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Predictors of risk-reducing surgery intentions following genetic counseling for hereditary breast and ovarian cancer

Mary Kathleen Ladd,[1,2] Beth N. Peshkin,[1,2] Leigha Senter,[3] Shari Baldinger,[4] Claudine Isaacs,[1,2] Hannah Segal,[1,2] Samantha Philip,[1,2] Chloe Phillips,[1,2] Kate Shane,[3] Aimee Martin,[1,2] Veronique Weinstein,[1,2] Robert Pilarski,[3] Joanne Jeter,[3] Kevin Sweet,[3] Bonnie Hatten,[4] Elisabeth J. Wurtmann,[4] Shanda Phippen,[4] Della Bro,[4] Marc D. Schwartz[1,2]

[1]Georgetown Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC 20057

[2]Jess and Mildred Fisher Center for Hereditary Cancer and Clinical Genomics Research, Georgetown University, Washington, DC 20057

[3]Division of Human Genetics, Department of Internal Medicine and Comprehensive Cancer Center, The Ohio State University, Columbus, OH 43210

[4]Virgina Piper Cancer Institute, Allina Health, Minneapolis, MN 55404

Correspondence to: Marc D. Schwartz, schwartm@georgetown.edu

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Abstract

Risk-reducing mastectomy (RRM) and salpingo-oophorectomy (RRSO) are increasingly used to reduce breast and ovarian cancer risk following *BRCA1/BRCA2* testing. However, little is known about how genetic counseling influences decisions about these surgeries. Although previous studies have examined intentions prior to counseling, few have examined RRM and RRSO intentions in the critical window between genetic counseling and test result disclosure. Previous research has indicated that intentions at this time point predict subsequent uptake of surgery, suggesting that much decision-making has taken place prior to result disclosure. This period may be a critical time to better understand the drivers of prophylactic surgery intentions. The aim of this study was to examine predictors of RRM and RRSO intentions. We hypothesized that variables from the Health Belief Model would predict intentions, and we also examined the role of affective factors. Participants were 187 women, age 21–75, who received genetic counseling for hereditary breast and ovarian cancer. We utilized multiple logistic regression to identify independent predictors of intentions. 49.2% and 61.3% of participants reported intentions for RRM and RRSO, respectively. Variables associated with RRM intentions include: newly diagnosed with breast cancer (OR = 3.63, 95% CI = 1.20–11.04), perceived breast cancer risk (OR = 1.46, 95% CI = 1.17–1.81), perceived pros (OR = 1.79, 95% CI = 1.38–2.32) and cons of RRM (OR = 0.81, 95% CI = 0.65–0.996), and decision conflict (OR = 0.80, 95% CI = 0.66–0.98). Variables associated with RRSO intentions include: proband status (OR = 0.28, 95% CI = 0.09–0.89), perceived pros (OR = 1.35, 95% CI = 1.11–1.63) and cons of RRSO (OR = 0.72, 95% CI = 0.59–0.89), and ambiguity aversion (OR = 0.79, 95% CI = 0.65–0.95). These data provide support for the role of genetic counseling in fostering informed decisions about risk management, and suggest that the role of uncertainty should be explored further.

Keywords

Hereditary breast/ovarian cancer, Intentions, Risk-reducing mastectomy, Risk-reducing oophorectomy, Genetic counseling, Decision-making

Implications

Practice: The results provide support for the role of genetic counseling in fostering informed decisions about risk management, and suggest that genetic counselors could be proactive in addressing concerns about prophylactic surgery, and facilitating appropriate follow-up and support for their patients.

Policy: The important role genetic counselors play in helping to foster informed risk management decisions suggests that all at-risk women need access to a genetic counselor.

Research: Research is needed to evaluate the role of ambiguity aversion and uncertainty following the receipt of genetic test results, to determine whether patients may require additional support.

INTRODUCTION

Genetic testing for pathogenic variants in *BRCA1* and *BRCA2* (*BRCA*) is central to the clinical care of women at high risk for hereditary breast and ovarian cancer (HBOC) [1]. Women who carry a pathogenic variant have up to a 72% lifetime risk of developing breast cancer and up to a 44% lifetime risk of developing ovarian cancer (including fallopian tube and primary peritoneal cancers), compared to a 12.4% and 1.3% lifetime risk, respectively, in the general population [2, 3]. The most effective options for reducing these extremely high cancer risks are risk-reducing mastectomy (RRM) and risk-reducing bilateral salpingo-oophorectomy (RRSO). RRM refers to the prophylactic removal of both breasts, or in newly diagnosed patients it may entail the removal of the affected breast for treatment, and removal of the unaffected breast for risk reduction. RRSO refers to the prophylactic removal of both ovaries and fallopian tubes. The National Comprehensive Cancer Network (NCCN) recommends that female *BRCA* mutation carriers have a RRSO after they have finished child bearing, and consider having a RRM [1].

