

Supplementary Material

Mendelian randomization implicates hyperlipidaemia as a risk factor for colorectal cancer

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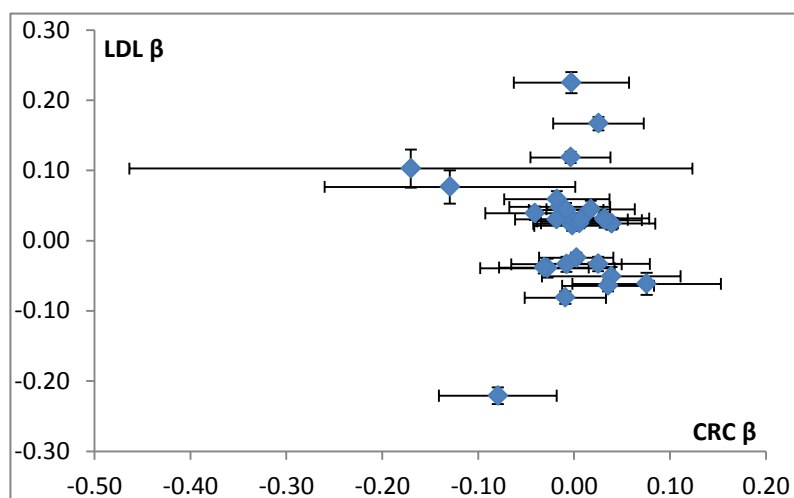
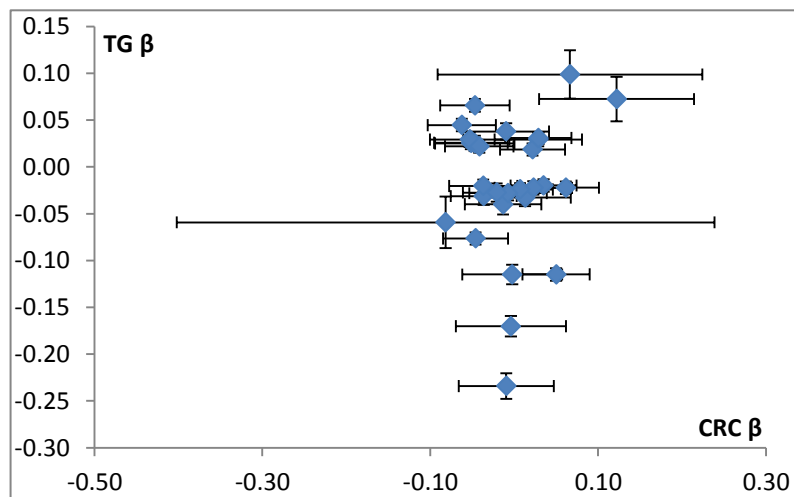
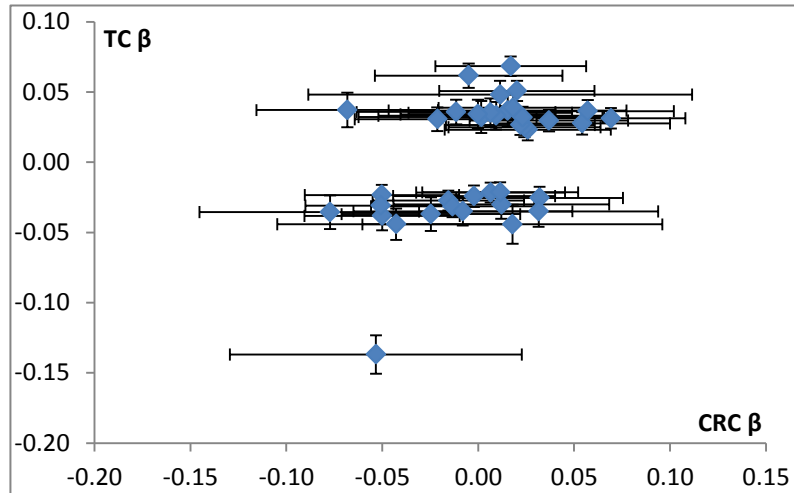
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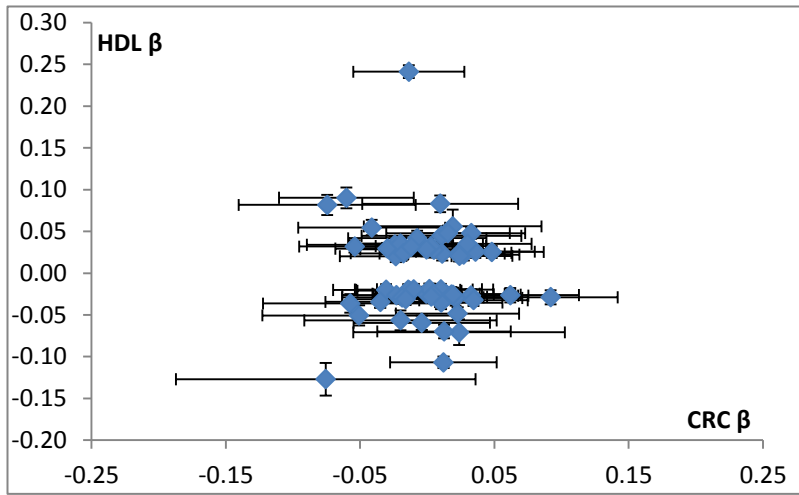
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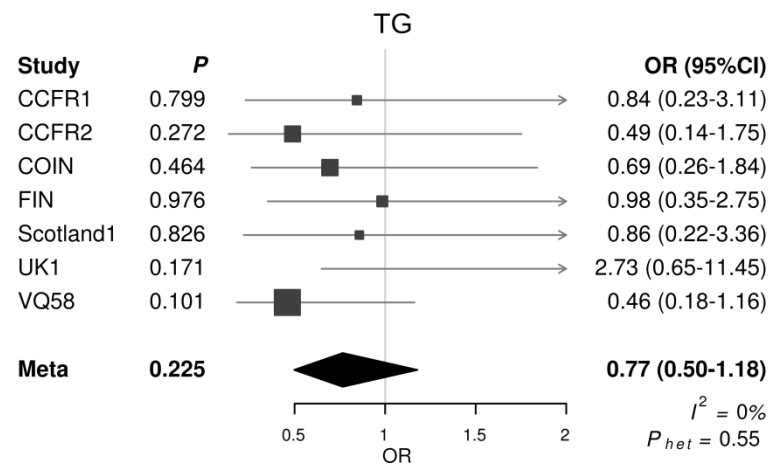
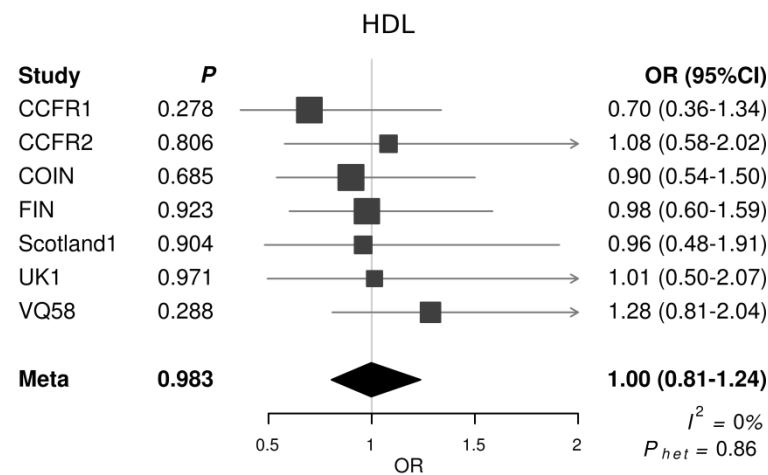
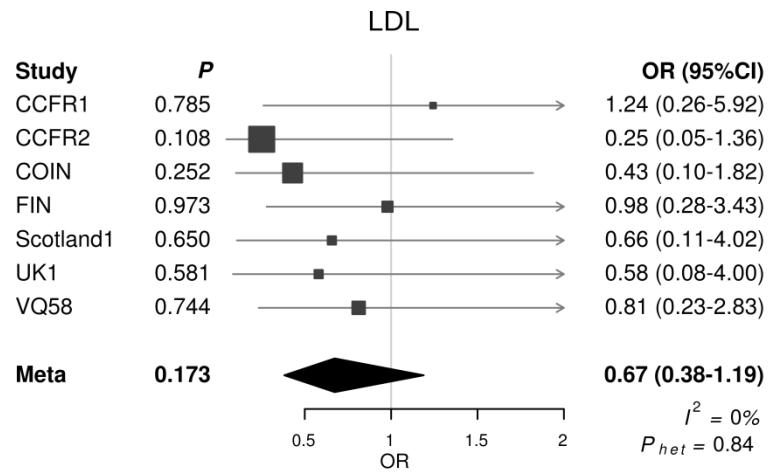
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Supplementary Figure 1: SNP-specific effects for risk of colorectal cancer. For each figure, the effect size of the respective measure for total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL), is plotted against the effect of colorectal cancer (CRC). Each point represents a SNP that was found to be associated with the trait effect. Lipid trait data obtained from the Global Lipids Genetics Consortium (GLGC) (Willer CJ, *et al.* Nat Genet 2013, doi: 10.1038/ng.2797).





