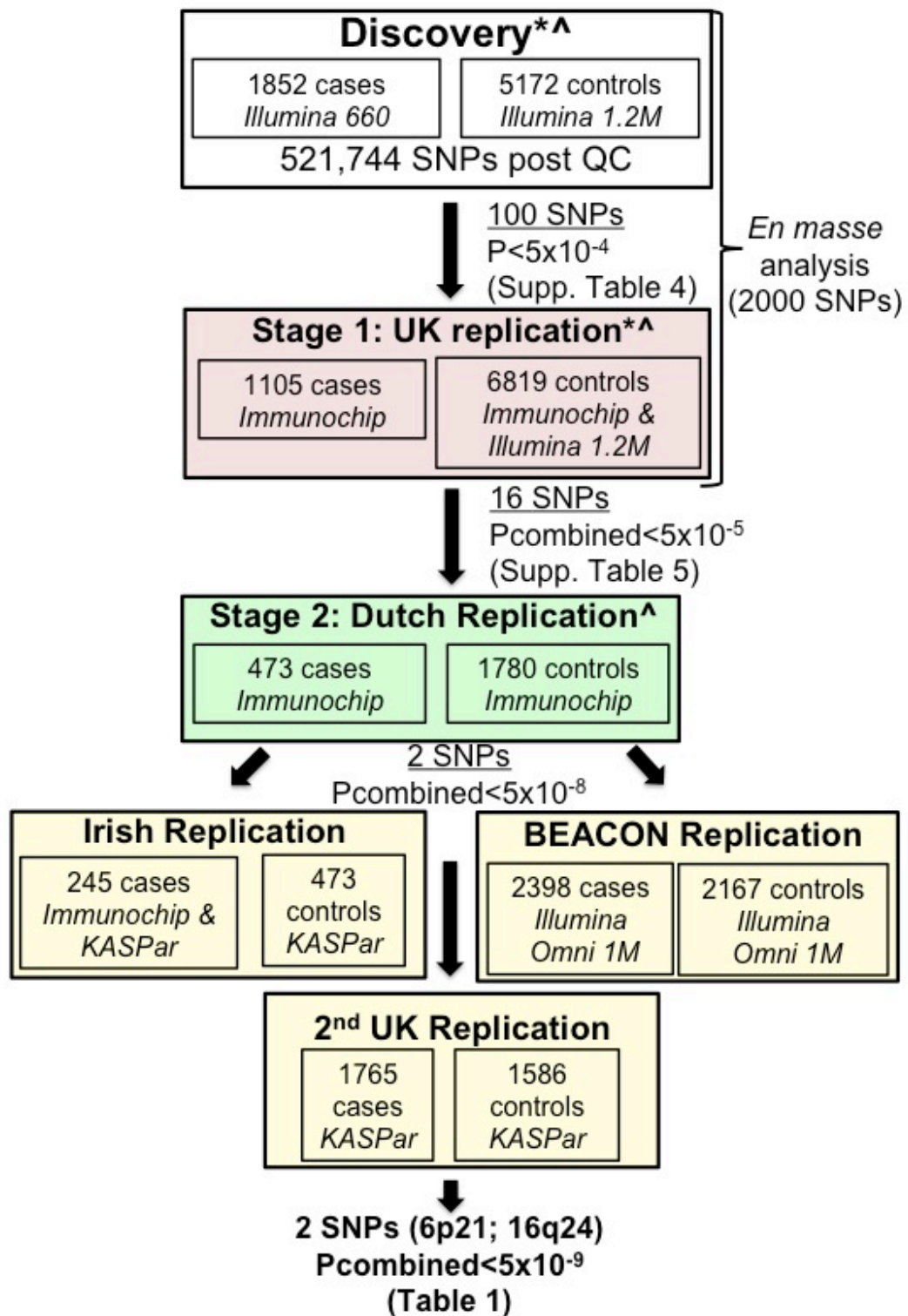


## **SUPPLEMENTARY NOTE**

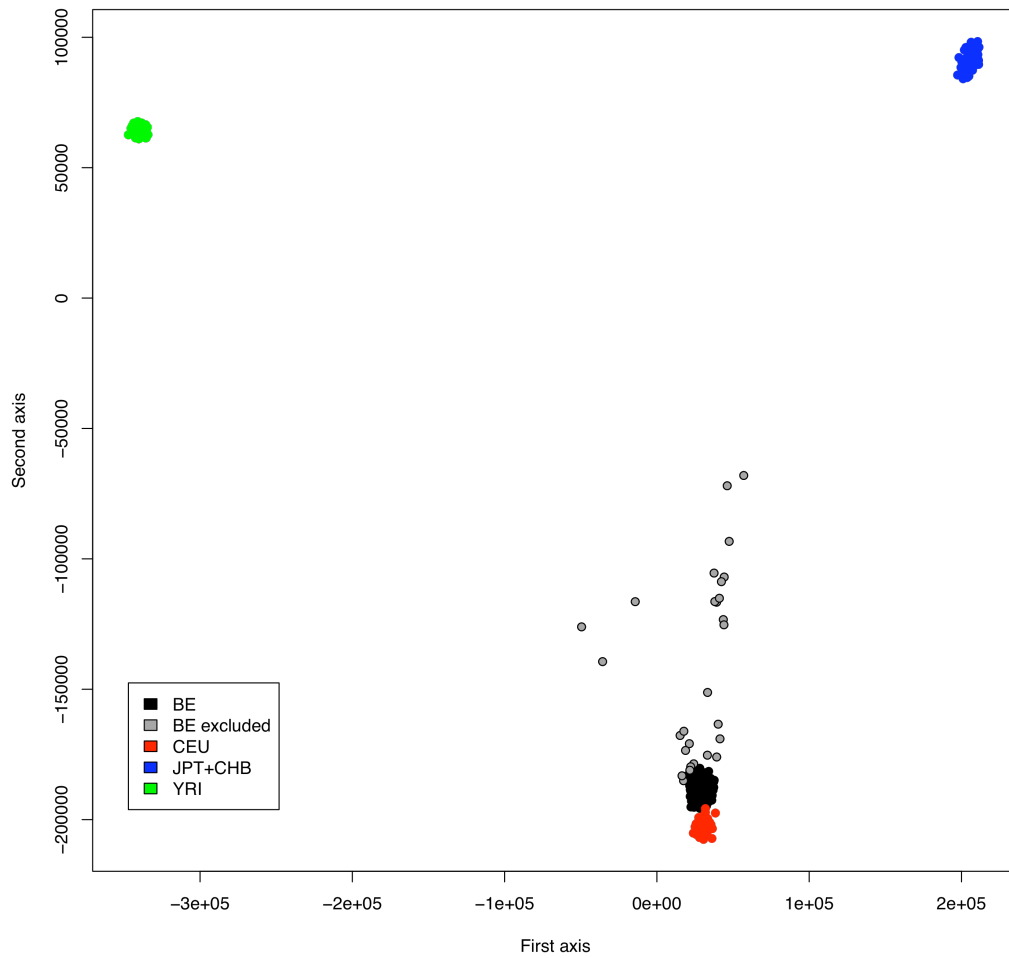
**Common variants at the MHC locus and at chromosome 16q24.1 predispose to Barrett's esophagus.**

The Esophageal Adenocarcinoma Genetics Consortium and the Wellcome Trust Case Control Consortium 2

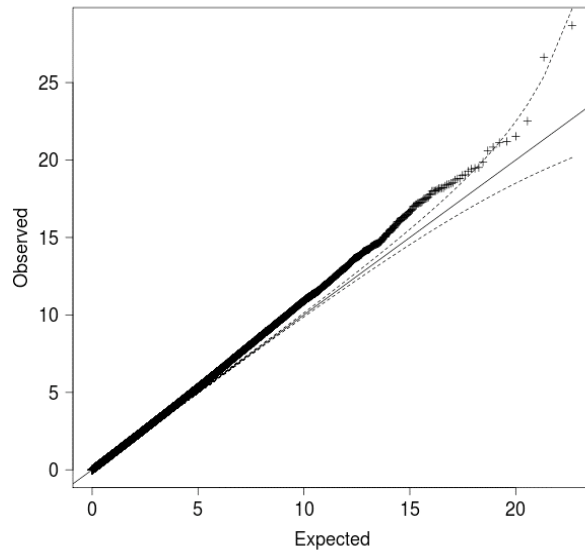
A full list of authors and affiliations appears at the end of the Supplementary Note



