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Factors Determining Dissemination of Results and Uptake of Genetic Testing in Families with Known *BRCA1/2* Mutations

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Abstract

Background—Uptake of genetic testing remains low, even in families with known *BRCA1* and *BRCA2* (*BRCA1/2*) mutations, despite effective interventions to reduce risk. We report disclosure and uptake patterns by *BRCA1/2*-positive individuals to at-risk relatives, in the setting of no-cost genetic counseling and testing.

Methods—Relatives of *BRCA1/2*-positive individuals were offered cost-free and confidential genetic counseling and testing. If positive for a *BRCA1/2* mutation, participants were eligible to complete a survey about their disclosure of mutation status and the subsequent uptake of genetic testing by at-risk family members.

Results—One hundred and fifteen of 142 eligible individuals responded to the survey (81%). Eighty-eight (77%) of those surveyed disclosed results to all at-risk relatives. Disclosure to first-degree relatives (FDRs) was higher than to second-degree relatives (SDRs) and third-degree relatives (TDR) (95% vs. 78%; p <0.01). Disclosure rates to male versus female relatives were similar, but reported completion of genetic testing was higher among female versus male FDRs (73% vs. 49%; p<0.01) and SDRs (68% vs. 43%; p<0.01), and among members of maternal versus paternal lineages (63% vs. 0%; p<0.01). Men were more likely than women to express general difficulty discussing positive *BCRA1/2* results with at-risk family members (90% vs. 70%; p = 0.03), while women reported more emotional distress associated with disclosure than men (48% vs. 13%; p < 0.01).

Discussion—We report a very high rate of disclosure of genetic testing information to at-risk relatives. However, uptake of genetic testing among at-risk individuals was low despite cost-free testing services, particularly in men, SDRs, and members of paternal lineages. The complete lack of testing among paternally related at-risk individuals and the lower testing uptake among men

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signify a significant barrier to testing and a challenge for genetic counselors and physicians working with high-risk groups. Further research is necessary to ensure that family members understand their risk and the potential benefits of genetic counseling.

Introduction

Strategies exist to decrease cancer risk among *BRCA1/2* mutation carriers, yet rates of genetic testing use, even in families with known mutations, remain low. Due to privacy regulations, genetic counselors and physicians rely on mutation-positive individuals to disseminate complex genetic risk information and to encourage at-risk relatives to seek genetic counseling. Disclosure of test results is highest to first-degree relatives (FDRs) (Claes *et al.*, 2003; Wagner Costalas *et al.*, 2003; McGivern *et al.*, 2004) and to female relatives (Claes *et al.*, 2003; Wagner Costalas *et al.*, 2003; Sermijn *et al.*, 2004). However, prior studies were limited by small sample sizes, barriers in the testing process, and few male participants. Understanding factors that influence how and to whom *BRCA1/2* mutation carriers communicate risk information will enable more effective patient and family counseling. The goal of this study was to evaluate disclosure patterns by *BRCA1*/*2*-positive individuals to at-risk relatives in a cost-free genetic counseling and testing environment.

Materials and Methods

Study design

The Known Mutation in the Family Study (KMFS) conducted by the University of Pennsylvania Cancer Risk Evaluation Program (CREP) was designed to offer genetic counseling and testing to members of families with known *BRCA1/2* mutations. Genetic counseling and testing services were cost free when conducted through the University of Pennsylvania. Services were not limited by geography, as mutation testing blood collection kits were sent by mail to research participants and counseling was offered by telephone if patients were unable or unwilling to be seen at the University of Pennsylvania or by a local provider. The goal was to assess disclosure and testing uptake patterns as well as factors influencing disclosure of genetic information within families with known *BRCA1/2* mutations.

In January 2001, all *BRCA1/2* mutation carriers in the CREP database were identified and informed that their relatives over the age of 18 were eligible for a CREP study involving *BRCA1/2* mutation-positive families. Those relatives interested in testing signed informed consent for enrollment in a University of Pennsylvania Institutional Review Board (IRB)-approved protocol. Relatives completed a Health History Questionnaire to provide information on their personal cancer, medical, and reproductive history, and completed pretest genetic counseling. Genetic testing was performed by Myriad Genetics Laboratories (Salt Lake City, UT). Results were made available to study participants within 3 months. Each participant received results in person or by telephone, depending on their preference.

Following an interactive communication session regarding genetic testing outcomes, each participant received a letter delineating the contents of the communication session. Mutation-positive participants received a letter describing the following: genetic transmission to children and within families, cancer risk information, and cancer risk management strategies (recommended screening practices, medical and genetics follow-up). Additionally, each letter clearly delineated family members at risk for having inherited a *BRCA1/2* mutation (e.g., your sister, Alice; your aunt, Jane). Genetic counselors encouraged disclosure of positive mutation status during conversations with study participants and reiterated this message within the letter mailed to each mutation carrier.

