

# Familial Effects of *BRCA1* Genetic Mutation Testing: Changes in Perceived Family Functioning

Antoinette M. Stroup<sup>1</sup> and Ken R. Smith<sup>2</sup>

<sup>1</sup>Utah Cancer Registry and <sup>2</sup>Department of Family and Consumer Studies and Huntsman Cancer Institute, University of Utah, Salt Lake City, Utah

## Abstract

This study expands recent research that examines how the receipt of *BRCA1* genetic test results affects family adaptability and cohesion 1 year after genetic risk notification. Study participants were members of a large Utah-based kindred with an identified mutation at the *BRCA1* locus. The final sample, 90 men and 132 women, contributed information before genetic testing (baseline) and 4 months and/or 1 year after receipt of genetic test results. After controlling for other factors such as family coping resources (Family Crises-Oriented Personal Evaluation Scale) and strains (Family Strains Index) and the tested individual's anxiety levels before genetic testing (state anxiety subscale), men and women reported significant declines in family cohesion 1 year after genetic risk notification ( $P < 0.01$ ). There is suggestive evidence that carrier men reported increasing

adaptability 1 year after risk notification (+0.21 points per month;  $P < 0.10$ ). Having a carrier sister had a positive influence on women's perceived family cohesion and adaptability levels, whereas a personal history of cancer, having a great deal of caregiving involvement for a female relative with cancer, anxiety, and some types of coping resources had a negative effect on men's perceived family cohesion and adaptability levels. Although results showed that tested parents are perceiving a decline in family functioning after genetic risk notification, there is no evidence to suggest that the decline is due to carrier status. In fact, it is other life circumstances that exist at the time of the genetic testing process that seem to influence the degree to which families adjust to the experience and test results. (Cancer Epidemiol Biomarkers Prev 2007;16(1):135-41)

## Introduction

The strong likelihood that carriers of a *BRCA1* gene mutation will develop breast and ovarian cancer has led a number of researchers to examine the potential psychological and behavioral effects of genetic testing for *BRCA1* mutations for individuals (1-6). Mutations in *BRCA1* are observed in ~50% of families with autosomal dominant breast cancer predisposition and in 80% of families with both breast and ovarian cancer (7). Female *BRCA1* carriers are at increased risk for breast and ovarian cancers (8) and male carriers have an increased risk of prostate cancer (9). Data from the Breast Cancer Linkage Consortium indicate that by the age of 70 years, female *BRCA1* mutation carriers have an 85% risk for developing breast cancer and a 63% risk for developing ovarian cancer. The cumulative risk of either cancer by this age is ~94% for female mutation carriers.

The implications of genetic risk notification for families, however, have not been explored as thoroughly. According to Halbert (10), *BRCA1/2* carriers reported greater uncertainty about familial implications and greater stress surrounding the management of familial concerns 1 month after risk notification compared with noncarriers. McInerney-Leo et al. (11) reported significant declines in family cohesion and expression levels among tested high-risk men and women 6 to 9 months after genetic risk notification, compared with those who did not undergo genetic testing. However, they did not find

differences in family cohesion and expressive levels between carriers and noncarriers.

This study expands on the recent but limited research examining how the receipt of genetic test results affects family functioning. The approach adopted here relies on psychosocial and coping theory to examine familial effects of *BRCA1* testing up to 1 year after genetic risk notification while also accounting for potential gender differences, the family's coping resources and strains, and the tested individual's anxiety level before genetic testing. Hierarchical linear modeling techniques are used to examine family functioning over time.

The psychosocial stress perspective (12) and the Resiliency Model of Family Stress, Adjustment, and Adaptation (hereafter called the Resiliency Model; refs. 13, 14) are used to model changes in family adaptability and cohesion due to notification of *BRCA1* mutation status (Fig. 1). Like individuals, families develop and operate with specific patterns of interaction, resources, and coping strategies to function as a social unit. The Resiliency Model emphasizes *family* coping and social resources in the stress process. The model also recognizes that existing family typology (hereafter referred to as family functioning) and existing family strains (pile-up) moderate the effect of stressful life events, leading to family crisis, maladjustment, or adaptation (13, 14). In this study, an individual's genetic test result (A factor) may disrupt or fortify a family's functioning (X factor) with the end result determined in part by existing family functioning patterns (T factor) and family strains (a factor) and coping strategies (B factor). The approach depicted in Fig. 1 represents a merging of stress and family functioning models appropriate for addressing three key research questions:

- Does *BRCA1* carrier status affect perceptions of family adaptability and cohesion up to 1 year after genetic testing?
- To what extent do family coping strategies and resources influence cohesion and adaptability levels after the receipt of *BRCA1* mutation test results?
- Do other life circumstances such as existing family strains, familial and individual history of breast cancer, and