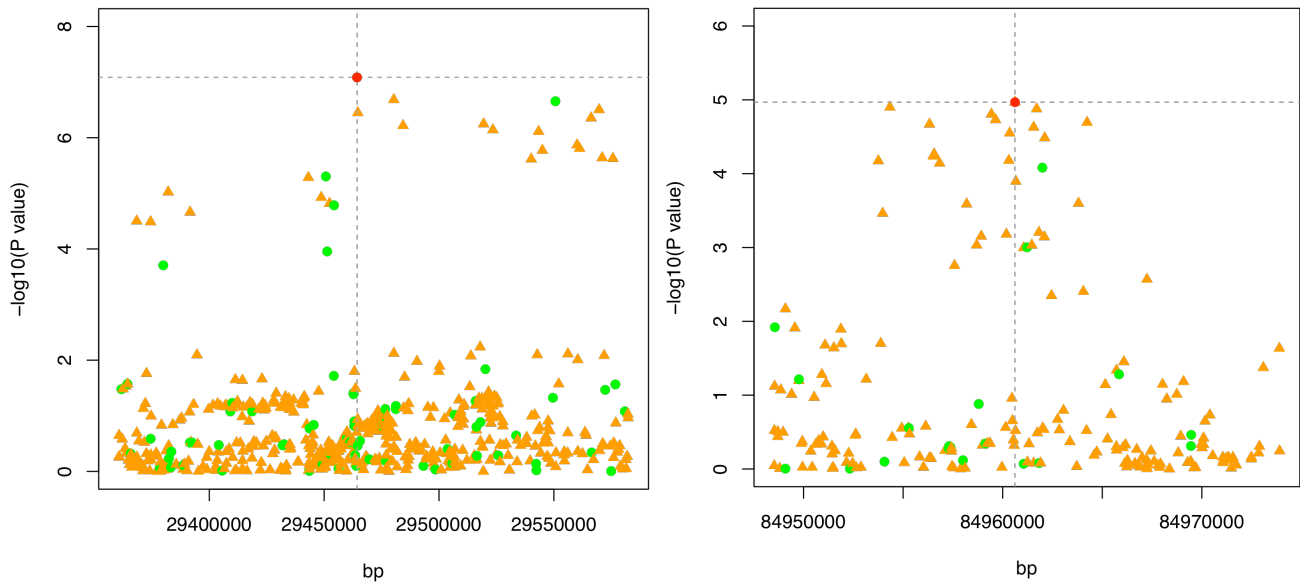
**Supplementary Figure 1** Outline of the analysis workflow. \*HLA alleles imputed, <sup>^</sup>C&M; Sex stratified analysis; Subset of sample (5%) also genotyped with KASPar at top 2 SNPs. Replication stages are coloured, pink- stage 1, green- stage 2, yellow-stage 3.



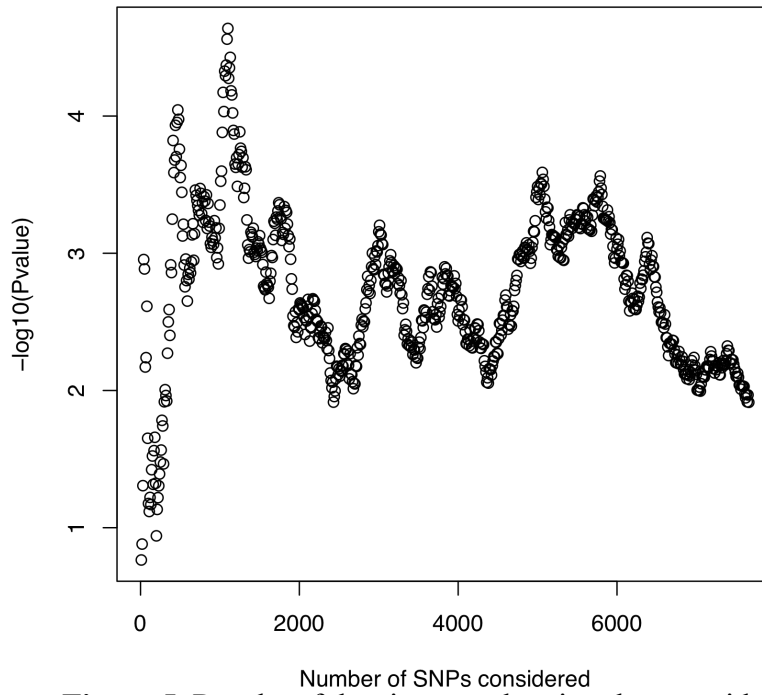
**Supplementary Figure 2.** Plot of the first two principal components computed from the Hapmap samples (CEU: red, YRI: green, JPT&CHB: blue) and then projected on to the cases (black) to show ancestry outliers. The case individuals that were excluded based on this analysis are shown in grey.



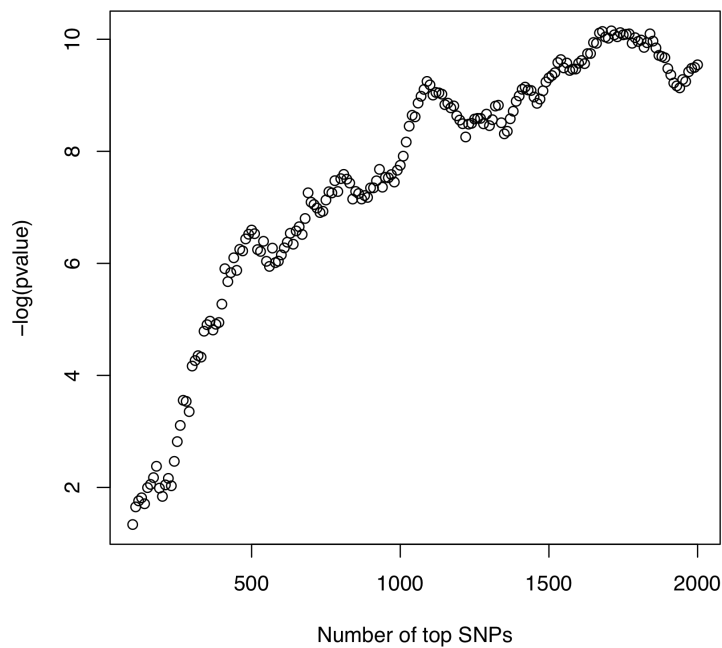
**Supplementary Figure 3.** Quantile-Quantile Plot showing the observed and the expected chi squared statistics of the discovery analysis, with 1 PCA as a covariate.  $\lambda=1.05$ , and when standardized to a population of 1000 cases and 1000 controls,  $\lambda_{1000}=1.019$ .



**Supplementary Figure 4.** Regional association plots showing imputation results at the two hit regions, chromosome 6p21 on the left and 16q34 on the right. Green circles represent the genotyped SNPs and orange triangles represent imputed SNPs. The top SNPs found in the discovery genotype data are shown as red circles.



**Supplementary Figure 5.** Results of the sign test showing the two-sided P values for the number of pruned SNPs that have the same direction of effects in the discovery and replication samples.



**Supplementary Figure 6.** Results of the score analysis where a score is calculated for each replication individual, based on the number of risk alleles carried by each individual weighted by the log of the odds ratio from the discovery data. The P value is testing for evidence of higher scores in the cases sample compared to the controls sample.

**Supplementary Table 1** Characteristics of discovery and replication case (CA) and control (CO) populations after exclusions

	Discovery		Stage 1		Stage 2		Stage 3					
	UK CA n=1852	UK CO n=5172	UK CA n=1105	UK CO n=6819	Dutch CA n=473	Dutch CO n=1780	Irish CA n=245	Irish CO n=473	UK CA n=1765	UK CO n=1586	BEACON CA n=2398	BEACON CO n=2167
<b>Sex</b>												
Males	1488	2609	783	3270	350	1054	157	166	1260	717	1822	1703
Females	364	2563	319	3512	123	726	57	304	494	889	576	464
Not stated	0	0	3	0		0	21	3	11	68		
<b>Age</b>												
<=40	85	1237	25		12			301	30	236	122	97
41-50	320	702	66		21			89	167	168	320	242
51-60	601	3178	154		77			65	362	291	637	573
61-70	646	46	324		57			15	716	294	671	755
70+	199	0	316		57			0	481	134	648	500
Not reported	1	9	220	6819	249	1780	245	3	9	463	0	0
<b>Reported Ethnicity</b>												
White Caucasian	1836	5172	1094	6819	472	1780	245	473	1765	1568	2349	2161
Other	0	0	0	0	0	0	0	0	0	0	7	6
Not reported	16	0	11	0	1	0	0	0	0	0	42	0
<b>CASE ONLY Prague Criteria Measurements</b>												
<b>Circumferential (C) length/cm</b>												
Mean	4.05		3.59		NA		NA		3.13			
95% CI	3.91-4.18		3.38-3.80						2.96-3.30			
Range	0-22		0-23						0-17			
<b>Maximal (M) length/cm</b>												
Mean	4.60		4.65		4.37		5.12		4.58			
95% CI	4.47-4.74		4.47-4.84		4.01-4.73		4.51-5.72		4.43-4.73			
Range	1-24		1-23		1-15		1-17		1-17			
<b>CASE ONLY Intestinal Metaplasia</b>												
Positive (%)	90	NA	66	NA	80	NA	100	NA	83		100	

