Supplementary Table 1: The late toxicity endpoints recorded in the RAPPER breast cohorts (11)

Trial	Toxicity endpoint and scale	Grade
IMRT and RACE	**Photographic assessment** of late shrinkage (IMRT Trial) and distortion (RACE)	1 = none/minimal 2 = mild 3 = marked
IMRT and RACE	**Clinical assessment** of late toxicity	
	Shrinkage	0 = None 1 = A little 2 = Quite a bit 3 = Very much
	Telangiectasia	
	Induration	
	Breast edema	
IMRT and Manchester	**Clinical assessment** (LENT-SOM) of late toxicity	
	Telangiectasia	0 = None 1 = Minimal (>1 per cm^2) 2 = Moderate (1-4 per cm^2) 3 = Severe (>4 per cm^2)
	Pigmentation	0 = None 1 = Transitory, slight 2 = Permanent, marked
	Breast edema	0 = None 1 = Asymptomatic 2 = Symptomatic 3 = Secondary dysfunction
IMRT and Manchester	**Patient reported** (EORTC BR23)	
	Breast pain	1 = Not at all 2 = A little 3 = Quite a bit 4 = Very much
	Breast sensation	

Supplementary Table 2: RTOG acute toxicity grades definition

RTOG grade	Skin symptoms
0	No visible change to skin
1	Faint or dull erythema
2a	Tender or bright erythema
2b	Patchy moist desquamation
3	Confluent moist desquamation

Supplementary Table 3: Statistically significant non-genetic factors for acute and five-year toxicity

Toxicity endpoint	**Important non-genetic factors**
Acute toxicity	post-operative breast infection (p=0.01), BMI (p=0.03), hormone treatment (p<0.001), chemotherapy treatment (p=0.02) and breast volume (p=0.04)
Telangiectasia at 5 years	age (p=0.004), breast boost (p=0.009), BMI (p<0.001), post-operative breast infection (p<0.001), trial treatment arm (p=0.05), volume receiving >107% of prescribed dose (p=0.02), tamoxifen use (p=0.05)
Breast edema at 5 years	breast boost (p=0.004), breast volume (p<0.001)
Shrinkage assessed photographically at 5 years	BMI (p<0.001), trial treatment arm (p=0.006), surgical cosmesis (p=0.002)
Induration at 5 years	Aromatase inhibitor (p=0.04), breast boost (p<0.001), post-operative breast infection (p=0.01), trial treatment arm (p=0.01), volume receiving <95% of prescribed dose (p<0.001), surgical defect (p<0.001)
Overall toxicity (STAT[a]) at 5 years	breast boost (p<0.001), BMI (p=0.002), post-operative breast infection (p=0.001), trial treatment arm (p=0.008), volume receiving <95% of prescribed dose (p<0.001), breast volume (p<0.001), surgical defect (p=0.006), surgical cosmesis (p=0.002)

[a]Standardized total average toxicity

Supplementary Table 4: Results from residual analyses of the effect of individual risk variants on acute and two-year toxicity

Variant	Adjusted beta[a], standard error, p-value																										
	Acute toxicity			Telangiectasia			Edema			Shrinkage			Induration			Pigmentation			Pain			Oversensitivity			Overall (STAT[b])		
rs10069690	-0.01	0.05	0.82	-0.02	0.06	0.70	0.01	0.05	0.92	0.01	0.05	0.87	-0.01	0.05	0.91	-0.09	0.06	0.12	-0.05	0.05	0.33	0.02	0.06	0.67	-0.03	0.05	0.52
rs1011970	-0.03	0.06	0.64	0.02	0.06	0.81	0.05	0.06	0.43	0.02	0.06	0.79	-0.04	0.06	0.55	-0.03	0.07	0.69	-0.02	0.06	0.76	0.00	0.06	0.96	0.03	0.06	0.62
rs1045485	-0.01	0.07	0.93	0.04	0.08	0.59	-0.08	0.07	0.29	-0.04	0.07	0.51	-0.09	0.07	0.23	0.09	0.08	0.26	-0.01	0.07	0.87	-0.09	0.08	0.22	0.01	0.07	0.90
rs10472076	-0.03	0.05	0.56	0.02	0.05	0.73	0.10	0.05	0.05	0.02	0.05	0.61	0.05	0.05	0.35	0.07	0.06	0.19	-0.05	0.05	0.28	-0.05	0.05	0.37	0.00	0.05	0.93
rs1053338	0.00	0.07	0.99	-0.02	0.07	0.80	-0.08	0.07	0.24	0.13	0.06	0.04	0.00	0.07	0.95	-0.03	0.08	0.70	0.05	0.07	0.46	0.11	0.08	0.16	0.08	0.07	0.26
rs10759243	0.03	0.06	0.66	0.07	0.06	0.30	-0.03	0.06	0.60	-0.07	0.06	0.26	-0.01	0.06	0.81	0.07	0.07	0.27	-0.01	0.06	0.91	0.04	0.06	0.53	0.00	0.06	0.97
rs10941679	-0.08	0.05	0.14	-0.05	0.06	0.36	0.01	0.05	0.85	-0.02	0.05	0.69	0.09	0.05	0.11	-0.01	0.06	0.91	-0.01	0.05	0.88	-0.02	0.06	0.70	-0.03	0.05	0.54
rs10995190	-0.02	0.07	0.77	0.05	0.07	0.46	-0.01	0.07	0.88	-0.01	0.07	0.90	0.02	0.07	0.83	0.13	0.08	0.09	0.00	0.07	1.00	0.06	0.08	0.43	0.03	0.07	0.66
rs11075995	0.06	0.06	0.31	0.01	0.06	0.85	-0.08	0.06	0.18	-0.04	0.05	0.49	-0.06	0.06	0.25	-0.01	0.06	0.93	-0.06	0.06	0.26	-0.02	0.06	0.78	-0.04	0.05	0.43
rs11199914	0.01	0.06	0.93	0.09	0.06	0.14	-0.03	0.06	0.57	0.03	0.06	0.64	-0.08	0.06	0.18	-0.11	0.07	0.09	-0.01	0.06	0.90	0.06	0.06	0.31	0.02	0.06	0.71
rs11242675	-0.04	0.05	0.50	-0.01	0.06	0.90	0.10	0.05	0.06	0.03	0.05	0.57	-0.03	0.05	0.54	-0.01	0.06	0.82	0.02	0.05	0.68	-0.04	0.06	0.47	0.02	0.05	0.70
rs11249433	-0.03	0.06	0.65	0.06	0.06	0.30	0.09	0.06	0.14	-0.09	0.06	0.10	-0.06	0.06	0.33	0.14	0.07	0.04	-0.05	0.06	0.36	-0.05	0.06	0.46	0.00	0.06	0.98
rs11552449	-0.02	0.06	0.72	0.01	0.06	0.82	-0.10	0.06	0.12	0.00	0.06	0.95	0.08	0.06	0.22	-0.04	0.07	0.56	-0.01	0.06	0.87	0.11	0.07	0.09	-0.01	0.06	0.90
rs11571833	0.05	0.28	0.87	0.39	0.30	0.19	-0.10	0.29	0.72	-0.47	0.28	0.09	-0.31	0.27	0.24	-0.05	0.30	0.87	-0.12	0.29	0.68	-0.32	0.32	0.30	-0.26	0.29	0.37
rs11627032	0.04	0.06	0.48	0.00	0.06	0.95	-0.07	0.06	0.25	0.05	0.06	0.35	-0.04	0.06	0.52	-0.04	0.07	0.58	0.05	0.06	0.37	0.11	0.06	0.06	0.01	0.06	0.85
rs11780156	0.02	0.06	0.73	0.01	0.07	0.84	-0.04	0.06	0.57	-0.02	0.06	0.79	-0.01	0.06	0.89	-0.03	0.07	0.70	0.02	0.07	0.81	0.09	0.07	0.19	-0.01	0.06	0.93
rs11814448	-0.28	0.19	0.14	-0.09	0.19	0.62	-0.11	0.18	0.55	-0.06	0.18	0.76	-0.23	0.18	0.20	0.03	0.19	0.88	-0.01	0.20	0.96	0.22	0.21	0.29	-0.06	0.18	0.73
rs11820646	-0.08	0.05	0.11	-0.05	0.05	0.32	0.00	0.05	1.00	0.02	0.05	0.63	0.01	0.05	0.78	-0.01	0.05	0.81	0.00	0.05	0.96	0.07	0.05	0.16	0.02	0.05	0.71
rs12048493	0.00	0.06	1.00	0.01	0.06	0.83	-0.11	0.06	0.06	0.01	0.06	0.92	-0.01	0.06	0.92	-0.10	0.07	0.14	-0.06	0.06	0.31	-0.03	0.06	0.66	-0.09	0.06	0.10
rs12405132	0.05	0.05	0.35	0.01	0.05	0.90	0.08	0.05	0.10	-0.04	0.05	0.37	-0.08	0.05	0.11	0.05	0.05	0.39	0.01	0.05	0.88	-0.01	0.05	0.87	0.04	0.05	0.41
rs12493607	-0.06	0.05	0.25	0.02	0.05	0.65	-0.06	0.05	0.22	-0.04	0.05	0.36	-0.11	0.05	0.03	0.00	0.06	0.98	-0.04	0.05	0.44	0.00	0.05	1.00	-0.01	0.05	0.77
rs12662670	-0.07	0.08	0.40	-0.08	0.09	0.37	0.03	0.08	0.69	-0.02	0.08	0.76	0.02	0.08	0.81	0.01	0.09	0.88	0.07	0.08	0.42	0.01	0.09	0.95	0.03	0.08	0.74
rs12710696	0.03	0.05	0.57	-0.04	0.05	0.47	-0.05	0.05	0.33	0.00	0.05	0.93	-0.02	0.05	0.75	-0.06	0.06	0.31	-0.06	0.05	0.21	-0.03	0.05	0.60	-0.10	0.05	0.05
rs1292011	0.06	0.05	0.19	-0.01	0.05	0.89	0.07	0.05	0.13	0.03	0.05	0.56	0.08	0.05	0.09	0.03	0.05	0.58	-0.06	0.05	0.22	-0.01	0.05	0.91	-0.02	0.05	0.75
rs13162653	-0.05	0.05	0.32	0.04	0.05	0.41	-0.01	0.05	0.83	-0.03	0.05	0.50	-0.06	0.05	0.23	0.04	0.06	0.52	0.05	0.05	0.38	-0.03	0.06	0.64	0.02	0.05	0.71