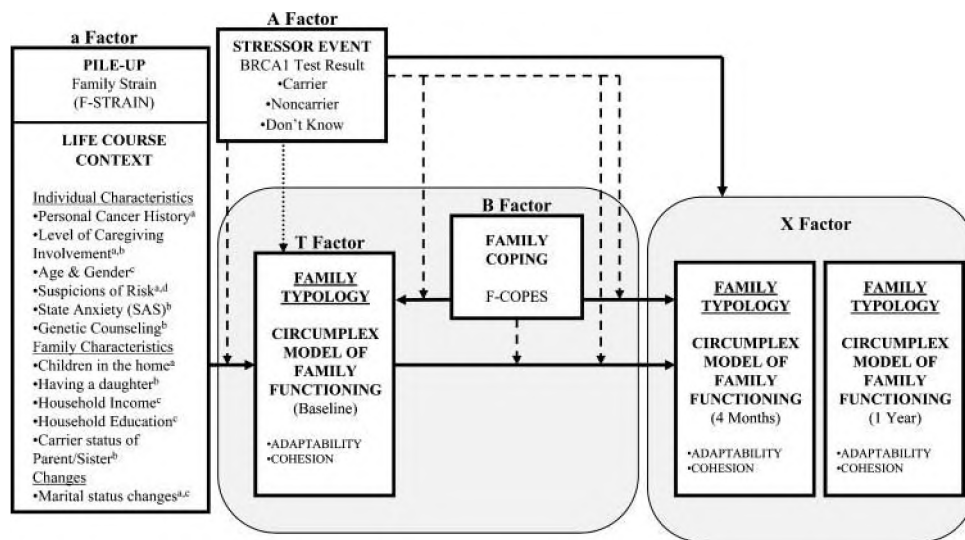
Received 3/8/06; revised 11/2/06; accepted 11/9/06.

**Grant support:** National Cancer Institute grant CA63681, the National Human Genome Research Institute grant HG00199, the National Center for Research Resources grant M01-RR00064, and the Marriner S. Eccles Graduate Fellowship, University of Utah, Graduate School, 1998-1999.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

**Requests for reprints:** Antoinette M. Stroup, Utah Cancer Registry, Suite 106B, 650 Komar Drive, Salt Lake City, UT 84108. Phone: 801-581-8407; Fax: 801-581-4560. E-mail: Nan.Stroup@hsc.utah.edu

Copyright © 2007 American Association for Cancer Research.  
doi:10.1158/1055-9965.EPI-06-0178



**Figure 1.** Genetic testing, family stress, and family functioning model. —, direct effect; - - - -, interaction effect; ·····, effect for unobservable heterogeneity. <sup>a</sup>, timing-Sequencing Context. <sup>b</sup>, linked-lives context. <sup>c</sup>, position in the social structure. <sup>d</sup>, anticipated event mechanism.

the carrier status of other family members moderate the effects of genetic test results on family cohesion and adaptability levels?

## Materials and Methods

Data were collected as part of a longitudinal study on the psychosocial and behavioral consequences of *BRCA1* mutation testing. Study participants were members of a large kindred of Northern European descent (K2082) with an identified mutation at the *BRCA1* locus (15). All subjects in the study are descendants of a founding couple (four to five generations earlier) known to be *BRCA1* mutation carriers. The full sample consists of 111 geographically distinct households (nuclear families) spread throughout Utah and Idaho, with an average of 3.3 children. Information for this study was gathered before genetic testing (baseline) and 4 months and 1 year after receipt of *BRCA1* genetic test results. All baseline interviews (that preceded genetic counseling) were conducted from September 1994 to March 1997, following a rolling recruitment strategy wherein participants were undergoing genetic counseling and testing shortly after consenting to participate. One-year (after receipt of test results) follow-up surveys were completed by July 1999. A detailed description of recruitment methods, eligibility criteria, and protocol for the longitudinal study are available elsewhere (16).

Individuals who were <18 years of age, not competent to provide informed consent, and untested members who were not at risk because they knew that their parents or grandparents tested negative for a *BRCA1* mutation (16) were excluded. The protocol included strict guidelines wherein parents are interviewed and offered genetic testing before their adult children. All survey data save genetic test results were stored at a centralized facility, and interviews were conducted via telephone. Informed written consent was obtained from each eligible member before enrollment, and genetic counseling was offered to all interested family members before and after genetic testing.

Of the 759 eligible members, 408 (53.75%) completed the baseline interview. The sample in this study was further restricted to members who completed the baseline and at least one of the two follow-up interviews (4 months and/or 1 year) and have living children ( $N = 259$  parents).

## Measures

**Family Functioning.** Family cohesion and adaptability levels were measured before (baseline) and 4 months and 1 year after

genetic testing using the Family Adaptability and Cohesion Evaluation Scales (FACES II). The FACES II scale has been shown to be a highly reliable and valid measure of family functioning (17, 18). Cohesion is defined as the emotional bonding that family members have toward one another. Adaptability is defined as the ability of the family to change in power structure, roles, and relationships to adjust to various situational stressors.

**BRCA1 Mutation Status.** *BRCA1* mutation carrier status was determined after the baseline interview but before the 4-month follow-up, and defined as positive/carrier, negative/noncarrier, and carrier status unknown.

**Coping Resources.** Family coping data was collected at baseline using the Family Crises-Oriented Personal Evaluation Scale (F-COPES; ref. 14), which measures how a family uses available familial and social resources in response to life events, including acquiring support from extended family members, mobilizing family members in a crisis, passive appraisal (accepting problematic issues), reframing (redefining stressful events to make them more manageable), and seeking spiritual support.

**Family Strains.** Existing family strains were measured at baseline by a number of factors, including the Family Strains Index (F-STRAIN; ref. 14). F-STRAIN captures stress from family, work, financial, and caregiving responsibilities "which can render a family vulnerable to the effect of a subsequent stressor or change" (13). Other factors, including the participant's history of cancer or cancer-related surgery, level of caregiving involvement for a female, maternal relative with cancer, age, gender, marital status, general anxiety level, and suspicions of cancer risk, may also capture the pile-up of demands and strains in the family not measured by F-STRAIN.

