

Supplementary Information

A Mendelian randomization study of the effects of blood lipids on breast cancer risk

Nowak et al.

Supplementary Table 1

Genetic variants used in instrumental variable analysis for blood lipids.

Supplementary Table 2

Genetic variants used in instrumental variable analysis for genes encoding drug targets.

Genetic variants used in instrumental variable analysis for genes encoding drug targets

Gene	rsid	SNP_hg19	lipid_eff ct_allele	lipid_oth r_allele	ldl_b	ldl_se	ldl_p	breast_ca ncr_oth er_allele	breast_ca ncr_eff ct_allele	bca_b	bca_se	bca_p	erpos_b	erpos_se	erpos_b	erneg_b	erneg_se	erneg_p
PCSK9	rs11206514	chr1:55156004	a	c	5.07E-02	4.10E-03	9.95E-33	C	A	7.00E-03	7.00E-03	3.16E-01	-3.90E-03	8.30E-03	6.40E-01	2.73E-02	1.25E-02	2.91E-02
PCSK9	rs11591147	chr1:55505647	g	t	4.97E-01	1.80E-02	8.58E-143	G	T	-4.42E-02	2.73E-02	1.06E-01	-2.40E-02	3.21E-02	4.55E-01	-6.22E-02	5.17E-02	2.28E-01
PCSK9	rs12067569	chr1:55528629	a	g	8.85E-02	1.00E-02	1.97E-17	G	A	2.00E-04	1.75E-02	9.90E-01	-9.70E-03	2.09E-02	6.44E-01	2.50E-03	3.18E-02	9.37E-01
PCSK9	rs2483205	chr1:55518316	c	t	5.14E-02	5.30E-03	4.74E-20	C	T	-7.80E-03	6.90E-03	2.61E-01	-8.20E-03	8.20E-03	3.14E-01	-9.40E-03	1.25E-02	4.53E-01
PCSK9	rs4927193	chr1:55509872	t	c	3.52E-02	5.60E-03	4.27E-11	T	C	-2.40E-03	9.90E-03	8.10E-01	4.20E-03	1.18E-02	7.21E-01	-1.60E-02	1.80E-02	3.74E-01
PCSK9	rs572512	chr1:55517344	t	c	4.78E-02	4.70E-03	5.31E-26	C	T	7.20E-03	7.40E-03	3.28E-01	8.20E-03	8.80E-03	3.50E-01	4.80E-03	1.34E-02	7.20E-01
PCSK9	rs7552841	chr1:55518752	t	c	3.68E-02	4.40E-03	5.40E-15	C	T	-7.10E-03	7.70E-03	3.58E-01	-6.00E-04	9.20E-03	9.51E-01	-1.11E-02	1.41E-02	4.33E-01
CETP	rs11076174	chr16:57003146	t	c	1.80E-01	7.50E-03	2.28E-127	T	C	-2.18E-02	1.20E-02	6.79E-02	-1.86E-02	1.42E-02	1.90E-01	-3.56E-02	2.18E-02	1.03E-01
CETP	rs117040820	chr16:57005762	t	c	1.81E-01	2.16E-02	2.23E-14	C	T	4.29E-02	3.43E-02	2.12E-01	5.05E-02	4.11E-02	2.20E-01	-3.30E-03	6.41E-02	9.59E-01
CETP	rs118146573	chr16:57000938	g	a	2.62E-01	7.40E-03	2.03E-236	G	A	-4.30E-03	1.01E-02	6.68E-01	-1.40E-03	1.20E-02	9.06E-01	-2.63E-02	1.85E-02	1.54E-01
CETP	rs12597002	chr16:57002404	c	a	8.49E-02	3.90E-03	1.13E-102	C	A	-1.33E-02	6.80E-03	4.98E-02	-2.07E-02	8.00E-03	1.03E-02	5.00E-03	1.23E-02	6.85E-01
CETP	rs12720873	chr16:57006072	a	g	9.54E-02	1.39E-02	1.88E-10	G	A	1.51E-02	1.91E-02	4.29E-01	1.28E-02	2.27E-02	5.73E-01	2.54E-02	3.54E-02	4.73E-01
CETP	rs1864163	chr16:56997233	g	a	2.25E-01	4.20E-03	0.00E+00	G	A	-6.90E-03	7.20E-03	3.35E-01	-7.70E-03	8.60E-03	3.71E-01	-1.41E-02	1.31E-02	2.80E-01
