Supplementary Table 1 – Genotype Frequencies in Cases and Controls

Polymorphism	MAF	Cancer Set	Controls Common	Controls Heterozygote	Controls Rare	Cases Common	Cases Heterozygote	Cases Rare
PTGS1								
rs1330344 (01)	0.21	Set 1	1413	748	112	1395	683	112
rs10306122 (04)	0.07	Set 1	1969	285	10	1902	271	9
rs10306194 (05)	0.16	Set 1	1594	610	53	1578	543	49
rs4836887 (07)	0.13	Set 1	1702	543	33	1665	492	31
rs10306108 (08)	0.07	Set 1	1952	306	13	1867	302	12
rs10306146 (15)	0.13	Set 1	1699	529	28	1670	477	27
PTGS2								
rs4648310 (01)	0.04	Set 1	2119	153	4	2062	119	4
rs689467 (02)	0.07	Set 1	1978	293	9	1881	303	11
rs2206593 (03)	0.05	Set 1	2042	222	6	1950	222	13
rs5275 (04)	0.34	Set 1	996	1010	259	927	985	260
*rs5277 (09)	0.16	Set 1	1562	639	56	1573	550	51
*rs5277 (09)	0.16	Set 2	1570	624	42	1469	619	57
*rs5277 (09)	0.16	Set 1 / 2	3132	1263	98	3042	1169	108
rs20424 (11)	0.02	Set 1	2183	91	0	2118	74	0
rs4648276 (17)	0.12	Set 1	1732	489	35	1667	463	39
PTGIS								
rs6090990 (03)	0.25	Set 1	1261	841	139	1205	819	140
*rs5602 (04)	0.49	Set 1	510	1157	570	550	1022	579
*rs5602 (04)	0.49	Set 2	530	1107	598	556	1055	514
*rs5602 (04)	0.49	Set 1 / 2	1040	2264	1168	1106	2077	1093
*rs6090996 (05)	0.21	Set 1	1410	770	90	1441	639	99
*rs6090996 (05)	0.21	Set 2	1446	732	94	1382	705	91
*rs6090996 (05)	0.21	Set 1 / 2	2856	1502	184	2823	1344	190
rs508757 (06)	0.20	Set 1	1467	711	89	1417	659	95
rs707528 (08)	0.49	Set 1	572	1159	537	561	1055	559
*rs477627 (11)	0.16	Set 1	1612	592	68	1549	596	40
*rs477627 (11)	0.16	Set 2	1636	569	69	1571	557	47
*rs477627 (11)	0.16	Set 1 / 2	3248	1161	137	3120	1153	87

Polymorphism	MAF	Cancer Set	Controls Common	Controls Heterozygote	Controls Rare	Cases Common	Cases Heterozygote	Cases Rare
PTGIS								
rs693649 (12)	0.20	Set 1	1440	741	91	1428	675	79
rs6012696 (13)	0.07	Set 1	1969	299	10	1876	305	11
*rs556731 (14)	0.05	Set 1	2046	218	6	2020	160	3
*rs556731 (14)	0.05	Set 2	2077	190	5	1958	201	10
*rs556731 (14)	0.05	Set 1 / 2	4123	408	11	3978	361	13
rs6095543 (15)	0.16	Set 1	1590	619	55	1501	611	71
rs1393343 (16)	0.22	Set 1	1373	799	103	1365	705	117
rs574113 (17)	0.34	Set 1	998	1008	271	968	949	273
rs501908 (18)	0.10	Set 1	1831	417	29	1736	425	27
*rs8183919 (19)	0.29	Set 1	1131	960	185	1068	894	223
*rs8183919 (19)	0.29	Set 2	1141	948	188	1057	909	206
*rs8183919 (19)	0.29	Set 1 / 2	2272	1908	373	2125	1803	429
rs1066894 (20)	0.31	Set 1	1087	951	228	1092	871	2181
rs476496 (21)	0.24	Set 1	1306	794	127	1269	769	127
PTGES								
rs2302821 (03)	0.08	Set 1	1902	353	12	1872	298	14
rs4837404 (04)	0.35	Set 1	957	1029	277	928	976	274
rs10739757 (05)	0.10	Set 1	1808	436	17	1710	435	26
*rs10448290 (06)	0.09	Set 1	1888	375	9	1795	355	25
*rs10448290 (06)	0.09	Set 2	1906	349	17	1810	343	19
*rs10448290 (06)	0.09	Set 1 / 2	3794	724	26	3605	698	44
rs12553596 (13)	0.07	Set 1	1940	306	6	1859	300	17
PTGDS								
rs11787588 (01)	0.27	Set 1	1213	885	166	1211	820	144
rs10781530 (03)	0.31	Set 1	1531	684	56	1478	631	74
rs908839 (04)	0.47	Set 1	634	1135	493	594	1080	499
PGDS								
rs10516950 (02)	0.44	Set 1	709	1136	433	673	1082	432
rs1045435 (03)	0.39	Set 1	841	1068	359	862	993	326

