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Research Article

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Genetic Testing in a Population-Based Sample of Breast and Ovarian Cancer Survivors from the REACH Randomized Trial: Cost Barriers and Moderators of Counseling Mode

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Abstract

Background: This study evaluates predictors of *BRCA1/2* testing among breast and ovarian cancer survivors who received genetic counseling as part of a randomized trial and evaluates moderators of counseling mode on testing uptake.

Methods: Predictors of *BRCA1/2* testing within one year post-counseling were evaluated using multivariable logistic regression in a population-based sample of breast and ovarian cancer survivors at increased hereditary risk randomly assigned to in-person counseling (IPC; $n = 379$) versus telephone counseling (TC; $n = 402$). Variables that moderated the association between counseling mode and testing were identified by subgroup analysis.

Results: Testing uptake was associated with higher perceived comparative mutation risk [OR = 1.32; 95% confidence interval (CI), 1.11–1.57] in the adjusted analysis. Those without cost barriers had higher testing uptake (OR = 18.73; 95% CI, 7.09–49.46). Psychologic distress and perceived comparative mutation risk moderated the effect of counseling and testing. Uptake between IPC versus TC did not differ at low levels of distress and risk, but differed at high distress (26.3% TC vs. 44.3% IPC) and high perceived comparative risk (33.9% TC vs. 50.5% IPC).

Conclusions: Cost concerns are a strong determinant of testing. Differences in testing uptake by counseling mode may depend on precounseling distress and risk perceptions.

Impact: Cost concerns may contribute to low testing in population-based samples of at-risk cancer survivors. Precounseling psychosocial characteristics should be considered when offering in-person versus telephone counseling. *Cancer Epidemiol Biomarkers Prev; 26(12); 1772–80. ©2017 AACR.*

Introduction

For breast and ovarian cancer survivors at increased risk for having *BRCA1/2* mutations (1), genetic testing can personalize treatment, estimate the risk of new cancers, and inform risk management and discussions with family members. Population-based studies suggest that less than 60% of breast and ovarian cancer survivors at increased risk for a *BRCA1/2* mutation undergo genetic testing (2–6). Much of our understanding of the factors associated with genetic testing decisions comes from studies of healthy at-risk individuals or cancer survivors self-referred to genetics clinics where testing uptake is high (2, 7). Existing population-based studies have focused on access and clinical factors (e.g., cost barriers, age of diagnosis; refs. 4, 8), yet the potential psychosocial (e.g., individual distress, social support, informed decision-making) and treatment implications (e.g., prophylactic surgery) of testing may also be salient concerns.

The psychosocial and treatment-related complexity of genetic testing is part of why genetic counseling is a standard of care for survivors at increased risk (1); however, only 40%–50% of survivors who meet the guidelines for a genetics referral are referred to or receive genetic counseling (4, 8). To address access barriers, genetic counselors are increasingly using alternative counseling delivery methods, such as telephone-based counseling (9). Our randomized controlled noninferiority trial of in-person versus telephone-based genetic counseling for breast and ovarian cancer survivors at increased hereditary cancer risk, the Risk Education and Assessment for Cancer Heredity (REACH) trial, found that telephone-based counseling was noninferior on key patient-reported outcomes such as distress and decisional satisfaction (5, 10). A secondary aim of the REACH trial was to examine factors associated with genetic testing decisions. However, genetic testing uptake in REACH

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Note: Clinical Trial registration ID: NCT01346761.

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was low overall (~30%), with lower testing uptake among survivors receiving telephone-based counseling (5, 10), suggesting the need to not only identify predictors of testing decisions, but also to determine whether in-person versus telephone-based counseling yielded different uptake depending on patient characteristics or patient perceptions of counseling.

To address the secondary aim of the trial, we evaluated psychosocial, clinical, and access factors in *BRCA1/2* testing decisions among breast and ovarian cancer survivors at increased hereditary cancer risk. We also evaluated moderators of the impact of in-person versus telephone-based genetic counseling on genetic testing uptake. This study addresses limitations of previous research by examining predictors from multiple domains in a population-based sample of cancer cases considered at increased risk for hereditary breast and ovarian cancer (HBOC) who received genetic counseling as part of a clinical trial and by evaluating patient perceptions of counseling in relation to testing decisions. Results are intended to inform the literature and care delivery on predictors of testing uptake in breast and ovarian cancer survivors at increased risk and advance research on who may be more or less likely to test if they receive in-person versus telephone-based counseling.

Hypotheses were guided by the Extended Parallel Process Model (EPPM; ref. 11) and the Ottawa Decision Support Framework (ODSF; ref. 12). When applied to genetic testing, the EPPM suggests that survivors who believe they are at increased risk for hereditary cancers may undergo genetic testing if they believe testing can help them manage risk. Therefore, we hypothesized that women with higher perceived risk of carrying a mutation, with more precounseling cancer-specific distress, and higher perceived personal control would be more likely to test, adjusting for other factors such as perceived cost barriers.

In the context of genetic counseling, the ODSF (12) suggests that patient-centered counseling helps patients assimilate complex information about testing, cancer risk, and medical management, addresses patient concerns, and increases personal control (13–17). We hypothesized that higher counselor patient-centeredness would predict higher testing uptake. We examined counseling-related variables and psychosocial variables as moderators of in-person versus telephone-based counseling based on prior literature suggesting differential responses to counseling methods (18–20).

Materials and Methods

Trial design and oversight

We describe the REACH trial in detail elsewhere (5, 10). Briefly, REACH was a family cluster randomized, two-group, equivalency/noninferiority trial comparing in-person to telephone counseling for women at high risk for *BRCA1/2* mutations (NCT01346761). Random assignment began in August 2010 and ended in September 2012 with one-year outcome assessments completed in February 2014. This study was conducted in accordance with the ethical guidelines outlined in the Belmont Report. The University of Utah and University of New Mexico Institutional Review Boards approved the study. All participants provided informed consent.