Variant	Adjusted beta[a], standard error, p-value																										
	Acute toxicity			Telangiectasia			Edema			Shrinkage			Induration			Pigmentation			Pain			Oversensitivity			Overall (STAT[b])		
rs132390	-0.20	0.13	0.12	-0.10	0.14	0.46	0.07	0.14	0.60	0.14	0.12	0.23	-0.09	0.13	0.51	-0.19	0.15	0.18	-0.06	0.12	0.65	-0.04	0.13	0.77	0.00	0.13	0.99
rs13267382	0.07	0.05	0.15	-0.01	0.05	0.90	-0.10	0.05	0.06	0.02	0.05	0.63	-0.02	0.05	0.63	0.05	0.05	0.37	-0.06	0.05	0.20	-0.09	0.05	0.09	-0.05	0.05	0.28
rs13281615	0.08	0.05	0.10	-0.06	0.05	0.21	-0.05	0.05	0.32	-0.09	0.05	0.04	-0.04	0.05	0.42	0.11	0.05	0.03	-0.08	0.05	0.12	-0.08	0.05	0.12	-0.04	0.05	0.45
rs13329835	0.01	0.06	0.83	0.10	0.06	0.09	0.05	0.06	0.39	-0.06	0.05	0.28	0.09	0.06	0.14	-0.08	0.06	0.23	-0.04	0.06	0.54	-0.01	0.06	0.81	0.00	0.06	0.95
rs13365225	0.03	0.07	0.60	-0.01	0.07	0.84	0.08	0.07	0.21	0.07	0.06	0.28	-0.02	0.07	0.81	0.05	0.07	0.49	0.03	0.07	0.70	-0.06	0.07	0.42	0.09	0.06	0.16
rs13387042	-0.04	0.05	0.39	-0.01	0.05	0.79	0.06	0.05	0.23	0.00	0.04	0.91	0.09	0.05	0.06	0.04	0.05	0.39	-0.01	0.05	0.88	-0.01	0.05	0.82	0.02	0.05	0.72
rs1353747	-0.07	0.08	0.39	0.06	0.08	0.48	-0.03	0.08	0.67	0.05	0.07	0.54	-0.01	0.08	0.90	-0.02	0.09	0.81	-0.10	0.08	0.22	-0.09	0.09	0.32	-0.01	0.08	0.94
rs1432679	-0.02	0.05	0.66	0.01	0.05	0.82	-0.04	0.05	0.43	0.11	0.05	0.02	0.07	0.05	0.16	-0.02	0.05	0.69	0.04	0.05	0.45	0.00	0.05	0.93	0.04	0.05	0.42
rs1436904	-0.06	0.05	0.28	-0.01	0.05	0.86	0.06	0.05	0.27	-0.08	0.05	0.08	0.04	0.05	0.37	0.14	0.05	0.01	0.04	0.05	0.46	0.04	0.05	0.43	0.03	0.05	0.50
rs146699004	-0.06	0.05	0.31	-0.02	0.06	0.71	-0.02	0.05	0.69	-0.07	0.05	0.20	0.03	0.05	0.64	-0.11	0.06	0.08	-0.04	0.05	0.47	0.03	0.06	0.59	-0.06	0.05	0.26
rs1550623	-0.01	0.06	0.84	-0.08	0.07	0.23	-0.01	0.06	0.92	0.02	0.06	0.78	-0.11	0.06	0.09	0.04	0.07	0.53	0.03	0.06	0.68	0.03	0.07	0.63	-0.02	0.06	0.79
rs16857609	0.10	0.06	0.08	-0.03	0.06	0.54	0.05	0.05	0.40	-0.03	0.05	0.62	-0.07	0.05	0.20	0.04	0.06	0.53	-0.11	0.06	0.05	-0.10	0.06	0.10	-0.01	0.05	0.91
rs17529111	0.06	0.06	0.28	-0.05	0.06	0.38	-0.02	0.06	0.74	-0.03	0.05	0.61	-0.06	0.06	0.27	0.04	0.06	0.56	0.01	0.06	0.88	0.03	0.06	0.66	0.02	0.06	0.71
rs17817449	0.04	0.05	0.44	-0.03	0.05	0.59	-0.07	0.05	0.15	-0.05	0.05	0.33	-0.02	0.05	0.66	-0.09	0.06	0.11	-0.04	0.05	0.44	-0.07	0.05	0.17	-0.12	0.05	0.01
rs17879961	-0.53	0.86	0.54	1.47	0.83	0.08	0.00	0.87	1.00	-0.06	0.82	0.94	-1.55	0.85	0.07	0.59	0.85	0.49	-1.11	0.86	0.20	-1.01	0.87	0.25	-0.55	0.84	0.51
rs2012709	0.08	0.05	0.12	-0.02	0.05	0.75	0.05	0.05	0.30	0.05	0.05	0.29	0.07	0.05	0.15	0.01	0.05	0.90	-0.01	0.05	0.82	0.02	0.05	0.75	0.03	0.05	0.47
rs2016394	-0.07	0.05	0.17	-0.02	0.05	0.63	0.07	0.05	0.16	0.04	0.05	0.37	0.04	0.05	0.36	0.06	0.05	0.28	-0.10	0.05	0.04	-0.05	0.05	0.29	0.03	0.05	0.58
rs204247	-0.10	0.05	0.04	-0.03	0.05	0.57	0.05	0.05	0.27	-0.13	0.05	0.003	-0.01	0.05	0.78	-0.04	0.05	0.46	0.07	0.05	0.18	-0.02	0.05	0.76	-0.01	0.05	0.76
rs2046210	0.00	0.05	0.96	0.05	0.05	0.36	0.11	0.05	0.03	0.04	0.05	0.44	0.03	0.05	0.52	0.04	0.05	0.46	0.05	0.05	0.35	0.04	0.05	0.39	0.11	0.05	0.01
rs2236007	0.12	0.06	0.07	-0.08	0.07	0.22	0.02	0.06	0.74	-0.02	0.06	0.73	0.06	0.06	0.34	-0.04	0.07	0.55	0.07	0.06	0.24	-0.01	0.07	0.86	-0.01	0.06	0.91
rs2363956	-0.08	0.05	0.09	0.03	0.05	0.55	0.00	0.05	0.99	-0.01	0.05	0.80	0.06	0.05	0.21	0.02	0.05	0.67	0.03	0.05	0.51	0.08	0.05	0.14	0.02	0.05	0.66
rs2380205	-0.01	0.05	0.78	0.03	0.05	0.54	-0.07	0.05	0.14	-0.02	0.05	0.60	0.02	0.05	0.64	-0.03	0.05	0.60	0.02	0.05	0.67	-0.02	0.05	0.71	-0.05	0.05	0.27
rs2588809	-0.04	0.06	0.50	0.04	0.07	0.57	0.03	0.06	0.69	0.02	0.06	0.69	0.04	0.06	0.52	-0.12	0.07	0.09	-0.09	0.06	0.15	-0.11	0.07	0.10	-0.08	0.06	0.18
rs2736108	-0.01	0.06	0.80	0.00	0.06	0.94	0.03	0.06	0.64	-0.05	0.05	0.39	-0.01	0.06	0.81	0.11	0.06	0.09	-0.02	0.06	0.67	0.10	0.06	0.08	0.06	0.05	0.26
rs2823093	0.05	0.06	0.42	-0.03	0.06	0.63	0.01	0.06	0.82	0.03	0.05	0.53	0.02	0.06	0.68	0.12	0.06	0.06	0.02	0.06	0.76	0.04	0.06	0.46	0.04	0.05	0.44
rs2943559	0.10	0.09	0.27	-0.01	0.09	0.93	0.00	0.09	0.98	0.16	0.08	0.05	-0.01	0.09	0.87	0.03	0.10	0.80	0.05	0.09	0.61	0.04	0.10	0.66	0.07	0.08	0.40
rs2981579	0.00	0.05	0.99	0.04	0.05	0.46	0.00	0.05	0.99	-0.06	0.05	0.24	-0.04	0.05	0.44	-0.02	0.06	0.72	-0.01	0.05	0.87	0.01	0.05	0.91	0.00	0.05	0.93

Variant	Adjusted beta[a], standard error, p-value																										
	Acute toxicity			Telangiectasia			Edema			Shrinkage			Induration			Pigmentation			Pain			Oversensitivity			Overall (STAT[b])		
rs3760982	-0.05	0.05	0.28	-0.09	0.05	0.07	0.08	0.05	0.09	0.04	0.05	0.43	0.06	0.05	0.19	0.04	0.05	0.41	-0.01	0.05	0.76	-0.05	0.05	0.30	-0.01	0.05	0.90
rs3803662	-0.08	0.05	0.14	0.04	0.05	0.47	0.04	0.05	0.47	0.00	0.05	0.99	-0.04	0.05	0.49	0.06	0.06	0.35	-0.07	0.05	0.16	-0.05	0.06	0.34	0.03	0.05	0.56
rs3817198	0.03	0.05	0.63	-0.02	0.06	0.69	0.01	0.05	0.88	-0.02	0.05	0.72	-0.06	0.05	0.27	-0.06	0.06	0.31	-0.02	0.05	0.67	-0.08	0.06	0.13	-0.04	0.05	0.42
rs3903072	-0.04	0.05	0.37	0.03	0.05	0.58	-0.03	0.05	0.51	-0.02	0.05	0.67	0.00	0.05	0.95	0.07	0.05	0.21	0.01	0.05	0.79	0.05	0.05	0.28	0.03	0.05	0.55
rs4245739	0.06	0.05	0.28	0.07	0.05	0.22	-0.02	0.05	0.67	0.00	0.05	0.98	0.03	0.05	0.61	-0.02	0.06	0.70	0.12	0.05	0.02	0.13	0.06	0.02	0.06	0.05	0.22
rs4593472	0.05	0.05	0.38	0.02	0.05	0.66	-0.03	0.05	0.57	0.05	0.05	0.33	0.00	0.05	0.93	0.14	0.06	0.01	0.06	0.05	0.29	0.01	0.06	0.80	0.08	0.05	0.12
rs4808801	0.04	0.05	0.43	-0.03	0.05	0.52	0.00	0.05	0.93	-0.01	0.05	0.87	-0.05	0.05	0.28	0.00	0.06	0.94	0.04	0.05	0.46	-0.01	0.05	0.91	-0.01	0.05	0.77
rs4849887	0.01	0.08	0.94	-0.08	0.08	0.36	0.03	0.08	0.69	0.04	0.08	0.61	0.05	0.08	0.56	0.06	0.09	0.46	0.00	0.08	1.00	0.10	0.08	0.22	0.03	0.08	0.68
rs4973768	-0.01	0.05	0.88	0.03	0.05	0.55	-0.07	0.05	0.14	-0.01	0.04	0.84	0.02	0.05	0.65	0.02	0.05	0.73	-0.02	0.05	0.66	-0.06	0.05	0.27	-0.03	0.05	0.57
rs527616	-0.02	0.05	0.72	-0.01	0.05	0.83	-0.08	0.05	0.13	0.00	0.05	0.99	0.04	0.05	0.38	0.06	0.05	0.25	0.09	0.05	0.06	0.02	0.05	0.73	0.08	0.05	0.09
rs6001930	-0.09	0.08	0.25	-0.05	0.08	0.52	-0.02	0.08	0.78	-0.01	0.07	0.91	-0.10	0.08	0.19	-0.02	0.08	0.81	0.09	0.08	0.27	-0.04	0.08	0.62	-0.02	0.07	0.74
rs616488	-0.04	0.05	0.49	0.02	0.05	0.76	-0.08	0.05	0.12	0.00	0.05	0.96	0.03	0.05	0.51	-0.14	0.06	0.02	-0.01	0.05	0.83	-0.04	0.06	0.43	-0.03	0.05	0.51
rs6472903	-0.02	0.07	0.80	-0.02	0.07	0.76	0.07	0.07	0.33	0.06	0.07	0.35	0.11	0.07	0.12	0.01	0.08	0.90	-0.04	0.07	0.54	-0.10	0.07	0.16	-0.06	0.07	0.41
rs6504950	0.05	0.06	0.33	-0.09	0.06	0.13	-0.01	0.06	0.81	-0.02	0.05	0.73	-0.04	0.06	0.52	0.11	0.06	0.07	0.03	0.06	0.64	0.08	0.06	0.16	0.01	0.05	0.78
rs6507583	-0.09	0.10	0.33	-0.22	0.09	0.02	-0.13	0.09	0.14	-0.16	0.08	0.07	-0.14	0.09	0.11	0.04	0.10	0.71	0.24	0.09	0.01	0.22	0.10	0.03	-0.05	0.09	0.60
rs6678914	0.01	0.05	0.84	-0.02	0.05	0.65	0.00	0.05	0.97	-0.09	0.05	0.06	-0.06	0.05	0.25	0.00	0.06	0.95	-0.01	0.05	0.79	0.08	0.05	0.16	-0.01	0.05	0.87
rs6762644	-0.01	0.05	0.80	0.02	0.05	0.66	0.00	0.05	0.95	-0.04	0.05	0.41	0.01	0.05	0.89	-0.06	0.06	0.32	0.09	0.05	0.07	0.02	0.05	0.71	-0.03	0.05	0.61
rs6796502	0.09	0.08	0.31	-0.01	0.09	0.87	-0.18	0.08	0.03	-0.01	0.08	0.84	-0.09	0.08	0.27	0.00	0.09	0.99	-0.15	0.08	0.07	0.02	0.09	0.81	-0.02	0.08	0.82
rs6828523	-0.15	0.08	0.06	0.04	0.08	0.64	-0.14	0.08	0.08	-0.09	0.07	0.22	-0.06	0.08	0.42	-0.08	0.09	0.36	0.04	0.08	0.60	-0.10	0.08	0.22	-0.14	0.08	0.07
rs6964587	-0.05	0.05	0.28	-0.09	0.05	0.09	0.10	0.05	0.05	0.00	0.05	0.95	-0.01	0.05	0.84	0.03	0.06	0.58	-0.07	0.05	0.19	-0.06	0.05	0.29	-0.02	0.05	0.66
rs704010	0.02	0.05	0.69	-0.01	0.05	0.88	-0.02	0.05	0.64	0.02	0.05	0.61	-0.05	0.05	0.35	0.08	0.06	0.17	0.08	0.05	0.10	-0.01	0.05	0.92	0.03	0.05	0.55
rs7072776	-0.05	0.06	0.35	-0.01	0.06	0.89	0.03	0.06	0.58	0.06	0.05	0.29	-0.04	0.06	0.52	0.09	0.06	0.16	-0.01	0.06	0.80	-0.08	0.06	0.20	0.03	0.05	0.54
rs720475	-0.02	0.06	0.72	0.04	0.06	0.48	0.01	0.06	0.89	0.00	0.05	0.95	-0.06	0.06	0.31	-0.03	0.06	0.59	0.05	0.06	0.35	0.01	0.06	0.88	0.00	0.05	0.95
rs72755295	0.00	0.18	0.98	-0.20	0.20	0.31	0.40	0.19	0.03	0.02	0.18	0.93	0.50	0.19	0.01	0.04	0.21	0.86	0.27	0.18	0.14	-0.03	0.19	0.87	0.26	0.18	0.15
rs745570	0.02	0.05	0.64	-0.06	0.05	0.26	-0.01	0.05	0.85	-0.01	0.05	0.76	-0.04	0.05	0.45	0.02	0.05	0.79	0.08	0.05	0.11	0.01	0.05	0.78	0.06	0.05	0.24
rs75915166	0.09	0.12	0.42	0.03	0.12	0.83	0.06	0.11	0.61	0.06	0.10	0.60	0.06	0.11	0.59	0.03	0.13	0.79	0.17	0.11	0.15	-0.05	0.12	0.71	0.07	0.11	0.49
rs7707921	-0.13	0.06	0.03	-0.01	0.06	0.81	0.04	0.06	0.49	0.04	0.05	0.42	0.01	0.06	0.89	0.03	0.06	0.68	0.05	0.06	0.36	0.08	0.06	0.20	0.09	0.06	0.12

