



**Karolinska  
Institutet**

This is supplementary material for an author produced version of a paper accepted by **ANNALS OF ONCOLOGY**. This paper has been peer-reviewed but does not include the final publisher proof-corrections or journal pagination.

**Breast cancer genetic risk profile is differentially associated with interval and screen-detected breast cancers.**

**J. Li, J. Holm, J. Bergh, M. Eriksson, H. Darabi, L.S. Lindström, S. Törnberg, P. Hall and K. Czene.**

**DOI: <https://doi.org/10.1093/annonc/mdu565>**

Access to the published version may require subscription.  
Published with permission from: **Elsevier**

© 2019, Elsevier.

Licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0

International <http://creativecommons.org/licenses/by-nc-nd/4.0/>



**Supplementary Table S1.** Single nucleotide polymorphisms (SNPs) included in the construction of polygenic risk scores from effect sizes for breast cancer overall, estrogen receptor (ER)-negative (ER-neg) and ER-positive (ER-pos) diseases [10].

SNP	Allele	Overall	ER-neg	ER-pos	SNP	Allele	Overall	ER-neg	ER-pos
rs10069690	T	0.0239	0.1133	-0.0052	rs2363956	T	0.0261	0.1183	-0.0046
rs1011970	T	0.0490	0.1097	0.0372	rs2380205	T	-0.0232	0.0004	-0.0404
rs1045485	C	-0.0362	-0.0461	-0.0320	rs2588809	T	0.0646	0.0116	0.0796
rs10472076	C	0.0410	0.0442	0.0307	rs2736108	T	-0.0641	-0.1094	-0.0506
rs10759243	A	0.0528	0.0085	0.0706	rs2823093	A	-0.0754	-0.0144	-0.0886
rs10771399	G	-0.1475	-0.1766	-0.1262	rs2943559	G	0.1252	0.0961	0.1296
rs10941679	G	0.1132	0.0250	0.1449	rs2981579	A	0.2251	0.0169	0.2757
rs10995190	A	-0.1551	-0.1347	-0.1631	rs3760982	A	0.0538	0.0491	0.0524
rs11075995	T	0.0361	0.0968	0.0202	rs3803662	A	0.2035	0.1415	0.2198
rs11199914	T	-0.0619	0.0165	-0.0831	rs3817198	C	0.0718	0.0544	0.0792
rs11242675	C	-0.0588	-0.0726	-0.0556	rs3903072	T	-0.0574	-0.0222	-0.0614
rs11249433	G	0.0947	-0.0004	0.1156	rs4245739	C	0.0287	0.1519	-0.0039
rs11552449	T	0.0779	0.0520	0.0852	rs4808801	G	-0.0673	-0.0805	-0.0668
rs11571833	T	0.2318	0.3797	0.2223	rs4849887	T	-0.0848	-0.0862	-0.0912
rs11780156	T	0.0668	0.0361	0.0808	rs4973768	T	0.0897	0.0587	0.0973
rs11814448	C	0.1972	0.2123	0.1840	rs527616	C	-0.0436	-0.0215	-0.0432
rs11820646	T	-0.0447	-0.0458	-0.0457	rs554219	G	0.1167	0.0094	0.1312
rs12422552	C	0.0322	0.0220	0.0364	rs6001930	C	0.1262	0.1146	0.1234
rs12493607	C	0.0515	0.0040	0.0622	rs616488	G	-0.0601	-0.1154	-0.0331
rs12662670	G	0.1303	0.1669	0.1133	rs6472903	G	-0.0917	-0.0697	-0.0918
rs12710696	T	0.0380	0.1002	0.0127	rs6504950	A	-0.0683	-0.0329	-0.0721
rs1292011	G	-0.0813	-0.0177	-0.0963	rs6678914	A	-0.0111	-0.0893	0.0058
rs132390	C	0.1035	0.0502	0.1072	rs6762644	G	0.0640	0.0253	0.0659
rs13281615	G	0.0908	0.0183	0.1054	rs6828523	A	-0.0992	0.0203	-0.1332
rs13329835	G	0.0731	0.0138	0.0846	rs704010	T	0.0676	0.0415	0.0771
rs13387042	G	-0.1285	-0.0428	-0.1518	rs7072776	A	0.0565	-0.0659	0.0802
rs1353747	G	-0.0820	-0.0880	-0.0667	rs720475	A	-0.0564	-0.0009	-0.0713
rs1432679	C	0.0649	0.0676	0.0650	rs75915166	A	0.0236	0.1245	0.0187
rs1436904	G	-0.0549	-0.0075	-0.0659	rs7726159	A	0.0353	0.0301	0.0433
rs1550623	G	-0.0571	-0.0601	-0.0537	rs78540526	T	0.1622	-0.0999	0.2104
rs16857609	T	0.0696	0.0798	0.0695	rs7904519	G	0.0568	0.0606	0.0493
rs17356907	G	-0.0967	-0.0731	-0.1045	rs8170	A	0.0309	0.1323	-0.0045
rs17529111	C	0.0447	0.0363	0.0442	rs865686	G	-0.1070	-0.0110	-0.1366
rs17817449	G	-0.0726	-0.1227	-0.0682	rs889312	C	0.1112	0.0524	0.1374
rs17879961	G	0.3098	-0.0818	0.4109	rs941764	G	0.0617	0.0349	0.0710
rs2016394	A	-0.0509	-0.0034	-0.0683	rs9693444	A	0.0705	0.0834	0.0682
rs204247	G	0.0491	0.0044	0.0625	rs9790517	T	0.0470	0.0206	0.0511
rs2046210	A	0.0460	0.1141	0.0269	rs999737	T	-0.0792	-0.0317	-0.0846
rs2236007	A	-0.0831	-0.0488	-0.0996					