CETP	rs289714	chr16:57007451	a	g	2.14E-01	5.00E-03	0.00E+00	G	A	5.80E-03	8.60E-03	4.99E-01	2.20E-03	1.02E-02	8.33E-01	1.30E-02	1.56E-02	4.05E-01
CETP	rs4784745	chr16:57014875	a	g	8.04E-02	5.50E-03	3.50E-46	A	G	-1.47E-02	6.50E-03	2.46E-02	-1.46E-02	7.80E-03	6.11E-02	-1.25E-02	1.19E-02	2.94E-01
CETP	rs5880	chr16:57015091	g	c	3.07E-01	9.00E-03	1.37E-233	G	C	-7.80E-03	1.54E-02	6.10E-01	-1.40E-02	1.84E-02	4.46E-01	6.00E-04	2.83E-02	9.83E-01
CETP	rs5883	chr16:57007353	t	c	1.15E-01	8.40E-03	1.76E-31	C	T	1.44E-02	1.43E-02	3.13E-01	2.35E-02	1.70E-02	1.65E-01	-1.41E-02	2.63E-02	5.93E-01
CETP	rs9923854	chr16:57017002	g	t	8.44E-02	9.70E-03	1.53E-15	T	G	9.00E-04	1.06E-02	9.34E-01	7.20E-03	1.26E-02	5.71E-01	-3.00E-04	1.93E-02	9.88E-01
NPC1L1	rs17655652	chr7:44580991	t	c	2.80E-02	4.40E-03	2.18E-10	T	C	-1.43E-02	7.70E-03	6.29E-02	-1.91E-02	9.30E-03	3.93E-02	-7.90E-03	1.40E-02	5.70E-01
NPC1L1	rs2072183	chr7:44579180	c	g	3.86E-02	4.70E-03	7.12E-16	G	C	7.60E-03	8.00E-03	3.44E-01	1.06E-02	9.50E-03	2.67E-01	-2.30E-03	1.45E-02	8.74E-01
NPC1L1	rs217406	chr7:44573761	g	c	3.88E-02	5.20E-03	4.09E-14	C	G	1.30E-02	9.00E-03	1.49E-01	1.75E-02	1.08E-02	1.04E-01	-5.50E-03	1.65E-02	7.40E-01
LDLR	rs2738464	chr19:11242307	c	g	4.22E-02	6.10E-03	2.73E-10	G	C	-8.80E-03	9.90E-03	3.74E-01	-1.14E-02	1.18E-02	3.37E-01	3.10E-03	1.81E-02	8.65E-01
LDLR	rs5742911	chr19:11243445	a	g	6.06E-02	5.70E-03	4.83E-24	A	G	-8.00E-03	6.90E-03	2.46E-01	-1.04E-02	8.20E-03	2.03E-01	4.00E-03	1.25E-02	7.50E-01
LDLR	rs6511720	chr19:11202306	g	t	2.21E-01	6.10E-03	3.85E-262	G	T	1.40E-03	1.03E-02	8.95E-01	4.00E-04	1.23E-02	9.72E-01	2.02E-02	1.85E-02	2.77E-01
LDLR	rs6511721	chr19:11206575	g	a	6.06E-02	5.10E-03	1.35E-29	G	A	-5.70E-03	6.90E-03	4.08E-01	-7.90E-03	8.20E-03	3.31E-01	3.20E-03	1.24E-02	8.00E-01
LDLR	rs688	chr19:11227602	t	c	5.40E-02	3.70E-03	1.01E-43	C	T	6.50E-03	6.20E-03	2.97E-01	1.06E-02	7.40E-03	1.55E-01	1.02E-02	1.13E-02	3.67E-01
LDLR	rs73015030	chr19:11207516	g	a	1.52E-01	1.48E-02	2.62E-22	G	A	2.29E-02	2.04E-02	2.62E-01	3.05E-02	2.45E-02	2.13E-01	9.60E-03	3.73E-02	7.96E-01
HMGCR	rs10515198	chr5:74641560	a	g	5.99E-02	6.10E-03	5.99E-22	G	A	2.50E-03	1.03E-02	8.10E-01	-7.40E-03	1.23E-02	5.48E-01	-5.00E-03	1.88E-02	7.92E-01
HMGCR	rs12916	chr5:74656539	c	t	7.33E-02	3.80E-03	7.79E-78	T	C	1.13E-02	6.30E-03	7.17E-02	1.36E-02	7.50E-03	6.89E-02	1.05E-02	1.15E-02	3.60E-01
HMGCR	rs2303152	chr5:74641707	a	g	4.23E-02	6.40E-03	1.04E-09	G	A	7.70E-03	1.02E-02	4.48E-01	2.22E-02	1.21E-02	6.72E-02	5.00E-04	1.86E-02	9.79E-01