Participants

We used the Utah Population Database (21) to identify breast and ovarian cancer patients who were then recruited through the Utah Cancer Registry. Eligible women were between the ages of 25 and 74 years, living in Utah with telephone access, had a personal or family history suggestive of HBOC meeting National Comprehensive Cancer Network criteria for a referral to genetic counseling at the time of the study and were willing to travel to in-person counseling at the nearest of 14 clinics from 8 rural and 6 urban areas. Women with prior genetic counseling and/or *BRCA1/2* testing were excluded. Only women who completed pretest genetic counseling and had known testing information were included in this analysis to allow for tests of genetic counseling variables (see Fig. 1, CONSORT).

The interventions were telephone versus in-person genetic counseling [see Kinney and colleagues (5) for details on counseling sessions]. Counseling was delivered by five board-certified genetic counselors using a semistructured protocol, counselor checklists, and standard visual aids. Visual aids were used during the counseling sessions in both study arms. Those who received telephone counseling were mailed visual aids to view during the session. Regardless of counseling mode, counselors explored the emotional aspects of testing, including the impact of a personal cancer history and anticipated reactions to test results [see Kinney and colleagues (5)]. Following telephone counseling, women who chose to have genetic testing were mailed a saliva genetic testing kit with instructions and were then offered posttest counseling with the same genetic counselor who conducted their initial counseling session. Women counseled in person who chose to have genetic testing were given the option of giving a sample immediately following in-person counseling or taking home a test kit to send a sample later. The cost of genetic testing was not covered by the study; however, if cost was identified as a barrier to testing during the counseling sessions, counselors discussed financial assistance programs. Women were instructed to contact counselors if they encountered financial barriers to testing. Pre- and posttest sessions were conducted by the same genetic counselor. Intervention fidelity was assessed with review of 10% of randomly selected audiotapes of counseling sessions.

Data collection

Assessments occurred at prerandomization (i.e., baseline), 1 week after genetic counseling, and 12 months after the last counseling session. Factors hypothesized to potentially influence how a participant perceived counseling were assessed at baseline. Factors that reflected the counseling process (e.g., patient-centeredness, education about the cost of testing) were assessed 1 week after counseling. Genetic testing that occurred within 12 months of counseling was chosen to allow for women who may have needed more time to make a decision.

Measures

Testing decision outcome. Testing was defined as completion of testing within 12 months after the counseling session. The majority (92%) of the genetic testing was completed through the study with verified testing status through Myriad Laboratories.

Predictors. Psychosocial factors included precounseling cancer-specific distress [Impact of Event Scale (IES); $\alpha = 0.90$; ref. 22] and perceived risk of having a genetic mutation compared with other women their age (i.e., perceived comparative risk for a mutation; ref. 23). A score of 20 or above on the IES, which can range from 0–75, was considered clinically significant distress (22, 24). A risk score of 4 or 5 on the scale of 1–5 indicated that women perceived themselves to be at higher risk than other women their age.

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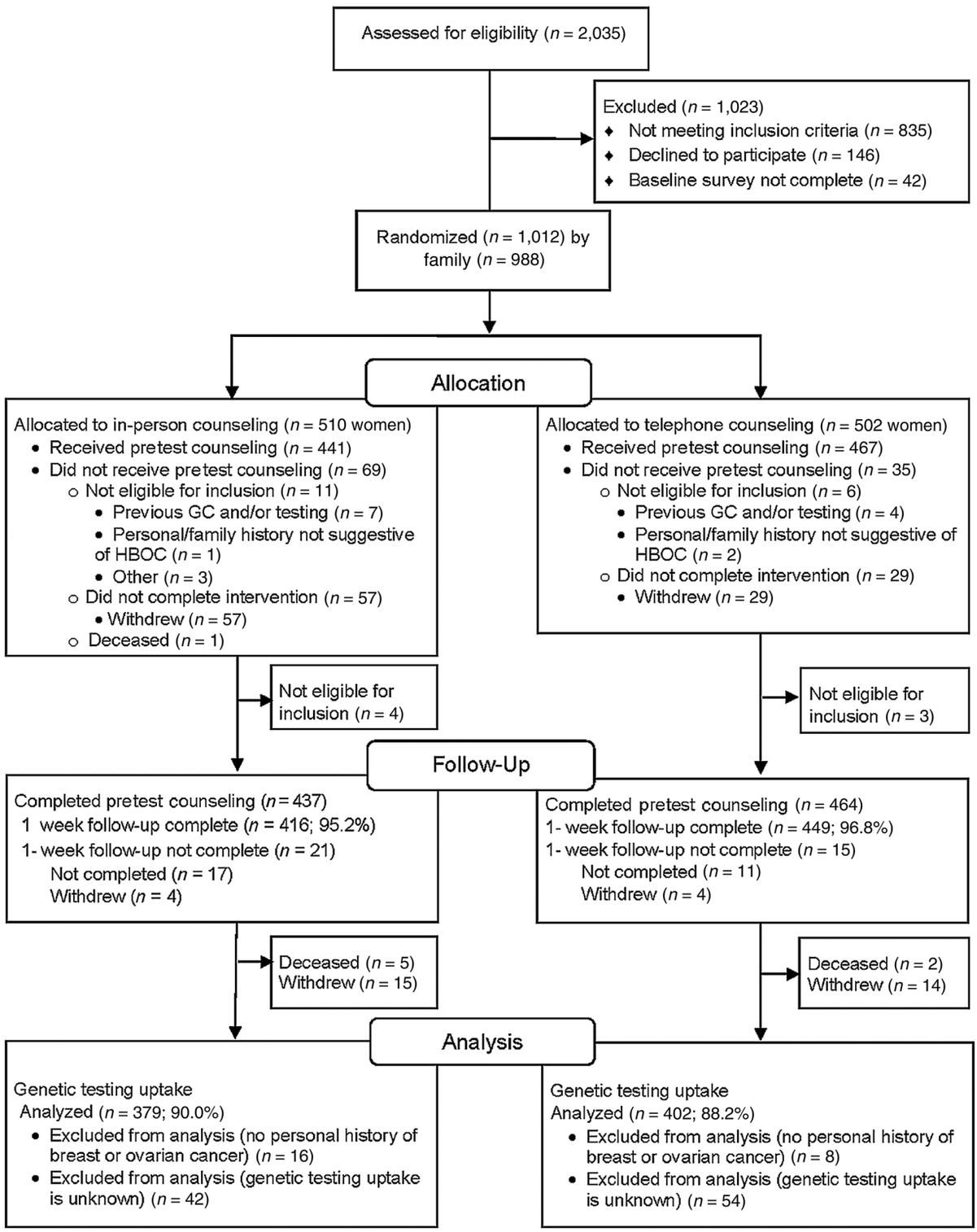