Level of caregiving involvement is considered because it has the potential to change family dynamics. Caregiving may also influence how the tested parent perceives his or her family functioning, and, if a relative with a history of cancer is female and related through the maternal branch of the kindred, the family's sensitivity toward cancer risk may be heightened. Level of caregiving involvement was assessed at baseline with two questions, whether the participant had a female, maternal relative with a history of cancer and if he/she was involved in care of that relative. Those with an affected relative and (a) had no caregiving involvement, (b) had some caregiving involvement, and (c) had a great deal of caregiving involvement were compared with those with no affected relatives.

General anxiety level (or state anxiety) was measured at baseline using the state anxiety subscale (SAS) of Spielberger's State-Trait Anxiety Inventory (19). It is considered here to control for initial levels of anxiety (at the individual level) before obtaining genetic test results.

Prior suspicions of cancer risk were measured at baseline by a single question where participants were asked if they knew or suspected that they came from a family with members that have an elevated risk for developing breast and ovarian cancer. If they said they knew or suspected, they were considered "suspicious."

**Other Variables.** Other baseline variables included in the analyses were the presence of children in the home, the gender composition of the participant's children, household income, and the highest education level by either parent (household education). Receipt of genetic counseling was measured at the 4-month follow-up and is an indicator for whether the participant received genetic counseling after being tested. Because the follow-up counseling session was not mandatory, not all participants opted to receive their test results from a genetic counselor.

**Statistical Analysis.**  $\chi^2$  analyses and *t* tests by sex were used to evaluate gender differences in mutation status, family functioning, and other key demographic variables as *BRCA1* mutations confer varying risks of cancer by sex. We then used hierarchical linear modeling to assess changes in family functioning while simultaneously accounting for family functioning levels before genetic testing, the correlation of measures for each participant over time (repeated observations), and unequal variances (heteroskedasticity) in the outcome variable between individuals (20). Another advantage of using hierarchical linear modeling is that we were able to include more cases in the final analysis as participants who completed the baseline and at least one of the two follow-up interviews (4 months and/or 1 year) were eligible for inclusion in this study.

Hierarchical linear modeling has two phases of estimation. Phase 1 is often referred to as the level 1 or repeated measures phase, which uses simple regression techniques to estimate patterns of change over time for each individual given his or her initial family functioning scores (measured at baseline) and rates of change as a function of time. The dependent variables are perceived adaptability and cohesion, measured separately, and the independent variable is time (0-12 months) since the baseline interview. These regressions generate an intercept ( $\pi_{0i}$ ) and slope ( $\pi_{1i}$ ) statistic, representing each individual's baseline family functioning and growth trajectory up to the 1-year interview, respectively. These estimates are then used in the second phase of the analysis, the level 2 or person-level phase. Phase 2 estimates average baseline family functioning levels among all study participants ( $\beta_{00}$ ) and the differences in baseline family functioning levels ( $\beta_{01}$ ) according to family/individual characteristics as well as the residual variation in baseline family functioning levels ( $r_{0i}$ ) after controlling for other factors. The growth trajectory of family functioning after genetic risk notification is estimated using the same technique, which estimates the relative effect of family/individual characteristics on the average growth trajectory of family functioning ( $\beta_{10}$ ), the differences in the growth trajectory ( $\beta_{11}$ ), and the residual variation in growth patterns ( $r_{1i}$ ).

The sample comprises sets of siblings, but approximately half of the female sample (60 of 132) and of the male sample (46 of 90) have only one sibling represented from their nuclear family. Nonetheless, to account for the possibility of correlated responses arising from having multiple siblings in the sample, we reestimated the models that make adjustments for this correlation using generalized estimating equations (21). Results from these models do not differ appreciably from those that

make no such adjustment. Accordingly, models reported here are not based on adjustments for familial clustering but they do adjust for correlated responses due to the fact that we rely on repeated responses from the same subject.

In this study, we estimated changes in family adaptability and cohesion separately and stratified the analyses by sex. We first conducted a preliminary hierarchical linear modeling analyses using an unconditional model (i.e., level 2 or person-level predictor variables excluded from the model) to assess the extent of variability in family functioning scores at baseline ( $\beta_{00}$ ) and changes by the 1-year interview ( $\beta_{10}$ ). We then estimated the influence of person/familial characteristics on family functioning scores in the final, multivariate model, which included all predictor variables.

## Results

Of the 259 (63% of 408) individuals who were eligible for the study, 206 (80%) completed and returned the 4-month, mailed, self-report FACES II survey. Fifty-three (20%) failed to return the survey or skipped the 4-month interview entirely. Another 12 participants were deleted from the 4-month pool of participants because they were missing five or more items on the FACES II survey. Overall, there were 194 (75% of the 259) usable FACES II surveys at 4 months. At the 1-year interview, 245 (95% of 259) participants were eligible for the final analysis. In the end, a total of 222 (90 men and 132 women) participant surveys were used in the final analysis.

Individual and familial characteristics for men and women are described in Table 1. Although the men and women in our sample had high rates of genetic counseling attendance, men were more likely to attend at least one genetic counseling session after being tested compared with women (86.7% and 77.3%, respectively). Women were more likely to have had a history of cancer or cancer-related surgery (31.8% versus 11.1%) and previous exposure to a great deal of caregiving involvement (30.3% versus 14.4%). Women were also more likely to report higher amounts of family coping, and, although suggestive ( $P < 0.10$ ), women also report higher family strain and general anxiety than men.

