

Online-only material accompanying manuscript entitled “Survival after bilateral risk-reducing mastectomy in healthy *BRCA1* and *BRCA2* mutation carriers”

Breast Cancer Research and Treatment

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Table S1. *BRCA1*-associated breast cancer characteristics

	BRRM	Surveillance	P-value^a
N	8 (3%)	268 (97%)	
Age at diagnosis, median (IQR)	45 (34 - 48)	44 (35 - 50)	0.781
Behavior, n/N (%)			
In situ	0/7 (0%)	32/263 (12%)	0.326
Invasive	7/7 (100%)	231/263 (88%)	
Bloom & Richardson differentiation grade, n/N (%)			
I	0/6 (0%)	9/245 (4%)	0.753
II	2/6 (33%)	55/245 (22%)	
III	4/6 (67%)	181/245 (74%)	
pT-status, n/N (%)			
0 (in situ)	0/5 (0%)	32/248 (13%)	0.652
1	4/5 (80%)	159/248 (64%)	
2	1/5 (20%)	57/248 (23%)	
pN-status, n/N (%)			
0	5/6 (83%)	202/242 (83%)	0.969
1	1/6 (17%)	32/242 (13%)	
2	0/6 (0%)	6/242 (3%)	
3	0/6 (0%)	2/242 (1%)	
Positive ER-status^b, n/N (%)	2/6 (33%)	47/218 (22%)	0.491
Positive PR-status^b, n/N (%)	1/6 (17%)	35/213 (16%)	0.988
Positive Her2-status^c, n/N (%)	0/4 (0%)	10/166 (6%)	0.613
Triple-negative^d, n/N (%)	2/4 (50%)	126/160 (78%)	0.191

Abbreviations: BRRM, bilateral risk-reducing mastectomy; IQR, interquartile range; n/N, number out of total number of women with non-missing data on the variable of interest; ER, estrogen receptor; PR, progesterone receptor.

^aDifferences between the BRRM and the surveillance group were tested by using Chi-square for categorical variables, and the two-sample Wilcoxon rank-sum (Mann-Whitney) test for continuous variables

^bHormone receptors were considered positive if staining was seen in $\geq 10\%$ of the nuclei, according to the Dutch national guidelines for breast cancer treatment.

^cHer2 receptor status was scored according to international guidelines. An equivocal immunohistochemical result (2+) was followed by fluorescence in situ hybridization.

^dER-negative, PR-negative and Her2-negative.

Table S2. Differences between *BRCA1/2* mutation carriers (combined) with known and unknown screening status in the surveillance group

	Screening status		P-value ^a
	Known	Unknown	
N	865 (50%)	864 (50%)	
Had screening ^b , n/N (%)	761/865 (88%)	-	
Screening modality ^b			
Mx and MRI, n/N (%)	537/761 (71%)	-	
MRI only, n/N (%)	102/761 (13%)	-	
Mx only, n/N (%)	74/761 (10%)	-	
Unknown, n/N (%)	48/761 (6%)	-	
Breast cancer, n/N (%)	249/865 (29%)	163/864 (19%)	<0.001
Age at diagnosis, median years (IQR)	43 (35 - 50)	46 (38 - 53)	0.035
Behavior, n/N (%)			
In situ	31/247 (13%)	37/159 (23%)	0.005
Invasive	216/247 (87%)	122/159 (77%)	
Bloom & Richardson differentiation grade, n/N (%)			
I	14/230 (6%)	6/141 (4%)	0.875
II	76/230 (33%)	47/141 (33%)	
III	140/230 (61%)	88/141 (63%)	
pT-status, n/N (%)			
0	31/239 (13%)	37/145 (25%)	0.013
1	157/239 (66%)	81/145 (56%)	
2	49/239 (20%)	27/145 (19%)	
3	2/239 (1%)	0/145 (0%)	
pN-status, n/N (%)			
0	189/231 (82%)	113/140 (81%)	0.412
1	34/231 (15%)	23/140 (16%)	
2	6/231 (2%)	1/140 (1%)	
3	2/231 (1%)	3/140 (2%)	
Positive ER-status ^c , n/N (%)	80/210 (38%)	46/109 (42%)	0.477
Positive PR-status ^c , n/N (%)	54/208 (26%)	36/105 (34%)	0.124
Positive Her2-status ^d , n/N (%)	10/158 (6%)	8/84 (10%)	0.516
Triple-negative ^e , n/N (%)	97/156 (62%)	46/81 (57%)	0.421
Treatment primary breast cancer, n/N (%)			
Chemotherapy	140/245 (57%)	80/162 (49%)	0.124
Endocrine therapy	55/241 (23%)	36/149 (24%)	0.761
Targeted therapy	8/241 (3%)	8/149 (5%)	0.321
Radiotherapy	64/241 (27%)	35/149 (23%)	0.499
Ovarian cancer, n/N (%)	21/865 (2%)	28/864 (3%)	0.308
Death, n/N (%)	34/865 (4%)	47/864 (5%)	0.138
Cause of death, n/N (%)			
Breast cancer	19/865 (2.2%)	8/864 (0.9%)	0.033
Ovarian cancer	7/865 (0.8%)	14/864 (1.6%)	0.124
Other malignancy	8/865 (0.9%)	20/864 (2.3%)	0.022
Not due to malignancy	0/865 (0%)	5/864 (0.8%)	0.008

Abbreviations: n/N, number out of total number of women with non-missing data on the variable of interest; Mx, mammography; MRI, magnetic resonance imaging; IQR, interquartile range; ER, estrogen receptor; PR, progesterone receptor.

^a Differences between the groups were tested by using Chi-square for categorical variables, and the two-sample Wilcoxon rank-sum (Mann-Whitney) test for continuous variables

^b Derived from self-reported data

^c Hormone receptors were considered positive if staining was seen in $\geq 10\%$ of the nuclei, according to the Dutch national guidelines for breast cancer treatment.

^d Her2 receptor status was scored according to international guidelines. An equivocal immunohistochemical result (2+) was followed by fluorescence in situ hybridization.

^e ER-negative, PR-negative and Her2-negative.