Figure 1.

Consolidated Standards of Reporting Trials (CONSORT) flowchart. GC, genetic counseling; HBOC, hereditary breast and ovarian cancer. CONSORT flow diagram depicting study recruitment and retention.

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Counseling factors were ascertained after the counseling session and included perceived personal control about the next steps, decisions, and information related to breast and/or ovarian cancer (Perceived Personal Control Questionnaire; $\alpha = 0.82$; ref. 25), and patients' ratings of the counselor's patient-centered communication (an adapted 13-item scale reflecting perceptions of their counselor's informativeness, interpersonal sensitivity, and partnership building; $\alpha = 0.90$; ref. 26).

Covariates. Covariates were selected for evaluation based on literature review (7, 8, 19, 20).

Sociodemographic factors included self-reported age, education, income, employment, marital status, and race/ethnicity. Clinical factors included personal cancer history and number of relatives affected by breast and ovarian cancer. Accessibility factors included rural/urban residence (27) and cost barriers. Cost barriers to testing, including lack of insurance coverage for the test, lack of insurance, fear of losing employment, or fear of losing health or life insurance, were assessed one week after genetic counseling with two questions asking about the main and other reasons why they had not yet tested. Response options included: desire to not know *BRCA* status, concerns about ability to cope with cancer risk, lack of insurance coverage for the test, lack of insurance, fear of losing employment, and fear of losing health or life insurance. Participants also had the option of listing other barriers to testing. "Other" responses were double-coded ($\kappa = 0.79$; 95% CI, 0.72–0.86). Cost barriers were divided into short-term (e.g., "Insurance will not cover the cost of the test") and long-term concerns (e.g., "Concerns about getting health or life insurance in the future").

Psychosocial factors included precounseling state anxiety (Brief Symptom Inventory-18; $\alpha = 0.90$; ref. 28), mental health (12-item SF-12v2™ Health Survey; $\alpha = 0.90$; ref. 29), physical health (12-item SF-12v2™ Health Survey; $\alpha = 0.88$; ref. 29), *BRCA1/2* knowledge (10-item adapted index representing the number of items correctly answered; ref. 30), and post-counseling social support (Interpersonal Support Evaluation List; $\alpha = 0.76$; ref. 31) and decisional conflict (Decisional Conflict Scale; $\alpha = 0.89$; ref. 32).

Statistical analysis

We restricted analysis to participants with known testing status. Bivariate association between a variable and testing uptake was assessed using simple logistic regression model. A multivariable logistic regression model was fitted using backward variable selection for a parsimonious model of the independent predictors of genetic testing uptake. The cluster effect of family (randomization unit) was insignificant based on a generalized linear mixed effects model ($P = 0.4$). Therefore, all analyses were conducted without the random effect of cluster.

Variables had to have a significance of $P < 0.10$ to be retained in the model (33). We chose this P value to assure that we retained potentially significant variables and accounted for confounders (33). Collinearity concerns among variables were evaluated using variance inflation factors (VIF) approach and not identified (i.e., the VIFs ~1). Bias-reducing penalized likelihood optimization was applied for logistic regression fitting (34). We included ORs per a half SD increase for continuous variables retained in the multivariable logistic model to aid their interpretation. For each putative moderator tested, an interaction of the counseling method (telephone vs. in-person) by the factor was added separately to the logistic regression model and tested. Moderators evaluated included cancer-specific distress, perceived risk of a genetic mutation compared to population risk, counselor patient-centeredness, cost barriers, decisional conflict, education, social support, and family history of cancer (18–20). Model goodness-of-fit was examined using the deviance test.

We conducted sensitivity analysis to compare results from those with known testing status ($n = 781$; per protocol) to those with known and unknown testing status ($n = 877$; intent-to-treat). We imputed 100 datasets to estimate genetic testing uptake among the 96 survivors with missing testing status using age, education, health care coverage status, breast cancer history, ovarian cancer history, baseline physical health, and baseline anxiety. All analyses were conducted using SAS version 9.4 (SAS Institute Inc.).