Polymorphism TBXAS1	MAF	Cancer Set	Controls Common	Controls Heterozygote	Controls Rare	Cases Common	Cases Heterozygote	Cases Rare
rs6971207 (01)	0.01	Set 1	2228	50	0	2127	59	2
rs2267681(02)	0.42	Set 1	771	1084	404	764	1044	367
rs7810415 (03)	0.48	Set 1	573	1172	503	558	1074	534
rs3779134 (04)	0.12	Set 1	1771	467	37	1680	466	37
rs194149 (05)	0.28	Set 1	1187	884	194	1131	872	172
rs11973494 (08)	0.22	Set 1	1385	765	120	1383	688	112
rs2284205 (09)	0.16	Set 1	1615	595	64	1545	587	53
rs2107901 (11)	0.17	Set 1	1578	622	64	1528	566	67
rs10487665 (12)	0.09	Set 1	1878	381	15	1821	355	16
rs2190087 (13)	0.23	Set 1	1325	821	117	1255	806	114
rs1557967 (14)	0.2	Set 1	1455	733	85	1397	698	92
rs1003816 (15)	0.1	Set 1	1827	415	20	1741	400	36
rs41728 (16)	0.12	Set 1	1749	493	26	1675	459	44
*rs41727 (17)	0.1	Set 1	1846	413	9	1767	378	32
*rs41727 (17)	0.1	Set 2	1881	367	29	1765	370	34
*rs41727 (17)	0.1	Set 1 / 2	3727	780	38	3532	748	66
rs2267701 (20)	0.14	Set 1	1669	548	31	1602	520	47
rs740150 (21)	0.19	Set 1	1507	674	93	1411	697	77
rs10487667 (23)	0.25	Set 1	1280	832	160	1170	852	154
rs2267706 (25)	0.23	Set 1	1358	782	118	1269	781	118
rs22861987 (28)	0.38	Set 1	880	1054	319	785	1064	317
rs2286196 (29)	0.19	Set 1	1474	704	89	1397	708	72
rs2267692 (30)	0.35	Set 1	964	1011	292	906	968	295
rs1015572 (31)	0.05	Set 1	2047	204	8	1978	198	4
rs1015570 (32)	0.39	Set 1	859	1040	361	786	1036	340
rs2299887 (37)	0.4	Set 1	838	1043	375	792	1026	355
rs10544451 (38)	0.24	Set 1	1301	826	120	1230	799	121

*SNP completed in Set 1 and Set 2

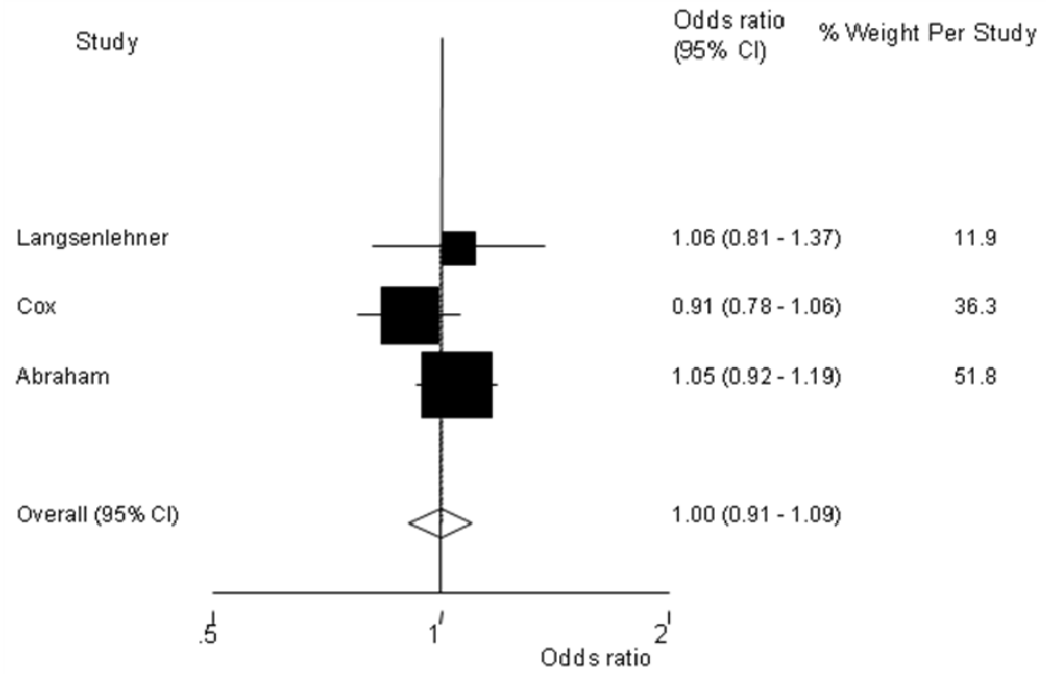
Supplementary Table 2 - Per Allele Risk for Multimarker Tags