RRSO reduces risk for ovarian cancer by over 80% [4] and when performed premenopausally may

also reduce breast cancer risk, especially in *BRCA2* carriers under age 50 [5]. Although this surgery is recommended by the NCCN, it is associated with significant side effects, including surgical menopause, increased risks for cardiovascular diseases, cognitive impairment, and osteoporosis [6]. RRM reduces the risk for breast cancer by about 90% [7, 8] and can also have psychological benefits, like reducing cancer-related distress [9]. However, this surgery can also have undesirable consequences, such as negative impacts on sexuality and body image [9, 10], and surgical complications [11]. Additionally, neither of these surgeries completely eliminates the risk for breast and ovarian cancer. Clearly, decision-making about risk-reducing surgery is complex, with multiple factors to weigh and trade-offs to consider [12, 13]. To provide the best care for women at risk for HBOC, it is critical for practitioners to better understand how women make these difficult risk management decisions.

Studies that have examined risk-reducing surgery intentions prior to genetic counseling have found that in addition to sociodemographic predictors, cognitive and affective factors such as perceived cancer risk, perceived benefits, cancer worry, distress, and uncertainty reduction predict RRM and RRSO intentions [14–20]. Much less is known about how intentions are impacted by genetic counseling since few studies have examined intentions during the window between genetic counseling and the receipt of the test result. This is a crucial window because previous research has indicated that intentions at this time point predict subsequent uptake of prophylactic surgery [21]. In contrast to pre-counseling intentions which may not reflect accurate comprehension of personal risk, the implications of a positive test result, or the risks and benefits of RRM/RRSO, post-counseling intentions are likely to be more informed. Learning the drivers of these decisions could help genetic counselors to better understand their patients' decision processes, and tailor genetic counseling to facilitate informed decisions. Further, understanding the predictors of post-counseling intentions may help to identify women who could benefit from additional decision support. Previous research suggests that decision support is of particular benefit to those women who have not reached decisions about RRM and RRSO prior to receipt of test results [13].

The Health Belief Model (HBM) is a well-established framework to understand and predict the adoption of a wide range of preventive health behaviors [22–24]. The framework posits that the likelihood of an individual engaging in a preventive health behavior is influenced by their perceived susceptibility to and perceived seriousness of the disease, self-efficacy for engaging in the behavior, their beliefs about whether the advantages of engaging in the health behavior outweigh the disadvantages, and cues to action. In this study, we focus on perceived benefits, perceived barriers, and perceived susceptibility as key HBM constructs that we predicted would be associated with RRM and RRSO intentions after genetic counseling, but prior to the receipt of test results.

Although we expect the cognitive HBM constructs to predict risk-reducing surgery intentions, as noted above, previous studies have found that affect is a strong predictor of RRM and RRSO intentions prior to genetic counseling. Emotional factors may be particularly salient prior to the provision of extensive information during genetic counseling. The information and decision support provided during genetic counseling could reduce the role that negative affect plays in decision-making. However, clinical observations suggest that the discussion of the risks and benefits surrounding testing and surgery options during genetic counseling can lead to feelings of uncertainty and worry [25] which may manifest as delayed or deferred decisions about risk-reducing surgery [26]. Thus, we examined whether affective factors including distress and uncertainty predict RRM and RRSO intentions after accounting for HBM factors following completion of genetic counseling.

METHOD

Participants

Participants were women undergoing genetic testing for HBOC who completed a baseline survey prior to randomization in a randomized controlled trial of post-test decision support. Participants were recruited from the clinical cancer genetics programs at the Lombardi Comprehensive Cancer Center (Washington, DC), Ohio State University Comprehensive Cancer Center (Columbus, OH), and Virginia Piper Cancer Institute (Minneapolis, MN). Eligible participants were women age 21–75 who received in-person genetic counseling for HBOC but who had not yet received genetic test results. Participants included women who were either affected or unaffected with breast cancer, but excluded those diagnosed with other cancers, besides nonmelanoma skin cancer. We included women who were newly diagnosed with breast cancer (i.e., who had not yet initiated definitive breast cancer treatment) but excluded newly diagnosed women who had already scheduled a bilateral mastectomy. We included both probands and women who had relatives with a *BRCA* pathogenic variant. We excluded participants who had been diagnosed with bilateral or metastatic breast cancer, had a previous bilateral mastectomy, were candidates for testing for another hereditary cancer syndrome, or had previously used breast cancer chemoprevention. We also excluded women who could not communicate in English or lacked the cognitive capacity to provide informed consent.

