Supplementary files

Supplementary Table 1: SNPs proxied for gallstones (general, female-specific and male-specific)

SNP		Beta	SE	EAF	Other allele	Effect allele	P value	Sample size	F statistics
SNPs proxied for gallstones (general)									
1	rs765299456	0.016574	0.00063	0.060744	A	G	3.58E-152	361141	11.31974
2	rs56266464	0.01646	0.000628	0.060728	G	A	3.83E-151	361141	11.16251
3	rs114938914	0.016436	0.000627	0.060915	C	T	2.82E-151	361141	11.16227
4	rs111617668	0.016425	0.000626	0.061012	C	T	2.21E-151	361141	11.1635
5	rs79835740	0.016437	0.000627	0.060897	A	T	2.15E-151	361141	11.16054
6	rs3923912	0.016453	0.000627	0.060793	A	C	1.09E-151	361141	11.16445
7	rs767464042	0.016569	0.000628	0.060768	C	T	2.08E-153	361141	11.31824
8	rs77725792	0.01649	0.000626	0.060837	G	A	1.38E-152	361141	11.22155
9	rs115445558	0.017098	0.000604	0.065375	G	C	4.53E-176	361141	12.90189
10	rs6756629	0.016461	0.000616	0.062655	G	A	2.21E-157	361141	11.49489
11	rs11887534	0.017225	0.000603	0.065427	G	C	4.62E-179	361141	13.10362
12	rs75331444	0.017307	0.000605	0.065062	G	A	1.60E-179	361141	13.1607
13	rs41360247	0.016568	0.000615	0.062712	T	C	1.62E-159	361141	11.65355
14	rs4953023	0.016639	0.000616	0.062501	G	A	2.44E-160	361141	11.71668
15	rs76866386	0.017249	0.000604	0.065196	T	C	6.44E-179	361141	13.09713
16	rs56132765	0.016725	0.000625	0.060695	G	A	2.29E-157	361141	11.51892
17	rs72875462	0.016717	0.000625	0.060814	C	A	1.36E-157	361141	11.5293
18	rs4076834	0.01721	0.000612	0.06365	T	G	4.57E-174	361141	12.75038
19	rs9753033	0.016582	0.000627	0.060456	A	T	3.75E-154	361141	11.28136
20	rs4507142	0.016636	0.000627	0.060346	G	A	7.85E-155	361141	11.33468
21	rs4614977	0.016582	0.000627	0.060468	C	G	4.91E-154	361141	11.2833
22	rs60567145	0.01968	0.00084	0.042774	T	G	2.72E-121	361141	11.45378