Gene[a]	Multimarker TagSNPs	Haplotype*	Frequency	P-value	OR	95% CIs
TBXAS1						
	rs 2267681 (02); rs 7810415 (03) CC	h00	0.45	0.83	0.99	0.91-1.08
	rs 2267681 (02); rs 7810415 (03) TC	h10	0.07	0.12	0.99	0.91-1.08
	rs 2299887 (37); rs 194149 (05) GG	h00	0.57	0.85	0.99	0.91-1.08
	rs 194149 (05); rs 11973494 (08) AA	h11	0.14	0.42	0.95	0.84-1.08
	rs2299887 (37); rs1015570 (32); rs2267692 (30) ACA	h110	0.12	0.73	0.98	0.86-1.11
	rs1015570 (32); rs11973494 (08); rs2284205 (09) GAA	h011	0.06	0.62	0.95	0.78-1.16
	rs 10487665 (12); rs 1557967 (14) AG	h00	0.8	0.6	0.97	0.88-1.08
PTGDS	rs908839 (04); rs10781530 (03) GC	h11	0.03	0.98	1.11	0.92-1.35

*0 = common allele
1 = rare allele

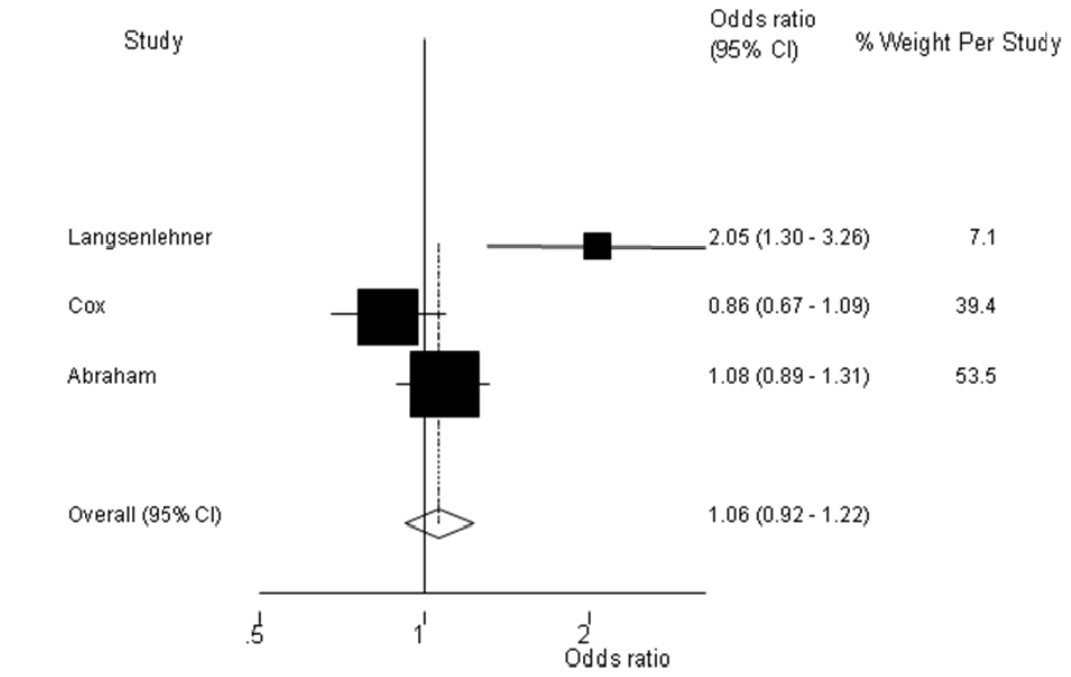
Supplementary Table 3 – Meta-analysis of Langsenlehner, Cox and Abraham studies