Variant	Adjusted beta[a], standard error, p-value																										
	Acute toxicity			Telangiectasia			Edema			Shrinkage			Induration			Pigmentation			Pain			Oversensitivity			Overall (STAT[b])		
rs7726159	0.01	0.06	0.89	0.03	0.06	0.65	0.02	0.06	0.67	0.02	0.05	0.67	0.05	0.06	0.40	-0.02	0.06	0.78	-0.01	0.06	0.92	0.05	0.06	0.44	0.03	0.05	0.55
rs78540526	0.13	0.10	0.18	0.00	0.10	0.96	0.00	0.10	0.99	0.01	0.09	0.90	-0.01	0.10	0.95	0.05	0.11	0.66	0.26	0.10	0.01	0.06	0.10	0.60	0.12	0.09	0.18
rs7904519	0.01	0.05	0.84	-0.04	0.05	0.40	0.05	0.05	0.34	0.04	0.05	0.40	-0.01	0.05	0.89	-0.09	0.05	0.11	0.05	0.05	0.37	-0.02	0.05	0.65	-0.01	0.05	0.81
rs8170	-0.09	0.06	0.16	0.02	0.06	0.72	0.06	0.06	0.31	-0.03	0.06	0.61	0.04	0.06	0.53	0.01	0.07	0.93	0.06	0.06	0.31	0.08	0.06	0.22	-0.02	0.06	0.80
rs865686	0.12	0.05	0.02	0.05	0.05	0.28	-0.02	0.05	0.63	-0.04	0.05	0.40	-0.02	0.05	0.72	0.04	0.05	0.46	0.01	0.05	0.78	0.03	0.05	0.59	0.01	0.05	0.91
rs889312	-0.06	0.05	0.30	-0.08	0.05	0.15	0.02	0.05	0.76	-0.02	0.05	0.68	-0.04	0.05	0.46	-0.01	0.06	0.91	0.06	0.05	0.23	-0.02	0.06	0.77	-0.01	0.05	0.88
rs9257408	-0.08	0.05	0.11	-0.08	0.05	0.13	-0.02	0.05	0.67	-0.02	0.05	0.69	0.00	0.05	0.93	-0.01	0.05	0.82	-0.04	0.05	0.42	-0.05	0.05	0.32	-0.03	0.05	0.49
rs941764	0.05	0.05	0.35	0.05	0.05	0.32	0.09	0.05	0.06	-0.03	0.05	0.58	0.05	0.05	0.33	0.04	0.06	0.48	-0.03	0.05	0.59	-0.06	0.05	0.25	0.03	0.05	0.53
rs9693444	-0.10	0.05	0.06	-0.05	0.05	0.38	-0.04	0.05	0.49	0.07	0.05	0.18	0.00	0.05	0.96	-0.03	0.06	0.57	-0.02	0.05	0.75	-0.07	0.06	0.19	-0.06	0.05	0.23
rs9790517	0.17	0.06	0.01	0.08	0.06	0.18	0.02	0.06	0.80	0.02	0.06	0.76	0.07	0.06	0.27	-0.01	0.07	0.88	-0.02	0.06	0.77	0.04	0.06	0.56	0.03	0.06	0.66
rs999737	0.05	0.06	0.40	-0.03	0.06	0.60	-0.06	0.06	0.29	0.02	0.06	0.74	-0.06	0.06	0.30	-0.03	0.07	0.65	0.05	0.06	0.45	-0.04	0.06	0.49	-0.06	0.06	0.34

[a]beta estimates are for the association between polygenic risk score and change in residual toxicity; a positive beta represents an increased risk of toxicity and a negative beta represents reduced risk of toxicity

[b]Standardized total average toxicity

Supplementary Table 5: Results from residual analyses of individual risk variants and five-year toxicity

Variant	Adjusted beta[a], standard error, p-value														
	Telangiectasia			Edema			Shrinkage			Induration			Overall toxicity (STAT[b])		
rs10069690	0.05	0.07	0.46	0.05	0.07	0.45	0.005	0.07	0.95	-0.05	0.07	0.48	0.001	0.07	0.99
rs1011970	0.01	0.08	0.89	0.15	0.08	0.05	-0.08	0.08	0.32	-0.002	0.08	0.98	0.02	0.08	0.82
rs1045485	0.05	0.09	0.57	0.03	0.09	0.73	0.06	0.10	0.55	-0.11	0.10	0.27	0.04	0.10	0.66
rs10472076	0.02	0.06	0.72	-0.02	0.06	0.75	-0.06	0.07	0.34	0.07	0.06	0.28	0.05	0.07	0.41
rs1053338	-0.08	0.09	0.38	0.05	0.09	0.60	-0.01	0.09	0.93	0.01	0.09	0.94	0.03	0.09	0.78
rs10759243	0.09	0.08	0.27	-0.05	0.08	0.55	0.03	0.08	0.75	-0.12	0.08	0.13	-0.004	0.08	0.96
rs10941679	0.02	0.07	0.82	-0.03	0.07	0.69	-0.04	0.07	0.53	-0.03	0.07	0.63	-0.03	0.07	0.68
rs10995190	0.09	0.09	0.32	0.05	0.09	0.56	0.05	0.09	0.55	-0.04	0.09	0.65	0.01	0.09	0.90
rs11075995	0.04	0.07	0.55	-0.11	0.07	0.13	0.07	0.07	0.31	0.03	0.07	0.73	-0.001	0.07	0.99
rs11199914	0.03	0.08	0.67	0.07	0.07	0.33	-0.05	0.08	0.53	-0.04	0.08	0.59	-0.02	0.08	0.82
rs11242675	-0.07	0.07	0.31	-0.03	0.06	0.70	0.03	0.07	0.64	-0.06	0.07	0.42	-0.11	0.07	0.12
rs11249433	0.09	0.08	0.25	0.04	0.07	0.54	-0.13	0.08	0.08	-0.11	0.08	0.16	-0.02	0.08	0.83
rs11552449	-0.16	0.08	0.06	-0.11	0.08	0.15	0.04	0.08	0.66	-0.01	0.08	0.88	-0.09	0.08	0.27
rs11571833	-0.38	0.36	0.29	-0.39	0.36	0.29	-0.38	0.40	0.34	-0.56	0.38	0.14	-0.79	0.38	0.04
rs11627032	0.04	0.08	0.58	-0.0002	0.07	1.00	0.11	0.08	0.15	0.11	0.08	0.16	0.04	0.08	0.61
rs11780156	0.09	0.08	0.27	0.14	0.08	0.07	-0.08	0.08	0.35	0.10	0.09	0.23	0.19	0.09	0.03
rs11814448	-0.16	0.24	0.49	-0.28	0.23	0.23	0.26	0.24	0.28	0.13	0.25	0.61	-0.13	0.24	0.59
rs11820646	-0.06	0.07	0.36	0.04	0.06	0.50	0.06	0.07	0.35	0.02	0.07	0.81	0.002	0.07	0.98
rs12048493	-0.09	0.08	0.25	-0.10	0.07	0.19	-0.06	0.08	0.47	0.01	0.08	0.92	-0.04	0.08	0.57
rs12405132	-0.04	0.06	0.55	-0.05	0.06	0.39	-0.04	0.06	0.49	-0.03	0.06	0.62	-0.07	0.07	0.28
rs12493607	-0.07	0.06	0.31	-0.01	0.06	0.93	0.001	0.06	0.99	-0.06	0.07	0.34	-0.10	0.07	0.14
rs12662670	-0.05	0.11	0.61	-0.09	0.10	0.36	-0.06	0.11	0.58	-0.02	0.11	0.89	-0.14	0.11	0.22
rs12710696	-0.01	0.06	0.88	-0.10	0.06	0.10	-0.05	0.07	0.41	-0.10	0.07	0.13	-0.09	0.07	0.17
rs1292011	-0.03	0.06	0.62	-0.05	0.06	0.43	0.01	0.06	0.83	0.01	0.07	0.91	-0.04	0.07	0.59

Variant	Adjusted beta[a], standard error, p-value														
	Telangiectasia			Edema			Shrinkage			Induration			Overall toxicity (STAT[b])		
rs13162653	-0.07	0.07	0.32	-0.11	0.07	0.10	-0.07	0.07	0.33	-0.09	0.07	0.21	-0.11	0.07	0.11
rs132390	-0.14	0.16	0.38	0.01	0.16	0.94	-0.06	0.17	0.70	-0.27	0.17	0.12	-0.19	0.17	0.27
rs13267382	-0.13	0.06	0.04	-0.06	0.06	0.31	-0.10	0.06	0.10	-0.02	0.06	0.77	-0.10	0.06	0.13
rs13281615	0.03	0.06	0.64	-0.12	0.06	0.05	0.05	0.06	0.44	-0.04	0.06	0.57	-0.06	0.06	0.37
rs13329835	0.06	0.07	0.40	0.08	0.07	0.25	0.02	0.08	0.81	0.10	0.08	0.21	0.09	0.08	0.26
rs13365225	-0.003	0.09	0.97	-0.04	0.08	0.64	-0.02	0.09	0.86	-0.21	0.09	0.02	-0.14	0.09	0.11
rs13387042	-0.01	0.06	0.80	0.05	0.06	0.36	0.04	0.06	0.47	-0.001	0.06	0.98	0.03	0.06	0.57
rs1353747	0.10	0.10	0.32	0.10	0.10	0.30	-0.07	0.10	0.47	0.02	0.11	0.84	0.12	0.11	0.24
rs1432679	0.01	0.06	0.86	-0.04	0.06	0.46	0.16	0.06	0.01	0.03	0.06	0.64	0.05	0.06	0.40
rs1436904	-0.04	0.07	0.51	0.03	0.06	0.69	0.05	0.07	0.46	-0.02	0.07	0.79	-0.03	0.07	0.67
rs146699004	-0.10	0.07	0.14	-0.01	0.07	0.87	-0.06	0.07	0.38	0.01	0.07	0.89	0.01	0.07	0.88
rs1550623	-0.003	0.08	0.97	-0.02	0.08	0.76	0.13	0.08	0.12	-0.12	0.08	0.15	0.02	0.09	0.77
rs16857609	0.02	0.07	0.73	0.03	0.07	0.65	-0.10	0.07	0.18	-0.05	0.07	0.51	-0.05	0.07	0.53
rs17529111	-0.02	0.07	0.83	-0.07	0.07	0.29	-0.03	0.07	0.72	-0.10	0.07	0.17	-0.12	0.07	0.09
rs17817449	-0.04	0.07	0.58	-0.04	0.06	0.50	0.05	0.07	0.49	-0.03	0.07	0.64	-0.03	0.07	0.64
rs17879961	2.36	0.88	0.01	0.82	0.88	0.35	1.82	0.87	0.04	-0.44	0.88	0.62	0.90	0.88	0.30
rs2012709	-0.04	0.06	0.53	-0.01	0.06	0.88	-0.02	0.06	0.73	-0.06	0.06	0.34	-0.02	0.06	0.75
rs2016394	-0.04	0.06	0.53	-0.01	0.06	0.81	-0.14	0.06	0.03	-0.04	0.06	0.56	-0.07	0.06	0.28
rs204247	0.05	0.06	0.47	0.07	0.06	0.25	-0.06	0.06	0.34	0.04	0.06	0.50	0.04	0.06	0.58
rs2046210	0.09	0.06	0.14	-0.04	0.06	0.49	0.04	0.07	0.55	-0.02	0.07	0.78	0.03	0.07	0.66
rs2236007	-0.07	0.08	0.35	-0.07	0.08	0.34	0.07	0.08	0.36	0.05	0.08	0.51	-0.06	0.08	0.46
rs2363956	0.05	0.06	0.38	-0.005	0.06	0.93	-0.05	0.06	0.42	-0.03	0.06	0.64	0.01	0.06	0.91
rs2380205	0.02	0.06	0.73	0.003	0.06	0.96	-0.07	0.06	0.28	0.02	0.06	0.79	-0.01	0.06	0.87
rs2588809	-0.01	0.08	0.86	0.001	0.08	0.99	0.08	0.08	0.30	0.01	0.08	0.90	-0.0001	0.08	1.00
rs2736108	0.06	0.07	0.40	0.04	0.07	0.60	-0.03	0.08	0.68	-0.06	0.08	0.41	-0.03	0.08	0.68
rs2823093	0.09	0.07	0.22	0.12	0.07	0.10	0.08	0.07	0.30	0.10	0.07	0.17	0.13	0.07	0.07
rs2943559	0.07	0.11	0.52	-0.16	0.11	0.13	-0.13	0.11	0.27	0.06	0.11	0.59	0.04	0.11	0.74