SNPs proxied for gallstones (female-specific)									
1	rs530899367	5.36251	0.403049	2.77E-06	G	A	2.26E-40	194153	30.91961
2	rs142658902	12.9777	1.46183	2.77E-06	C	T	6.88E-19	194153	181.2297
3	rs571907843	253.736	16.7862	1.38E-06	T	G	1.36E-51	194153	42113.61
4	rs186058156	7.1006	1.28062	1.38E-06	A	G	2.95E-08	194153	27.10503
5	rs564795640	14.2075	1.63881	1.38E-06	C	A	4.37E-18	194153	108.5619
6	rs181946550	6.61166	1.12722	1.38E-06	G	C	4.49E-09	194153	23.50027
7	rs190199103	13.4041	2.2646	1.38E-06	T	C	3.25E-09	194153	96.62525
8	rs112402510	4.32696	0.288185	1.38E-06	T	C	6.30E-51	194153	10.06439
9	rs61745528	33.0685	2.47528	1.38E-06	G	A	1.09E-40	194153	589.5832
10	rs140327735	22.6981	2.53161	1.38E-06	A	G	3.11E-19	194153	277.3308
11	rs200990091	49.6562	7.51078	1.38E-06	G	C	3.82E-11	194153	1334.508
12	rs141353328	83.9622	9.69515	1.38E-06	G	A	4.74E-18	194153	3864.8
13	rs10512330	83.901	9.69502	1.38E-06	T	G	5.01E-18	194153	3859.056
14	9:139982579_c_t	7.27613	1.01643	1.38E-06	C	T	8.18E-13	194153	28.46189
15	9:139983329_t_c	7.27613	1.01643	1.38E-06	T	C	8.18E-13	194153	28.46189
16	9:140242576_c_t	63.0052	5.93691	1.38E-06	C	T	2.65E-26	194153	2157.504
17	rs141392389	9.51429	1.34896	1.38E-06	G	A	1.76E-12	194153	48.66995
18	rs117603556	3.82829	0.291822	2.77E-06	T	C	2.68E-39	194153	15.757
19	rs140139872	7.70131	0.628336	1.38E-06	C	T	1.59E-34	194153	31.88598
20	rs140902738	4.49927	0.298886	1.38E-06	C	T	3.50E-51	194153	10.88197
21	rs115483407	56.21	3.95663	2.77E-06	A	C	8.80E-46	194153	3457.173
22	rs557107249	63.319	5.93657	1.38E-06	C	T	1.49E-26	194153	2179.29
23	rs201923549	6.08163	0.931573	1.38E-06	G	A	6.67E-11	194153	19.88308
24	rs143172698	69.1811	5.06164	1.38E-06	G	A	1.66E-42	194153	2607.158
25	rs113863556	18.7532	1.31891	1.38E-06	A	C	7.40E-46	194153	189.2226
26	rs188442884	3.20429	0.212356	4.15E-06	G	A	2.04E-51	194153	16.55842
27	rs140781249	7.91432	0.524292	4.15E-06	G	A	1.86E-51	194153	101.0582

28	rs144189579	12.0601	1.85461	1.38E-06	G	A	7.90E-11	194153	78.21247
29	rs141080835	9.58944	0.79501	1.38E-06	T	G	1.72E-33	194153	49.44203
30	rs138213755	29.9262	2.18559	2.77E-06	C	G	1.18E-42	194153	967.5887
31	rs200789814	62.9232	8.39683	1.38E-06	C	T	6.73E-14	194153	2151.829
32	rs114475684	6.93636	0.989582	4.15E-06	C	T	2.40E-12	194153	77.61668
33	rs61747143	8.77443	1.05165	1.38E-06	C	T	7.26E-17	194153	41.39326
34	rs374115679	5.72716	0.818539	1.38E-06	C	T	2.63E-12	194153	17.63264
SNPs proxied for gallstones (male-specific)									
1	rs368016704	124.107	19.6909	1.38E-06	C	T	2.93E-10	166988	7438.04
2	rs574804613	5.45247	0.684888	4.15E-06	C	T	1.72E-15	166988	41.24321
3	rs139416584	22.1108	2.77073	1.38E-06	A	T	1.47E-15	166988	226.3272
4	rs200018098	5.23309	0.859407	1.38E-06	C	T	1.14E-09	166988	12.66161
5	rs142528020	10.4342	1.73035	1.38E-06	A	G	1.64E-09	166988	50.34878
6	rs148625825	10.4342	1.73035	1.38E-06	G	T	1.64E-09	166988	50.34878
7	rs139435904	10.4342	1.73035	1.38E-06	A	C	1.64E-09	166988	50.34878
8	rs540763634	21.1285	2.44206	4.15E-06	G	C	5.11E-18	166988	621.4544
9	rs143303699	3.81205	0.698172	4.15E-06	C	T	4.77E-08	166988	20.15711
10	rs545716291	17.5641	2.22939	2.77E-06	C	T	3.33E-15	166988	285.735
11	rs528879612	32.5188	4.51717	1.38E-06	T	C	6.09E-13	166988	490.3228
12	rs141034739	252.138	27.8432	1.38E-06	C	T	1.37E-19	166988	35669.26
13	rs375212388	14.785	1.30962	1.38E-06	A	G	1.52E-29	166988	101.1219
14	rs137859753	7.19644	1.29149	6.92E-06	G	A	2.52E-08	166988	119.7991
15	rs145512248	124.291	19.6908	1.38E-06	C	T	2.76E-10	166988	7461.098
16	rs4151656	39.011	6.38863	1.38E-06	A	C	1.02E-09	166988	706.5576
17	rs533422258	9.48786	1.13969	2.77E-06	C	G	8.50E-17	166988	83.27644
18	rs149172104	83.4125	11.3685	2.77E-06	G	C	2.19E-13	166988	6691.041
19	rs550980322	4.14715	0.716276	2.77E-06	G	A	7.06E-09	166988	15.90413
20	rs148247595	13.4909	2.31258	1.38E-06	C	G	5.43E-09	166988	84.1861

