

Incidence and predictors of positive and negative effects of *BRCA1/2* genetic testing on familial relationships: a 3-year follow-up study

Julie Lapointe, OT, PhD Candidate^{1,2}, Karine Bouchard, MSc²,
Andrea Farkas Patenaude, PhD^{3,4}, Elizabeth Maunsell, PhD^{2,5,6}, Jacques Simard, PhD^{5,7},
and Michel Dorval, PhD^{1,2,6}; for the INHERIT BRCA^s Research Program

Purpose: Little is known about the long-term impact of *BRCA1/2* testing on the relationships between family members. We assessed the incidence of positive and negative family relationship effects of *BRCA1/2* testing in the 3 years after result disclosure and identified predictors of these effects.

Methods: A total of 485 women and 67 men who had undergone *BRCA1/2* testing were asked 3 years later whether having been tested had improved and/or disrupted relationships with their relatives. The associations with sociodemographic, medical, and psychosocial characteristics were assessed.

Results: Globally, 85.1% did not report any positive or negative effects of genetic testing on family relationships. Positive and negative effects were reported by 13.2% and 3.7% of participants, respectively. Reporting positive relationship effects was associated with older

age, intolerance for uncertainty, cancer-specific distress, and more social support. Low education, positive attitude toward prophylactic mastectomy, and low social support increased the likelihood of negative effects.

Conclusion: Our findings do not support the belief that family relationships are frequently disrupted by *BRCA1/2* testing. Understanding that most family relationships are unchanged long term by genetic testing may help genetic service providers encourage those considering testing to overcome hesitancy related to potential difficulties of communicating results to relatives.

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Key Words: *BRCA* genes; family communication; prospective study; psychosocial issues

INTRODUCTION

Genetic testing for cancer susceptibility is a family process.¹ Individuals undergoing testing first need to gather a precise family cancer history, which may entail asking relatives to recollect difficult past events. Further along in the process, the genetic test result will have medical and psychological implications not only for the counselee but also for his/her relatives. For instance, first-degree relatives of a *BRCA1* or *BRCA2* mutation carrier have a 50% risk of having this mutation. Female carriers have a lifetime risk of developing breast cancer, which varies between 43 and 85% and between 11 and 66% for ovarian cancer.^{2,3} To a lesser degree, *BRCA1/2* mutations also predispose males to certain types of cancer.^{4,5}

The psychological adjustment of individuals undergoing genetic testing for cancer susceptibility has been studied extensively.^{6–8} In general, no major long-term adverse psychological consequences seem to result from the genetic testing process with the exception of a consistently present subgroup of individuals who report distress.^{7,9,10} Although what causes psychological difficulties for this subgroup is still unclear, it has been proposed that psychological adaptation should be analyzed not

only at the individual perspective level but also in the context of the family interrelationships.¹¹

Presently, family members carry responsibility for notifying relatives about the presence of cancer-predisposing mutation.^{12,13} Some family members who have assumed the role of informant have encountered resistance to dispersion of information about familial mutations and sometimes feared to be the focus of resentment from relatives.¹⁴ Previous studies have shown that individuals undergoing *BRCA1/2* genetic testing share their test result with most, but not all, of their first-degree relatives quickly after it is disclosed.^{15,16} Motivations to communicate include the desire to obtain social support and to offer advice about preventive health strategies.^{15,17} Reasons for not communicating results to relatives include lack of a close relationship, infrequent communication, or thinking that the genetic information might upset a particular relative.^{17–19}

Despite accumulating knowledge on the psychological and communication aspects of genetic testing, little is known about the effects of the testing process on family relationships per se. Although positive family relationship effects have been

¹Faculté de Pharmacie, Université Laval, Québec, Canada; ²URESP, Centre de Recherche FRSQ du Centre Hospitalier Affilié Universitaire de Québec, Québec, Canada;

³Department of Psychosocial Oncology and Palliative Care, Dana-Faber Cancer Institute; Boston, Massachusetts, USA; ⁴Department of Psychiatry, Harvard Medical School, Boston, Massachusetts, USA; ⁵Faculté de Médecine, Université Laval; Québec, Canada; ⁶Centre des Maladies du Sein Deschênes-Fabia, Hôpital du Saint-Sacrement, Québec, Canada;

⁷Laboratoire de Génomique des Cancers, Centre de Recherche du CHUQ-CHUL, Québec, Canada. Correspondence: Michel Dorval (mdorval@uresp.ulaval.ca)

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reported more frequently than negative ones, these results come mainly from cross-sectional studies with small samples and with a time since result disclosure, which varied considerably between subjects.^{20–25} Only a few studies were specifically conducted to quantify the effects of the genetic testing process on family relationships.^{26–28} Data on the incidence of long term (i.e., >1 year) of family relationship effects after the receipt of test result are still lacking.

Two characteristics have been reported to be associated with negative effects on family relationships: mutation carrier status and lack of open communication.^{25,27} In the months following the test result disclosure, a decrease in the level of family cohesion and expressiveness have also been reported.^{26,28} To the best of our knowledge, no study has yet evaluated how other sociodemographic, medical, and psychosocial characteristics are associated with the incidence of long-term effects on family relationships in the context of *BRCA1/2* genetic testing. Identification of the possible relationship effects and their modifiable factors can help to develop strategies to relieve concern about possible adverse impacts of genetic testing on family interrelationships, which may in turn encourage testing for those at high risk of being mutation carriers.