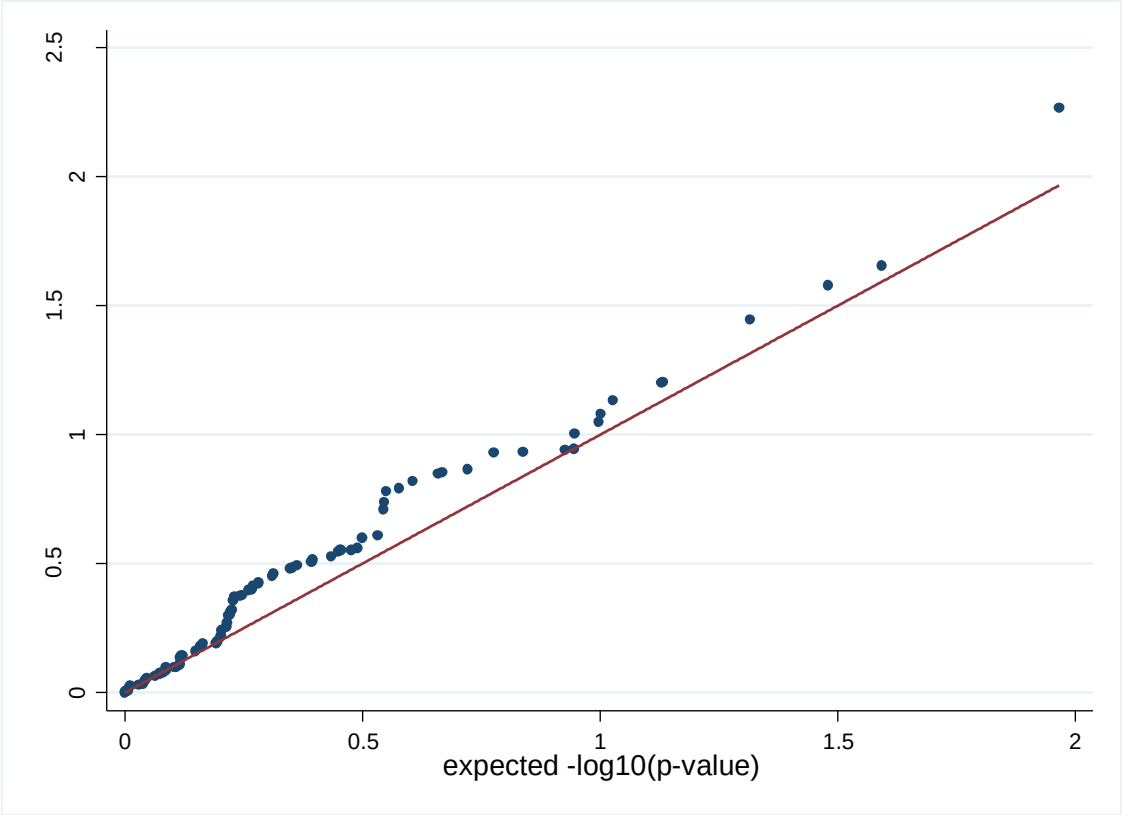
Variant	Adjusted beta[a], standard error, p-value														
	Telangiectasia			Edema			Shrinkage			Induration			Overall toxicity (STAT[b])		
rs2981579	-0.07	0.06	0.29	-0.03	0.06	0.67	0.06	0.07	0.37	0.05	0.07	0.42	-0.03	0.07	0.68
rs3760982	-0.04	0.06	0.55	0.12	0.06	0.04	0.09	0.06	0.17	0.07	0.06	0.26	0.08	0.06	0.23
rs3803662	-0.10	0.07	0.14	0.002	0.07	0.98	-0.03	0.07	0.71	0.07	0.07	0.31	0.03	0.07	0.69
rs3817198	-0.08	0.07	0.25	0.06	0.07	0.34	-0.14	0.07	0.05	-0.02	0.07	0.73	-0.06	0.07	0.40
rs3903072	0.01	0.06	0.85	-0.06	0.06	0.34	-0.01	0.06	0.82	-0.07	0.06	0.26	-0.03	0.06	0.68
rs4245739	0.11	0.07	0.11	0.06	0.07	0.41	0.06	0.07	0.43	-0.01	0.07	0.94	0.05	0.07	0.50
rs4593472	-0.01	0.07	0.85	0.01	0.07	0.83	0.05	0.07	0.48	0.03	0.07	0.70	0.04	0.07	0.56
rs4808801	0.01	0.07	0.84	0.03	0.06	0.64	0.06	0.07	0.37	-0.05	0.07	0.43	-0.02	0.07	0.75
rs4849887	0.03	0.11	0.78	-0.19	0.10	0.05	0.04	0.11	0.74	-0.13	0.11	0.25	-0.11	0.11	0.31
rs4973768	0.07	0.06	0.27	0.11	0.06	0.05	0.03	0.06	0.66	-0.02	0.06	0.77	0.08	0.06	0.19
rs527616	-0.02	0.06	0.75	-0.003	0.06	0.95	-0.01	0.06	0.82	0.02	0.06	0.76	-0.001	0.06	0.99
rs6001930	-0.04	0.10	0.67	-0.10	0.09	0.29	0.07	0.10	0.48	-0.003	0.10	0.97	-0.05	0.10	0.59
rs616488	-0.06	0.07	0.35	-0.11	0.06	0.07	0.14	0.07	0.04	-0.08	0.07	0.24	-0.07	0.07	0.28
rs6472903	-0.01	0.09	0.90	0.06	0.08	0.50	0.07	0.09	0.44	-0.04	0.09	0.69	-0.05	0.09	0.57
rs6504950	0.08	0.07	0.24	0.05	0.07	0.50	-0.02	0.07	0.82	0.19	0.07	0.01	0.15	0.07	0.04
rs6507583	-0.06	0.11	0.61	-0.04	0.11	0.69	0.04	0.11	0.71	-0.15	0.12	0.20	-0.17	0.11	0.14
rs6678914	-0.04	0.07	0.51	0.07	0.06	0.31	-0.14	0.07	0.04	0.01	0.07	0.89	-0.0002	0.07	1.00
rs6762644	0.07	0.06	0.26	-0.07	0.06	0.25	0.04	0.07	0.53	0.07	0.07	0.28	0.02	0.07	0.76
rs6796502	-0.14	0.10	0.18	-0.17	0.10	0.08	0.13	0.10	0.20	-0.09	0.10	0.36	-0.19	0.10	0.07
rs6828523	-0.01	0.10	0.90	0.003	0.10	0.97	-0.24	0.10	0.02	-0.16	0.10	0.13	-0.14	0.11	0.20
rs6964587	-0.10	0.07	0.13	0.22	0.06	0.0007	-0.06	0.07	0.34	-0.07	0.07	0.31	-0.04	0.07	0.60
rs704010	0.05	0.06	0.47	0.11	0.06	0.06	0.04	0.06	0.58	0.06	0.06	0.37	0.15	0.06	0.02
rs7072776	-0.02	0.07	0.78	-0.03	0.07	0.65	0.03	0.07	0.71	0.02	0.08	0.78	-0.02	0.08	0.74
rs720475	0.04	0.07	0.57	-0.05	0.07	0.44	0.07	0.07	0.33	-0.01	0.07	0.89	-0.03	0.07	0.65
rs72755295	0.14	0.23	0.54	-0.09	0.22	0.68	-0.08	0.24	0.74	-0.08	0.24	0.75	0.11	0.24	0.66
rs745570	-0.02	0.06	0.75	0.001	0.06	0.98	-0.03	0.06	0.63	0.09	0.07	0.19	0.07	0.07	0.29
rs75915166	-0.22	0.15	0.14	0.14	0.14	0.31	0.05	0.15	0.72	0.15	0.15	0.32	-0.04	0.15	0.79

Variant	Adjusted beta[a], standard error, p-value														
	Telangiectasia			Edema			Shrinkage			Induration			Overall toxicity (STAT[b])		
rs7707921	-0.11	0.07	0.12	-0.02	0.07	0.82	0.02	0.08	0.79	-0.03	0.08	0.69	-0.06	0.08	0.47
rs7726159	0.09	0.07	0.18	0.04	0.07	0.58	0.10	0.07	0.16	0.05	0.07	0.53	0.08	0.07	0.30
rs78540526	-0.09	0.13	0.50	0.11	0.12	0.36	0.004	0.13	0.98	0.09	0.13	0.48	0.0004	0.13	1.00
rs7904519	0.002	0.06	0.98	0.05	0.06	0.41	-0.01	0.06	0.91	-0.004	0.06	0.95	-0.004	0.06	0.95
rs8170	0.07	0.08	0.39	-0.06	0.08	0.40	-0.04	0.08	0.60	0.05	0.08	0.52	0.03	0.08	0.70
rs865686	0.15	0.06	0.02	0.04	0.06	0.50	-0.04	0.06	0.56	-0.05	0.06	0.41	0.05	0.06	0.42
rs889312	0.04	0.07	0.57	-0.07	0.07	0.30	-0.04	0.07	0.62	-0.07	0.07	0.31	-0.02	0.07	0.78
rs9257408	-0.03	0.06	0.64	-0.11	0.06	0.07	-0.09	0.06	0.15	-0.03	0.06	0.61	-0.05	0.07	0.47
rs941764	0.08	0.07	0.25	-0.04	0.06	0.56	0.04	0.07	0.60	-0.05	0.07	0.47	-0.0002	0.07	1.00
rs9693444	0.01	0.07	0.84	0.10	0.06	0.11	0.04	0.07	0.51	0.05	0.07	0.42	0.11	0.07	0.11
rs9790517	0.09	0.08	0.27	-0.08	0.07	0.30	0.05	0.08	0.53	-0.08	0.08	0.32	0.02	0.08	0.83
rs999737	0.01	0.08	0.92	-0.06	0.07	0.40	0.06	0.08	0.44	0.04	0.08	0.65	0.04	0.08	0.61

[a]beta estimates are for the association between polygenic risk score and change in residual toxicity; a positive beta represents an increased risk of toxicity and a negative beta represents reduced risk of toxicity

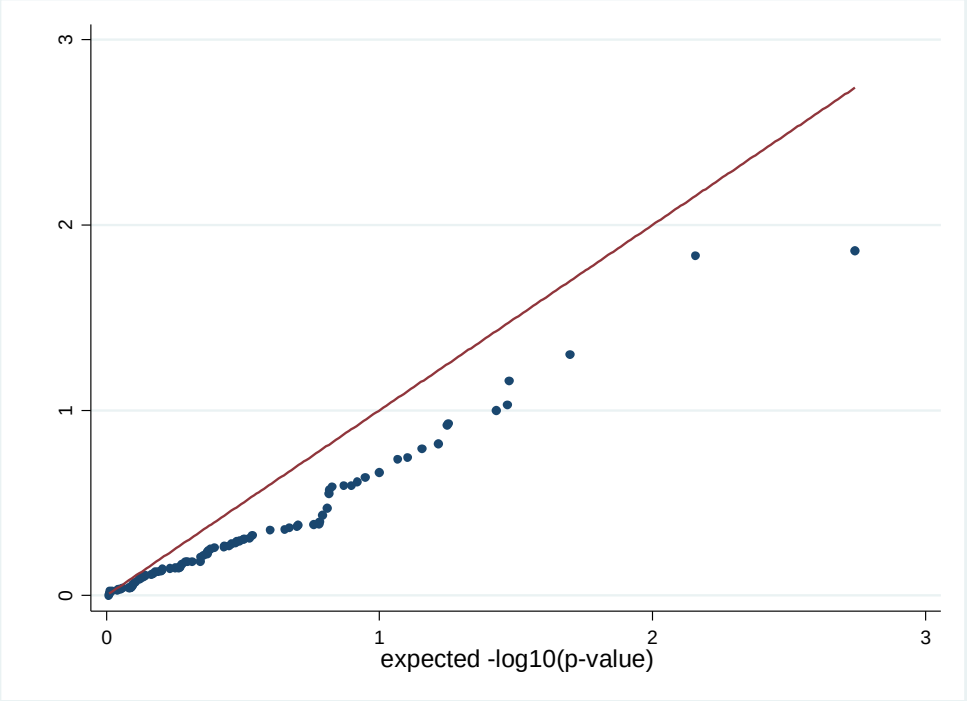
[b]Standardized total average toxicity

Supplementary Figure 1: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and acute toxicity

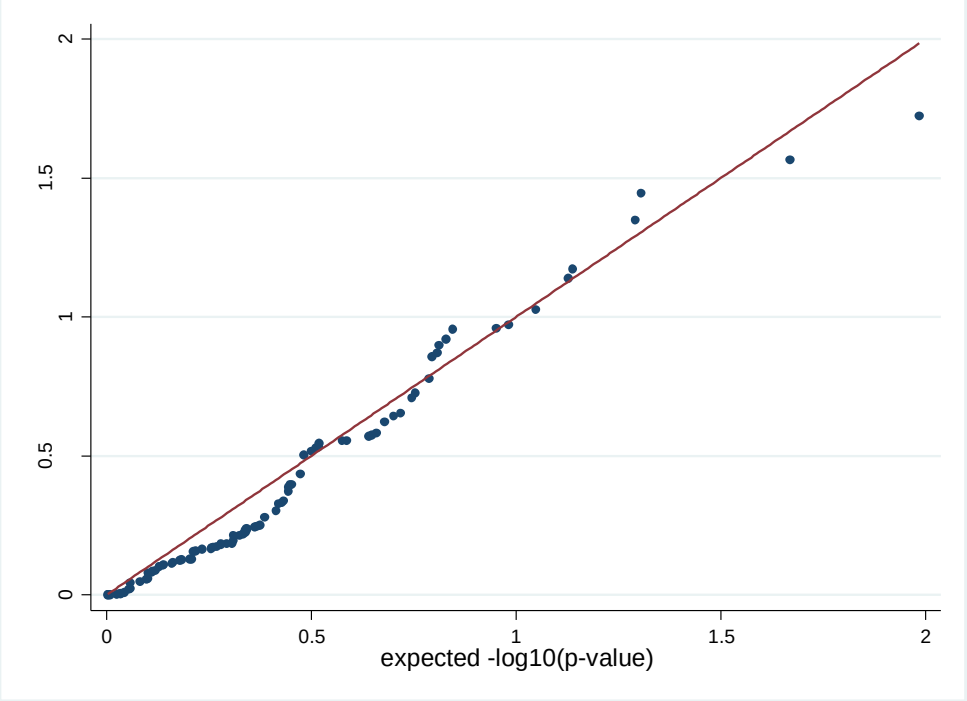


Supplementary Figure 2: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and standardised total average toxicity (STAT) score