Of 352 potentially eligible participants, 79 declined study contact, 86 who agreed to contact received their genetic test results before completing the baseline survey, and 187 (53.1%) completed the baseline survey prior to receiving test results. This report includes all individuals who completed a baseline survey regardless of whether they were ultimately randomized in the trial. Of the 187 women who completed a baseline survey, six were excluded because they were administered an incorrect version of the survey. For the RRM analysis, two were excluded due to missing data on the outcome variable. For the RRSO analysis, one participant was excluded due to missing data on the outcome variable and 12 participants who previously had their ovaries removed were ineligible.

Procedure

Genetic counselors at each study site assessed patient eligibility during their pretest counseling session, explained the study to potentially eligible patients, and asked if they were interested in participation. Participants who met eligibility criteria, and agreed to participate, were enrolled immediately following their genetic counseling appointment. These women were contacted by the study staff and given the option to complete the baseline questionnaire electronically or over the telephone. Electronic surveys were completed using the HIPAA-compliant REDCap data capture tool hosted at Georgetown University [27]. Participants completed an Institutional Review Board approved verbal or electronic consent form prior to completion of the baseline survey. Participants were required to complete the baseline survey after the pretest genetic counseling session but prior to result disclosure. Following the interview and receipt of participants' test results, the research assistant randomized eligible participants to one of several decision support interventions. This paper focuses only on pre-randomization baseline data.

Measures

Control variables

Sociodemographics. We assessed age, race/ethnicity, relationship status, education, employment, and Jewish ancestry.

Medical history. We assessed personal and family cancer history and used this information to calculate lifetime breast cancer risk with the BRCAPRO model [28].

HBM variables

Perceived breast/ovarian cancer risk. We measured quantitative perceived risk by asking participants to rate their risk on a scale from 0 (definitely will not get breast/ovarian cancer) to 100 (definitely will get breast/ovarian cancer). For participants previously diagnosed with breast cancer, the items asked about the likelihood of developing a new breast cancer. We have used this measure in prior research [15, 29].

Perceived pros and cons for RRM. We measured six pros (Risk-reducing mastectomy would reduce my risk for developing breast cancer) and eight cons (I am worried that risk-reducing mastectomy would change the way I feel about my appearance) of RRM on a 4-point Likert scale ranging from "not at all important" to "very important." This scale was adapted from a measure used in previous studies [21]. Cronbach's alpha was 0.76 for the pros and 0.73 for the cons.

Perceived pros and cons for RRSO. Adapted from a previous study [21], we measured six pros (Having my ovaries removed would reduce my worry about developing ovarian cancer) and seven cons (I don't want to go on hormone replacement therapy) of RRSO on a 4-point Likert scale from "not at all important" to "very important." Cronbach's alpha was 0.61 for the pros and 0.75 for the cons.

Affective/uncertainty variables

Cancer distress. We measured cancer distress using the Impact of Event Scale [30], a 15-item Likert-style scale, where higher scores indicate more distress. Reliability in the present study was 0.91.

Perceived stress. We used the 4-item Perceived Stress Scale [31]. This measure asks participants how often they have felt or thought a certain way in the last month. Items are scored on a 5-point Likert scale from "never" to "very often." Cronbach's alpha in the present study was 0.78.

Decisional conflict. We measured decisional conflict regarding the management of one's breast cancer risk with the 10-item version of the Decisional Conflict Scale [32]. Items were scored on a weighted 3-point scale, where higher scores indicate greater decisional conflict. Participants were asked to respond to questions like "Do you feel sure about what to choose?" with "yes," "unsure," or "no." Cronbach's alpha in the present study was 0.87.

Perceived uncertainty. We used Baty's 12-item measure to evaluate perceived uncertainty about genetic counseling and testing [25]. Items were scored on a 5-point Likert scale, from "very certain" to "very uncertain," where higher scores represented greater uncertainty. Consistent with previous research [25], we calculated perceived uncertainty using the average of five items that assessed uncertainty about

health care, positive outcomes of testing, and coping with results. Cronbach's alpha for in the present study was 0.72.

Ambiguity aversion. We measured aversion to ambiguity regarding medical tests and treatment using the 6-item AA-Med Scale [33]. Participants were asked to rate statements like "I would not have confidence in a medical test or treatment if experts had conflicting opinions about it" on a 5-point Likert scale, from "strongly disagree" to "strongly agree," where higher scores indicate greater ambiguity aversion. Cronbach's alpha was 0.79.

Outcome variables

Surgery intentions. We assessed participants' intentions for RRM a with a single face-valid item, "If you were to learn that you have a mutation in the *BRCA1* or *BRCA2* gene, would you have a bilateral risk-reducing mastectomy to reduce your risk for breast cancer?" with options on a 5-point scale ranging from "I definitely would not" to "I definitely would." Because responses to this item were not normally distributed, we dichotomized this variable, with those responding "I definitely would not/I probably would not/I am not really sure" categorized as "no intention for RRM," and those answering "I probably would/I definitely would" categorized as "intention for RRM." For RRSO we used a similar item, asking "If you were to learn that you have a mutation in the *BRCA1* or *BRCA2* gene, would you have your ovaries removed for risk reduction?" and we dichotomized the variable in the same way as RRM.

