

Age at breast cancer diagnosis of proband	Probabilities (%)					
	No Mutation	BRCA1 Mutation	BRCA2 Mutation	PALB2 Mutation	CHEK2 Mutation	ATM Mutation
30	87.3	5.2	3.8	1.0	1.6	1.1
35	90.1	3.3	3.0	1.0	1.6	1.1
40	92.2	2.0	2.3	0.9	1.5	1.1
45	93.4	1.5	1.8	0.8	1.5	1.0
50	94.5	1.0	1.3	0.6	1.5	1.0
55	95.1	0.7	1.2	0.5	1.5	1.0
60	95.6	0.5	1.1	0.5	1.4	1.0
65	95.8	0.3	1.1	0.4	1.4	0.9
70	96.1	0.2	1.1	0.4	1.3	0.9
75	96.5	0.2	0.8	0.3	1.3	0.9

Table S1: Mutation carrier probability, corresponding to Figure 2 (a). BOADICEA mutation carrier probabilities for a female in the UK, born in 1975 with unknown family history as a function of her breast cancer diagnosis age

Age at breast cancer diagnosis of mother	Probabilities (%)					
	No Mutation	BRCA1 Mutation	BRCA2 Mutation	PALB2 Mutation	CHEK2 Mutation	ATM Mutation
30	36.8	42.8	16.0	2.2	1.4	0.9
35	47.4	31.9	15.3	2.6	1.7	1.1
40	58.3	22.1	13.4	2.7	2.1	1.4
45	65.6	17.0	11.1	2.5	2.3	1.5
50	72.2	12.5	9.0	2.3	2.4	1.6
55	76.5	9.2	8.3	2.0	2.4	1.6
60	79.7	7.1	7.4	1.8	2.4	1.6
65	81.6	5.6	7.3	1.6	2.4	1.6
70	83.2	4.6	6.8	1.5	2.3	1.6
75	84.9	4.1	5.8	1.4	2.3	1.5

Table S2: Mutation carrier probability, corresponding to Fig 2 (b) BOADICEA mutation carrier probabilities for a female in the UK, born in 1975 who was diagnosed with breast cancer at age 30 and whose mother was diagnosed with breast cancer, as a function of her mother's age at diagnosis.

Family/study	Implied relative risk (RR) in the true negative	Estimated Standardised Incidence Rate (SIR) in prospective studies
<i>Present study</i>		
Figure 3a	BRCA1: RR=0.75 BRCA2: RR=0.81	
Figure 3c	BRCA1 family: RR=1.07 BRCA2 family: RR=1.22	
Figure 3e	BRCA1 family: RR=1.16 BRCA2 family: RR=1.43	
Figure 3g	BRCA1 family: RR=1.13 BRCA2 family: RR=1.31	
<i>Published studies</i>		
Smith et al ¹		All (prospective analysis): 2.1; 95% CI 0.4 to 6.2
Kurian et al ²		All (retrospective): 0.39; 95% CI, 0.04 to 3.81
Rowan E et al ³		All: 2.9; 95% CI 1.0 to 8.6
Korde et al ⁴		All (prospective): 0.82 (95% CI 0.39-1.51) With family history of breast cancer: 1.33 (95%CI: 0.41-2.91)
Domchek et al ⁵		All (prospective): 0.52 (95%CI: 0.13-2.09) No stratification by family history.
Harvey et al ⁶		All: 1.14 (95% CI: 0.51-2.53) With family history: 1.29 (95% CI: 0.58-2.88) No family history: 0.48 (95% CI: 0.12-1.93)

Table S3: Contrasting the relative risks of breast cancer for women who test negative for the family mutations in

BOADICEA and published studies.