A) STAT score at two years

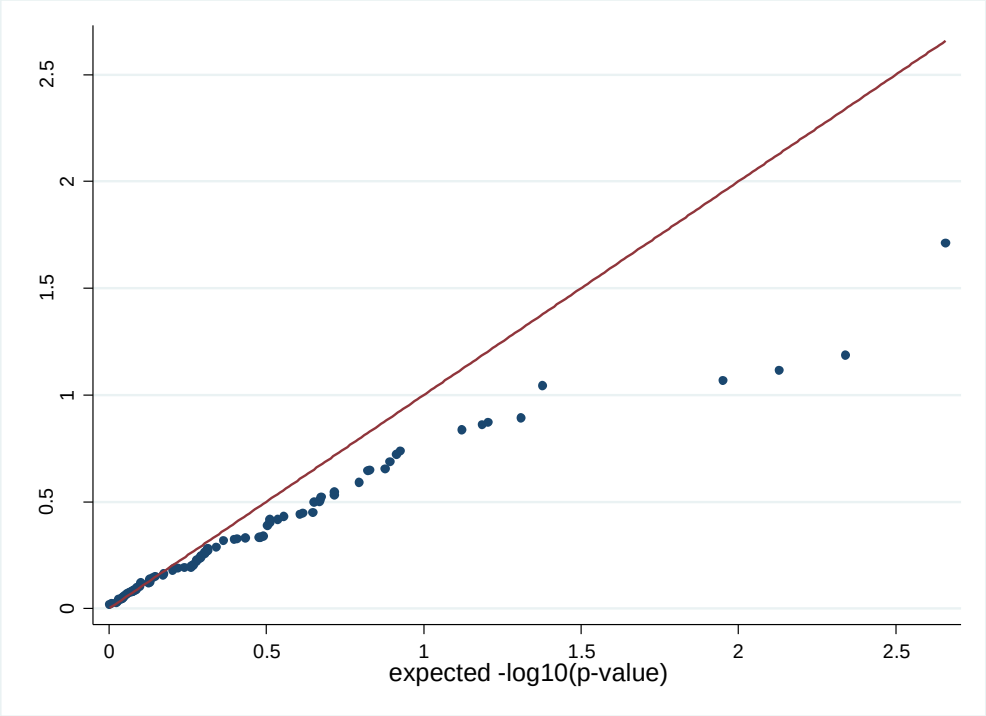


B) STAT score at five years

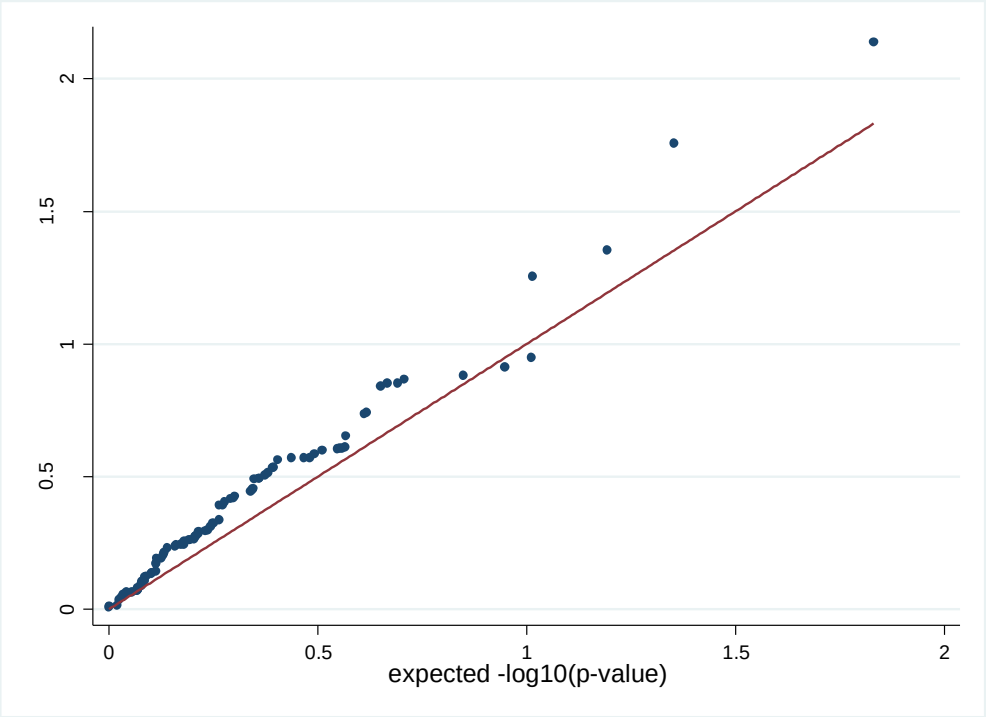


Supplementary Figure 3: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and telangiectasia

A) Telangiectasia at two years

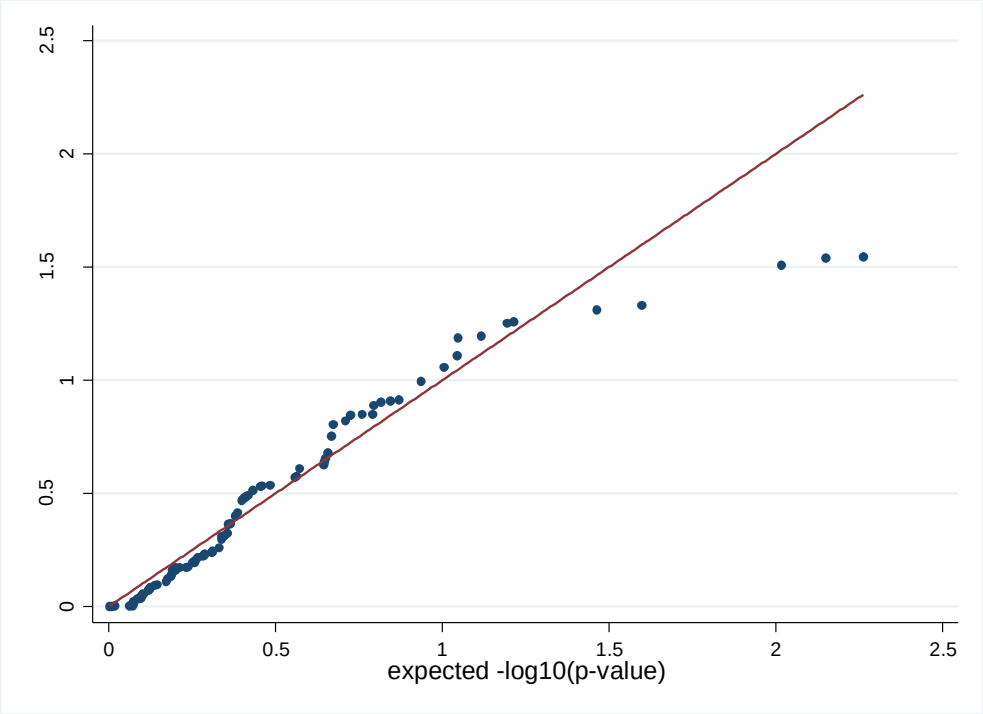


B) Telangiectasia at five years

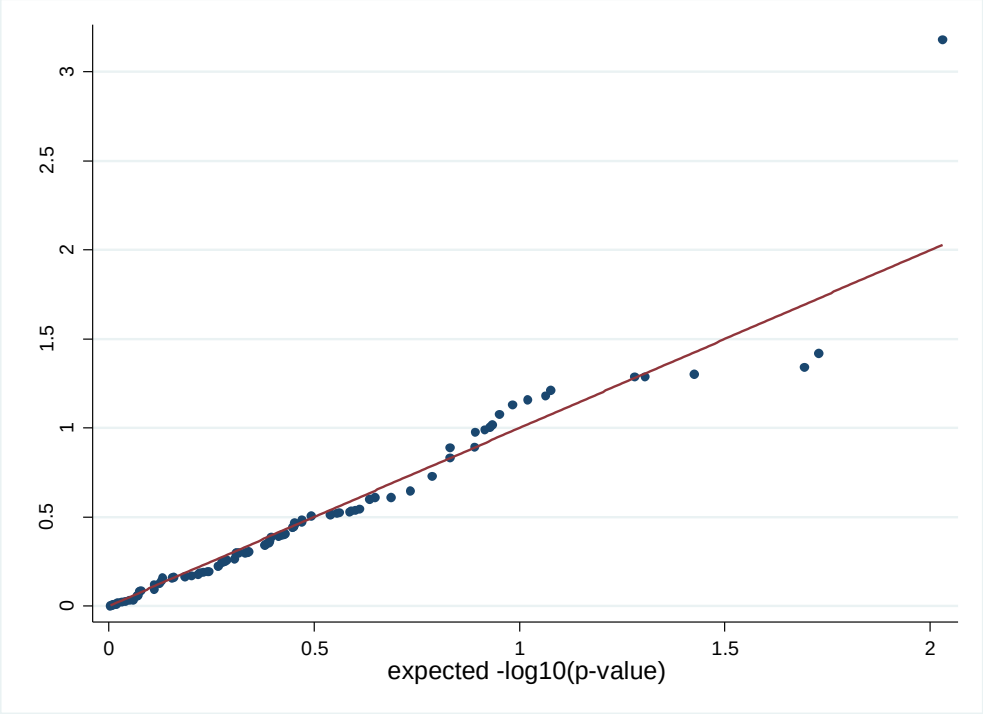


Supplementary Figure 4: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and edema

A) Edema at two years

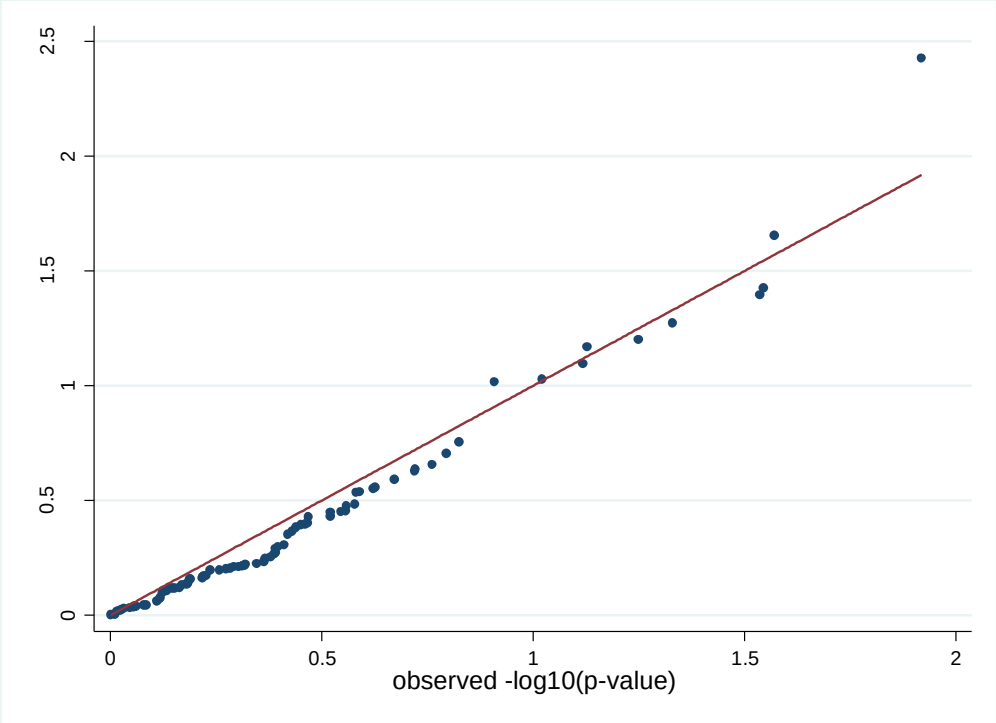


B) Edema at five years

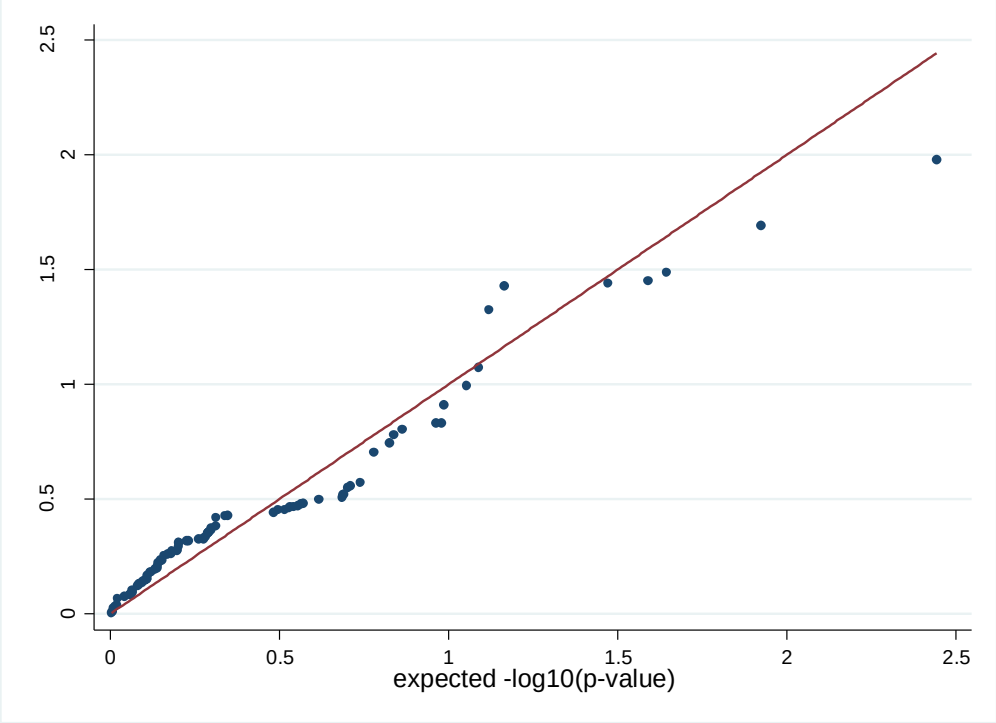


Supplementary Figure 5: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and breast shrinkage