Statistical analysis

After characterizing the sample in terms of demographics, family history, and lifetime risk of breast cancer, we used chi-square and *t*-tests to examine bivariate associations with RRM and RRSO intentions. Next, we used multiple logistic regression to identify independent predictors of intentions for RRM and RRSO. Guided by our conceptual model, in the initial model, we included personal demographic and medical history variables with bivariate associations at the $p < .10$ level. In the next step, we included the HBM variables of perceived pros and cons of RRM/RRSO (i.e., perceived benefits and barriers) and perceived risk (perceived susceptibility). In the final model, we included affect-related variables, based on significant bivariate associations. For the small amount of missing data we employed mean substitution. All analyses were performed using Statistical Analysis Software (SAS) version 9.4, SAS Inc. (Cary, NC).

RESULTS

Participants were primarily non-Hispanic white (72.7%), employed full-time (64.8%), and did not have a known *BRCA* mutation in their family (83.8%). The average age of participants was 47.5 years (SD = 12.5) and women had an average lifetime risk of breast cancer of 14.5%.

RRM results

Of the 179 women in this analysis, 88 (49.2%) reported that they probably or definitely would obtain a RRM if they were found to have a *BRCA* mutation. Table 1 displays the bivariate associations between our baseline variables and RRM intentions. The following variables had bivariate associations ($p < .10$) with RRM intentions: being employed, no family history of ovarian cancer, being newly diagnosed with breast cancer, higher objective breast cancer risk, higher perceived breast cancer risk, greater perceived pros and lower perceived cons of RRM, lower perceived uncertainty, and lower decisional conflict.

To evaluate the independent contribution of specific HBM and affective components, we utilized logistic regression with hierarchical variable entry. As seen in Table 2, we first entered background demographic and clinical variables that were associated with RRM intentions. These variables (employment, family history of ovarian cancer, and personal breast cancer history), in combination, were significantly associated with RRM intentions (χ^2 (5, N = 179) = 20.17, $p = .001$).

In Model 2, we added the HBM variables of perceived pros, perceived cons, and perceived susceptibility. These variables, in combination, strongly predicted RRM intentions over and above the clinical and demographic variables already in the model ($\Delta\chi^2$ (3) = 53.05, $p < .0001$).

In the final model, we added all affective/uncertainty variables with $p < .10$ bivariate associations to RRM intentions (perceived uncertainty and decisional conflict). The combined contribution of perceived uncertainty and decision conflict approached statistical significance ($\Delta\chi^2$ (2) = 5.87, $p = .053$). In this final model, the following variables independently predicted RRM intentions: being newly diagnosed with breast cancer (OR = 3.63, 95% CI = 1.20–11.04), perceived risk of breast cancer (OR = 1.46, 95% CI = 1.17–1.81), perceived pros of RRM (OR = 1.79, 95% CI = 1.38–2.32), perceived cons of RRM (OR = 0.81, 95% CI = 0.65–0.996), and decision conflict (OR = 0.80, 95% CI = 0.66–0.98). Compared to women who were previously diagnosed with breast cancer, those who were newly diagnosed with breast cancer were more than three and a half times as likely to have high RRM intentions. Each half standard deviation increase in perceived breast cancer risk was associated with 46% increased odds of having high RRM intentions and each half standard deviation increase in perceived pros of RRM was associated with 79% increased odds of high RRM intentions. In contrast, each half standard deviation

Table 1 | Bivariate associations between categorical and continuous predictors and risk-reducing mastectomy (RRM) intentions