Supplementary Figure 2: Meta-analysis OR for colorectal cancer per unit increase in genetic risk score, using the restricted SNP list for low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride (TG). Horizontal lines: 95% CIs. Box: OR point estimate; its area is proportional to the weight of the study. Diamond: overall summary estimate, with confidence interval given by its width. Vertical line: null value (OR = 1.0).



Supplementary Table 1: Median and range of standard deviations of lipid trait measurements in European cohorts of the Global Lipids Genetics Consortium from which genetic instruments were derived. Data obtained from Willer CJ, *et al.* Nat Genet 2013, doi: 10.1038/ng.2797.

	HDL (mg/dL)	LDL (mg/dL)	TC (mg/dL)	TG (mg/dL)
Median of SD	14.8	36.2	42.5	89.5
(range)	(10.7-28.3)	(22.4-78.6)	(30.2-59.9)	(36.3-176.4)

Supplementary Table 2: Effect size and standard error for each measure for blood lipids and CRC risk for SNPs used as instrumental variables.

(a) Total cholesterol (TC)

SNP ID	TC β	TC SE	CRC β	CRC SE	SNP ID	TC β	TC SE	CRC β	CRC SE
rs1077514	-0.0301	0.0052	0.01209	0.028716	rs7570971	0.0297	0.0039	0.036884	0.021067
rs2287623	-0.0273	0.0036	-0.01554	0.020127	rs2290159	-0.0369	0.0061	-0.02465	0.023742
rs11694172	0.0277	0.0041	0.054226	0.023352	rs12916	0.0684	0.0036	0.016941	0.020029
rs11563251	0.0368	0.0059	0.015338	0.031614	rs6882076	0.0508	0.0037	0.0202	0.020648
rs13315871	-0.0355	0.0061	-0.07722	0.034769	rs3177928	0.0482	0.005	0.01143	0.051042
rs2758886	0.0232	0.0039	0.025796	0.022094	rs2814982	-0.0441	0.0057	-0.04276	0.031595
rs9376090	-0.0254	0.004	0.032015	0.022201	rs9488822	0.0341	0.0053	-0.00012	0.020622
rs1997243	0.0332	0.005	0.00933	0.031257	rs12670798	0.0364	0.0041	0.057099	0.022941
rs3780181	-0.0442	0.0071	0.017876	0.039889	rs2072183	0.0358	0.0045	-0.01149	0.026442
rs10904908	0.025	0.0036	0.0241	0.020227	rs2081687	-0.0382	0.0052	-0.05009	0.020629
rs11603023	-0.0216	0.0036	0.006481	0.019819	rs2255141	-0.0314	0.0039	-0.01331	0.021688
rs4883201	-0.035	0.0056	0.031514	0.031799	rs10128711	0.0307	0.0043	-0.02127	0.021978
rs314253	-0.0233	0.0037	-0.05024	0.020508	rs11065987	-0.0309	0.0036	-0.05071	0.020079
rs138777	-0.0214	0.0037	0.011402	0.02073	rs1169288	0.0318	0.0039	0.023109	0.021263
rs4253772	0.0322	0.0058	0.001592	0.032643	rs2000999	0.0617	0.0044	-0.00497	0.024956
rs12027135	0.0266	0.0036	0.022066	0.019795	rs10401969	-0.1369	0.007	-0.0533	0.038833
rs7515577	0.0372	0.0063	-0.06823	0.024144	rs492602	0.0313	0.0037	0.06922	0.019809
rs2642442	0.0353	0.0052	0.006334	0.02176	rs2277862	-0.0349	0.0052	-0.008	0.029111
rs514230	0.0388	0.0053	0.018197	0.019782	rs2902940	-0.0241	0.0039	-0.00217	0.021552

(b) Triglyceride (TG)

