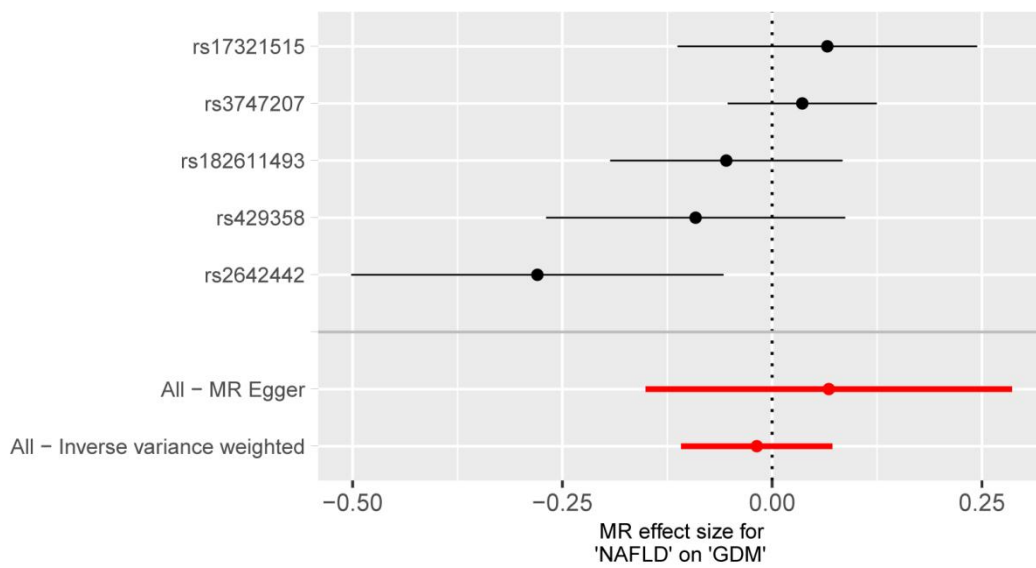


Fig S2. The forest plot of the causal effect of NAFLD on GDM

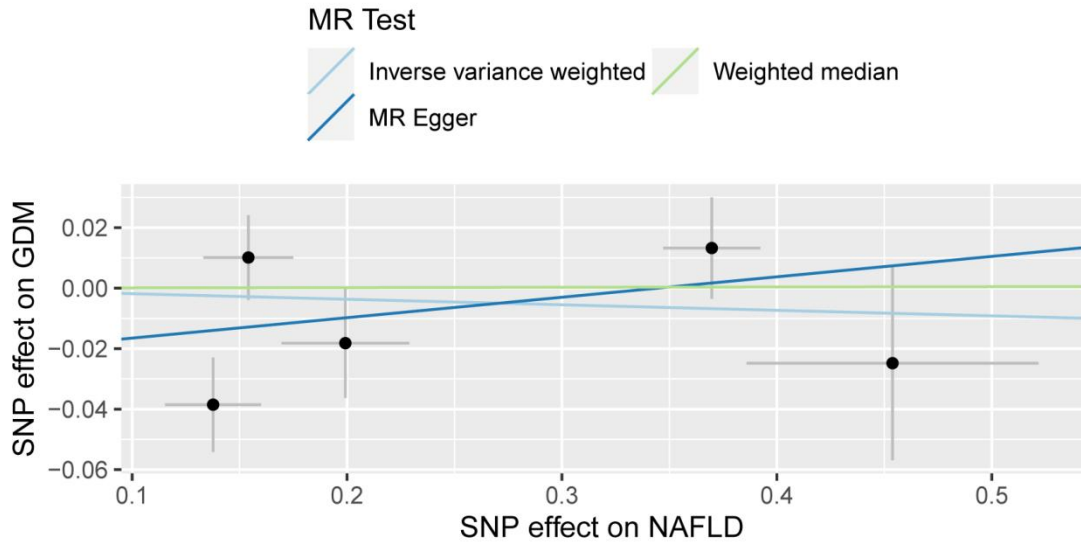


Fig S3. The scatter plot of the causal effect of NAFLD on GDM

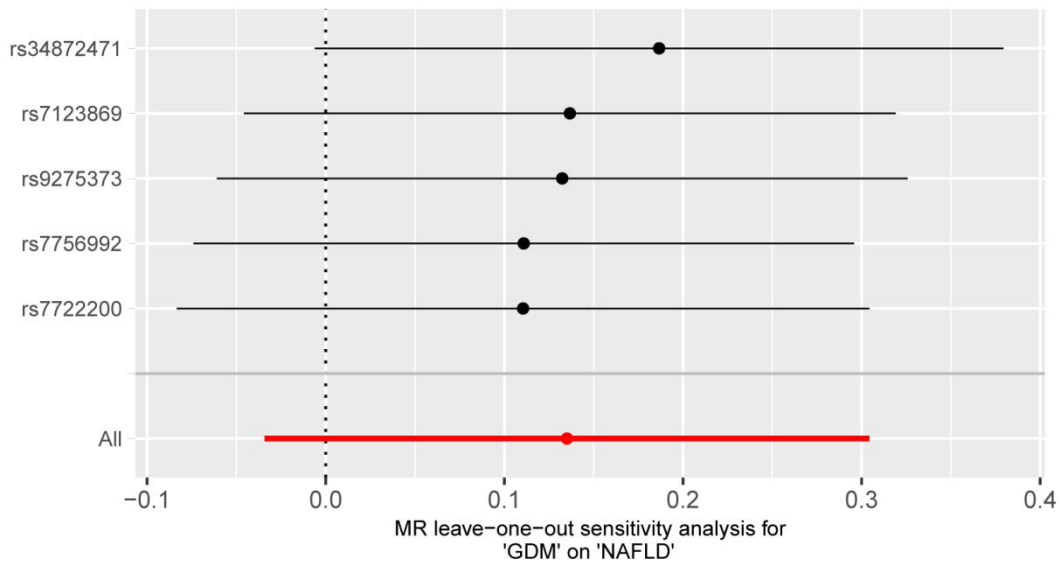