21	rs73701083	4.68002	0.521883	1.38E-06	A	G	3.06E-19	166988	10.12655
22	rs569718323	3.53021	0.527098	2.77E-06	T	C	2.13E-11	166988	11.52392
23	rs12115676	5.78604	0.715397	4.15E-06	G	A	6.11E-16	166988	46.44536
24	9:139915320_g_a	10.7108	1.37186	2.77E-06	G	A	5.87E-15	166988	106.1424
25	9:139973444_c_t	3.78367	0.616567	2.77E-06	C	T	8.45E-10	166988	13.23823
26	9:139973872_c_t	3.78367	0.616567	2.77E-06	C	T	8.45E-10	166988	13.23823
27	rs201691089	7.02147	0.843017	1.38E-06	G	T	8.22E-17	166988	22.79581
28	rs200798287	5.34853	0.65871	2.77E-06	G	A	4.70E-16	166988	26.45494
29	rs185706535	34.2337	4.64106	1.38E-06	T	C	1.64E-13	166988	543.5741
30	rs143864010	5.35147	0.867272	1.38E-06	T	C	6.82E-10	166988	13.24099
31	rs141467923	61.3989	9.84532	2.77E-06	A	G	4.49E-10	166988	3560.014
32	rs139690921	7.90578	0.953411	1.38E-06	A	C	1.12E-16	166988	28.90043
33	rs144019457	5.45347	0.621403	1.38E-06	G	A	1.71E-18	166988	13.75059
34	rs557569790	5.39961	0.743202	2.77E-06	T	C	3.74E-13	166988	26.96274
35	rs200752877	11.74	1.31111	1.38E-06	G	A	3.45E-19	166988	63.74434
36	rs371236140	18.3386	2.88764	1.38E-06	C	T	2.15E-10	166988	155.624
37	rs148140313	6.20733	1.01684	2.77E-06	G	A	1.03E-09	166988	35.63456
38	rs4369791	53.9837	9.28265	1.38E-06	T	A	6.05E-09	166988	1358.261
39	rs142119092	4.77446	0.795299	1.38E-06	G	A	1.94E-09	166988	10.53939
40	rs61742056	4.74729	0.548916	1.38E-06	G	A	5.26E-18	166988	10.41977
41	rs200603379	10.198	1.1453	1.38E-06	G	A	5.43E-19	166988	48.09443
42	rs200139706	15.891	2.67956	1.38E-06	C	T	3.03E-09	166988	116.8277
43	rs377620137	15.6473	2.54231	1.38E-06	C	T	7.54E-10	166988	113.2695
44	rs144441435	17.6492	2.05272	2.77E-06	T	C	8.18E-18	166988	288.5153
45	rs150855218	17.5627	1.96886	7.73E-06	C	A	4.70E-19	166988	799.5839

Supplementary Table 2: SNPs proxied for cholecystectomy (general)