**Supplementary Table 2** Discovery sample collection cohorts.

Site	Number of cases (post QC)
Aberdeen Royal Infirmary, Aberdeen	5 (5)
Addenbrookes Hospital, Cambridge	3 (3)
Alexandra Hospital, Redditch	21 (21)
Altnagelvin Hospital, Londonderry	24 (24)
Antrim & Whiteabbey United Hospitals, Antrim	59 (59)
Ayr Hospital, Ayr	8 (6)
Barnsley Hospital NHS Foundation Trust, Barnsley	23 (23)
Barts and The London, London	23 (20)
Belfast City Hospital, Belfast	13 (13)
Blackpool Victoria Hospital, Blackpool	26 (25)
Bronglais General Hospital, Aberystwyth	19 (17)
City Hospital Birmingham, Birmingham	13 (11)
Conquest Hospital, St Leonard on Sea	7 (7)
Countess of Chester Hospital, Chester	44 (42)
Craigavon Area Hospital, Craigavon	43 (40)
Cumberland Infirmary, Carlisle	26 (24)
Darent Valley Hospital, Dartford	15 (15)
Derriford Hospital, Plymouth	9 (9)
Gartnavel General Hospital, Glasgow	7 (6)
George Eliot Hospital, Nuneaton	8 (8)
Glasgow Royal Infirmary, Glasgow	14 (13)
Gloucestershire Royal Hospital, Gloucester	166 (148)
Good Hope Hospital, Sutton Coldfield	8 (8)
Guy's Hospital, London	12 (10)
Hairmyres Hospital, East Kilbride	12 (12)
Harrogate District Hospital, Harrogate	24 (24)
Hereford County Hospital, Hereford	3 (3)
John Radcliffe Hospital, Oxford	19 (17)
Kettering General Hospital, Kettering	18 (18)
Lagan Valley Hospital, Lisburn	19 (17)
Leicester General Hospital, Leicester	111 (96)
Leicester Royal Infirmary, Leicester	137 (131)
Lister Hospital, Stevenage	16 (14)
Maidstone Hospital Kent Oncology Centre, Maidstone	8 (7)
Mater Infirmorium Hospital, Belfast	29 (28)
May Day University Hospital, Croydon	18 (15)
Neath Port Talbot Hospital, Port Talbot	4 (4)

New Cross Hospital, Wolverhampton	7 (7)
Ninewells Hospital, Dundee	41 (40)
Nobles Hospital, Braddan	6 (5)
North Manchester General Hospital, Manchester	18 (17)
North Tyneside General Hospital, North Shields	30 (27)
Northampton General Hospital, Northampton	5 (5)
QEII East & North Hertfordshire NHS Trust, Welwyn Garden City	46 (44)
Queen Alexandra Hospital, Portsmouth	96 (92)
Queen Elizabeth Hospital, Birmingham	4 (4)
Queen Elizabeth Hospital, Kings Lynn	11 (11)
Queen Margaret Hospital, Dunfermline	19 (19)
Queen Mary's Hospital NHS Trust, Sidcup	10 (8)
Queens Medical Centre, Nottingham	52 (48)
Rotherham General Hospital, Rotherham	5 (5)
Royal Albert Edward Infirmary NHS Trust, Wigan	53 (48)
Royal Alexandra Hospital, Paisley	21 (20)
Royal Bournemouth Hospital, Bournemouth	6 (6)
Royal Cornwall Hospital, Truro	8 (8)
Royal Derby Hospital, Derby	35 (31)
Royal Devon & Exeter NHS Foundation Trust, Exeter	2 (2)
Royal Infirmary of Edinburgh, Edinburgh	19 (17)
Royal Lancaster Infirmary, Lancaster	11 (9)
Royal Liverpool Hospital, Liverpool	28 (24)
Royal Oldham Hospital, Oldham	9 (8)
Royal Sussex County Hospital, Brighton	18 (16)
Royal Victoria Hospital, Belfast	56 (56)
Russell's Hall Hospital, Dudley	19 (18)
Sandwell General Hospital, Lyndon	24 (18)
Southern General, Glasgow	3 (2)
St Mark's Hospital, Harrow	13 (13)
St Mary's Hospital, London	1 (1)
St Richard's Hospital, Chichester	9 (8)
Stepping Hill Hospital, Stockport	16 (13)
Tameside General Hospital, Ashton-under-Lyne	1 (1)
Taunton & Somerset NHS Trust (Musgrove Park), Taunton	24 (21)
Torbay Hospital, Torquay	55 (49)
Ulster Community Hospitals Trust, Belfast	14 (14)
University Hospitals Coventry and Warwickshire, Coventry	11 (10)
Victoria Hospital, Kirkcaldy	23 (21)
Victoria Infirmary, Glasgow	2 (2)



Wansbeck General Hospital, Ashington	32 (29)
Warwick Hospital, Warwick	12 (9)
Western General Hospital, Edinburgh	74 (70)
Weston General Hospital , Weston-Super-Mare	2 (2)
Wexham Park Hospital, Slough	8 (8)
Worcestershire Royal Hospital, Worcester	4 (4)
Wycombe Hospital, High Wycombe	4 (4)
Yeovil Hospital, Yeovil	10 (10)
York District Hospital, York	7 (5)

**Supplementary Table 3** Sample exclusions in the discovery data

	PreQC	Int	Sex	Het/ CR	Ancestry	Identity	Related	Phenotype	Unique Exc	PostQC
cases	1991	1	10	67	28	14	24	2	138	1852
58C	2930	32	11	163	57	1	20	0	256	2673
UKBS	2737	23	14	111	51	8	54	0	236	2499

Numbers of individuals excluded where column headings are: PreQC: the number of samples for which genotypes were available, Int: signal intensity from the chip outlying, Sex: sex modeled from X chromosome intensity mismatched with supplied sex, Het/CR: call rate and heterozygosity, Ancestry: HapMap PCA population exclusions Identity: <90% concordant with initial Sequenom genotypes, Relatedness: >5%IBD, Phenotype: Incorrect assignment of phenotype. Unique Exc: the number of unique sample excluded, PostQC: the number of samples carried through to the analysis stage.

**Supplementary Table 4** The top 100 ranked SNPs at which replication was attempted in the Stage 1 replication.

Chr	rsID	Position	Risk Allele	Cases RAF	Controls RAF	Discovery P value	Discovery OR	95% CI	Stage 1 UK Replication P value	Stage 1 UK Replication OR	95%CI	Meta P value
1	rs7522642	44335891	C	0.36	0.33	1.55E-04	1.17	(1.08-1.27)	0.176	0.937	(0.852-1.03)	4.62E-02
1	rs1503832	114291212	C	0.27	0.24	1.83E-04	1.19	(1.08-1.30)	0.242	0.94	(0.847-1.04)	3.77E-02
1	rs4448517	114681615	G	0.22	0.19	6.64E-05	1.22	(1.10-1.34)	0.185	1.08	(0.964-1.21)	9.71E-05
1	rs7513382	158638733	G	0.5	0.46	1.29E-04	1.16	(1.08-1.25)	0.103	1.08	(0.985-1.18)	7.10E-05
1	rs7511950	185322184	G	0.23	0.2	1.01E-04	1.2	(1.10-1.32)	0.725	0.98	(0.876-1.10)	5.65E-03
2	rs3072	20741887	C	0.41	0.36	2.64E-07	1.23	(1.14-1.33)	0.222	1.06	(0.966-1.16)	2.43E-06
2	rs1377238	50252406	A	0.88	0.85	1.02E-04	1.24	(1.11-1.38)	0.311	0.936	(0.825-1.06)	2.17E-02
2	rs11126740	79754603	A	0.39	0.35	1.10E-05	1.19	(1.10-1.29)	0.220	0.943	(0.859-1.04)	1.00E-02
2	rs1365943	137282639	G	0.61	0.57	1.72E-04	1.16	(1.07-1.25)	0.225	1.06	(0.966-1.16)	2.62E-04
2	rs7583748	142571761	G	0.11	0.089	9.42E-05	1.3	(1.14-1.48)	0.359	1.08	(0.921-1.26)	3.46E-04
2	rs6756958	157845179	C	0.99	0.98	1.38E-04	1.75	(1.31-2.34)	0.604	1.09	(0.781-1.53)	1.23E-03
2	rs17270248	169674758	T	0.09	0.06	5.13E-06	1.42	(1.22-1.65)	0.191	0.888	(0.743-1.06)	8.19E-03