Supplementary Table 3

Mendelian randomization results using genetic variants associated with blood lipid levels ($P < 5 \times 10^{-8}$) as instrumental variables.

Mendelian randomization results using all independent genetic variants associated with blood lipid levels ($P < 5 \times 10^{-8}$) as instrumental variables for low-density lipoprotein-cholesterol (LDL), high-density lipoprotein-cholesterol (HDL) and triglycerides (TG). Outcomes are risk of any breast cancer (BCA), risk of estrogen receptor positive (ERpos) and negative (ERneg) breast cancer.

	LDL	b	se	95% lci	95% uci	p	OR	95% LCI	95% UCI	Q' p-value
BCA	IVW	0.048	0.025	-0.001	0.098	0.055	1.050	0.999	1.103	3.33E-16
	Egger	0.004	0.039	-0.073	0.081	0.917	1.004	0.930	1.084	
	Intercept	0.003	0.002	-0.001	0.008	0.140	1.003	0.999	1.008	
	Median	0.045	0.025	-0.003	0.094	0.064	1.046	0.997	1.098	
Erpos	IVW	0.041	0.028	-0.014	0.095	0.144	1.041	0.986	1.100	1.59E-11
	Egger	-0.022	0.043	-0.106	0.062	0.604	0.978	0.899	1.064	
	Intercept	0.005	0.002	0.000	0.010	0.056	1.005	1.000	1.010	
	Median	0.010	0.029	-0.047	0.066	0.742	1.010	0.954	1.068	
Erneg	IVW	0.037	0.037	-0.036	0.109	0.321	1.037	0.965	1.115	5.19E-06
	Egger	0.028	0.058	-0.086	0.143	0.629	1.029	0.917	1.153	
	Intercept	0.001	0.003	-0.006	0.007	0.851	1.001	0.994	1.007	
	Median	0.051	0.047	-0.040	0.143	0.271	1.053	0.961	1.154	
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	HDL	b	se	95% lci	95% uci	p	OR	95% LCI	95% UCI	Q' p-value
BCA	IVW	0.096	0.032	0.034	0.158	0.003	1.101	1.034	1.171	7.06E-26
	Egger	0.056	0.053	-0.049	0.160	0.295	1.057	0.953	1.174	
	Intercept	0.002	0.003	-0.003	0.007	0.350	1.002	0.997	1.007	
	Median	0.054	0.027	0.001	0.108	0.047	1.056	1.001	1.114	
Erpos	IVW	0.103	0.034	0.037	0.169	0.002	1.109	1.038	1.185	9.68E-17
	Egger	0.048	0.057	-0.063	0.159	0.401	1.049	0.939	1.172	
	Intercept	0.003	0.003	-0.002	0.008	0.221	1.003	0.998	1.008	
	Median	0.048	0.032	-0.013	0.110	0.125	1.050	0.987	1.116	
Erneg	IVW	0.086	0.046	-0.004	0.177	0.062	1.090	0.996	1.194	2.40E-10
	Egger	0.108	0.078	-0.045	0.262	0.166	1.114	0.956	1.299	
	Intercept	-0.001	0.004	-0.008	0.006	0.725	0.999	0.992	1.006	
	Median	0.051	0.049	-0.046	0.148	0.303	1.052	0.955	1.159	
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	TG	b	se	95% lci	95% uci	p	OR	95% LCI	95% UCI	Q' p-value
BCA	IVW	-0.096	0.043	-0.181	-0.011	0.026	0.908	0.834	0.989	6.19E-26
	Egger	-0.124	0.073	-0.266	0.019	0.089	0.884	0.766	1.019	
	Intercept	0.002	0.004	-0.006	0.009	0.636	1.002	0.994	1.009	
	Median	-0.093	0.031	-0.154	-0.033	0.002	0.911	0.857	0.967	
Erpos	IVW	-0.099	0.047	-0.191	-0.007	0.036	0.906	0.826	0.993	3.99E-19
	Egger	-0.139	0.079	-0.293	0.016	0.078	0.871	0.746	1.016	
	Intercept	0.003	0.004	-0.005	0.011	0.529	1.003	0.995	1.011	
	Median	-0.087	0.036	-0.158	-0.017	0.015	0.916	0.854	0.983	
Erneg	IVW	-0.106	0.055	-0.213	0.001	0.052	0.899	0.808	1.001	6.99E-07
	Egger	-0.094	0.092	-0.274	0.086	0.308	0.911	0.761	1.090	
	Intercept	-0.001	0.005	-0.010	0.009	0.865	0.999	0.990	1.009	
	Median	-0.089	0.057	-0.201	0.023	0.121	0.915	0.818	1.024	