We were able to investigate these effects in a prospective study we initiated in 1998 aimed at assessing quality of life, health-related behaviors, and family communication issues. Multiple sources were used to identify relevant variables to include in the follow-up questionnaires.^{29–32} At the time we planned the study, conceptual frameworks on psychosocial aspects of genetic testing were not well established. However, our work adheres basically to the Family System Genetic Illness model, which entails that the genetic information of one family member influences the entire family and that family dynamics will go into different phases over time.³³

The objectives of this prospective study were to assess the incidence of positive and negative effects on family relationships of *BRCA1/2* testing 3 years after result disclosure and to identify predictors of these effects.

MATERIALS AND METHODS

This study was part of the INHERIT BRCA (Interdisciplinary Health Research International Team on Breast Cancer susceptibility) research program in which *BRCA1/2* genetic testing was provided to French-speaking individuals in the province of Québec, Canada, who had a family history suggestive of an inherited breast and/or ovarian cancer susceptibility.³⁴ Methodological details have been described previously.^{34,35} In brief, all women and men who had undergone *BRCA1/2* testing between 1998 and 2004 were invited to participate in a longitudinal psychosocial study. Data were collected through four different mailed self-report questionnaires, the first administered shortly after the education session conducted before genetic testing and then the others 1, 12, and 36 months after disclosure of the genetic test result. This study was approved by the institutional ethics review boards of all participating institutions. All participants provided signed, informed consent.

Positive and negative effects on family relationships

Reports of the incidence of positive and negative effects on family relationships were collected in the 3-year follow-up questionnaire using the following question: “Did the fact that you had genetic testing improve relationships with any of your relatives?” The incidence of negative effects was assessed by a similar question: “Did the fact that you had genetic testing disrupt relationships with any of your relatives?” Participants answering “yes” to either question were then asked to identify, from a preestablished list, the family member(s) with whom these effects were experienced.

Predictors of family relationship effects

Sociodemographic, medical, and psychosocial characteristics potentially associated with these outcomes were assessed shortly after the pretest education session and/or 1 month and 12 months after result disclosure. Sociodemographic characteristics included gender, age, educational level, marital status, and having children. Medical variables included the genetic test result (carrier, noncarrier, and inconclusive), a personal cancer history before testing, having had a cancer diagnosis in the period after result disclosure, any cancer diagnosis in the family in the last 12 months, and deaths of family members from all causes in the last 12 months. The order in which participants were informed of their *BRCA1/2* test result within their family was also considered. A number of psychosocial variables were assessed. Consistent with the classification proposed by Kasparian *et al.*,³⁶ these measures pertained to psychological adjustment, knowledge, risk perception, decision-related outcomes, and social support. A detailed description of these psychosocial measures and time when assessed are provided in [Table 1](#).

Statistical analysis

The 3-year incidences of positive and negative effects on relationships and their 95% confidence interval (CI) were computed. The proportions of participants reporting positive and negative effects on relationships with each type of first-degree relatives and the spouse were computed. Because of how the question was formulated, the number of living relatives in each category is not available, and, therefore, specific incidences of effects for each first-degree relative could not be computed. All potential predictors were dichotomized ([Table 1](#)). This was done to facilitate group comparisons and to deal with the fact that most characteristics were not normally distributed. To identify predictors of positive and negative effects, we proceeded in two steps. First, we identified statistically significant univariate associations with the Fisher exact test (bilateral $P \leq 0.05$). Second, using multivariate logistic regression models, we forced the entry of the genetic test result and then—with a forward stepwise selection procedure (inclusion criterion $P \leq 0.05$ and removal criterion $P > 0.10$)—retained significant variables. To account for the few missing data, two approaches were used, dummy variables and listwise deletion.⁴⁴ As the findings were unchanged by the choice of method, results with missing data treated with dummy variables are presented. Multilevel models

Table 1 Overview of the psychosocial variables considered as possible predictors of positive or negative effects of genetic testing on family relationships

Variables	Measure (response scale)	No. of items (study α^a)	Possible range	Categories used for analyses ^b	Assessment time points		
					Pretest	1 mo	12 mo
Psychological adjustment							
General psychological distress in past 7 days	Psychiatric Symptom Index (PSI) ³⁷ (never, occasionally, quite often, and very often)	14 (0.88)	0–100	0: Low distress: $\leq 26/100^c$ 1: Moderate to high distress: $>26/100$	✓	✓	✓
Cancer-specific distress in past 7 days	Impact of Events Scale (IES) ^{38,39} (not at all, rarely, sometimes, and often)	15 (0.87)	0–75	0: Low distress: $<8.6/75^d$ 1: Moderate to high distress: $\geq 8.6/75$	✓	✓	✓
Tolerance for uncertainty	Abridged version of Freeston <i>et al.</i> ⁴⁰ (5 points ranging from “not at all in agreement” to “totally in agreement”)	13 (0.94)	0–52	0: Tolerant: $\leq 24/52^e$ 1: Intolerant: $>24/52$	✓	✓	✓
Risk perception							
Cancer risk perception	Investigator developed: “Would you say that your risk of getting cancer (or a new cancer) between now and the end of your life is:” (very low, low, average, high, very high)	1	1–5	0: Very low, low or average risk 1: Very high or high risk		✓	
Knowledge							
Knowledge about genetic breast and ovarian cancer susceptibility	Adapted from Lerman <i>et al.</i> ³² (true or false)	19 (NA)	0–100	0: Higher median ($\geq 56/100$) 1: Lower median ($<56/100$)	✓		
Decision-related outcomes							
Attitude toward prophylactic mastectomy	Investigator developed: “Please indicate which of the following statements best reflects your current feelings about prophylactic mastectomy:” (I will never have this operation; I have no intention now, but maybe in future; I am considering this possibility now; I have made the decision to undergo; not applicable)	1	1–5	0: Never or no intention 1: Consider or has taken the decision			✓