Fig S4. The result of leave-one-out sensitivity analysis of the causal effect of GDM on NAFLD

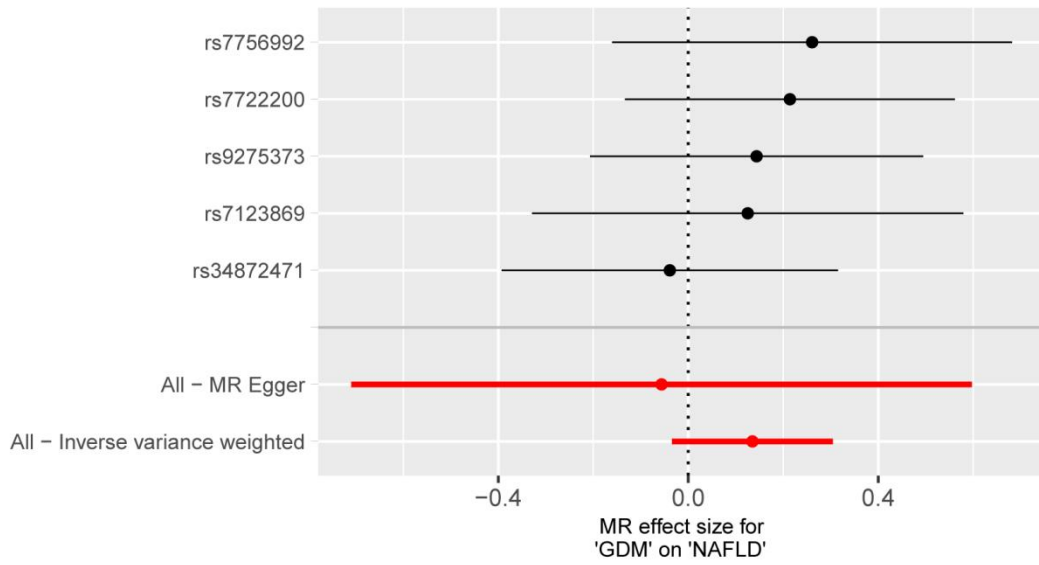


Fig S5. The forest plot of the causal effect of GDM on NAFLD

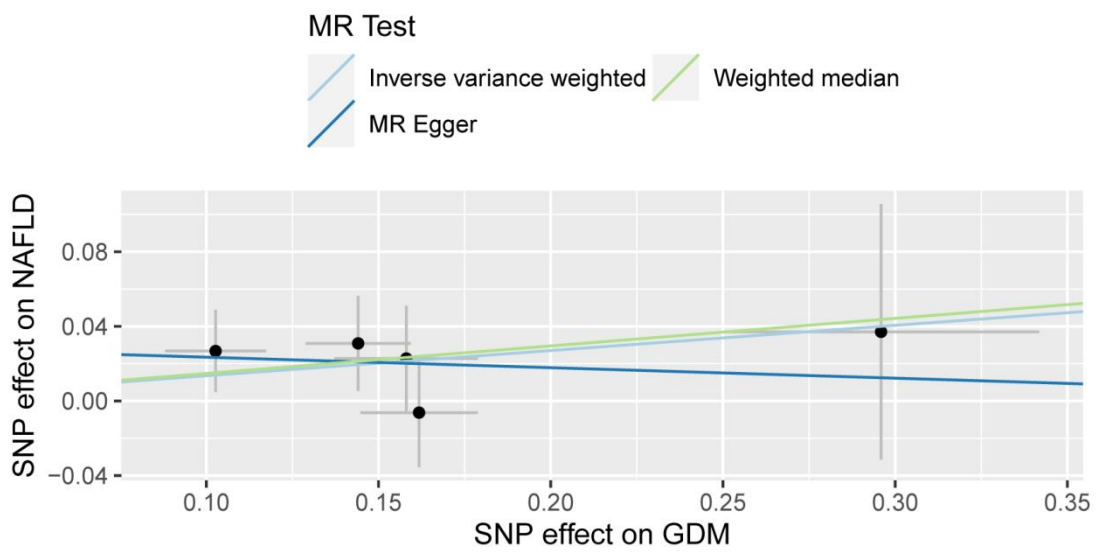


Fig S6. The scatter plot of the causal effect of GDM on NAFLD