FAMILIAL EFFECTS OF BRCA1 GENETIC MUTATION TESTING:

CHANGES IN PERCEIVED FAMILY FUNCTIONING

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ABSTRACT

This study expands recent research that examines how the receipt of BRCA1 genetic test results affects family adaptability and cohesion one 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 prior to 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 (F-COPES) and strains (F-STRAIN), and the tested individual's anxiety levels prior to genetic testing (SAS), men and women reported significant declines in family cohesion one year after genetic risk notification ($p<.01$). Compared to non-carriers, carrier men reported increasing adaptability one year after risk notification (+0.21 points per month, $p<.10$). Having a carrier sister seemed to have a positive influence on women's perceived family cohesion and adaptability levels, while 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 impact 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 which 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.

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INTRODUCTION

Individuals undergoing predictive genetic testing to determine their susceptibility to late-onset cancers may experience a range of responses associated with the receipt of this type of information. A significant portion of the research investigating psychosocial outcomes following genetic testing have specifically examined testing for *BRCA1* and *BRCA2* mutations. Mutations in *BRCA1* are observed in approximately 50% of families with autosomal dominant breast cancer predisposition, and in 80% of families with both breast and ovarian cancer cases (1). Female *BRCA1* carriers are at increased risk for breast and ovarian cancers (2). Male carriers have an increased risk of prostate cancer (3). Data from the Breast Cancer Linkage Consortium (BCLC) indicate that by the age of 70, 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 approximately 94% for female mutation carriers.

The strong likelihood that carriers of a *BRCA1* gene mutation will develop breast and ovarian cancer has lead a number of researchers to examine the potential psychological and behavioral effects of genetic testing for *BRCA1* mutations for individuals (4-9). 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 one month after risk notification compared to non-carriers. McInerney-Leo et al.(11) reported significant declines in family cohesion and expression levels among tested, high-risk men and women 6-9 months after genetic risk notification compared to those who did not undergo genetic testing. However, they did not find differences in family relationships between carriers and noncarriers.

This study expands on the recent but limited research examining how the receipt of genetic test results impacts family functioning. The approach adopted here relies on psychosocial and coping theory to examine familial effects of *BRCA1* testing up to one 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. Hiearchical linear modeling (HLM) techniques are used to examine family functioning over time.

The psychosocial stress perspective (PSP) (12) and the Resiliency Model of Family Stress, Adjustment, and Adaptation (hereafter called the Resiliency Model) (13, 14) are used as frameworks to model changes in family adaptability and cohesion due to notification of *BRCA1* mutation status (Figure 1). Like individuals, families develop and operate with specific patterns of interaction, resources, and coping strategies in order 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 impact 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 Figure 1 represents a merging of stress and family functioning models appropriate for addressing three key research questions:

(a) Does *BRCA1* carrier status affect perceptions of family adaptability and cohesion up to one year after genetic testing?

(b) To what extent do family coping strategies and resources influence cohesion and adaptability levels after the receipt of *BRCA1* mutation test results?

(c) Do other life circumstances such as existing family strains, familial and individual history of breast cancer, and the carrier status of other family members moderate the effects of genetic test results on family cohesion and adaptability levels?

Figure 1

MATERIALS AND METHODS

Data were collected as part of a large 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 comprises 111 distinct nuclear families in the Utah and Idaho areas. Information for this study was gathered prior to genetic testing (baseline) and 4 months and 1 year after receipt of *BRCA1* genetic test results. A detailed description of recruitment methods, eligibility criteria, and protocol for the longitudinal study are available elsewhere (16).

Individuals who were less than 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. Due to ethical and logistical considerations, 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 prior to

enrollment, and genetic counseling was offered to all interested family members prior to and after genetic testing.

Of the 759 eligible members, 408 completed the baseline interview (53.75%). The sample in this study was restricted further 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 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 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 in order to adjust to various situational stressors.

BRCA1 Mutation Status. BRCA1-mutation carrier status was defined as positive/carrier, negative/non-carrier, and carrier status unknown .

Coping Resources. Family coping data was collected at baseline using the Family Crises-Oriented Personal Evaluation Scale (F-COPES) (14), which measures how a family utilizes 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 in order to make them more manageable), and seeking spiritual support.

Family Strains. Existing family strains were measured by a number of factors, including the Family Strains Index (F-STRAIN) (14). F-STRAIN captures stress from family, work,

financial, and caregiving responsibilities "which can render a family vulnerable to the impact 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 capture the pile-up of demands and strains in the family.

