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1 Simulation

1.1 Supplementary Figures

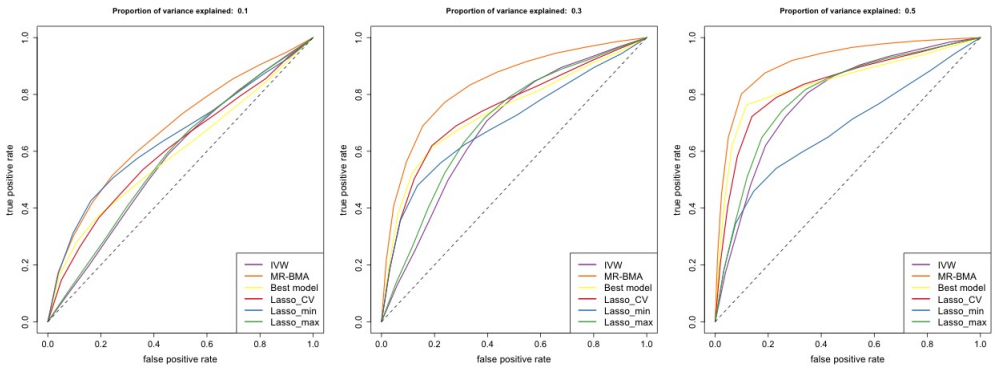

Figure 1: Receiver Operating Characteristic (ROC) curve for setting A including a moderate number of risk factors ($d = 12$) of which 4 are true positive effects. Proportion of variance explained is set to 0.1 (left) 0.3 (middle) and 0.5 (right).

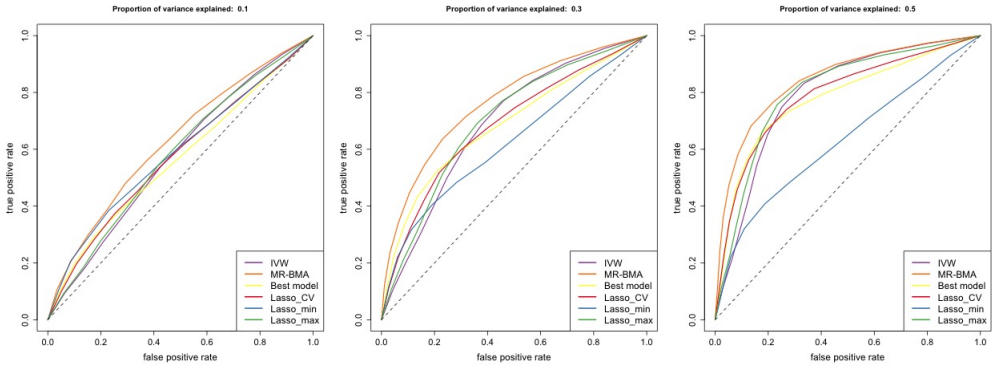

Figure 2: Receiver Operating Characteristic (ROC) curve for setting B including a moderate number of risk factors ($d = 12$) of which 8 are true positive effects. Proportion of variance explained is set to 0.1 (left) 0.3 (middle) and 0.5 (right).

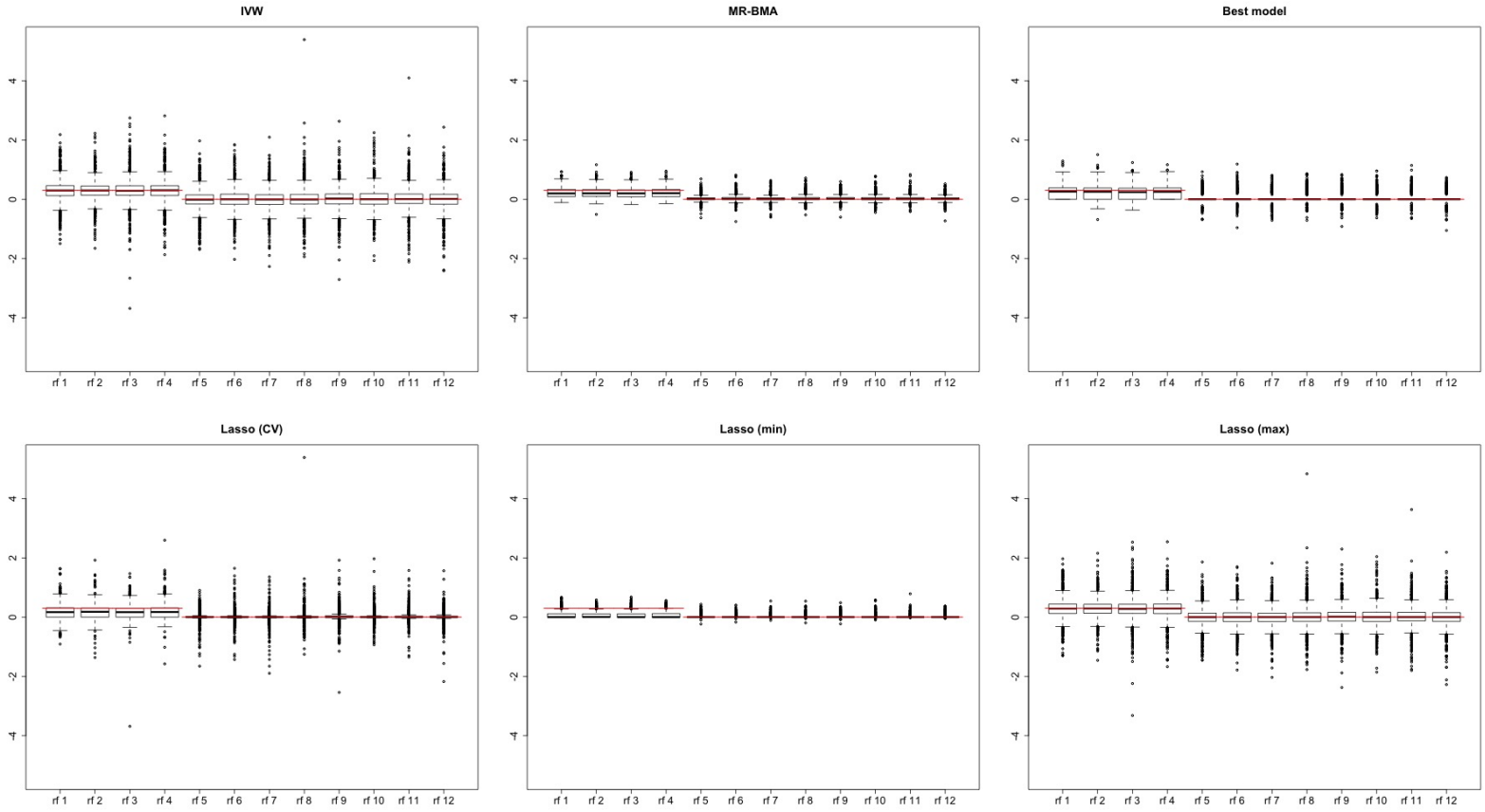

Figure 3: Boxplots of the causal effect estimates for setting A including a moderate number of risk factors ($d = 12$) of which 4 are true positive effects. The true causal effects are marked in red. From top left to bottom right are the competing approaches: IVW, MR-BMA, best model and Lasso with its three implementations (cross-validation, maximum penalty and minimum penalty). Proportion of variance explained is set to 0.3.