Men and women reported average levels of cohesion at baseline compared with a normed national population with a mean of 64.9 (SD, 8.4; refs. 17, 18). However, they reported slightly higher levels of adaptability at baseline (normed population mean, 49.9; SD, 6.6). Family coping among this sample, while slightly lower compared with a normed population, falls within 1 SD of mean values, which are 93.12 (SD, 14.05) for men and 95.64 (SD, 13.24) for women. Family strain (F-STRAIN) scores in this sample were within normal limits, 4.0 to 11.0 (13). Population norms for general anxiety levels (SAS) are not available because general anxiety is dependent on the individual and the situation evoking the anxious response. However, when compared with hospitalized cancer patients, this sample reports lower anxiety levels (22). The psychometric properties of SAS, F-STRAIN, F-COPES, and FACES II were assessed with Chronbach's  $\alpha$  statistic and found to have good (0.69) to excellent (0.92) internal consistency (Table 1).

According to Table 2, there were significant amounts of variability in initial family functioning levels reported by both men and women ( $r_{0i}$ ) in this study, although the amount of residual variance dramatically declined compared with the unconditional model (results not shown). Men and women reported significant declines in family cohesion ( $\beta_{10}$ ;  $P < 0.01$ ), and no significant changes in family adaptability were found. Table 2 also shows that women reported a steeper decline in family cohesion levels compared with men ( $\beta_{10}$ ;  $-0.23$  versus  $-0.19$ ); unlike the men in this study, women reported greater

**Table 1. Participant characteristics by sex (N = 222)**

Characteristic	Men (N = 90)	Women (N = 132)
Carrier status		
Carrier	24.4	27.3
Noncarrier	67.8	67.4
Don't know carrier status	7.8	5.3
Cancer/cancer-related surgery	11.1*	31.8*
No children living in the home	26.7	19.7
Marital status		
Stayed married by 1 y	100.0	93.2
Stayed single by 1 y	0.0	4.5
Married at baseline/single by 1 y	0.0	2.3
Has at least one living daughter	100.0	89.4
Suspect higher risk for cancer	60.0	64.4
Caregiving involvement		
No caregiving involvement	17.8	14.4
Some caregiving involvement	24.4	21.2
A great deal of caregiving involvement	14.4*	30.3*
No female, maternal relative with history of cancer	43.3	34.1
Carrier status of relatives		
Parent carrier at baseline	12.2	6.8
Parent carrier at 4 mo	18.9	18.2
Sister carrier at baseline	6.7	3.0
Sister carrier at 4 mo	32.2	20.5
Received genetic counseling	86.7 <sup>†</sup>	77.3 <sup>†</sup>
Median household income (\$1,000)	42.5	42.5
Mean household education (y)	15.06	15.08
Mean age at baseline (y)	44.86	43.21
Mean SAS <sup>‡</sup>	29.88 <sup>§</sup>	31.77 <sup>§</sup>
Mean F-STRAIN <sup>  </sup>	6.43 <sup>§</sup>	8.04 <sup>§</sup>
Mean F-COPES <sup>¶</sup>	86.4*	93.7*
Family functioning outcomes**		
Mean FACES II at baseline	61.32	61.97
Mean cohesion at baseline	65.79	66.78
Mean adaptability at baseline	56.84	57.17

NOTE: Frequency percentages reported, unless otherwise noted. *P* values refer to  $\chi^2$  analyses with Fisher's exact tests (right tailed) between men and women.

\**P* < 0.01.

<sup>†</sup>*P* < 0.05.

<sup>‡</sup>SAS: Chronbach's  $\alpha$  for internal consistency calculated at 0.92.

<sup>§</sup>*P* < 0.10.

<sup>||</sup>F-STRAIN: Chronbach's  $\alpha$  for internal consistency calculated at 0.69.

<sup>¶</sup>F-COPES: Chronbach's  $\alpha$  for internal consistency calculated at 0.82, subscales range 0.32-0.83.

\*\*FACES: Chronbach's  $\alpha$  for internal consistency calculated at 0.88, 0.89, 0.87 at baseline, 4 mo, and 1 yr respectively. Males ranged from 0.87-0.90 and females ranged from 0.87-0.89 for all three time periods.

variability in the amount of decline in cohesion levels after genetic testing ( $r_{11}$ ; *P* < 0.05).

Although the men and women in our study did not know their *BRCA1* mutation carrier status at baseline, we included it in our baseline model to ascertain initial differences, if any, in

family cohesion and adaptability between (as yet unknown) carrier and noncarrier families. Table 3 shows that there are no differences in cohesion and adaptability levels between carrier, noncarrier, and unknown carrier status families before genetic risk notification. However, being a male *BRCA1* mutation carrier is associated with a positive influence on family adaptability, increasing adaptability by +0.21 points per month more than noncarrier families (*P* < 0.10).

General anxiety levels (SAS) and family strains (F-STRAIN) had significant negative effects on cohesion and adaptability levels before genetic testing for both men and women, ranging from -0.14 to -0.31. Family coping levels (F-COPES) also had expected effects, as men and women report greater cohesion and adaptability levels at baseline with increasing social and coping resources (ranging from +0.15 to +0.21).

