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Long Term Outcomes of *BRCA1/BRCA2* Testing: Risk Reduction and Surveillance

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Abstract

Purpose—For *BRCA1/BRCA2* gene testing to benefit public health, mutation carriers must initiate appropriate risk management strategies. There has been little research examining the long-term use and prospective predictors of the full range of risk management behaviors among women who have undergone *BRCA1/2* testing. We evaluated long-term uptake and predictors of risk reducing mastectomy (RRM), risk reducing oophorectomy (RRBSO), chemoprevention and cancer screening among women at a mean of 5.3 years post testing.

Patients and Methods—Participants were 465 women who underwent *BRCA1/2* testing. Prior to genetic counseling, we measured family/personal cancer history, sociodemographics, perceived risk, cancer-specific and general distress. We contacted patients at a mean of 5.3-years post-testing to measure use of: RRM; RRBSO; chemoprevention; breast and ovarian cancer screening.

Results—Among participants with intact breasts and/or ovaries at the time of testing, *BRCA1/2* carriers were significantly more likely to obtain RRM (37%) and RRBSO (65%) compared to women who received uninformative (RRM=6.8%; RRBSO=13.3%) or negative (RRM=0%; RRBSO=1.9%) results. Among carriers, pre-counseling anxiety was associated with subsequent uptake of RRM. RRO was predicted by age. Carriers were also more likely have used breast cancer chemoprevention and have obtained a screening MRI.

Conclusion—This prospective evaluation of the uptake and predictors of long-term management outcomes provides a clearer picture of decision making in this population. By a mean of 5.3 years post-testing, more than 80% of carriers had obtained RRM, RRBSO or both, suggesting that *BRCA1/2* testing is likely to favorably impact breast and ovarian cancer outcomes.

The increasing use of *BRCA1/2* testing will impact public health only if receipt of a positive test result leads to increased use of breast and ovarian cancer risk reduction strategies. Among mutation carriers, risk reducing mastectomy (RRM) reduces breast cancer risk by about 90%[1–4] and risk reducing bilateral salpingo-oophorectomy (RRBSO) reduces ovarian cancer risk by 85–90% and breast cancer risk by about 50% if performed premenopausally.[5,6] Additionally, RRBSO has been demonstrated to reduce all-cause and cancer-specific mortality in carriers.[7] The efficacy of other risk management options such as chemoprevention[8] and breast and ovarian cancer screening are under investigation. To date, there have been no U.S. studies to prospectively evaluate the full spectrum of long-term risk

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management decisions and predictors of these decisions among women undergoing *BRCA1/2* testing.

Long-Term Use of Risk Reduction Strategies

Initial research suggested low rates of RRM ranging from 0%–15% among unaffected mutation carriers and 18%–48% among carriers previously affected with breast cancer.[9–14] More recent U.S. studies examining RRM from 3–5 years post-testing have reported rates of 20%–36% for unaffected carriers and 49% for affected carriers.[15–18] Outside of the U.S., rates are more variable, ranging from under 10% to about 50%.[4,17–22] Given clear guidelines recommending RRBSO after the completion of child-bearing,[23] RRBSO is more common than RRM. In U.S. studies, long-term uptake of RRBSO has ranged from 51%–71%.[15,16,18,24,25] Outside of the U.S., rates are more variable, ranging from 29%–73%.[18–22] The few studies that have evaluated the long-term use of chemoprevention (tamoxifen/raloxifene) among *BRCA1/2* carriers report variable use, ranging from 0% in an Australian sample[21] to over 20% in a U.S. and Canadian sample.[26]

There have been only a few studies examining mammography among carriers over the long-term. In the 3–5 years following testing, rates have ranged from 80% receiving annual mammograms[21] to 97.5% having received at least one mammogram at a mean of 4.4 years post testing.[18] Data about the efficacy of breast magnetic resonance imaging (MRI) in high risk women emerged in the early 2000s,[27,28] and was incorporated into American Cancer Society guidelines in 2007.[29] The limited research on uptake of MRI screening among carriers varies widely by country, ranging from 2.2% in Israel to over 90% in the Netherlands.[18]

