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## Factors Associated with Interest in Gene-Panel Testing and Risk Communication Preferences in Women from *BRCA1/2* Negative Families

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### Abstract

Scientific advances have allowed the development of multiplex gene-panels to assess many genes simultaneously in women who have tested negative for *BRCA1/2*. We examined correlates of interest in testing for genes that confer modest and moderate breast cancer risk and risk communication preferences for women from *BRCA* negative families. Female first-degree relatives of breast cancer patients who tested negative for *BRCA1/2* mutations (N= 149) completed a survey assessing multiplex genetic testing interest and risk communication preferences. Interest in testing was high (70%) and even higher if results could guide risk-reducing behavior changes such as taking medications (79%). Participants preferred to receive genomic risk communications from a variety of sources including: primary care physicians (83%), genetic counselors (78%), printed materials (71%) and the web (60%). Factors that were independently associated with testing interest were: perceived lifetime risk of developing cancer (odds ratio (OR)=1.67; 95% confidence interval (CI) 1.06–2.65) and high cancer worry (OR=3.12; CI 1.28–7.60). Findings suggest that women from *BRCA1/2* negative families are a unique population and may be primed for behavior change. Findings also provide guidance for clinicians who can help

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#### Conflicts of Interest

Authors Kristina Flores, Laurie Steffen, Christopher McLouth, Belinda Vicuna, Amanda Gammon, Lucretia Vigil, Zoneddy Dayao, Melanie Royce, and Anita Kinney have no conflict of interest.

#### Compliance with Ethical Standards

##### Human Studies and Informed Consent

All procedures followed were in accordance with the ethical standards of University of Utah on human experimentation and with the 1964 Helsinki declaration and it later amendments or comparable ethical standards. Informed consent was obtained from all participants included in the study.

#### Animal Studies

No animal studies were carried out by the authors for this article.

develop genomic risk communications, promote informed decision making and customize behavioral interventions.

### Keywords

Gene-panel; genetic testing; *BRCA1/2* negative; hereditary breast cancer; informed decision-making

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## INTRODUCTION

The translation of genetic information is at the forefront of cancer prevention and control and is especially relevant for women at high risk for Hereditary Breast and Ovarian Cancer (HBOC). When HBOC is suspected, genetic testing for mutations in the *BRCA1/2* breast cancer susceptibility genes is an evidence-based strategy that informs medical management options (e.g., prophylactic mastectomy and/or oophorectomy, tamoxifen therapy), helps women to make informed decisions about cancer prevention, and has been shown to improve patient survival when testing leads to risk reducing strategies (BradburyPatrick-Miller & Domchek, 2015). Genetic cancer information not only impacts the affected individual but also has clinical and psychosocial implications for family members. Without a prior family history of a *BRCA* mutation, a *BRCA* negative test result is “uninformative”, (other genetic mutations may contribute to cancer in the family), and the patient and their family members may have lingering concerns about their cancer risk, genetic testing options beyond *BRCA1* or *BRCA2*, or cancer prevention options (Kotsopoulos et al., 2014). Thus, strategies to improve genetic risk communication for *BRCA* negative families is an important emerging issue.

Until recently, genetic testing for HBOC focused mainly on assessing for mutations in *BRCA1/2*, but technological advances in DNA sequencing have made it possible to test multiple, even hundreds, of genes simultaneously using multiplex gene-panels (Desmond et al., 2015). Recent studies of the clinical utility of gene-panel testing for hereditary breast and ovarian cancer have found that gene-panel testing can identify actionable variants that would have otherwise gone undetected with *BRCA1/2* testing alone (Daly et al., 2016; Desmond et al., 2015; Lincoln et al., 2015). Newer research exploring the utilization of SNP panels (often in conjunction with other data including *BRCA1/2* and other high/moderate risk genes or breast density measurements) for breast cancer risk assessment in the general population further highlight how genetic testing considerations may become increasingly pertinent for unaffected women (Evans et al., 2012; Li et al., 2016; Mavaddat et al., 2015).

There is a broad range in the number of people reporting interest in genetic testing (28% to over 90%) in the general population and in high-risk individuals (Bottorff et al., 2002; Graves et al., 2011; Henneman et al., 2013; Hoberg-Vetti et al., 2016; Meisel et al., 2015; Ramirez et al., 2015; Sussner et al., 2011; Vermeulen et al., 2014). Studies vary widely based on the questions asked, the context of the genetic testing, and on population characteristics such as income, age, education, and country. Most recently, intense research and media attention have elevated public interest in genetic testing for HBOC (Evans et al., 2014; Lebo et al., 2015). Family members may believe that gene-panel testing can provide

more cancer risk information and cancer prevention options. In most cases, unaffected family members from *BRCA* negative families do not meet criteria for further cancer genetic testing ("National Comprehensive Cancer Network Guidelines Version 2.2016 Genetic/Familial High Risk Assessment: Breast and Ovarian,") nor is it likely their medical insurance covers genetic testing in this context. However, family members may ultimately desire genetic counseling and genetic testing to cope with lingering concerns. Thus, it is important to understand why relatives seek genetic testing, what they hope to gain from testing, and to provide them with relevant information to understand their risks and benefits in the context of the genetic evaluation that has already occurred in their family.