^aIf there was more than one measurement point, the lowest observed Cronbach alpha was reported. ^b0 category = reference category. ^cCut-off value for highest quintile observed in the general population of Québec. ^dScale developer’s proposed cut-off point. ^eCut-off corresponds to observed median value in this study. ^fCut-off point determined by lower tertile (<2 persons) in this population. NA, not applicable.

Table 1 Continued on next page

Table 1 Continued.

Variables	Measure (response scale)	No. of items (study α^a)	Possible range	Categories used for analyses ^b	Assessment time points		
					Pretest	1 mo	12 mo
Attitude toward salpingo-oophorectomy	Investigator developed: "Please indicate which of the following statements best reflects your current feelings about prophylactic ovariectomy: (1) I will never have this operation; I have no intention now, but maybe in future; I am considering this possibility now; I have made the decision to undergo; not applicable)	1	1-5	0: Never or no intention for now 1: Consider or has taken the decision			✓
Social support							
Number of confidants	Developed by Santé Québec ¹¹ : "How many people around you are available as confidants?" (open ended)	1	0-∞	0: Limited network ^f 1: Extended network	✓		
Number of close relationships	Developed by Santé Québec ¹¹ : "How many people around you are close to you and express affection?" (open ended)	1	0-∞	0: Limited network ^g 1: Extended network	✓		
Satisfaction with social support to confide about testing	Investigator developed: "Overall, to what extent are you satisfied with the support available to you for confiding in someone concerning your genetic test?" (4-point ranging from "very satisfied" to "very unsatisfied")	1	1-4	0: Satisfied and very satisfied 1: Unsatisfied and very unsatisfied		✓	✓

^aIf there was more than one measurement point, the lowest observed Cronbach alpha was reported. ^b0 category = reference category. ^cCut-off value for highest quintile observed in the general population of Québec. ^dScale developer's proposed cut-off point. ^eCut-off corresponds to observed median value in this study. ^fCut-off point determined by lower tertile (<2 persons) in this population. ^gCut-off point determined by lower tertile (<5 persons) in this population. NA, not applicable.

were used to adjust for possible family clustering effects.⁴⁵ The SAS 9.2 package (SAS Institute, Cary, NC) was used.

RESULTS

Initially, 750 (86.7%) individuals agreed to participate and completed the pretest questionnaire. Over the course of the study, 25 subjects died and 31 were no longer eligible due to their participation in another study. Of the remaining 694 subjects, 142 (18.9%) were excluded from the present analyses because they did not complete all follow-up questionnaires. Thus, a total of 552 individuals (79.5% of the 694 subjects eligible at follow-up) from 201 families completed the 3-year follow-up. The average number of participants per family was 2.7 (range: 1–23). Participants' mean age was 51.3 years (range: 18–87). When compared with the initial cohort, the final cohort displayed similar characteristics (Table 2). The intraclass correlation coefficients— used to estimate the family cluster effects or the degree of similarity between responses of family members— were 0.05 for positive family relationship effects and 0.25 for negative effects.

Overall, 470 participants (85.1%) did not report any effect— positive or negative— of genetic testing on their family relationships. The 3-year incidences of positive and negative effects on family relationships were 13.2% (95% CI: 10.3–16.1) and 3.7% (95% CI: 2.1–5.3), respectively. Eight participants (1.4%)

Table 2 Comparison of initial and final cohorts at pretest questionnaire according to sociodemographic and psychosocial characteristics

Characteristics	Initial cohort (n = 750), n (%) ^a	Final cohort (n = 552), n (%) ^a
Gender		
Women	645 (86)	485 (88)
Age		
<40 yr	142 (19)	98 (18)
40–59 yr	412 (55)	312 (56)
≥60 yr	196 (26)	142 (26)
Education		
> High school	530 (71)	374 (71)
Having children		
Yes	599 (81)	421 (80)
Personal history of cancer		
Yes	310 (41)	219 (40)
Genetic test result		
Carrier	144 (22)	114 (21)
Noncarrier	195 (29)	163 (30)
Inconclusive	330 (49)	275 (49)
High general psychological distress		
Yes	257 (34)	167 (32)
Moderate to high cancer-specific psychological distress		
Yes	350 (47)	244 (47)

^aBecause of missing data, number of participants does not always add to total.

reported both positive and negative effects. Proportion of participants reporting positive and negative effects of genetic testing on relationships with each type of first-degree relatives and their spouse are displayed in Figure 1. For both positive and negative effects, sisters were the relatives most frequently reported to be involved. For positive effects, daughters were the second most frequently involved family members.