SNP ID	TG β	TG SE	CRC β	CRC SE	SNP ID	TG β	TG SE	CRC β	CRC SE
rs6831256	0.0258	0.0035	-0.05147	0.022375	rs17145738	-0.1149	0.0053	-0.00234	0.030283
rs998584	0.0293	0.0037	0.028818	0.026524	rs11776767	0.022	0.0035	-0.04156	0.020802
rs38855	0.0187	-0.0033	0.021875	0.019777	rs1495741	-0.0399	0.0056	-0.01322	0.023308
rs1832007	-0.0327	0.0047	0.013001	0.02786	rs12678919	-0.1702	0.0056	-0.00389	0.033468
rs3198697	-0.0198	0.0034	0.03502	0.019973	rs2954029	-0.0764	0.0033	-0.04592	0.019766
rs8077889	0.0252	0.0042	-0.04698	0.024063	rs10761731	-0.0312	0.0047	-0.03631	0.019982
rs7248104	-0.0222	0.0034	0.061516	0.020096	rs2068888	-0.0241	0.0034	0.007017	0.01987
rs731839	-0.0224	0.0036	0.022942	0.023526	rs174546	0.0447	0.0034	-0.06247	0.020693
rs2131925	0.0657	0.0035	-0.04681	0.021047	rs964184	-0.2341	0.0069	-0.00946	0.028865
rs1260326	-0.1148	0.0034	0.050007	0.020408	rs11613352	-0.028	0.0039	-0.00728	0.02345
rs645040	0.0293	0.004	-0.05304	0.024076	rs2412710	0.0988	0.0132	0.06647	0.080463
rs442177	0.0309	0.0033	0.028915	0.020135	rs11649653	-0.0274	0.005	-0.02074	0.020645
rs9686661	0.0379	0.0044	-0.0096	0.026116	rs5756931	-0.0203	0.0035	-0.03693	0.020723

(c) Low Density Lipoprotein (LDL)

SNP ID	LDL β	LDL SE	CRC β	CRC SE	SNP ID	LDL β	LDL SE	CRC β	CRC SE
rs267733	-0.0331	0.0053	0.025045	0.027557	rs2479409	-0.0642	0.0041	0.035458	0.024391
rs2710642	0.0239	0.0038	-0.00191	0.020767	rs629301	0.1669	0.0049	0.025453	0.024105
rs10490626	-0.0508	0.0069	0.038907	0.036863	rs1367117	0.1186	0.004	-0.00367	0.021263
rs2030746	0.0214	0.0038	-0.0019	0.020167	rs4299376	-0.0812	0.0045	-0.00916	0.021638
rs1250229	0.0243	0.0042	0.03899	0.023305	rs3757354	-0.0382	0.0044	-0.03148	0.023902
rs7640978	-0.0392	0.0069	-0.0279	0.03577	rs1800562	-0.0615	0.008	0.075604	0.039531
rs17404153	-0.0336	0.0054	-0.00794	0.029441	rs1564348	0.0481	0.005	-0.01494	0.026778
rs4530754	0.0275	0.0036	1.05E-05	0.019691	rs11136341	0.0447	0.0062	0.017329	0.023505
rs4722551	0.0391	0.0049	-0.04085	0.026366	rs11220462	0.059	0.0059	-0.01805	0.028013
rs10102164	0.0316	0.0045	0.031518	0.023917	rs8017377	0.0303	0.0038	-0.01824	0.022132
rs4942486	-0.0243	0.0037	0.002276	0.019768	rs7206971	0.0292	0.0055	0.031978	0.019796
rs1801689	0.1028	0.0139	-0.17021	0.149789	rs6511720	-0.2209	0.0061	-0.07952	0.031259
rs364585	0.0249	0.0038	0.005459	0.020436	rs4420638	0.2251	0.0077	-0.00282	0.030684
rs2328223	0.0299	0.005	0.006866	0.025082	rs6029526	0.0436	0.0052	-0.00828	0.019841
rs5763662	0.0767	0.0121	-0.12953	0.066657					

(d) High Density Lipoprotein (HDL)