Despite little evidence to support ovarian cancer screening, it is often recommended for *BRCA1/2* carriers who have not obtained RRBSO. Although few studies have examined long-term use of such screening, a recent report indicated that up to 75% of *BRCA1/2* carriers with intact ovaries had received at least one transvaginal ultrasound (TVU) in the three years following testing.[20] This is higher than previous reports which focused on the year following testing.[10,30]

Gaps in current research

Despite increased research on long-term management outcomes following *BRCA1/2* testing, gaps remain. Few studies have examined the full range of risk reduction and screening options, and we are aware of no studies that have evaluated the long-term management decisions of mutation carriers, as well as those who received uninformative and negative test results. Finally, only one study evaluated pre-test psychosocial predictors of long-term management outcomes.[20] This study followed a small cohort (N=154) in the United Kingdom for 3 years. They found that neither cancer worry nor general mental health prior to testing was related to subsequent risk management behaviors among carriers and definitive negatives. However, given multiple studies documenting associations between pre-testing distress and short-term risk management outcomes,[13,31,32] additional investigation of predictors of long-term management outcomes in U.S. based samples is warranted. The purpose of this study was to describe the long term uptake of the full range of breast and ovarian cancer risk management options among women who have received *BRCA1/2* test results and to identify predictors of these decisions.

Method

Participants

Participants were women aged 25–75 who had received genetic counseling and testing through the clinical genetics research program at the Lombardi Comprehensive Cancer Center from 1998 to 2005 and had agreed to be contacted for future research via active participation in a familial cancer registry (FCR). We excluded the small number of otherwise eligible participants who had a *BRCA1/2* variant of uncertain clinical significance (N=19). Characteristics of participants in the FCR have been described previously.[13]

All participants had enrolled in one of four prior studies. Two of these were observational studies of the short-term outcomes of genetic testing and are described in detail elsewhere.[14,30,33] The other two studies were trials of interventions in *BRCA1/2* carriers that were delivered after standard pre- and post-test genetic counseling—one evaluated a psychosocial telephone counseling intervention[34] and the other evaluated an interactive decision aid.[35,36] Both trials employed usual care control groups and only mutation carriers were randomized. The present paper includes 51 carriers who were randomized to the intervention arms in these studies. These individuals did not differ significantly on any of our study outcomes from carriers who participated the observational studies or who were randomized to usual care.

Of 661 potentially eligible women, five were deceased at the time of contact and we had incorrect contact information for 26. Of the 630 eligible women, 118 (18.7%) declined participation and 47 (7.4%) could not be reached after repeated attempts. Our final sample (N=465) represents 73.8% of those who were eligible and for whom we had correct contact information. Participants (N=465) differed from eligible non-participants (N=165) on two variables. Non-participants were more likely to be married and less likely to be Jewish ($p<.05$).

Procedure

After being identified through our FCR, we sent eligible individuals a study packet containing: informed consent/HIPAA documentation and a print version of the survey. Interested individuals could complete the 30-minute survey and return via mail or complete the survey via telephone. All participants provided informed consent.

Measures

Control and Predictor Variables

Sociodemographics: We assessed age, race, education, marital status, employment status, and religion.

Genetic Test Result: We classified results as ‘positive’ if a deleterious mutation was identified; ‘uninformative’ if a deleterious mutation was not identified in affected individuals who were the first in their family to be tested; and ‘negative’ in women who did not to carry a mutation previously identified in their family.

Time Since Genetic Testing: We calculated time between receipt of test results and the completion of the study survey. Since all women who received uninformative results were previously affected with breast or ovarian cancer, we simply used the mean time since the receipt of test result as our predictor. For mutation carriers, some of whom had been previously affected, we created a three-level variable comparing those who were unaffected with breast or ovarian cancer to those who were diagnosed within the previous 10 years to those who were diagnosed more than 10 years ago.