Predictors of positive effects

An inconclusive test result was marginally less likely to be associated with report of positive family relationship effects than either positive or negative results. Five other characteristics were associated with positive effects on family relationships in the multivariate model (Table 3). Age ≥60 years was associated with positive effects on family relationships. Two were psychological adjustment variables, namely moderate to high cancer-specific distress and intolerance for uncertainty. Having an extended support network, as defined by the number of confidants and close relationships, was also associated with the incidence of positive effects.

Predictors of negative effects

The test result was not associated with the report of negative family relationship effects, although, again, participants who had an inconclusive result tended to less frequently report such effects than mutation carriers. Only three other variables were associated with the incidence of negative effects in the multivariate model: having a low educational level, considering or having decided to undergo a prophylactic mastectomy and being unsatisfied with social support available for confiding about testing (Table 4).

DISCUSSION

Our findings do not support the belief that family relationships are frequently disrupted by BRCA1/2 testing. To our knowledge, this study is the first to have evaluated both prospectively and in the long term the effects of BRCA1/2 genetic testing on family relationships on a large cohort with good participation of both women and men who have undergone testing. The great majority of relationships with family members were unaffected by getting testing results, as reported by the tested individual.

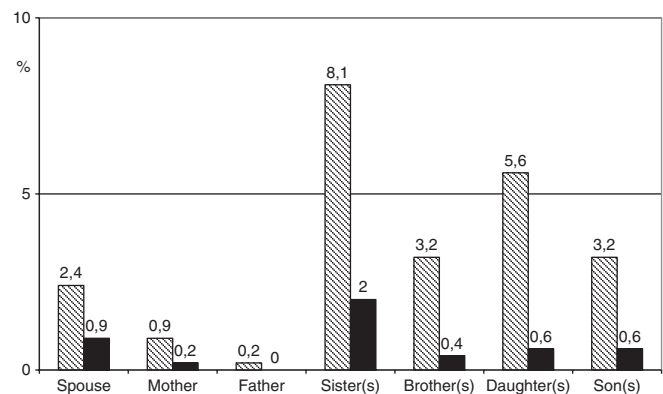


Figure 1 Proportion of participants reporting positive and negative effects of genetic testing on relationships with spouse and first-degree relatives (n = 552). ▨ positive effects; ■ negative effects.

Table 3 Multivariate logistic regression model of characteristics associated with positive family relationship effects at 3-yr postresult disclosure

Characteristics (no. of missing data)	Total N	Incidence of positive effects		Adjusted		
		n	Percentage	OR	95% CI	P
<i>BRCA1/2</i> genetic test result	(0)					
Carrier	114	17	14.9	1.0	Reference	
Noncarrier	163	23	14.1	1.0	0.5–2.0	0.9
Inconclusive	275	30	10.9	0.5	0.2–1.0	0.05
Age ^a	(0)					
<40 yr	77	4	5.2	1.0	Reference	
40–59 yr	298	26	8.7	2.1	0.7–6.4	0.2
≥60 yr	158	39	24.7	7.3	2.4–22.4	<0.01
Cancer-specific psychological distress ^b	(26)					
Low	281	25	8.9	1.0	Reference	
High	245	42	17.1	2.1	1.2–3.8	0.02
Tolerance for uncertainty ^c	(20)					
Tolerant	274	7	2.6	1.0	Reference	
Intolerant	258	12	4.7	2.8	1.5–5.1	<0.01
Number of confidants ^a	(27)					
Limited network	90	5	5.6	1.0	Reference	
Extended network	435	61	14.0	3.1	1.2–8.5	0.03
Number of close relationships ^a	(28)					
Limited network	161	12	7.5	1.0	Reference	
Extended network	363	54	14.9	2.0	1.0–4.1	0.05

^aMeasure taken at pretest. ^bAlthough cancer-specific psychological distress was assessed at different time points, only the pretest measure was associated with the report of positive effects in the multivariate logistic regression model. ^cAlthough tolerance for uncertainty was assessed at different time points, only the measure taken at 12 months postdisclosure was associated with the report of positive effects in the multivariate logistic regression model.

CI, confidence interval; OR, odds ratio.

Table 4 Multivariate logistic regression model of characteristics associated with negative family relationship effects at 3-yr postresult disclosure

Characteristics (no. of missing data)	Total N	Incidence of negative effects		Adjusted		
		n	Percentage	OR	95% CI	P
<i>BRCA1/2</i> genetic test result	(0)					
Carrier	114	7	6.1	1.0	Reference	
Noncarrier	163	8	4.9	1.5	0.4–5.5	0.51
Inconclusive	275	5	1.8	0.3	0.1–1.3	0.10
Educational level ^a	(25)					
> High school	374	7	1.9	1.0	Reference	
≤ High school	153	11	7.2	5.2	1.7–15.7	<0.01
Attitude toward prophylactic mastectomy ^b	(38)					
Never or no intention	412	10	2.4	1.0	Reference	
Considering or has made the decision	11	3	27.3	15.2	2.0–116.7	0.01
NA ^c	91					
Satisfaction with social support to confide about testing ^d	(35)					
Satisfied	499	12	2.4	1.0	Reference	
Unsatisfied	18	5	27.8	11.2	2.6–48.0	<0.01

^aMeasure taken at pretest. ^bMeasure taken at 12 months postresult disclosure. ^cNA, not applicable because the participant was either a man or a woman who had a bilateral mastectomy to treat breast cancer. ^dAlthough satisfaction with social support to confide about testing was assessed at different time points, only the measure taken at 1 month postdisclosure was associated with the report of negative effects in the multivariate logistic regression model.

