Supplementary Table 1: List of primers used for PCR and Sanger sequencing to confirm variations

Name	Sequence 5'->3'	Tm	Size (bp)
BRCA1-13F	CAGCAGCTGAAATTTGTGAG	55	475
BRCA1-13R	GCAAAGGTATAACGCTATTGTC		
BRCA2-5F	CAGCAGCTGAAATTTGTGAG	55	475
BRCA2-5R	GCAAAGGTATAACGCTATTGTC		
OGG1-1F	TAGGTGAAATGAGCGGTG	54	702
OGG1-1R	TTATACCGCTGGATCCTTAC		
BRCA2-11-DR	GAAGTTTGCTGGCCTGTTGA	57	678
BRCA2-11-DF	TGCTCCGTTTTAGTAGCAGTT		
BRCA2-27-F	AGATTGATGACCAAAAGAACTGC	54	376
BRCA2-27-R	TTCAGTCTGAGATAATCTTCTG		

Supplementary Table 2: Variants in BRCA genes present in F2.2, previously reported to represent independently minor, but cumulatively significant, increased risk for breast cancer

Variant Nomenclature	avsnp144	Secondary primary breast cancer OR dom (p-value)	AF-Exac
BRCA1:NM_007294:exon10:c.3548A>G:p.K1183R	rs16942	1.00 (1.00)	C=0.3490/42150
BRCA1:NM_007294:exon15:c.4837A>G:p.S1613G	rs1799966	1.00 (1.00)	C=0.3496/42424
BRCA2:NM_000059:exon10:c.1114A>C:p.N372H	rs144848	1.11(0.29)	C=0.2779/33565
BRCA2:NM_000059:exon27:c.9976A>T:p.K3326X	rs11571833	1.34(0.36)	T=0.0070/848

Supplementary table 3: List of common at risk breast cancer SNPs present in F2.2 and F1.1 patients out *BRCA* genes.

	Locus	Gene	rs ID	Genotype	Alleles	Func.refgene	Variant nomenclature	#MAF	1000g2015	ExAC_ALL	ExAC_AFR	CLINSIG	OR[a]	CI[b]	P-value[c]	Combined P-value[d]	OR[a]	CI[b]	P-value[c]	Combined P-value[d]
F2.2	1p36.13	**KLHDC7A**	rs2992756	C/C	C/T	upstream	NA	0.49	0.552117	NA	NA	NA	1.07	1.05-1.09	2.7×10^{-11}	9.9×10^{-16}	1.03	1-1.07	4.2×10^{-02}	1.1×10^{-01}
	1q22	**TRIM46**	rs4971059	A/A	G/A	intronic	NA	0.35	0.429912	NA	NA	NA	1.06	1.04-1.09	3.7×10^{-09}	1.3×10^{-11}	1.03	1-1.07	5.7×10^{-02}	4.2×10^{-01}
	1q32.1	**MDM4**	rs4245739	A/C	A/C	UTR3	NM_002393:c.*32C>A	0.26	0.785942	0.7694	0.7750	NA	1	0.98-1.02	9.0×10^{-01}	9.8×10^{-01}	1.12	1.09-1.17	9.2×10^{-11}	3.1×10^{-23}
	7q21.2	**AKAP9**	rs6964587	G/T	G/T	exonic	AKAP9:NM_005751:exon8:c.1389G>T:p.M463I	0.39	0.372204	0.3829	0.5114	Benign	1.03	1.01-1.05	2.1×10^{-03}	1.8×10^{-09}	1.02	0.98-1.05	3.5×10^{-01}	4.5×10^{-02}
	11q22.3*	**KDELC2**	rs11374964	GA/GA	G/GA	UTR3	NM_153705:c.*38_*39insT	0.42	0.483027	0.4644	0.4094	NA	1.02	1.01-1.04	5.9×10^{-03}	-	0.94	0.92 – 0.96	3.6×10^{-08}	4.1×10^{-13}
	14q13.3	**PAX9**	rs2236007	G/A	G/A	intronic	NA	0.21	0.166334	0.1897	0.0717	NA	0.93	0.91-0.96	3.1×10^{-08}	1.9×10^{-18}	0.95	0.91-0.99	1.4×10^{-02}	8.0×10^{-03}
F1.1	11q22.3*	**KDELC2**	rs11374964	GA/GA	G/GA	UTR3	NM_153705:c.*38_*39insT	0.42	0.483027	0.4644	0.4094	NA	1.02	1.01-1.04	5.9×10^{-03}	-	0.94	0.92 – 0.96	3.6×10^{-08}	4.1×10^{-13}

All SNPs were reviewed in reference [1]

[#]MAF reported in OncoArray controls

[a]Odds ratio (OR) reported for ER-positive and ER-negative breast cancer in OncoArray

[b]95% Confidence Interval (CI) reported for ER-positive and ER-negative breast cancer in OncoArray

[c]p-value reported for ER-positive and ER-negative breast cancer in OncoArray

[d]Combined meta-analysis p-value for ER-positive and ER-negative breast cancer

Supplementary table 4 : The BRCA2 K3326X Confers susceptibility to multi-organ cancers

Cancer	**Cancer kind**	**OR (95%)**	**P value**	**Population**	**References**
Upper aerodigestive tract cancer	-Oral cavity -**Larynx** -Esophagus	2.53 51.89 to 3.38)	$3x10^{-10}$	European Latin American and Indian population	[2]
Urinary tract cancer	**-Bladder** -Renal cell carcinoma -Prostate cancer	**ORmeta= 1.60** 1.45 (1.12-1.94)	***P*meta= 0.010** $P_{meta} = 0.013$	European descent	[3]
Hormone-related cancers	-Breast -Invasive ovarian -**Serous ovarian cancer** **-Estrogen receptor negative breast cancer**	1.28 (1.17-1.40) 1.26 (1.1-1.43) **1.46 (1.2 - 1.70)** **1.50 (1.28 - 1.76)**	$5.9\ 10^{-6}$ $3.8\ 10^{-3}$ **3.4x10-5** **4.1x10-5**	iCOGS study population	[4]

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