IVW Inverse variance-weighted method

Egger MR Egger method

Intercept Intercept term from MR Egger regression

Median Weighted Median method. Bowden et al. Genet Epidemiol 2016;40(4):304-314. PMID 27061298.

Q' p-value Q' heterogeneity test using modified second order weighting for two-sample Mendelian randomization studies. Bowden et al. Improving the accuracy of two-sample summary data Mendelian randomization: moving beyond the NOME assumption. Preprint manuscript posted on bioRxiv February 27, 2018. doi: <https://doi.org/10.1101/159442>

Supplementary Table 4

Mendelian randomization results using genetic variants associated with blood lipid levels ($P < 5 \times 10^{-8}$) as instrumental variables. For each lipid, all variants associated with any of the other two lipids ($P < 0.001$) have been excluded.

Mendelian randomization results using independent genetic variants associated with blood lipid levels ($P < 5 \times 10^{-8}$) as instrumental variables for low-density lipoprotein-cholesterol (LDL), high-density lipoprotein-cholesterol (HDL) and triglycerides (TG). Outcomes are risk of any breast cancer (BCA), risk of estrogen receptor positive (ERpos) and negative (ERneg) breast cancer. For each lipid, all variants that are also associated with any of the other two lipids ($P < 0.001$) have been excluded.