SNP		Beta	SE	EAF	Other allele	Effect allele	P value	Sample size	F statistics
SNPs proxied for general cholecystectomy									
1	rs11802588	0.002476	0.000403	C	C	G	8.30E-10	462933	37.69916
2	rs28473566	-0.00807	0.000545	G	G	A	1.20E-49	462933	219.3736
3	rs11691033	-0.00451	0.000436	T	T	A	3.60E-25	462933	107.4022
4	rs4665972	0.00359	0.000414	T	T	C	4.20E-18	462933	75.23726
5	rs13427681	0.002338	0.000406	G	G	C	8.50E-09	462933	33.15177
6	rs1047891	-0.00299	0.000433	C	C	A	5.10E-12	462933	47.65797
7	rs112732186	0.002501	0.00042	G	G	T	2.70E-09	462933	35.39666
8	rs11887534	0.043735	0.000812	G	G	C	#######	462933	2903.362
9	rs2741044	0.002532	0.000443	G	G	A	1.10E-08	462933	32.70803
10	rs10935751	-0.00261	0.000442	C	C	T	3.80E-09	462933	34.71872
11	rs4681516	-0.00492	0.000407	G	G	C	1.10E-33	462933	146.3147
12	rs2290846	0.005136	0.000446	G	G	A	9.60E-31	462933	132.8824
13	rs9371004	-0.00314	0.000406	T	T	C	1.00E-14	462933	59.84855
14	rs1201467	-0.00386	0.00066	G	G	C	4.80E-09	462933	34.2879
15	rs2288153	0.003223	0.000468	C	C	T	6.00E-12	462933	47.34448
16	rs7802555	-0.007	0.000581	A	A	C	1.90E-33	462933	145.2101
17	rs714583	-0.00455	0.000488	T	T	A	1.00E-20	462933	87.09168
18	rs146652454	0.006885	0.001243	C	C	T	3.10E-08	462933	30.66692
19	rs1293297	0.003841	0.000618	G	G	C	5.10E-10	462933	38.64319
20	rs2470048	0.002543	0.000444	C	C	T	9.90E-09	462933	32.87017
21	rs1993453	-0.0047	0.000427	A	A	G	3.80E-28	462933	121.0006
22	rs686030	0.005877	0.000579	C	C	A	3.30E-24	462933	103.0333
23	rs10900221	0.005046	0.000472	G	G	A	1.10E-26	462933	114.2817
24	rs2393969	0.003516	0.000404	A	A	C	3.20E-18	462933	75.73822

25	rs2727270	0.003704	0.00063	C	C	T	4.10E-09	462933	34.55703
26	rs72931779	0.00481	0.000677	C	C	G	1.20E-12	462933	50.44449
27	rs3862794	0.003246	0.000462	T	T	C	2.10E-12	462933	49.42266
28	rs2393776	0.003916	0.000415	G	G	A	4.20E-21	462933	88.87447
29	rs932784	0.007651	0.001376	T	T	A	2.70E-08	462933	30.9293
30	rs28929474	0.018479	0.001449	C	C	T	3.10E-37	462933	162.5709
31	rs41276920	-0.00475	0.000713	G	G	A	2.70E-11	462933	44.41727
32	rs76818081	0.007874	0.001337	G	G	A	3.80E-09	462933	34.7021
33	rs150844304	0.007165	0.00127	A	A	C	1.70E-08	462933	31.81152
34	rs11644920	0.002922	0.00044	A	A	T	3.00E-11	462933	44.19886
35	rs17138478	0.003928	0.000602	C	C	A	6.70E-11	462933	42.61232
36	rs1801689	0.006991	0.001171	A	A	C	2.40E-09	462933	35.63988
37	rs11543269	-0.00364	0.000613	C	C	T	2.80E-09	462933	35.29803
38	rs212099	-0.007	0.000544	T	T	A	7.80E-38	462933	165.3226
39	rs681343	0.004502	0.000402	C	C	T	4.50E-29	462933	125.2514
40	rs8112972	0.005261	0.000613	G	G	A	9.00E-18	462933	73.72623
41	rs2733737	-0.003	0.000418	T	T	C	6.60E-13	462933	51.65837
42	rs708686	0.002969	0.000455	C	C	T	7.00E-11	462933	42.51746
43	rs1800961	0.012424	0.001163	C	C	T	1.20E-26	462933	114.1377
44	rs4814175	-0.00227	0.000413	A	A	T	3.80E-08	462933	30.24742
45	rs41281265	0.002348	0.000424	A	A	G	3.20E-08	462933	30.59838

