

Estimating the effect of liver and pancreas volume and fat content on risk of diabetes: A Mendelian randomization study

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Supplementary Table 1. Summary statistics of FinnGen studies used.

Trait	Code	Name	N cases	N controls	Age cases (years), mean	Traits included
Type 2 diabetes	E4_DM2_STRICT	Type 2 diabetes, strict (exclude DM1)	29,166	183,185	59.88	E4_DM2COMA E4_DM2KETO E4_DM2REN E4_DM2OPHTH E4_DM2NEU E4_DM2PERIPH E4_DM2NASCOMP E4_DM2NOCOMP
Type 1 diabetes	E4_DM1_STRICT	Type 1 diabetes, strict (exclude DM2)	2649	183,674	18.60	E4_DM1COMA E4_DM1KETO E4_DM1REN E4_DM1OPHTH E4_DM1NEU E4_DM1PERIPH E4_DM1NASCOMP E4_DM1NOCOMP

Supplementary Table 2a. The summary of 10 liver fat, 11 liver volume, 9 pancreas fat and 17 pancreas volume genetic variants from the GWAS of the respective exposures in UK Biobank.

Exposure	RSID	Chromosome	Position	Effect allele	Other allele	PVE	Beta	SE	P	Closest gene
Liver fat	rs2642438	1	220970028	G	A	0.1	0.05	0.008	1.E-10	<i>MARC1</i>
Liver fat	rs4665985	2	27753878	C	A	0.1	0.05	0.009	2.E-08	<i>C2orf16</i>
Liver fat	4:100472229_ GATTTATAGT TCAGAGA_G	4	100472229	G	GATTTATAG TTCAGAGA	0.1	-0.05	0.009	2.E-09	<i>MTTP</i>
Liver fat	rs112875651	8	126506694	A	G	0.1	-0.05	0.008	9.E-11	<i>TRIB1</i>
Liver fat	rs7029757	9	132566666	A	G	0.1	-0.08	0.013	5.E-09	<i>TOR1B</i>
Liver fat	rs11446981	10	113950257	TA	T	0.2	-0.06	0.009	4.E-13	<i>GPAM</i>
Liver fat	rs55714539	19	18207397	C	A	0.1	0.05	0.008	2.E-08	<i>MAST3</i>
Liver fat	rs58542926	19	19379549	T	C	1.6	0.33	0.015	3.E-116	<i>TM6SF2</i>
Liver fat	rs429358	19	45411941	C	T	0.4	-0.12	0.011	1.E-30	<i>APOE</i>
Liver fat	rs738409	22	44324727	G	C	1.8	0.23	0.009	2.E-133	<i>PNPLA3</i>
Liver volume	rs193084249	1	26987646	G	A	0.1	0.14	0.023	7.E-10	<i>ARID1A</i>
Liver volume	rs1260326	2	27730940	C	T	0.2	-0.06	0.007	5.E-19	<i>GCKR</i>
Liver volume	rs79287178	3	172294500	A	G	0.2	0.15	0.021	8.E-13	<i>TNFSF10</i>
Liver volume	rs1009064	6	52623490	C	G	0.1	-0.04	0.007	1.E-08	<i>GSTA2</i>
Liver volume	rs753444559	6	127066487	GA	G	0.2	-0.05	0.007	1.E-12	<i>RSPO3</i>
Liver volume	rs4240624	8	9184231	A	G	0.4	-0.14	0.012	1.E-31	<i>PPP1R3B</i>
Liver volume	rs7896518	10	65104500	G	A	0.2	-0.05	0.007	4.E-13	<i>REEP3</i>
Liver volume	rs10881959	10	93507964	T	G	0.1	0.05	0.007	7.E-11	<i>TNKS2</i>
Liver volume	rs139974673	15	44027885	C	T	0.3	0.21	0.023	5.E-21	<i>PDIA3</i>

Liver volume	16:53812783_TTTTG_T	16	53812783	T	TTTTG	0.1	0.04	0.007	3.E-09	
Liver volume	rs58489806	19	19456917	T	C	0.1	0.08	0.012	3.E-11	MAU2
Pancreas fat	rs775103516	1	51397564	A	AAT	0.2	-0.07	0.009	3.E-13	FAF1
Pancreas fat	rs11679492	2	208834477	T	C	0.1	0.05	0.009	1.E-08	PLEKHM3
Pancreas fat	rs4733612	8	129569999	A	G	0.2	-0.07	0.010	9.E-12	
Pancreas fat	9:136138765_GCGCCCACC ACTA_G	9	136138765	G	GCGCCCACC CACTA	0.2	0.08	0.011	3.E-13	ABO
Pancreas fat	rs2270911	10	49313245	T	C	0.1	0.06	0.011	2.E-08	FAM25C
Pancreas fat	rs751370420	12	4122179	A	AAAG	0.2	-0.06	0.009	2.E-11	PARP11
Pancreas fat	rs7405380	16	88975910	C	G	0.2	0.06	0.009	6.E-13	PABPN1L
Pancreas fat	rs10422861	19	33894846	T	C	0.4	0.09	0.009	2.E-22	PEPD
Pancreas fat	rs13040225	20	48830772	T	A	0.2	0.06	0.009	2.E-11	CEBPB
Pancreas volume	rs2336240	1	33915751	C	T	0.1	0.04	0.008	3.E-08	PHC2
Pancreas volume	rs11120180	1	213825272	C	G	0.1	0.05	0.010	1.E-08	PROX1
Pancreas volume	2:239798829_AG_A	2	239798829	A	AG	0.1	0.06	0.011	2.E-08	TWIST2
Pancreas volume	rs36153289	6	109133485	G	C	0.1	-0.04	0.008	2.E-08	ARMC2
Pancreas volume	rs9482770	6	127443092	C	T	0.2	0.06	0.008	3.E-14	RSPO3
Pancreas volume	rs7819154	8	129558351	A	C	0.2	-0.07	0.008	6.E-15	
Pancreas volume	9:136138765_GCGCCCACC ACTA_G	9	136138765	G	GCGCCCACC CACTA	0.1	-0.07	0.010	8.E-12	ABO