Where there were changes, the positive effects were nearly four times more frequent than negative ones. The incidences observed are in line with those previously reported in either cross-sectional or shorter-term follow-up studies.^{20–25,27} These studies have also reported, similar to this study, more positive than negative family relationship effects.^{20–22,24,27} Taken together, these results offer reassurance about potential family effects to individuals considering *BRCA1/2* testing.

The association between psychological adjustment difficulties, such as cancer distress and intolerance for uncertainty, and the more frequent reporting of positive effects of genetic testing is intriguing. Little is known about the effect of psychological distress on family relationships in the context of genetic testing. With respect to family reactions to genetic testing for cancer susceptibility, Koehly *et al.*⁴⁶ observed that a communal coping strategy, defined by the use of group support to cope, is sometimes used by family members. Some qualitative studies have also reported that the genetic testing process had stimulated communication, improved connections, and brought individuals to address this potential threat together, as a family.^{47–49} Furthermore, this phenomenon of communal coping is consistent with the Family System Genetic Illness model which conceives of the family as an important source of support.³³ It may be hypothesized that individuals who have more cancer-related distress benefited or elicited more from the family communal support. A possible scenario might be that distressed individuals turned more to their family members to adjust to the threat of genetic information, and this may have enhanced relationships. For some participants, intolerance for uncertainty may have been relieved by receipt of a genetic test result. Those previously much burdened by difficulty tolerating uncertainty about cancer risk may have been pleased to share their relief with family members. Lessening of the anxiety associated with uncertainty may have enhanced the relationship with relatives. The fact that individuals with psychological adjustment difficulties reported positive relationship effects later on suggests that it could be relevant to develop strategies which may help patients enlist their relatives in ways which enhance group support and family communal coping.⁵⁰

Our observation that a favorable attitude toward prophylactic mastectomy is associated with negative effects on family relationships supports the need for professionals preparing patients considering this procedure about this possible consequence. Previously, qualitative studies have reported negative familial effects such as relatives being shocked and upset following family discussion about a woman's wish to have prophylactic mastectomy.^{51,52} A case history described how family pressure for a high-risk women to undergo prophylactic mastectomy may be associated with distress.⁵³ However, this is the first time that there has been quantitative evidence of the extent to which considering or having decided to have prophylactic mastectomy was associated with the report of negative effects in family relationships.

In this prospective study, different measures of social support were associated with positive and negative effects. One previous study reported that receiving support from family members played an important role in affecting relationship bonds

throughout the testing process.⁴⁸ Although it seems intuitive that strong social support is associated with more frequent reports of positive effects and unsatisfying social support with negative effects, the fact that significant associations were observed for these characteristics when measured years before the outcomes suggests the presence of a causal pathway. It may, therefore, be relevant to assess the availability of and satisfaction with social support early on during the genetic testing process to offer relevant, timely and situation-specific professional support and advice on ways to seek and receive social support.⁵⁴

To our knowledge, this is the first time that older age has been associated with positive family relationship effects in the context of *BRCA1/2* testing. A possible explanation could be that older individuals often assume a pivotal role within their family with respect to support and information sharing about genetic testing.⁵⁵ This role may create opportunities to experience positive effects on family relationships related to genetic testing by feeling efficacious about moving others to testing or to improved surveillance or surgery.

The fact that sisters were the most frequently involved relatives for both positive and negative effects is in line with previous findings. Sisters are among the relatives with whom *BRCA1/2* testing is the most frequently discussed.^{16–18,56} They may also face similar immediate decisions, which may help them to build positive bonds as they share information and experiences in deciding what steps to take to deal with hereditary susceptibility. Our data may also offer reassurance to parents who worry considerably about potential adverse effects of genetic testing on the relationship with their daughters, as in our study, the perceived impact on these relationships, when present, was positive.

The observation that individuals with an inconclusive test result tended to report less frequent family relationship effects, either positive or negative, may suggest that they have less opportunity for the kind of communication about results that could lead to changes in their relationships with family members. Communication between relatives about inconclusive results may be less frequent either because this result is not considered very informational or because its meaning is more difficult to convey. They may also not have to face the same burden of communicating to potential at-risk relatives or of facing difficult medical decisions as the ones facing individuals from mutation-positive families.⁵⁷

The design and methods of this study have several strengths that increase confidence in our findings. This is the first study to be conducted prospectively for such an extended time period when compared with effects over the first 6–12 months previously reported. Our design resulted in a uniform follow-up for all subjects, which is very important because family dynamics change over time. Furthermore, a wide range of sociodemographic, medical, and psychosocial characteristics was assessed at different time points along the genetic testing process, including before the test result disclosure. As a result, we identified several predictors of both positive and negative family effects, which deepen our understanding of this new research area. The sample size, which is twice as large as those of previous studies,

allowed us to examine infrequent outcomes in multivariate analyses. Finally, the statistical approach took into account the family cluster effects, which mean that standard error estimates were not biased by the fact that some participants were recruited from the same family.