Categorical predictors	Full sample *N* = 179	Intention for RRM *N* (%)	No intention for RRM *N* (%)	*p*
Married				
No	56	32 (57.1%)	24 (42.9%)	.148
Yes/living together	121	55 (45.5%)	66 (54.5%)	
Education				
College or less	95	45 (47.4%)	50 (52.6%)	.610
More than college	84	43 (51.2%)	41 (48.8%)	
Race				
Non-Hispanic white	128	66 (51.6%)	62 (48.4%)	.498
Hispanic/non-white	48	22 (45.8%)	26 (54.2%)	
Employment				
<Full-time	63	25 (39.7%)	38 (60.3%)	.062
Full-time	116	63 (54.3%)	53 (45.7%)	
Jewish decent				
Yes	24	11 (45.8%)	13 (54.2%)	.834
No	135	65 (48.15%)	70 (51.85%)	
Breast cancer				
Unaffected	92	40 (43.5%)	52 (56.5%)	.001
Affected	41	15 (36.6%)	26 (63.4%)	
Newly diagnosed	46	33 (71.7%)	13 (28.3%)	
Children				
Yes	120	59 (49.2%)	61 (50.8%)	.919
No	54	27 (50%)	27 (50%)	
Proband status				
Relative	29	13 (44.8%)	16 (55.2%)	.610
Proband	150	75 (50%)	75 (50%)	
Breast cancer family history				
Yes	133	64 (48.1%)	69 (51.9%)	.372
No	41	23 (56.1%)	18 (43.9%)	
Ovarian cancer family history				
Yes	40	15 (37.5%)	25 (62.5%)	.067
No	134	73 (54.5%)	61 (45.5%)	
Continuous predictors	**Full sample *M* (*SD*)**	**Intention for RRM *M* (*SD*)**	**No intention for RRM *M* (*SD*)**	***p***
Age	47.5 (12.5)	46.3 (12.0)	48.7 (12.9)	.192
Lifetime breast cancer risk	14.5 (7.5)	15.6 (8.1)	13.3 (6.8)	.053
Pros of RRM	18.95 (3.4)	20.4 (2.1)	17.6 (3.8)	<.0001
Cons of RRM	19.0 (4.8)	18.0 (4.5)	20.0 (5.0)	.006
Perceived breast cancer risk	41.4 (27.4)	48.8 (27.0)	34.3 (26.1)	.0004
Perceived uncertainty	2.2 (0.7)	2.1 (0.7)	2.3 (0.7)	.026
Ambiguity aversion	17.5 (4.7)	16.9 (4.6)	18.0 (4.6)	.119
Cancer distress	23.8 (17.0)	24.6 (16.2)	23.2 (17.7)	.580
Perceived stress	5.4 (3.0)	5.4 (3.0)	5.5 (3.0)	.752
Decision conflict	29.1 (24.2)	23.1 (23.3)	34.9 (23.8)	.001

increase in perceived cons of RRM was associated with 19% decreased odds of high RRM intentions and each half standard deviation increase in decision conflict was associated with a 20% decrease in the odds of having high RRM intentions.

RRSO analysis

Of the 168 women included in this analysis, 103 (61.3%) responded that if they were found to have a *BRCA* mutation, they probably or definitely would obtain a RRSO. Table 3 displays the bivariate associations between our baseline predictors and RRSO intentions. The following variables exhibited $p < .10$ association with RRSO intentions: being non-Hispanic white, having a relative with a *BRCA* mutation, higher perceived ovarian cancer risk, greater pros and weaker cons of RRSO, and lower ambiguity aversion.

Table 2 | Logistic regression models of risk-reducing mastectomy (RRM) intentions

	Model 1				Model 2				Model 3			
Predictor	OR	95% CI	χ^2	*p*	OR	95% CI	χ^2	*p*	OR	95% CI	χ^2	*p*
Employed	1.52	0.77–2.96	1.48	.223	2.05	0.89–4.71	2.87	.090	2.18	0.93–5.12	3.18	.075
Family history ovarian cancer	0.52	0.23–1.15	2.61	.106	0.37	0.14–0.99	3.92	.048	0.38	0.14–1.06	3.41	.065
Breast cancer history												
Newly diagnosed vs. affected	3.67	1.45–9.27	7.54	.006	3.08	1.04–9.06	4.15	.042	3.63	1.20–11.04	5.18	.023
Unaffected vs. affected	1.32	0.59–2.97	0.44	.506	1.12	0.42–3.00	0.05	.816	1.28	0.48–3.45	0.24	.623
Lifetime breast cancer risk[a]	1.14	0.97–1.35	2.48	.116	1.05	0.86–1.29	0.25	.616	1.03	0.83–1.27	0.07	.796
Perceived risk[a]					1.43	1.16–1.77	11.39	<.001	1.46	1.17–1.81	11.60	<.001
Pros of RRM[a]					1.84	1.41–2.38	20.90	<.0001	1.79	1.38–2.32	19.25	<.0001
Cons of RRM[a]					0.74	0.61–0.91	8.62	.003	0.81	0.65–0.996	3.97	.046
Perceived uncertainty[a]									0.92	0.76–1.12	0.63	.428
Decision conflict[a]									0.80	0.66–0.98	4.73	.030

[a]The units on all continuous variables are a half standard deviation. Model 1: $\chi^2 = 20.17$, $df = 5$, $p = .001$; model fit: −2log-L = 227.93. Model 2: $\chi^2 = 73.22$, $df = 8$, $p < .0001$; model fit: −2log-L = 174.88. Model 3: $\chi^2 = 79.09$, $df = 10$, $p < .0001$; model fit: −2log-L = 169.01. Model 2 vs. Model 1: $\chi^2 = 53.05$, $df = 3$, $p < .0001$. Model 3 vs. Model 2: $\chi^2 = 5.87$, $df = 2$, $p = .053$.
The shaded gray area depicts the predictors not included in each model.