The increased availability of complex genomic information poses challenges to clinicians as well as patients. Medical professionals, who are tasked with interpreting test results for patients or family members, have concerns about gene-panels that include variants of unknown significance (VUS) and examine genes that have low clinical validity (i.e., how accurately the test predicts disease risk) and clinical utility (i.e., how useful the test is for medical decision-making) (Easton et al., 2015). Testing multiple genes simultaneously can lead to unanticipated results by revealing risks for other cancer syndromes or diseases. Inappropriate referrals for genetic testing are not uncommon (McCarthy et al., 2013; Teng et al., 2014; Trivers et al., 2011). Physicians report inappropriately referring average risk individuals for testing or failing to refer individuals that meet criteria for genetic testing (Trivers et al., 2011).

Multiple individual and system-level factors inform the decision to use gene-panel testing including clinic, socioeconomic, cognitive and emotional factors (BradburyPatrick-Miller & Domchek, 2015; Cragun et al., 2015; Easton et al., 2015; Powers et al., 2014). Given that the majority of women who undergo testing actually test negative for *BRCA1/2* mutations, it is important to understand attitudes toward multiplex testing and risk communication preferences among *BRCA1/2* negative family members. Although the individual with cancer is the most informative person to receive genetic testing in a high risk family, they may not be the first person in the family to become aware of additional genetic testing options. When the cause of cancer is unknown in a family, relatives without cancer may gravitate toward new tests to help clarify their own cancer risks and healthcare options. The importance of understanding individual attitudes and preferences in genetic testing is underscored by national initiatives, such as Precision Medicine (Collins et al., 2015), (which calls for assessing individual variability in genes, environment, and lifestyle to improve treatment and prevention healthcare decisions) and recommendations to incorporate genomic information into behavior change interventions (McBride et al., 2015). Precision medicine and health behavior change can potentially be realized without promoting unnecessary genetic testing by more effectively communicating genetic information to entire families.

Currently, we know very little about the perspectives of unaffected women from *BRCA1/2* negative families toward gene-panel testing and the most effective ways to communicate information about genetic testing to promote health behaviors (McBride et al., 2015). We address this gap by examining interest in and preferences for receiving information about gene-panel testing for modest to moderate increases in breast cancer risk for members of *BRCA* negative families. Specifically, we examined the association of multiple potential

psychological, behavioral, demographic and clinical factors with interest in genetic testing for members of *BRCA1/2* negative families. Such information can help guide risk communication strategies for clinicians in speaking with patients about gene-panel testing by having a better understanding of what relatives are seeking through additional testing. With this insight, genetic counselors can provide a more tailored discussion on the potential risks and benefits of gene-panel testing and the importance of identifying the most informative person to test within the family. Targeted communication strategies can better help women make informed decisions about whether or not to undergo gene-panel testing, risk reduction strategies and screening to improve cancer outcomes.

## METHODS

### Participants

Study participants *were the sisters or daughters of female breast cancer patients* who were enrolled in a large clinical trial, the Risk Education and Assessment for Cancer Heredity (REACH) Project (Kinney et al., 2014). The REACH Project was a cluster randomized trial that tested 1) the equivalency of *BRCA1/2* testing uptake and 2) non-inferiority of changes in psychosocial and informed decision-making measures among women who received remote telephone genetic counseling or in-person genetic counseling. Women in the telephone counseling arm who chose to have *BRCA1/2* testing received a genetic test kit and women in the in-person counseling group either gave a sample directly in the clinic or, if they preferred, received a genetic test kit. Detailed information about the study's population-based recruitment strategy, interventions, theoretical rationale, and outcomes are published elsewhere (Kinney et al., 2014). For the current study, only REACH participants who tested negative for a *BRCA1/2* gene mutation were mailed a letter, family contact form, and a postage-paid envelope asking their permission to invite their potentially eligible sisters and/or daughters (the participants of this study) to participate in a survey. Relatives of *BRCA* negative breast cancer patients were contacted by mail and/or telephone to screen for eligibility. Eligibility criteria for the current study included: 1) age 40–74 years (i.e., eligible for mammography screening at the time of the study); 2) resident of the United States; 3) no prior diagnosis of cancer (except non-melanoma skin cancer); 4) no prior *BRCA1/2* testing or genetic counseling; and 5) no bilateral mastectomy. They were mailed a study packet that included a consent cover letter, study questionnaire, tape measure with instructions, and a postage-paid return envelope. Out of list of 214 potential participants, 33 could not be contacted, 15 were ineligible and 17 refused participation. The overall cooperation rate was 89.8% (149/149+17). We did not find any statistical differences in participants compared to non-participants when we compared the two groups by available information including mean age, rural vs urban residence or Utah vs other state residence. The University of Utah Institutional Review Board approved the study.

### Measures and Procedures

**Perceived Risk**—Perceived risk was evaluated with an item assessing lifetime risk (Lipkus et al., 2000): “In your opinion, how likely is it that you will get breast cancer in your lifetime?”. Response options were ‘Very unlikely’, ‘Unlikely’, ‘50-50 chance’, ‘Likely’, and ‘Very Likely’.