Heterozygote Risk



Heterogeneity Chi-squared = 2.23 (d.f. = 2) p=0.33; Test of OR = 1; z = 0.05 p = 0.96

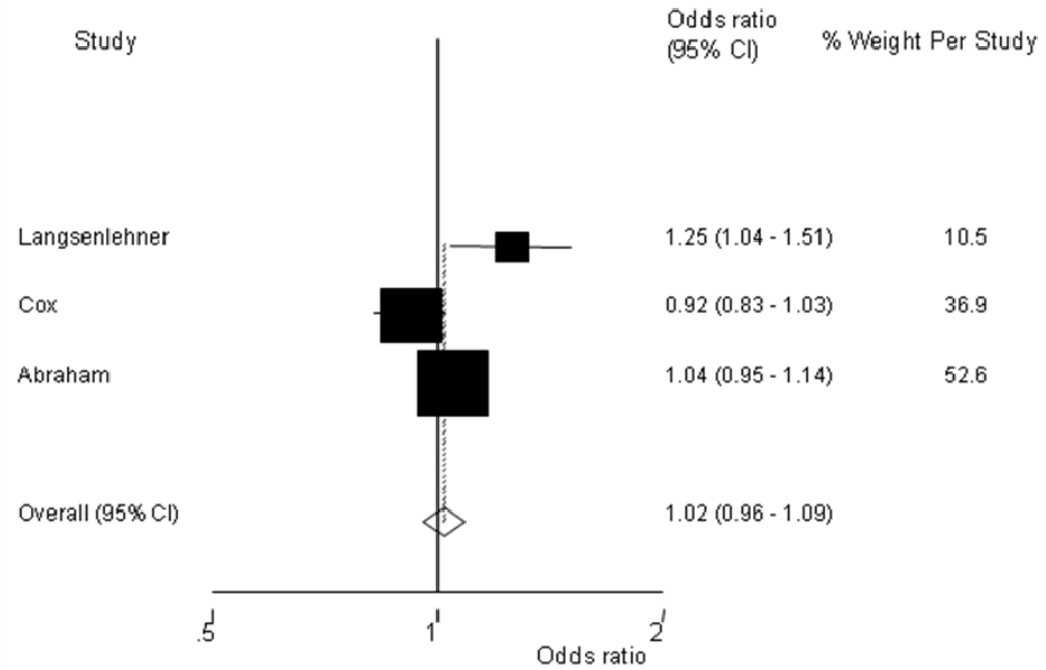
*Homozygote Risk



Heterogeneity Chi-squared = 10.99 (d.f. = 2) p=0.004; Test of OR = 1; z = 0.80 p = 0.42

***The difference in our estimates and those of the Cox paper can be explained by the fact that Cox et al presented multi-variate adjusted ORs.**

Per Allele Risk



Heterogeneity Chi-squared = 8.31 (d.f. = 2) p=0.02; Test of OR = 1; z = 0.58 p = 0.56

Supplementary Table 4: Prostaglandin TagSNP Incident Cases and Prevalent Cases Survival Analysis