Mutation carriers identified between January 2001 and December 2002 as a part of the KMFS were eligible to complete a questionnaire regarding their familial communication of *BRCA1/2* results. (Survey was conducted as a part of a University of Pennsylvania IRB-approved protocol, as an adjunct to the KMFS.) The questionnaire was derived from common themes in the literature regarding barriers and facilitators of dissemination of risk information. Items were reviewed by a panel of experts for face validity and understandability. In addition, the survey was piloted in a group of 30 participants (not included in this study) and revised.

This survey was mailed in August 2004 and again to nonresponders in December 2004. The survey listed names of at-risk FDRs and those second-degree relatives (SDRs) who did not have a living or available intervening FDR or SDR (e.g., cousins were included if both the parent and intervening aunt or uncle was deceased). The name of the initial mutation carrier who informed survey participants of their genetic risk was excluded from the survey. Participants were allowed to write in names of additional relatives who they believed were at risk or to whom mutation results were disclosed. Participants were asked whether they disclosed positive testing status to at-risk relatives and whether or not the relatives received genetic testing. The survey included general demographics questions regarding marital status, education level, employment status, household income, and health insurance status. Participants were asked about methods of disclosure, including whether they relied on other family members to disseminate risk information, about topics included in disclosure discussions, and whether they recommended testing to at-risk relatives.

In addition to questions asking participants to quantify general difficulty and confidence levels disclosing genetic risk, participants were surveyed about factors influencing disclosure. Participants were first asked about general reasons for choosing to share genetic risk information and about reasons that might have made it hard, in general, to share results with family members. In addition, they answered questions about reasons that might have made it easier, in general, to share. In instances in which participants did not share results, they were asked to describe the factors that played a role in decisions not to disclose. Appendix A includes the survey questions regarding disclosure decisions.

Statistical analysis

Questions regarding factors influencing disclosure were answered using a 4-point scale, with 1 signifying a factor playing no role in disclosure decisions and 4 signifying a factor playing a large role (see Appendix A). Contingency tables were created to evaluate the relationship between explanatory factors that may have contributed to disclosure decisions, the occurrence of disclosure, genetic testing uptake, and gender differences. Two-sided Fisher's exact tests (FETs), odds ratios (ORs), and 95% confidence intervals (CIs) were computed.

Results

Patient population

Nine of the original 142 surveys (6%) were returned due to incorrect mailing addresses, and 1 survey from a deceased patient was excluded from the total. Overall, 115 of 132 surveys from 47 families were included in the final analysis, representing an 87.1% response rate. An average of 2.4 individuals responded from each of the 47 families, with a median number of two participants from each family; in 39 of the 47 families represented, one to three family members completed surveys about communication of risk status. Table 1 describes the demographics of the survey population. Our population was predominantly Caucasian (93%), married (85%), employed (65%), college educated or above (68%), had an income > $50,000 per year (70%), and had health insurance (95%). Eighty-three of the

respondents were female (72%), and 32 were male (28%). Forty-three participants (37.4%) had a personal history of breast cancer, while 12 (10.7%) had an ovarian cancer history and 8 (7.0%) had a history of other cancers.

Disclosure of BRCA1/2-positive test results to at-risk relatives

Of 115 respondents, all disclosed to at least some at-risk relatives. Eighty-eight (77%) disclosed positive *BRCA1/2* mutation status to all at-risk family members, while 27 (23%) survey participants disclosed to at least one, but not all, at-risk family members. Based on pedigree analysis, survey participants had 655 FDRs and SDRs without living FDRs who were at risk for inheriting *BRCA1/2* mutations. Survey results, presented in Table 2, show that participants disclosed positive mutation status to 588 of the 655 at-risk relatives (89.9%). Four hundred and twenty-eight of the 450 (95%) FDRs at risk were; informed versus 160 of the 205 (78%) SDRs ($p < 0.01$; OR=8.41, CI = 4.36–17.02).

Data regarding disclosure patterns are presented in Table 3. While there was a trend toward statistical significance with regard to disclosure to sisters (99%) versus brothers (94%) ($p = 0.051$; OR = 4.65, CI=0.90–45.44), disclosure to both were very high and there was no difference between disclosure to mothers versus fathers, daughters versus sons, or female FDRs versus male FDRs. There were also no differences in disclosure rates between aunts and uncles, maternally related SDRs versus paternally related SDRs, or nieces versus nephews. Members of younger generations (children, nieces, and nephews of surveyed individuals) were more likely to be told of their mutation status than members of older generations (siblings, aunts, uncles, and parents) (94.9% vs. 89.1%; $p = 0.01$; OR=2.27, CI = 1.14–5.0).

Uptake of genetic testing based on degree of relation and gender

While disclosure rates were quite high, reported uptake of genetic testing was much lower. Survey participants reported that only 260 of the 428 FDRs (60.7%) informed of their risk received genetic testing. Only 74 of the 160 more distant relatives (46.5%) pursued testing. Overall, only 56.8% of those told were tested, based on knowledge of family testing patterns among those surveyed.