Table 3 | Bivariate associations between categorical and continuous predictors and risk-reducing salpingo-oophorectomy (RRSO) intentions

Categorical predictors	Full sample *N* = 168	Intention for RRSO *N* (%)	No intention for RRSO *N* (%)	*p*
Married				
No	54	32 (59.3%)	22 (40.7%)	.739
Yes/living together	113	70 (61.95%)	43 (38.05%)	
Education				
College or less	85	57 (67.1%)	28 (32.9%)	.122
More than college	83	46 (55.4%)	37 (44.6%)	
Race				
Non-Hispanic white	118	79 (66.95%)	39 (33.05%)	.008
Hispanic/non-white	47	21 (44.7%)	26 (55.3%)	
Employment				
<Full-time	56	32 (57.1%)	24 (42.6%)	.433
Full-time	112	71 (63.4%)	41 (36.6%)	
Jewish decent				
Yes	22	8 (36.4%)	14 (63.6%)	.686
No	127	75 (59.1%)	52 (40.9%)	
Breast cancer				
Unaffected	89	61 (68.5%)	28 (31.5%)	.119
Affected	35	18 (51.4%)	17 (48.6%)	
Newly diagnosed	44	24 (54.55%)	20 (45.45%)	
Children				
Yes	110	70 (63.6%)	40 (36.4%)	.275
No	53	29 (54.7%)	24 (45.3%)	
Proband status				
Relative	28	23 (82.1%)	5 (17.9%)	.013
Proband	140	80 (57.1%)	60 (42.9%)	
Breast cancer family history				
Yes	123	74 (60.2%)	49 (39.8%)	.585
No	40	26 (65.0%)	14 (35.0%)	
Ovarian cancer family history				
Yes	37	25 (67.6%)	12 (32.4%)	.377
No	126	75 (59.5%)	51 (40.5%)	
Continuous predictors	**Full sample *M* (*SD*)**	**Intention for RRSO *M* (*SD*)**	**No intention for RRSO *M* (*SD*)**	***p***
Age	46.5 (12.0)	47.1 (12.0)	45.4 (11.6)	.399
Lifetime breast cancer risk	14.9 (7.6)	15.4 (8.3)	14.2 (6.5)	.325
Pros of RRSO	19.8 (3.0)	20.2 (2.6)	19.1 (3.5)	.020
Cons of RRSO	16.9 (4.5)	15.8 (4.4)	18.5 (4.3)	.0001
Perceived ovarian cancer risk	27.2 (23.6)	30.6 (23.1)	21.4 (23.4)	.013
Perceived uncertainty	2.19 (0.7)	2.2 (0.7)	2.2 (0.7)	.571
Ambiguity aversion	17.5 (4.7)	16.6 (4.4)	19.0 (4.9)	.002
Cancer distress	23.6 (17.1)	22.9 (17.1)	24.7 (17.2)	.505
Perceived stress	5.3 (3.0)	5.4 (3.0)	5.2 (3.0)	.708
Decision conflict	28.5 (24.3)	26.5 (24.2)	31.6 (24.2)	.187

As displayed in Table 4, we used the same approach as for RRM to identify the independent contribution of specific HBM components. On the first step, the demographic and clinical variables that were associated ($p < .10$) with RRSO (race and proband status) were significantly associated with RRSO intentions (χ^2 (2, N = 168) = 12.29, p = .002). In Model 2, the HBM variables (perceived pros, perceived cons, and perceived susceptibility) entered together were strong predictors of RRSO intentions over and above the variables already in the model ($\Delta\chi^2$ (3) = 21.72, $p < .0001$). Finally, ambiguity aversion, the only affect-related variable that was significantly associated with RRSO, significantly added to the model ($\Delta\chi^2$ (1) = 6.68, p = .010). The following variables were independent predictors of RRSO intentions in the final model: proband status (OR = 0.28, 95% CI = 0.09–0.89), perceived pros of

Table 4 | Logistic regression models of risk-reducing salpingo-oophorectomy (RRSO) intentions

	Model 1				Model 2				Model 3			
Predictor	OR	95% CI	χ^2	*p*	OR	95% CI	χ^2	*p*	OR	95% CI	χ^2	*p*
Race	2.32	1.15–4.67	5.50	.019	1.69	0.77–3.67	1.76	.185	1.76	0.80–3.87	1.95	.163
Proband status	0.34	0.12–0.96	4.15	.042	0.33	0.11–1.01	3.75	.053	0.28	0.09–0.89	4.65	.031
Perceived risk[a]					1.09	0.90–1.31	0.77	.379	1.05	0.87–1.28	0.28	.595
Pros of RRSO[a]					1.32	1.09–1.59	8.28	.004	1.35	1.11–1.63	9.26	.002
Cons of RRSO[a]					0.69	0.56–0.84	13.78	.0002	0.72	0.59–0.89	9.12	.003
Ambiguity aversion[a]									0.79	0.65–0.95	6.31	.012