	LDL	b	se	95% lci	95% uci	p	OR	95% LCI	95% UCI	Q' p-value
BCA	IVW	0.114	0.048	0.020	0.208	0.017	1.121	1.021	1.231	3.97E-08
	Egger	0.169	0.129	-0.084	0.422	0.191	1.184	0.919	1.525	
	Intercept	-0.002	0.005	-0.012	0.007	0.647	0.998	0.988	1.007	
	Median	0.148	0.048	0.054	0.243	0.002	1.160	1.055	1.275	
ERpos	IVW	0.153	0.053	0.050	0.257	0.004	1.166	1.051	1.293	1.08E-05
	Egger	0.165	0.152	-0.133	0.463	0.278	1.179	0.876	1.588	
	Intercept	0.000	0.006	-0.012	0.011	0.934	1.000	0.988	1.011	
	Median	0.193	0.059	0.077	0.309	0.001	1.213	1.080	1.362	
ERneg	IVW	0.028	0.064	-0.097	0.152	0.663	1.028	0.908	1.165	0.041
	Egger	0.130	0.173	-0.209	0.469	0.451	1.139	0.812	1.598	
	Intercept	-0.004	0.007	-0.017	0.009	0.523	0.996	0.983	1.009	
	Median	0.034	0.083	-0.129	0.196	0.685	1.034	0.879	1.216	
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	HDL	b	se	95% lci	95% uci	p	OR	95% LCI	95% UCI	Q' p-value
BCA	IVW	0.075	0.058	-0.039	0.189	0.198	1.078	0.962	1.208	0.003
	Egger	0.117	0.168	-0.212	0.447	0.485	1.125	0.809	1.563	
	Intercept	-0.001	0.005	-0.012	0.009	0.787	0.999	0.988	1.009	
	Median	0.085	0.066	-0.045	0.214	0.200	1.088	0.956	1.239	
ERpos	IVW	0.123	0.056	0.013	0.233	0.028	1.131	1.014	1.263	0.169
	Egger	0.053	0.161	-0.263	0.369	0.742	1.054	0.769	1.446	
	Intercept	0.002	0.005	-0.008	0.012	0.641	1.002	0.992	1.012	
	Median	0.119	0.073	-0.024	0.262	0.102	1.127	0.977	1.300	
ERneg	IVW	0.015	0.106	-0.192	0.221	0.890	1.015	0.825	1.248	0.003
	Egger	0.466	0.289	-0.101	1.032	0.108	1.593	0.904	2.808	
	Intercept	-0.015	0.009	-0.033	0.003	0.096	0.985	0.967	1.003	
	Median	0.046	0.118	-0.185	0.277	0.697	1.047	0.831	1.319	
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	TG	b	se	95% lci	95% uci	p	OR	95% LCI	95% UCI	Q' p-value
BCA	IVW	-0.110	0.133	-0.371	0.151	0.407	0.896	0.690	1.163	0.153
	Egger	-0.463	0.401	-1.248	0.323	0.248	0.630	0.287	1.381	
	Intercept	0.013	0.014	-0.015	0.041	0.350	1.013	0.985	1.042	
	Median	-0.120	0.117	-0.349	0.108	0.302	0.887	0.705	1.114	
ERpos	IVW	-0.111	0.202	-0.507	0.285	0.583	0.895	0.602	1.330	0.036
	Egger	-0.361	0.707	-1.747	1.025	0.610	0.697	0.174	2.788	
	Intercept	0.009	0.025	-0.040	0.059	0.707	1.010	0.961	1.061	
	Median	-0.058	0.140	-0.332	0.216	0.679	0.944	0.717	1.242	
ERneg	IVW	-0.151	0.290	-0.719	0.418	0.603	0.860	0.487	1.519	0.056
	Egger	-1.478	0.537	-2.529	-0.426	0.006	0.228	0.080	0.653	
	Intercept	0.050	0.019	0.013	0.088	0.009	1.052	1.013	1.092	
	Median	-0.200	0.207	-0.607	0.206	0.335	0.819	0.545	1.229	

IVW Inverse variance-weighted method

Egger MR Egger method

Intercept Intercept term from MR Egger regression

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Supplementary Table 5

Results from MR-PRESSO applied after excluding genetic variants associated with other lipids ($P < 0.001$).

MR-PRESSO (Mendelian randomization pleiotropy residual sum and outlier) results using independent genetic variants associated with blood lipid levels (P<5e-08) as instrumental variables for low-density lipoprotein-cholesterol (LDL), high-density lipoprotein-cholesterol (HDL) and triglycerides (TG). Outcomes are risk of any breast cancer (BCA), risk of estrogen receptor positive (ERpos) and negative (ERneg) breast cancer. For each lipid, all variants that are also associated with any of the other two lipids (P<0.001) have been excluded.