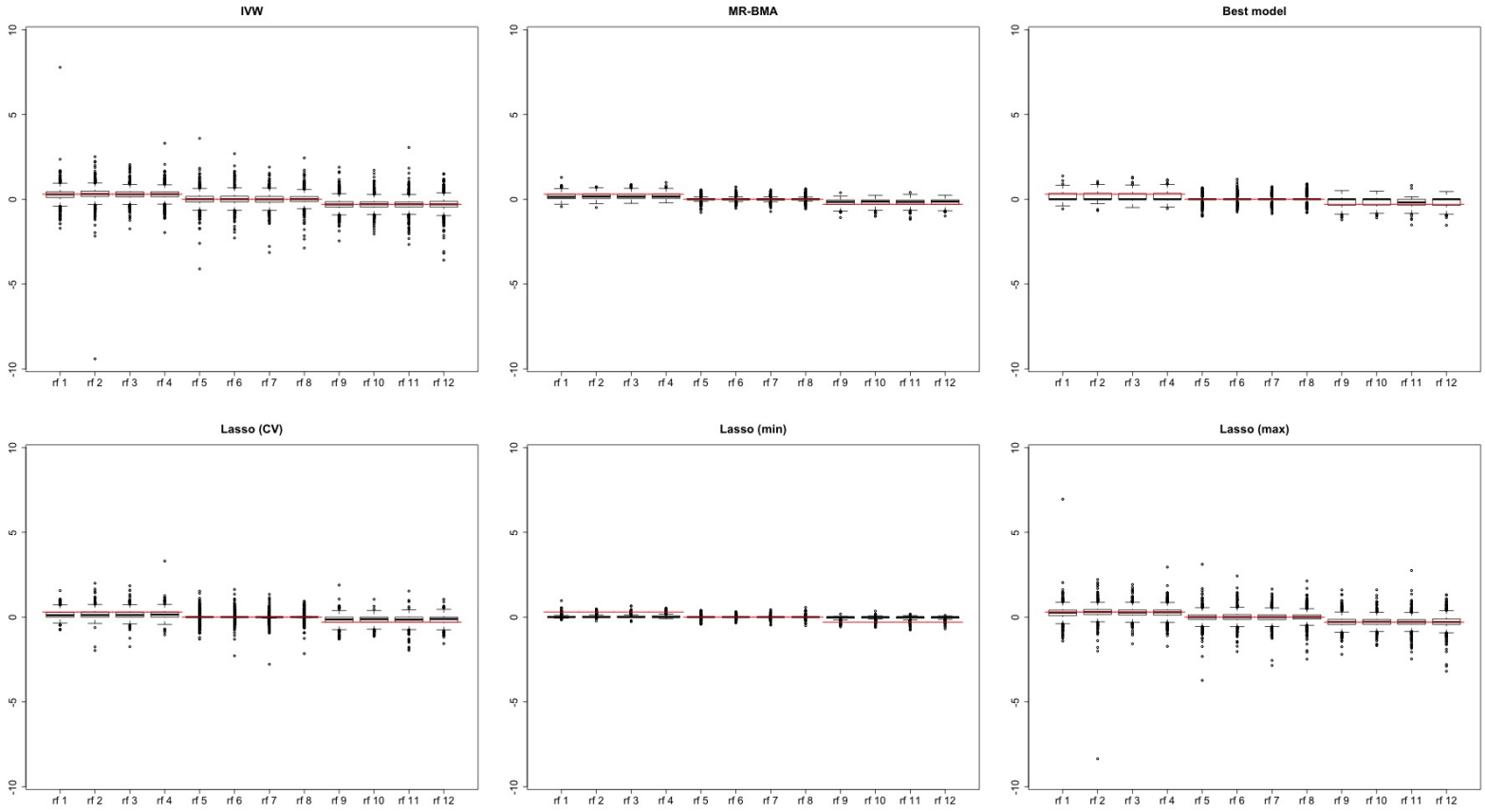

Figure 4: Boxplots of the causal effect estimates for setting B including a moderate number of risk factors ($d = 12$) of which 4 have a positive and 4 have a negative causal effect. The true causal effects are marked in red. From top left to bottom right are the competing approaches: IVW, MR-BMA, best model and Lasso with its three implementations (cross-validation, maximum penalty and minimum penalty). Proportion of variance explained is set to 0.3.

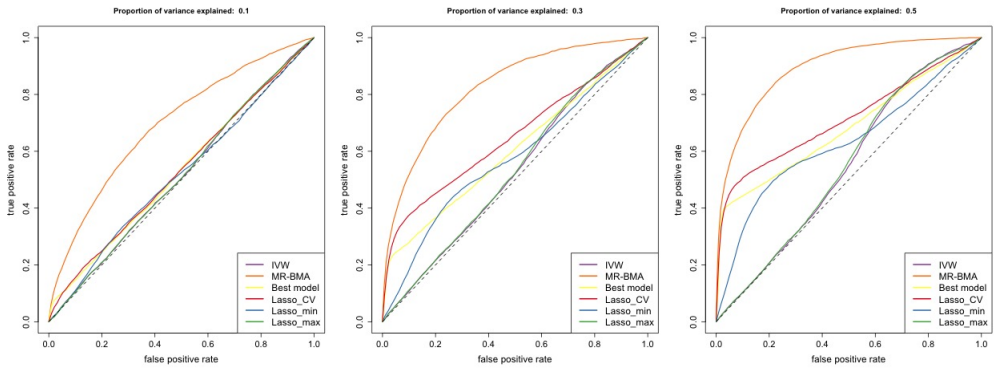

Figure 5: Receiver Operating Characteristic (ROC) curve for setting A including a large number of risk factors ($d = 92$) of which 4 are true positive effects. Proportion of variance explained is set to 0.1 (left) 0.3 (middle) and 0.5 (right).

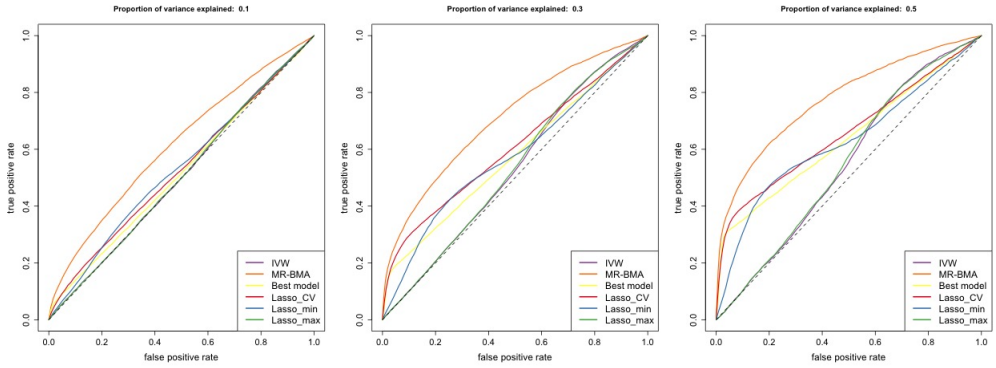

Figure 6: Receiver Operating Characteristic (ROC) curve for setting B including a large number of risk factors ($d = 92$) of which 8 are true positive effects. Proportion of variance explained is set to 0.1 (left) 0.3 (middle) and 0.5 (right).

