

Impact of a panel of 88 SNPs on the risk of breast
cancer in high risk women: Results from two
randomised tamoxifen prevention trials

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Supplementary material

Table S1: Distribution of the number SNP failures per sample, by treatment and trial

	0	1-5	6-10	11+
ALL	917 (82.8%)	145 (13.1%)	20 (1.8%)	25 (2.3%)
ALL: CASE	317 (77.9%)	62 (15.2%)	15 (3.7%)	13 (3.2%)
ALL: CONTROL	600 (85.7%)	83 (11.9%)	5 (0.7%)	12 (1.7%)
IBIS-I	717 (87.5%)	80 (9.8%)	5 (0.6%)	17 (2.1%)
IBIS-I: CASE	230 (87.5%)	26 (9.9%)	1 (0.4%)	6 (2.3%)
IBIS-I: CONTROL	487 (87.6%)	54 (9.7%)	4 (0.7%)	11 (2.0%)
MARSDEN	200 (69.4%)	65 (22.6%)	15 (5.2%)	8 (2.8%)
MARSDEN: CASE	87 (60.4%)	36 (25.0%)	14 (9.7%)	7 (4.9%)
MARSDEN: CASE (TISSUE)	1 (2.6%)	20 (51.3%)	12 (30.8%)	6 (15.4%)
MARSDEN: CASE (BLOOD)	86 (81.9%)	16 (15.2%)	2 (1.9%)	1 (1.0%)
MARSDEN: CONTROL	113 (78.5%)	29 (20.1%)	1 (0.7%)	1 (0.7%)

Table S2: Sample characteristics by trial. BMI: body mass index; Cont: Control; ER: estrogen-receptor; FDR: number of affected first-degree relatives; IQR: inter-quartile range; OR: odds ratio; TC: Tyrer-Cuzick model.

Factor	Value	IBIS (Case)	IBIS (Cont)	P (IBIS)	Mars (Case)	Mars (Cont)	P (Mars)
Total		256	532		103	104	
Treatment	Placebo	158	321		56	56	
	Tamoxifen	98	211		47	48	
ER Status	Positive	192	393		73	73	
	Negative	45	97		19	20	
	Unknown	19	42		11	11	
Age(y)	Median (IQR)	50 (46-54)	50 (46-54)	0.9	48 (44-54)	48 (44-54)	0.7
Age menarche (y)	<12	56 (22%)	129 (24%)	0.9	25 (25%)	23 (22%)	0.9
	12	51 (20%)	89 (17%)		16 (16%)	16 (15%)	
	>12	145 (58%)	309 (59%)		61 (60%)	65 (62%)	
	Unknown	4	5		1	0	
Nulliparous	Parous	42 (16%)	71 (13%)	0.31	19 (18%)	14 (13%)	0.41
	Age first (IQR)	23.0 (21.0-27.0)	24.0 (21.0-26.0)	0.7	25.0 (21.0-28.0)	26.0 (22.0-28.0)	0.9
	Unknown	6	10		0	0	
Menopause	Pre	127 (50%)	254 (48%)	0.32	61 (59%)	51 (49%)	0.043
	Peri	11 (4%)	19 (4%)		7 (7%)	8 (8%)	
	Post	118 (46%)	259 (49%)		35 (34%)	45 (43%)	
BMI (kg/m2)	Median (IQR)	26.4 (23.3-29.1)	25.8 (23.4-29.9)	0.6	23.1 (22.0-26.6)	23.4 (21.5-26.3)	0.46
	Unknown	5	7		6	1	
FDR	0	35 (14%)	51 (10%)	0.37	4 (4%)	4 (4%)	1.0
	1	181 (71%)	401 (75%)		80 (78%)	81 (78%)	
	>1	40 (16%)	80 (15%)		19 (18%)	19 (18%)	
TC OR	Median (IQR)	2.41 (1.89-3.03)	2.16 (1.76-2.71)	<0.001	2.63 (2.10-3.28)	2.39 (1.96-3.24)	0.11
SNP88	Median(IQR)	1.13 (0.82-1.58)	0.99 (0.70-1.39)	<0.001	1.13 (0.81-1.70)	1.08 (0.84-1.41)	0.6

Table S3: Number of failures by SNP.