Pancreas volume	rs2163150	10	49335932	C	T	0.2	-0.07	0.009	2.E-16	
Pancreas volume	rs10509540	10	90023033	C	T	0.1	-0.05	0.008	2.E-09	<i>RNLS</i>
Pancreas volume	14:101306841 _TC_T	14	101306841	T	TC	0.2	-0.05	0.008	1.E-12	<i>RTL1</i>
Pancreas volume	rs72802342	16	75234872	A	C	0.2	0.11	0.014	8.E-15	<i>CTRB2</i>
Pancreas volume	rs7405380	16	88975910	C	G	0.1	-0.05	0.008	2.E-09	<i>PABPN1L</i>
Pancreas volume	rs150747780	18	864347	GA	G	0.1	0.07	0.012	4.E-09	<i>ADCYAP1</i>
Pancreas volume	rs1226053	18	1421021	C	G	0.1	0.04	0.008	1.E-08	
Pancreas volume	rs922048	18	56876386	T	A	0.1	0.05	0.008	3.E-09	<i>GRP</i>
Pancreas volume	rs653395	19	49268194	A	G	0.1	0.05	0.008	1.E-08	<i>FGF21</i>
Pancreas volume	rs9330813	22	46364161	A	G	0.1	-0.05	0.008	1.E-09	<i>WNT7B</i>

PVE: phenotypic variation explained; SE: standard error; P: p-value.

Supplementary Table 2b. The summary of 10 liver fat, 11 liver volume, 9 pancreas fat and 17 pancreas volume genetic variants and their proxies (where necessary) from the GWAS of type 1 and type 2 diabetes.

Exposure	Index SNP	Proxy SNP	Proxy chromosome	Proxy position	r ²	Type 2 diabetes			Type 1 diabetes		
						Beta	SE	P	Beta	SE	P
Liver fat	rs2642438					0.005	0.009	0.590	0.054	0.026	0.035
Liver fat	rs4665985					-0.039	0.010	8.E-05	-0.035	0.027	0.189
Liver fat	4:100472229_G ATTTATAGTTC AGAGA_G	rs10007794	4	100478740	1.00	0.017	0.010	0.078	0.018	0.027	0.512
Liver fat	rs112875651					-0.002	0.009	0.820	0.039	0.026	0.131
Liver fat	rs7029757					-0.028	0.015	0.065	0.007	0.042	0.861
Liver fat	rs11446981	rs1129555	10	113910721	0.85	0.027	0.009	0.004	0.036	0.026	0.165
Liver fat	rs55714539					-0.001	0.009	0.920	0.011	0.027	0.670
Liver fat	rs58542926					0.090	0.016	1.E-08	-0.016	0.044	0.718
Liver fat	rs429358					-0.093	0.012	3.E-14	-0.009	0.036	0.800
Liver fat	rs738409					0.055	0.010	3.E-08	0.029	0.028	0.307
Liver volume	rs193084249					0.078	0.029	0.006	-0.016	0.075	0.830
Liver volume	rs1260326					0.059	0.009	6.E-12	0.033	0.024	0.166
Liver volume	rs79287178					0.020	0.026	0.440	0.028	0.069	0.682
Liver volume	rs1009064					0.016	0.009	0.061	0.033	0.025	0.184
Liver volume	rs753444559	rs1101557	6	127067996	0.98	-0.044	0.008	1.E-07	0.075	0.023	0.001
Liver volume	rs4240624					-0.070	0.015	2.E-06	0.030	0.041	0.473
Liver volume	rs7896518					-0.018	0.008	0.033	-0.008	0.024	0.743
Liver volume	rs10881959					0.007	0.009	0.440	-0.015	0.024	0.523
Liver volume	rs139974673					-0.041	0.026	0.110	-0.022	0.074	0.764