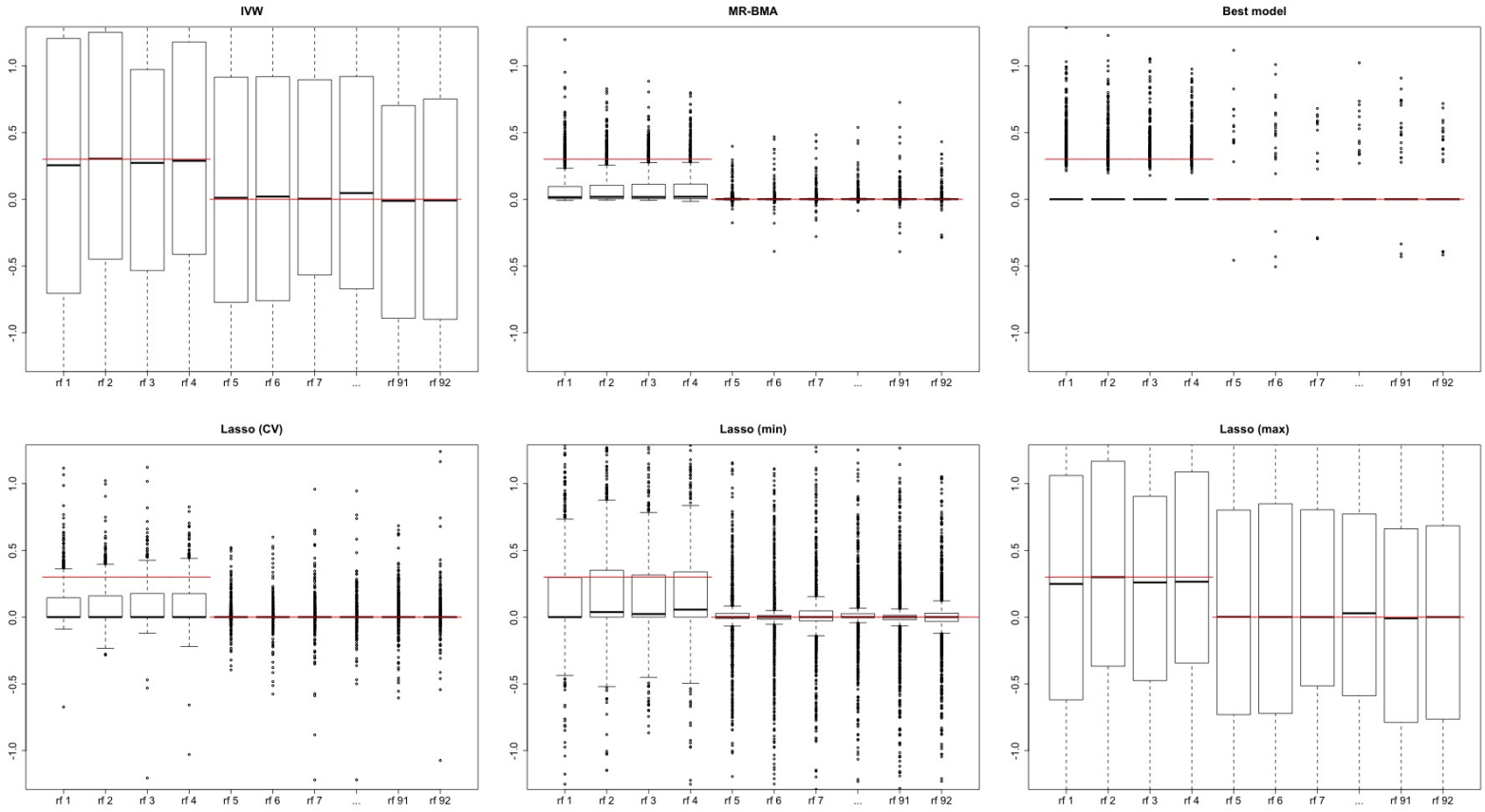

Figure 7: Boxplots of the causal effect estimates for setting A including a large number of risk factors ($d = 92$) of which 4 are true positive effects. Risk factors 8 to 90 are omitted. The true causal effects are marked in red. From top left to bottom right are the competing approaches: IVW, MR-BMA, best model and Lasso with its three implementations (cross-validation, maximum penalty and minimum penalty). Proportion of variance explained is set to 0.3.

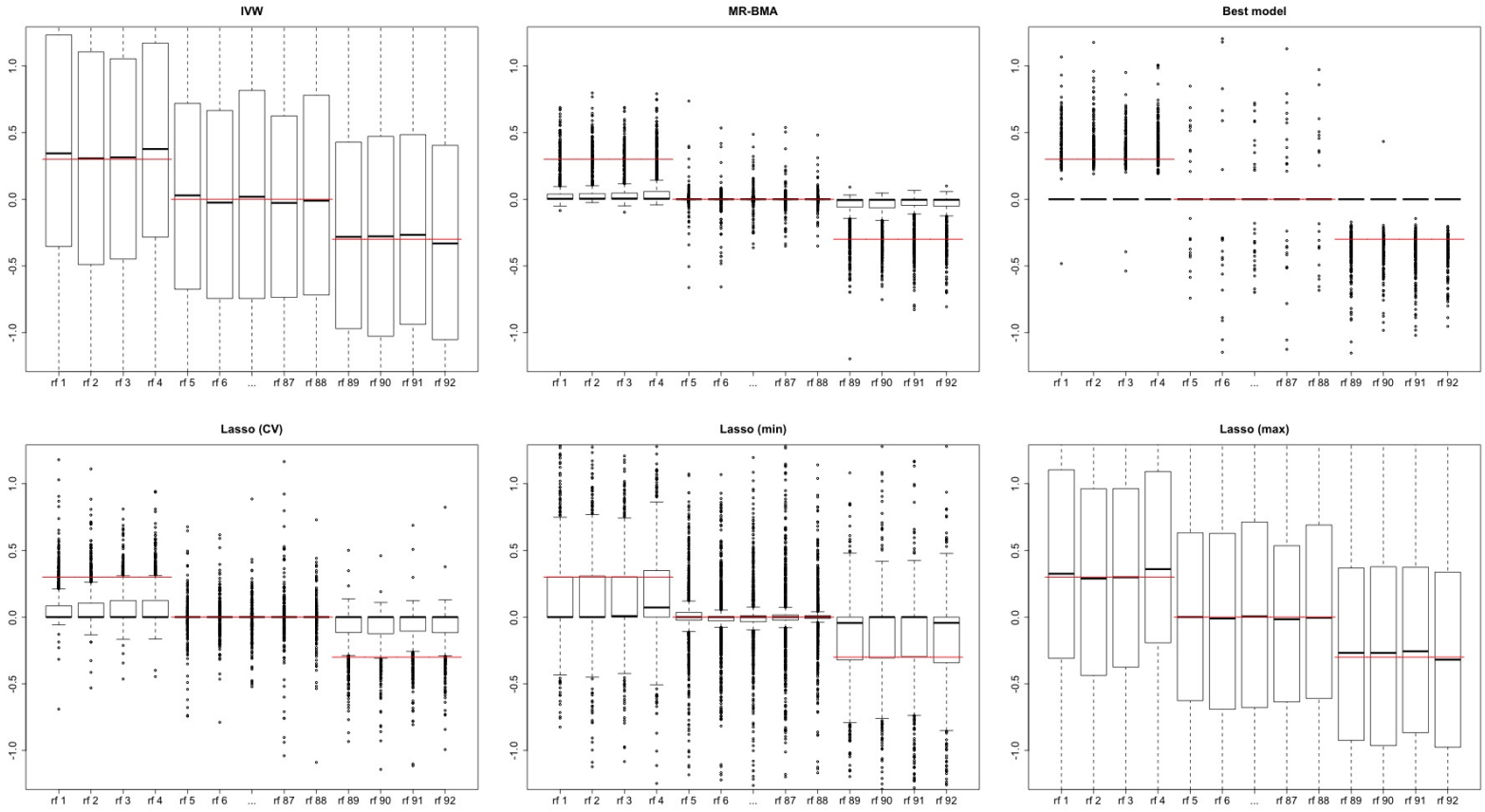

Figure 8: Boxplots of the causal effect estimates for setting B including a large number of risk factors ($d = 92$) of which 4 have a positive and 4 have a negative causal effect. Risk factors 7 to 86 are omitted. The true causal effects are marked in red. From top left to bottom right are the competing approaches: IVW, MR-BMA, best model and Lasso with its three implementations (cross-validation, maximum penalty and minimum penalty). Proportion of variance explained is set to 0.3.

