

Reactions to Direct-To-Consumer BRCA Test Results



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Goals of study

Inherited *BRCA1* and *BRCA2* gene mutations convey a high risk for breast and ovarian cancer, but current guidelines limit *BRCA* mutation testing to women with early-onset cancer and relatives of mutation-positive cases. Benefits and risks of providing this information directly to consumers are unknown. In addition, growing activity in the area of whole genome and exome sequencing has raised the question of how to deal with unexpected medically relevant information, yet there is little published data to inform this discussion.

This study focused on reactions of individuals who received the results of testing for three mutations that predispose one to hereditary breast and ovarian cancer (HBOC): *BRCA1* 185delAG and 5382insC, and *BRCA2* 6174delT, most common in people with Ashkenazi Jewish ancestry. *BRCA1* mutations confer upon women a breast cancer risk of about 60% and an ovarian cancer risk of about 40%; *BRCA2* mutations confer a breast cancer risk of about 50% and an ovarian cancer risk of about 20% (Chen & Parmigiani 2007). Among all predictive genetic tests currently available directly to consumers, *BRCA1/2* mutation testing can be considered the most actionable, with proven clinical utility (Domchek *et al.* 2010).

Our interview-based study aimed to collect empirical data on the benefits and harms experienced by consumers who purchased 23andMe's Personal Genome Service® (PGS®) that includes testing for these three relatively common *BRCA1/2* mutations. We report here the experiences of individuals who were faced with unexpected genetic information that has personal, medical, and family health consequences.

Methods

We invited all 136 *BRCA1* and *BRCA2* mutation-positive individuals in the 23andMe customer database who had chosen to view their *BRCA1/2* report to participate in this IRB-approved study. We also invited 160 mutation-negative customers who were matched for age, sex and ancestry. Semi-structured phone interviews were completed for 32 mutation carriers and 31 non-carriers (Table 1).

Table 1: Demographic characteristics of cases (those with one of three *BRCA1/BRCA2* variants) and controls (those without any of three variants) who completed interviews.

	Cases (n=32)		Controls (n=31)	
	Females	Males	Females	Males
Completed Interview	16	16	18	13
Age Range	30-73	26-62	27-73	23-66
Mean Ages by Sex	51	43	50	43
Mean Ages by Group	47		47	

Questions addressed personal and family history of cancer, decision and timing of viewing the *BRCA1/2* report, recollection of the result, emotional responses, perception of personal cancer risk, information sharing, and actions taken or planned. The interviews were taped, coded and transcribed. Four researchers reviewed and scored the anonymous transcripts independently and their findings were reconciled. Mutation status as recalled by each participant was independently confirmed through inspection of the database.

Results

Ancestry and awareness of test

Six of 32 mutation-positive participants did not report knowledge of any Ashkenazi Jewish ancestry; one reported Indian ancestry, consistent with previous identification of his *BRCA1* 185delAG mutation in breast cancer patients in India (Vaidyanathan *et al.* 2009). At the time of purchase, 13/32 (41%) mutation-positive participants ("cases") were aware that *BRCA1/2* testing was included in the PGS®, compared to 20/31 (65%) of mutation-negative participants ("controls"). Twenty of 32 (63%) cases were aware that having Ashkenazi Jewish ancestry confers higher chance of having one of the three *BRCA* mutations, compared to 13 of 31 (42%) controls.

Emotional reactions

Ten of 16 mutation-positive women were not surprised by their *BRCA1/2* test result (Table 2), including five who had been previously tested, one who had close relatives known to be mutation-positive, and four with a strong family history. The 12 mutation-positive men who were not surprised cited the following as reasons: two already knew about their mutation, one had a mutation-positive aunt, some had a positive family history of breast and ovarian cancer and others had realized they were at risk by having Ashkenazi Jewish ancestry.

Table 2. Emotional responses to *BRCA* testing results.