		INCIDENT CASES			PREVALENT CASES		
†Gene/SNP	MAF**	P-trend	Hazard ratio (HR) Per Allele	95% CI**	P-trend	Hazard ratio (HR) Per Allele	95% CI**
PTGDS							
PTGDS(01) rs11787588	0.27	0.40	1.09	0.89 - 1.34	0.26	0.83	0.60 - 1.15
PTGDS(03) rs10781530	0.31	0.44	0.93	0.76 - 1.13	0.01	1.47	1.11 - 1.95
PTGDS(04) rs908839	0.47	1.00	1.00	0.84 - 1.20	0.47	0.9	0.68 - 1.19
PTGES							
PTGES(03) rs2302821	0.08	0.27	1.20	0.88 - 1.64	0.13	1.48	0.91 - 2.39
PTGES(04) rs4837404	0.35	0.53	1.06	0.88 - 1.28	0.03	0.73	0.54 - 0.98
PTGES(05) rs10739757	0.1	0.05	0.75	0.55 - 1.02	0.32	1.24	0.82 - 1.89
PTGES (06) rs10448290	0.09	0.01	0.66	0.47 - 0.94	0.71	1.1	0.68 - 1.76
††PTGES(13) rs12553596 (set 1 & 2 combined)	0.07	0.01	0.71	0.54 - 0.95	0.61	1.11	0.75 - 1.65
PTGIS							
PTGIS(03) rs6090990	0.25	0.76	0.97	0.79 - 1.19	0.86	0.97	0.70 - 1.34
PTGIS(04) rs5602	0.49	0.76	1.03	0.86 - 1.22	0.4	0.89	0.67 - 1.17
PTGIS(05) rs6090996	0.21	0.93	1.01	0.82 - 1.25	0.15	0.75	0.50 - 1.12
PTGIS(06) rs508757	0.2	0.13	1.17	0.96 - 1.44	0.63	0.91	0.62 - 1.34
PTGIS(08) rs707528	0.49	0.30	0.91	0.77 - 1.09	0.06	1.31	0.99 - 1.74
PTGIS(11) rs477627	0.16	0.23	1.16	0.91 - 1.48	0.51	0.88	0.59 - 1.31
PTGIS(12) rs693649	0.2	0.67	0.95	0.76 - 1.20	0.02	1.49	1.07 - 2.06
PTGIS(13) rs6012696	0.07	0.69	1.07	0.77 - 1.50	0.61	1.11	0.75 - 1.65
PTGIS(14) rs556731	0.05	0.32	0.77	0.45 - 1.32	0.38	0.72	0.33 - 1.58
PTGIS(15) rs6095543	0.16	0.55	0.93	0.73 - 1.18	0.85	1.04	0.73 - 1.48
PTGIS (16) rs1393343	0.22	0.20	1.14	0.93 - 1.39	0.96	0.99	0.70 - 1.41
PTGIS (17) rs574113	0.34	0.98	1.00	0.84 - 1.20	0.07	1.3	0.99 - 1.71
PTGIS (18) rs501908	0.1	0.21	1.19	0.92 - 1.54	0.50	0.85	0.52 - 1.39
PTGIS (19) rs8183919	0.29	0.37	0.92	0.76 - 1.11	0.1	1.28	0.96 - 1.70
PTGIS (20) rs1066894	0.31	0.49	1.07	0.89 - 1.30	0.57	0.92	0.69 - 1.23
PTGIS (21) rs476496	0.24	0.67	1.05	0.85 - 1.29	0.93	0.99	0.71 - 1.37
PTGS1							
PTGS1(01) rs1330344	0.21	0.71	1.04	0.85 - 1.28	0.25	1.21	0.88 - 1.66
PTGS1(04) rs10306122	0.07	0.31	0.83	0.57 - 1.21	0.40	0.76	0.40 - 1.47
PTGS1(05) rs10306194	0.16	0.75	0.96	0.75 - 1.24	0.86	0.96	0.64 - 1.45
PTGS1(07) rs4836887	0.13	0.07	0.77	0.58 - 1.03	0.66	1.10	0.72 - 1.68
PTGS1(08) rs10306108	0.07	0.83	1.04	0.74 - 1.46	0.50	1.18	0.74 - 1.88
PTGS1(15) rs10306146	0.13	0.08	0.77	0.58 - 1.04	0.98	1.01	0.65 - 1.57
PTGS2							
PTGS2(01) rs4648310	0.04	0.50	1.18	0.74 - 1.86	0.33	0.59	0.19 - 1.85
PTGS2(02) rs689467	0.07	0.43	0.87	0.62 - 1.23	0.86	1.05	0.58 - 1.92
PTGS2(03) rs2206593	0.05	0.32	1.20	0.85 - 1.69	0.94	0.98	0.56 - 1.72
PTGS2(04) rs5275	0.34	0.86	1.02	0.85 - 1.22	0.36	1.15	0.86 - 1.54
PTGS2(09) rs5277	0.16	0.22	1.16	0.92 - 1.47	0.15	0.74	0.48 - 1.14
††PTGS2(11) rs20424 (set 1 & 2 combined)	0.02	0.47	0.8	0.44 - 1.46	0.37	0.64	0.24 - 1.71
PTGS2(17) rs4648276	0.12	0.12	1.22	0.95 - 1.57	0.25	1.26	0.86 - 1.85
PGDS							
PGDS(02) rs10516950	0.44	0.89	0.99	0.82 - 1.18	0.17	1.21	0.92 - 1.58
PGDS(03) rs1045435	0.39	0.67	0.96	0.80 - 1.15	0.62	1.07	0.82 - 1.41
TBXAS1							
TBXAS1(01) rs6971207	0.01	0.33	1.36	0.76 - 2.41	0.05	0	0.00 - E
††TBXAS1(02) rs2267681 (set 1 & 2 combined)	0.42	0.06	1.13	0.99 - 1.29	0.77	0.97	0.78 - 1.20
TBXAS1(03) rs7810415	0.48	0.82	0.98	0.82 - 1.17	0.76	1.04	0.79 - 1.38
TBXAS1(04) rs3779134	0.12	0.19	1.19	0.93 - 1.52	0.35	0.8	0.50 - 1.28
TBXAS1(05) rs194149	0.28	0.11	1.17	0.97 - 1.42	0.5	0.9	0.65 - 1.23
TBXAS1(08) rs11973494	0.22	0.07	1.22	0.99 - 1.50	0.67	0.93	0.67 - 1.30
TBXAS1(09) rs2284205	0.16	0.07	1.24	0.98 - 1.57	0.6	0.9	0.61 - 1.33