[a]The units on all continuous variables are a half standard deviation. Model 1: $\chi^2 = 12.29$, $df = 2$, $p = .002$; model fit: −2log-L = 211.94. Model 2: $\chi^2 = 34.01$, $df = 5$, $p < .0001$; model fit: −2log-L = 190.22. Model 3: $\chi^2 = 40.69$, $df = 6$, $p < .0001$; model fit: −2log-L = 183.53. Model 2 vs. Model 1: $\chi^2 = 21.72$, $df = 3$, $p < .0001$. Model 3 vs. Model 2: $\chi^2 = 6.68$, $df = 1$, $p = .010$.
The shaded gray area depicts the predictors not included in each model.

RRSO (OR = 1.35, 95% CI = 1.11–1.63), perceived cons of RRSO (OR = 0.72, 95% CI = 0.59–0.89), and ambiguity aversion (OR = 0.79, 95% CI = 0.65–0.95). Those with a relative with a *BRCA* mutation were over 3.5 times more likely to have intentions for RRSO. Each half standard deviation increase in perceived pros of RRSO was associated with 35% increased odds of high RRSO intentions. Each half standard deviation increase in perceived cons of RRSO was associated with 28% decreased odds of high RRSO intentions and each half standard deviation increase in ambiguity aversion was associated with a 21% decrease in the odds of having high RRSO intentions.

DISCUSSION

We evaluated intentions for RRM and RRSO following genetic counseling but prior to the receipt of genetic test results. We predicted that the HBM variables of perceived risk, and perceived pros and perceived cons of surgery would be important predictors following genetic counseling. We also tested whether affect and uncertainty were associated with intentions over and above the HBM variables. Consistent with our predictions, HBM variables were strong predictors of RRM and RRSO intentions even after controlling for sociodemographics and personal/family cancer history. However, the role of affect and uncertainty was less clear.

We found that 49.2% of participants reported that they probably or definitely would obtain a RRM if they received a positive *BRCA* test result and 61.3% reported that they would probably or definitely obtain a RRSO. These rates are higher than studies of pre-counseling risk-reducing surgery intentions [15, 34] and are comparable to the actual rates of RRM and RRSO reported in studies of *BRCA* mutation carriers. For example, in one study, at a mean of 5 years post-testing, 37% of *BRCA* mutation carriers had obtained RRM and 65% had obtained RRSO [35]. More recent studies have shown comparable but slightly higher rates of uptake [36]. This is consistent with our previous report documenting that post-counseling intentions were highly predictive of subsequent surgical decisions [21].

As expected, the HBM variables that we assessed in this study were important predictors of RRM and RRSO intentions. In particular, perceived benefits and barriers were strong predictors of RRM and RRSO intentions. These associations remained after controlling for relevant sociodemographic, objective risk, and cancer history variables. Recent conceptualizations of informed medical decision-making describe concordance between attitudes and decisions as a key component of informed decisions [37]. The fact that our participants' intentions are broadly concordant with their preferences, along with previous research suggesting that patients have increased knowledge following genetic counseling [38], provides evidence that genetic counseling facilitates informed decisions about risk-reducing surgery.

In contrast to studies of pre-counseling intentions [15, 17, 39], distress and worry were not associated with risk-reducing surgery intentions. This could reflect the impact of genetic counseling on reducing distress, fostering more accurate risk comprehension, and providing information about the full range of management alternatives [40]. However, this finding must be considered in the context of previous studies that have identified reduction of worry as a key motivator of risk-reducing surgery [41, 42]. It is certainly possible that distress may reemerge as a motivator for surgery following the receipt of a positive test result.

Although distress was not related to risk-reducing surgery intentions, uncertainty in the form of decision conflict and ambiguity aversion emerged as an independent predictor of RRM and RRSO. Higher decisional conflict regarding RRM was associated with lower intentions for obtaining the surgery. Abundant research has documented that individuals with high levels of decisional conflict are less likely to behaviorally implement a health decision [43–45]. In this study, high decision conflict likely reflects that these participants are early in the decision process and have not reached a final decision. Those who have already decided to proceed with

RRM in the event of a positive test result have lower decision conflict than those who are undecided or who favor screening. These results are consistent with our previous research in which those who rapidly reach a management decision maintain low decision conflict and high decision satisfaction in the short and longer term [13].