Medical/Family History: Prior to genetic counseling we assessed number of first and second degree relatives affected with breast and/or ovarian cancer. We created two variables to measure time since cancer diagnosis. As carriers included affected and unaffected women, we created a three level variable comparing those who were: unaffected vs. diagnosed with breast or ovarian cancer within 10 years versus diagnosed 10+ years earlier. Since all uninformatives were affected with breast and/or ovarian cancer, we calculated the time between diagnosis and the survey date.

Pre-Testing Distress: For cancer-specific distress, all participants completed the 15-item, reliable (alpha=.88) Impact of Events Scale (IES).[37] For general distress, 90 participants completed the 20-item State Anxiety Inventory (STAI) and 375 participants completed the anxiety sub-scale of the Brief Symptom Inventory (BSI). Both measures are reliable (alphas=.85–.91). To create a single measure of general distress, we converted raw scores on both the STAI and BSI to standard z-scores. We then used these standard scores as our single measure of general distress.

Perceived Risk: Participants completed slightly different measures of breast cancer perceived risk before genetic counseling. The measures assessed perceived risk for developing breast cancer (or developing breast cancer again) using a Likert-style response scale. We created a single measure by dichotomizing each measure to reflect the highest perceived risk rating versus all other levels.

Outcome Variables

Risk Reducing Surgeries: We assessed RRM and RRBSO by asking participants whether they had each surgery and whether the surgery was for cancer treatment, prevention, or other indication. Participants who reported having one or both breasts removed for prevention were classified as having RRM and participants who reported having their ovaries removed for prevention were classified as having had RRBSO.

Chemoprevention: We assessed whether unaffected participants had used tamoxifen or raloxifene and why. If they reported using either agent for risk reduction purposes, they were classified as using chemoprevention.

Surveillance: We assessed date of last mammogram, date of last TVU and date of last CA-125. We also assed whether each participant had **ever** had a screening MRI.

Statistical Analysis

We characterized the sample in terms of sociodemographics, family/personal history of cancer, and genetic test results. We tabulated the uptake of management outcomes separately for carriers, uninformatives, and negatives. For RRM and RRBSO, we used chi-squares and t-tests to identify bivariate predictors of uptake among carriers and uninformatives (uptake among negatives was too low to conduct such analyses). We used logistic regression to identify independent predictors of uptake among carriers and uninformatives. For chemoprevention and surveillance we compared uptake among participants who received positive, uninformative and negative results using chi-square analyses.

RESULTS

Sample Characteristics

Overall, 144 (31%) participants received positive results, 261 (56.1%) received uninformative results and 60 (12.9%) received negative results. The mean time between

receipt of genetic test result and study participation was 5.3 years (SD=1.2 years). The majority of participants were white (94%), affected with breast and/or ovarian cancer (77%), college educated (95%) and married (77%). Participants had a mean age of 52.5 years (SD=10.1) and a mean of 2.3 (SD=1.6) relatives affected with breast or ovarian cancer.

RRM

We excluded 33 participants who had both breasts removed for treatment of bilateral breast cancer. Of the remaining 432 women, 13.4% (N=58) had already undergone RRM prior to referral for genetic counseling/testing. Of the remaining 374 women, 37% (40/108) of those who received positive results, 6.8% (14/206) of those who received uninformative results and 0% (0/60) of definitive negatives opted for RRM (χ^2_2 (N=374)=64.5, p<.001). Overall, 48.5% of carriers (64/132) opted for RRM either before or after testing.

Predictors of RRM Following Testing

Carriers—As displayed in Table 1, younger age (t(106)=2.4, p=.02); higher pre-counseling cancer distress (t(106)=2.3, p=.02) and anxiety (t(106)=2.0, p=.04); more recently diagnosed with breast or ovarian cancer (χ^2_2 (N=108)=7.1, *p*=.03); and having intact ovaries pre-genetic counseling (χ^2_2 (N=108)=7.6, p=.006) were associated with receipt of RRM following testing.