This study also has some potential limitations. Possible selection bias is one. Even if initial participation and retention were fairly high, we cannot definitively exclude the possibility that the family relationship effects experienced by nonparticipating subjects differed from those of participants. However, the observation that no major difference exists between the characteristics of the initial cohort and those still in the study 3 years later is reassuring. The use of a single question to measure negative and positive family relationship effects is another potential limitation. The dichotomous items used in this study assessed either the presence or the absence of effects but did not provide further information about their causes, timing, or extent. It is possible that these items were subject to response bias, such as social desirability and accuracy of recall. We can speculate that family effects were more likely to be reported if they occurred close to the measurement time and/or if they were large effects. As we asked questions about effects at one time period, 3 years after disclosure, it is possible that later effects were disproportionately remembered and reported. Recognizing that our study questions were not designed to gather in-depth information about relationship effects, these clear and simple items still enabled a quantitative assessment of such effects. Finally, this study might have overlooked other potential predictors of family relationship effects; family communication is probably one of them. Even if the genetic test result per se is known to be communicated to a great proportion of first-degree relatives,^{15,16} less is known about the manner of telling, the information conveyed, and subsequent discussions about hereditary cancer.¹ Clearly, this important research area is embedded with several challenges, including the development of valid and sensitive measures of the unfolding process of family communication.

Future research using mixed qualitative and quantitative methods can explore further the range, nature, quality, and personal impact of such relationship effects. Future longitudinal research over a more extended period of time could also help clarify longer-term impact on family and individual life course development.⁵⁸ One could hypothesize that nodal points of heightened psychosocial strain would occur with transitions in family/individual member development and significant health events, such as cancer diagnosis or cancer death, in the immediate or extended family.⁵⁹

This study underscores the importance of medical genetics professionals discussing with their patients potential family effects that might be encountered when undergoing genetic testing for breast and ovarian cancer susceptibility. It also highlights particular subgroups of subjects who may merit stronger or more long-lasting professional support. This may include younger women who are leaning toward undergoing prophylactic mastectomy, which may be an increasingly large group as more second-generation daughters of mutation carriers are

tested. However, additional and more in-depth study of the causes, timing, and extent of effects on family relationships during the course of the genetic testing process is still needed. The communication of genetic test result is clearly important to subsequent family relationship effects. Determination of the relevant factors which predispose to positive effects should be addressed in future research on the manner of telling, the information conveyed, and subsequent discussions about hereditary cancer.¹ Because previous research efforts have tended to focus on negative effects,⁶⁰ we suggest that studying positive and neutral effects is just as important. A better understanding of how *BRCA1/2* testing can positively affect family dynamics may suggest strategies for genetic service providers to help individuals get the greatest benefit from their testing experience and relieve the burden of concern for those considering testing about the impact of family disclosure on relationships with close relatives.

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DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Patenaude AF. *Genetic Testing for Cancer: Psychological Approaches for Helping Patients and Families*. American Psychological Association: Washington, 2005.
2. Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with *BRCA1* or *BRCA2* mutations detected in case Series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet* 2003;72:1117–1130.
3. Antoniou AC, Cunningham AP, Peto J, et al. The BOADICEA model of genetic susceptibility to breast and ovarian cancers: updates and extensions. *Br J Cancer* 2008;98:1457–1466.
4. Risch HA, McLaughlin JR, Cole DE, et al. Population *BRCA1* and *BRCA2* mutation frequencies and cancer penetrances: a kin-cohort study in Ontario, Canada. *J Natl Cancer Inst* 2006;98:1694–1706.
5. Tai YC, Domchek S, Parmigiani G, Chen S. Breast cancer risk among male *BRCA1* and *BRCA2* mutation carriers. *J Natl Cancer Inst* 2007;99:1811–1814.
6. Braithwaite D, Emery J, Walter F, Prevost AT, Sutton S. Psychological impact of genetic counseling for familial cancer: a systematic review and meta-analysis. *Fam Cancer* 2006;5:61–75.
7. Meiser B. Psychological impact of genetic testing for cancer susceptibility: an update of the literature. *Psychooncology* 2005;14:1060–1074.
8. Hamilton JG, Lobel M, Moyer A. Emotional distress following genetic testing for hereditary breast and ovarian cancer: a meta-analytic review. *Health Psychol* 2009;28:510–518.