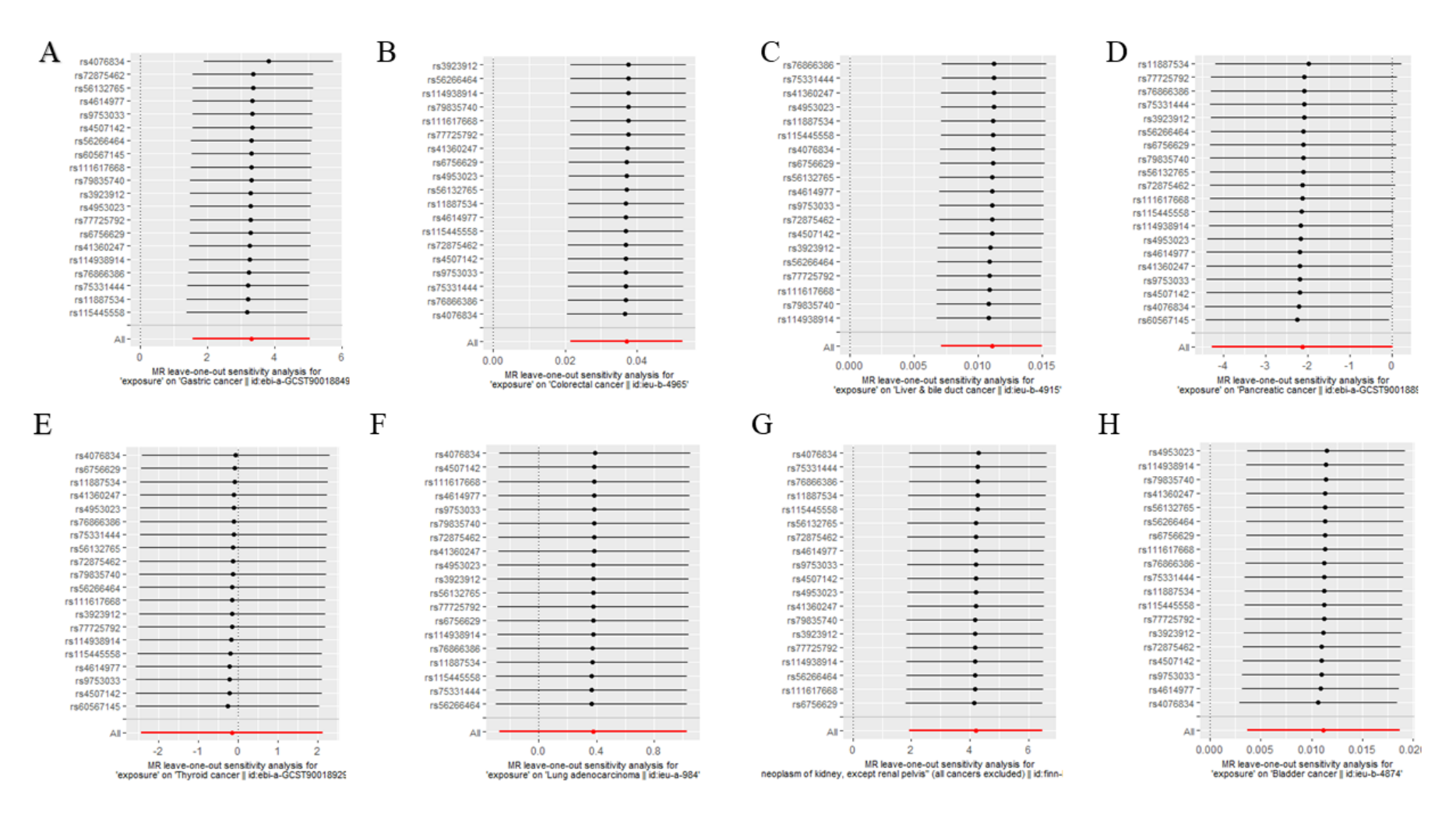
Supplementary Table 3: Data resources

	Phenotype		Year	Consortium	Ancestry	Gender	Study reference	Data sources	Phenotype link / ICD code
Exposures	Gallstones	7,157 / 353,984	2018	UK Biobank	European	Males and Females		UKBB GWAS Imputed v3	K80
		5,575 / 188,578	2018	UK Biobank	European	Females			
		1,582 / 165,406	2018	UK Biobank	European	Males			
	Cholecystectomy	26,145 / 436,788	2018	UK Biobank	European	Males and Females			Z90
Outcomes	Stomach cancer	1,029 / 474,058	2021	Meta-analyses with the UK Biobank and FinnGen	European	Males and Females	Nat Genet 53, 1415–1424 (2021)	IEU OpenGWAS (ebi-a-GCST90018849)	C16
	Colorectal cancer	5,657 / 372,016	2021	Meta-analyses with the UK Biobank and FinnGen	European	Males and Females	Nat Genet 53, 1415–1424 (2021)	IEU OpenGWAS (ieu-b-4965)	C18
	Liver and bile duct cancer	350 / 371,666	2021	Meta-analyses with the UK Biobank and FinnGen	European	Males and Females	Nat Genet 53, 1415–1424 (2021)	IEU OpenGWAS (ieu-b-4915)	C22.0, C22.1 / C23