In terms of RRSO, participants who reported high ambiguity aversion also reported lower RRSO intentions. On the one hand, this finding might be surprising since RRSO is recommended for all *BRCA* mutation carriers and unequivocally reduces the risk of developing ovarian cancer [1, 4, 46]. Thus, one might expect that individuals who are high in ambiguity aversion would favor RRSO. However, the immediate period following genetic counseling and prior to receipt of genetic test results is a highly uncertain period and the decision to obtain an RRSO raises additional uncertainties. For example, there is ongoing uncertainty surrounding the probability of testing positive and the risk for developing ovarian cancer. The majority of women in the study do not have a family history of ovarian cancer. Thus, a positive result from genetic testing would be their only indicator of increased risk of this cancer, which may require some time to assimilate after initial uncertainty about the implications of risk information obtained from genetic testing. For premenopausal women, the uncertainty and decision conflict around RRSO may be related to how the surgery may affect quality of life (e.g., menopausal symptoms and sexual functioning) and how to manage the potential side effects of the surgery, including the appropriateness of hormone therapy. These data suggest that genetic counselors could be proactive in eliciting these concerns and facilitating appropriate follow-up and support for these patients.

This study has several limitations. First, as a cross-sectional analysis of intentions, it is important to extend these findings to prospectively evaluate predictors of uptake of these surgeries. Although intentions may change after participants receive their test results, previous research suggests that post-counseling attitudes are significant predictors of actual uptake of risk-reducing surgery [21]. Second, given the study's 53% participation rate, caution must be taken in generalizing these findings. Third, this study includes participants who had recently been diagnosed with breast cancer, breast cancer survivors, and unaffected women. Further, we included both probands (i.e., first person in family to be tested) as well as individuals from families in which a pathogenic variant had previously been identified. The content of pretest genetic counseling, including discussions of risk-reducing surgery options, differs somewhat for these groups. Our sample size precluded examination of differences in predictors of risk-reducing surgery intentions across these groups, but this remains a question for future research. Fourth, although we focused on surgical intentions surrounding the identification of a *BRCA* pathogenic variant (by far the most commonly mutated genes in this population), about 85% of our participants had broader multigene panel testing. We did not evaluate prophylactic surgery intentions associated with genetic mutations other than *BRCA1* and *BRCA2*. Additionally, due to participant burden considerations, we did not assess a number of variables that may have predicted intentions. For example, we did not assess physician recommendation for surgery despite prior evidence suggesting that it is a predictor of surgical decisions [47]. Finally, while we were guided in part by the HBM, we did not assess all HBM components and instead added an assessment of affective and decision-making factors that are not part of the HBM. A more complete assessment of HBM variables might have yielded additional associations that could have altered our conclusions.

Despite these limitations, the data reported here provide support for the role of genetic counseling in fostering informed risk management decisions. Participant attitudes were the strongest and most consistent predictors of both RRM and RRSO intentions. This contrasts with studies of pre-counseling intentions in which negative affect is a more important predictor [17]. It is certainly possible that affective factors will reemerge as important predictors among women who learn that they carry a mutation. However, it is reassuring that following genetic counseling, patients' intentions appear to be broadly consistent with their preferences. Finally, these data suggest that the role of uncertainty should be further explored. Decision conflict and ambiguity aversion were inversely associated with intentions. Although it has already been established that additional decision support can reduce decision conflict and aid decision-making in the genetic testing context [13], future research should evaluate the role of ambiguity aversion and specific forms of uncertainty following the receipt of test results to determine whether additional support is required.

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Compliance with Ethical Standards

Conflict of Interest: Ms. M.K. Ladd, Ms. B.N. Peshkin, Ms. S. Baldinger, Dr. C. Isaacs, Ms. H. Segal, Ms. S. Philip, Ms. C. Phillips, Ms. K. Shane, Ms. A. Martin, Ms. V. Weinstein, Mr. R. Pilarski, Dr. J. Jeter, Mr. K. Sweet, Ms. B. Hatten, Ms. E.J. Wurtmann, Ms. S. Phippen, Ms. D. Bro, and Dr. M.D. Schwartz report no conflicts of interest. Ms. L. Senter has received honoraria from Ambry Genetics for a presentation at a sponsored conference unrelated to the content of this study. Ms. L. Senter is also a consultant for Astra Zeneca focused in the genetic testing and PARP inhibitor therapy in ovarian cancer patients; this topic is unrelated to the content of this study.

Authors' Contributions: Ms. B.N. Peshkin, Dr. C. Isaacs and Dr. M.D. Schwartz conceived and designed the study. Ms. L. Senter and Ms. S. Baldinger contributed to the study design. Ms. L. Senter, Ms. S. Baldinger, Dr. C. Isaacs, Ms. C. Phillips, Ms. K. Shane, Ms. A. Martin, Ms. V. Weinstein, Mr. R. Pilarski, Dr. J. Jeter, Mr. K. Sweet, Ms. B. Hatten, Ms. E.J.Wurtmann., Ms. S. Philip and Ms. D. Bro recruited study participants. Ms. M.K. Ladd, Ms. H. Segal, and Ms. S. Philip collected data. Ms. M.K. Ladd and Dr. M.D. Schwartz performed data analysis. All authors contributed to the writing of this manuscript.

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

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