2 Application

2.1 Supplementary Tables

A) Model averaging

	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	LDL.D	0.523	-0.227
2	XS.VLDL.TG	0.243	-0.125
3	S.HDL.TG	0.237	-0.103
4	IDL.TG	0.222	-0.120
5	Gln	0.190	-0.074
6	S.VLDL.TG	0.172	-0.070
7	XXL.VLDL.TG	0.157	0.078
8	S.LDL.C	0.139	0.059
9	Serum.TG	0.125	-0.056
10	Est.C	0.093	0.030

B) Individual models

	risk factor(s)	*PP*	$\hat{\theta}_{\gamma}$
1	LDL.D,S.HDL.TG	0.026	-0.376,-0.398
2	LDL.D,S.VLDL.TG	0.021	-0.485,-0.379
3	LDL.D,Serum.TG	0.008	-0.454,-0.365
4	S.HDL.TG	0.008	-0.433
5	Est.C,IDL.TG	0.008	0.393,-0.625
6	LDL.D,XS.VLDL.TG	0.007	-0.339,-0.324
7	XS.VLDL.TG	0.007	-0.373
8	LDL.D,M.VLDL.TG	0.006	-0.545,-0.408
9	Gln,LDL.D,S.HDL.TG	0.005	-0.353,-0.357,-0.437
10	S.HDL.TG,XXL.VLDL.TG	0.005	-0.653,0.45

Table 1: Ranking of risk factors (top ten) for age-related macular degeneration according to their marginal inclusion probability (*MIP*) A) and the best ten individual model according to their posterior probability (*PP*) B). Calculation is based on all genetic variants $n = 148$ including the *LIPC* region. Abbreviations: rf=risk factor, *MIP*=marginal inclusion probability, MACE= model-averaged causal effect, *PP*=posterior probability for indivudal model.

	rs	region	q M1	q M2	min q
1	rs6859	APOE	17.007	17.388	17.007
2	rs492602	FUT2	15.526	13.899	13.899
3	rs174532	MYRF	11.939	11.078	11.078
4	rs6489818	MAPKAPK5	11.226	10.857	10.857
5	rs103294	AC245884.7	8.857	9.255	8.857
6	rs4465830	ZNF335	7.395	11.127	7.395
7	rs3817588	GCKR	7.263	8.095	7.263
8	rs261342	LIPC	7.11	8.107	7.11
9	rs2710642	EHBP1	6.662	6.955	6.662
10	rs903319	SLC2A2	8.06	6.567	6.567
11	rs2587534	AL160408.6	6.498	6.063	6.063
12	rs9491696	RSPO3	6.317	5.658	5.658
13	rs8176720	ABO	5.415	4.972	4.972
14	rs688	LDLR	4.85	5.178	4.85
15	rs1689797	LINC01344	4.638	5.325	4.638
16	rs1781930	AKR1C8P	4.978	4.585	4.585
17	rs2925979	CMIP	4.66	4.516	4.516
18	rs6882076	TIMD4	5.742	4.023	4.023
19	rs7703051	HMGCR	4.581	3.988	3.988
20	rs38855	MET	4.636	3.896	3.896
21	rs702485	DAGLB	4.863	3.892	3.892
22	rs3741414	INHBC	3.873	4.434	3.873
23	rs2602836	ADH5	3.724	4.357	3.724
24	rs4148218	ABCG8	3.967	3.592	3.592
25	rs3822072	FAM13A	3.549	3.858	3.549
26	rs9930333	FTO	3.351	3.428	3.351
27	rs7225700	THCAT158	3.127	3.305	3.127
28	rs6680658	GALNT2	3.124	3.675	3.124
29	rs2328223	SNX5	3.189	2.867	2.867
30	rs1800562	HFE	3.307	2.857	2.857

Table 2: q-statistic for all $n = 148$ genetic variants for the best individual model 1 (M1: LDL.D, and S.HDL.TG), and model 2 (M2: LDL.D, and S.VLDL.TG), and the minimum q of each variant in both models. This table displays the 30 variants with the largest minimum q and the region they fall in.

	rs	region	Cd M1	Cd M2	min Cd
1	rs261342	LIPC	0.989	1.087	0.989
2	rs4465830	ZNF335	0.188	0.108	0.108
3	rs6859	APOE	0.081	0.076	0.076
4	rs174532	MYRF	0.062	0.062	0.062
5	rs3817588	GCKR	0.058	0.085	0.058
6	rs5880	CETP	0.056	0.071	0.056
7	rs103294	AC245884.7	0.045	0.044	0.044
8	rs686030	TTC39B	0.054	0.04	0.04
9	rs7703051	HMGCR	0.039	0.045	0.039
10	rs1689797	LINC01344	0.037	0.031	0.031
11	rs2710642	EHBP1	0.031	0.033	0.031
12	rs2587534	AL160408.6	0.02	0.018	0.018
13	rs799160	intergenic	0.017	0.016	0.016
14	rs894210	intergenic	0.015	0.022	0.015
15	rs10493326	DOCK7	0.011	0.017	0.011
16	rs515135	APOB(intergenic)	0.019	0.011	0.011
17	rs2068888	CYP26A1	0.012	0.011	0.011
18	rs7225700	THCAT158	0.011	0.012	0.011
19	rs1515110	NR	0.014	0.01	0.01
20	rs1800562	HFE	0.01	0.012	0.01
21	rs3741414	INHBC	0.01	0.016	0.01
22	rs10401969	SUGP1	0.009	0.025	0.009
23	rs903319	SLC2A2	0.02	0.008	0.008
24	rs2980885	AC091114.1	0.007	0.01	0.007
25	rs2923084	AMPD3	0.007	0.008	0.007
26	rs3198697	PDXDC1	0.007	0.01	0.007
27	rs2925979	CMIP	0.007	0.007	0.007
28	rs688	LDLR	0.007	0.01	0.007
29	rs6882076	TIMD4	0.006	0.016	0.006
30	rs2326077	intergenic	0.006	0.006	0.006

Table 3: Cook's distance (Cd) based on $n = 148$ genetic variants including *LIPC* for the best individual model 1 (M1: LDL.D, and S.HDL.TG), and model 2 (M2: LDL.D, and S.VLDL.TG), and the minimum Cook's distance of each variant in any of the models. This table displays the 30 variants with the largest minimum Cook's distance and the region they fall in.