**Cancer Worry**—We measured the frequency and intensity of cancer worry with a validated 3-item scale (Jensen et al., 2010; McCaul et al.). Two items measured worry intensity: “How bothered are you about getting breast cancer?” and “How worried are you about getting breast cancer?” Responses ranged from ‘not at all’ to ‘extremely’ on a 5-point Likert scale. Worry frequency was measured by asking participants “During the past week, how often have you worried about getting breast cancer?” The items were summed to create the worry variable. Internal consistency was very good (Cronbach’s  $\alpha=.82$ ). Scores less than 7 were considered ‘low worry’ and scores greater than or equal to 7 were considered ‘high worry’.

**Clinical Factors**—We assessed: 1) whether or not a participant reported having talked with their provider about a family history of cancer, ‘Yes’, ‘No’, 2) if the participant reported having 2 or more close blood relatives with breast cancer (based on a short family history of cancer questionnaire), if a participant reported having had 3) a clinical breast exam and 4) mammography within the last 2 years based on self-reported date of last procedure.

**Lifestyle**—Participants were asked. “Over the past month, how many servings of fruits [vegetables] did you eat per day?” Response options were, ‘0’, ‘1’, ‘2’, ‘3’, ‘4’ or ‘5 or more’. The number of fruit and vegetable servings per day from the two questions were combined and assessed as less than 5 or 5 or more in accordance with national dietary guidelines (“US Department of Agriculture. Dietary Guidelines for Americans. <http://www.health.gov/dietaryguidelines/>”). For physical activity, we assessed if participants engaged in at least 150 minutes of self-reported moderate intensity exercise or 75 minutes of high intensity exercise per week using the International Physical Activity Questionnaire Short Form (IPAQ).

**Sociodemographics**—We assessed age, marital status, income, education and rural or urban residence. Rural or urban status was ascertained using Rural-Urban Commuting Area Codes by zip code as previously described (Kinney et al., 2014).

**Outcome Variables**—The questionnaire included a brief summary about genetic testing with information about *BRCA1/2* testing and other genetic changes that may relate to either small or moderate increases in breast cancer risk (i.e., gene-panel/multiplex testing). The primary outcome, interest in multiplex testing, was assessed by a single item asking participants “If genetic testing could tell you that you may have a slightly to moderately increased risk of developing breast cancer, how likely is it that you would want a genetic test?” We further asked participants if they were interested in this type of genetic testing if it could provide information about risk-based screening (mammograms, breast MRI, or other screening procedures); if their risk could be lowered by taking medications; and if their risk could be lowered by diet and exercise. Response options were “I would definitely not have the test”, “I would probably not have the test”, “I would probably have the test”, “I would definitely have the test”. Responses were dichotomized into “would definitely or probably not have the test” or “would definitely or probably have the test”. Items were adapted from a survey by Graves *et al.*, 2011.

We assessed participants' preferred method of receiving information about gene-panel testing including print or written information, web-based information, computer kiosk touch screen in a clinic, discussion with a nurse, discussion with a primary care physician, discussion with a cancer specialist such as an oncologist, discussion with a genetic counselor/cancer risk specialist. Possible responses were: "Not at All", "A Little", "Somewhat", or "Very Much". Responses were dichotomized by interest into "Not at All/A Little" and "Somewhat/Very Much".

### Data Analyses

Sociodemographics, clinical and behavioral factors, cancer worry, perceived risk, and preferences for receiving genetic testing information were characterized in the study population using descriptive statistics in SPSS version 22. Independent variables with non-normal distributions were dichotomized and variables were screened for collinearity. Unadjusted odds ratios (ORs) and 95% and confidence intervals (CI) were estimated to ascertain association between each independent variable and interest in genetic testing. Logistic regression was used to delineate the independent association of potential factors with interest in genetic testing. Variables that were crudely associated with interest in testing based on a  $p$  value  $<0.20$  were entered into the multivariate model. Variables were removed by backward elimination based on the probability of a likelihood-ratio statistic for variable removal of 0.10. To account for family clustering, we tested the final model using generalized mixed modeling in MPlus (version 7). There were 100 family clusters in the sample, with an average cluster size of 2. The design effect for genetic testing was essentially 0 and results were the same whether or not clustering was taken into account. However, the final adjusted model was evaluated taking clustering into account.

## RESULTS

Characteristics of the study population are presented in Table 1. The mean age of participants was 53 years ( $SD \pm 9.4$  yrs). A majority of women were married (80%) and had annual incomes equal to or above \$50,000 (67%). Most participants had at least some college education (83%). Participants indicated that they had talked with a personal healthcare provider about their family history of breast cancer (69%) and reported having had a clinical breast exam (73%) or a mammogram (77%) in the last two years at the time of questionnaire completion. Sixty four percent of women reported having 2 or more first or second degree relatives with a breast cancer diagnosis. Over one-third of women reported high levels of cancer worry.