Data regarding uptake of genetic testing among informed relatives are presented in Table 4. Uptake of genetic testing by FDRs was significantly higher among female relatives compared to male (73% vs. 49%; $p< 0.01$; OR=2.75, CI=1.79–4.21). Sisters were more likely to be tested than brothers (79% vs. 53%; $p < 0.01$; OR=3.28, CI = 1.91–5.67), and daughters were more likely to be tested than sons (57% vs. 53%; $p=0.01$; OR=2.84, CI = 1.21–6.80). Among SDRs, 68% of female relatives versus 43% of male relatives were tested ($p < 0.01$; OR = 2.85, CI = 132–6.18). Nieces were significantly more likely than nephews to be tested (83% vs. 24%; $p<0.01$; OR=15.71, CI = 4.05–64.36). In addition, uptake of genetic testing was significantly higher among members of older than younger generations (653% vs. 50.3%; $p<0.01$; OR = 1.86, CI = 1.27–2.72). Lastly, while disclosure to at-risk members of maternal versus paternal lineages was not significantly different (67.8% vs. 55.6%; $p=0.41$), no paternally related family members chose to receive genetic testing (63.8% vs. 0.0%; $p < 0.01$).

Methods and content of disclosure

The most common methods for disclosure of positive test results were discussions in person (87.0%) or over the telephone (76.5%). Writing letters or e-mails describing results were less frequent methods of disclosure (Table 5). There were no statistically significant differences between methods used by people who disclosed to all at-risk relatives versus

those who disclosed to only some at-risk relatives. In addition, gender did not influence the methods used for disclosure.

Participants discussed many recommended topics with family members, including chance of having a mutation and cancer risk for people with a mutation. Table 6 presents data regarding the topics discussed with one or more relatives. Eighty-nine percent of those surveyed cither strongly recommended or suggested genetic testing to their relatives during disclosure conversations. Despite these recommendations, uptake of testing in at-risk relatives was only 57%.

Disclosure patterns and motivations to share positive BRCA status

Participants were asked about reasons for choosing to share, reasons that might have made it easy to share, and reasons that might have made it hard to share positive mutation status with family members. Greater than 90% of participants stated that the following factors were significant reasons for choosing to share genetic risk information: a feeling of obligation toward family members (93.2% full disclosers and 96.3% partial disclosers), a belief that disclosing risk information would help relatives make medical decisions (97.7% full and 96.3% partial), a desire to provide relatives risk information (95.4% full and 92.5% partial), and a desire for relatives to be tested (95.4% full and 100% partial). There were no statistical differences between those who disclosed to all versus those who disclosed to some at-risk relatives with regard to the aforementioned factors. Other factors, including physician/geneticist recommendation to disclose, previous agreements with family members regarding disclosure, encouragement by other family members to disseminate information, direct inquiry by family members, and the need for emotional support from family members, were infrequently listed as a reason for disclosure by both full and partial disclosure participants, with no difference between the two groups.

More people who disclosed to some at-risk relatives compared to those who disclosed to all at-risk relatives felt that the following reasons made it difficult to discuss genetic risk information (Table 7): lack of close relationships with some relatives (46% vs. 15%; $p \leq 0.01$; OR=0.21, CI=0.07–0.62), confusion about which relatives were at risk for inheriting a *BRCA1/2* mutation (30% vs. 12%; $p = 0.04$; OR = 3.2, CI = 0.94–11.11), belief that relatives did not want to know about genetic test results (30% vs. 7%; $p<0.01$; OR=5.62, CI = 1.48–21.79), and belief that relatives did not understand how genetic risk information applied to them (35% vs. 15%; $p = 0.05$; OR =2.98, CI = 0.95–8.95).

In contrast, factors such as emotional difficulty with sharing, lack of comfort discussing complex information, fear of upsetting relatives, guilt or anxiety regarding test results, or belief that the genetics information was too personal to share were not significantly different between full and partial disclosers. Only 36.5% of participants who told all at-risk relatives and 40.1% of those who disclosed to only some at-risk relatives noted difficulty sharing due to emotional discomfort ($p = 0.82$). About 17.4% full and 14.8% partial disclosers thought that the complexity of information made it difficult to share ($p = 1.0$). About 23.3% full and 185% partial disclosers reported feeling guilty or anxious about test results ($p = 0.79$), and 13.8% full and 14.8% partial disclosers thought that the personal nature of the information was a barrier to disclosure ($p = 1.0$).