SNP	Chr	Position	Case	Control	All
rs616488	1	10566215	3 (0.8%)	0 (0.0%)	3 (0.3%)
rs11249433	1	121280613	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs12405132	1	145644984	2 (0.6%)	0 (0.0%)	2 (0.2%)
rs12048493	1	149906413	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs72755295	1	242034263	3 (0.8%)	5 (0.8%)	8 (0.8%)
rs11552449	1	114448389	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs4245739	1	204518842	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs1045485	2	202149589	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs16857609	2	218296508	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs12710696	2	19320803	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs13387042	2	217905832	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs1550623	2	174212894	2 (0.6%)	0 (0.0%)	2 (0.2%)
rs2016394	2	172972971	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs4849887	2	121245122	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs12493607	3	30682939	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs6796502	3	46866866	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs6762644	3	4742276	2 (0.6%)	1 (0.2%)	3 (0.3%)
rs1053338	3	63967900	0 (0.0%)	2 (0.3%)	2 (0.2%)
rs4973768	3	27416013	1 (0.3%)	1 (0.2%)	2 (0.2%)
rs6828523	4	175846426	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs9790517	4	106084778	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs1432679	5	158244083	1 (0.3%)	1 (0.2%)	2 (0.2%)
rs13162653	5	16186489	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs2012709	5	32567732	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs10472076	5	58184061	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs1353747	5	58337481	2 (0.6%)	1 (0.2%)	3 (0.3%)
rs7707921	5	81538046	1 (0.3%)	3 (0.5%)	4 (0.4%)
rs10069690	5	1279790	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs10941679	5	44706498	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs2736108	5	1297488	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs889312	5	56031884	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs204247	6	13722523	3 (0.8%)	2 (0.3%)	5 (0.5%)
rs9257408	6	28916252	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs11242675	6	1318878	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs12662670	6	151918856	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs2046210	6	151948366	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs4593472	7	130667121	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs720475	7	144074929	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs6964587	7	91630620	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs13267382	8	117209548	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs9693444	8	29509616	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs13365225	8	36858483	2 (0.6%)	0 (0.0%)	2 (0.2%)
rs6472903	8	76230301	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs11780156	8	129194641	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs13281615	8	128355618	1 (0.3%)	3 (0.5%)	4 (0.4%)
rs2943559	8	76417937	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs1011970	9	22062134	2 (0.6%)	1 (0.2%)	3 (0.3%)

rs10759243	9	110306115	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs865686	9	110888478	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs7904519	10	114773927	2 (0.6%)	3 (0.5%)	5 (0.5%)
rs11814448	10	22315843	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs10995190	10	64278682	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs704010	10	80841148	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs11199914	10	123093901	2 (0.6%)	3 (0.5%)	5 (0.5%)
rs2380205	10	5886734	0 (0.0%)	3 (0.5%)	3 (0.3%)
rs2981579	10	123337335	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs7072776	10	22032942	1 (0.3%)	1 (0.2%)	2 (0.2%)
rs11820646	11	129461171	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs3817198	11	1909006	1 (0.3%)	2 (0.3%)	3 (0.3%)
rs3903072	11	65583066	1 (0.3%)	2 (0.3%)	3 (0.3%)
rs554219	11	69331642	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs75915166	11	69379161	1 (0.3%)	1 (0.2%)	2 (0.2%)
rs12422552	12	14413931	2 (0.6%)	2 (0.3%)	4 (0.4%)
rs10771399	12	28155080	2 (0.6%)	0 (0.0%)	2 (0.2%)
rs17356907	12	96027759	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs1292011	12	115836522	0 (0.0%)	2 (0.3%)	2 (0.2%)
rs11571833	13	32972626	0 (0.0%)	2 (0.3%)	2 (0.2%)
rs2236007	14	37132769	9 (2.5%)	19 (3.0%)	28 (2.8%)
rs941764	14	91841069	0 (0.0%)	2 (0.3%)	2 (0.2%)
rs11627032	14	93104072	3 (0.8%)	0 (0.0%)	3 (0.3%)
rs2588809	14	68660428	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs999737	14	69034682	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs17817449	16	53813367	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs11075995	16	53855291	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs13329835	16	80650805	1 (0.3%)	2 (0.3%)	3 (0.3%)
rs3803662	16	52586341	0 (0.0%)	0 (0.0%)	0 (0.0%)
chr17:29230520:D	17	29166302	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs6504950	17	53056471	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs745571	17	77781387	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs527616	18	24337424	0 (0.0%)	2 (0.3%)	2 (0.2%)
rs1436904	18	24570667	1 (0.3%)	1 (0.2%)	2 (0.2%)
rs6507583	18	42399590	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs2363956	19	17394124	1 (0.3%)	1 (0.2%)	2 (0.2%)
rs3760982	19	44286513	0 (0.0%)	1 (0.2%)	1 (0.1%)
rs4808801	19	18571141	19 (5.3%)	38 (6.0%)	57 (5.7%)
rs8170	19	17389704	3 (0.8%)	1 (0.2%)	4 (0.4%)
rs2823093	21	16520832	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs6001930	22	40876234	1 (0.3%)	0 (0.0%)	1 (0.1%)
rs132390	22	29621477	0 (0.0%)	0 (0.0%)	0 (0.0%)
rs17879961	22	29121087	0 (0.0%)	0 (0.0%)	0 (0.0%)