Overall the percentage of participants that reported interest in genetic testing was relatively high with 70% of women having reported that they would either definitely or probably have a genetic test if it could tell them if they have a slightly to moderately increased risk of developing breast cancer. Interest in genetic testing increased somewhat based on behavioral modification scenarios (Figure 1): 74% of women indicated they would definitely or probably have genetic testing if testing could tell them whether or not they should have a mammogram, breast MRI or other screening more frequently, and 79% of women indicated they would have a genetic test if testing could tell them whether or not their risk of breast

cancer could be lowered by taking medications. Interest in genetic testing also increased in the scenario where testing could tell them whether or not their risk could be lowered by diet or exercise (77%).

The most frequently cited preferred source of information about genetics and cancer risk was with a primary care physician (83%; Figure 2), followed by a genetic counselor or cancer risk specialist (78%), and a cancer specialist such as an oncologist (77%).

The unadjusted ORs, 95% CIs and p values for each independent variable with overall interest in gene-panel testing are shown in Table 2. Marital status, rural/urban residence, having had a mammogram in the past two years, consuming 5 or more servings of fruits and vegetables daily, high levels of cancer worry, and increased perceived lifetime risk of developing cancer met the criteria ( $p < .20$ ) for entry into the logistic model. The final adjusted logistic model included cancer worry and perceived lifetime risk of developing cancer (Table 3). Participants reporting higher levels of cancer worry were more likely to indicate interest in genetic testing than those with lower cancer worry levels (OR=3.12, 95% CI 1.28, 7.60,  $p=0.009$ ). Higher perceived lifetime risk was associated with interest in genetic testing (OR=1.67, 95% CI=1.06 to 2.65,  $p=0.031$ ). Perceived risk and worry did not interact with each other to predict genetic testing (result not shown).

## DISCUSSION

This study is one of the first to examine interest in gene-panel testing, prior to genetic counseling, among first-degree relatives of *BRCA1/2* negative breast cancer patients. We found that the percentage of women reporting interest in gene-panel testing was high for members of *BRCA1/2* negative families and that the percentage of women reporting interest in testing increased if the test could inform them about customized behavior changes to reduce their risk or personalize screening. A previous study did not find increased interest in genetic testing for breast cancer risk when testing could provide recommendations for behavior change (Graves et al., 2011). Our results showed some increase and suggest that some women from *BRCA* negative families may be especially receptive to behavior change recommendations based on genetic test results and would prefer to receive genetic information from many sources especially their primary care provider and a genetic counselor. Family members generally are not included in their relative's genetic counseling session. Those with high levels of worry and risk may benefit from enhanced cancer genetic information about genetic risk. Particularly if further genetic testing is not warranted for family members, addressing the limitations of genetic testing in the context of important areas of interest can help to improve cancer genetic communication for members of *BRCA* negative families.

In this study, interest in gene-panel testing was particularly high if testing could tell participants whether or not taking medications could reduce their risk of cancer (79%). Currently, the US Preventive Services Task Force recommends that clinicians and patients at increased risk make shared informed decisions about taking medications to reduce their risk for breast cancer (e.g., tamoxifen or raloxifene to reduce primary breast cancer risk and recurrence) (Moyer et al., 2013; Powers et al., 2014). Adherence to medication for the

prevention of primary breast cancer in patients is suboptimal, and although adjuvant hormonal therapy has been shown to reduce hormone-sensitive breast cancer recurrence and mortality rates, medication adherence in this population remains low (Nelson et al., 2013). Our results suggest that members of *BRCA* negative families may be especially interested in information regarding medication use for cancer risk reduction.

Rural and urban residence, fruit and vegetable intake, mammography screening with the past 2 years, cancer worry, and perceived lifetime risk were associated with interest in genetic testing in bivariate analyses. Some of these factors deserve further discussion based on their potential applications. Within their small communities and with fewer health care providers to choose from, rural dwellers may perceive gene-panel testing as a greater threat to their privacy and confidentiality and may also have a greater need for accessing information to help them make informed decisions about gene-panel testing and mitigate high cancer worry (Kelly et al., 2007). The opportunity to improve access to genetic counseling is especially important for rural women because they have limited access to genetic risk specialists, are often diagnosed with late stage breast cancer compared to their urban counterparts (Nguyen-Pham et al., 2014), and experience disparities in breast cancer treatment including being less likely to receive radiation and surgery (Markossian et al., 2012). Unmarried participants reported a greater interest in genetic testing, but this factor was not significant in multivariable analysis. The relationship between marital status and interest in cancer genetic testing is inconsistent across studies and could be a reflection of the different populations studied (Anderson et al., 2014; Graves et al., 2011; Weinrich et al., 2002). However, our current finding (unmarried women were more interested in testing) is consistent with findings from our previous study regarding interest in multiplex testing for colorectal cancer risk (Anderson et al., 2014). Younger age has been found to be associated with interest in genetic testing in other studies, but it was not significantly associated with interest in genetic testing for this population of women. Compared to our previous study that included younger men and women below age 40 who were at increased risk for familial colorectal cancer, the current study's lower age limit was 40. It is possible that our study participants' previous knowledge of their family *BRCA1/2* mutation status led them to discuss these results with family members and share information and opinions that played a greater role in their reported interest beyond the influence of age or marital status alone. Having had a mammogram within the previous two years was also crudely associated with interest in genetic testing and may be representative of women who are already empowered to seek cancer screening based on familial risk.