Liver volume	16:53812783_T TTTG_T	rs11075985	16	53805207	0.86	-0.120	0.008	1.E-45	0.020	0.024	0.406
Liver volume	rs58489806					0.075	0.015	2.E-07	-0.016	0.040	0.686
Pancreas fat	rs775103516	rs113170275	1	51479997	0.85	0.010	0.009	0.270	-0.037	0.025	0.138
Pancreas fat	rs11679492					-0.026	0.009	0.002	0.039	0.024	0.101
Pancreas fat	rs4733612					-0.039	0.009	3.E-05	-0.031	0.027	0.256
Pancreas fat	9:136138765_G CGCCCACCAC TA_G	rs495828	9	136154867	0.84	-0.052	0.010	4.E-07	0.066	0.029	0.023
Pancreas fat	rs2270911					0.022	0.011	0.036	-0.001	0.030	0.984
Pancreas fat	rs751370420	rs7307879	12	4124107	0.71	-0.002	0.009	0.840	0.035	0.025	0.165
Pancreas fat	rs7405380	rs12444726	16	88982789	0.77	0.008	0.010	0.420	0.066	0.025	0.009
Pancreas fat	rs10422861					-0.021	0.009	0.016	-0.034	0.025	0.179
Pancreas fat	rs13040225					-0.038	0.008	5.E-06	0.044	0.024	0.067
Pancreas volume	rs2336240					-0.011	0.009	0.190	0.012	0.025	0.633
Pancreas volume	rs11120180					-0.015	0.011	0.170	0.004	0.030	0.894
Pancreas volume	2:239798829_A G_A	rs35291227	2	239800707	0.94	-0.002	0.013	0.880	0.032	0.039	0.421
Pancreas volume	rs36153289	rs11153132	6	109139055	0.91	0.005	0.009	0.590	-0.002	0.024	0.924
Pancreas volume	rs9482770					-0.013	0.008	0.110	0.010	0.024	0.686
Pancreas volume	rs7819154					0.039	0.009	3.E-05	0.030	0.027	0.269
Pancreas volume	9:136138765_G CGCCCACCAC TA_G	rs495828	9	136154867	0.84	-0.052	0.010	4.E-07	0.066	0.029	0.023

Pancreas volume	rs2163150										
Pancreas volume	rs10509540					0.008	0.009	0.400	-0.124	0.027	4.E-06
Pancreas volume	14:101306841_TC_T	rs34337125	14	101307703	0.85	0.024	0.009	0.005	0.102	0.026	6.E-05
Pancreas volume	rs72802342					-0.120	0.016	1.E-13	0.269	0.043	4.E-10
Pancreas volume	rs7405380	rs12444726	16	88982789	0.77	0.008	0.010	0.420	0.066	0.025	0.009
Pancreas volume	rs150747780	rs13381552	18	864109	0.86	0.001	0.013	0.930	0.076	0.038	0.045
Pancreas volume	rs1226053					0.005	0.009	0.580	-0.025	0.025	0.320
Pancreas volume	rs922048					-0.015	0.009	0.079	0.030	0.024	0.211
Pancreas volume	rs653395	rs62132802	19	49270872	0.72	-0.004	0.010	0.670	0.034	0.033	0.294
Pancreas volume	rs9330813					0.009	0.010	0.380	0.011	0.035	0.743

For one pancreas volume SNP (rs2163150), neither the index nor proxy SNPs were available in either GWAS. Where proxy SNPs were used, this SNP was the same across both GWAS despite the best available proxy SNPs being identified in GWAS independently. r^2 : measure of linkage disequilibrium between index and proxy SNP; SE: standard error; P: p-value.

Supplementary Table 3. MR-PRESSO horizontal pleiotropy assessment for the MR for liver and pancreas fat/volume exposures for type 1 and type 2 diabetes, including MR results before (raw) and after outlier removal.

Exposure	Outcome	Analysis	Causal estimate	Lower CI	Upper CI	t-statistic	P	Global test RSSobs	Global test P	Distortion coefficient	Distortion P
Liver fat	Type 2 diabetes	Raw	1.27	1.08	1.49	2.88	0.018	88.93	<0.001	-1.04	0.843
Liver fat	Type 2 diabetes	Outlier-corrected	1.27	1.21	1.34	9.06	1.E-04				
Liver fat	Type 1 diabetes	Raw	1.07	0.90	1.27	0.72	0.49	13.60	0.343		
Liver fat	Type 1 diabetes	Outlier-corrected									
Liver volume	Type 2 diabetes	Raw	1.37	0.82	2.27	1.20	0.26	365.15	<0.001	-15.30	1
Liver volume	Type 2 diabetes	Outlier-corrected	1.44	1.24	1.69	4.62	0.010				
Liver volume	Type 1 diabetes	Raw	0.92	0.67	1.27	-0.50	0.63	18.68	0.151		
Liver volume	Type 1 diabetes	Outlier-corrected									
Pancreas fat	Type 2 diabetes	Raw	1.02	0.76	1.37	0.13	0.9	111.30	<0.001	-67.93	1
Pancreas fat	Type 2 diabetes	Outlier-corrected	1.06	0.87	1.29	0.59	0.59				
Pancreas fat	Type 1 diabetes	Raw	1.26	0.82	1.92	1.04	0.33	29.80	0.005	-40.95	0.544
Pancreas fat	Type 1 diabetes	Outlier-corrected	1.47	1.02	2.12	2.04	0.08				
Pancreas volume	Type 2 diabetes	Raw	0.76	0.62	0.93	-2.60	0.019	98.67	<0.001	-48.56	0.008
Pancreas volume	Type 2 diabetes	Outlier-corrected	0.83	0.74	0.94	-2.98	0.011				
Pancreas volume	Type 1 diabetes	Raw	1.55	0.85	2.84	1.42	0.18	101.86	<0.001	1131.72	<0.001
Pancreas volume	Type 1 diabetes	Outlier-corrected	0.96	0.67	1.36	-0.24	0.82				