Table S4: Summary statistics for each SNP. MAF is the minor allele frequency from the data. COGS estimates used to form the SNP score are also given for comparison. HWE tests based on the number of homozygotes, where the observed number of homozygotes divided by expected is also given for cases and controls separately.

SNP	Chr	MAF	MAF	MAF	OR	OR COGS	O/E	O/E
		ctl	case	COGS			ctl	case
rs616488	1	31	35	33	1.23	0.94(0.92-0.96)	0.98	1.01
rs11249433	1	46	41	40	0.83	1.09(1.07-1.12)	0.98	1.05
rs12405132	1	36	38	36	1.04	0.95(0.93-0.97)	0.99	1.00
rs12048493	1	42	41	41	0.96	1.06(1.04-1.07)	0.93	1.05
rs72755295	1	4	4	3	0.83	1.16(1.1-1.22)	1.00	1.00
rs11552449	1	17	14	16	0.77	1.07(1.04-1.09)	1.01	1.01
rs4245739	1	27	25	26	0.92	1.03(1.01-1.05)	0.97	0.93
rs1045485	2	12	12	13	1.03	0.97(0.94-1)	0.99	0.99
rs16857609	2	27	29	26	1.15	1.08(1.06-1.11)	1.04	1.04
rs12710696	2	37	40	36	1.14	1.04(1.02-1.06)	1.02	1.03
rs13387042	2	48	47	49	0.98	0.88(0.86-0.9)	1.00	1.01
rs1550623	2	15	15	16	0.96	0.95(0.92-0.97)	0.97	0.95
rs2016394	2	45	45	48	1.01	0.95(0.94-0.97)	1.03	0.99
rs4849887	2	9	8	10	0.93	0.91(0.88-0.94)	1.00	0.98
rs12493607	3	33	33	34	1.04	1.06(1.04-1.08)	0.98	1.01
rs6796502	3	10	8	9	0.88	0.92(0.89-0.95)	0.99	1.01
rs6762644	3	41	42	40	1.07	1.07(1.05-1.09)	0.95	1.08
rs1053338	3	14	14	13	1.11	1.08(1.05-1.11)	0.98	0.99
rs4973768	3	47	48	47	1.08	1.10(1.08-1.12)	1.04	1.03
rs6828523	4	11	10	12	0.97	0.90(0.87-0.93)	1.01	1.01
rs9790517	4	19	19	22	1.02	1.05(1.03-1.08)	1.00	1.02
rs1432679	5	47	48	43	1.06	1.07(1.05-1.09)	0.99	1.06
rs13162653	5	42	45	45	1.14	0.94(0.92-0.96)	1.00	0.95
rs2012709	5	46	46	46	0.99	1.05(1.04-1.07)	1.00	0.97
rs10472076	5	38	40	38	1.05	1.05(1.03-1.07)	1.06	0.98
rs1353747	5	10	8	10	0.74	0.92(0.89-0.95)	0.99	1.00
rs7707921	5	25	26	23	1.05	0.93(0.91-0.95)	1.05	0.98
rs10069690	5	26	28	26	1.07	1.06(1.04-1.09)	1.01	0.95
rs10941679	5	26	27	25	1.03	1.12(1.1-1.15)	0.99	0.98
rs2736108	5	29	30	29	1.05	0.94(0.92-0.96)	1.00	0.94
rs889312	5	29	28	28	0.96	1.12(1.1-1.15)	1.01	1.08
rs204247	6	43	44	44	1.09	1.05(1.03-1.07)	0.99	0.98
rs9257408	6	40	40	41	1.04	1.05(1.03-1.07)	1.06	0.91
rs11242675	6	37	38	38	1.04	0.96(0.94-0.98)	0.98	1.04
rs12662670	6	9	10	7	1.02	1.17(1.13-1.22)	1.02	0.98
rs2046210	6	36	38	34	1.07	1.08(1.06-1.1)	1.05	0.94
rs4593472	7	35	34	35	0.99	0.95(0.93-0.96)	1.04	0.95
rs720475	7	29	23	25	0.72	0.94(0.92-0.96)	1.01	0.96
rs6964587	7	39	40	39	1.10	1.05(1.03-1.07)	0.96	0.98
rs13267382	8	34	38	36	1.20	1.05(1.03-1.07)	0.99	0.98
rs9693444	8	33	34	32	1.06	1.07(1.05-1.09)	1.03	1.05
rs13365225	8	15	16	17	1.07	0.94(0.91-0.96)	1.00	1.00