2	rs6742549	231160095	G	0.63	0.59	1.39E-04	1.16	(1.08-1.26)	0.801	1.01	(0.923-1.11)	2.10E-03
3	rs11716163	31782580	T	0.32	0.28	2.12E-05	1.2	(1.10-1.30)	0.133	0.927	(0.839-1.02)	2.23E-02
3	rs17070791	64433972	C	0.036	0.024	1.50E-04	1.57	(1.24-1.98)	0.621	0.933	(0.709-1.23)	1.02E-02
3	rs819848	157218708	G	0.32	0.29	4.60E-05	1.19	(1.09-1.29)	0.060	1.1	(0.996-1.21)	1.53E-05
3	rs9812221	166709890	C	0.25	0.22	5.41E-05	1.21	(1.10-1.32)	0.503	1.04	(0.931-1.16)	4.33E-04
3	rs7374644	172423777	C	0.72	0.68	3.13E-05	1.19	(1.10-1.29)	0.634	0.976	(0.884-1.08)	3.76E-03
3	rs2636054	177849508	T	0.31	0.27	1.23E-04	1.18	(1.08-1.28)	0.958	1	(0.907-1.11)	2.96E-03
4	rs4550900	155551224	T	0.26	0.23	1.08E-04	1.19	(1.09-1.30)	0.939	1	(0.902-1.12)	2.52E-03
4	rs4057791	164444582	A	0.39	0.35	3.69E-05	1.18	(1.09-1.28)	0.333	1.05	(0.954-1.15)	1.65E-04
4	rs11938564	187449128	G	0.26	0.23	1.42E-04	1.19	(1.09-1.30)	0.876	0.991	(0.89-1.10)	4.71E-03
5	rs702628	53432695	C	0.34	0.31	4.11E-05	1.18	(1.09-1.29)	0.619	1.02	(0.93-1.13)	5.31E-04
5	rs10053323	117897564	C	0.21	0.18	1.46E-04	1.21	(1.09-1.33)	0.385	1.05	(0.938-1.18)	5.38E-04
5	rs2731672	176775080	T	0.27	0.24	1.64E-04	1.18	(1.08-1.29)	8.03E-03	1.15	(1.04-1.28)	4.38E-06

6	rs9467504	25522304	G	0.18	0.15	9.79E-05	1.23	(1.11-1.36)	0.954	0.996	(0.884-1.12)	3.54E-03
6	rs1892250	25877003	C	0.91	0.88	1.38E-04	1.27	(1.12-1.44)	0.020	1.19	(1.03-1.37)	1.04E-05
6	rs9393692	26384629	G	0.55	0.52	3.99E-05	1.17	(1.09-1.27)	0.382	1.04	(0.951-1.14)	2.17E-04
6	rs13211507	28365356	T	0.906	0.88	5.85E-06	1.32	(1.17-1.49)	0.028	1.17	(1.02-1.35)	1.09E-06
6	rs9257809	29464310	A	0.902	0.87	2.78E-07	1.36	(1.21-1.53)	0.061	1.14	(0.994-1.31)	2.97E-07
6	rs9261290	30146626	T	0.89	0.87	1.58E-06	1.32	(1.18-1.48)	0.151	1.1	(0.965-1.26)	4.56E-06
6	rs9262143	30760760	C	0.88	0.85	4.27E-07	1.33	(1.19-1.48)	0.073	1.12	(0.989-1.28)	5.44E-07
6	rs886403	31065597	T	0.74	0.71	4.47E-05	1.19	(1.10-1.30)	0.380	1.05	(0.947-1.15)	2.38E-04
6	rs4143332	31456344	G	0.88	0.86	1.09E-04	1.25	(1.11-1.39)	0.242	1.08	(0.949-1.23)	2.21E-04
6	rs2734583	31613459	A	0.88	0.86	2.37E-05	1.27	(1.14-1.42)	0.225	1.08	(0.952-1.23)	6.28E-05
6	rs1270942	32026839	A	0.89	0.87	4.92E-05	1.27	(1.13-1.43)	0.558	1.04	(0.91-1.19)	5.46E-04
6	rs3129963	32488186	A	0.83	0.81	5.32E-05	1.22	(1.11-1.35)	0.506	1.04	(0.927-1.17)	4.42E-04
6	rs9275686	32795548	G	0.8	0.77	9.52E-05	1.2	(1.09-1.31)	0.893	1.01	(0.903-1.12)	2.05E-03

6	rs924974	100869934	T	0.38	0.35	1.53E-04	1.17	(1.08-1.26)	0.311	0.953	(0.867-1.05)	2.58E-02
7	rs2107785	80802211	T	0.913	0.89	1.41E-05	1.32	(1.16-1.50)	0.746	0.976	(0.841-1.13)	1.85E-03
7	rs851727	146997887	T	0.962	0.946	1.45E-04	1.4	(1.18-1.67)	0.044	1.24	(1.01-1.52)	2.63E-05
7	rs1860218	153276785	G	0.34	0.31	5.20E-05	1.19	(1.09-1.29)	0.164	1.07	(0.972-1.18)	6.72E-05
7	rs3734960	154315086	C	0.29	0.26	2.13E-05	1.21	(1.11-1.32)	0.037	1.11	(1.01-1.23)	4.60E-06
7	rs35936561	155880035	A	0.39	0.36	1.03E-05	1.19	(1.10-1.29)	0.276	1.05	(0.96-1.15)	4.75E-05
8	rs11993663	10070304	A	0.36	0.32	4.35E-05	1.19	(1.09-1.29)	0.709	1.02	(0.926-1.12)	8.04E-04
8	rs12156009	11322629	A	0.54	0.5	5.73E-05	1.17	(1.08-1.26)	0.186	1.06	(0.971-1.16)	9.05E-05
8	rs2898290	11471318	T	0.5	0.47	2.02E-04	1.16	(1.07-1.25)	0.062	1.09	(0.996-1.19)	5.38E-05
8	rs13273672	11649790	C	0.34	0.3	8.20E-08	1.25	(1.15-1.36)	0.376	1.04	(0.948-1.15)	2.99E-06
8	rs6998330	21284826	T	0.19	0.16	1.94E-04	1.21	(1.10-1.34)	0.376	0.948	(0.842-1.07)	2.40E-02
8	rs12679938	59661239	G	0.33	0.3	1.93E-04	1.17	(1.08-1.27)	0.474	0.965	(0.876-1.06)	1.78E-02
8	rs2954866	76048661	A	0.87	0.85	1.61E-04	1.23	(1.11-1.38)	0.601	0.966	(0.85-1.10)	1.14E-02

8	rs2945756	134755247	A	0.35	0.32	1.94E-05	1.19	(1.10-1.29)	0.820	1.01	(0.919-1.11)	6.39E-04
8	rs13272742	137348023	A	0.89	0.86	1.69E-04	1.24	(1.11-1.39)	0.490	0.955	(0.836-1.09)	1.57E-02
9	rs1800651	70841425	G	0.28	0.24	9.70E-05	1.19	(1.09-1.30)	0.730	0.982	(0.884-1.09)	5.70E-03
9	rs11265889	91532610	A	0.28	0.25	9.49E-05	1.19	(1.09-1.29)	0.300	0.947	(0.855-1.05)	2.05E-02
9	rs9696872	92781054	C	0.66	0.62	8.87E-05	1.17	(1.08-1.27)	0.780	1.01	(0.924-1.11)	1.56E-03
9	rs913913	99337413	A	0.25	0.22	1.44E-04	1.19	(1.09-1.31)	0.144	1.08	(0.973-1.21)	1.18E-04
9	rs7861786	126041281	G	0.7	0.67	1.94E-04	1.17	(1.08-1.26)	0.210	0.94	(0.853-1.04)	4.02E-02
10	rs6593440	44617535	C	0.9	0.87	3.63E-05	1.28	(1.14-1.45)	0.285	1.08	(0.938-1.24)	1.21E-04
10	rs7091469	52742174	T	0.19	0.16	1.42E-05	1.25	(1.13-1.39)	0.758	0.981	(0.869-1.11)	1.75E-03
10	rs7895043	71016742	C	0.49	0.46	8.41E-05	1.17	(1.08-1.26)	0.426	1.04	(0.948-1.14)	4.49E-04
11	rs949538	88542052	G	0.93	0.91	1.49E-04	1.31	(1.14-1.50)	0.566	1.05	(0.891-1.23)	1.09E-03
11	rs7116731	113835228	A	0.6	0.56	2.20E-05	1.18	(1.09-1.27)	0.304	0.953	(0.87-1.04)	9.15E-03
11	rs633040	131236636	T	0.68	0.63	1.61E-05	1.19	(1.10-1.29)	0.785	1.01	(0.922-1.11)	5.19E-04