SNP ID	HDL β	HDL SE	CRC β	CRC SE	SNP ID	HDL β	HDL SE	CRC β	CRC SE
rs12748152	-0.0506	0.0062	-0.05079	0.036697	rs6450176	-0.0254	0.0039	0.004788	0.022856
rs12145743	0.0203	0.0036	-0.02339	0.02124	rs605066	0.0281	0.0049	0.005003	0.020148
rs4650994	-0.021	0.0034	-0.01312	0.01977	rs4731702	0.0294	0.0034	-0.02976	0.019758
rs1047891	-0.0269	0.0039	0.032468	0.021828	rs9987289	0.0817	0.0062	-0.07449	0.033657
rs2606736	-0.0246	0.0043	-0.00083	0.020414	rs2293889	-0.0312	0.0035	-0.01604	0.020209
rs2290547	-0.0297	0.0046	0.0211	0.025386	rs581080	0.0419	0.0045	-0.00744	0.026288
rs2013208	0.0254	0.0036	0.048114	0.01973	rs1883025	-0.0698	0.0041	0.012553	0.025375
rs13326165	-0.0289	0.0043	0.091868	0.025455	rs2923084	-0.0256	0.0045	0.018078	0.026258
rs6805251	-0.02	0.0035	-0.03059	0.020186	rs3136441	0.0545	0.0047	-0.04138	0.0279
rs10019888	-0.027	0.0046	0.01505	0.026872	rs7134375	0.0207	0.0035	0.023898	0.020136
rs3822072	-0.0251	0.0034	0.014044	0.022235	rs7134594	0.0354	0.0048	-0.01978	0.01973
rs2602836	-0.0192	0.0034	0.001673	0.019974	rs4759375	0.056	0.0102	0.019022	0.033759
rs1936800	-0.02	0.0034	-0.01417	0.019779	rs4765127	0.0324	0.005	0.00276	0.020981
rs702485	0.0243	0.0034	0.023978	0.019807	rs838880	-0.0484	0.0039	0.022615	0.023429
rs4142995	-0.0263	0.0037	-0.02289	0.020512	rs1532085	-0.1068	0.0035	0.012131	0.020267
rs4917014	0.0222	0.0036	0.027166	0.021148	rs2652834	0.0285	0.0043	-0.0006	0.025061
rs17173637	-0.0363	0.0057	-0.05727	0.033185	rs3764261	0.2412	0.0039	-0.01363	0.021083
rs970548	0.0258	0.0039	0.035886	0.022568	rs16942887	0.0831	0.0051	0.009637	0.029645
rs12801636	0.0235	0.0042	0.011193	0.023759	rs2925979	0.0351	0.0037	0.029883	0.024405
rs499974	-0.0263	0.0044	0.061846	0.026051	rs11869286	0.0319	0.0037	-0.05404	0.021108
rs4983559	-0.0197	0.0036	-0.01004	0.022409	rs4148008	-0.028	0.0038	0.00307	0.021227
rs1121980	-0.0196	0.0034	0.010172	0.019927	rs4129767	0.0237	0.0034	-0.01774	0.019943
rs17695224	-0.029	0.0039	-0.01857	0.022818	rs7241918	0.0902	0.0064	-0.0601	0.025622
rs4660293	-0.0353	0.004	0.01031	0.023392	rs12967135	-0.0262	0.0045	0.019321	0.023572
rs1689800	-0.0344	0.0036	-0.035	0.020788	rs7255436	0.0316	0.0053	-0.01196	0.022159
rs4846914	0.0479	0.0034	0.03285	0.020435	rs737337	-0.0565	0.0061	-0.01983	0.036536

rs12328675	0.0447	0.0052	0.010666	0.030301	rs386000	0.0479	0.0047	0.015518	0.023475
rs2972146	-0.0323	0.0035	0.034505	0.020641	rs1800961	-0.127	0.0099	-0.07554	0.056898
rs13107325	-0.0708	0.0078	0.023783	0.040182	rs6065906	-0.0594	0.0044	-0.00408	0.025891

Supplementary Table 3: SNP lists used in the restricted analysis for HDL, LDL, and TG, as *per Holmes et al* (Eur Heart J 2015, doi: 10.1093/eurheartj/eh571).

(a) HDL

rs12145743	rs2602836	rs1689800	rs7134594	rs7255436
rs4650994	rs702485	rs12328675	rs4759375	rs737337
rs1047891	rs4142995	rs13107325	rs838880	rs386000
rs2606736	rs4917014	rs6450176	rs2652834	
rs2290547	rs17173637	rs605066	rs16942887	
rs2013208	rs12801636	rs4731702	rs2925979	
rs13326165	rs499974	rs2293889	rs11869286	
rs6805251	rs4983559	rs2923084	rs4148008	
rs10019888	rs17695224	rs3136441	rs4129767	
rs3822072	rs4660293	rs7134375	rs12967135	

(b) LDL

rs267733	rs364585
rs2710642	rs2328223
rs1250229	rs5763662
rs4942486	rs8017377
rs1801689	

(c) TG

rs38855	rs9686661
rs1832007	rs11776767
rs3198697	rs10761731
rs8077889	rs2068888
rs7248104	rs2412710
rs645040	rs11649653
rs442177	rs5756931

Supplementary Data: Pairwise R² calculations for the SNPs used as instrumental variables.

Separate file