rs6472903	8	15	16	18	1.07	0.91(0.89-0.93)	0.99	1.00
rs11780156	8	20	17	16	0.82	1.07(1.04-1.09)	1.01	0.95
rs13281615	8	42	46	40	1.12	1.10(1.08-1.12)	1.00	1.01
rs2943559	8	10	8	7	0.79	1.13(1.09-1.17)	1.00	1.00
rs1011970	9	18	18	17	1.01	1.06(1.03-1.08)	1.02	1.01
rs10759243	9	29	28	29	0.89	1.05(1.03-1.08)	1.04	1.03
rs865686	9	36	33	38	0.90	0.90(0.88-0.92)	0.97	1.00
rs7904519	10	47	47	46	1.00	1.05(1.03-1.07)	0.97	0.97
rs11814448	10	2	2	2	0.92	1.27(1.19-1.36)	1.00	1.00
rs10995190	10	13	10	16	0.80	0.86(0.83-0.88)	1.01	1.01
rs704010	10	40	43	38	1.13	1.08(1.06-1.1)	0.99	1.07
rs11199914	10	32	32	32	0.99	0.95(0.93-0.97)	1.05	0.96
rs2380205	10	44	42	44	0.91	0.99(0.97-1.01)	0.95	0.92
rs2981579	10	44	47	40	1.13	1.27(1.24-1.29)	1.01	1.07
rs7072776	10	28	28	29	1.01	1.07(1.05-1.09)	0.96	1.03
rs11820646	11	41	38	41	0.88	0.95(0.93-0.97)	1.01	0.92
rs3817198	11	34	36	31	1.11	1.07(1.05-1.09)	0.96	0.96
rs3903072	11	45	46	47	1.04	0.95(0.93-0.97)	1.04	1.05
rs554219	11	13	15	12	1.18	1.26(1.23-1.3)	0.99	0.99
rs75915166	11	6	7	6	1.16	1.31(1.26-1.36)	0.99	1.00
rs12422552	12	27	29	26	1.11	1.04(1.02-1.07)	1.00	0.97
rs10771399	12	12	9	12	0.75	0.86(0.83-0.89)	0.99	0.98
rs17356907	12	28	27	30	0.97	0.91(0.9-0.93)	0.96	1.06
rs1292011	12	42	39	42	0.85	0.92(0.9-0.94)	0.93	1.03
rs11571833	13	2	2	1	1.01	1.27(1.15-1.4)	1.00	1.00
rs2236007	14	22	21	21	1.00	0.93(0.91-0.95)	0.98	1.00
rs941764	14	35	37	34	1.16	1.07(1.05-1.09)	0.97	0.99
rs11627032	14	26	26	27	1.03	0.94(0.92-0.96)	1.02	0.99
rs2588809	14	16	14	16	0.90	1.08(1.05-1.11)	1.02	0.99
rs999737	14	24	22	23	0.88	0.92(0.9-0.94)	0.99	0.98
rs17817449	16	41	36	40	0.81	0.93(0.91-0.95)	1.04	0.91
rs11075995	16	23	23	24	1.02	1.04(1.02-1.06)	1.00	0.98
rs13329835	16	21	24	22	1.19	1.08(1.06-1.11)	0.99	1.02
rs3803662	16	31	33	26	1.08	1.24(1.21-1.26)	0.96	1.00
chr17:29230520:D	17	26	24	27	0.94	0.95(0.93-0.97)	0.99	0.98
rs6504950	17	25	28	28	1.19	0.94(0.92-0.96)	0.97	0.96
rs745571	17	49	47	50	0.91	1.05(1.04-1.07)	1.03	1.08
rs527616	18	35	35	38	0.97	0.95(0.93-0.97)	1.02	0.92
rs1436904	18	40	38	40	0.89	0.96(0.94-0.97)	1.01	0.93
rs6507583	18	8	7	7	0.90	0.91(0.88-0.94)	1.00	1.00
rs2363956	19	49	47	49	0.92	1.03(1.01-1.05)	0.99	1.00
rs3760982	19	50	49	46	0.99	1.05(1.03-1.07)	0.99	1.06
rs4808801	19	36	35	35	0.98	0.93(0.91-0.94)	1.02	1.01
rs8170	19	18	19	19	1.09	1.04(1.02-1.07)	1.04	1.03
rs2823093	21	27	27	27	0.96	0.93(0.91-0.95)	1.00	0.95
rs6001930	22	10	12	11	1.16	1.12(1.09-1.16)	1.03	0.99
rs132390	22	4	4	4	0.98	1.14(1.08-1.2)	1.00	1.00
rs17879961	22	0	0	0	1.41	1.37(1.21-1.55)	1.00	1.00