Level of caregiving involvement is considered because it has the potential to change family dynamics; influence how the tested parent perceives his or her family functioning; and, if a relative with a history of cancer is famale and related through the maternal branch of the kindred, the family's sensitivity toward cancer risk may be heightened. Thus, these members may be more aware of the risks and consequences of cancer.

General anxiety level (or state anxiety) is 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) prior to obtaining genetic test results.

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

Other Variables. Other variables included in the analyses are receipt of genetic counseling, 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).

Statistical Analysis

Chi-square 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 (HLM) to assess changes in family functioning while simultaneously accounting for family functioning levels prior to 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 HLM is that we were able to include more cases in the final analysis. Unlike repeated measures analysis of variances (ANOVA), multivariate analysis of variance (MANOVA), structural equation modeling, and time-series analysis, HLM does not assume all participants have the same number of observations over time and that data was collected at equally spaced intervals (21). With HLM, participants who completed the baseline and at least one of the two follow-up interviews (4-months and/or 1-year) are eligible for inclusion in this study.

HLM has two phases of estimation. The first phase is often referred to as the Level-1 or repeated measures phase. This phase assesses 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. For the Level-1 analysis, the dependent variables are perceived adaptability and cohesion, and the independent variable is time (0 to 12 months) since the baseline interview. In other words, a simple regression is estimated for each subject where the only dependent variable is time since the baseline interview. These regressions generate an intercept (π_{0i}) and slope (π_{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. This phase estimates average baseline

family functioning levels among all study participants (β_{00}) and the differences in baseline family functioning levels (β_{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 also estimated using the same technique so results will show the relative effect of family/individual characterics on the average growth trajectory of family functioning (β_{10}), the differences in the growth trajectory (β_{11}), and the residual variation in growth patterns (r_{1i}). It is at this level (Level-2) that we hope to uncover the role of *BRCA1* mutation status in changing family functioning patterns one year after this information is disclosed.

In this study, we estimated changes in family adaptability and cohesion separately, and stratified the analyses by sex. We first conducted a preliminary HLM 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 (β_{00}) and changes by the 1-year interview (β_{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 individuals who were eligible for the study (63% of 408), 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 5 or more items on the FACES II survey. Overall, there were 194 usable FACES II surveys at 4 months (75% of the 259). At the 1-year interview, 245 participants (95% of 259) were eligible for the final

analysis; however, only a total of 222 (90 men and 132 women) participants were used because of missing data.

Individual and familial characteristics for men and women are described in Table 1. Men were more likely to attend at least one genetic counseling session compared to women, but women were more likely to have had a history of cancer or cancer-related surgery and previous exposure to a great deal of care giving involvement. Women were also more likely to report higher amounts of family coping, family strain, and general anxiety than men.

Table 1

The sample of individuals in this study reported slightly higher levels of cohesion and adaptability and family coping compared to a normed population (17, 18), which is 65 (SD=8.4) for cohesion and 50 (SD=6.6) for adaptability. Family strain (F-STRAIN) scores in this sample were within normal limits, 4.0-11.0 (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 to 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. However, men and women only reported significant declines in family cohesion (β_{10}) ($p < .01$). No significant changes in family adaptability were found. Table 2 also shows that women reported a steeper decline in family cohesion levels compared to men (β_{10}) (- 0.23 versus - 0.19); and, unlike the

men in this study, there was a significant variation in the amount of change reported among women (r_{1i}) ($p<.01$).

Table 2

As shown in Table 3, there remains a significant amount of unexplained variability in cohesion and adaptability levels prior to genetic testing (r_{0i}) ($p < .01$) and significant decreases in cohesion levels reported by men and women (β_{10}) ($p < .01$), despite controlling for many potential risk and protective factors. Significant variation in cohesion levels over time also remains among the women in our study (r_{1i}) ($p < .05$).

Table 3 about here

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 non-carrier families. Table 4 shows that not only were there no differences in cohesion and adaptability levels between carrier, noncarrier, and unknown carrier status families prior to genetic risk notification, but being a *BRCA1* mutation carrier seemed to only affect changes in familial adaptability for the men (coefficient = 0.21, $p < .10$). Interestingly, being a carrier is associated with a positive influence on family adaptability, increasing adaptability by +0.21 points per month more than non-carrier families.

Tables 4 and 5 about here

General anxiety levels (SAS) and family strains (F-STRAIN) had significant negative effects on cohesion and adaptability levels prior to 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 4, men's anxiety level (SAS) prior to genetic testing had a significant negative effect on family cohesion levels one year after genetic testing. Increasing levels of family coping resources (F-COPES) prior to 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 conducted the same 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 with F-COPES were not associated with changes in male cohesion or adaptability (results not shown).