	Cases (n=32)		Controls (n=31)	
	Females (n=16)	Males (n=16)	Females (n=18)	Males (n=13)
Were you surprised by this result?				
Yes	6	4	1	0
No	10	12	17	13
How did you feel about this information?				
Extremely upset (cried, lost sleep had thoughts of suicide...)	0	0	0	0
Moderately upset (couldn't stop thinking about the result, felt moderate anxiety)	3	1	0	0
Somewhat upset (initial disappointment, transient anxiety)	3	6	0	0
Neutral	9	8	7	8
Relieved	1	1	10	5
Extremely relieved (if had high anxiety before)	0	0	1	0

Eleven women and 14 men received the unexpected result that they are carriers of one of three *BRCA1/2* mutations. None reported extreme anxiety and four reported moderate anxiety that was transitory (Table 2). Four women and six men in this group described their response as neutral.

Table 3: Actions taken after positive *BRCA1/2* results.

	Cases (n=32)	
	Females (n=16)	Males (n=16)
What did you do next?		
Talk to family/friends	7	7
Consult my primary care doctor	4	1
Consult a genetic counselor	3	
Consult a cancer specialist (OB/GYN, oncologist)	6	
Consult a cancer geneticist	2	
Had physical breast/ovarian exam and breast imaging	5	
Had risk-reducing mastectomy	1	
Had risk-reducing oophorectomy (removal of ovaries)	2	
Did online research	1	2
Quit smoking, changed diet		1

Actions taken and planned

Sharing of *BRCA1/2* test results with physicians was more common amongst cases (19/32 or 60%) than controls (8/31 or 26%); within the mutation-positive group, sharing the information was more common amongst women (13/16 or 81%) than men (6/16 or 38%).

Most mutation-positive women sought medical advice and four underwent risk-reducing procedures after confirmatory mutation testing (Table 3).

The 11 mutation-positive women who received this information through 23andMe for the first time took or planned the following actions: one prophylactic mastectomy, three planned mastectomies, three oophorectomies, and four planned oophorectomies (after childbearing). Five said they had breast exams and breast imaging after getting their results, and the seven who neither had nor were planning to have mastectomies reported that they would continue to have regular breast cancer monitoring. 13/16 mutation-positive men reported that they would get screened for prostate cancer.

Male carriers realized that their test results implied genetic risk for female relatives, and several of them felt considerably burdened by this fact. 75% of mutation-positive women and 31% of mutation-positive men were planning to make sure that their family members would get tested.

Female carrier: "While the results were shocking and a little stressful, ultimately I think this could potentially change my life, and it obviously made a difference for my aunt, who was able to catch pre-cancer early. So I think all in all, it's a positive thing. We would have never known, because there are no (affected) first and second-degree relatives. So until somebody ended up with breast or ovarian cancer I don't think we would have known."

Male carrier: "My mother saw a genetic counselor as a result of my testing and my little sister saw a genetic counselor as a result of my test."

Sharing mutation information with family members led to screening of at least 30 relatives and identification of 13 additional carriers. Controls did not report inappropriate actions, such as foregoing cancer screening

Overall response to testing

All but one of the 32 mutation-positive participants reported that they appreciated learning their *BRCA1/2* status. Thirty of 32 cases and 30 of 31 controls said they would purchase the PGS® again. The participants found the PGS® worthwhile for several reasons, the most significant being that some mutation carriers felt it may have saved their lives or the lives of relatives who tested *BRCA1/2* positive as a result of the primary participant being tested. One male carrier said he would rather not have known. One mutation-positive woman said she already knew her results and didn't learn anything new.

Conclusions

- Direct access to *BRCA1/2* mutation tests provided clear benefits to participants.
- The high level of sharing with physicians for mutation-positive women most likely reflects the actionability of the test results.
- The vast majority took or were planning preventative actions including prophylactic surgery or screening.
- The unexpected information created a ripple effect as relatives of newly identified carriers also sought testing.
- Six mutation carriers did not report Ashkenazi Jewish ancestry – need to consider that many with mutation may not be aware of such ancestry.
- Overall, participants, whether they knew before signing up or not that the test included *BRCA1/2*, appreciated learning their *BRCA1/2* status.

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References

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