Table S5: Calibration coefficients from conditional logistic regression model on log odds of each predictor.

Group	Predictor	Calibration (95% CI)
Overall	SNP88	46% (19 to 74%)
	TC	71% (37 to 106%)
IBIS-I	SNP88	56% (24 to 87%)
	TC	77% (38 to 116%)
Marsden	SNP88	14% (-43 to 71%)
	TC	55% (-13 to 123%)
Placebo	SNP88	54% (18 to 90%)
	TC	79% (36 to 123%)
Tamoxifen	SNP88	36% (-7 to 78%)
	TC	59% (4 to 114%)
ER+	SNP88	56% (23 to 88%)
	TC	60% (21 to 99%)
ER-	SNP88	-2% (-62 to 59%)
	TC	112% (34 to 190%)

Table S6: Observed and expected number of cancers by 10-year risk group decile, in the placebo arm. SE, standard error; χ^2 , the chi-squared statistic component used in a Hosmer-Lemeshow test.

Decile	Observed	Expected	SE	χ^2
1	24	19.6	4.3	1.1
2	34	23.9	4.7	4.6
3	32	28.5	5.0	0.5
4	26	30.1	5.2	0.6
5	38	32.3	5.4	1.1
6	31	35.9	5.6	0.8
7	41	37.1	5.7	0.5
8	31	42.6	6.0	3.7
9	42	47.9	6.4	0.8
10	64	63.5	7.1	0.0

Table S7: Additional interaction subgroup tests for the SNP score.

	Comparison	P
Age	Per year	0.49
Menopause status	Pre and Peri vs Post	1.0
BMI	kg/m2	0.49
Nulliparous	Children / not	0.47
Age at first birth	Per year	0.19
Age at menarche	Per year	0.39
TC family history only	Odds ratio	0.7
TC All	Odds ratio	0.6

Table S8: Main results, using SNP score with imputed SNP values where missing.

Result	IQ-OR	95% CI	LR- χ^2	P	mC	mC 95% CI
SNP88	1.40	1.15 - 1.70	11.8	<0.001	0.58	0.53 - 0.62
IBIS	1.46	1.19 - 1.79	13.4	<0.001	0.59	0.54 - 0.64
MARSDEN	1.10	0.72 - 1.66	0.2	0.7	0.53	0.43 - 0.62
- Het. (trial)				0.18		
TC	1.45	1.21 - 1.73	17.6	<0.001	0.55	0.51 - 0.60
TC x SNP88 (df=1)	1.64	1.36 - 1.98	29.6	<0.001	0.61	0.56 - 0.65
			$\Delta\chi^2_1 = 13.1$	<0.001		
SNP88 subgroups						
ER+	1.50	1.19 - 1.87	12.8	<0.001	0.59	0.53 - 0.64
ER-	0.95	0.57 - 1.61	0.0	0.9	0.51	0.40 - 0.62
- Het. (ER)				0.071		
Placebo	1.54	1.19 - 2.00	10.9	<0.001	0.61	0.55 - 0.66
Tamoxifen	1.22	0.93 - 1.61	2.1	0.15	0.53	0.46 - 0.60
- Het. (treatment)				0.27		
Placebo, ER+	1.51	1.13 - 2.01	8.0	0.005	0.60	0.54 - 0.67
Placebo, ER-	1.38	0.63 - 3.01	0.7	0.41	0.58	0.44 - 0.73
- Het. (placebo:ER)				0.7		
Tamoxifen, ER+	1.47	1.03 - 2.09	4.8	0.028	0.56	0.48 - 0.65
Tamoxifen, ER-	0.72	0.39 - 1.36	1.0	0.31	0.44	0.28 - 0.60
- Het. (tamoxifen:ER)				0.048		
TC subgroups						
ER+	1.33	1.10 - 1.60	9.2	0.002	0.55	0.49 - 0.60
ER-	1.94	1.22 - 3.07	8.8	0.003	0.59	0.49 - 0.68
- Het. (ER)				0.23		
Placebo	1.54	1.21 - 1.96	13.3	<0.001	0.55	0.49 - 0.61
Tamoxifen	1.31	1.02 - 1.68	4.6	0.032	0.56	0.50 - 0.63
- Het. (treatment)				0.6		
IBIS-I	1.44	1.19 - 1.73	15.3	<0.001	0.55	0.50 - 0.60
MARSDEN	1.28	0.94 - 1.73	2.6	0.11	0.56	0.47 - 0.66
- Het. (trial)				0.6		
TC x SNP88 subgroups						
ER+	1.64	1.33 - 2.01	23.5	<0.001	0.60	0.55 - 0.66
ER-	1.56	0.95 - 2.54	3.2	0.072	0.59	0.48 - 0.71
Placebo	1.84	1.43 - 2.38	24.6	<0.001	0.63	0.58 - 0.69
Tamoxifen	1.42	1.08 - 1.87	6.4	0.011	0.57	0.50 - 0.65