**Supplementary Table S2.** Distribution of polygenic risk scores (PRS) in different datasets. Abbreviations: SD: standard deviation

	<i>n</i>	<b>PRSO<sub>overall</sub></b>		<b>PRSE<sub>Rneg</sub></b>		<b>PRSE<sub>Rpos</sub></b>	
		<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>
<b>LIBRO-1</b>							
Controls	5537	-0.221	0.972	-0.133	0.996	-0.221	0.968
Screen-detected	1865	0.011	0.980	-0.045	0.982	0.021	0.985
Interval	782	-0.086	1.010	-0.028	1.037	-0.087	0.999
<b>SASBAC</b>							
Controls	1378	-0.211	0.972	-0.124	0.988	-0.209	0.975
Screen-detected	694	0.027	1.000	0.014	0.979	0.028	1.001
Interval	197	-0.102	0.961	-0.006	1.045	-0.120	0.966
<b>MERCK</b>							
Screen-detected	95	-0.113	1.037	-0.102	1.000	-0.110	1.014
Interval	98	-0.127	0.913	-0.127	0.913	-0.186	0.895

**Supplementary Table S3.** Association between polygenic risk score (PRS) in quartiles and breast cancer risk (age-adjusted). Quartiles were based on the distribution of PRS in cancer-free controls. Logistic regression models were used to estimate the odds ratios (ORs) and corresponding 95% confidence intervals (CI), with the lowest quartile (Q1) as the reference. Continuous effects of PRS per standard deviation increase were also estimated. Abbreviations: Screen, screen-detected;  $P_{Wald}$ , Pvalue based on Wald test. \*Cancer-free controls for LIBRO-1 were comprised of 5,537 participants of the Karolinska Mammography Project for Risk Prediction of Breast Cancer (KARMA) mammography screening study.

PRS <sub>overall</sub> quartile (range)	Controls	Screen-detected cancers				Interval cancers			
		Cases	OR	95% CI	$p_{Wald}$	Cases	OR	95% CI	$p_{Wald}$
*LIBRO-1									
Q1 (-3.498 to -0.891)	1384	207	1.00	Reference		115	1.00	Reference	
Q2 (-0.89 to -0.225)	1384	402	1.93	1.57 to 2.37	<0.001	160	1.37	1.04 to 1.79	0.024
Q3 (-0.225 to 0.418)	1384	488	2.47	2.02 to 3.02	<0.001	214	1.83	1.41 to 2.36	<0.001
Q4 (0.419 to 4.012)	1385	768	4.21	3.47 to 5.10	<0.001	293	2.64	2.06 to 3.39	<0.001
Continuous variable	5537	1865	1.70	1.59 to 1.81	<0.001	782	1.49	1.37 to 1.63	<0.001
SASBAC									
Q1 (-3.203 to -0.873)	345	77	1.00	Reference		29	1.00	Reference	
Q2 (-0.871 to -0.227)	344	132	1.73	1.26 to 2.37	0.001	44	1.55	0.94 to 2.53	0.083
Q3 (-0.227 to 0.435)	344	185	2.41	1.78 to 3.27	<0.001	50	1.75	1.08 to 2.83	0.023
Q4 (0.436 to 3.942)	345	300	3.91	2.92 to 5.24	<0.001	74	2.58	1.64 to 4.07	<0.001
Continuous variable	1378	694	1.67	1.51 to 1.84	<0.001	197	1.46	1.25 to 1.71	<0.001