	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.677	0.332
2	L.HDL.C	0.254	0.099
3	Gln	0.164	-0.055
4	Tyr	0.114	-0.034
5	HDL.D	0.085	0.023
6	XS.VLDL.TG	0.079	-0.018
7	Ace	0.069	0.017
8	LDL.D	0.061	-0.014
9	IDL.TG	0.061	-0.011
10	S.VLDL.TG	0.059	-0.013
11	Serum.TG	0.054	-0.013
12	XXL.VLDL.TG	0.053	0.015
13	Serum.C	0.047	-0.009
14	HDL.C	0.045	0.008
15	M.HDL.C	0.045	-0.009
16	His	0.043	-0.008
17	S.HDL.TG	0.043	-0.006
18	S.VLDL.C	0.038	-0.004
19	M.VLDL.C	0.038	-0.004
20	XL.HDL.TG	0.037	0.004
21	Val	0.034	0.006
22	ApoA1	0.034	-0.005
23	ApoB	0.033	-0.004
24	L.VLDL.C	0.032	-0.004
25	M.VLDL.TG	0.032	0.004
26	Ala	0.030	0.004
27	Cit	0.030	0.004
28	XL.VLDL.TG	0.029	-0.003
29	L.VLDL.TG	0.028	-0.001
30	S.LDL.C	0.028	0.000
31	LDL.C	0.027	-0.002
32	Lac	0.026	0.003
33	Ile	0.025	0.001
34	Leu	0.024	0.001
35	IDL.C	0.024	-0.001
36	Urea	0.023	0.000
37	Glc	0.023	-0.001
38	Pyr	0.023	0.000
39	SM	0.023	-0.002
40	Phe	0.022	0.000
41	Tot.FA	0.022	-0.001
42	VLDL.D	0.022	0.001
43	TotPG	0.022	-0.002
44	Alb	0.022	-0.002
45	Est.C	0.021	0.000
46	Gly	0.021	0.002
47	Glol	0.021	0.001
48	Crea	0.020	-0.001
49	AcAce	0.019	0.000

Table 4: Ranking of risk factors for age-related macular degeneration according to their marginal inclusion probability (*MIP*) after excluding genetic variants in the *LIPC, FUT2* and *APOE* region $n = 145$. Abbreviations: rf=risk factor, *MIP*=marginal inclusion probability, MACE= model-averaged causal effect.

	rs	region	Q M1	Q M2	Q M3	Q M4	Q M5	Q M6	min Q
1	rs103294	AC245884.7	13.03	13.155	10.253	11.936	11.203	14.449	10.253
2	rs6489818	MAPKAPK5	11.244	9.575	7.592	10.53	10.356	9.883	7.592
3	rs6882076	TIMD4	9.536	9.118	9.712	6.708	6.503	10.504	6.503
4	rs2587534	AL160408.6	5.931	8.936	7.9	6.551	6.735	8.409	5.931
5	rs903319	SLC2A2	7.514	6.651	5.481	7.275	7.255	6.379	5.481
6	rs9491696	RSPO3	5.651	5.974	7.465	5.017	4.971	5.479	4.971
7	rs1781930	AKR1C8P	5.176	4.259	5.251	4.996	5.072	4.851	4.259
8	rs8176720	ABO	3.929	6.312	7.846	4.592	4.734	5.197	3.929
9	rs1689797	LINC01344	6.403	4.747	3.815	4.635	4.587	5.648	3.815
10	rs38855	MET	3.768	5.98	5.388	5.082	4.973	5.205	3.768
11	rs702485	DAGLB	3.569	3.439	3.946	3.887	3.768	3.597	3.439
12	rs3822072	FAM13A	5.105	3.376	4.495	4.504	4.606	4.099	3.376
13	rs2710642	EHBP1	3.632	3.432	4.271	4.381	4.714	3.318	3.318
14	rs6680658	GALNT2	3.216	3.885	4.225	3.926	3.527	3.577	3.216
15	rs9693857	AC022784.6	4.752	3.147	3.216	3.966	4.246	3.601	3.147
16	rs2923084	AMPD3	5.067	2.814	2.805	2.956	2.944	3.933	2.805
17	rs174532	MYRF	2.708	4.701	2.946	3.405	3.927	4.12	2.708
18	rs2925979	CMIP	3.135	3.14	2.629	3.417	3.486	3.142	2.629
19	rs499974	RN7SL786P	3.109	3.324	3.722	2.597	2.616	3.09	2.597
20	rs688	LDLR	2.562	5.557	5.382	3.97	4.071	4.856	2.562
21	rs12145743	RRNAD1	2.78	2.413	2.793	2.711	2.541	2.587	2.413
22	rs7264396	FER1L4	2.74	3.251	3.486	2.562	2.372	3.438	2.372
23	rs5880	CETP	5.433	2.877	2.346	2.687	2.73	4.246	2.346
24	rs1515110	NR	2.213	3.003	2.272	2.999	2.733	2.575	2.213
25	rs3761445	MAFF	2.379	2.911	2.233	2.655	2.551	2.205	2.205
26	rs9930333	FTO	3.872	2.154	2.579	3.299	3.245	2.299	2.154
27	rs17173637	AOC1	2.405	2.595	3.956	2.365	2.147	3.062	2.147
28	rs17789218	intergenic	3.72	2.12	2.249	3.145	3.219	3.512	2.12
29	rs10773105	SCARB1	2.088	2.945	2.805	2.245	2.243	2.801	2.088
30	rs7703051	HMGCR	5.974	3.24	2.076	3.246	3.319	4.009	2.076

Table 5: q-statistic for $n = 145$ genetic variants after excluding *LIPC, FUT2* and *APOE* the best individual model 1 (M1: XL.HDL.C), model 2 (M1: L.HDL.C), model 3 (M3: L.HDL.C and Glutamine), model 4 (M4: XL.HDL.C and XS.VLDL.TG), model 5 (M5: IDL.TG and XL.HDL.C), model 6 (M6: HDL.D) and the minimum q-statistic for in any model. This table displays the 30 variants with the largest minimum q and the region they fall in.

	rs	region	*Cd* M1	*Cd* M2	*Cd* M3	*Cd* M4	*Cd* M5	*Cd* M6	min *Cd*
1	rs5880	CETP	0.234	0.277	0.12	0.122	0.122	0.297	0.12
2	rs4465830	ZNF335	0.216	0.311	0.121	0.106	0.113	0.271	0.106
3	rs1689797	LINC01344	0.061	0.098	0.047	0.047	0.048	0.086	0.047
4	rs686030	TTC39B	0.072	0.062	0.034	0.04	0.033	0.062	0.033
5	rs174532	MYRF	0.052	0.027	0.028	0.039	0.057	0.039	0.027
6	rs903319	SLC2A2	0.047	0.025	0.02	0.024	0.024	0.021	0.02
7	rs1800961	HNF4A	0.015	0.033	0.017	0.013	0.014	0.011	0.011
8	rs9491696	RSPO3	0.016	0.013	0.026	0.01	0.011	0.02	0.01
9	rs7897379	REEP3	0.017	0.018	0.014	0.013	0.009	0.024	0.009
10	rs499974	RN7SL786P	0.016	0.021	0.014	0.009	0.009	0.018	0.009
11	rs103294	AC245884.7	0.028	0.026	0.066	0.023	0.039	0.009	0.009
12	rs1515110	NR	0.008	0.025	0.014	0.012	0.008	0.016	0.008
13	rs894210	intergenic	0.008	0.046	0.04	0.023	0.011	0.018	0.008
14	rs10773105	SCARB1	0.015	0.042	0.021	0.009	0.008	0.04	0.008
15	rs702485	DAGLB	0.013	0.014	0.011	0.008	0.007	0.014	0.007
16	rs17788930	FNBP4	0.014	0.014	0.007	0.011	0.01	0.014	0.007
17	rs2602836	ADH5	0.016	0.011	0.006	0.011	0.011	0.016	0.006
18	rs4983559	AL590326.2	0.008	0.013	0.006	0.007	0.009	0.006	0.006
19	rs11045163	intergenic	0.009	0.01	0.005	0.006	0.007	0.007	0.005
20	rs2278236	ANGPTL4	0.01	0.015	0.044	0.005	0.005	0.01	0.005
21	rs355838	COBLL1	0.013	0.007	0.004	0.009	0.008	0.008	0.004
22	rs688	LDLR	0.005	0.011	0.006	0.025	0.029	0.004	0.004
23	rs10493326	DOCK7	0.003	0.017	0.009	0.021	0.014	0.004	0.003
24	rs6680658	GALNT2	0.003	0.011	0.007	0.007	0.003	0.008	0.003
25	rs217386	NPC1L1	0.006	0.006	0.004	0.003	0.003	0.006	0.003
26	rs10019888	C4orf52	0.003	0.002	0.002	0.002	0.002	0.002	0.002
27	rs205262	C6orf106	0.002	0.005	0.002	0.003	0.002	0.006	0.002
28	rs17789218	intergenic	0.034	0.003	0.002	0.017	0.017	0.031	0.002
29	rs3996352	intergenic	0.003	0.004	0.002	0.005	0.004	0.008	0.002
30	rs9930333	FTO	0.002	0.002	0.003	0.004	0.004	0.002	0.002