The influences of individual anxiety and family coping on cohesion and adaptability patterns after genetic risk notification, however, are only evident among the men in our study. According to Table 3, men's anxiety level (SAS) before genetic testing had a significant negative effect on family cohesion levels 1 year after genetic testing. Increasing levels of family coping resources (F-COPES) before genetic testing also had a negative effect on both cohesion and adaptability for the men, dropping -0.01 points per month for every unit increase in F-COPES. To explore this unexpected finding, we repeated the analyses replacing the composite F-COPES score with specific coping subscales (i.e., acquiring support from extended family members, mobilizing family members in a crisis, passive appraisal, reframing, and seeking spiritual support). We found that among men, cohesion levels seemed to be most sensitive to coping strategies that included reframing, whereas adaptability levels seemed to be affected by coping strategies that included seeking spiritual support. All other types of coping mechanisms measured within F-COPES were not associated with changes in male cohesion or adaptability (results not shown).

Changes in family functioning differed by gender with respect to personal cancer history. Although based only on a small number of men, our results suggest that men (but not women) with a history of cancer experienced a decline in cohesion and adaptability, -0.27 and -0.34 points per month, respectively.

The carrier status of sisters and/or parents also affected men and women differently. Whereas men were not affected, women with a carrier sister reported significant increases in both family cohesion and adaptability levels, +0.20 and +0.24 points per month, respectively.

Table 4 shows that women who had a great deal of caregiving involvement for a relative with cancer perceive higher adaptability levels before genetic testing compared with women who did not have an affected relative (+3.09). The results are similar for men, although men reported higher

**Table 2. Multivariate-multilevel estimation of initial (baseline) family cohesion and adaptability and subsequent changes (slope) 1 yr after BRCA1 genetic risk notification by sex**

Final estimation of fixed and random effects	Cohesion, coefficient (SE)		Adaptability, coefficient (SE)	
	Men	Women	Men	Women
Baseline intercept, $\beta_{00}$	65.43* (0.46)	66.59* (0.42)	56.73* (0.50)	57.00* (0.49)
Slope, $\beta_{10}$	-0.19* (0.05)	-0.23* (0.04)	-0.04 (0.04)	-0.06 (0.05)
Residual variance: intercept, $r_{0i}$	9.51* (71 df)	12.70* (110 df)	13.60* (71 df)	18.93* (110 df)
Residual variance: month slope, $r_{1i}$	0.005 (71 df)	0.047 <sup>†</sup> (110 df)	0.002 (71 df)	0.04 <sup>†</sup> (110 df)
Random error, level 1, $e_{ti}$	13.33	15.53	12.83	17.53

NOTE: Final estimation controls for carrier status, age, children in the home, household education, household income, marital status, suspicions of risk, genetic counseling, cancer history, having a daughter, carrier status of parent and/or sister, caregiving of maternal relative with cancer, anxiety level (SAS), family strain (F-STRAIN), family coping levels (F-COPES), and carrier status-suspicions of risk interaction.  $\beta_{00}$ , mean FACES II score before genetic testing (baseline).  $\beta_{10}$ , mean rate of change in FACES II scores per month among tested parents.  $r_{0i}$ , residual random effect in mean FACES II scores before genetic testing (baseline).  $r_{1i}$ , residual random effect in mean rates of change in FACES II scores among tested parents.  $e_{ti}$ , random error for person *i* at time *t*.

\**P* < 0.01.

<sup>†</sup>*P* < 0.05.

**Table 3. Significant factors associated with initial (baseline) family cohesion and adaptability and subsequent changes (slope) 1 yr after BRCA1 genetic risk notification: men**

Final estimation of fixed effects	Cohesion		Adaptability	
	Intercept coefficient (SE)	Slope coefficient (SE)	Intercept coefficient (SE)	Slope coefficient (SE)
Carrier	-2.13 (1.50)	0.16 (0.13)	-2.64 (1.64)	0.21* (0.13)
Don't know carrier status	-2.81 (2.83)	0.02 (0.28)	-4.26 (3.10)	-0.05 (0.27)
Age 18-40 y	2.06* (1.44)	-0.10 (0.11)	1.72 (1.25)	-0.16 (0.11)
No children living in home	-0.37 (1.17)	-0.03 (0.11)	0.45 (1.28)	-0.07 (0.11)
Household education	0.41 (0.29)	-0.02 (0.03)	0.32 (0.32)	-0.02 (0.03)
Household income	-0.02 (0.02)	-0.00 (0.00)	-0.03 (0.02)	-0.00 (0.00)
Married to single	—	—	—	—
Stayed single	—	—	—	—
Suspect higher risk	-0.14 (1.17)	-0.02 (0.11)	-1.77 (1.27)	0.07 (0.11)
Attended genetic counseling	-3.09 (2.24)	0.01 (0.22)	-5.37 <sup>†</sup> (2.45)	0.01 (0.22)
Cancer history	0.57 (1.52)	-0.27* (0.15)	-0.02 (1.66)	-0.34 <sup>†</sup> (0.15)
Has a daughter	—	—	—	—
Parent carrier	-0.09 (1.97)	-0.11 (0.14)	-1.55 (2.16)	-0.13 (0.14)
Sister carrier	0.43 (1.89)	-0.04 (0.12)	3.47* (2.08)	0.07 (0.12)
No caregiving	2.40* (1.43)	-0.05 (0.14)	2.43 (1.57)	-0.13 (0.14)
Some caregiving	0.76 (1.36)	-0.05 (0.14)	-1.19 (1.49)	-0.19 (0.14)
A great deal of caregiving	3.37 <sup>†</sup> (1.65)	-0.02 (0.18)	3.72 <sup>†</sup> (1.81)	-0.29* (0.17)
Carrier × suspect	-0.74 <sup>†</sup> (2.50)	0.10 (0.24)	-1.65 (2.77)	0.29 (0.24)
SAS	-0.14 <sup>†</sup> (0.07)	-0.01 <sup>†</sup> (0.01)	-0.24 <sup>‡</sup> (0.07)	-0.01 (0.01)
F-STRAIN	-0.31 <sup>‡</sup> (0.08)	0.00 (0.01)	-0.24 <sup>‡</sup> (0.08)	0.01 (0.01)
F-COPES	0.18 <sup>‡</sup> (0.04)	-0.01 <sup>†</sup> (0.00)	0.17 <sup>‡</sup> (0.05)	-0.01 <sup>‡</sup> (0.00)