	Pancreatic cancer	1,196 / 475,049	2021	Meta-analyses with the UK	European	Males and Females	Nat Genet 53, 1415–1424 (2021)	IEU OpenGWAS (ebi-a-GCST90018893)	C25

Thyroid cancer	1,054 / 490,920	2021	Biobank and FinnGen Meta-analyses with the UK Biobank and FinnGen	European	Males and Females	Nat Genet 53, 1415–1424 (2021)	IEU OpenGWAS (ebi-a-GCST90018929)	C73
Lung cancer	11,245 / 54,619	2022	TRICL	European	Males and Females		IEU OpenGWAS (ieu-a-984)	C34
Kidney cancer	971 / 174,006	2021	FinnGen Biobank	European	Males and Females		IEU OpenGWAS (finn-b-C3_KIDNEY_NOTRENALPELVIS)	C64
Bladder cancer	1,279 / 372,016	2021	MRC IEU	European	Males and Females		IEU OpenGWAS (ieu-b-4874)	C67
Female breast cancer	17,389 / 240,341	2021	Meta-analyses with the UK Biobank and FinnGen	European	Females	Nat Genet 53, 1415–1424 (2021).	GWAS Catalog	C50
Endometrial cancer	2,188 / 237,839	2021	Meta-analyses with the UK Biobank and FinnGen	European	Females	Nat Genet 53, 1415–1424 (2021).	IEU OpenGWAS (ebi-a-GCST90018838)	C53
Cervical cancer	909 / 238,249	2021	Meta-analyses with the UK Biobank and FinnGen	European	Females	Nat Genet 53, 1415–1424 (2021).	IEU OpenGWAS (ebi-a-GCST90018817)	C54