†Gene/SNP	MAF**	INCIDENT CASES P-trend	Hazard ratio (HR) Per Allele	95% CI**	PREVALENT CASES P-trend	Hazard ratio (HR) Per Allele	95% CI**
TBXAS1(11) rs2107901	0.17	0.96	1.01	0.79 - 1.28	0.07	1.39	0.99 - 1.94
TBXAS1(12) rs10487665	0.09	0.22	1.20	0.90 - 1.61	0.34	0.77	0.45 - 1.34
TBXAS1(13) rs2190087	0.23	0.84	1.02	0.83 - 1.26	0.56	1.1	0.80 - 1.51
TBXAS1(14) rs1557967	0.2	0.49	1.08	0.87 - 1.34	0.27	0.82	0.57 - 1.18
TBXAS1(15) rs1003816	0.1	0.84	1.03	0.78 - 1.37	0.87	1.03	0.68 - 1.57
TBXAS1(16) rs41728	0.12	0.83	1.03	0.79 - 1.34	0.58	1.12	0.75 - 1.67
TBXAS1(17) rs41727	0.1	0.75	1.05	0.79 - 1.39	0.98	1	0.64 - 1.55
TBXAS1(20) rs2267701	0.14	0.66	1.06	0.82 - 1.36	0.59	0.89	0.59 - 1.35
TBXAS1(21) rs740150	0.19	0.84	0.98	0.78 - 1.22	0.45	0.87	0.59 - 1.26
TBXAS1(23) rs10487667	0.25	0.18	1.15	0.94 - 1.39	0.61	0.92	0.67 - 1.27
TBXAS1(25) rs2267706	0.23	0.86	1.02	0.83 - 1.25	0.86	1.03	0.73 - 1.45
TBXAS1(28) rs22861987	0.38	0.13	1.16	0.96 - 1.39	0.79	1.04	0.78 - 1.39
TBXAS1(29) rs2286196	0.19	0.26	1.13	0.91 - 1.40	0.73	0.93	0.64 - 1.37
TBXAS1(30) rs2267692	0.35	0.12	1.16	0.97 - 1.38	0.87	1.02	0.77 - 1.36
TBXAS1(31) rs1015572	0.05	0.63	1.11	0.73 - 1.68	0.62	0.85	0.43 - 1.66
TBXAS1(32) rs1015570	0.39	0.62	0.95	0.79 - 1.15	0.64	0.94	0.71 - 1.24
TBXAS1(37) rs2299887	0.4	0.93	0.99	0.83 - 1.19	0.63	0.93	0.70 - 1.24
TBXAS1(38) rs10544451	0.24	0.71	1.04	0.85 - 1.28	0.46	1.13	0.82 - 1.54

†All genes assessed in set1 (cases=2270 and controls=2280) only unless P</= 0.05 for either P-trend or P-heterogeneity in original analysis.

††Results shown are combined set 1 and 2 data (cases=4470 and controls=4560).

* The values for these SNPs are absent due to their low frequency.

**Abbreviations: MAF - Minor Allele Frequency; 95%CI - 95% Confidence Interval.