To identify independent predictors of RRM, we included these variables in a backward logistic regression model. After removing non-significant variables, receipt of RRM was associated with intact ovaries at baseline (odds ratio [OR]=4.5; 95% CI=1.5 to 14.3) and higher self-reported anxiety prior to genetic counseling (OR=1.5, 95% CI = 1.0 to 2.2).

Uninformatives—As displayed in Table 1, younger age (t(204)=1.96, p=.05); less time since cancer diagnosis (Welch-Satterthwaite t(18.4)=2.86, p=.01); and higher pre-counseling cancer distress (t(204)=1.82, p=.07) were associated with RRM following testing. Since only 14 uninformatives opted for RRM post-testing we could not conduct multivariate analyses.

RRBSO

We could not determine oophorectomy status for two participants, 20 (4.3%) had their ovaries removed for ovarian cancer treatment and 40 (8.6%) had their ovaries removed for reasons other than cancer risk reduction. Of the remaining 403 women, 48 (11.9%) had RRBSO prior to genetic counseling. Of the 355 women with intact ovaries at the time of counseling, 65% (65/100) of carriers, 13.3% (27/203) of uninformatives, and 1.9% (1/52) of negatives obtained RRBSO (χ^2_2 (N=358)=111.2, p<.001). Overall, 72.7% of carriers (93/128) and 19.5% of uninformatives (43/220) had RRBSO either before or after testing.

Predictors of RRBSO Following Testing

Carriers—As displayed in Table 2, being age 40 or older (χ^2_1 (N=100)=20.7, *p* <.001); and having been diagnosed with breast cancer more than 10 years ago (χ^2_2 (N=100)=8.7, *p*=.01) were associated with RRBSO following testing. When included in a backward logistic regression, only age was independently associated with RRBSO (OR=8.7; 95% CI=3.3 to 23.3).

Uninformatives—As displayed in Table 2, having obtained an RRM prior to genetic counseling (χ^2_1 (N=203)=4.8, p=.03) and higher breast cancer perceived risk (χ^2_1 (N=203)=7.4, p=.007) were associated with RRBSO following testing. In multivariate modeling, receipt of RRM prior to testing (OR=3.8, 95% CI = 1.3 to 10.8) and high

perceived risk for breast cancer (OR=4.0, 95% CI=1.6 to 10.1) were independently associated with RRBSO.

Chemoprevention

We evaluated use of breast cancer chemoprevention among unaffected participants. We did not evaluate use in affected participants (i.e., affected carriers and all uninformatives) because many of these women used tamoxifen as adjuvant treatment for their breast cancer). Overall, 17% of unaffected carriers and 1.7% of negatives reported using tamoxifen/raloxifene for chemoprevention (χ^2_1 (N=106)=7.9, p=.005). The low number of participants who used chemoprevention precluded evaluating predictors of use.

Screening

Receipt of a mammogram in the previous year was not related to test result among unaffected (Carriers=82%; Negatives=66%; χ^2_1 (N=81)=2.3, p=.13) or affected (Carriers = 92%; Uninformatives=89%; χ^2_1 (N=220)=0.2, p=.65) participants. Given the low number of nonadherent participants, we did not evaluate predictors of mammography. Forty-six percent of unaffected carriers reported at least one screening MRI compared to 11% of negatives (χ^2_1 (N=80)=12.2, p<.001). Fifty-one percent of affected carriers and 27% of uninformatives reported at least one screening MRI (χ^2_1 (N=220)=8.1, p=.005). Among carriers, none of the baseline predictors was significantly associated with MRI use. Among uninformatives, younger age (t(182=2.7, p=.008) and being more recently diagnosed with cancer (Satterthwaite-Welch t(124.7)=2.2, p=.03) were associated with receipt of MRI.

Among participants with intact ovaries (N=254), 56% of carriers reported a CA-125 in the previous year compared to 33% of uninformatives and 12% of negatives (χ^2_2 (N=254)=18.0, p<.001). Similarly, 42% of carriers, 26% of uninformatives and 20% of negatives (χ^2_2 (N=254)=5.4, p=.07) reported a transvaginal ultrasound in the prior year. Given the low number of carriers with intact ovaries (N=35), we did not examine predictors of ovarian cancer screening.