Gender and motivations for sharing positive BRCA1/2 status

Greater than 90% of men and women surveyed reported the following motivations for sharing genetic risk information: a feeling of obligation toward family members (93.8% men and 94.0% women), a belief that disclosing risk information would help relatives make medical decisions (93.8% men and 98.8% women), a desire to provide relatives risk

information (93.8% men and 95.1% women), and a desire for relatives to be tested (93.9% men and 96.3% women). As noted in Table 8, the need for emotional support was a significant motivation for sharing positive mutation status among women (70%) compared to men (34%) ($p<0.01$; OR=0.22, CI =0.09–0.59). Men were more likely to cite direct inquiry regarding test results as a reason for sharing, though this was not statistically significant (70% men vs. 51% women; p=0.08; OR = 2.2, CI = 0.83–6.19). There was no statistically significant gender-based difference in the following motivations for sharing positive *BRCA1/2* results: feeling obligated to share, being encouraged by health professionals to share, making agreements with family members prior to receiving results, being encouraged by other family members, feeling that information could help relatives make medical decisions, needing advice from family members for medical decision making, providing relatives information regarding their own risk, or encouraging relatives to get tested.

Gender and reasons that might have made It easier to share positive BRCA1/2 status

Although there was no evidence that physician recommendation was a definitive reason participants chose to share positive *BRCA1/2* results with family members, 65% of women and 43% of men surveyed reported that physician recommendations made it easier to share results with relatives ($p = 0.051$; OR=2.44, CI = 0.95–6.25). While not statistically significant between genders, greater than 85% of men and women surveyed believed that the following factors made it easier to share: a good understanding of results (87.1% men and 91.4% women; $p = 049$), a close relationship with relatives (93.6% men and 91.4% women; $p = 1.0$), belief that disclosure would help relatives with medical decision making (96.8% men and 93.8% women; $p = 1.0$), and the belief that relatives might want to be tested (90.3% men and 91.4% women; $p = 1.0$).

Gender and difficulty discussing positive BRCA1/2 results

As shown in Table 8, men reported significantly more difficulty, in general, discussing positive *BRCA1/2* results with family members than women (90% vs. 70%; $p = 0.03$; OR = 4.24, CI = 1.13–23.50). However, 48% of women reported emotional difficulty versus 13% of men ($p<0.01$, two-sided FET; OR = 6.25, CI = 1.92–25). There were no gender-based differences with regard to whether the following topics made it difficult to share results: complexity of information, lack of close relationships with relatives, poor understanding of who was at risk for *BRCA1/2* mutations, disinterest in or poor understanding of applicability of test results among relatives, fear of upsetting relatives, guilt or anxiety regarding positive test results, or the desire for privacy regarding positive test status.

Discussion

Our study demonstrates a very high disclosure of genetic testing information in known mutation carriers; subjects reported an overall 90% disclosure rate, with 95% disclosure to FDRs and 78% disclosure to SDRs. Compared to other studies of known mutation carriers, our overall disclosure rate is higher, but the disclosure to FDRs is similar (Blandy *et al.*, 2003; McGivem *et al.*, 2004). In studies of *BRCA1/2* testing and disclosure patterns in high-risk families after genetic testing, both positive and negative results were discussed within families, but disclosure was highest among *BRCA1/2*-positive study participants to FDRs (Hughes *et al.*, 2002; Claes *et al.*, 2003; Wagner Costalas *et al.*, 2003). In addition, distant relatives were more likely to be told about conclusive (definitively positive or negative) rather than inconclusive genetic results (Claes *et al.*, 2003). While these studies suggest that *BRCA1/2*-positive individuals understand the need to disseminate genetic information to at-risk relatives, it is unclear how much at-risk *BRGA 1/2*-positive individuals and families comprehend regarding gene transmission, degree of risk among affected relatives, and

prophylactic/screening practices. Some studies suggest that despite genetic counseling, comprehension remains low (Blandy *et al.*, 2003). Additional research on comprehension and retention of genetic counseling information by mutation carriers is necessary so that more effective practices can be created.

A larger percentage of participants who disclosed test results selectively rather than to all at-risk relatives noted that lack of a close relationship made it more difficult to share. This supports previous data that suggest that, despite counseling efforts, mutation carriers describe decreased disclosure to relatives with whom affected individuals have difficult or distant relationships (Julian-Reynier *et at.,* 1996; Green *et al.,* 1997; Hughes *et al.,* 2002; Forrest *et al.,* 2003; McGivem *et al.,* 2004), or with whom there is an FDR available to discuss positive family results (Claes *et al.,* 2003; Peterson *et al.,* 2003; McGivern *et al.,* 2004). In this family context, it is concerning that a person several times removed from the actual genetic counseling process provides genetic risk information to other family members, potentially distorting the content of the transmitted information. There is limited data on the content of genetic risk discussions among extended families.