For two analyses (liver fat and volume vs. type 1 diabetes) no outliers were detected. Global test: detecting horizontal pleiotropy; Distortion test: test for significant distortion in MR causal estimates before and after outlier removal. CI: 95% confidence interval; P: p-value; RSSobs: observed residual sum of squares; MR: Mendelian randomisation.

Supplementary Table 4. Pleiotropy coefficients per genetic variant for MR analyses where outliers were detected using MR-PRESSO.

Exposure	Outcome	SNP	RSSobs	P	Gene
Liver fat	Type 2 diabetes	rs1129555	0.002	<0.01	<i>GPAM</i>
Liver fat	Type 2 diabetes	rs429358	0.005	<0.01	<i>APOE</i>
Liver fat	Type 2 diabetes	rs4665985	0.003	<0.01	<i>C2orf16</i>
Liver fat	Type 2 diabetes	rs10007794	2.E-05	1	<i>MTTP</i>
Liver fat	Type 2 diabetes	rs112875651	1.E-04	1	<i>TRIB1</i>
Liver fat	Type 2 diabetes	rs2642438	7.E-05	1	<i>MARC1</i>
Liver fat	Type 2 diabetes	rs55714539	1.E-04	1	<i>MAST3</i>
Liver fat	Type 2 diabetes	rs58542926	3.E-04	1	<i>TM6SF2</i>
Liver fat	Type 2 diabetes	rs7029757	1.E-04	1	<i>TOR1B</i>
Liver fat	Type 2 diabetes	rs738409	6.E-07	1	<i>PNPLA3</i>
Liver volume	Type 2 diabetes	rs1009064	9.E-04	<0.011	<i>GSTA2</i>
Liver volume	Type 2 diabetes	rs11075985	0.013	<0.011	
Liver volume	Type 2 diabetes	rs1260326	0.008	<0.011	<i>GCKR</i>
Liver volume	Type 2 diabetes	rs139974673	0.016	<0.011	<i>PDIA3</i>
Liver volume	Type 2 diabetes	rs58489806	0.003	<0.011	<i>MAU2</i>
Liver volume	Type 2 diabetes	rs1101557	1.E-03	0.011	<i>RSPO3</i>
Liver volume	Type 2 diabetes	rs4240624	0.001	0.473	<i>PPP1R3B</i>
Liver volume	Type 2 diabetes	rs10881959	7.E-05	1	<i>TNKS2</i>
Liver volume	Type 2 diabetes	rs193084249	0.001	1	<i>ARID1A</i>
Liver volume	Type 2 diabetes	rs7896518	4.E-06	1	<i>REEP3</i>
Liver volume	Type 2 diabetes	rs79287178	9.E-04	1	<i>TNFSF10</i>
Pancreas fat	Type 2 diabetes	rs11679492	8.E-04	<0.009	<i>PLEKHM3</i>
Pancreas fat	Type 2 diabetes	rs13040225	0.002	<0.009	<i>CEBPB</i>
Pancreas fat	Type 2 diabetes	rs4733612	0.002	<0.009	
Pancreas fat	Type 2 diabetes	rs495828	0.003	<0.009	<i>ABO</i>
Pancreas fat	Type 2 diabetes	rs10422861	8.E-04	0.009	<i>PEPD</i>
Pancreas fat	Type 2 diabetes	rs2270911	5.E-04	0.477	<i>FAM25C</i>