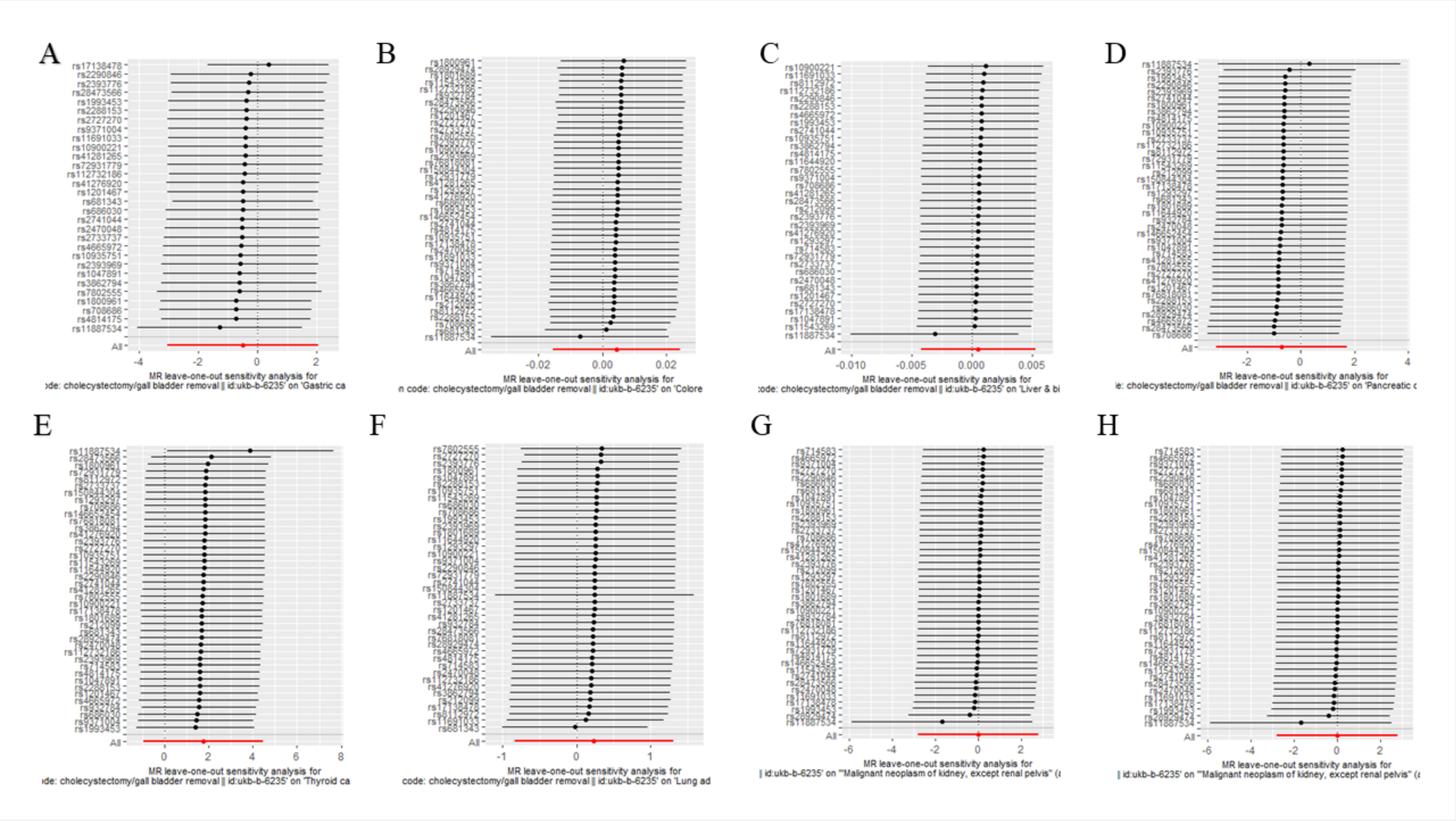
Ovarian cancer	843 / 60,614	2021	Meta-analyses with the UK Biobank and FinnGen	European	Females	Nat Genet 53, 1415–1424 (2021).	IEU OpenGWAS (ebi-a-GCST90018668)	C56
Prostate cancer	79,148 / 61,106	2018	meta-analyses of Europeans	European	Males	Nat Genet. 2018 Jul;50(7):928-936.	IEU OpenGWAS (ebi-a-GCST006085)	C61

Supplementary Figure 1: Leave one out plot for the MR analysis between gallstones and cancers



Footnote:(A) stomach cancer (B) colorectal cancer (C) liver and bile duct cancer (D) pancreatic cancer (E) thyroid cancer (F) lung cancer (G) kidney cancer (H) bladder cancer.

Supplementary Figure 2: Leave one out plot for the MR analysis between cholecystectomy and cancers



Footnote:(A) stomach cancer (B) colorectal cancer (C) liver and bile duct cancer (D) pancreatic cancer (E) thyroid cancer (F) lung cancer (G) kidney cancer (H) bladder cancer.