A) Breast shrinkage at two years

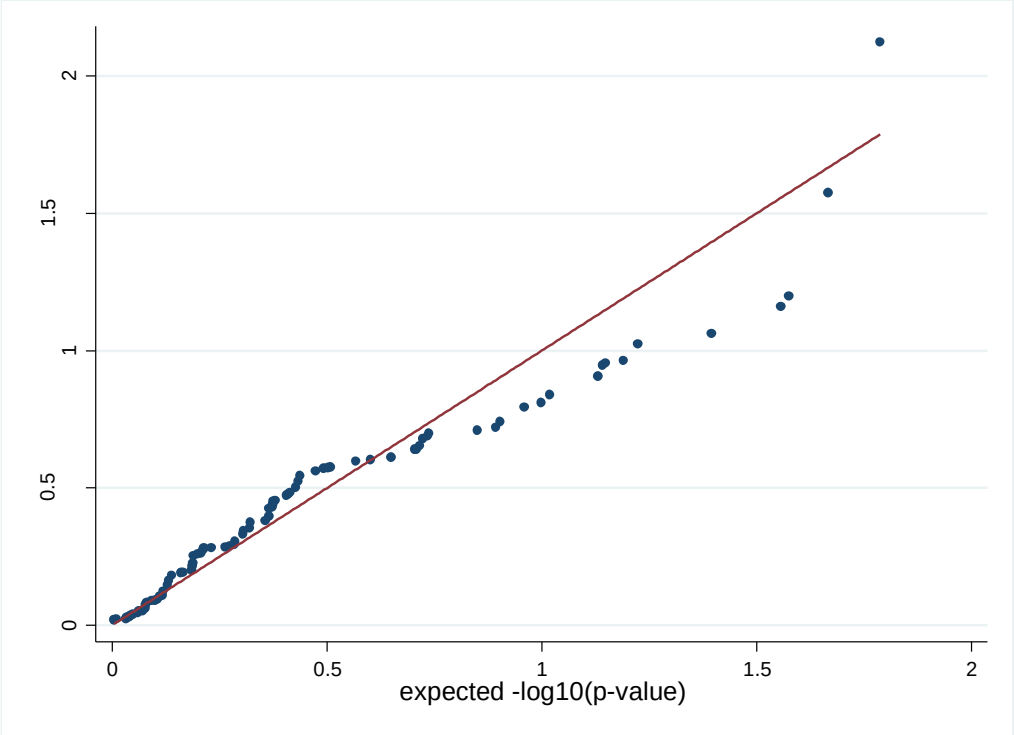


B) Breast shrinkage at five years

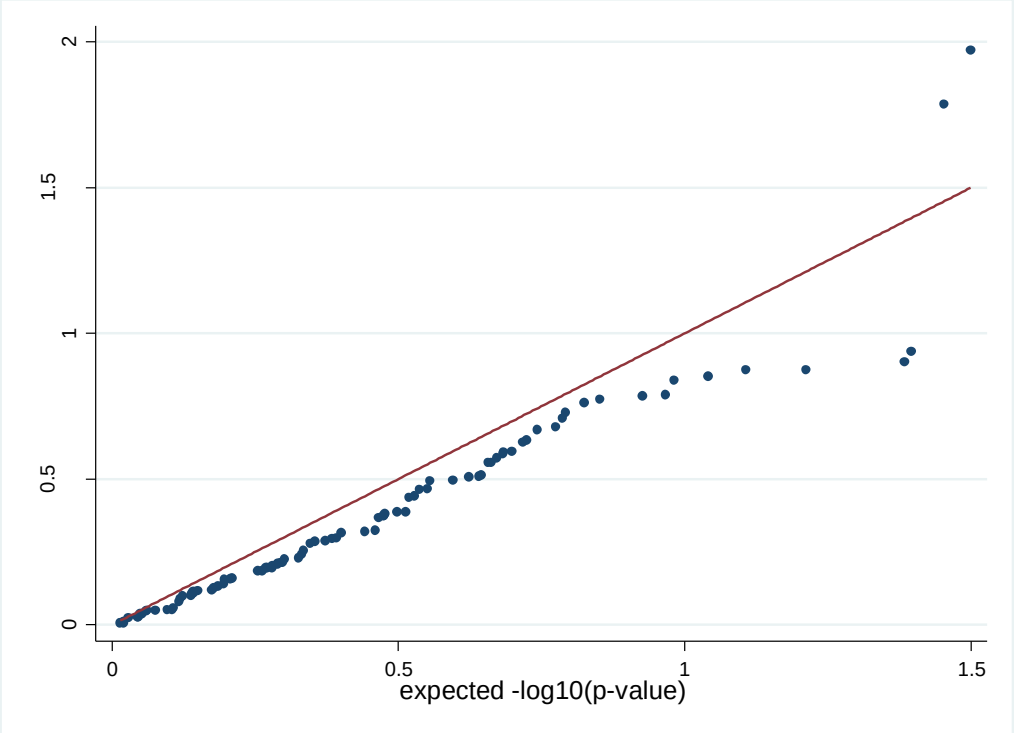


Supplementary Figure 6: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and breast induration

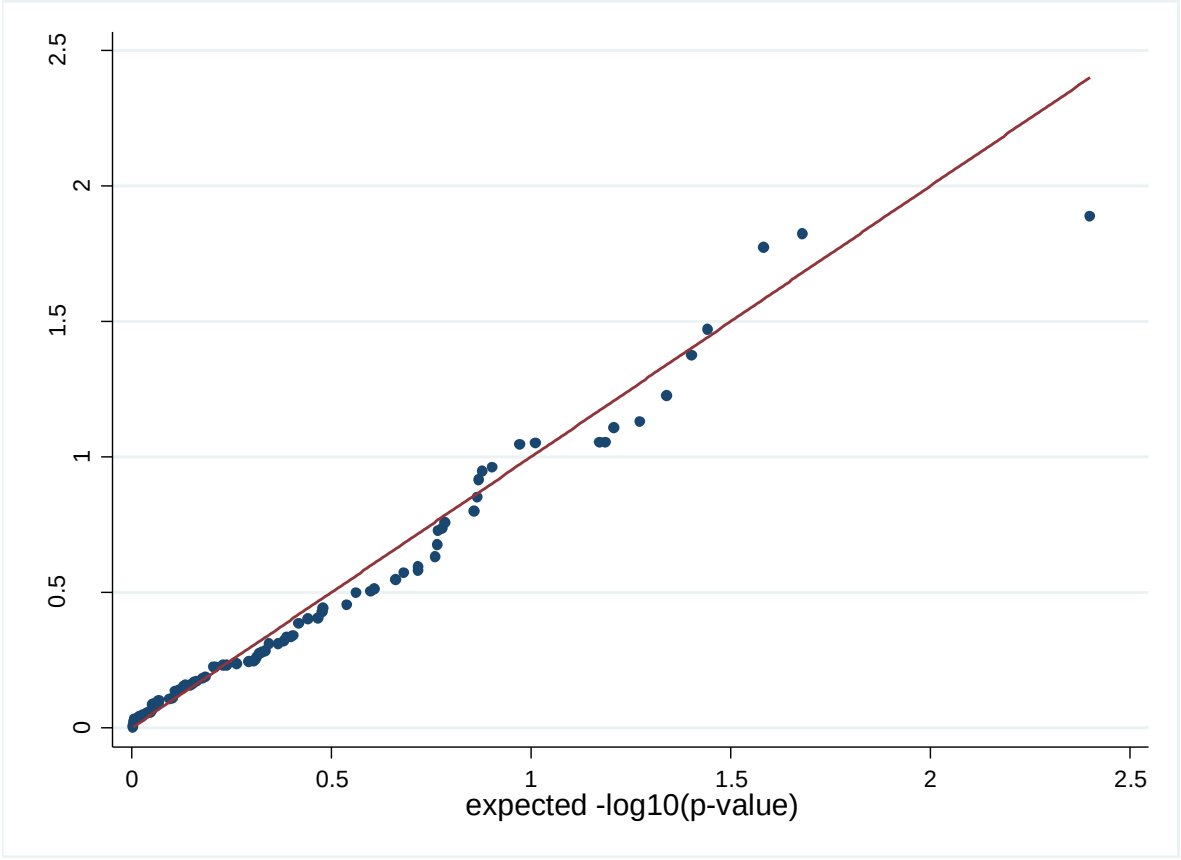
A) Induration at two years



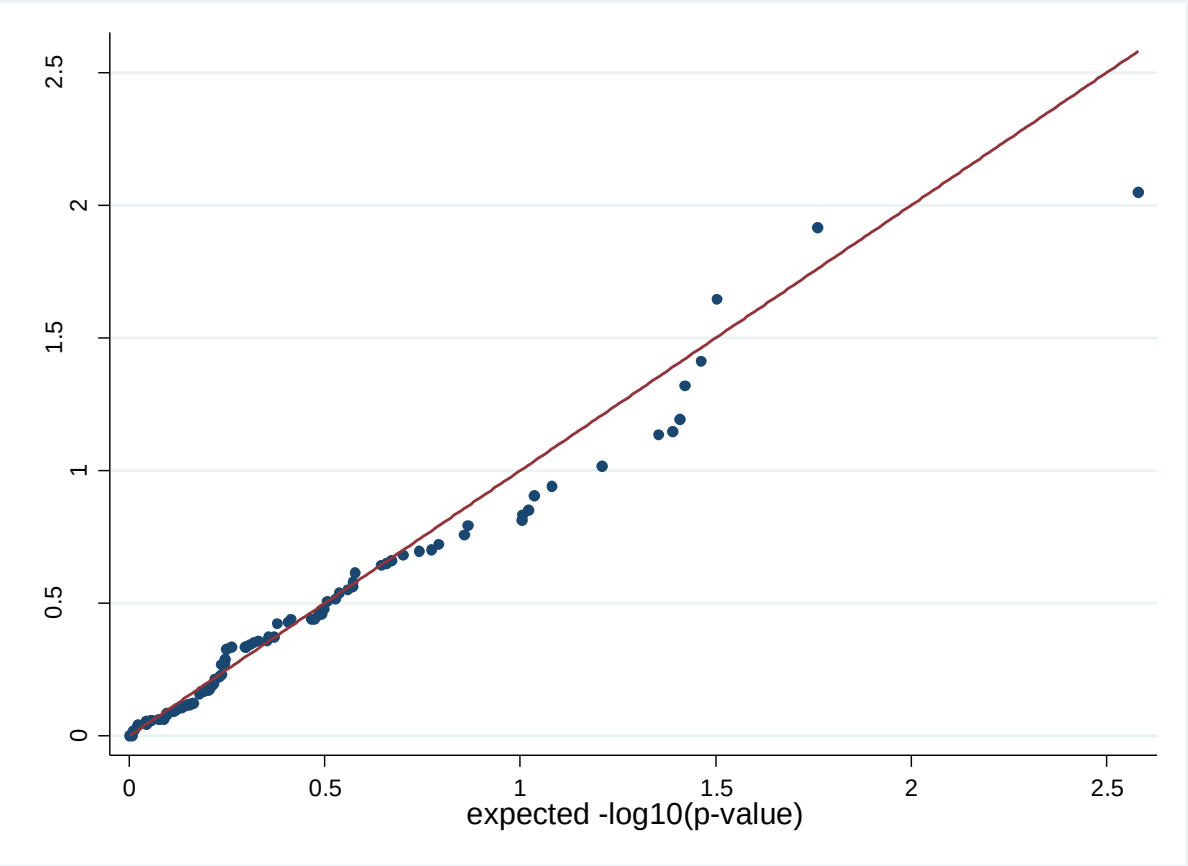
B) Induration at five years



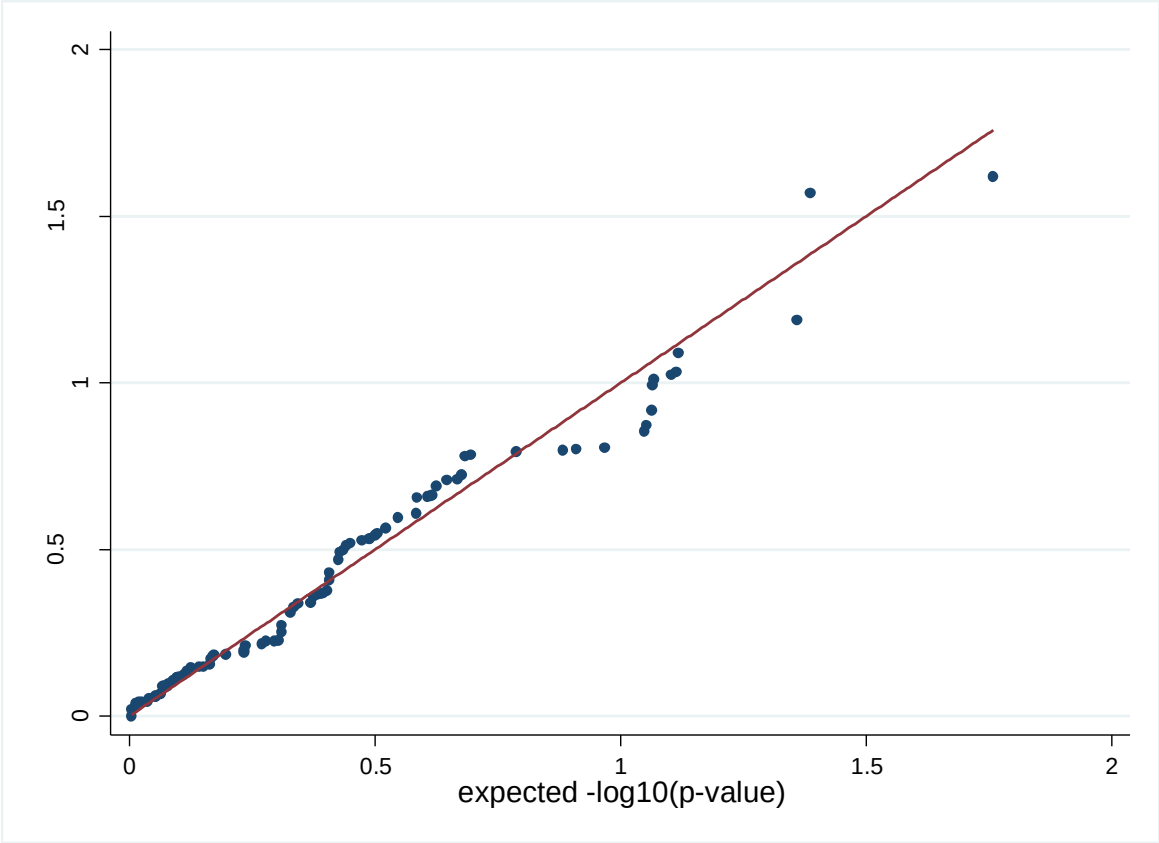
Supplementary Figure 7: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and breast pigmentation at two years



Supplementary Figure 8: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and breast pain at two years