Our data regarding disclosure to female and male relatives indicate no difference at either the FDR or SDR level. This is discordant with previous studies that describe disclosure patterns among high-risk mutation-positive, mutation-negative, and mutation-indeterminate individuals (Julian-Reynier *et al,* 2000; Claes *et al.,* 2003; Daly *et al,* 2001; Wagner Costalas *et al.,* 2003). In one study of only mutation-positive individuals, the disclosure rate to female and male relatives was equal, consistent with our data (McGivern *et al.,* 2004). Another study of mutation-positive individuals showed a statistically significant increased disclosure to daughters versus sons, but otherwise equal disclosure to female versus male relatives (Blandy *et al.,* 2003). One hypothesis to explain high disclosure to all at-risk relatives among members of mutation-positive families is that individuals disseminate risk information widely so that other at-risk relatives can receive counseling and testing, regardless of gender or strength of relationship. High-risk individuals report this rationale in numerous studies (Green *et al,* 1997; Hughes *et al,* 2002; McGivern *et al,* 2004). However, poor uptake of genetic counseling and testing by at-risk relatives suggests that there is not a strong correlation between dissemination of risk information and a change in behaviors among informed relatives. Indeed, our survey participants encouraged testing to the majority of at-risk relatives, yet despite decreased barriers to testing, the rate of genetic testing remained low.

Disclosure was higher to members of younger generations while testing uptake was higher in members of older generations. This testing uptake pattern may reflect the perception that *BRCA1/2* genes predispose to late onset cancers (breast and prostate), or that as people age, they develop increasing concern regarding health issues. Alternatively, this may indicate increased value or concern for the health of younger family members, and thus a stronger tendency to disclose test results to this population.

Despite very high disclosure rates (90%) and free genetic counseling and testing for family members, participants described a substantially lower uptake of testing (57% total, 61% in FDR, and 47% in SDRs). This is consistent with other studies that demonstrate poor uptake despite communication of positive *BRCA1/2* status within families (Claes *et al,* 2003; Landsbcrgen *et al,* 2005). Our uptake data are limited in that they arc based on survey participants' knowledge of relatives' testing behavior, not on actual test results. Notably, we found that no members of at-risk paternally related families decided to pursue testing, despite disclosure patterns similar to those among maternally related at-risk individuals. This suggests a significant gap in understanding of genetic risk in these kindreds. Other research suggests that there is decreased reporting of breast cancer cases and risk along

paternal lineages (Green *et al*, 1997; Quillin *et al*, 2006). In one study of 46 women from hereditary breast and ovarian cancer (HBOC) families, only 13 women (28%) knew about paternally related cancers of any kind, and only 4 (9%) knew of paternal relatives with breast or ovarian cancers specifically (Green *et al.*, 1997). Additional research is necessary to learn how to effectively identify and screen people in at-risk paternally related lineages, and also to impact the communication patterns regarding cancer risk within these families.

An additional limitation of the disclosure and uptake data from our 115 participants is that these individuals were members of 47 kindreds and multiple individuals from a single kindred could participate. This impacts descriptive data in the study such as race and ethnicity, and also may impact interpretation of the data, since it is possible that intrafamilial factors influence disclosure patterns in ways that are not captured in the structure of our survey. We were not able to account for the potential intrafamilial factors in our statistical design due to the small sample size and the structure of the survey design. We acknowledge the potentially confounding influence created when individuals within the same extended family reported disclosure and uptake patterns. Substantial correlation within patient or family may reduce the power of comparison across groups. However, for the comparisons presented, these correlations are likely to bias our analyses toward the null; for example, if patients vary in their propensity to report to family members and this propensity influences the probability of a family member having been told, the ability to identify differences in FDRs versus SDRs or men versus women would be significantly reduced. In addition, individuals were reporting on factors that influenced their own disclosure patterns which potentially will differ among family members. The study population was based on families with known *BRCA1/2* mutations. This may bias the reporting in favor of disclosure and genetic counseling, as participants are from kindreds in whom some individuals had already proactively sought genetic counseling and testing.

Our survey participants included 32 men with known *BRCA1/2* mutations. Male participants reported more general difficulty discussing *BRCA1/2* result than female participants, but few of the specific factors mentioned in our survey were associated with distress or difficulty with disclosure. There are very few studies that study male *BRCA1/2* mutation carriers and their decision-making patterns. Research suggests that male inheritance patterns of *BRCA1/2* mutations are not well understood among at-risk family members. In one study, knowledge of HBOC was measured by a survey using true/false statements in members of high-risk families who had received genetic counseling; those who had inconclusive genetic testing results reported increased confusion regarding transmission of *BRCA1/2* mutations through males (Claes *et al*, 2003). In another study, following genetic counseling, only 27% of surveyed individuals were correct regarding the risk of transmission of *BRCA1/2* mutations by male carriers (Blandy *et al*, 2003). Additionally, the same study found that men informed of risk had trouble believing and accepting the information provided (Blandy *et al*, 2003).