		Causal estimate	SE	P-value	OR	95% LCI	95% UCI	MR-PRESSO global heterogeneity p-value	Q' p-value
LDL									
BCA	IVW (initial)	0.114	0.048	0.021	1.121	1.021	1.231	<0.001	3.97E-08
	IVW (after outlier removal)	0.090	0.037	0.020	1.094	1.018	1.176	0.109	0.102
ERPos	IVW (initial)	0.153	0.053	0.006	1.166	1.051	1.293	<0.001	1.08E-05
	IVW (after outlier removal)	0.129	0.043	0.004	1.138	1.047	1.237	0.125	0.124
Erneg	IVW (initial)	0.028	0.064	0.666	1.028	0.908	1.165	0.048	0.041
	IVW (after outlier removal)	0.031	0.055	0.577	1.032	0.926	1.150	0.438	0.438
HDL									
BCA	IVW (initial)	0.075	0.058	0.209	1.078	0.962	1.208	0.002	0.003
	IVW (after outlier removal)	0.072	0.051	0.171	1.074	0.973	1.187	0.092	0.090
Erpos	IVW (initial)	0.123	0.056	0.037	1.131	1.014	1.263	0.202	0.169
		-	-	-	-	-	-	-	-
Erneg	IVW (initial)	0.015	0.106	0.891	1.015	0.825	1.248	0.003	0.003
	IVW (after outlier removal)	0.084	0.091	0.365	1.088	0.910	1.301	0.115	0.108
TG*									
BCA	IVW (initial)	-0.110	0.133	0.468	0.896	0.690	1.163	0.316	0.153
		-	-	-	-	-	-	-	-
Erpos	IVW (initial)	-0.111	0.202	0.621	0.895	0.602	1.330	0.149	0.036
		-	-	-	-	-	-	-	-
Erneg	IVW (initial)	-0.151	0.290	0.639	0.860	0.487	1.519	0.037	0.056
		-	-	-	-	-	-	-	-

*(too few variants to exclude outliers)

IVW (initial)

Inverse variance-weighted analysis

IVW (after outlier removal)

Inverse variance-weighted analysis after removal of outlying variants identified by the MR-PRESSO heterogeneity test

Q' p-value

Q' heterogeneity test using modified second order weighting for two-sample Mendelian randomization studies. Bowden et al. Improving the accuracy of two-sample summary data Mendelian randomization: moving beyond the NOME assumption. Preprint manuscript posted on biorxiv February 27, 2018. doi: <https://doi.org/10.1101/159442>

MR-PRESSO global heterogeneity p-value

MR-PRESSO global heterogeneity test. Verbanck et al. Nat Genet 2018;50(5):693-698. PMID: 29686387.

Supplementary Table 6

Results from MR-PRESSO applied without excluding genetic variants associated with other lipids.

MR-PRESSO (Mendelian randomization pleiotropy residual sum and outlier) results using independent genetic variants associated with blood lipid levels (P<5e-08) as instrumental variables for low-density lipoprotein-cholesterol (LDL), high-density lipoprotein-cholesterol (HDL) and triglycerides (TG). Outcomes are risk of any breast cancer (BCA), risk of estrogen receptor positive (ERpos) and negative (ERneg) breast cancer.