Results

Participants had a personal history of breast cancer ($n = 715$; 91.5%), ovarian cancer ($n = 63$, 8.1%), or both cancers ($n = 3$, 0.4%). The average age was 56.6 years ($SD = 7.7$ years). The majority had health insurance ($n = 761$, 97.4%) and an established health care provider ($n = 697$, 89.2%). The majority of the sample was non-Hispanic white (n = 738, 94.5%). A total of 241 (30.9%) women obtained testing. Cost represented 38.9% ($n = 142$) of the primary barriers to testing cited one week after genetic counseling. No one cited concern about losing employment as a primary barrier to testing, although 12 people cited concerns about losing health or life insurance or future insurability for themselves or their family as a primary barrier. Long-term cost concerns (which included concerns related to future insurability) were less common than out-of-pocket cost concerns (e.g., lack of insurance coverage for the test) that were endorsed by 17.7% of survivors (Table 1). Long-term cost concerns did not differ by income level ($\chi^2 = 2.30$; df = 3; $P = 0.51$). Short-term cost concerns differed by income level ($\chi^2 = 16.15$; df = 3; $P = 0.001$). Survivors earning \$50–69 K reported higher short-term cost concerns. Those earning between \$30–49 K and those earning between \$50–69 K had similar health insurance coverage ($\chi^2 = 0.14$; df = 1; $P = 0.712$). Survivors earning at least \$50 K were more likely to have a college degree ($\chi^2 = 56.21$; df = 3; $P < 0.0001$).

Independent focal predictors of testing uptake

After adjusting for other independent variables, testing uptake was associated with higher cancer-specific distress (OR = 1.01; 95% CI, 1.002–1.03; equivalent to $OR_{0.5\ SD} = 1.11$; 95% $CI_{0.5\ SD}$ = 1.01–1.21) and perceived comparative risk (OR = 1.32; 95% CI, 1.11–1.57; equivalent to $OR_{0.5\ SD} = 1.16$; 95% $CI_{0.5\ SD}$ = 1.06–1.28; Table 2). Cancer-specific distress and perceived comparative risk were not considerably linearly correlated ($r = 0.08$; 95% CI, 0.01–0.15).

Testing was also independently associated with lower ratings of counselor patient-centeredness (OR = 0.45; 95% CI, 0.30–0.68; equivalent to $OR_{0.5\ SD} = 0.83$; 95% $CI_{0.5\ SD} = 0.75$–0.91). Cost barriers exhibited the largest effect on testing uptake. Testing uptake was independently associated with the absence of short-term cost barriers (OR = 18.73; 95% CI, 7.09–49.46) and long-term cost barriers (OR = 6.64; 95% CI, 1.15–38.41; Table 2).

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Table 1. Descriptive statistics and bivariate analysis of genetic testing uptake

	(*N* = 781)		
Primary variables of interest	***Mean (SD)*/N (%)**	**OR (95% CI)[a]**	***P***
Precounseling cancer distress[b]	*15.18 (14.24)*	1.01 (1.00–1.02)	0.051
Precounseling perceived comparative risk[c]	*2.99 (1.10)*	1.42 (1.23–1.63)	<0.0001
Perceptions of patient centeredness	*4.25 (0.48)*	0.80 (0.58–1.11)	0.179
Perceived personal control	*1.55 (0.36)*	1.14 (0.74–1.77)	0.542
Covariates			
Decisional conflict	*27.90 (13.39)*	0.97 (0.96–0.98)	<0.0001
Social support	*8.53 (1.91)*	0.93 (0.86–1.00)	0.061
Age	*56.58 (7.71)*	1.02 (1.00–1.04)	0.063
Anxiety	*2.65 (2.99)*	1.00 (0.95–1.05)	0.920
Physical health	*49.79 (9.05)*	0.99 (0.97–1.00)	0.106
Mental health	*51.25 (8.92)*	0.99 (0.97–1.01)	0.307
Knowledge	*7.05 (1.44)*	1.08 (0.97–1.21)	0.153
Intervention			
In-person (ref.)	379 (48.53)		
Telephone	402 (51.47)	0.68 (0.50–0.92)	0.013
Short-term cost concerns			
Yes (ref.)	138 (17.67)		
No	643 (82.33)	17.46 (6.71–45.43)	<0.0001
Long-term cost concerns			
Yes (ref.)	27 (3.46)		
No	754 (96.54)	8.26 (1.54–44.43)	0.014
Relatives with breast or ovarian cancer			
0 FDR/SDR (ref.)	411 (52.62)		0.0001
1 FDR/SDR	216 (27.66)	1.55 (1.08–2.22)	
≥2 FDR/SDR	154 (19.72)	2.27 (1.54–3.35)	
Residence			
Urban (ref.)	658 (84.25)		0.019
Rural	123 (15.75)	1.61 (1.08–2.40)	
Marital status			
Not married (ref.)	151 (19.33)		0.773
Married	630 (80.67)	1.06 (0.72–1.56)	
Education			
High school or less (ref.)	166 (21.25)		0.939
Some college	287 (36.75)	1.00 (0.66–1.51)	
Bachelor's or more	328 (42.00)	0.95 (0.63–1.42)	
Income ($)			
≤29,999 (ref.)	86 (11.44)		0.153
30,000–49,999	148 (19.68)	0.68 (0.38–1.20)	
50,000–69,999	145 (19.28)	0.57 (0.32–1.01)	
≥70,000	373 (49.60)	0.86 (0.53–1.41)	

Abbreviations: FDR, first-degree relative; ref, reference group; SDR, second-degree relative.
[a]ORs per one-point increase on continuous scales.
[b]Observed scores ranged 0–63 on scale of 0–75.
[c]Scale ranged from 1–5; 3 = perceived "the same" risk as other women their age.

Results with imputed data were consistent with results from known testing outcomes.

Moderators of counseling

Precounseling cancer distress and perceived comparative risk of an inherited gene mutation modified the effect of the type of counseling and completion of genetic testing ($P = 0.003$, $P = 0.038$, respectively, for the interaction effect). For clinical interpretation, precounseling cancer-specific distress was plotted at values indicative of clinically significant distress (20 or above) and perceived comparative risk of a genetic mutation was plotted at values indicating high versus average or lower perceived risk.