Table 6: Cook's distance (Cd) based on $n = 145$ genetic variants after excluding *LIPC, FUT2* and *APOE* the best individual model 1 (M1: XL.HDL.C), model 2 (M1: L.HDL.C), model 3 (M3: L.HDL.C and Glutamine), model 4 (M4: XL.HDL.C and XS.VLDL.TG), model 5 (M5: IDL.TG and XL.HDL.C), model 6 (M6: HDL.D) and the minimum Cook's distance for in any model. This table displays the 30 variants with the largest minimum Cook's distance and the region they fall in.

$p = 0.01$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.603	0.305
2	L.HDL.C	0.288	0.111
3	HDL.D	0.087	0.031
4	HDL.C	0.024	0.008
5	Gln	0.019	-0.007
6	Tyr	0.011	-0.003
7	XS.VLDL.TG	0.010	-0.002
8	IDL.TG	0.009	-0.002
9	Ace	0.009	0.002
10	S.HDL.TG	0.009	-0.002

$p = 0.05$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.643	0.320
2	L.HDL.C	0.270	0.105
3	Gln	0.089	-0.030
4	HDL.D	0.084	0.027
5	Tyr	0.055	-0.016
6	XS.VLDL.TG	0.044	-0.009
7	Ace	0.038	0.010
8	IDL.TG	0.036	-0.007
9	HDL.C	0.033	0.008
10	LDL.D	0.031	-0.007

$p = 0.1$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.687	0.337
2	L.HDL.C	0.253	0.098
3	Gln	0.153	-0.051
4	Tyr	0.100	-0.029
5	HDL.D	0.080	0.022
6	XS.VLDL.TG	0.073	-0.016
7	Ace	0.066	0.017
8	IDL.TG	0.060	-0.011
9	LDL.D	0.054	-0.012
10	S.VLDL.TG	0.053	-0.012

$p = 0.2$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.738	0.355
2	Gln	0.267	-0.089
3	L.HDL.C	0.238	0.093
4	Tyr	0.225	-0.069
5	XS.VLDL.TG	0.121	-0.029
6	XXL.VLDL.TG	0.116	0.041
7	Ace	0.108	0.026
8	S.VLDL.TG	0.105	-0.028
9	Serum.TG	0.099	-0.027
10	LDL.D	0.093	-0.022

$p = 0.3$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.758	0.357
2	Tyr	0.374	-0.122
3	Gln	0.345	-0.112
4	XXL.VLDL.TG	0.263	0.110
5	L.HDL.C	0.238	0.095
6	Serum.TG	0.191	-0.067
7	S.VLDL.TG	0.173	-0.053
8	XS.VLDL.TG	0.153	-0.038
9	Ace	0.135	0.031
10	LDL.D	0.128	-0.032

Table 7: Parameter check for the prior probability p, ranging from $p = 0.01$ to $p = 0.3$. This reflects 0.49 to 14.7 expected causal risk factors. We used $p = 0.1$ in the main analysis. Abbreviations: *MIP*=marginal inclusion probability, MACE= model-averaged causal effect.

$\sigma = 0.1$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.498	0.126
2	L.HDL.C	0.454	0.106
3	HDL.D	0.260	0.052
4	HDL.C	0.109	0.016
5	Gln	0.104	-0.014
6	XS.VLDL.TG	0.100	-0.012
7	LDL.D	0.099	-0.013
8	S.HDL.TG	0.098	-0.013
9	S.VLDL.TG	0.082	-0.009
10	Tyr	0.076	-0.008

$\sigma = 0.3$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.687	0.314
2	L.HDL.C	0.267	0.096
3	Gln	0.177	-0.053
4	Tyr	0.124	-0.032
5	XS.VLDL.TG	0.095	-0.020
6	HDL.D	0.091	0.024
7	Ace	0.081	0.018
8	LDL.D	0.073	-0.015
9	IDL.TG	0.071	-0.012
10	S.VLDL.TG	0.066	-0.013

$\sigma = 0.5$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.687	0.338
2	L.HDL.C	0.251	0.097
3	Gln	0.155	-0.052
4	Tyr	0.103	-0.030
5	HDL.D	0.082	0.022
6	XS.VLDL.TG	0.076	-0.017
7	Ace	0.067	0.017
8	IDL.TG	0.060	-0.011
9	LDL.D	0.055	-0.012
10	S.VLDL.TG	0.053	-0.012

$\sigma = 0.7$

#	risk factor	*MIP*	$\hat{\theta}_{\text{MACE}}$
1	XL.HDL.C	0.675	0.339
2	L.HDL.C	0.254	0.100
3	Gln	0.131	-0.045
4	Tyr	0.089	-0.027
5	HDL.D	0.079	0.023
6	XS.VLDL.TG	0.061	-0.014
7	Ace	0.055	0.014
8	IDL.TG	0.050	-0.010
9	S.VLDL.TG	0.045	-0.011
10	Serum.TG	0.043	-0.011

Table 8: Parameter check for the prior variance σ^2, ranging from $\sigma = 0.1$ to $\sigma = 0.7$. We used $\sigma = 0.5$ in the main analysis. Abbreviations: *MIP*=marginal inclusion probability, MACE= model-averaged causal effect.