9. van Oostrom I, Meijers-Heijboer H, Lodder LN, et al. Long-term psychological impact of carrying a BRCA1/2 mutation and prophylactic surgery: a 5-year follow-up study. *J Clin Oncol* 2003;21:3867–3874.
10. Lerman C, Croyle RT, Tercyak KP, Hamann H. Genetic testing: psychological aspects and implications. *J Consult Clin Psychol* 2002;70:784–797.
11. Smith KR, West JA, Croyle RT, Botkin JR. Familial context of genetic testing for cancer susceptibility: moderating effect of siblings' test results on psychological distress one to two weeks after BRCA1 mutation testing. *Cancer Epidemiol Biomarkers Prev* 1999;8(4 Pt 2):385–392.
12. Godard B, Hurlimann T, Letendre M, Egalité N; INHERIT BRCA. Guidelines for disclosing genetic information to family members: from development to use. *Fam Cancer* 2006;5:103–116.
13. Sermijn E, Goelen G, Teugels E, et al. The impact of proband mediated information dissemination in families with a BRCA1/2 gene mutation. *J Med Genet* 2004;41:e23.
14. d'Agincourt-Canning L. Experiences of genetic risk: disclosure and the gendering of responsibility. *Bioethics* 2001;15:231–247.
15. Hughes C, Lerman C, Schwartz M, et al. All in the family: evaluation of the process and content of sisters' communication about BRCA1 and BRCA2 genetic test results. *Am J Med Genet* 2002;107:143–150.
16. Patenaude AF, Dorval M, DiGianni LS, Schneider KA, Chittenden A, Garber JE. Sharing BRCA1/2 test results with first-degree relatives: factors predicting who women tell. *J Clin Oncol* 2006;24:700–706.
17. McGivern B, Everett J, Yager GG, Baumiller RC, Hafertepen A, Saal HM. Family communication about positive BRCA1 and BRCA2 genetic test results. *Genet Med* 2004;6:503–509.
18. Finlay E, Stopfer JE, Burlingame E, et al. Factors determining dissemination of results and uptake of genetic testing in families with known BRCA1/2 mutations. *Genet Test* 2008;12:81–91.
19. MacDonald DJ, Sarna L, van Servellen G, Bastani R, Giger JN, Weitzel JN. Selection of family members for communication of cancer risk and barriers to this communication before and after genetic cancer risk assessment. *Genet Med* 2007;9:275–282.
20. Esplen MJ, Madlensky L, Butler K, et al. Motivations and psychosocial impact of genetic testing for HNPCC. *Am J Med Genet* 2001;103:9–15.
21. Liede A, Metcalfe K, Hanna D, et al. Evaluation of the needs of male carriers of mutations in BRCA1 or BRCA2 who have undergone genetic counseling. *Am J Hum Genet* 2000;67:1494–1504.
22. Metcalfe KA, Liede A, Trinkaus M, Hanna D, Narod SA. Evaluation of the needs of spouses of female carriers of mutations in BRCA1 and BRCA2. *Clin Genet* 2002;62:464–469.
23. Bradbury AR, Dignam JJ, Ibe CN, et al. How often do BRCA mutation carriers tell their young children of the family's risk for cancer? A study of parental disclosure of BRCA mutations to minors and young adults. *J Clin Oncol* 2007;25:3705–3711.
24. Hayat Roshanai A, Lampic C, Rosenquist R, Nordin K. Disclosing cancer genetic information within families: perspectives of counselees and their at-risk relatives. *Fam Cancer* 2010;9:669–679.
25. Manne S, Audrain J, Schwartz M, Main D, Finch C, Lerman C. Associations between relationship support and psychological reactions of participants and partners to BRCA1 and BRCA2 testing in a clinic-based sample. *Ann Behav Med* 2004;28:211–225.
26. McInerney-Leo A, Biesecker BB, Hadley DW, et al. BRCA1/2 testing in hereditary breast and ovarian cancer families II: impact on relationships. *Am J Med Genet A* 2005;133A:165–169.
27. van Oostrom I, Meijers-Heijboer H, Duivenvoorden HJ, et al. A prospective study of the impact of genetic susceptibility testing for BRCA1/2 or HNPCC on family relationships. *Psychooncology* 2007;16:320–328.
28. Stroup AM, Smith KR. Familial effects of BRCA1 genetic mutation testing: changes in perceived family functioning. *Cancer Epi Biomarkers Prev* 2007;16:135–141.
29. Baum A, Friedman AL, Zakowski SG. Stress and genetic testing for disease risk. *Health Psychol* 1997;16:8–19.
30. Botkin JR, Croyle RT, Smith KR, et al. A model protocol for evaluating the behavioral and psychosocial effects of BRCA1 testing. *J Natl Cancer Inst* 1996;88:872–882.
31. Hallowell N, Richards M. Understanding life's lottery. An evaluation of studies of genetic risk awareness. *J Health Psychol* 1997;2:31–43.
32. Lerman C, Narod S, Schulman K, et al. BRCA1 testing in families with hereditary breast-ovarian cancer. A prospective study of patient decision making and outcomes. *JAMA* 1996;275:1885–1892.
33. Rolland JS, Williams JK. Toward a biopsychosocial model for 21st-century genetics. *Fam Process* 2005;44:3–24.
34. Simard J, Dumont M, Moisan AM, et al.; INHERIT BRCA. Evaluation of BRCA1 and BRCA2 mutation prevalence, risk prediction models and a multistep testing approach in French-Canadian families with high risk of breast and ovarian cancer. *J Med Genet* 2007;44:107–121.