Cancer worry and perceived lifetime risk were significant predictors of interest in genetic testing. Women with higher levels of cancer worry were three times as likely to report interest in gene-panel testing as those with low cancer worry levels, a finding that is consistent with other studies (Cameron et al., 2006; Graves et al., 2010). Cancer-specific worry has been positively correlated with intentions to have a genetic test for hereditary breast and ovarian and colorectal cancer susceptibility (Codori et al., 1999; Lerman et al., 1994). Consistent with Leventhal's Common-Sense Model of self-regulation for health threat cognition and behavior, worry or emotional arousal can motivate protective action (i.e., engaging in strategies to reduce distress) (Cameron et al., 2001). Risk perception has also been shown to play a salient role in how cancer patients and their families cope with



breast cancer and has been positively associated with interest in and utilization of genetic testing (Croyle et al., 1993; Graves et al., 2010; Lerman et al., 1994). Furthermore, cancer risk and illness perceptions have been shown to predict cancer worry in healthy women (Gibbons et al., 2015) and influence behavior change (Cameron et al., 2009). Risk perception and worry in at-risk women from *BRCA1/2* negative families may drive interest in genetic testing and behavior change. In some cases this could lead to the adoption of unnecessary tests or behaviors if a woman perceives her risk to be high and feels the need to do something to reduce this risk; overuse of cancer screening has been associated with perceived cancer risk in *BRCA1/2* negative women (Milhabet et al., 2013). Additional time may need to be spent educating a patient on the limitations of gene-panel testing and clarifying who the most informative person would be to undergo testing in the family in order to maximize benefit for the patient. Based on results from this study, emotional and cognitive factors of risk and worry may help to identify family members that could most benefit from additional or targeted cancer genetic information. More studies are needed that address the psychosocial and behavioral effects of gene panel testing for members of *BRCA1/2* negative families.

Genetic counseling strategies, such as the tiered-binned model, are designed to provide patients with the most pertinent information to support informed decision-making for genetic testing followed by need-based patient specific information. Bradbury et al. found that previously tested *BRCA1/2* negative patients were more likely to go forward with multiplex testing after tiered/binned counseling compared to *BRCA1/2* untested patients (BradburyPatrick-MillerEgleston et al., 2015). Patients that received testing did not have significant changes in anxiety, depression, cancer worry and uncertainty. The majority of *BRCA1/2* untested patients however declined multiplex (gene-panel) testing. Breast cancer worry, greater uncertainty, and greater perceived utility were all associated with making less informed decisions about gene-panel testing. In our study, participants with no prior exposure to genetic counseling showed a high interest in genetic testing. Interest in gene-panel testing may change based on the information received in pre-test counseling and understanding the potential factors that contribute to genetic testing may further inform the clinical and personal utility of genetic communication strategies.

The vast majority of women in this study reported that they prefer to get their genetic testing information from their primary care physicians followed by a cancer risk specialist/genetic counselor. A recent study found that only a fraction of women who receive a physician referral for genetic testing also receive genetic counseling to help them make an informed decision. The ABOUT (American BRCA Outcomes and Utilization of Testing) study showed that of women who received *BRCA* testing ordered by their physician only 36.8% received genetic counseling. However, women who received genetic counseling reported more knowledge about and satisfaction with *BRCA* testing. Since patients consistently report that they prefer to talk with their primary care providers about genetic information and testing, it is especially important that providers have a conversation about genetic counseling with their patients. Unfortunately, primary care providers often lack sufficient knowledge of hereditary cancer risk and management, which may impede recognition of appropriate times to refer patients for genetic counseling (Cohn et al., 2015).

Most of the study participants indicated that they were ‘Somewhat’ or ‘Very interested’ in getting information from a variety of sources including print materials and via the Internet whereas getting information by computer kiosk was the least preferable mode of communication. Women who participated in the REACH Project received high quality, personalized print genetic information and structured in-person or telephone genetic counseling, and may have discussed or shared this information with their relatives (i.e., the participants in this study). It is possible that many of the study participants were primed to expect high quality information from various sources. Our results agree with similar studies showing that a majority of participants prefer to receive genetic information through a physician or genetic counselor and also prefer print materials (Anderson et al., 2014; McGuire et al., 2009).

### Study Limitations

Our study had several limitations. While we measured interest in gene-panel testing we did not measure reasons for this interest or whether or not women participated in follow-up genetic counseling or testing. We do not know the extent of discussions about *BRCA* status among family members but found that family clustering did not have a significant effect on the results (data not shown). The relatively small sample size and homogenous study population (well educated, non-Hispanic white, married) are limitations and underscore the need to replicate our findings with diverse populations. Interest in gene-panel testing may be determined by other factors such as cost, concern about genetic discrimination, and the perceived benefit of the genetic information assessed, including the likelihood of clear risk management strategies (BradburyPatrick-Miller & Domchek, 2015; Cragun et al., 2015; Easton et al., 2015; Powers et al., 2014). Finally, gene-panel testing is a complicated and rapidly evolving field. We did not measure participants’ genetic literacy, their cancer knowledge or how they interpret small to moderate increases in cancer risk due to genetic variants. Additional research could be especially helpful in this regard.