12	rs2239073	2408761	C	0.44	0.41	3.47E-05	1.18	(1.09-1.27)	0.583	1.03	(0.937-1.12)	4.45E-04
12	rs2037744	16191109	A	0.14	0.11	7.54E-05	1.27	(1.13-1.43)	0.357	0.937	(0.816-1.08)	1.56E-02
12	rs10771272	26291854	G	0.84	0.81	1.82E-04	1.21	(1.09-1.33)	0.920	1.01	(0.896-1.13)	3.49E-03
12	rs11564281	38644957	A	0.13	0.11	1.22E-04	1.26	(1.12-1.42)	0.840	1.01	(0.879-1.17)	2.06E-03
12	rs4768467	41584140	G	0.77	0.74	4.87E-05	1.2	(1.10-1.31)	0.666	1.02	(0.923-1.13)	7.43E-04
12	rs11176874	66482939	G	0.48	0.45	7.71E-05	1.17	(1.08-1.26)	0.171	0.939	(0.858-1.03)	3.44E-02
12	rs17110081	70325202	A	0.15	0.13	1.47E-04	1.24	(1.11-1.39)	0.436	1.05	(0.925-1.20)	7.10E-04
13	rs9506800	21675161	A	0.36	0.32	1.64E-04	1.17	(1.08-1.27)	0.126	0.928	(0.842-1.02)	5.66E-02
13	rs3923500	85657509	C	0.82	0.78	1.88E-05	1.23	(1.12-1.35)	0.058	1.11	(0.996-1.24)	7.69E-06
13	rs1751036	94516666	C	0.051	0.038	7.97E-05	1.5	(1.22-1.83)	0.079	0.813	(0.645-1.02)	6.67E-02
13	rs7322495	109789286	C	0.27	0.24	7.84E-05	1.2	(1.09-1.31)	0.706	1.02	(0.918-1.13)	1.08E-03
14	rs12883673	80550575	A	0.9	0.88	1.60E-04	1.26	(1.12-1.42)	0.022	0.846	(0.733-0.977)	1.49E-01
15	rs1820995	55120263	A	0.61	0.57	8.16E-05	1.17	(1.08-1.26)	0.782	0.987	(0.902-1.08)	4.80E-03

15	rs2218260	56001502	C	0.43	0.39	4.24E-05	1.17	(1.09-1.27)	0.047	1.1	(1.00-1.20)	1.04E-05
15	rs12148329	78788333	G	0.17	0.14	1.29E-04	1.22	(1.10-1.36)	0.126	0.906	(0.799-1.03)	4.75E-02
15	rs1457853	93325178	A	0.38	0.34	6.06E-05	1.18	(1.09-1.27)	0.668	1.02	(0.929-1.12)	8.10E-04
15	rs2535483	95357916	T	0.27	0.24	3.67E-05	1.2	(1.10-1.31)	0.108	1.09	(0.981-1.21)	2.65E-05
16	rs2043633	5759275	T	0.63	0.59	6.04E-05	1.17	(1.08-1.27)	0.021	1.11	(1.02-1.22)	5.21E-06
16	rs7205607	7914506	A	0.41	0.37	1.49E-04	1.16	(1.08-1.26)	0.772	1.01	(0.924-1.11)	2.11E-03
16	rs6497831	25233567	T	0.67	0.64	1.62E-04	1.17	(1.08-1.26)	0.640	1.02	(0.931-1.12)	1.48E-03
16	rs9936833	84960619	C	0.42	0.38	8.18E-06	1.2	(1.11-1.29)	6.24E-05	1.21	(1.10-1.32)	2.08E-09
17	rs1105936	3857362	G	0.85	0.81	2.63E-05	1.24	(1.12-1.37)	0.540	0.965	(0.86-1.08)	5.73E-03
17	rs11658327	28991792	C	0.89	0.86	1.97E-05	1.28	(1.14-1.43)	0.692	0.974	(0.857-1.11)	3.27E-03
17	rs1001865	78508277	T	0.3	0.27	1.78E-04	1.18	(1.08-1.29)	0.123	0.924	(0.836-1.02)	6.60E-02
18	rs9955953	5760922	A	0.06	0.04	1.67E-04	1.42	(1.18-1.70)	0.747	0.966	(0.784-1.19)	8.42E-03
18	rs17188857	21707077	A	0.85	0.82	2.02E-06	1.28	(1.15-1.41)	0.211	0.927	(0.823-1.04)	4.85E-03



18	rs7233779	30697224	G	0.88	0.85	1.43E-04	1.23	(1.11-1.37)	0.661	1.03	(0.904-1.17)	1.33E-03
18	rs12956753	65544165	T	0.24	0.21	1.26E-04	1.2	(1.09-1.31)	0.839	1.01	(0.907-1.13)	2.31E-03
19	rs10423674	18678903	C	0.7	0.66	5.14E-05	1.18	(1.09-1.28)	0.412	1.04	(0.946-1.14)	3.00E-04
19	rs4802138	47696238	T	0.28	0.24	2.04E-04	1.18	(1.08-1.29)	0.800	1.01	(0.913-1.12)	2.67E-03
19	rs17835915	57399786	A	0.17	0.15	1.18E-04	1.23	(1.11-1.37)	0.171	0.916	(0.809-1.04)	4.10E-02
20	rs6039511	958089	T	0.07	0.05	1.94E-04	1.37	(1.16-1.62)	0.373	0.913	(0.746-1.12)	2.10E-02
20	rs4814019	11456980	C	0.34	0.3	4.01E-06	1.21	(1.12-1.32)	0.419	0.96	(0.87-1.06)	2.40E-03
21	rs3916645	9884717	A	0.035	0.023	7.09E-05	1.64	(1.28-2.09)	0.759	0.952	(0.697-1.30)	3.25E-03
21	rs2824400	17920408	A	0.64	0.59	9.35E-06	1.19	(1.10-1.29)	0.782	1.01	(0.925-1.11)	3.90E-04
22	rs8136975	48313720	C	0.41	0.38	1.60E-04	1.16	(1.07-1.26)	0.444	0.964	(0.879-1.06)	1.68E-02

**Supplementary Table 5** All additional loci at which replication was attempted in the Stage 1 and Stage 2 replication

(Results for lead SNPs on 6p21 and 16q24 are presented in Table 1).

Chr	rsID	Position	Risk allele	Discovery					Stage 1 replication P value	Stage 2 replication P value	Meta P
				Cases RAF	Controls RAF	Discovery P value	Discovery OR	95% CI			
1	rs7513382	158638733	C	0.496	0.463	1.29x10 <sup>-4</sup>	1.16	(1.08-1.25)	0.103	(-) 0.0370	3.95x10 <sup>-3</sup>
2	rs3072	20741887	G	0.408	0.363	2.64x10 <sup>-7</sup>	1.23	(1.14-1.33)	0.222	0.0180	1.45x10 <sup>-7</sup>
5	rs2731672	176775080	A	0.274	0.240	1.64x10 <sup>-4</sup>	1.18	(1.08-1.29)	8.03x10 <sup>-3</sup>	0.289	3.24x10 <sup>-6</sup>
6	rs13211507	28365356	A	0.906	0.880	5.85x10 <sup>-6</sup>	1.32	(1.17-1.49)	0.028	1.02x10 <sup>-3</sup>	8.77x10 <sup>-9</sup>
6	rs9262143	30760760	G	0.882	0.852	4.27x10 <sup>-7</sup>	1.33	(1.19-1.48)	0.073	0.0111	2.18x10 <sup>-8</sup>
7	rs1860218	153276785	G	0.338	0.306	5.20x10 <sup>-5</sup>	1.19	(1.09-1.29)	0.164	(-) 0.111	2.20x10 <sup>-3</sup>
7	rs3734960	154315086	G	0.292	0.259	2.13x10 <sup>-5</sup>	1.21	(1.11-1.32)	0.037	0.340	3.97x10 <sup>-6</sup>
8	rs13273672	11649790	G	0.344	0.301	8.20x10 <sup>-8</sup>	1.25	(1.15-1.36)	0.376	(-) 0.619	3.43x10 <sup>-5</sup>
8	rs8180912	11677400	A	0.224	0.191	3.63x10 <sup>-6</sup>	1.25	(1.14-1.37)	0.163	0.966	3.47x10 <sup>-5</sup>
13	rs3923500	85657509	G	0.818	0.785	1.88x10 <sup>-5</sup>	1.23	(1.12-1.35)	0.058	0.0340	7.77x10 <sup>-7</sup>
15	rs2218260	56001502	G	0.433	0.393	4.24x10 <sup>-5</sup>	1.17	(1.09-1.27)	0.047	0.261	6.50x10 <sup>-6</sup>
15	rs2535483	95357916	A	0.273	0.238	3.67x10 <sup>-5</sup>	1.2	(1.10-1.31)	0.108	0.0105	1.22x10 <sup>-6</sup>
16	rs2043633	5759275	A	0.629	0.588	6.04x10 <sup>-5</sup>	1.17	(1.08-1.27)	0.021	0.0177	3.12x10 <sup>-7</sup>
19	rs10423674	18678903	G	0.700	0.661	5.14x10 <sup>-5</sup>	1.18	(1.09-1.28)	0.412	0.564	3.56x10 <sup>-4</sup>

(-) Direction of risk opposite to that in the discovery population. All P values are 2-sided.