Among survivors at clinically significant levels of cancer distress, 26.3% of survivors who received telephone-counseling tested compared with 44.3% of those who received in-person counseling (OR = 0.45; 95% CI, 0.27–0.76; Fig. 2). In contrast, among those with lower levels of distress, 27.0% tested after telephone-counseling compared with 30% after in-person counseling (OR = 0.86; 95% CI, 0.59–1.26; Fig. 2). Among survivors who believed that they were at higher risk for a genetic mutation compared with other women their age, 33.9% of those who received telephone-counseling tested compared with 50.5% of those who received in-person counseling (OR = 0.50; 95% CI, 0.29–0.87; Fig. 3). In contrast, among survivors who believed they had the same or lower risk for a mutation compared with other women their age, 23.8% tested who received telephone counseling compared with 29.8% who received in-person counseling (OR = 0.74; 95% CI, 0.51–1.07; Fig. 3).

Education was of marginal significance as a moderator of counseling mode and genetic testing uptake ($P = 0.055$). Those with a high school education or lower appeared less likely to test if they received telephone-counseling compared with in-person counseling (OR = 0.23; 95% CI, 0.11–0.50), whereas testing uptake by counseling mode did not differ among those with some college (OR = 0.66; 95% CI, 0.37–1.17) or a bachelor's degree or more (OR = 0.68; 95% CI, 0.40–1.17). No other

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Table 2. Multivariable predictors of genetic testing uptake

	(*N* = 781[a])			
Primary variables of interest	***Mean (SD)*/N (%)**	**OR (95% CI)[b]**	**$OR_{0.5\ SD}$[c] (95% $CI_{0.5\ SD}$)**	***P***
Precounseling cancer distress	*15.18 (14.24)*	1.01 (1.002–1.03)	1.11 (1.01–1.21)	0.026
Precounseling perceived comparative risk	*2.99 (1.10)*	1.32 (1.11–1.57)	1.16 (1.06–1.28)	0.002
Perceptions of patient-centeredness	*4.25 (0.48)*	0.45 (0.30–0.68)	0.83 (0.75–0.91)	0.0001
Covariates				
Residence				
Urban (ref.)	658 (84.25)			0.057
Rural	123 (15.75)	1.57 (0.99–2.49)		
Relatives with breast or ovarian cancer				
0 FDR/SDR (ref.)	411 (52.62)			0.010
1 FDR/SDR	216 (27.66)	1.45 (0.96–2.21)		
≥2 FDR/SDR	154 (19.72)	2.09 (1.29–3.40)		
Intervention				
In-person (ref.)	379 (48.53)			
Telephone	402 (51.47)	0.53 (0.37–0.76)		0.0005
Short-term cost concerns				
Yes (ref.)	138 (17.67)			
No	643 (82.33)	18.73 (7.09–49.46)		<0.0001
Long-term cost concerns				
Yes (ref.)	27 (3.46)			
No	754 (96.54)	6.64 (1.15–38.41)		0.034
Social support	*8.53 (1.91)*	0.90 (0.82–0.99)	0.91 (0.83–0.99)	0.035
Decisional conflict	*27.9 (13.39)*	0.95 (0.94–0.97)	0.72 (0.65–0.80)	<0.0001

Abbreviations: FDR, first-degree relative; ref., reference group; SDR, second-degree relative.
[a]Model shows estimates after adjustment for other variables.
[b]ORs per one-point increase on the scale for continuous variables.
[c]Equivalent ORs and 95% CI per 0.50 SD increase in continuous variables; provided to aid clinical interpretation. Categorical ORs and 95% CI estimates remain the same as footnote "b".
The goodness of fit of this model indicated adequate model fit ($P = 0.43$).

moderators were significant, including family cancer history which was moderately correlated (polyserial correlation = 0.45; $P < 0.001$) with precounseling perceived comparative risk for a genetic mutation.

Discussion

This article examined predictors of genetic testing uptake among a population-based sample of breast and ovarian cancer survivors at increased risk for HBOC who received either telephone or in-person genetic counseling as part of a randomized controlled trial. Our data show that women without cost barriers to testing are more likely to complete genetic testing. Findings suggest that survivors entering counseling with high cancer distress or high perceived comparative risk for a mutation may respond differently to telephone versus in-person counseling, and indicate that more patient-centered counseling may yield lower testing uptake.

From a policy perspective, results highlight the importance of addressing cost barriers to testing. Long-term cost concerns did not differ by income. Short-term cost concerns were similar across incomes with the exception of those earning between $50,000–$69,000 a year who were more likely to report short-term cost concerns as a barrier. This income bracket and above was

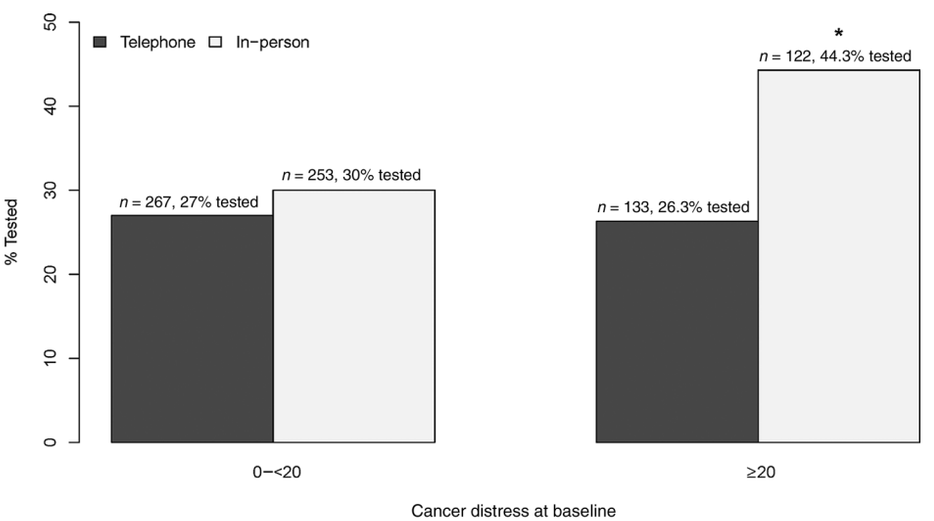

Figure 2.
Clinically significant precounseling cancer distress modifies counseling method's effect on testing uptake. *, statistically significant difference observed. A score of 20 or above was considered clinically significant. Among survivors at clinically significant levels of cancer distress, 26.3% of survivors who received telephone counseling tested compared with 44.3% of those who received in-person counseling (OR = 0.45; 95% CI, 0.27–0.76).