### Practice Implications

Interest in clinic-based and direct-to-consumer gene-panel testing is increasing (Roberts et al., 2013) yet physicians report lacking the time and expertise to discuss genetic test results with patients and have concerns about high VUS rates and the clinical utility of large scale genetic tests (Powell et al., 2012; Selkirk et al., 2014). Genetic counselors, report similar challenges in: 1) interpreting the results and clinical utility for some variants assessed by gene-panel tests; 2) providing appropriate informed consent; and 3) determining the most appropriate candidates for panel testing (Wolfe Schneider et al., 2014). Our study informs the need for the development of effective methods of communicating genetic information and testing strategies for members of high risk cancer families. By knowing what factors are associated with interest in testing, providers can be better prepared to offer genetic counseling referrals or other resources to the most appropriate family members. Based on our results, diverse strategies of communication with women who test negative for *BRCA* mutations and their family members should be utilized. Patients should be given more resources, such as information on genetic counseling and testing, and action plans, working alongside their primary care providers if appropriate, to make sure that they have access to genetic counseling so that they can better understand their cancer risk and increase their

satisfaction with a testing decision. A specific opportunity for family genetic communication sharing arises after a patient receives a *BRCA* negative test result, yet patients with a *BRCA* negative test result are less likely to share genetic information with their family members who may benefit from it (Himes et al., 2016; Patenaude et al., 2006). Genetic counselors can play a significant role in developing and disseminating materials and strategies that increase genetic information sharing within *BRCA* negative families. The sharing of family genetic information may help to balance public perceptions about the benefits and risks of additional genetic testing.

Our study's findings suggest that women from *BRCA1/2* negative families represent a unique population with a high level of interest in gene-panel testing driven by unmitigated perceived risk and cancer worry. These women may be especially motivated for customized behavior change. Clinicians should pay special attention to threat perceptions (i.e., perceived risk and worry) when designing risk communications as well as informed decision-making and behavior change interventions with the goal of effectively leveraging these potential factors with evidence-based risk communications. Interest in multiplex testing for breast cancer susceptibility may create a teachable moment that can be used by clinicians to counsel about behavior change. Health messages can include broadly applicable recommendations such as increasing fruit and vegetable intake and physical activity, healthy behaviors that are associated with decreases in incidence and mortality from cancer and other chronic disease (Kabat et al., 2015; Petersen et al., 2015).

### Research Recommendations

More research is needed to: 1) determine if cognitive and emotional factors are important for gene-panel testing interest and decisions and 2) develop genetic communication tools for cancer families. Negative mutations testers and their family members are an understudied population that will benefit from further research. As gene-panel testing becomes increasingly integrated into standard care, many families may need to make informed decisions about gene-panel testing and medical management. Further research should address the adoption of preventive behaviors in the context of gene-panel testing across diverse populations, and ultimately ascertain if gene-panel testing translates into improved cancer outcomes.

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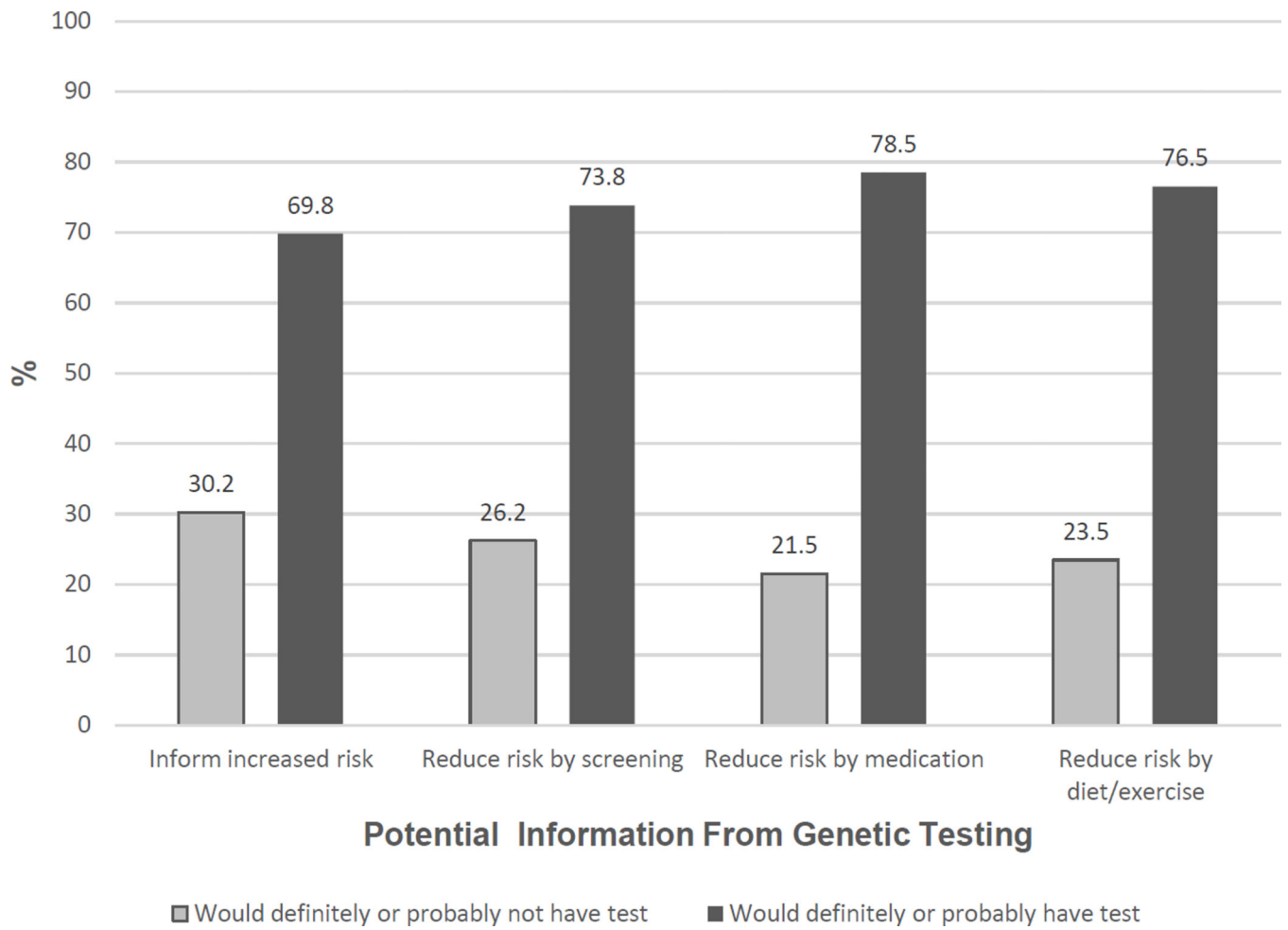
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**Figure 1.**  
Interest in Genetic Testing by Potential Utility of Results