\**P* < 0.10.†*P* < 0.05.‡*P* < 0.01.

family functioning along both cohesion and adaptability dimensions. A more salient difference, however, is that changes in family functioning only seem to be affected by men's caregiving responsibilities/roles and that the changes are only significant and *negative* along the adaptability dimension (-0.29).

## Discussion

This study expands previous research conducted by McInerney-Leo et al. (11) who reported no significant changes in family cohesion, expressiveness, and conflict up to 6 to 9

months after BRCA1/2 genetic testing. However, their measures and analytic approach varied markedly from this study. In contrast to this study, which uses the Family Adaptability and Cohesion Evaluation Scales, McInerney-Leo et al. (11) used the Family Relationship Index, a subscale of the Family Environment Scale. We also accounted for additional factors that were likely to confound the effects of genetic testing such as individual anxiety levels, family coping resources, existing family strains, and the carrier status of other family members. Finally, we analyzed data from more points in time (baseline, 4 months, and 1 year) using a different analytic approach (hierarchical linear modeling).

**Table 4. Significant factors associated with initial (baseline) family cohesion and adaptability and subsequent changes (slope) 1 yr after BRCA1 genetic risk notification: women**

Final estimation of fixed effects	Cohesion		Adaptability	
	Intercept coefficient (SE)	Slope coefficient (SE)	Intercept coefficient (SE)	Slope coefficient (SE)
Carrier	-1.13 (1.20)	-0.09 (0.13)	-1.53 (1.37)	-0.13 (0.14)
Don't know carrier status	-0.85 (2.29)	0.17 (0.24)	-1.85 (2.63)	0.32 (0.25)
Age (continuous)	-0.02 (0.05)	0.01 (0.01)	0.03 (0.06)	0.00 (0.01)
No children living in home	1.99 (1.41)	0.17 (0.15)	0.99 (1.62)	0.28* (0.16)
Household education	-0.16 (0.23)	0.03 (0.02)	0.13 (0.27)	0.02 (0.03)
Household income	-0.05 <sup>†</sup> (0.02)	0.00 (0.00)	-0.06 <sup>†</sup> (0.03)	0.00 (0.00)
Married to single	-8.75 <sup>‡</sup> (3.05)	0.25 (0.32)	-2.86 (3.51)	0.29 (0.33)
Stayed single	-6.01 <sup>‡</sup> (2.38)	0.05 (0.25)	-1.67 (2.74)	-0.21 (0.26)
Suspect higher risk	-2.26 <sup>†</sup> (1.09)	0.03 (0.11)	-3.21 <sup>‡</sup> (1.25)	0.10 (0.12)
Attended genetic counseling	-3.29 <sup>†</sup> (1.41)	0.12 (0.15)	-4.79 <sup>‡</sup> (1.62)	0.18 (0.16)
Cancer history	0.26 (1.11)	-0.07 (0.11)	0.27 (1.28)	-0.02 (0.12)
Has a daughter	-3.30* (1.77)	-0.07 (0.18)	-2.63 (2.04)	-0.05 (0.19)
Parent carrier	-2.59* (1.59)	0.06 (0.13)	-2.72 (1.89)	0.07 (0.14)
Sister carrier	1.07 (2.36)	0.20* (0.11)	4.58* (2.81)	0.24 <sup>†</sup> (0.12)
No caregiving	2.62* (1.46)	-0.08 (0.15)	3.08* (1.68)	-0.08 (0.16)
Some caregiving	1.51 (1.39)	-0.21 (0.14)	1.70 (1.60)	-0.10 (0.15)
A great deal of caregiving	1.45 (1.22)	-0.02 (0.13)	3.09 <sup>†</sup> (1.41)	-0.03 (0.14)
Carrier × suspect	-0.30 (2.69)	0.44 (0.27)	0.04 (3.10)	0.43 (0.29)
SAS	-0.13 <sup>†</sup> (0.06)	0.00 (0.01)	-0.14* (0.07)	0.00 (0.01)
F-STRAIN	-0.18 <sup>†</sup> (0.08)	0.01 (0.01)	-0.23 <sup>‡</sup> (0.09)	0.01 (0.01)
F-COPES	0.15 <sup>‡</sup> (0.04)	-0.00 (0.00)	0.21 <sup>‡</sup> (0.04)	-0.00 (0.00)

\**P* < 0.10.†*P* < 0.05.‡*P* < 0.01.

Gender of the tested individual moderated the effect of genetic test results as women did not report significant changes in overall family functioning after being notified of their genetic status. Male carriers, on the other hand, reported increasing familial adaptability. It is possible that men who learn that they are carriers are faced with this novel challenge that they had not previously considered as seriously as women had. Given this new status, men's increased levels of adaptability may reflect a need or willingness for greater flexibility within the family to accommodate their new position and health threat. Whereas the same could be said for female carriers, these women are likely to have contemplated being a carrier in light of the extensive female cancer history in the sample families. Accordingly, changes in adaptability may have already happened well before receiving genetic test results. We did not find significant effects of carrier status on family cohesion, a result that is consistent with those of McInerney-Leo et al. (11).