Pancreas fat	Type 2 diabetes	rs113170275	2.E-04	1	FAF1
Pancreas fat	Type 2 diabetes	rs12444726	5.E-05	1	PABPN1L
Pancreas fat	Type 2 diabetes	rs7307879	4.E-07	1	PARP11
Pancreas fat	Type 1 diabetes	rs495828	0.009	0.009	ABO
Pancreas fat	Type 1 diabetes	rs10422861	0.005	0.09	PEPD
Pancreas fat	Type 1 diabetes	rs12444726	0.003	0.243	PABPN1L
Pancreas fat	Type 1 diabetes	rs113170275	6.E-04	1	FAF1
Pancreas fat	Type 1 diabetes	rs11679492	9.E-04	1	PLEKHM3
Pancreas fat	Type 1 diabetes	rs13040225	0.001	1	CEBPB
Pancreas fat	Type 1 diabetes	rs2270911	3.E-04	1	FAM25C
Pancreas fat	Type 1 diabetes	rs4733612	3.E-04	1	
Pancreas fat	Type 1 diabetes	rs7307879	6.E-04	1	PARP11
Pancreas volume	Type 2 diabetes	rs34337125	0.002	<0.016	RTL1
Pancreas volume	Type 2 diabetes	rs72802342	0.010	<0.016	CTRB2
Pancreas volume	Type 2 diabetes	rs495828	0.001	0.016	ABO
Pancreas volume	Type 2 diabetes	rs7819154	5.E-04	0.368	
Pancreas volume	Type 2 diabetes	rs11153132	3.E-04	0.688	ARMC2
Pancreas volume	Type 2 diabetes	rs1226053	3.E-04	0.896	
Pancreas volume	Type 2 diabetes	rs10509540	4.E-05	1	RNLS
Pancreas volume	Type 2 diabetes	rs11120180	6.E-08	1	PROX1
Pancreas volume	Type 2 diabetes	rs12444726	3.E-05	1	PABPN1L
Pancreas volume	Type 2 diabetes	rs13381552	5.E-04	1	ADCYAP1
Pancreas volume	Type 2 diabetes	rs2336240	1.E-06	1	PHC2
Pancreas volume	Type 2 diabetes	rs35291227	2.E-04	1	TWIST2
Pancreas volume	Type 2 diabetes	rs62132802	3.E-04	1	FGF21
Pancreas volume	Type 2 diabetes	rs922048	8.E-06	1	GRP
Pancreas volume	Type 2 diabetes	rs9330813	2.E-05	1	WNT7B
Pancreas volume	Type 2 diabetes	rs9482770	8.E-06	1	RSPO3
Pancreas volume	Type 1 diabetes	rs10509540	0.012	<0.016	RNLS

Pancreas volume	Type 1 diabetes	rs72802342	0.061	<0.016	<i>CTRB2</i>
Pancreas volume	Type 1 diabetes	rs12444726	0.008	0.016	<i>PABPN1L</i>
Pancreas volume	Type 1 diabetes	rs34337125	0.007	0.032	<i>RTL1</i>
Pancreas volume	Type 1 diabetes	rs13381552	0.013	0.08	<i>ADCYAP1</i>
Pancreas volume	Type 1 diabetes	rs7819154	0.004	0.384	
Pancreas volume	Type 1 diabetes	rs11120180	4.E-04	1	<i>PROX1</i>
Pancreas volume	Type 1 diabetes	rs11153132	5.E-04	1	<i>ARMC2</i>
Pancreas volume	Type 1 diabetes	rs1226053	0.002	1	
Pancreas volume	Type 1 diabetes	rs2336240	6.E-05	1	<i>PHC2</i>
Pancreas volume	Type 1 diabetes	rs35291227	0.004	1	<i>TWIST2</i>
Pancreas volume	Type 1 diabetes	rs495828	0.002	1	<i>ABO</i>
Pancreas volume	Type 1 diabetes	rs62132802	0.003	1	<i>FGF21</i>
Pancreas volume	Type 1 diabetes	rs922048	1.E-04	1	<i>GRP</i>
Pancreas volume	Type 1 diabetes	rs9330813	0.001	1	<i>WNT7B</i>
Pancreas volume	Type 1 diabetes	rs9482770	3.E-04	1	<i>RSPO3</i>

No outliers were detected for analyses of liver fat and volume vs. type 1 diabetes, so these do not appear here. RSSobs: observed residual sum of squares; P: p-value; MR: Mendelian randomisation.

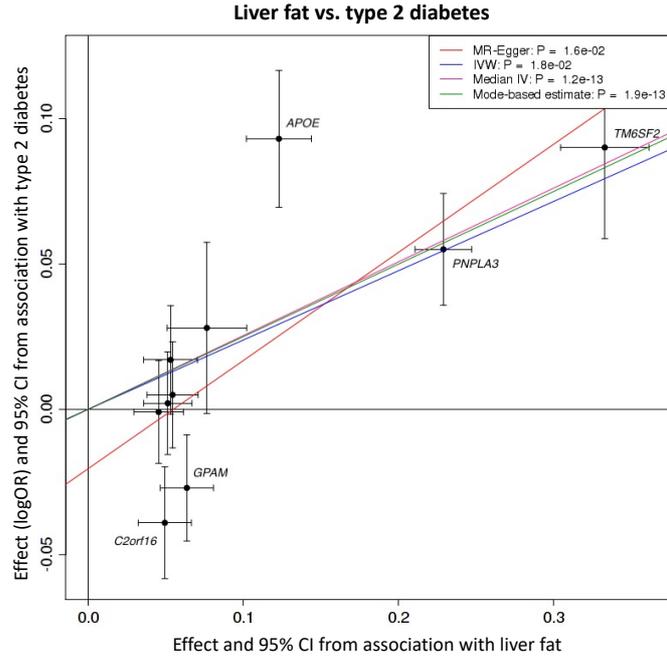
Supplementary Table 5. Results of the MR study testing causal association between liver and pancreas fat/volume and type 1 and type 2 diabetes using FinnGen.