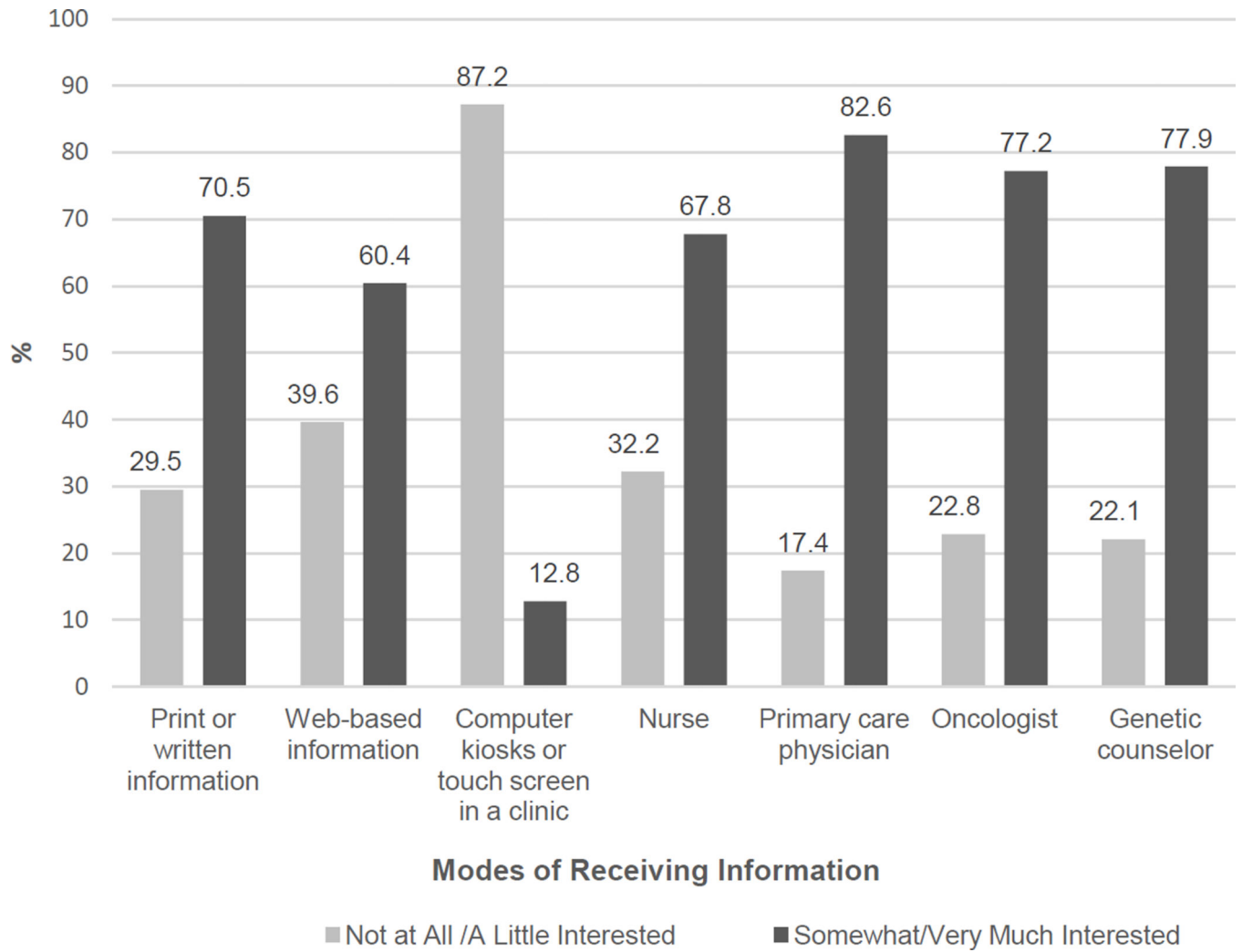
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**Figure 2.** Preferences for Receiving Information about Genetics and Cancer Risk