**Supplementary Table 6** Table of association with imputed classical HLA alleles.

HLA allele	Discovery						Stage 1 UK Replication						Combined		
	Case MAF	Con MAF	missing data proportion	Beta	SE	P value	Case MAF	Con MAF	missing data proportion	Beta	SE	P value	Beta	SE	P value
HLADQB*201	0.13	0.15	0.02	-0.20	0.06	4.36 x 10 <sup>-4</sup>	0.17	0.16	0.10	0.03	0.07	6.70 x 10 <sup>-1</sup>	-0.10	0.04	1.67 x 10 <sup>-2</sup>
<b>HLAC*701</b>	<b>0.15</b>	<b>0.18</b>	<b>0.02</b>	<b>-0.18</b>	<b>0.05</b>	<b>4.96 x 10<sup>-4</sup></b>	<b>0.01</b>	<b>0.01</b>	<b>0.05</b>	<b>0.21</b>	<b>0.30</b>	<b>4.79 x 10<sup>-1</sup></b>	<b>0.35</b>	<b>0.19</b>	<b>6.44 x 10<sup>-2</sup></b>
<b>HLAB*801</b>	<b>0.13</b>	<b>0.15</b>	<b>0.05</b>	<b>-0.20</b>	<b>0.06</b>	<b>5.88 x 10<sup>-4</sup></b>	<b>0.13</b>	<b>0.14</b>	<b>0.03</b>	<b>0.11</b>	<b>0.07</b>	<b>1.10 x 10<sup>-1</sup></b>	<b>0.02</b>	<b>0.10</b>	<b>8.66 x 10<sup>-1</sup></b>
HLAC*1701	0.01	0.01	0.02	0.72	0.24	2.96 x 10 <sup>-3</sup>	0.01	0.01	0.05	-0.21	0.30	4.79 x 10 <sup>-1</sup>	0.35	0.19	6.44 x 10 <sup>-2</sup>
<b>HLAA*101</b>	<b>0.18</b>	<b>0.20</b>	<b>0.03</b>	<b>-0.13</b>	<b>0.05</b>	<b>7.49 x 10<sup>-3</sup></b>	<b>0.18</b>	<b>0.19</b>	<b>0.06</b>	<b>0.07</b>	<b>0.06</b>	<b>2.53 x 10<sup>-1</sup></b>	<b>0.11</b>	<b>0.04</b>	<b>5.26 x 10<sup>-3</sup></b>
HLADQB*602	0.16	0.14	0.02	0.15	0.06	7.86 x 10 <sup>-3</sup>	0.13	0.14	0.10	-0.01	0.07	8.61 x 10 <sup>-1</sup>	0.09	0.04	4.71 x 10 <sup>-2</sup>
HLADQA*501	0.22	0.24	0.05	-0.12	0.05	1.31 x 10 <sup>-2</sup>	0.22	0.24	0.06	-0.11	0.06	3.99 x 10 <sup>-2</sup>	-0.11	0.04	1.28 x 10 <sup>-3</sup>
HLADQA*102	0.20	0.18	0.05	0.10	0.05	3.87 x 10 <sup>-2</sup>	0.19	0.18	0.06	0.04	0.06	5.53 x 10 <sup>-1</sup>	0.08	0.04	4.95 x 10 <sup>-2</sup>
HLAA*2501	0.03	0.02	0.03	0.26	0.13	4.77 x 10 <sup>-2</sup>	0.02	0.02	0.06	0.21	0.19	2.61x 10 <sup>-1</sup>	0.24	0.11	2.33x 10 <sup>-2</sup>

HLA alleles shown in bold also showed evidence of a protective effect on disease risk when analysed using GENECLUSTER.  $\log_{10}BF = 3.71$  for the single mutation mode

**Supplementary Table 7A** Table of association at rs9257809 (chromosome 6) with only the cases that have intestinal metaplasia

Cohort	Beta	SE	P value	N cases	N controls	p-het
Discovery	-0.294	0.062	2.04x 10 <sup>-6</sup>	1662	5172	
Stage 1	-0.214	0.084	0.011	734	6819	
Stage 2	-0.389	0.122	0.001	379	1780	
UK rep2	-0.126	0.0808	0.118	1318	1586	
Irish	0.045	0.153	0.767	245	473	
BEACON	-0.125	0.072	0.083	2396	2167	
<b>meta</b>	<b>-0.201</b>	<b>0.034</b>	<b>3.87x10<sup>-9</sup></b>			0.063

**Supplementary Table 7B** Table of association at rs9936833 (chromosome 16) with only the cases that have intestinal metaplasia

_	Beta	SE	P value	N cases	N controls	p-het
Discovery	0.182	0.042	1.37 x10 <sup>-5</sup>	1662	5172	
Stage 1	0.198	0.056	4.58 x10 <sup>-4</sup>	734	6819	
Stage 2	0.122	0.086	0.154	379	1780	
UK rep2	0.005	0.054	0.931	1318	1586	
Irish	0.083	0.114	0.468	245	473	
BEACON	0.151	0.043	5.02 x 10 <sup>-4</sup>	2397	2165	
<b>meta</b>	<b>0.139</b>	<b>0.023</b>	<b>8.51x10<sup>-10</sup></b>			0.137

**Supplementary Table 8** Results for SNPs associated with Circumference (C) and Maximal length (M) measurement of the Barrett's segment at  $P < 10^{-5}$ .

SNPs associated with C measurements

Chr	rsID	Position	Discovery					
			A1	A2	MAF	Beta	SE	P value
3	rs1912785	147884861	A	G	0.41	-0.15	0.03	$7.81 \times 10^{-6}$
12	rs1531228	13520648	A	G	0.14	0.20	0.05	$9.40 \times 10^{-6}$
15	rs12901001	84660480	A	G	0.35	0.15	0.03	$5.50 \times 10^{-6}$

SNPs associated with M measurements

Chr	rsID	Position	A1	A2	Discovery				Stage 1 UK Replication			Stage 2 Dutch Replication			Meta		
					MAF	Beta	SE	P	Beta	SE	P	Beta	SE	P	Beta	SE	P
9	rs10123313	4278098	A	G	0.01	-0.72	0.14	$1.62 \times 10^{-7}$	-0.13	0.18	0.48	0.16	0.41	0.70	-0.45	0.10	$1.53 \times 10^{-5}$
5	rs1004385	111706536	A	G	0.11	0.25	0.05	$1.21 \times 10^{-6}$									
5	rs6594591	111719360	A	G	0.10	-0.24	0.05	$6.14 \times 10^{-6}$									
5	rs821735	111695471	A	C	0.11	-0.23	0.05	$7.68 \times 10^{-6}$									
12	rs12425938	60770659	A	G	0.15	-0.19	0.04	$8.91 \times 10^{-6}$									
12	rs9669389	60776776	A	G	0.15	-0.19	0.04	$9.26 \times 10^{-6}$									

**Supplementary Table 9** Sex-stratified analysis of 16 SNPs for which replication was attempted

Male-only analysis (M): Discovery: 1488 cases, 2611 controls. UK replication: 785 cases, 3270 controls. NL replication: 350 cases, 1054 controls. Female-only analysis (F): Discovery 364 cases, 2564 controls. UK replication: 319 cases, 3512 controls. NL replication: 123 cases, 726 controls.

rsID	Sex	Risk allele	Discovery		Stage 1 UK Replication		Stage 2 Dutch Replication		Meta		P <sub>interaction</sub>			
			OR (95%CI)	P	OR	P	OR	P	OR	P	Dis	UK rep	D rep	Meta
rs7513382	M	C	1.17 (1.07-1.28)	9.63x10 <sup>-4</sup>	1.04 (0.93-1.17)	0.44	0.81 (0.68-0.96)	0.01	1.06 (1-1.14)	0.07	0.38	0.37	0.21	0.13
	F	C	1.25 (1.07-1.46)	5.69x10 <sup>-3</sup>	1.14 (0.97-1.33)	6.29x10 <sup>-3</sup>	0.98 (0.75-1.28)	0.90	1.16 (1.05-1.29)	4.53x10 <sup>-3</sup>				
rs3072	M	G	1.24 (1.13-1.37)	5.96x10 <sup>-6</sup>	1.03 (0.92-1.16)	0.56	1.24 (1.04-1.48)	0.01	1.17 (1.09-1.25)	6.60x10 <sup>-6</sup>	0.52	0.83	0.51	0.57
	F	G	1.16 (0.98-1.37)	0.08	1.05 (0.89-1.25)	0.08	1.11 (0.84-1.47)	0.45	1.11 (1-1.24)	0.06				
rs2731672	M	A	1.11 (1-1.23)	0.05	1.12 (0.99-1.28)	0.07	1.09 (0.89-1.33)	0.43	1.10 (1.03-1.19)	7.12x10 <sup>-3</sup>	0.04	0.42	0.55	0.02
	F	A	1.39 (1.16-1.67)	3.17x10 <sup>-4</sup>	1.24 (1.03-1.50)	2.05x10 <sup>-4</sup>	1.22 (0.9-1.64)	0.20	1.29 (1.15-1.46)	1.98x10 <sup>-5</sup>				
rs13211507	M	A	1.43 (1.23-1.64)	1.73x10 <sup>-6</sup>	1.25 (1.05-1.50)	0.01	1.42 (1.08-1.87)	0.01	1.36 (1.23-1.51)	4.52x10 <sup>-9</sup>	0.11	0.15	0.79	0.05
	F	A	1.14 (0.88-1.45)	0.32	1 (0.78-1.29)	0.3	1.5 (0.99-2.26)	0.06	1.13 (0.96-1.33)	0.14				
rs9257809	M	A	1.47 (1.28-1.69)	5.26x10 <sup>-8</sup>	1.23 (1.04-1.46)	0.02	1.46 (1.12-1.9)	4.76x10 <sup>-3</sup>	1.38 (1.25-1.53)	1.71x10 <sup>-10</sup>	0.09	0.12	0.79	0.01
	F	A	1.16 (0.91-1.47)	0.23	1.03 (1.31-80)	0.24	1.37 (0.91-2.05)	0.13	1.11 (0.95-1.3)	0.19				