		Causal estimate	SE	P-value	OR	95% LCI	95% UCI	MR-PRESSO global heterogeneity p-value	Q' p-value
LDL									
BCA	IVW (initial)	0.048	0.025	0.058	1.050	0.999	1.103	<2e-04	3.32E-16
	IVW (after outlier removal)	0.028	0.022	0.198	1.028	0.986	1.073	<2e-04	2.79E-07
ERPos	IVW (initial)	0.041	0.028	0.148	1.041	0.986	1.100	<2e-04	1.59E-11
	IVW (after outlier removal)	0.022	0.025	0.364	1.023	0.975	1.073	<2e-04	7.34E-06
Erneg	IVW (initial)	0.037	0.037	0.325	1.037	0.965	1.115	<2e-04	5.19E-06
	IVW (after outlier removal)	0.031	0.036	0.389	1.032	0.961	1.107	<2e-04	4.58E-05
HDL									
BCA	IVW (initial)	0.096	0.032	0.003	1.101	1.034	1.171	<2e-04	7.00E-26
	IVW (after outlier removal)	0.086	0.025	0.001	1.090	1.037	1.145	<2e-04	1.44E-09
Erpos	IVW (initial)	0.103	0.034	0.003	1.109	1.038	1.185	<2e-04	9.64E-17
	IVW (after outlier removal)	0.099	0.027	0.001	1.104	1.046	1.164	<2e-04	1.05E-05
Erneg	IVW (initial)	0.086	0.046	0.066	1.090	0.996	1.194	<2e-04	2.40E-10
	IVW (after outlier removal)	0.076	0.041	0.071	1.079	0.995	1.170	<2e-04	8.65E-06
TG									
BCA	IVW (initial)	-0.096	0.043	0.031	0.908	0.834	0.989	<2e-04	6.14E-26
	IVW (after outlier removal)	-0.109	0.027	1.72E-04	0.897	0.851	0.945	0.001	1.31E-03
Erpos	IVW (initial)	-0.099	0.047	0.041	0.906	0.826	0.993	<2e-04	3.98E-19
	IVW (after outlier removal)	-0.122	0.028	8.96E-05	0.885	0.837	0.936	0.051	4.52E-02
Erneg	IVW (initial)	-0.106	0.055	0.058	0.899	0.808	1.001	<2e-04	6.99E-07
	IVW (after outlier removal)	-0.091	0.044	0.046	0.913	0.837	0.996	0.051	1.36E-02

IVW (initial)

Inverse variance-weighted analysis

IVW (after outlier removal)

Inverse variance-weighted analysis after removal of outlying variants identified by the MR-PRESSO heterogeneity test

Q' p-value

Q' heterogeneity test using modified second order weighting for two-sample Mendelian randomization studies. Bowden et al. Improving the accuracy of two-sample summary data Mendelian randomization: moving beyond the NOME assumption. Preprint manuscript posted on biorxiv February 27, 2018. doi: <https://doi.org/10.1101/159442>

MR-PRESSO global heterogeneity p-value

MR-PRESSO global heterogeneity test. Verbanck et al. Nat Genet 2018;50(5):693-698. PMID: 29686387.

Supplementary Table 7

Mendelian randomization results of changes in blood lipids due to genetic variants in genes encoding drug targets.

The analysis takes into account the correlation between variants ($R^2 < 0.4$). References: Yavorska & Burgess Int J Epidemiol 2017;46(6):1734-1739. PMID: 28398548. Burgess et al. Stat Med 2016;35(11):1880-1906. PMID: 2661904.