**Table 1**

## Characteristics of the Study Population

Characteristic	N (%)
Race/Ethnicity	
Non-Hispanic white	146 (98.0)
Other/unreported	3 (2.0)
Married	
Yes	119 (79.9)
No	30 (20.1)
Education	
High school or less	25 (16.8)
Some college or more	124 (83.2)
Residence	
Urban	121 (81.2)
Rural	24 (16.1)
Missing	4 (2.7)
Annual Household Income	
< \$50,000	32 (21.5)
\$50,000	100 (67.1)
Missing	17 (11.4)
First or Second Degree Relative with Breast Cancer	
One	53 (35.6)
Two or more	96 (64.4)
Family History of Breast Cancer Discussed with Provider	
Yes	102 (68.5)
No	47 (31.5)
Clinical Breast Exam in Past 2 Years	
Yes	109 (73.2)
No	25 (16.8)
Missing, refused	15 (10.0)
Mammogram in Past 2 Years	
Yes	114 (76.5)
No	23 (15.4)
Missing, refused	12 (8.1)
Daily Servings Fruit and Vegetables	
< 5 servings a day	86 (57.7)
5 servings a day	62 (41.6)
Missing, refused	1 (0.7)
Exercise 75 Minutes of High Intensity or 150 Minutes of Moderate Intensity/Week	
Yes	69 (46.3)
No	65 (43.6)

Missing, refused	15 (10.1)
Cancer Worry	
Low Worry	92 (61.7)
High Worry	57 (38.3)
<hr/>	
Continuous Variables	Mean (SD)
<hr/>	
Age	53 (9.4)
Perceived Lifetime Risk of Developing Cancer	3.11 (0.91)
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**Table 2**

Crude Odds Ratios and 95% Confidence Intervals for Factors Associated with Interest in Genetic Testing

Variable	N (%)	OR (95% CI)	P value
Married			0.179
Yes	119 (79.9)	0.51 (0.19, 1.36)	
No	30 (20.1)	1.00 (Reference)	
Education			0.830
High school or less	25 (16.8)	1.00 (Reference)	
Some college or more	124 (83.2)	1.11 (0.44, 2.79)	
Residence			0.191
Rural	24 (16.6)	1.00 (Reference)	
Urban	121 (83.4)	1.83 (0.74, 4.51)	
Annual Household Income			0.492
< \$50,000	32 (24.2)	1.00 (Reference)	
\$50,000	100 (75.8)	1.35 (0.58, 3.15)	
First or Second Degree Relative with Breast Cancer			0.455
One	53 (35.6)	1.00 (Reference)	
Two or more	96 (64.4)	0.75 (0.36, 1.59)	
Family History of Breast Cancer Discussed with Provider			0.489
No	47 (31.5)	1.00 (Reference)	
Yes	102 (68.5)	1.30 (0.62, 2.73)	
Clinical Breast Exam in Past 2 Years			0.724
No	25 (18.7)	1.00 (Reference)	
Yes	109 (81.3)	1.18 (0.46, 3.02)	
Mammogram in Past 2 Years			0.175
No	23 (16.8)	1.00 (Reference)	
Yes	114 (83.2)	1.30 (0.75, 4.73)	
Daily Servings Fruit and Vegetables			0.135
< 5 servings a day	86 (58.1)	1.00 (Reference)	
5 servings a day	62 (41.9)	0.58 (0.29, 1.18)	
Exercise 75 Minutes of High Intensity or 150 Minutes of Moderate Intensity/Week			0.878
No	65 (48.5)	1.00 (Reference)	
Yes	69 (51.5)	1.17 (0.55, 2.50)	
Cancer Worry			0.001
Low Worry	92 (61.7)	1.00 (Reference)	
High Worry	57 (38.3)	4.12 (1.75, 9.70)	
Continuous Variables	Mean (SD)	OR (95% CI)	P
Age	53 (9.4)	0.99 (0.95, 1.02)	0.443
Perceived Lifetime Risk of Developing Cancer	3.11 (0.91)	1.98 (1.28, 3.07)	0.002

**Table 3**

Multivariable Logistic Regression Model for Interest in Genetic Testing

Variable	OR (95% CI)	P value
Cancer Worry		0.009
Low Worry	1.00 (Reference)	
High Worry	3.12 (1.28, 7.60)	
Perceived Lifetime Risk of Developing Cancer	1.67 (1.06, 2.65)	0.031

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