Family Notification and Cascade Screening After *BRCA* Genetic Testing

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Background

Deleterious mutations in the *BRCA1* or *BRCA2* genes confer an estimated 80% lifetime risk of breast cancer and 40% lifetime risk of ovarian cancer.[1] An important public health genetics strategy is to promote genetic testing for the relatives of individuals with known *BRCA* mutations, which is known as cascade screening. Established clinical guidelines recommend genetic counseling and testing for those with a known mutation in the family.[2,3]

Why Promote Cascade Screening?

- BRCA mutations are autosomal dominant, which means immediate relatives are at 50% risk
- Enhanced screenings (mammograms, breast MRI) can aid early cancer detection[4]
- Cancer risk reduction through medication, mastectomy and/or oophorectomy[5]
- Relatives without the mutation can avoid unnecessary interventions
- Testing for specific mutations is less expensive than full gene sequencing
- Testing for a known family mutation provides the most informative results

Methods

As part of a cooperative agreement with the Centers for Disease Control and Prevention, a phone survey of *BRCA* positive and true negative women was created by the Michigan Department of Community Health Cancer Genomics Program and conducted by eight Michigan centers staffed with genetics providers. The centers administering the survey had provided genetic counseling to the respondents.

Eligible women met the following criteria:

- Counseled at one of eight facilities with genetics providers from Oct. 1, 2007 – Sept. 30, 2009
- Had *BRCA* testing, either before or after the counseling visit
- Were deleterious mutation positive or were negative for a known family mutation (true negative)

Seven of the eight facilities attempted inclusion of all of patients meeting criteria. One facility contacted a random subset of their eligible patients. The survey included questions on personal cancer history, *BRCA* results, family notification of testing and results, and subsequent testing in relatives.

Family communication and follow-up questions:

- Did you tell any family members that you were having *BRCA* testing?
  - Approximately how many family members did you tell?
- Did you share your *BRCA* test result with any family members?
  - Approximately how many family members did you share your results with?
- Of the family members that you notified about your results, how many have had *BRCA* testing since your test?
  - How many of these family members had a *BRCA* mutation?

The frequency of notification and mean number of relatives notified, tested and found positive were calculated.

References & Acknowledgements

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Results

Of eligible respondents, 138 (54.6%) completed the survey. Follow-up time from first counseling visit to date of survey ranged from 1.7 to 4.9 years. Some patients with deleterious mutations had testing prior to their first counseling visit. Time elapsed since first counseling visit was not significantly different in those with and without a cancer history or between those with/without a deleterious mutation (data not shown).

The majority of both positive and true negative women told a family member that they were having testing (92.8%) and notified their family about their test results (98.5%, Table 1).

Table 1. Cascade screening: family notification about *BRCA* testing and results

Cascade Screening Action	Positive	True Negative	Fisher's Exact Test p-value
Told family about BRCA testing?			0.49
Yes	87 (90.6%)	41 (97.6%)	
No	7 (7.3%)	1 (2.4%)	
Not sure	2 (2.1%)	0	
Told family about BRCA results?			1.00
Yes	93 (97.9%)	42 (100.0%)	
No	2 (2.1%)	0	

Table 2. Number of relatives notified, tested, and found to have a deleterious mutation among *BRCA* positive and true negative respondents

Cascade Screening Action	Positive	True Negative	T-Test p-value
	mean ± SD (range)	*mean ± SD (range)*	
How many relatives told about BRCA testing?	7.3 ± 7.4 (0, 50)	8.5 ± 8.8 (0, 50)	0.42
How many relatives told about BRCA results?	11.7 ± 10.0 (0, 50)	9.2 ± 6.0 (2.5, 30)	0.08*
How many relatives had subsequent testing?†	2.2 ± 2.3 (0, 12.5)	1.1 ± 1.7 (0, 8)	<0.01*
How many relatives were found positive?‡	1.2 ± 1.5 (0, 9)	1.4 ±1.7 (0, 7)	0.68

*p-value for unequal variances

†Includes relatives notified of results

‡Includes relatives who had testing

If relatives who were not notified about results or did not pursue testing are taken into account, there was an average of 0.9 ± 1.4 relatives found to be *BRCA* positive for every positive respondent. The number of relatives told about test results and the number who went on for testing was greater for positive vs. true negative respondents (Table 2).

Table 3. Number of relatives notified and tested among respondents with and without a personal history of cancer

Cascade Screening Action	Personal Cancer History	No Personal Cancer History	T-Test p-value
	mean ± SD (range)	*mean ± SD (range)*	
How many relatives told about BRCA testing?	7.4 ± 8.3 (0, 50)	7.9 ± 7.5 (0, 50)	0.73
How many relatives told about BRCA results?	12.1 ± 10.4 (2, 50)	9.8 ± 7.5 (0, 45)	0.14*
How many relatives had subsequent testing?	2.4 ± 2.7 (0, 12.5)	1.4 ± 1.6 (0, 7.5)	0.01*

*p-value for unequal variances

There was a significant difference in the number of relatives pursuing subsequent testing when comparing respondents with or without a personal cancer history at the time of testing. Personal cancer history did not appear to influence the number of relatives told about *BRCA* testing prior to notification about results (Table 3).

Length of time elapsed between first counseling visit and the survey was not predictive of the number of relatives told about BRCA testing or the number of relatives notified about results; time elapsed was also not predictive of the number of relatives pursuing subsequent testing (data not shown).

Conclusion

While almost all women communicated with at least one family member about their *BRCA* testing and results, only a small proportion of the relatives notified about test results were known to have pursued subsequent *BRCA* testing. This was true even for women with a *BRCA* mutation and/or with a personal cancer history.

Our results suggest that these women were willing to disclose *BRCA* –related information to relatives. Assessment of other impediments to further testing in relatives is needed; these may include the information communicated by the proband, the information understood by family members, and other barriers experienced by relatives. The identification of impediments to testing should prompt the development of novel strategies to advance appropriate follow-up by relatives.

Promoting the uptake of cascade screening will serve to maximize the public health potential of *BRCA* testing by identifying those at highest risk of mutation in the most cost efficient manner. Most importantly, high-risk relatives who pursue testing and discover a deleterious mutation can engage in screenings and interventions to reduce their risk of cancer. These individuals should not be denied this opportunity.