2.2 Supplementary Figures

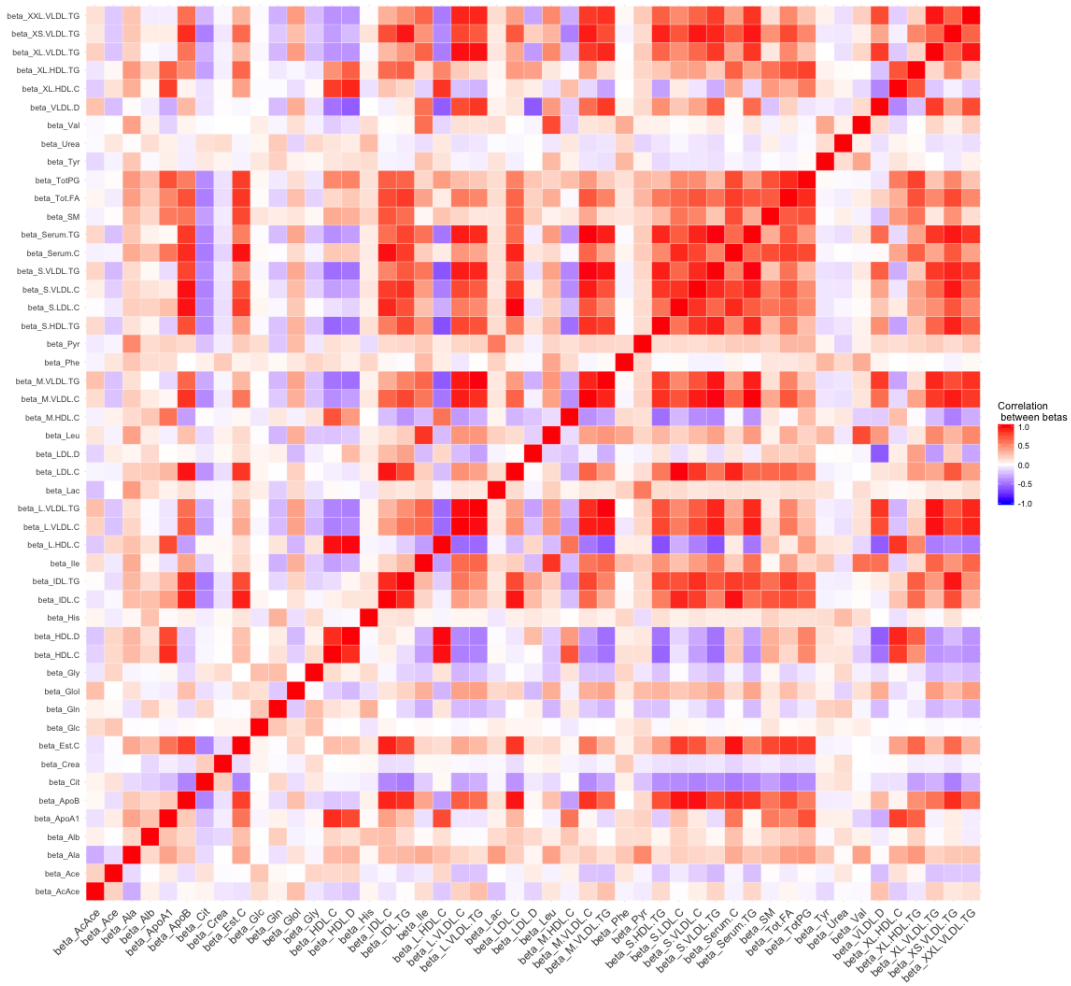

Figure 9: Genetic correlation between metabolite measurements based on the $n = 148$ instrumental genetic variants.

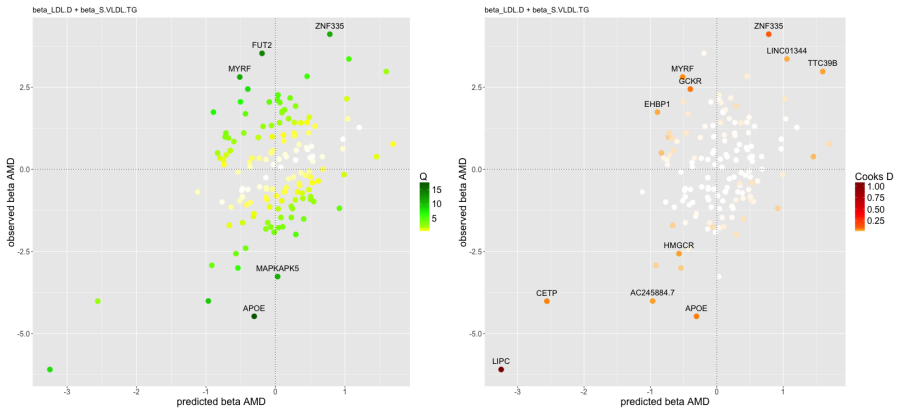

Figure 10: Diagnostic plot of the predicted associations with AMD (x-axis) based on the for the second best individual model 2 (M2: LDL diameter (LDL.D) and TG in small VLDL (S.VLDL.TG)) against the observed associations with AMD (y-axis). Model 1 including LDL diameter (LDL.D), and TG content in small HDL (S.HDL.TG) is shown in the main manuscript. The color code shows: left) the q-statistic for outliers and right) Cook's distance for influential points. Any genetic variant with q-statistic > 10 or Cook's distance $> 4/n$ is marked by a label indicating the gene region.

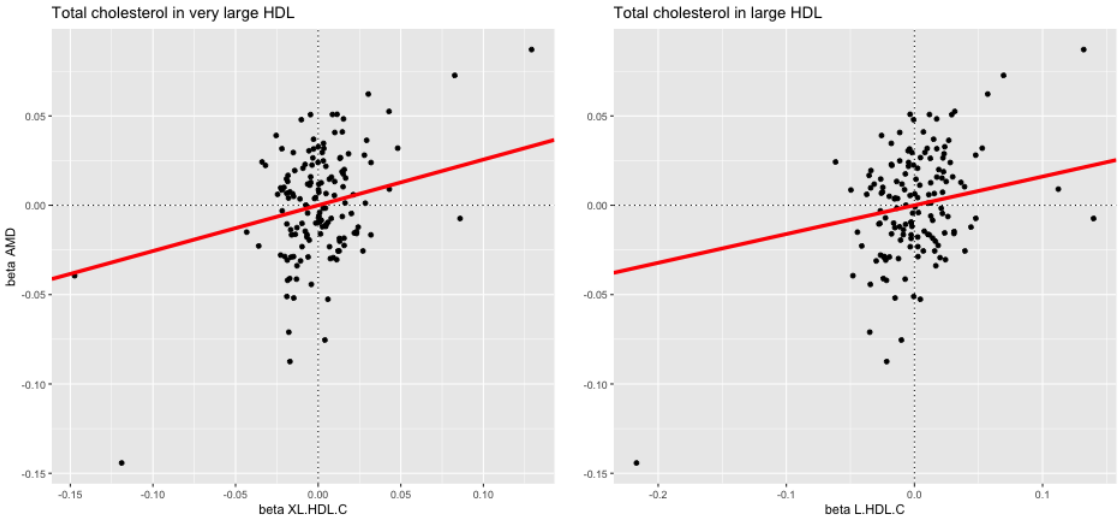

Figure 11: Scatterplot of association with A) XL.HDL.C B) L.HDL.C on the x-axis against the association with AMD y-axis after excluding the *LIPC*, *FUT2* and *APOE* gene regions. The MACE of each risk factor on AMD is marked in red.