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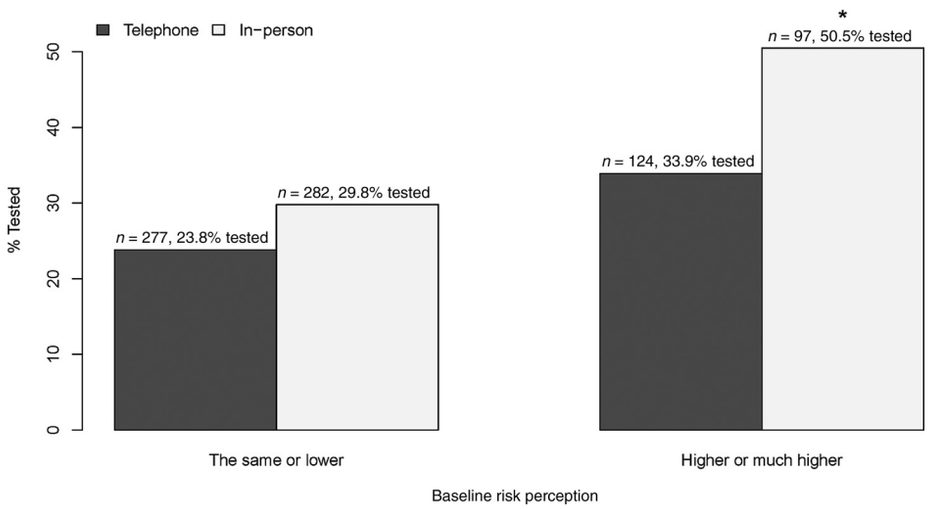

Figure 3.
High baseline precounseling perceived comparative risk of inherited gene mutation modifies counseling method's effect on testing uptake. *, statistically significant difference observed. Among survivors who believed that they were at higher risk for a genetic mutation compared with other women their age, 33.9% of those who received telephone counseling tested compared with 50.5% of those who received in-person counseling (OR = 0.50; 95% CI, 0.29–0.87).

more likely to be college educated, but had similar insurance coverage as those earning $30,000–$49,000. They may have been an educated group of women more used to consuming health information compared with those earning less than them who were less likely to have a college degree. Thus, financial strain from testing and indicated procedures may have been a more salient barrier to testing compared to other factors such as its perceived lack of benefit for managing health.

At the time our study was conducted, the cost of *BRCA* sequencing was over $3,000 (35). The cost of testing has dropped due to the Supreme Court's ruling on *BRCA* patenting (36). *BRCA* sequencing is now available for less than $300 (37). Most insurance companies cover the cost of *BRCA* testing for populations indicated by the National Comprehensive Cancer Network guidelines (38). Many genetic testing laboratories provide financial assistance programs for uninsured and underinsured individuals. However, coverage varies for multi-gene panel testing (39) and for preventative services (e.g., prophylactic surgery, surveillance magnetic resonance imaging) following a positive test, which places some survivors at risk of being able to afford the cost of a test itself, but unable to afford and benefit from the interventions indicated by the test (40). These concerns are compounded by the uncertain future of the Affordable Care Act, the repeal of which would disparately affect subgroups of the population with known disparities accessing and utilizing genetic services and associated preventative services (16, 41). Yet a priority of the national Precision Medicine Initiative is to address insurance coverage to enable access to genomic discoveries and guideline-concordant genetic care delivery (42).

This study has implications for the practice of genetic counseling. Our moderation analysis results suggest that survivors who enter counseling with high levels of cancer-specific distress or high perceived comparative risk for a mutation will be more likely to test if they receive in-person counseling and less likely to test if they receive telephone counseling. Counselor response to nonverbal cues of distress exhibited by survivors may have magnified the effects of precounseling cancer-specific distress and perceived comparative risk for a mutation by prompting more discussion about the perceived threat of cancer and carrying a mutation. In contrast, unaddressed nonverbal cues of distress may have impeded information exchange or discussion of distress as a barrier to testing in telephone-counseling. Research should evaluate patient–counselor interactions [e.g., linguistic analysis for counselor and survivor affective word use (43), session length, survivor question frequency, etc.] to understand the function of distress and perceived comparative risk in these counseling delivery methods.

Moderation results suggest that survivors with a high school education or less may be less likely to test if they receive telephone counseling than if they receive in-person counseling. This result must be interpreted cautiously, as it was of only borderline statistical significance. The logistics of sending in a sample may have been more of a barrier for this subgroup. Alternatively, even though visual aids were used in both in-person and telephone-based counseling, those with less education in telephone counseling may have had more difficulty understanding material presented or had undetected questions about the information. Future research should examine whether those with lower educational attainment and health literacy show smaller knowledge gains after telephone counseling than in-person counseling. Additional materials (e.g., computer-based modules) to supplement telephone counseling or additional assistance overcoming logistical barriers to testing may be useful for those with less education.