While our survey did not specifically ask whether men were active in family discussions of risk, we did not find statistical differences in male survey participants' rates of disclosure or in factors impacting methods of disclosure. Some research suggests that men in high-risk families may be excluded from discussions of breast cancer (McAllister *et al.*, 1998), while other studies report male participation in family discussions regarding mutation status (McAllister *et al*, 1998; Liede *et al*, 2000). In mutation-positive men and women, women more frequently cited concern regarding personal risk as a reason to be tested, while men noted concern for children and family as more important factors influencing personal testing decisions (Liede *et al*, 2000). More targeted research to understand decisions by men regarding genetic testing and disclosure of risk status is needed.

Risk-reduction strategies, such as prophylactic surgery, chemoprevention, and enhanced breast cancer screening, have been shown to be effective, and are often a part of genetic counseling discussions with *BRGA1/2*-positive women. Similar risk-reduction strategies, such as prostate-specific antigen (PSA) screening, are not as well established for male *BRCA1/2* carriers. As research on appropriate cancer screening for male *BRCA1/2* carriers continues, integration of this data into genetic counseling sessions may increase the impact of these interventions. If proven methods to decrease cancer risk for men are established, this may enhance the perceived benefit of genetic counseling and testing among this population. An additional reason to seek genetic testing, apart from the potential changes in medical management, is to understand whether one's children are at risk for a *BRCA1/2* mutation. Low uptake of genetic testing in men in families with known *BRCA1/2* mutations may significantly limit information for female relatives.

We did not discover any factors that significantly contributed to participants' desire to talk about genetic risk with family members. Several issues were cited as contributing to difficulty in discussing results, though were not clearly deterrents. Similar to other studies (Hughes *et al*, 2002), the need for emotional support was a motivation for women who were sharing risk information. Women were also more likely (though not statistically significantly so) to value a physician recommendation for disclosure, which is consistent with previous reports regarding women seeking more medical care and advice.

In our study population, surveyed individuals are from families in which a known *BRCA1/2* mutation carrier had already been identified. Implied in our study design, participants were already aware of increased personal and family risk prior to enrollment. Our study population is drawn from families that may be more likely to communicate about risk status, as the participants are well-educated, middle-class, predominantly white members of families with multiple breast/ovarian cancer cases and known *BRCA1/2* mutations. The population does not differ greatly from other groups surveyed in the literature. The total number of survey participants in our study is small, yet still represents one of the largest analyses of male mutation carriers. It is possible that race, marriage status, income, education, and employment may be confounding variables, but the small sample size limits the usefulness of these comparisons.

Summary

In summary, our study demonstrates that people with positive *BRCA1/2* status usually inform at-risk relatives, but uptake of genetic testing remains relatively low among at-risk family members. Although participants disclosed positive mutation status to at-risk maternal and paternal relatives, no at-risk paternally related family members sought testing. These observations indicate a clear need for additional research and development of targeted genetic counseling to impact uptake of testing in high-risk men and people in high-risk paternally related lineages.

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Appendix A: Survey Questions Regarding Factors Influencing Disclosure

Please consider each of the following reasons for choosing to share your results with family members. Rate each reason on a scalc from 1–4 to indicate how much of a role it played in deciding to share your BRCA1/2 test results with family members.				
a. I felt obligated to share the information	1	2	3	4
b. I was encouraged by the health professional	1	2	3	4
c. I made an agreement to tell them before receiving my results	1	2	3	4

d. I was encouraged by other family members to share the information	1	2	3	4
e. I felt the information could help my relatives in making medical decisions	1	2	3	4
f. I was asked about the result by a family member	1	2	3	4
g. I needed emotional support from my family members	1	2	3	4
h. I needed advice from my family members in making medical decisions	1	2	3	4
i. I wanted to provide them information about their risk	1	2	3	4
j. I wanted to encourage them to get tested	1	2	3	4
Other:_____				

1 =No role

2= A small role

3 = A medium role

4 = A large role

Please consider each of the following reasons that might have made it hard in general to share your results with family members. Rate each reason on a scale from 1–4 to indicate how much of a role it played in deciding to share information.				
a. It was emotionally difficult to share the info.	1	2	3	4
b. The information was complex and I did not know what to say	1	2	3	4
c. I do not have a close relationship with some of my relative(s)	1	2	3	4
d. I did not know who was at risk for having a BRCA1/2 mutation	1	2	3	4
My relatives did not want to know about my test results	1	2	3	4
f. My relatives did not understand how the information applied to them	1	2	3	4
g. I did not want to upset my relative(s)	1	2	3	4
h. I felt guilty or anxious about my test result	1	2	3	4
i. I felt the information was too personal	1	2	3	4
Other:_____				

1 = No role

2 = A small role

3 = A medium role

4 = A large role

Please consider each of the following reasons that might have made It easier in general to share your results with family members. Rate each reason on a scalc from 1 to 4 to indicate how much of a role it played in deciding to share information:				
a. I had a good understanding of what my results meant	1	2	3	4
b. I have a dose relationship with some of my relatives	1	2	3	4

c. My doctor thought it was a good idea to tell my relatives	1	2	3	4
d. I thought it would help them make decisions about their healthcare	1	2	3	4
e. I thought they might want to get tested	1	2	3	4
f. I thought their children should know	1	2	3	4
g. I was asked about my results	1	2	3	4
Other:_____				