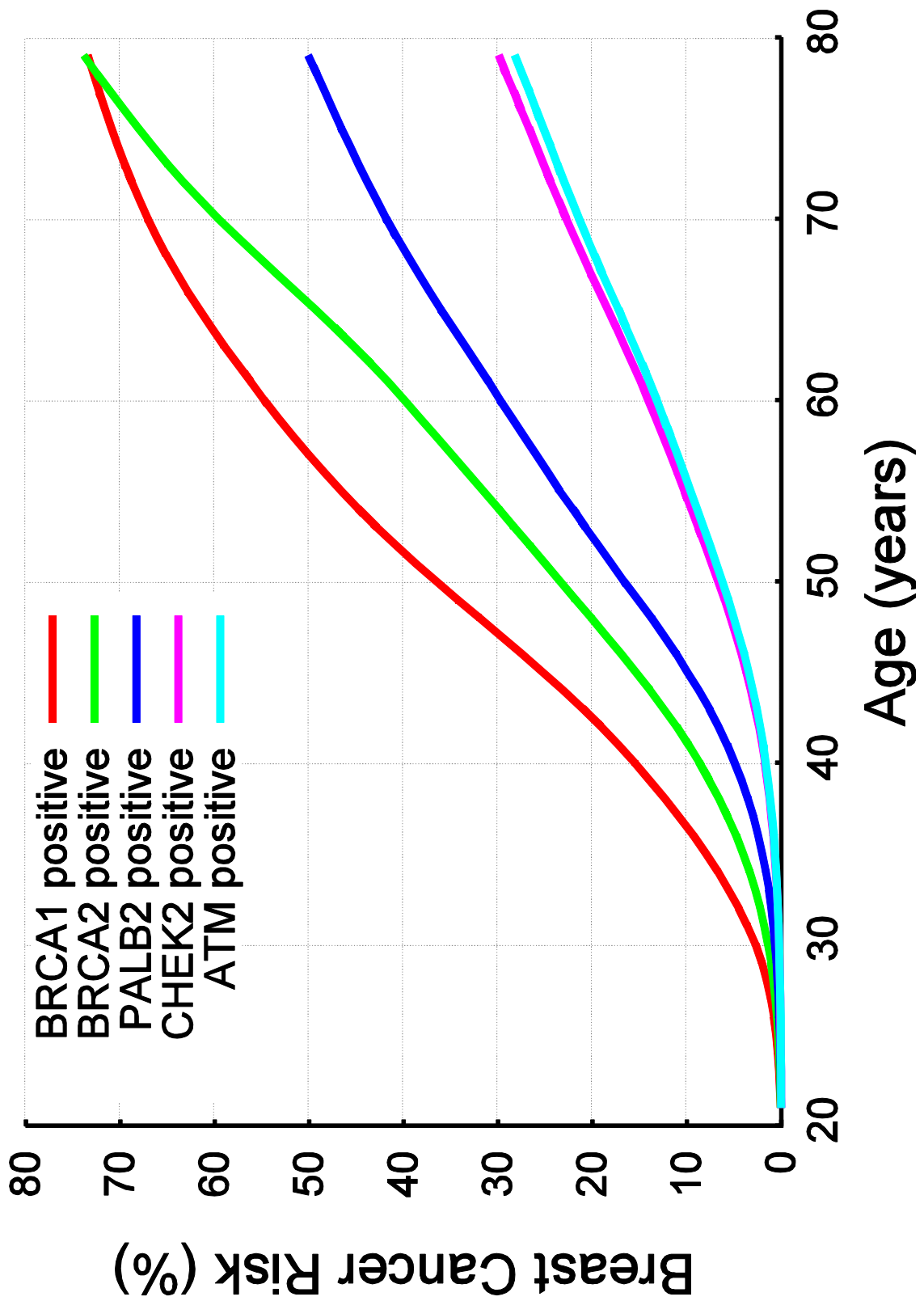


Fig S1. Breast Cancer Risk for Average Female. BOADICEA risk by mutation status for a female age 20 in the UK, born in 1975 with unknown family history (i.e. for the average female in the population).

1. Smith A, Moran A, Boyd MC, et al. Phenocopies in BRCA1 and BRCA2 families: evidence for modifier genes and implications for screening. *J Med Genet.* 2007;44(1):10-15.
2. Kurian AW, Gong GD, John EM, et al. Breast cancer risk for noncarriers of family-specific BRCA1 and BRCA2 mutations: findings from the Breast Cancer Family Registry. *J Clin Oncol.* 2011;29(34):4505-4509.
3. Rowan E, Poll A, Narod SA. A prospective study of breast cancer risk in relatives of BRCA1/BRCA2 mutation carriers. *J Med Genet.* 2007;44(8):e89; author reply e88.
4. Korde LA, Mueller CM, Loud JT, et al. No evidence of excess breast cancer risk among mutation-negative women from BRCA mutation-positive families. *Breast cancer research and treatment.* 2011;125(1):169-173.
5. Domchek SM, Gaudet MM, Stopfer JE, et al. Breast cancer risks in individuals testing negative for a known family mutation in BRCA1 or BRCA2. *Breast cancer research and treatment.* 2010;119(2):409-414.
6. Harvey SL, Milne RL, McLachlan SA, et al. Prospective study of breast cancer risk for mutation negative women from BRCA1 or BRCA2 mutation positive families. *Breast cancer research and treatment.* 2011;130(3):1057-1061.