The relation between higher patient-centeredness ratings and lower testing uptake in this study was unexpected. However, patient-centered care focused on the unique needs and preferences of a survivor given their family history, risk perception, knowledge, and stated concerns. Thus, a patient-centered approach may have yielded higher or lower testing uptake to the extent that counseling reflected a patient's readiness for testing. Survivors who were ambivalent about testing may have felt supported by their counselor to not rush a testing decision. In contrast, those who were further in the decision process may have received more directive counseling that addressed specific barriers. Similarly, a patient-centered focus might have allowed survivors at lower risk to feel comfortable declining testing. Research on the patient–counselor interaction is needed to better understand this counterintuitive result.

Limitations

Generalizability is limited by population characteristics of mostly non-Hispanic white women with relatively high income

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and education levels from one geographic area. Ethnic minorities and those with lower socioeconomic status face substantial disparities in genetic counseling and testing and may have additional factors that influence testing decisions (3). We did not assess the extent to which survivors discussed genetic counseling and testing with their family, friends, or health care providers, or the nature of those interactions. Finally, this study was conducted before the use of multigene panel testing. Certain psychosocial factors (e.g., concern about discovering unexpected positive results and secondary findings) may be more salient with adoption of multigene panel testing and whole genome sequencing.

Conclusion

The study's findings suggest that cost concerns are critical in testing decisions among survivors at risk for HBOC who receive genetic counseling. Our findings further suggest that telephone counseling, while improving access to qualified genetic counselors, may yield lower testing uptake among survivors who enter counseling with clinically significant cancer-specific distress or high perceived comparative risk for a mutation. In-person counseling may be indicated for survivors with elevated cancer distress or high perceived comparative risk for a mutation. Screening for psychosocial concerns, including distress, could help allocate in-person resources. Alternatively, counselors may consider the use of videotechnology or consider screening for psychosocial issues, including distress, prior to delivering telephone-based counseling to inform counseling (44). Research should examine if there are differential effects of video-enabled versus audio alone technologies among diverse populations and counselor–patient interactions during genetic counseling sessions to better understand the effect of cancer distress, perceived comparative risk for mutations, and counselor–patient centeredness during counseling.

Disclosure of Potential Conflicts of Interest

A. Gammon is a consultant/advisory board member for Invitae. No potential conflicts of interests were disclosed by the other authors.

Disclaimer

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References

1. Daly MB, Pilarski R, Axilbund JE, Berry M, Buys SS, Crawford B, et al. Genetic/familial high-risk assessment: breast and ovarian, version 2.2015. J Natl Compr Canc Netw 2016;14:153–62.
2. Ropka ME, Wenzel J, Phillips EK, Siadaty M, Philbrick JT. Uptake rates for breast cancer genetic testing: a systematic review. Cancer Epidemiol Biomarkers Prev 2006;15:840–55.
3. Levy DE, Byfield SD, Comstock CB, Garber JE, Syngal S, Crown WH, et al. Underutilization of *BRCA1/2* testing to guide breast cancer treatment: Black and Hispanic women particularly at risk. Genet Med 2011;13:349–55.
4. Kurian AW, Griffith KA, Hamilton AS, Ward KC, Morrow M, Katz SJ, et al. Genetic testing and counseling among patients with newly diagnosed breast cancer. JAMA 2017;317:531–4.
5. Kinney AY, Butler KM, Schwartz MD, Mandelblatt JS, Boucher KM, Pappas LM, et al. Expanding access to *BRCA1/2* genetic counseling with telephone delivery: A cluster randomized trial. J Natl Cancer Inst 2014;106:djv328.
6. Cragun D, Weidner A, Lewis C, Bonner D, Kim J, Vadaparampil ST, et al. Racial disparities in *BRCA* testing and cancer risk management across a population-based sample of young breast cancer survivors. Cancer 2017;123:2497–505.
7. Sweeny K, Ghane A, Legg AM, Huynh HP, Andrews SE. Predictors of genetic testing decisions: a systematic review and critique of the literature. J Genet Couns 2014;23:263–88.
8. Cragun D, Bonner D, Kim J, Akbari MR, Narod SA, Gomez-Fuego A, et al. Factors associated with genetic counseling and *BRCA* testing in a population-based sample of young Black women with breast cancer. Breast Cancer Res Treat 2015;151:169–76.
9. Cohen SA, Marvin ML, Riley BD, Vig HS, Rousseau JA, Gustafson SL. Identification of genetic counseling service delivery models in practice: a report from the NSGC Service Delivery Model Task Force. J Genet Couns 2013;22:411–21.
10. Kinney AY, Steffen LE, Brumbach BH, Kohlmann W, Du R, Lee JH, et al. Randomized noninferiority trial of telephone delivery of *BRCA1/2* genetic counseling compared with in-person counseling: 1-Year follow-up. J Clin Oncol 2016;34:2914–24.