Discussion

This is the first U.S. report to prospectively examine the full spectrum of long term risk management outcomes and predictors following *BRCA1/2* testing. At a mean of 5.3-years post testing, this report provides the longest follow-up to date. After testing, 37% of *BRCA1/2* carriers opted for RRM and 65% of opted for RRBSO. Overall, 91.2% of affected carriers and 63.9% of unaffected carriers obtained RRM and/or RRBSO prior to or following testing (data not shown). The 40.3% RRM uptake among affected carriers and 32.6% among unaffected carriers are comparable to[17,18] or higher than[15,16] previous U.S. reports. Our sample also had comparable or slightly higher uptake of RRBSO compared to prior reports.[15,16,18,24,25] These rates likely reflect our longer follow-up time compared to previous studies.[15–18] Our rates may also reflect a trend of increasing use of these surgeries. Recent reports indicate rising use of contralateral RRM among newly diagnosed breast cancer patients.[38–41] These data, coupled with emerging evidence of reduced mortality following risk reducing surgery,[7] suggest that *BRCA1/2* testing may beneficially impact cancer mortality.

Unique to this report was our evaluation of prospective predictors of RRM and RRBSO. Our finding that age was the only predictor of RRBSO among carriers reflects current guidelines recommending RRBSO by age 40.[23,42] RRM was associated with having intact ovaries and higher anxiety at the time of genetic counseling. Given the risk reduction associated with oophorectomy, individuals who had a prior oophorectomy may have been less motivated to

consider RRM. The association between anxiety and RRM contrasts with the only prior report to examine psychosocial predictors of long-term RRM.[20] However, it is consistent with prior studies documenting an association between distress and RRM in the year following testing.[13,31,32] These data highlight the paradox that while distress tends to be low among carriers,[33] even low level distress may impact management decisions.

Although limited by a small sample, we found that 17% of unaffected carriers reported using tamoxifen or raloxifene. These data contrast with recent reports indicating low overall use in the U.S.[43,44] However, these estimates are consistent with a prior study in which 12.4% of unaffected U.S. carriers reported using tamoxifen.[18] These data suggest that chemoprevention may be a viable management alternative for some *BRCA1/2* carriers.

Uninformative *BRCA1/2* test results are the most common result encountered in clinical practice and are associated with heterogeneous and difficult to quantify breast and ovarian cancer risks. Consistent with the limited prior research,[45,46] we found low rates of contralateral RRM (7%) and RRBSO (13.3%) among uninformatives. The greater uptake of contralateral RRM among younger patients likely reflects their higher lifetime risk compared to older patients. Predictors of RRBSO were perceived risk for breast cancer and having an RRM prior to genetic counseling. The fact that women with prior RRM were more likely to opt for RRBSO was not expected as uninformative test results are not typically associated with increased ovarian cancer risk. It is likely that both RRM and RRBSO reflect an overall greater perception of vulnerability to cancer. This is consistent with the fact that perceived risk for breast cancer was also associated with receipt of RRBSO.

Although mammography use was uniformly high, use of MRI was strongly associated with test result. Almost half of mutation carriers reported that they had received a screening MRI. Prior research has reported rates of MRI among U.S. and Canadian carriers ranging from about 25% to 48%.[18] Our results might reflect increased MRI screening consistent with the addition of annual MRI to management guidelines.[29] We also examined ovarian cancer screening. Consistent with prior studies and with the lack of demonstrated efficacy, rates of CA-125 and TVU were lower than rates of breast cancer screening. However, carriers were more likely than uninformatives and negatives to receive ovarian cancer screening.

The generalizability of these data are limited by the fact that they were collected from a single institution in which all participants were enrolled in clinical research studies. However, it is important to note that referrals were drawn from a diverse group of community providers across a large metropolitan area. The sample likely reflects the population typically seen at large cancer genetics referral centers. Even so, the fact that only 6% of participants were members of racial/ethnic minorities and 95% were college educated indicates that these results must be interpreted cautiously.