1 = No role

2= A small role

3 = A medium role

4 = A large role

For those relatives with whom you did *not* share your results, please rate each reason on a scale from 1–4 to indicate how much of a role it played in your not sharing the information.				
a. I do not know some of my relatives very well	1	2	3	4
b. I do not have a good relationship with some of my relatives	1	2	3	4
c. I did not believe the information would be useful to them	1	2	3	4
d. I was concerned about genetic discrimination	1	2	3	4
e. I did not think the relative could handle the information emotionally	1	2	3	4
f. I was worried about being responsible for causing problems in a relationship or marriage	1	2	3	4
g. My relative told me they did not want to know	1	2	3	4
h. I have not had time to tell my relatives	1	2	3	4
i. It is difficult to contact some of my relatives	1	2	3	4
j. A relative was having difficulties and I did not want to burden them	1	2	3	4
Other:_____				

1 = No role

2 = A small role

3 = A medium role

4 = A large role

Table 1

Demographics

Category	*n* (total = 115)	%
Gender		
Female	83	72.17
Male	32	27.83
Age		
18–39	15	13.04
40–59	73	63.48
60+	27	23.48
Unknown	0	0
Race/ethnicity		
Ashkenazi Jewish	28	24.35
Non-Ashkenazi/Caucasian	79	68.70
Unknown/Caucasian	7	6.09
Other	1	0.87
Relationship status		
Single/never married	6	5.22
Married	98	85.22
Divorced/separated	9	7.83
Widowed	2	1.74
Education level		
High school graduate or less	15	13.04
Some college	22	19.13
College graduate or beyond	78	67.83
Not collected	0	0.0
Employment status		
Unemployed	20	17.39
Full-time	58	50.43
Part-time	17	14.78
Retired	19	16.52
Not collected	1	0.87
Annual income		
<$20,000	4	3.45
$20,001–$50,000	19	16.52
$50,001–$75,000	17	14.78
$75,001–$100/100	21	18.26
>$100,000	42	36.52
Not collected	12	10.43
Health insurance status		
Insured	109	94.78
Uninsured	5	4.35

Category	*n* (total = 115)	%
Not collected	1	0.87

Table 2

Reported Mutation Status Disclosure and Testinc Uptake among FDRs and SDRs of Survey Participants

	Disclosure (number told/total number)	Testing uptake (total tested/total told)
	***n*/total (%)**	***n*/total (%)**
First-degree relatives		
Mother	8/9 (88.8)	7/8 (87.5)
Father	12/12 (100)	9/12 (75)
Sister	158/162 (97.5)	122/158 (77.2)
Brother	136/148 (91.9)	71/136 (52.2)
Daughter	61/65 (93.8)	36/61 (59.0)
Son	53/54 (98.1)	15/53 (28.3)
Total FDR	428/450 (95.1)	260/450 (60.7)
Second- and third-degree relatives		
Maternal aunt	28/42 (66.6)	17/28 (60.7)
Paternal aunt	7/13 (53.8)	0/7 (0.0)
Maternal uncle	31/45 (68.9)	20/31 (64.5)
Paternal uncle	3/5 (60.0)	0/3 (0.0)
Niece	50/54 (92.6)	30/50 (60.0)
Nephew	41/46 (89.0)	7/41 (17.1)
Total S+TDR	160/205 (78.0)	74/160 (46.3)
Total all relatives	588/655 (89.8)	334/655 (56.8)

Denominators in this table are calculated using missing and nonmissing data; the denominator includes all possible at-risk relatives who could be informed and subsequently tested for mutations.

Table 3

Disclosure Patterns in Families with Known BRCA1/2 Mutations

	Number/total (%) told[a,b]	*p*-value[c]	OR	CI
First-degree relative				
Mother vs. father	8/9 (89) vs. 12/12 (100)	0.43	—	—
Sister vs. brother	158/160 (99) vs. 136/144 (94)	0.051	4.65	0.90–45.44
Daughter vs. son	61/63 (97) vs. 53/54 (98)	1.00	0.60	0.01–11.85
Female vs. male	227/232 (98) vs. 201/210 (96)	0.28	2.0	0.6–7.8
Second-degree relative				
Maternal aunt vs. maternal uncle	28/42 (67) vs. 31/45 (69)	1.0	0.90	0.33–2.45
Paternal aunt vs. paternal uncle	7/16 (54) vs. 3/5 (60)	1.0	0.78	0.05–9.6
Maternal lineage vs. paternal lineage	59/87 (68) vs. 10/18 (56)	0.41	1.69	0.51–532
Niece vs. nephew	50/53 (94) vs. 41/46 (89)	0.47	2.0	0.37–13.77
Female vs. male	85/108 (78) vs. 75/96 (78)	1.0	1.03	0.5–2.13
FDR vs. SDR	428/442 (97) vs. 160/204 (78)	<0.01	8.4	436–17.07
Older vs. younger generation[d]	383/430 (89) vs. 205/216 (94)	0.01	2.27	1.14–5.00

[a] Percentages and ORs are calculated using nonmissing data only.