We also found that for men, unlike women, state anxiety levels had a significant negative effect on family cohesion regardless of carrier status. This suggests that men may be more vulnerable to the stress associated with the *BRCA1* genetic testing process than women, holding constant other factors. It is possible that other psychological states not assessed and used in this study (i.e., depressive symptoms, trait anxiety) might account for the remaining variance among men as regards cohesion declines over time. In particular, trait anxiety may capture a more persistent mood state, which may be a better predictor of family functioning in a long-term study such as this. The fact that there was no relationship between anxiety levels and change in cohesion among women might be further evidence that *BRCA1* genetic testing may not be a significant stressor event for women who are already at higher risk for breast and ovarian cancer (23).

Selection bias may also be playing a role in the effect of anxiety on perceived family functioning. Because all of the men in this sample have living daughters, they may have self-selected themselves into the project. Their anxiety may be linked to the heritability and risk factors associated with *BRCA1* mutations that predispose their daughters to developing breast and ovarian cancer. As such, these men may then choose to participate in this study, thereby affecting the relationship between anxiety level and family functioning.

The effect of family coping strategies also plays a significant role for both men and women in terms of perceived changes in family adaptability and cohesion. However, contrary to previous research, higher amounts of coping do not necessarily lead to better adjustment to stressful life events (24) or genetic testing (25). Among the men in this sample, higher amounts of family coping strategies before genetic testing decrease the degree to which families are able to adapt and interact after the genetic testing experience. More detailed analysis showed that families of male probands undergoing genetic testing, who cope by reframing or redefining stressful life events to make them more manageable, may suffer declines in family cohesiveness, and coping by seeking spiritual support may be detrimental to family adaptability. Why these attributes of coping are detrimental to families with a parent undergoing *BRCA1* genetic testing remains unanswered, and additional qualitative or ethnographic information will be needed to examine the process by which reframing has its effects. However, the psychosocial stress perspective and the Resiliency Model underscore the notion that the types and amount of coping strategies before genetic testing do not necessarily mean they are adequate or appropriate after genetic results are disclosed.

This study also found that other life circumstances alter the family's adjustment after genetic testing. Although the results are less consistent between men and women and between cohesion and adaptability, we found that having a history of

cancer, having a carrier sister, and being a caregiver for a first-degree female relative with cancer affect the family's adjustment after *BRCA1* genetic testing. Men with a history of cancer were shown to report greater rates of declining family adaptability and cohesion up to 1 year after genetic testing. Perhaps the genetic testing experience may have stimulated repressed negative feelings and experiences associated with previous cancer diagnosis and treatment. More research examining men's psychological response is needed to more fully understand the effects of *BRCA1* genetic testing.

We showed that, among women, having a carrier sister increases adaptability and cohesion. It is important to note that the increases in family adaptability and cohesion refer to the female proband's nuclear family and not family functioning between the proband and her siblings or parent. We did not consider the timing in which family members were tested and received their genetic test results because it was not always possible to know how results were communicated among family members. It was therefore not possible to know whether families in this study were affected by knowledge of their sisters' carrier status (increasing cohesiveness and adaptability). We also cannot rule out the possibility that preexisting levels of cohesiveness of the family facilitated communication of genetic test results, which in turn influenced other female members of the kindred to participate in this study.

Unlike women, men with a great deal of caregiving involvement for a female relative with cancer reported significantly greater rates of decline in adaptability relative to men who did not have affected relatives. The lack of significant effects on adaptability for women may arise because more women in this sample report being involved a great deal in the care of a relative with cancer and have already adapted accordingly. In contrast, men may be experiencing greater difficulty negotiating the effects of genetic testing on top of the financial, time, and, possibly, behavioral demands imposed by the caregiver role.

There are three noteworthy caveats to our findings. According to the Resiliency Model, how one appraises the potential effect of an event (i.e., perceiving an event as a potential source of stress) is a key element in the negotiation of life events. However, appraisal was not measured and, therefore, not accounted for in the analysis. A study of cancer-specific distress among women at high risk of breast and ovarian cancer (23) showed that women reported greater distress with the possibility of receiving a positive test result (*BRCA1/2* mutation carrier) than being tested or receiving a negative test result (*BRCA1/2* noncarrier). Future studies on family functioning and genetic testing should account for the family's appraisal of genetic risk notification. Second, the sample is predominantly Mormon and from Northern European descent; thus, generalizing the findings of this study may be limited to these populations. Finally, communication among family members as regards their genetic results may have biased our measure of "prior suspicions of cancer risk" because members who tested positive may have discussed their results with other members who had not completed the baseline interview.

The discovery of *BRCA1* gene mutations has broadened the practice of genetic testing into a more preventive context, allowing tested individuals to prepare for and, possibly, attenuate the effects of breast and ovarian cancer. This study expands previous research by examining longitudinal changes in family relationships as a result of genetic testing. Although results show that tested parents are perceiving a decline in family functioning after genetic risk notification, there is no evidence to suggest that the decline is due to carrier status. In fact, it is other life circumstances that exist at the time of the genetic testing process that seem to influence the degree to which families adjust to the experience and test results.