rs9262143	M	G	1.40 (1.23-1.6)	3.92x10 <sup>-7</sup>	1.2 (1.02-1.41)	0.02	1.31 (1.02-1.68)	0.04	1.32 (1.2-1.45)	8.94x10 <sup>-9</sup>	0.37	0.11	0.92	0.07
	F	G	1.25 (1-1.57)	0.05	1.05 (0.84-1.32)	0.06	1.27 (0.87-1.85)	0.21	1.13 (0.97-1.31)	0.12				
rs1860218	M	G	1.18 (1.07-1.31)	8.39x10 <sup>-4</sup>	1.07 (0.95-1.21)	0.26	0.88 (0.74-1.05)	0.17	1.09 (1.02-1.17)	0.01	0.59	0.96	0.99	0.73
	F	G	1.22 (1.03-1.44)	0.02	1.08 (0.91-1.29)	0.03	0.88 (0.66-1.17)	0.37	1.1 (0.98-1.23)	0.10				
rs3734960	M	G	1.18 (1.07-1.31)	1.49x10 <sup>-3</sup>	1.08 (0.96-1.22)	0.2	1.13 (0.92-1.38)	0.24	1.14 (1.06-1.23)	5.43x10 <sup>-4</sup>	0.90	0.87	0.58	0.96
	F	G	1.21 (1.01-1.45)	0.04	1.1 (0.91-1.32)	0.05	1.01 (0.74-1.38)	0.93	1.13 (1.01-1.28)	0.04				
rs13273672	M	G	1.25 (1.13-1.37)	8.07x10 <sup>-6</sup>	1 (0.89-1.13)	0.93	1.08 (0.9-1.31)	0.39	1.13 (1.06-1.22)	3.56x10 <sup>-4</sup>	0.83	0.56	0.02	0.43
	F	G	1.24 (1.04-1.47)	0.01	1.07 (0.90-1.28)	0.02	1.39 (1.05-1.85)	0.02	1.07 (0.96-1.2)	0.23				
rs8180912	M	A	1.22 (1.09-1.37)	5.27x10 <sup>-4</sup>	1.08 (0.94-1.24)	0.27	1.14 (0.92-1.42)	0.22	1.15 (1.07-1.26)	3.36x10 <sup>-4</sup>	0.81	0.64	0.04	0.38
	F	A	1.30 (1.06-1.59)	9.95x10 <sup>-3</sup>	1.02 (0.83-1.26)	0.02	0.76 (1.06-0.54)	0.11	1.08 (0.95-1.23)	0.25				
rs3923500	M	G	1.18 (1.05-1.32)	5.09x10 <sup>-3</sup>	1.11 (0.97-1.27)	0.14	1.18 (0.95-1.45)	0.13	1.15 (1.06-1.25)	6.56x10 <sup>-4</sup>	0.30	0.74	0.49	0.25
	F	G	1.33 (1.1-1.61)	3.09x10 <sup>-3</sup>	1.15 (0.95-1.40)	5.34x10 <sup>-3</sup>	1.34 (0.96-1.89)	0.09	1.25 (1.1-1.42)	4.79x10 <sup>-4</sup>				
rs2218260	M	G	1.19 (1.09-1.31)	2.23x10 <sup>-4</sup>	1.13 (1.01-1.26)	0.04	1.11 (0.93-1.32)	0.24	1.16 (1.08-1.24)	1.66x10 <sup>-5</sup>	0.35	0.31	0.58	0.11
	F	G	1.11 (0.95-1.29)	0.20	1.02 (0.86-1.20)	0.25	1.01 (0.77-1.33)	0.93	1.06 (0.95-1.17)	0.31				
rs2535483	M	A	1.16 (1.05-1.28)	4.29x10 <sup>-3</sup>	1.12 (0.98-1.27)	0.09	1.18 (0.97-1.44)	0.09	1.15 (1.07-1.24)	2.51x10 <sup>-4</sup>	0.15	0.33	0.46	0.52
	F	A	1.35 (1.12-1.61)	1.45x10 <sup>-3</sup>	1 (0.83-1.22)	1.66x10 <sup>-3</sup>	1.37 (1-1.88)	0.05	1.19 (1.06-1.35)	4.49x10 <sup>-3</sup>				

rs2043633	M	A	1.11 (1.01-1.2)	0.04	1.12 (1.00-1.26)	0.04	1.23 (1.04-1.45)	0.02	1.12 (1.06-1.2)	3.23x10 <sup>-4</sup>	0.06	0.66	0.46	0.51
	F	A	1.35 (1.16-1.59)	1.80x10 <sup>-4</sup>	1.07 (0.91-1.26)	1.67x10 <sup>-4</sup>	1.09 (0.83-1.43)	0.55	1.19 (1.07-1.32)	1.15x10 <sup>-3</sup>				
rs9936833	M	G	1.19 (1.08-1.30)	3.56x10 <sup>-4</sup>	1.18 (1.05-1.32)	4.06x10 <sup>-3</sup>	1.16 (0.96-1.39)	0.12	1.18 (1.1-1.26)	1.64x10 <sup>-6</sup>	0.72	0.61	0.09	0.84
	F	G	1.25 (1.06-1.47)	6.98x10 <sup>-3</sup>	1.24 (1.05-1.47)	8.15x10 <sup>-3</sup>	0.86 (0.64-1.15)	0.31	1.18 (1.06-1.32)	2.29x10 <sup>-3</sup>				
rs10423674	M	C	1.15 (1.04-1.27)	6.06x10 <sup>-3</sup>	1 (0.89-1.13)	0.93	0.98 (0.81-1.18)	0.80	1.07 (1-1.15)	0.05	0.48	0.27	0.30	0.19
	F	C	1.23 (1.04-1.44)	0.02	1.14 (0.96-1.35)	0.01	1.17 (0.88-1.56)	0.29	1.18 (1.05-1.31)	3.76x10 <sup>-3</sup>				



**Supplementary Table 10A** Results for SNPs associated with body mass index (BMI) or waist-hip ratio (WHR) that are genotyped in the discovery data. Risk alleles are given for the forward strand.

Chr	rsID	Position	Phenotype	Risk Allele	Gene	Reference	Discovery Risk allele	Discovery P value
1	rs1514175	74,764,232	BMI	A	<i>TNNI3K</i>	1	A	0.0780
1	rs1011731	170,613,171	WHR	G	<i>DNM3-PIGC</i>	2	G	0.752
2	rs2867125	612,827	BMI	C	<i>TMEM18</i>	1	T	0.846
2	rs10195252	165,221,337	WHR	T	<i>GRB14</i>	2	C	0.553
3	rs6795735	64,680,405	WHR	C	<i>ADAMTS9</i>	2	C	0.255
3	rs13078807	85,966,840	BMI	G	<i>CADM2</i>	1	G	0.0910
4	rs13107325	103,407,732	BMI	T	<i>SLC39A8</i>	1	C	0.897
6	rs987237	50,911,009	BMI/WC	G	<i>TFAP2B</i>	3	G	0.113
7	rs1055144	25,837,634	WHR	T	<i>NFE2L3</i>	2	T	0.407
9	rs10968576	28,404,339	BMI	G	<i>LRRN6C</i>	1	G	0.0858
12	rs718314	26,344,550	WHR	G	<i>ITPR2-SSPN</i>	3	A	0.756
12	rs7138803	48,533,735	BMI	A	<i>FAIM2</i>	1	A	0.647
12	rs1443512	52,628,951	WHR	A	<i>HOXC13</i>	3	A	0.0806
14	rs10146997	79,014,915	BMI/WC	G	<i>NRXN3</i>	4	G	9.63x10 <sup>-3</sup>
15	rs2241423	65,873,892	BMI	G	<i>MAP2K5</i>	1	G	0.142
18	rs571312	55,990,749	BMI	A	<i>MC4R</i>	1	A	0.0888
18	rs12970134	56,035,730	BMI/WC	A	<i>MC4R</i>	5	A	0.0991
19	rs29941	39,001,372	BMI	G	<i>KCTD15</i>	1	A	0.623
19	rs2287019	50,894,012	BMI	C	<i>QPCTL</i>	1	C	0.0932

**Supplementary Table 10B** Results in the BE discovery scan for tags of SNPs associated with BMI or WHR that were not genotyped in the discovery data. The genotyped tag SNPs are within 250kb and with  $r^2 > 0.8$  (according to 1000G CEU pilot1 June release). Risk alleles are given for the forward strand.