Analysis	OR	Lower CI	Upper CI	P	Egger intercept	Heterogeneity: Q	I ² MR-Egger
Liver fat vs. type 2 diabetes							
IVW	1.137	0.967	1.338	0.156		46.121, p=6E-7	
Weighted median	1.087	0.968	1.221	0.157			
MR-Egger	1.211	0.928	1.579	0.196	-0.009, p=0.566	44.144, p=5E-7	0.98
MBE	1.103	1.003	1.213	0.042			
Liver fat vs. type 1 diabetes							
IVW	1.123	0.919	1.371	0.287		7.704, p=0.564	
Weighted median	1.132	0.884	1.450	0.326			
MR-Egger	1.098	0.801	1.505	0.578	0.003, p=0.860	7.672, p=0.466	0.98
MBE	1.149	0.905	1.460	0.254			
Liver volume vs. type 2 diabetes							
IVW	1.415	0.892	2.244	0.171		155.070, p=3E-28	
Weighted median	1.435	1.201	1.714	7E-05			
MR-Egger	1.087	0.385	3.069	0.880	0.021, p=0.588	149.826, p=1E-27	0.86
MBE	1.511	1.277	1.788	2E-06			
Liver volume vs. type 1 diabetes							
IVW	1.153	0.828	1.604	0.419		3.356, p=0.972	
Weighted median	1.227	0.793	1.898	0.358			
MR-Egger	1.246	0.607	2.559	0.564	-0.006, p=0.703	3.299, p=0.951	0.84
MBE	1.273	0.751	2.158	0.370			
Pancreas fat vs. type 2 diabetes							
IVW	1.059	0.748	1.499	0.756		54.839, p=2E-9	
Weighted median	0.957	0.757	1.209	0.714			
MR-Egger	1.788	0.234	13.647	0.595	-0.035, p=0.626	52.529, p=1E-9	0.36

MBE	0.837	0.610	1.148	0.269			
Pancreas fat vs. type 1 diabetes							
IVW	1.588	0.836	3.015	0.200		23.745, p=0.001	
Weighted median	1.561	0.951	2.560	0.080			
MR-Egger	1.634	0.035	76.841	0.811	-0.002, p=0.989	23.744, p=6E-4	0.33
MBE	1.600	0.881	2.906	0.123			
Pancreas volume vs. type 2 diabetes							
IVW	0.799	0.603	1.058	0.136		114.044, p=8E-17	
Weighted median	0.850	0.715	1.011	0.060			
MR-Egger	0.227	0.078	0.662	0.016	0.072, p=0.032	83.042, p=2E-11	0.15
MBE	0.854	0.671	1.086	0.200			
Pancreas volume vs. type 1 diabetes							
IVW	1.214	0.623	2.364	0.577		81.831, p=8E-11	
Weighted median	1.044	0.614	1.775	0.875			
MR-Egger	5.066	0.298	86.147	0.279	-0.082, p=0.325	76.554, p=3E-10	0.20
MBE	0.887	0.386	2.038	0.778			

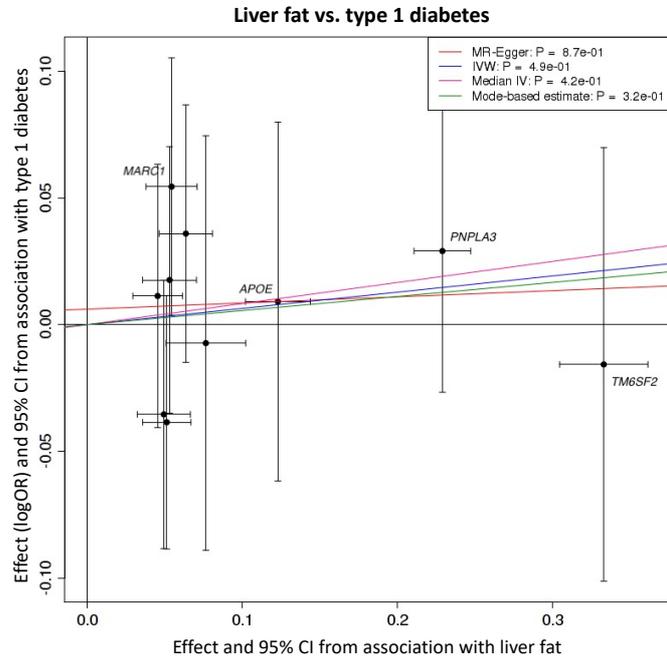
The odds ratio (OR) are per 1 standard deviation higher liver and pancreas fat/volume. CI: 95% confidence interval; IVW: inverse-variance weighted; MBE: mode-based estimate; MR: Mendelian randomisation.