Table S9: Main results, including tissue samples from Marsden controls and matching cases.

Result	IQ-OR	95% CI	LR- χ^2	P	mC	mC 95% CI
SNP88	1.38	1.15 - 1.65	12.9	<0.001	0.55	0.51 - 0.60
IBIS	1.45	1.17 - 1.78	12.6	<0.001	0.57	0.52 - 0.62
MARSDEN	1.21	0.86 - 1.70	1.2	0.28	0.51	0.43 - 0.59
- Het. (trial)				0.36		
TC	1.48	1.24 - 1.75	20.8	<0.001	0.56	0.52 - 0.60
TC x SNP88 (df=1)	1.67	1.40 - 2.01	33.9	<0.001	0.60	0.56 - 0.65
			$\Delta\chi^2_1 = 14.7$	<0.001		
SNP88 subgroups						
ER+	1.43	1.17 - 1.75	12.5	<0.001	0.56	0.51 - 0.61
ER-	1.06	0.69 - 1.64	0.1	0.8	0.52	0.42 - 0.62
- Het. (ER)				0.16		
Placebo	1.48	1.16 - 1.88	10.4	0.001	0.58	0.52 - 0.63
Tamoxifen	1.26	0.97 - 1.62	3.1	0.078	0.52	0.45 - 0.60
- Het. (treatment)				0.46		
Placebo, ER+	1.43	1.10 - 1.86	7.2	0.007	0.57	0.50 - 0.63
Placebo, ER-	1.38	0.70 - 2.71	0.9	0.35	0.58	0.44 - 0.71
- Het. (placebo:ER)				0.8		
Tamoxifen, ER+	1.42	1.04 - 1.92	5.3	0.022	0.55	0.47 - 0.63
Tamoxifen, ER-	0.88	0.52 - 1.48	0.2	0.6	0.46	0.31 - 0.61
- Het. (tamoxifen:ER)				0.10		
TC subgroups						
ER+	1.36	1.14 - 1.63	11.8	<0.001	0.56	0.50 - 0.61
ER-	1.97	1.23 - 3.15	8.9	0.003	0.59	0.49 - 0.68
- Het. (ER)				0.34		
Placebo	1.56	1.24 - 1.97	15.0	<0.001	0.55	0.49 - 0.61
Tamoxifen	1.36	1.06 - 1.75	6.0	0.014	0.57	0.51 - 0.64
- Het. (treatment)				0.7		
IBIS-I	1.44	1.19 - 1.73	15.3	<0.001	0.55	0.50 - 0.60
MARSDEN	1.39	1.05 - 1.84	5.5	0.019	0.58	0.50 - 0.66
- Het. (trial)				0.9		
TC x SNP88 subgroups						
ER+	1.66	1.36 - 2.04	26.0	<0.001	0.60	0.55 - 0.65
ER-	1.63	1.03 - 2.57	4.6	0.032	0.58	0.47 - 0.68
Placebo	1.81	1.43 - 2.31	25.9	<0.001	0.63	0.57 - 0.68
Tamoxifen	1.47	1.13 - 1.92	8.9	0.003	0.57	0.50 - 0.64