Chr	rsID	Position	Phenotype	Risk Allele	Gene	Reference	Tag SNP ( $r^2$ )	Tagged risk allele	Tag SNP P value
1	rs2815752	72,585,028	BMI	A	<i>NEGR1</i>	1	rs3101336 (0.96)	A	0.773
1	rs1555543	96,717,385	BMI	C	<i>PTBP2</i>	1	rs11165643 (1)	C	0.240
1	rs984222	119,305,366	WHR	G	<i>TBX15- WARS2</i>	2	rs10923724 (0.85)	G	0.452
1	rs543874	176,156,103	BMI	G	<i>SEC16B</i>	1	rs10913469 (0.96)	G	0.944
2	rs713586	25,011,512	BMI	C	<i>RBJ</i>	1	rs6752378 (1)	T	0.427
2	rs887912	59,156,381	BMI	T	<i>FANCL</i>	1	rs759250 (0.92)	T	0.929
4	rs10938397	44,877,284	BMI	G	<i>GNPDA2</i>	1	rs12641981 (0.90)	A	0.764
5	rs2112347	75,050,998	BMI	T	<i>FLJ35779</i>	1	rs253414 (0.81)	T	0.497
5	rs4836133	124,360,002	BMI	A	<i>ZNF608</i>	1	rs6864049 (1)	A	0.0840
5	rs6861681	173,295,064	WHR	A	<i>CPEB4</i>	2	rs7736263 (1)	A	0.386
6	rs1294421	6,688,148	WHR	G	<i>LY86</i>	2	rs1294433 (0.81)	T	0.977
6	rs206936	34,410,847	BMI	G	<i>NUDT3</i>	1	rs3798560 (1)	G	0.711
6	rs9491696	127,494,332	WHR	G	<i>RSPO3</i>	2	rs7766106 (0.96)	G	0.790
11	rs4929949	8,561,169	BMI	C	<i>RPL27A</i>	1	rs725502 (0.87)	T	0.784
11	rs10767664	27,682,562	BMI	A	<i>BDNF</i>	1	rs11030104 (0.90)	A	0.0308
11	rs3817334	47,607,569	BMI	T	<i>MTCH2</i>	1	rs7124681	T	0.162

							(0.94)		
16	rs12444979	19,841,101	BMI	C	<i>GPRC5B</i>	1	rs12446632 (0.88)	C	0.0892
16	rs7359397	28,793,160	BMI	T	<i>SH2B1</i>	1	rs4788102 (0.96)	C	0.633
16	rs1558902	52,361,075	BMI	A	<i>FTO</i>	1	rs9930333 (0.90)	A	0.571
19	rs3810291	52,260,843	BMI	A	<i>TMEM160</i>	1	rs2303108 (1)	G	0.0244
22	rs4823006	27,781,671	WHR	A	<i>ZNRF3- KREMEN1</i>	2	rs2294239 (0.90)	A	0.234

**Supplementary Table 11** Assay concordance between Illumina genotyping panels and Kaspar allele specific PCR.

		Discovery cases	Discovery and UK replication controls	UK and Irish cases	Dutch cases
		Illumina 670	Illumina 1.2	ImmunoChip	ImmunoChip
Concordance (sample size)					
rs9257809	Kaspar	1 (166)	0.99 (463)	1 (91)	1 (39)
rs9936833		1 (166)	1 (463)	0.99 (91)	1 (39)

## Supplementary Note

**DNA sample preparation.** Genomic DNA for all discovery cases was shipped to the Wellcome Trust Sanger Institute (WTSI), Cambridge. Where there was sufficient DNA, quality was validated using the Sequenom iPLEX assay designed to genotype 4 gender SNPs and 26 SNPs present on the Illumina Beadchips. DNA concentrations were quantified using a PicoGreen assay (Invitrogen) and an aliquot assayed by agarose gel electrophoresis. A DNA sample was considered to pass quality control if the DNA concentration was greater than or equal to 50 ng/ $\mu$ l, the DNA was not degraded, the sex assignment from the iPLEX assay matched that provided in the patient data manifest and genotypes were obtained for at least two thirds of the SNPs on the iPLEX.

**Discovery Sample Quality Control.** We used a Bayesian clustering approach to infer outlying individuals on the basis of call rate, heterozygosity, African or Asian ancestry (defined by a principal component analysis of the HapMap2 data; see Supplementary Figure 2) and average probe intensity. To obtain a set of putatively unrelated individuals we used a hidden Markov model (HMM) to infer identity by descent along the genome and then iteratively removed individuals to obtain a set with pair-wise identity by descent less than 5%. To guard against sample mishandling we removed samples if their inferred sex was discordant with the recorded sex or if less than 90% of the SNPs typed by Sequenom on entry to the sample handling (see above) agreed with the genome-wide data.

**Principal component analysis (PCA).** We performed Principal Component Analysis (PCA) on a subset of 205,842 post-QC SNPs (none from the MHC), selected so as to minimize the contribution from regions of strong linkage disequilibrium and to ensure that only genome-wide effects are detected. Principal component scores were computed for the combined dataset of post-exclusion case and control samples using the program SHELLFISH. Visual inspection of the SNP loadings suggests that the first principal component reflects genome-wide population structure (data not shown). It also significantly correlated with case-control status and was therefore included as covariate in association analysis.

### **PCA of BEACON samples.**

We performed Principal Component Analysis (PCA) as a two-step process using the SNPRelate software (<http://cran.r-project.org/web/packages/SNPRelate/index.html>). First, we used PCA to define a homogeneous set of European ancestry samples. We did this by running PCA on a set of

6,481 unrelated (except for six two-person families) subjects each of which was either an esophageal cancer case, a Barrett's esophagus case, or a control. A majority of these subjects (~97%) self-identified their race as "White" and a scatterplot of all subjects along the axes of the first two eigenvectors showed the majority of samples formed a tight cluster (data not shown). Therefore, we computed the medians and standard deviations (SD) of the first two eigenvectors and defined any sample that fell within a one SD rectangle of both eigenvector medians to be of homogeneous European ancestry (n=6,302). BE cases and all controls within the PCA defined European ancestry set were used in the replication analysis of rs9936833 and rs9257809.

Next, we performed PCA on these 6,302 subjects. For this analysis we used 66,554 non-monomorphic, autosomal SNPs that passed initial quality control, had missing call rate < 5%, minor allele frequency > 5%, and did not have an LD value > 0.2 between any two SNPs in a sliding window of 500K bases. We included the first four eigenvectors from this analysis as covariates in the association test model since they were significantly correlated with case-control status (of Barrett's esophagus vs. control) and a scree plot showed that the variance accounted for by each eigenvector flattened out after these four eigenvectors (data not shown). To check that only genome-wide variation was detected we computed the absolute value of the correlation coefficient of each of the four eigenvectors against the genotypes for each SNP and did not observe any localized regions of high correlations that would suggest an eigenvector had detected only local variation (data not shown). The lambda using these four eigenvectors was 1.037.

**Imputation.** SNPs were imputed using IMPUTE2 and the 1000 Genomes June 2010 release CEU reference population. Pre-QC there were 516123 SNPs on chromosome 6 and 235844 SNPs on chromosome 16. SNPs with info scores <0.5 were removed from the data, and following QC, 438040 SNPs remained on chr 6 (403914 imputed, 34126 genotyped) and 185980 SNPs remained on chr 16 (170206 imputed, 15774 genotyped).

**HLA imputation.** HLA\*IMP was used to impute classical HLA alleles using SNP genotype data for the discovery phase samples. The "MS\_NBS" set<sup>6</sup> of SNPs was selected to inform the imputation. This SNP set had been selected by the HLA\*IMP team for use in WTCCC2 studies. Best guess alleles imputed with a probability score greater than 0.7 were analysed. 145 different alleles imputed in all three datasets were investigated in the discovery, and alleles with the most significant associations were then imputed in the replication data. The "IMMUNOCHIP" set of SNPs, selected by the HLA\*IMP team was used to inform the replication phase HLA imputation.

**Testing for interactions.** To look for interactions between associated loci, we compared two logistic regression models. In the first (null) model, a separate parameter for each SNP specified the multiplicative increase in the odds of disease with each additional copy of the risk allele for that SNP. We compared this, using a likelihood ratio test, to a model for interaction in which there is a third parameter which modifies the effect associated with carrying risk alleles at both SNPs. There are many different ways to model both the marginal effects at each SNP and their joint effect<sup>7</sup>, and so there are many approaches to search for interactions. The procedure we adopted is perhaps the simplest (multiplicative model marginally at each SNP and a single additional parameter for multiplicative interactions) Similar analyses, using a binary indicator for male individuals, were used to test for interactions between sex and SNPs

**Meta-analysis.** A fixed effect meta-analysis was used to combine the evidence of association across the discovery and replication data sets. To do so, we first fit logistic regression models to each of the data sets as described in Methods, and then averaged the estimated effect size parameter across the data sets, weighting by precision of the estimates. Two-sided P-values were calculated assuming the combined data z-score to be normally distributed.

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