Figure S1



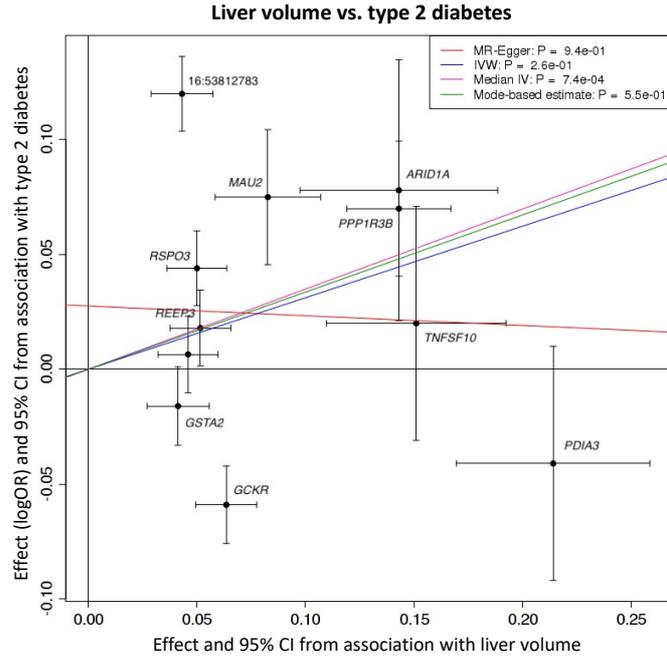
Supplementary Figure 1. Scatter plot of the main and sensitivity MR study investigating the effect of liver fat on type 2 diabetes. The x-axis represents the genetic association with liver fat; the y-axis represents the genetic association with risk of type 2 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.

Figure S2



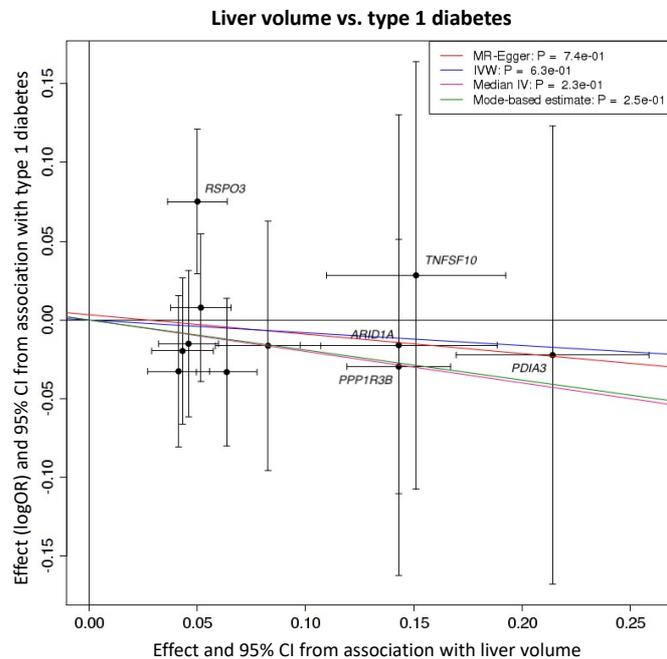
Supplementary figure 2. Scatter plot of the main and sensitivity MR study investigating the effect of liver fat on type 1 diabetes. The x-axis represents the genetic association with liver fat; the y-axis represents the genetic association with risk of type 1 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.

Figure S3



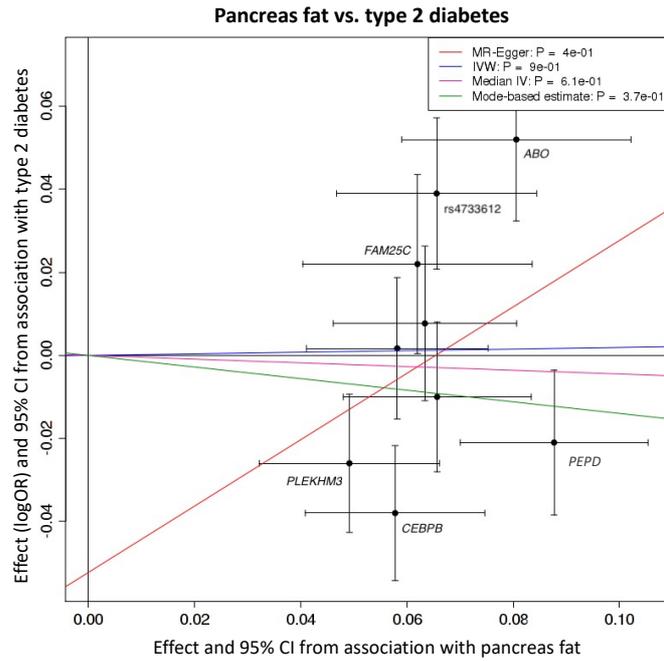
Supplementary figure 3. Scatter plot of the main and sensitivity MR study investigating the effect of liver volume on type 2 diabetes. The x-axis represents the genetic association with liver volume; the y-axis represents the genetic association with risk of type 2 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.