[b] Percent of people to which + mutation status was disclosed (told/told + not told).

[c] Two-sided Fisher's exact test (FET).

[d] Older generation (mother/father/aunt/uncle/sister/brother); younger generation (daughter/son/niece/nephew).

Table 4

Genetic Testing Uptake after Disclosure of Known *BRCA*1/2 Mutations

	Number tested/told (%)[a,b]	*p*-value[c]	OR	CI
First-degree relative				
Mother vs. father	7/9 (78) vs. 9/12 (75)	1.0	1.17	0.10–17.53
Sister vs. brother	122/155 (79) vs. 71/134 (53)	<0.01	3.28	1.91–5.67
Daughter vs. son	36/63 (57) vs. 15/47 (53)	0.01	2.84	1.21–6.80
Female vs. male	165/227 (73) vs. 95/193 (49)	<0.01	2.75	1.79–4.21
Second-degree relative				
Maternal aunt vs. maternal uncle	17/27 (63) vs. 20/31 (65)	1.0	0.94	0.28–3.14
Paternal aunt vs. paternal uncle	0/6 (0) vs. 0/3 (0)	—	—	—
Maternal lineage vs. paternal lineage	37/58 (63) vs. 0/9 (0)	<0.01	—	—
Niece vs. nephew	30/36 (83) vs. 7/29 (24)	<0.01	15.71	4.05–64.36
Female vs. male	47/69 (68) vs. 27/63 (43)	<0.01	2.85	1.32–6.18
FDR vs. SDR	260/420 (61) vs. 74/132 (56)	0.26	1.27	0.84–1.93
Older vs. younger generation[d]	246/377 (65) vs. 88/175 (50)	<0.01	1.86	1.27–2.72
Female FDR and SDR vs. male FDR and SDR	212/296 (72) vs. 122/256 (48)	<0.01	2.77	1.92–4.01

[a] Denominator represents nonmissing data only and represents the number of people who were informed of genetic risk and who had genetic testing, based on knowledge of survey participant. Several participants answered unknown, so the denominator docs not match the number given for number told in Table 2 or 3.

[b] Percent of people who received testing for *BRCA1/2* status after a family member was diagnosed with the mutation (number tested/total number).

[c] Two-sided Fisher's exact test (FET).

[d] Older generation (mother/father/aunt/uncle/sister/brother); younger generation (daughter/son/niece/nephew).

Table 5

Methods Used to Discuss Genetic Risk Information with Family Members

	***n*/total**	**%**
Discussed in person	100/115	87.0
Discussed over the telephone	88/115	76.5
Wrote a letter	12/115	10.4
Sent an e-mail	13/115	11.3
Asked another family member to tell someone	34/115	29.6

Table 6

Topics Discussed with One or More Relatives

	***n*/total**	**%**
Chance of having a mutation	98/115	85.2
Cancer risk for people with a mutation	102/115	88.7
Special screening guidelines for people with a mutation	81/115	70.4
How medical care can change for people with a mutation	80/115	69.6
Preventative surgery or medication options to reduce risk	89/115	78.3
Information about genetic discrimination	50/115	43.5

Table 7

Factors That Made It Harder to Share Positive Mutation Status

	Number (%)				
Factor	**Full disclosure**	**Partial disclosure**	***p*-value**	**OR**	**CI**
I do not have a close relationship with some of my relatives	13/86 (15%)	12/26 (46%)	<0.01	0.21	0.07–0.62
I did not know who was at risk for having a *BRCA1/2* mutation	10/86 (12%)	8/27 (30%)	0.04	3.2	0.94–11.11
My relatives did not want to know about my test results	6/86 (7%)	8/27 (30%)	<0.01	5.62	1.48–21.79
My relatives did not understand how the information applied to them	13/86 (15%)	9/26 (35%)	0.05	2.98	0.95–8.94

Table 8

Gender Differences Regarding Disclosure of Positive Mutation Status

	Number (%)				
Factor	**Female**	**Male**	***p*-value**	**OR**	**CI**
Need for emotional support is a motivation to share	57/82 (70%)	11/32 (34%)	<0.01	0.22	0.09–059
Experience general difficultly/distress discussing positive *BRCA1/2* results	57/82 (70%)	29/32 (91%)	0.03	4.24	1.13–23.50
Experienced emotional difficultly discussing positive *BRCA1/2* results	38/80 (48%)	4/32 (13%)	<0.01	6.25	1.92–25.0
Physician recommendation to share test results made it easier to disclose results	52/80 (65%)	13/30 (43%)	0.05	2.44	0.95–6.25