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11. Maloney EK, Lapinski MK, Witte K. Fear appeals and persuasion: a review and update of the Extended Parallel Process Model. Social and Personality Psychology Compass 2011;5:206–19.
12. Durand M-A, Stiel M, Boivin J, Elwyn G. Where is the theory? Evaluating the theoretical frameworks described in decision support technologies. Patient Educ Couns 2008;71:125–35.
13. O'Connor AM, Jacobsen MJ, Stacey D. An evidence-based approach to managing women's decisional conflict. J Obstet Gynecol Neonatal Nurs 2002;31:570–81.
14. Ormond KE. From genetic counseling to "genomic counseling." Mol Genet Genomic Med 2013;1:189–93.
15. Pieterse AH, Ausems MGEM, Van Dulmen AM, Beemer FA, Bensing JM. Initial cancer genetic counseling consultation: change in counselees' cognitions and anxiety, and association with addressing their needs and preferences. Am J Med Genet Assoc 2005;137A:27–35.
16. Cragun D, Kinney AY, Pal T. Care delivery considerations for widespread and equitable implementation of inherited cancer predisposition testing. Expert Rev Mol Diagn 2017;17:57–70.
17. Skirton H. The client's perspective of genetic counseling-a grounded theory study. J Genet Couns 2001;10:311–29.
18. Anderson B, McLosky J, Wasilevich E, Lyon-Callo S, Duquette D, Copeland G. Barriers and facilitators for utilization of genetic counseling and risk assessment services in young female breast cancer survivors. J Cancer Epidemiol 2012;2012:11.
19. Butrick M, Kelly S, Peshkin BN, Luta G, Nusbaum R, Hooker GW, et al. Disparities in uptake of *BRCA1/2* genetic testing in a randomized trial of telephone counseling. Genet Med 2015;17:467–75.
20. Gooding HC, Organista K, Burack J, Biesecker BB. Genetic susceptibility testing from a stress and coping perspective. Soc Sci Med 2006;62:1880–90.
21. Cannon-Albright LA, Thomas A, Goldgar DE, Gholami K, Rowe K, Jacobsen M, et al. Familiality of cancer in Utah. Cancer Res 1994;54:2378–85.
22. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. Psychosom Med 1979;41:209–18.
23. Gurmankin Levy A, Shea J, Williams SV, Quistberg A, Armstrong K. Measuring perceptions of breast cancer risk. Cancer Epidemiol Biomarkers Prev 2006;15:1893–8.
24. Bleiker EMA, Pouwer F, van der Ploeg HM, Leer J-WH, Adèr HJ. Psychological distress two years after diagnosis of breast cancer: frequency and prediction. Patient Educ Couns 2000;40:209–17.
25. Smets EM, Pieterse AH, Aalfs CM, Ausems MG, van Dulmen AM. The Perceived Personal Control (PPC) questionnaire as an outcome of genetic counseling: reliability and validity of the instrument. Am J Med Genet A 2006;140:843–50.
26. Epstein RM, Street RL Jr. Patient-centered communication in cancer care: Promoting healing and reducing suffering; National Cancer Institute, NIH Publication No. 07-6225. 2007. Available from: https://healthcaredelivery.cancer.gov/pcc/monograph.html.
27. University of Washington Rural Health Research Center. Rural-urban commuting area codes (Version 2.0); 2006. Available from: http://depts.washington.edu/uwruca/.
28. Derogatis LR. Brief Symptom Inventory 18: administration, scoring, and procedures manual. Minneapolis, MN: NCS Pearson, Inc.; 2000.
29. Ware J Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: Construction of scales and preliminary tests of reliability and validity. Med Care 1996;34:220–33.
30. Wang C, Gonzalez R, Milliron KJ, Strecher VJ, Merajver SD. Genetic counseling for *BRCA1/2*: a randomized controlled trial of two strategies to facilitate the education and counseling process. Am J Med Genet A 2005;134a:66–73.
31. Cohen S, Mermelstein R, Kamarck T, Hoberman HM. Measuring the functional components of social support. In: Sarason IG, Sarason BR, editors. Social support: theory, research and applications. Dordrecht, the Netherlands: Springer; 1985. p. 73–94.
32. O'Connor AM. Validation of a decisional conflict scale. Med Decis Making 1995;15:25–30.
33. Bursac Z, Gauss CH, Williams DK, Hosmer DW. Purposeful selection of variables in logistic regression. Source Code Biol Med 2008;3:17.
34. Firth D. Bias reduction of maximum likelihood estimates. Biometrika 1993;80:27–38.
35. Chang Y, Near AM, Butler KM, Hoeffken A, Edwards SL, Stroup AM, et al. ReCAP: Economic evaluation alongside a clinical trial of telephone versus in-person genetic counseling for *BRCA1/2* mutations in geographically underserved areas. J Oncol Pract 2016;12:59.
36. Cook-Deegan R, Niehaus A. After myriad: genetic testing in the wake of recent Supreme Court decisions about gene patents. Curr Genet Med Rep 2014;2:223–41.
37. Color Test. Available from: https://getcolor.com/kit/how-it-works.
38. Clain E, Trosman JR, Douglas MP, Weldon CB, Phillips KA. Availability and payer coverage of *BRCA1/2* tests and gene panels. Nat Biotechnol 2015;33:900–2.
39. Curnutte MA, Frumovitz KL, Bollinger JM, McGuire AL, Kaufman DJ. Development of the clinical next-generation sequencing industry in a shifting policy climate. Nat Biotechnol 2014;32:980–2.
40. Prince AER. Prevention for those who can pay: insurance reimbursement of genetic-based preventive interventions in the liminal state between health and disease. J Law Biosci 2015;2:365–95.
41. Karaca-Mandic P, Jena AB, Ross JS. Health and health care use among individuals at risk to lose health insurance with repeal of the Affordable Care Act. JAMA Intern Med 2017;177:590–3.
42. Trosman JR, Weldon CB, Douglas MP, Kurian AW, Kelley RK, Deverka PA, et al. Payer coverage for hereditary cancer panels: barriers, opportunities, and implications for the Precision Medicine Initiative. J Natl Compr Canc Netw 2017;15:219–28.
43. Kelly KM, Ellington L, Schoenberg N, Jackson T, Dickinson S, Porter K, et al. Genetic counseling content: how does it impact health behavior? J Behav Med 2015;38:766–76.
44. Eijzenga W, Bleiker EMA, Hahn DEE, Kluijt I, Sidharta GN, Gundy C, et al. Psychosocial aspects of hereditary cancer (PAHC) questionnaire: development and testing of a screening questionnaire for use in clinical cancer genetics. Psychooncology 2014;23:862–9.

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Genetic Testing in a Population-Based Sample of Breast and Ovarian Cancer Survivors from the REACH Randomized Trial: Cost Barriers and Moderators of Counseling Mode

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