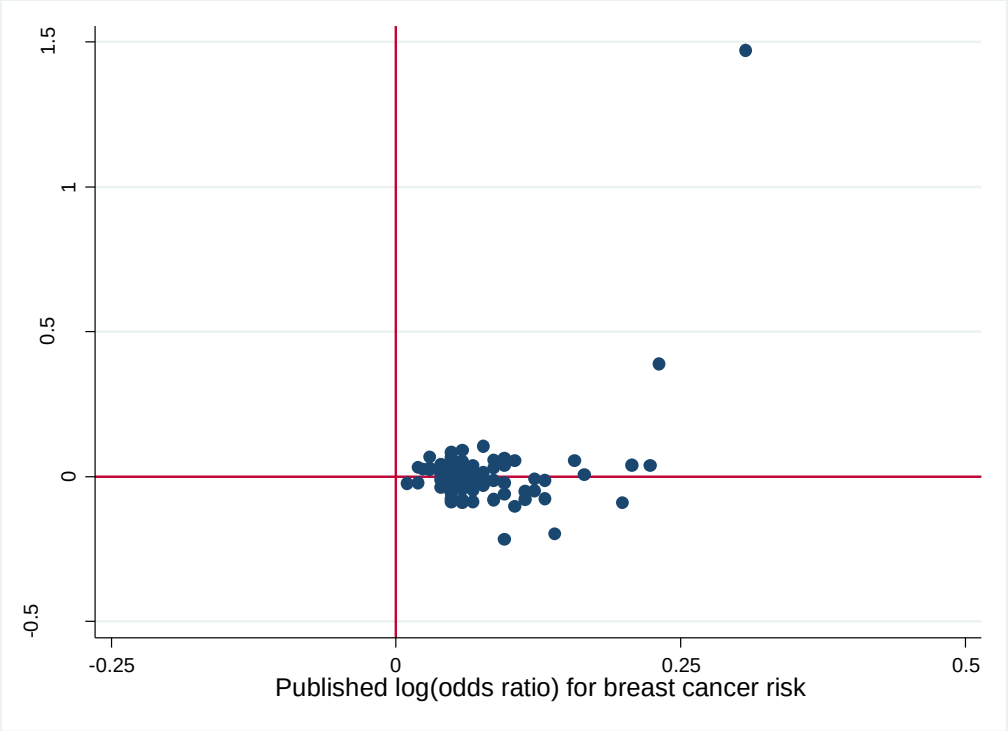


Supplementary Figure 9: -log$_{10}$(p-value) plot comparing expected p-values with observed p-values for the associations between individual breast cancer risk SNPs and breast sensitivity at two years

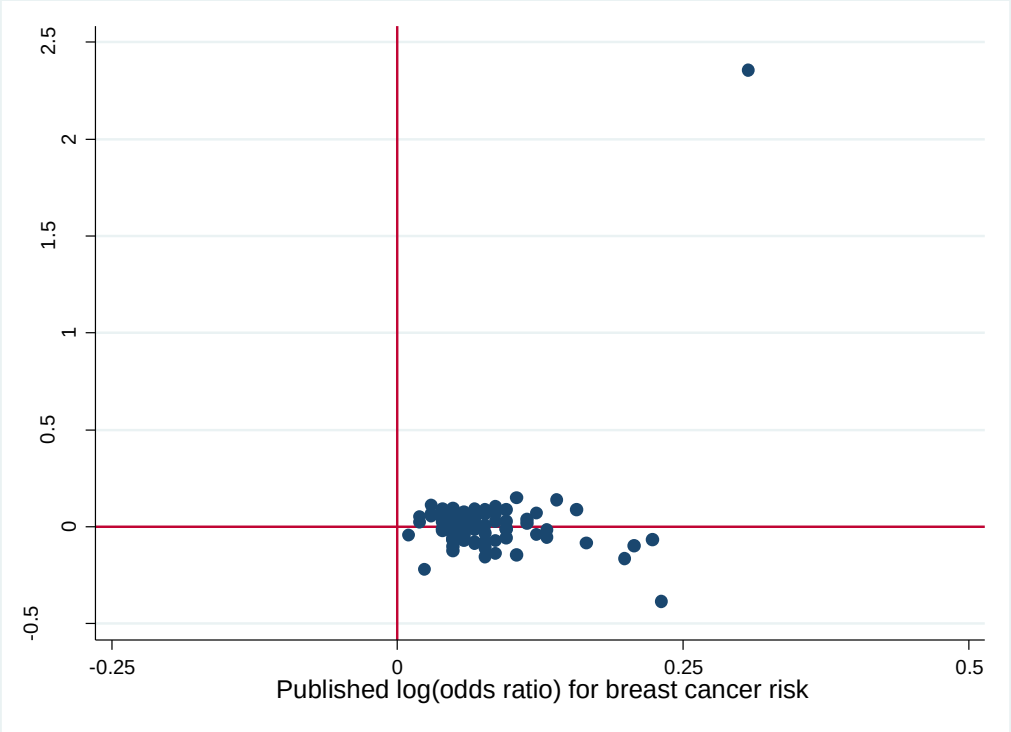


Supplementary Figure 10: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on telangiectasia

A) Telangiectasia at two years

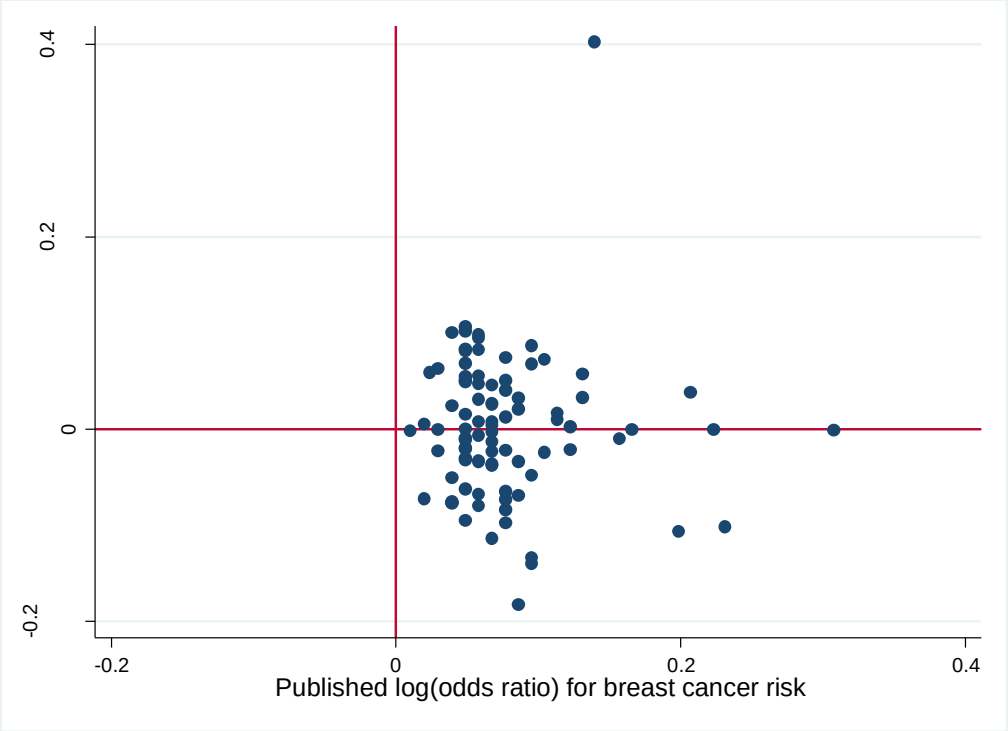


B) Telangiectasia at five years

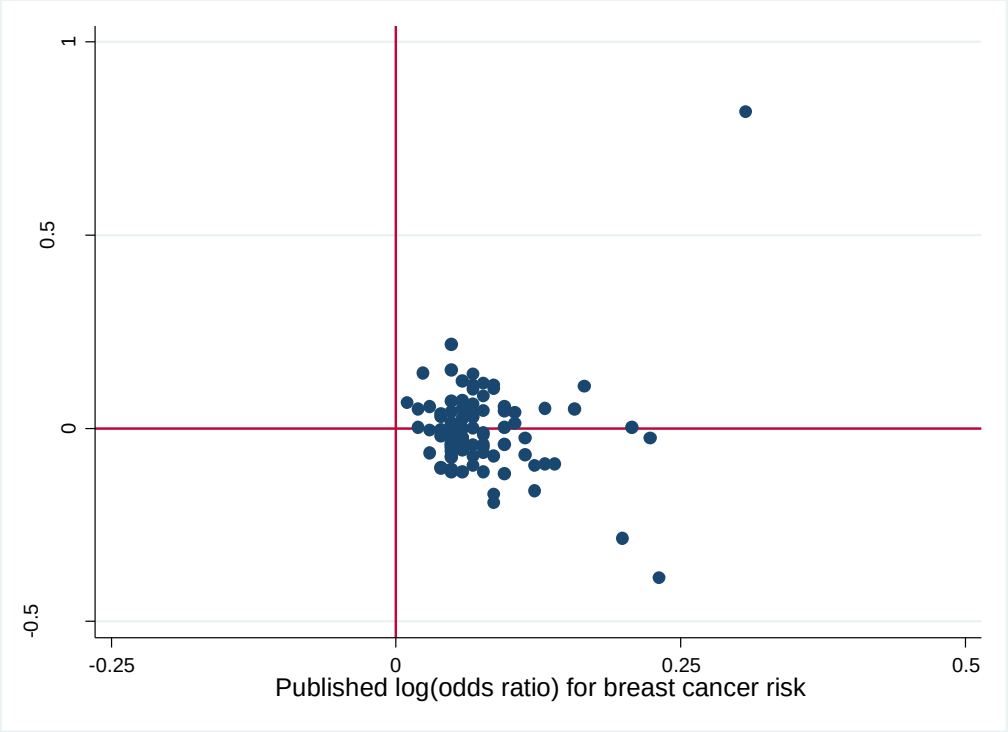


Supplementary Figure 11: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on breast edema

A) Edema at two years

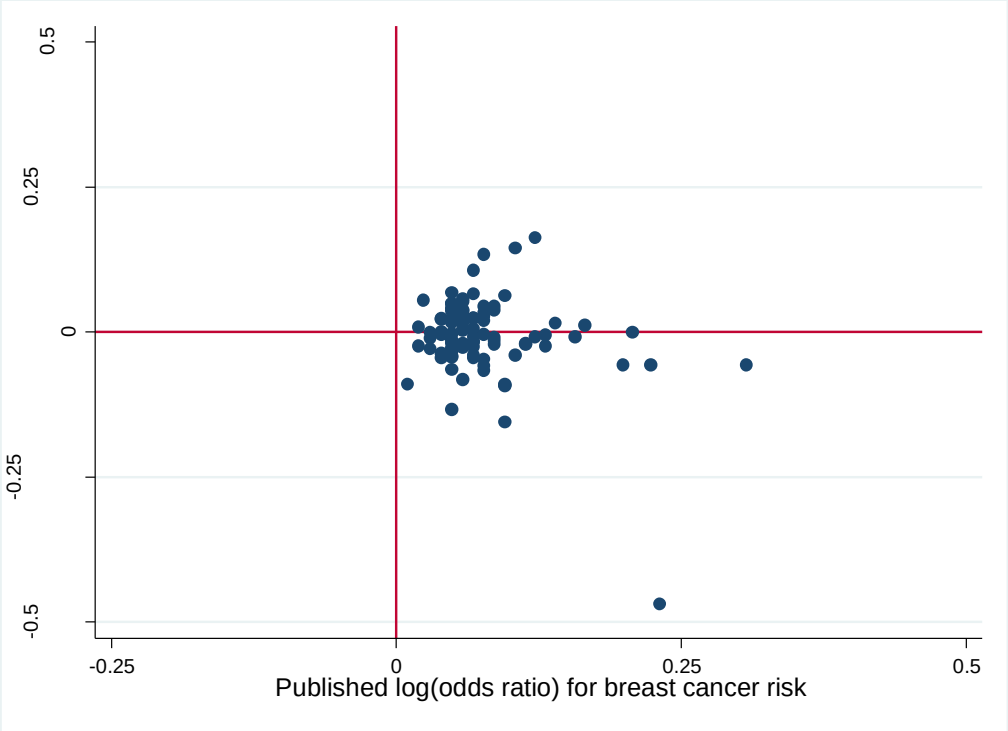


B) Edema at five years

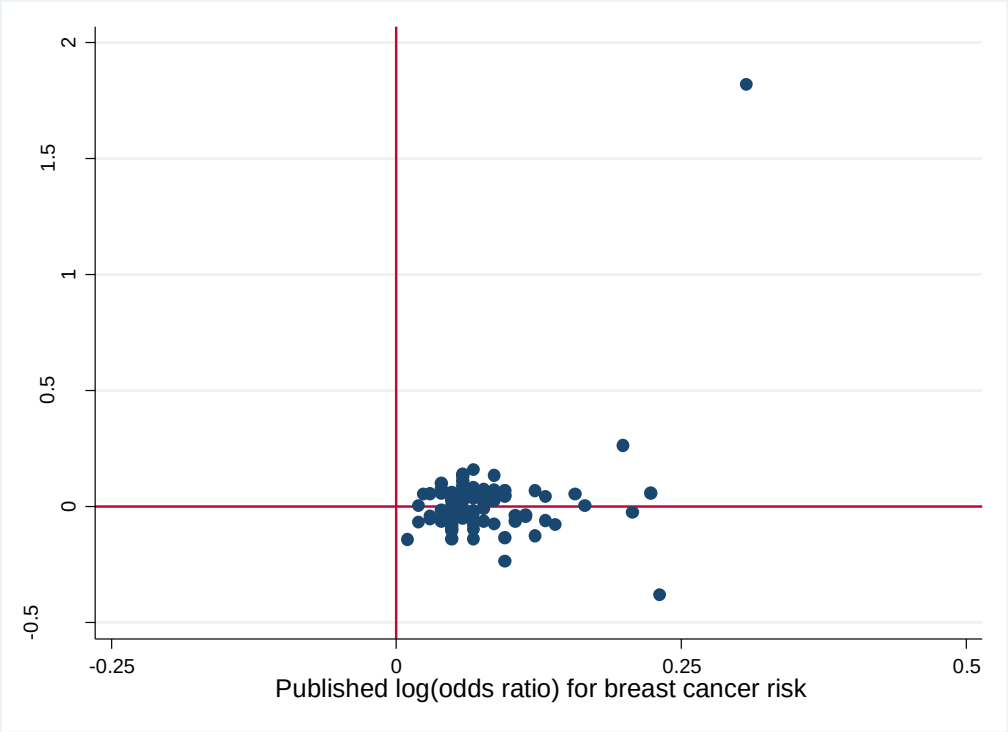


Supplementary Figure 12: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on breast shrinkage