Despite these limitations, this is the first U.S. study to prospectively evaluate the full spectrum of long-term management outcomes and predictors. With an average follow-up time of 5.3 years, this study provides a clearer picture of long-term decision making following testing. Our data document that the majority of carriers engage in RRM and/or RRBSO. These data, combined with reports of the risk and mortality reduction benefits of these behaviors, strongly suggest that the receipt of a positive *BRCA1/2* test result is likely to have a favorable impact on long-term breast and ovarian cancer outcomes.

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Table 1

Bivariate Predictors of Risk Reducing Mastectomy in Positives and Uninformatives

	Mutation Carriers		Uninformatives	
Variable	**RRM**	**No RRM**	**RRM**	**No RRM**
Mean Age (SD)	45.8 (8.2)	50.7 (11.0)*	49.7 (6.6)	54.7 (9.4)*
Education				
< College (%)	38 (95%)	67 (98.5%)	14 (100%)	186 (96.9%)
College + (%)	2 (5%)	1 (1.5%)	0 (0%)	6 (3.1%)
Religion/Ethnicity				
Jewish (%)	13 (32.5%)	22 (32.4%)	4 (28.6%)	78 (40.6%)
Non-Jewish (%)	27 (67.5%)	46 (67.6%)	10 (71.4%)	114 (59.4%)
Race				
Caucasian (%)	37 (94.9%)	64 (95.5%)	12 (85.7%)	171 (91.9%)
Non-Caucasian (%)	2 (5.1%)	3 (4.5%)	2 (14.3%)	15 (8.1%)
Marital Status				
Married/Partner (%)	31 (77.5%)	54 (79.4%)	10 (71.4%)	145 (75.5%)
Single/Widow/Divorced (%)	9 (22.5%)	14 (20.6%)	4 (28.6%)	47 (24.5%)
Pre-Test Perceived Breast Cancer Risk				
Extremely High (%)	19 (47.5%)	23 (33.8%)	4 (28.6%)	47 (24.5%)
< Extremely High (%)	21 (52.5%)	45 (68.2%)	10 (71.4%)	145 (75.5%)
Mean Years Since Testing (SD)	5.0 (1.1)	5.4 (1.2)	5.1 (1.1)	5.3 (1.2)
Baseline Ovary Status				
Ovaries Intact	36 (90%)	45 (66.2%)	12 (85.7%)	158 (82.3%)
Ovaries Removed	4 (10%)	23 (33.8%)**	2 (14.3%)	34 (17.7%)
Mean Years Since Cancer Dx (SD)++	--	--	6.8 (3.0)	9.4 (5.6)**
Time Since Cancer Diagnosis++				
No Cancer	14 (35%)	31 (42.5%)	--	--
< 10 Years	21 (52.5%)	19 (27.9%)	--	--
10+ Years	5 (12.5%)	18 (26.5%)*	--	--
Prior Use of Tamoxifen				
No	28 (70%)	53 (77.9%)	10 (71.4%)	127 (66.1%)
Yes	12 (30%)	15 (22.1%)	4 (28.6%)	65 (33.9%)
Mean Relatives with Breast Cancer (SD)	2.4 (1.1)	2.3 (1.2)	1.6 (1.1)	1.5 (1.1)
Mean Relatives with Ovarian Cancer (SD)	0.48 (.68)	0.60 (.74)	0.07 (.27)	0.24 (.53)

Variable	Mutation Carriers		Uninformatives	
	RRM	No RRM	RRM	No RRM
Mean Relatives with Breast and Ovarian Cancer (SD)	2.88 (1.3)	2.93 (1.7)	1.7 (1.1)	1.8 (1.3)
Pre-Test Mean IES (SD)	24.0 (14.9)	17.2 (14.9)*	26.2 (13.8)	19.4 (13.5) +
Pre-Test Mean Anxiety (SD)	0.28 (1.3)	−0.13 (.79)*	0.43 (1.3)	0.07 (.95)

** p<.01,

* p < .05,

+ p<.10

++ We used two measures of time since diagnosis. Since all uninformatives were affected with breast or ovarian cancer we used mean number of years since cancer diagnosis for uninformatives. Since carriers included both affected and unaffected women, we created a three-level variable to compare those who were unaffected to those who were diagnosed less than 10 years ago to those who were diagnosed more than 10 years ago.