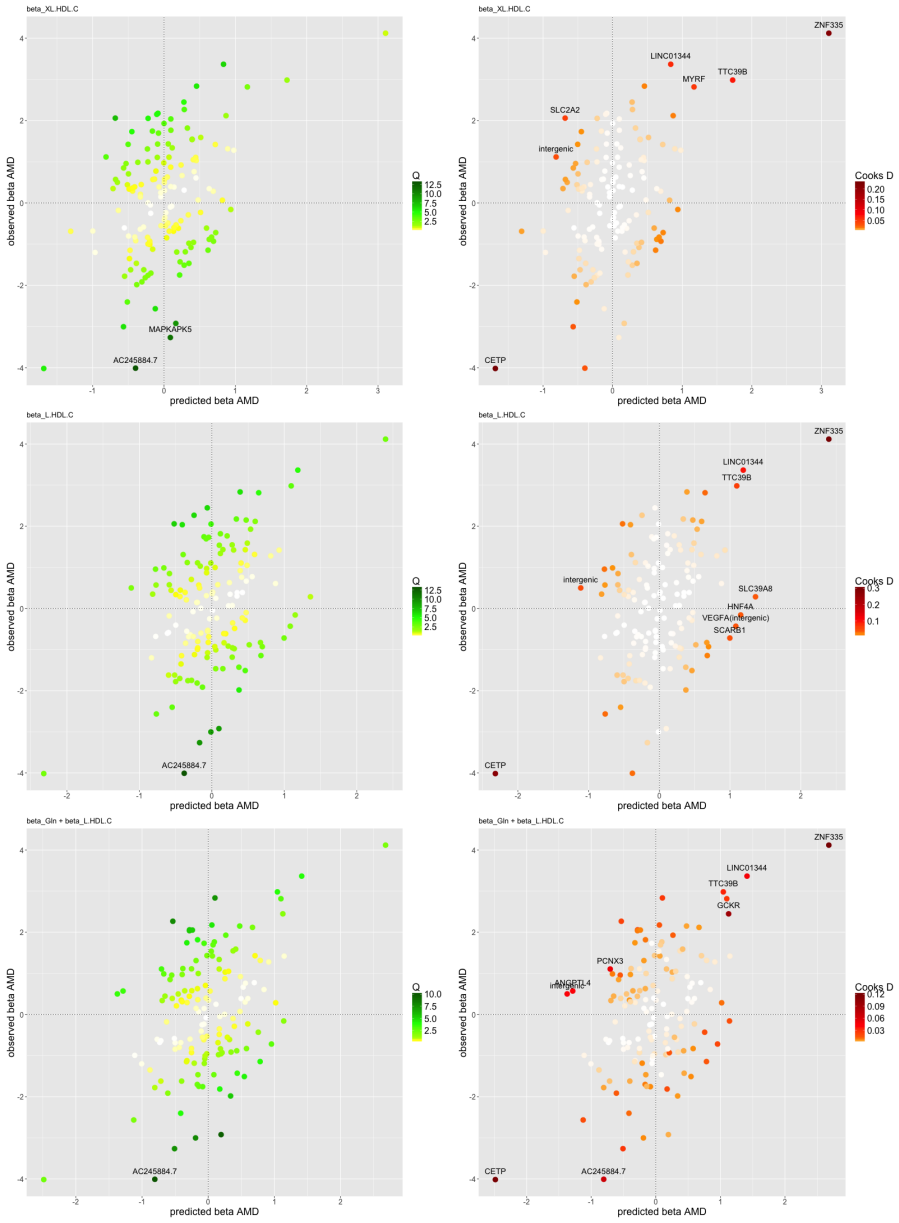

Figure 12: Diagnostic plot of the predicted associations with AMD (x-axis) based on the best individual model 1 (M1: XL.HDL.C), model 2 (M1: L.HDL.C), model 3 (M3: L.HDL.C and Glutamine), against the observed associations with AMD (y-axis). The color code shows: left) the q-statistic for outliers and right) Cook's distance for influential points. Any genetic variant with q-statistic > 10 or Cook's distance $> 4/n$ is marked by a label indicating the gene region. The *LIPC, FUT2* and *APOE* gene regions have been removed prior to this analysis.

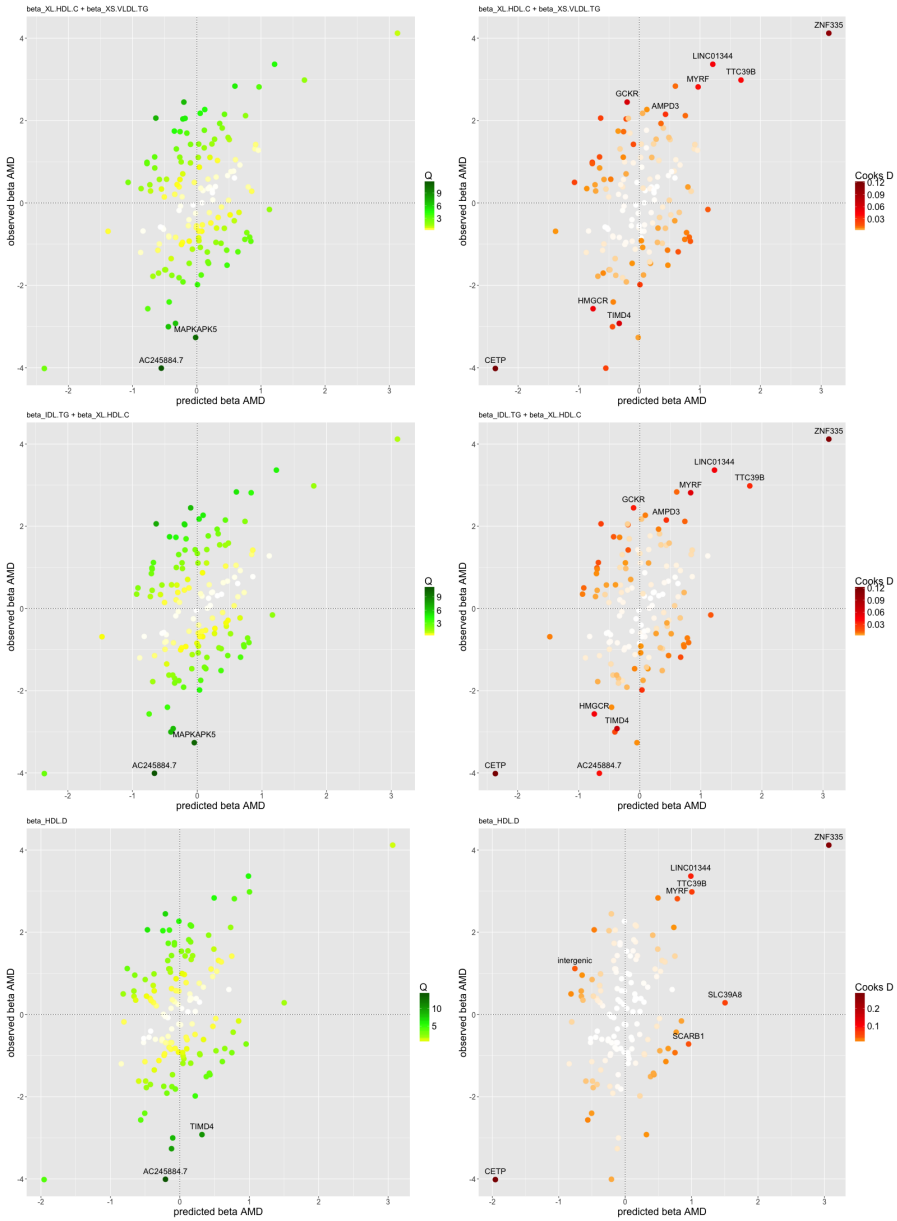

Figure 13: Diagnostic plot of the predicted associations with AMD (x-axis) based on the best individual model 4 (M4: XL.HDL.C and XS.VLDL.TG), model 5 (M5: IDL.TG and XL.HDL.C), model 6 (M6: HDL.D) against the observed associations with AMD (y-axis). The color code shows: left) the q-statistic for outliers and right) Cook's distance for influential points. Any genetic variant with q-statistic > 10 or Cook's distance $> 4/n$ is marked by a label indicating the gene region. The *LIPC, FUT2* and *APOE* gene regions have been removed prior to this analysis.