Genetic correlations considered in MR		b	se	95% lci	95% uci	p	OR	95% LCI	95% UCI	Q' p-value
PCSK9										
BCA	IVW	0.095	0.039	0.019	0.172	0.014	1.100	1.019	1.187	0.867
	Egger	0.090	0.083	-0.073	0.253	0.281	1.094	0.929	1.288	
	Egger intercept	0.000	0.005	-0.010	0.011	0.928	1.000	0.990	1.011	
Erpos	IVW	0.076	0.046	-0.014	0.166	0.099	1.079	0.986	1.181	0.893
	Egger	0.055	0.086	-0.113	0.223	0.523	1.056	0.893	1.249	
	Egger intercept	0.002	0.006	-0.009	0.013	0.739	1.002	0.991	1.013	
Erneg	IVW	0.123	0.072	-0.019	0.264	0.089	1.130	0.982	1.302	0.619
	Egger	0.102	0.114	-0.120	0.325	0.368	1.108	0.887	1.384	
	Egger intercept	0.002	0.007	-0.012	0.016	0.815	1.002	0.988	1.016	
CETP										
BCA	IVW	0.065	0.020	0.026	0.105	0.001	1.068	1.026	1.110	0.530
	Egger	-0.003	0.072	-0.143	0.138	0.972	0.997	0.866	1.148	
	Egger intercept	0.011	0.010	-0.010	0.031	0.311	1.011	0.990	1.032	
Erpos	IVW	0.078	0.024	0.031	0.124	0.001	1.081	1.032	1.133	0.390
	Egger	0.005	0.077	-0.147	0.157	0.948	1.005	0.864	1.170	
	Egger intercept	0.011	0.011	-0.011	0.033	0.315	1.011	0.989	1.034	
Erneg	IVW	0.065	0.037	-0.007	0.137	0.075	1.067	0.993	1.147	0.938
	Egger	0.034	0.103	-0.167	0.235	0.741	1.035	0.846	1.266	
	Egger intercept	0.005	0.015	-0.024	0.034	0.746	1.005	0.976	1.035	
NPC1L1										
BCA	IVW	0.334	0.131	0.076	0.591	0.011	1.396	1.079	1.806	0.667
	Egger	-0.329	1.655	-3.573	2.914	0.842	0.719	0.028	18.433	
	Egger intercept	0.022	0.056	-0.087	0.131	0.687	1.023	0.917	1.140	
Erpos	IVW	0.449	0.157	0.141	0.757	0.004	1.567	1.151	2.133	0.625
	Egger	-0.423	1.860	-4.068	3.222	0.820	0.655	0.017	25.089	
	Egger intercept	0.030	0.063	-0.093	0.152	0.637	1.030	0.911	1.164	
Erneg	IVW	0.057	0.239	-0.411	0.525	0.811	1.059	0.663	1.691	0.797
	Egger	-1.088	1.660	-4.341	2.164	0.512	0.337	0.013	8.709	
	Egger intercept	0.038	0.058	-0.076	0.152	0.509	1.039	0.927	1.165	
LDLR										
BCA	IVW	0.012	0.036	-0.057	0.082	0.726	1.013	0.944	1.086	0.413
	Egger	-0.034	0.053	-0.139	0.070	0.522	0.966	0.871	1.073	
	Egger intercept	0.005	0.004	-0.003	0.013	0.231	1.005	0.997	1.013	
Erpos	IVW	0.023	0.049	-0.074	0.119	0.642	1.023	0.929	1.127	0.249
	Egger	-0.045	0.063	-0.169	0.079	0.475	0.956	0.844	1.082	
	Egger intercept	0.007	0.005	-0.002	0.017	0.141	1.007	0.998	1.017	
Erneg	IVW	-0.070	0.063	-0.193	0.052	0.260	0.932	0.824	1.053	0.897
	Egger	-0.178	0.145	-0.462	0.106	0.220	0.837	0.630	1.112	
	Egger intercept	0.012	0.012	-0.011	0.035	0.309	1.012	0.989	1.035	
HMGCR										
BCA	IVW	0.146	0.085	-0.021	0.313	0.086	1.157	0.980	1.367	0.827
	Egger	0.224	0.398	-0.557	1.005	0.574	1.251	0.573	2.731	
	Egger intercept	-0.006	0.027	-0.059	0.048	0.835	0.994	0.942	1.049	
Erpos	IVW	0.159	0.101	-0.039	0.357	0.116	1.172	0.961	1.429	0.168
	Egger	0.088	0.391	-0.677	0.854	0.822	1.092	0.508	2.348	
	Egger intercept	0.005	0.027	-0.047	0.058	0.847	1.005	0.954	1.059	
Erneg	IVW	0.130	0.155	-0.174	0.434	0.402	1.139	0.840	1.543	0.798
	Egger	0.489	0.859	-1.196	2.173	0.570	1.630	0.302	8.788	
	Egger intercept	-0.026	0.059	-0.142	0.089	0.656	0.974	0.868	1.093	