Figure S4



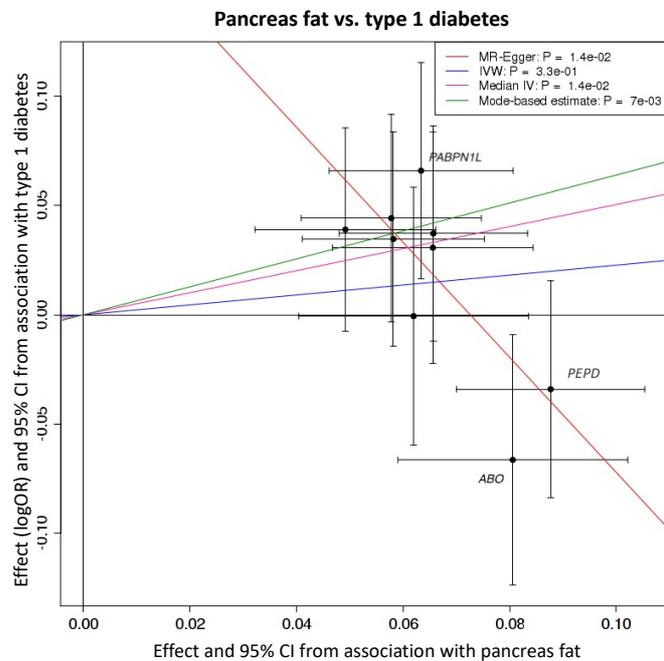
Supplementary figure 4. Scatter plot of the main and sensitivity MR study investigating the effect of liver volume on type 1 diabetes. The x-axis represents the genetic association with liver volume; the y-axis represents the genetic association with risk of type 1 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.

Figure S5



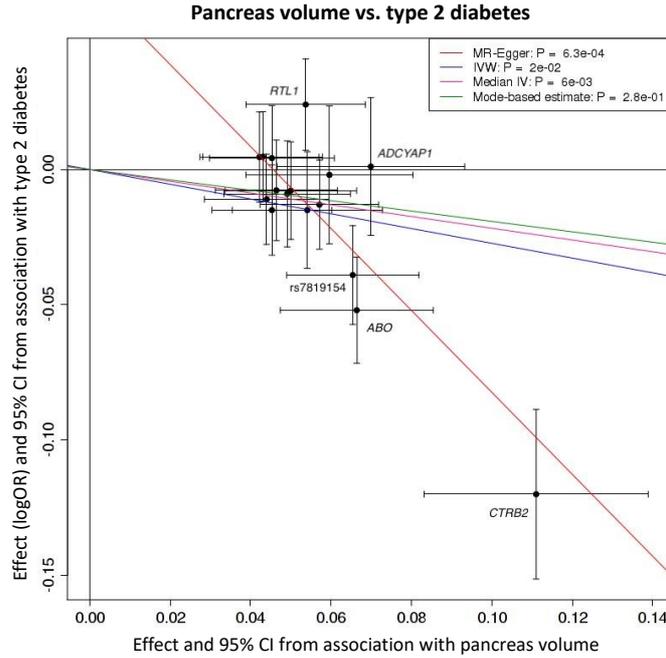
Supplementary figure 5. Scatter plot of the main and sensitivity MR study investigating the effect of pancreas fat on type 2 diabetes. The x-axis represents the genetic association with pancreas fat; the y-axis represents the genetic association with risk of type 2 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.

Figure S6



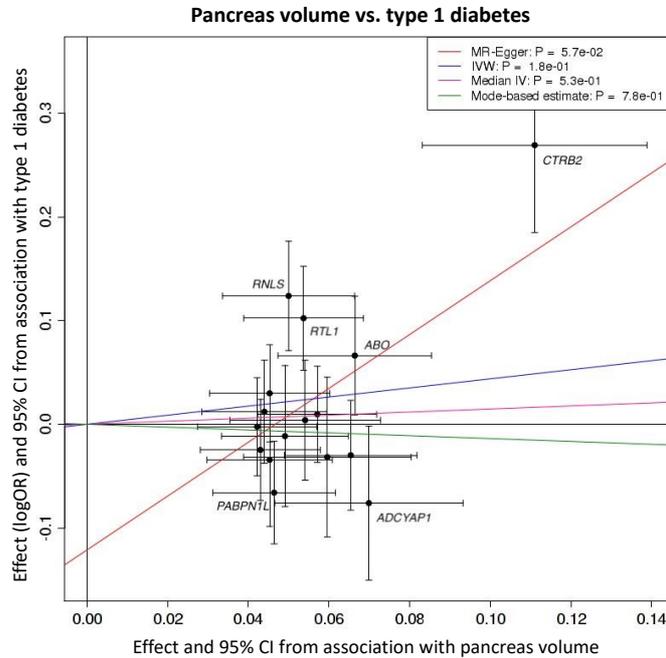
Supplementary figure 6. Scatter plot of the main and sensitivity MR study investigating the effect of pancreas fat on type 1 diabetes. The x-axis represents the genetic association with pancreas fat; the y-axis represents the genetic association with risk of type 1 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.

Figure S7



Supplementary figure 7. Scatter plot of the main and sensitivity MR study investigating the effect of pancreas volume on type 2 diabetes. The x-axis represents the genetic association with pancreas volume; the y-axis represents the genetic association with risk of type 2 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.

Figure S8



Supplementary figure 8. Scatter plot of the main and sensitivity MR study investigating the effect of pancreas volume on type 1 diabetes. The x-axis represents the genetic association with pancreas volume; the y-axis represents the genetic association with risk of type 1 diabetes. Each line represents a different MR method. CI, confidence intervals; MR, Mendelian randomization; OR, odds ratio.