The implications for genetic testing policies are clear. When individuals and families are interested in genetic testing, the informed consent process must be as comprehensive as possible. This process includes disclosure of the potential familial effects of the testing experience overall as well as the specific genetic result. Typically, the psychosocial intake involves gathering information about an individual's coping resources and strategies. Our research suggests that it would be valuable to expand that intake to include information about the life stresses (caregiving, work, and other anxieties) and the coping resources and strategies associated with the nuclear family as well. This will alert counselors to the possibility that individuals or families may be preoccupied with other more immediate concerns and events. If the counselor finds an excess of stress on the family, that individuals seeking testing have high levels of general anxiety, or that the family does not have adequate amounts and sources of support, this may have an effect on long-term familial adjustment after genetic testing. Therefore, the consent process should include either additional strategies for coping or a dialogue about the readiness of the individual to have blood drawn.

### Acknowledgments

We thank Diana Lane Reed, Deb Ma, and Jean Wylie for their invaluable assistance with this analysis, and Jeff Botkin and Vickie Venne for their helpful comments.

### References

- Croyle RT, Smith KR, Botkin JR, Baty B, Nash J. Psychological responses to BRCA1 mutation testing: preliminary findings. *Health Psychol* 1997;16:63-72.
- DudokdeWit AC, Duivenvoorden HJ, Passchier J, Niermeijer MF, Tibben A. Course of distress experienced by persons at risk for an autosomal dominant inheritable disorder participating in a predictive testing program: an explorative study. *Rotterdam/Leiden Genetics Workgroup. Psychosom Med* 1998;60:543-9.
- DudokdeWit AC, Tibben A, Duivenvoorden HJ, Niermeijer MF, Passchier J. Predicting adaptation to presymptomatic DNA testing for late onset disorders: who will experience distress? *Rotterdam Leiden Genetics Workgroup. J Med Genet* 1998;35:745-54.
- Lerman C, Croyle RT. Emotional and behavioral responses to genetic testing for susceptibility to cancer. *Oncology (Williston Park)* 1996;10:191-5,9; discussion 200-2.
- Smith KR, Ellington L, Chan AY, Croyle RT, Botkin JR. Fertility intentions following testing for a BRCA1 gene mutation. *Cancer Epidemiol Biomarkers Prev* 2004;13:733-40.
- 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;8:385-92.
- Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. *Breast Cancer Linkage Consortium. Am J Hum Genet* 1995;56:265-71.
- 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;72:1117-30.
- Thompson D, Easton DF. Cancer Incidence in BRCA1 mutation carriers. *J Natl Cancer Inst* 2002;94:1358-65.
- Halbert CH, Schwartz MD, Wenzel L, et al. Predictors of cognitive appraisals following genetic testing for BRCA1 and BRCA2 mutations. *J Behav Med* 2004;27:373-92.
- McNerney-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* 2005;133:165-9.
- Kaplan HB. Perspectives on psychosocial stress. In: Kaplan HB, editor. *Psychosocial stress: Perspectives on structure, theory, life course, and methods*. San Diego: Academic Press; 1996. p. 3-24.
- McCubbin HI, Thompson AI. *Family assessment inventories for research and practice*. Madison (WI): University of Wisconsin-Madison; 1991.
- McCubbin HI, Thompson AI, McCubbin MA. *Family assessment: Resiliency, coping, and adaptation—inventories for research and practice*. Madison (WI): University of Wisconsin-Madison; 1996.
- Goldgar DE, Fields P, Lewis CM, et al. A large kindred with 17q-linked breast and ovarian cancer: genetic, phenotypic, and genealogical analysis. *J Natl Cancer Inst* 1994;86:200-9.
- 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;88:872-82.
- Olson DH, McCubbin HI, Barnes H, Larsen A, Muxen M, Wilson M. *Family Inventories*. St. Paul: David H. Olson, Family Social Science, University of Minnesota; 1985.
- Olson DH, Portner J. Family adaptability and cohesion scales. In: Filsinger EE, editor. *Marriage and family assessment: a sourcebook for family therapy*. Beverly Hills (CA): Sage Publications; 1993. p. 299-315.
- Spielberger CD, Vagg PR, Barker LR, Donham GW, Westberry LG. The factor structure of the State-Trait Anxiety Inventory. In: Sarason IG, Spielberger CD, editors. *Stress and anxiety 7*. Washington (DC): Hemisphere Publishing; 1980. p. 95-109.
- Byrk AS, Raudenbush SW. *Hierarchical linear models: Applications and data analysis methods*. Advanced quantitative techniques in the social sciences. Newbury Park: Sage Publications; 1992.
- Liang KY, Zeger SL. Regression analysis for correlated data. *Annu Rev Public Health* 1993;14:43-68.
- Pancheri P, De Martino V, Spiombi G, Biondi M, Mosticoni S. Life stress events and state-trait anxiety in psychiatric and psychosomatic patients. In: Spielberger CD, Sarason IG, editors. *Stress and anxiety 10*. Washington (DC): Hemisphere Publishing; 1986. p. 367-95.
- Coyne JC, Kruus L, Racioppo M, Calzone KA, Armstrong K. What do ratings of cancer-specific distress mean among women at high risk of breast and ovarian cancer? *Am J Med Genet* 2003;116:222-8.
- Taylor SE, Aspinwall IG. Mediating and moderating processes in psychosocial stress. In: Kaplan HB, editor. *Psychosocial stress: Perspectives on structure, theory, life course, and methods*. San Diego: Academic Press; 1996. p. 71-110.
- Tibben A, Roos RA, Niermeijer MF. Psychological consequences of presymptomatic testing for Huntington's disease. *Lancet* 1997;349:809.