A) Shrinkage at two years

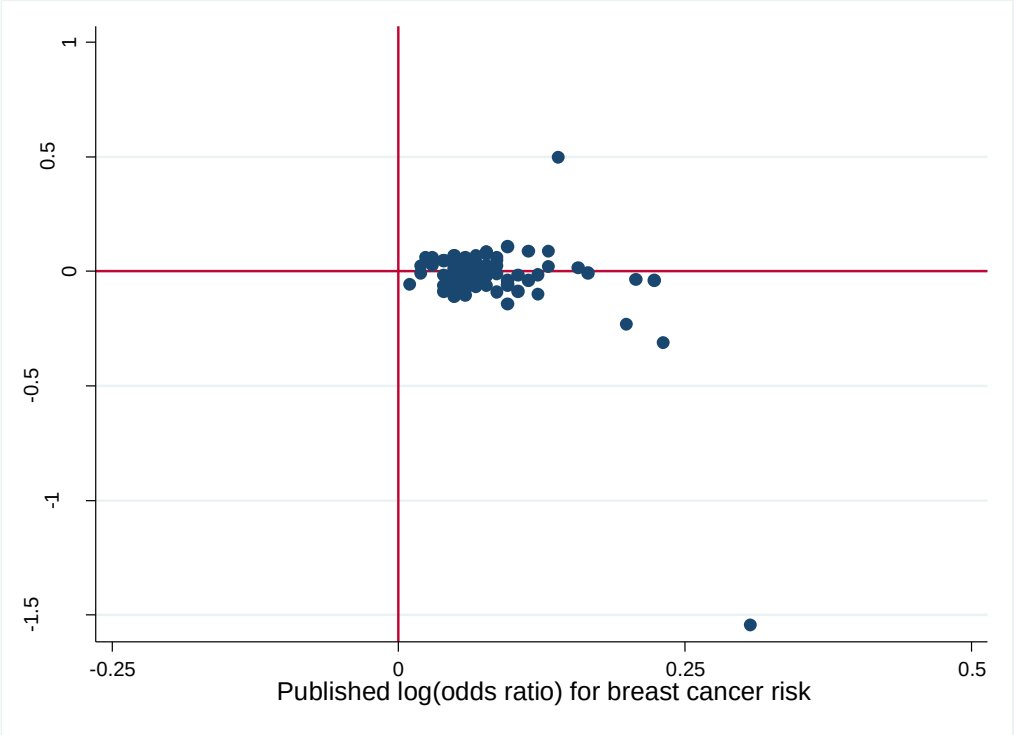


B) Shrinkage at five years

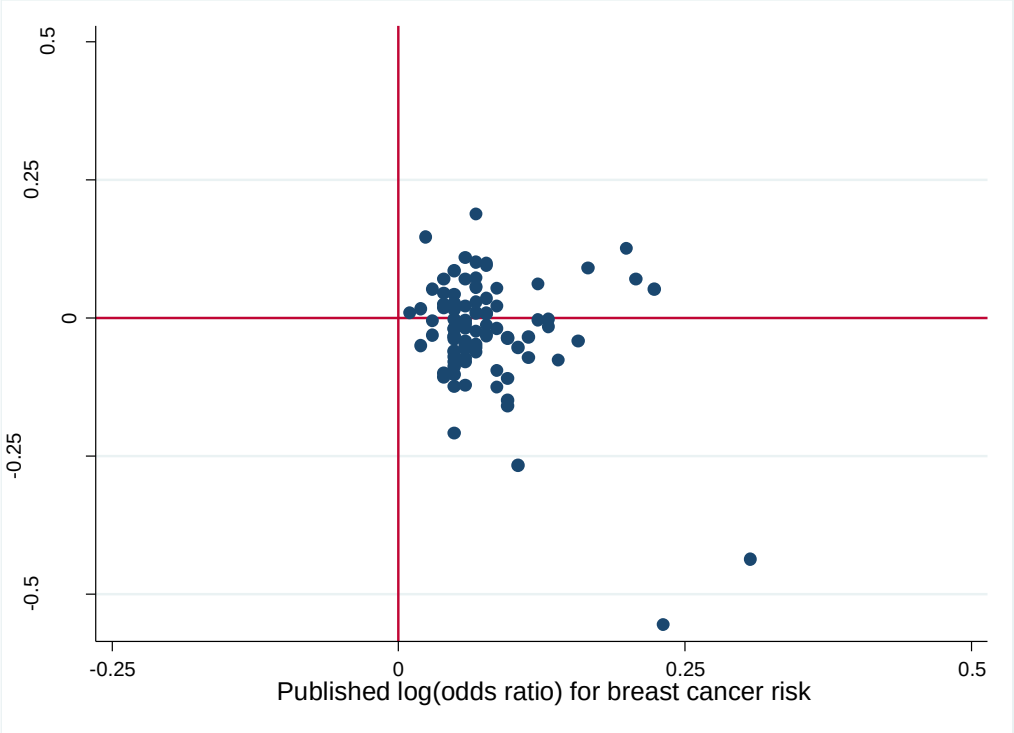


Supplementary Figure 13: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on induration

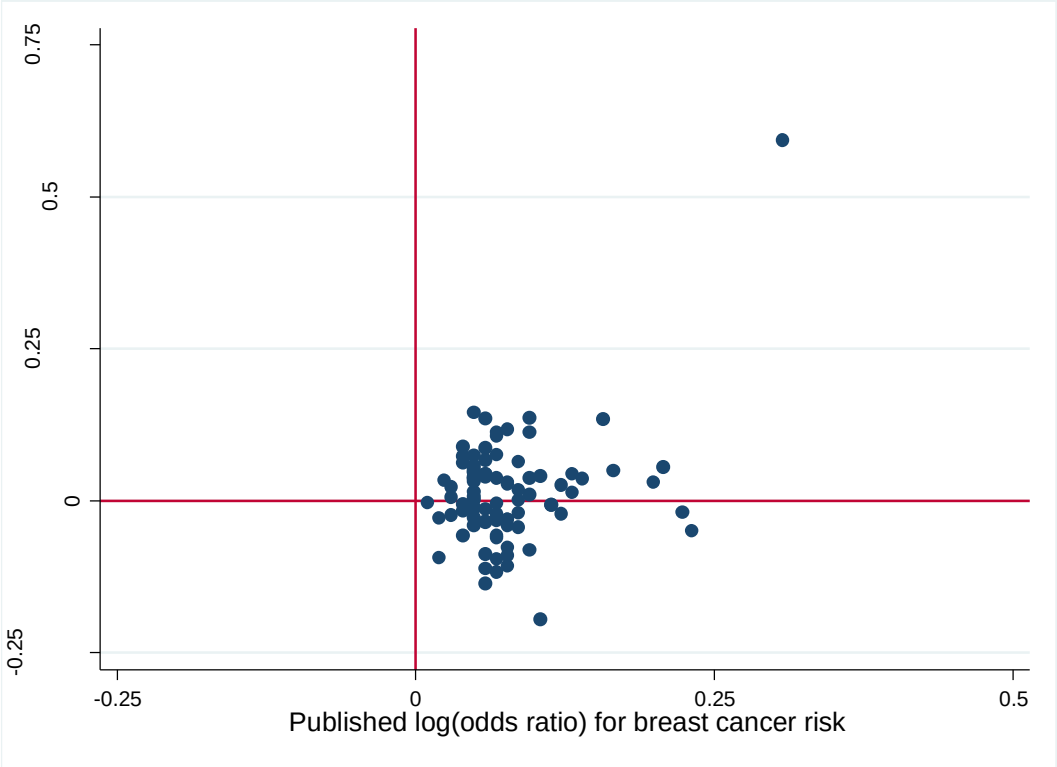
A) Induration at two years



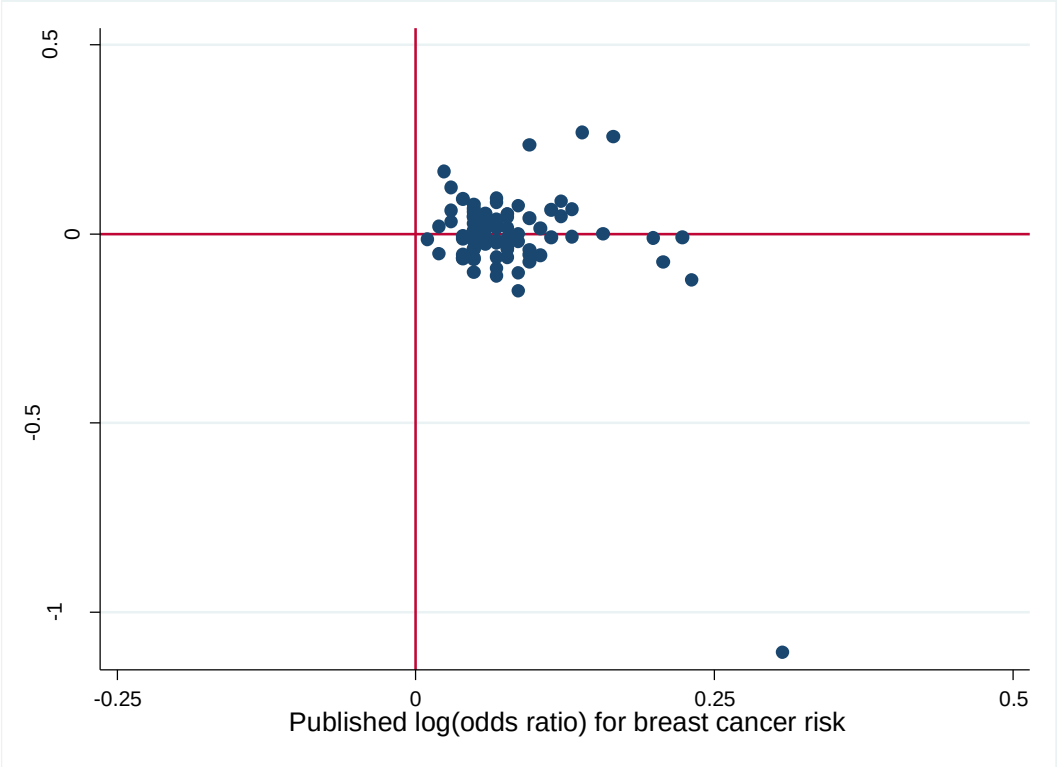
B) Induration at five years



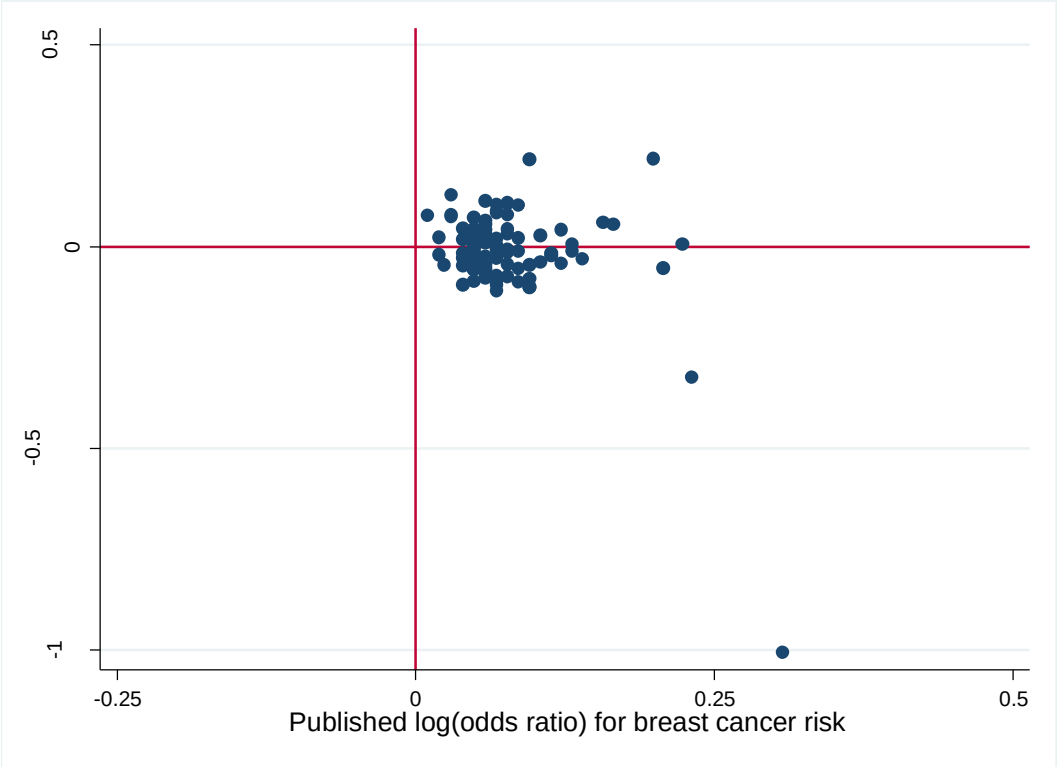
Supplementary Figure14: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on pigmentation at two years



Supplementary Figure 15: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on breast pain at two years



Supplementary Figure 16: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on breast sensitivity at two years



Supplementary Figure 17: Scatter plot of individual breast cancer risk variants comparing their effect on breast cancer risk with their effect on acute toxicity