Table 2

Bivariate Predictors of Risk Reducing Bilateral Salpingo Oophorectomy

	Mutation Carriers		Uninformatives	
Variable	**RRBSO**	**No RRBSO**	**RRBSO**	**No RRBSO**
Age				
< 40	9 (13.9%)	20 (57.1%)	1 (3.7%)	16 (9.0%)
40+	56 (86.2%)	15 (42.9%)**	26 (96.3%)	160 (91%)
Education				
<College (%)	3 (4.6%)	1 (2.9%)	1 (3.7%)	6 (3.4%)
College + (%)	62 (95.4%)	34 (97.1%)	26 (96.3)	170 (96.6%)
Religion/Ethnicity				
Jewish (%)	22 (33.8%)	6 (17.1%)	10 (37%)	70 (39.8%)
Non-Jewish (%)	43 (66.2%)	29 (82.9%)+	17 (70%)	106 (60.2%)
Race				
Caucasian (%)	62 (95.4%)	31 (93.9%)	25 (92.6%)	156 (91.2%)
Non-Caucasian (%)	3 (4.6%)	2 (6.1%)	2 (7.4%)	15 (8.8%)
Marital Status				
Married/Partner (%)	51 (78.5%)	25 (71.4%)	23 (85.2%)	135 (76.7%)
Single/Widow/Divorced (%)	14 (21.5%)	10 (28.6%)	4 (14.8%)	41 (23.3%)
Pre-Test Perceived Breast Cancer Risk				
Extremely High (%)	21 (32.3%)	13 (37.1%)	10 (37%)	27 (15.3%)
< Extremely High (%)	44 (67.7%)	22 (62.9%)	17 (63%)	149 (84.7%)**
Mean Years Since Testing (SD)	5.3 (1.1)	4.9 (.92)+	5.3 (1.2)	5.2 (1.1)
Baseline RRM Status				
No Prior RRM	55 (84.6%)	30 (85.7%)	20 (74.1%)	157 (89.2%)
Prior RRM	10 (15.4%)	5 (14.3%)	7 (25.9%)	19 (10.8%)*
Mean Years Since Cancer Dx (SD)++	--	--	8.6 (4.8)	9.5 (6.1)
Cancer Dx/Time Since Cancer Dx++				
No Cancer	19 (29.2%)	17 (48.6%)	--	--
< 10 Years	30 (46.2%)	17 (48.6%)	--	--
10+ Years	16 (24.6%)	1 (2.9%)*	--	--
Mean Relatives with Breast Cancer (SD)	2.4 (1.1)	2.2 (1.0)	1.9 (121)	1.5 (1.2)
Mean Relatives with Ovarian Cancer (SD)	0.51 (.66)	0.31 (.67)	0.22 (.42)	0.16 (.41)
Mean Relatives with Breast and Ovarian Cancer (SD)	2.9 (1.5)	2.5 (1.3)	2.1 (1.1)	1.7 (1.3)

Variable	Mutation Carriers		Uninformatives	
	RRBSO	No RRBSO	RRBSO	No RRBSO
Pre-Test Mean IES (SD)	20.7 (14.5)	22.7 (17.5)	22.3 (16.2)	20.3 (13.7)
Pre-Test Mean Anxiety (SD)	0.14 (1.1)	−0.07 (1.1)	0.20 (.83)	0.09 (.99)

** p<.01,

* p < .05,

+ p<.10

++ We used two measures of time since diagnosis. Since all uninformatives were affected with breast or ovarian cancer we used mean number of years since cancer diagnosis for uninformatives. Since carriers included both affected and unaffected women, we created a three-level variable to compare those who were unaffected to those who were diagnosed less than 10 years ago to those who were diagnosed more than 10 years ago.