35. Dorval M, Bouchard K, Maunsell E, et al.; INHERIT BRCA. Health behaviors and psychological distress in women initiating BRCA1/2 genetic testing: comparison with control population. *J Genet Couns* 2008;17:314–326.
36. Kasparian NA, Wakefield CE, Meiser B. Assessment of psychosocial outcomes in genetic counseling research: an overview of available measurement scales. *J Genet Couns* 2007;16:693–712.
37. Boyer R, Prévaille M, Légaré G, Valois P. [Psychological distress in a noninstitutionalized population of Quebec: normative results of the Quebec health survey]. *Can J Psychiatry* 1993;38:339–343.
38. Léger E, Freeston MH, Ladouceur R, Noreau L, Tremblay L. Les manifestations anxieuses chez les personnes ayant la sclérose en plaques ou une autre déficience physique. *Journal de Réadaptation Médicale* 1998;18:4–8.
39. Horowitz M, Wilner N, Alvarez W. Impact of Event Scale: a measure of subjective stress. *Psychosom Med* 1979;41:209–218.
40. Freeston MH, Rhéaume J, Letarte H, Dugas MJ, Ladouceur R. Why do people worry? *Pers Individ Dif* 1994;17:791–802.
41. Institut de la statistique du Québec. Enquête sociale et de santé 1998. Québec: Institut de la statistique du Québec, 2001.
42. Santé Québec. Cahier technique et méthodologique—enquête sociale et de santé 1992–1993. Québec: Santé Québec, 1994.
43. Horowitz M. Stress response syndromes and their treatment. In: Goldberg L, Breznitz S (eds). *Handbook of Stress: Theoretical and Clinical Aspects*. Free Press: New York, 1982:711–732.
44. Allison PD. Missing data techniques for structural equation modeling. *J Abnorm Psychol* 2003;112:545–557.
45. Lapointe J, Abdous B, Camden S, et al. Influence of the family cluster effect on psychosocial variables in families undergoing BRCA1/2 genetic testing for cancer susceptibility. *Psychooncology* 2011: e-pub ahead of print 2 March, 2011.
46. Koehly LM, Peters JA, Kuhn N, et al. Sisters in hereditary breast and ovarian cancer families: communal coping, social integration, and psychological well-being. *Psychooncology* 2008;17:812–821.
47. Kenen R, Ardern-Jones A, Eeles R. “Social separation” among women under 40 years of age diagnosed with breast cancer and carrying a BRCA1 or BRCA2 mutation. *J Genet Couns* 2006;15:149–162.
48. Douglas HA, Hamilton RJ, Grubs RE. The effect of BRCA gene testing on family relationships: A thematic analysis of qualitative interviews. *J Genet Couns* 2009;18:418–435.
49. d'Agincourt-Canning L. A gift or a yoke? Women's and men's responses to genetic risk information from BRCA1 and BRCA2 testing. *Clin Genet* 2006;70:462–472.
50. Miller SM, McDaniel SH, Rolland JS, Feetham SL, editors. *Individual, Families, and the New Era of Genetics*, 1st edn. Norton: London, 2006.
51. Lim J, Macluran M, Price M, Bennett B, Butow P; kConFab Psychosocial Group. Short- and long-term impact of receiving genetic mutation results in women at increased risk for hereditary breast cancer. *J Genet Couns* 2004;13:115–133.
52. Lloyd SM, Watson M, Oaker G, Sacks N, Querci della Rovere U, Gui G. Understanding the experience of prophylactic bilateral mastectomy: a qualitative study of ten women. *Psychooncology* 2000;9:473–485.
53. de Vries-Kragt K. The dilemmas of a carrier of BRCA1 gene mutations. *Patient Educ Couns* 1998;35:75–80.
54. Cohen S, Underwood LG, Gottlieb BH (eds). *Social Support Measurement And Intervention: A Guide For Health And Social Scientists*, 1st edn. Oxford University Press: New York, 2000.
55. Keenan KF, Simpson SA, Wilson BJ, et al. “It's their blood not mine”: who's responsible for (not) telling relatives about genetic risk? *Health Risk Soc* 2005;7:209–226.
56. Wagner Costalas J, Itzen M, Malick J, et al. Communication of BRCA1 and BRCA2 results to at-risk relatives: a cancer risk assessment program's experience. *Am J Med Genet C Semin Med Genet* 2003;119C:11–18.
57. Ardern-Jones A, Kenen R, Lynch E, Doherty R, Eeles R. Is no news good news? Inconclusive genetic test results in BRCA1 and BRCA2 from patients and professionals' perspectives. *Hered Cancer Clin Pract* 2010;8:1. Available at: <<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2832891/pdf/1897-4287-8-1.pdf>> Accessed August 26, 2011.
58. Rolland JS, Walsh F. Facilitating family resilience with childhood illness and disability. *Curr Opin Pediatr* 2006;18:527–538.
59. Rolland JS. Living with anticipatory loss in the new era of genetics: a life cycle perspective. In: Miller SM, McDaniel SH, Rolland JS, Feetham SL (eds). *Individuals, Families, and the New Era of Genetics: Biopsychosocial Perspectives*. Norton: New York, 2006:139–172.
60. Wiseman M, Dancyger C, Michie S. Communicating genetic risk information within families: a review. *Fam Cancer* 2010;9:691–703.