Changes in family functioning over time also differed between men and women with a history of cancer. While a history of cancer did not influence women's cohesion and adaptability levels after genetic testing, men experienced a sharper decline if they had a previous history of cancer, -0.27 and –0.34 points per month, respectively.

The carrier status of sisters and/or parents also affected men and women differently. While men were not affected, women with a carrier sister reported significant increases in both

family cohesion and adaptability levels, +0.20 points per month and +0.24 points per month, respectively.

Table 5 shows that women who had a great deal of care giving involvement for a relative with cancer perceive higher adaptability levels prior to genetic testing compared to women who did not have an affected relative (+3.09). The results are similar for men, although men reported higher 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 care giving 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 investigated changes in family cohesion, expressiveness, and conflict up to 6-9 months after *BRCA1/2* genetic testing. Although they did not report significant changes in family functioning between baseline and follow-up, their measures and analytic approach varied marketly from this analysis. McInerney-Leo et al. (11) used the Family Relationship Index (FRI), a subscale of the Family Environment Scale (FES) while we used the Family Adaptabality and Cohesion Evaluation Scales (FACES II). Both surveys measure some form of family functioning, however, the differences in our findings could be attributed in part to differences in the familial constructs used. The FRI primarily serves as an index of social support since all three subscales (cohesion, expressiveness, and conflict) focus on the degree to which family members are free to communicate their feelings and how committed each member is to helping other members of the family (11). High scores imply greater familial social support. FACES II goes beyond social support and measures other characteristics of family relationships. The cohesion subscale of

FACES II measures the degree to which families are appropriately bonded to each other through levels of family closeness and independence and well-established boundaries and coalitions. The adaptability subscale of FACES II measures the degree to which families are able to adjust to changing life circumstances through appropriate levels of assertiveness, discipline, and negotiation. Unlike the FRI, higher levels of cohesion and adaptability do not imply better family functioning. Instead, extreme levels of cohesion and adapatability may be detrimental to families as they might imply that families are too enmeshed (lack of boundaries and independence) or too chaotic (lack of structure, discipline, and rules). Another difference between the McInerney-Leo et al. (11) study and the current study is that we accounted for additional factors that were likely to confound the effects of genetic testing, including individual anxiety levels, family coping resources, existing family strains, the carrier status of other family members, household composition (having a daughter, having children in the home), and the level of care giving responsibilities for a relative with cancer. Finally, this study used a different analytic approach to studying family functioning changes over time. We not only looked at family outcomes using data up to one year after genetic risk notification, but we also analyzed data from more points in time (baseline, 4 months, and 1 year) using HLM techniques.

We found that the gender of the tested individual plays an important role in moderating the impact of genetic test results. Women did not report significant changes in overall family functioning after being notified of their genetic status while carrier men reported significant increases in family adaptability. At first glance, this finding might be surprising as most people would consider a positive genetic test result (carrier) to be a risk factor for declining family functioning, particularly for women. However, this finding is supported by a recent study that examined cancer-specific distress among women at high risk for breast and ovarian cancer (23).

Coyne and colleagues found that women who were rated as being high-risk were more distressed about their risk in general than undergoing genetic testing.

The reason for increasing familial adaptability among the male carriers in this study may lie in the psychological responses of the children. According to a recent study of children's long-term psychological effects of genetic testing for hereditary colorectal cancer (24), children of fathers who tested positive for the adenomatous polyposis coli (APC) gene mutation tended to have less psychological distress (anxiety and despression symptoms) and less behavioral problems than children of carrier mothers. The fact that all the men in this study had living children (daughters), reported significantly lower levels of general anxiety and family strain compared to women, and reported increasing levels in a dimension of family functioning that is characterized by an ability to adjust to changing life circumstances (adaptability) may reflect the same interactions between fathers and children as in the APC study.

Similar to the McInerney-Leo et al. (11) investigation, we did not find significant effects of carrier status on family cohesion. However, this is inconsistent with previous findings by Epslen et al. (25) wherein 50% of individuals who underwent genetic testing for the *MLH1* and *MLH2* mutations associated with hereditary nonpolyposis colorectal cancer (HNPCC) reported a positive impact on their relationships with their spouses and parents and 30% reported a positive impact with their children. One explanation for the discrepant results may be that the Epslen HNPCC study was based on a small (N=50) cross-sectional sample of men and women who were at various stages of genetic testing, which subjected the study to recall bias. In the present study, familial relationships are measured prior to genetic testing and again four months and one year after genetic test results have been disclosed. The prospective, longitudinal nature of this study limits the influence of recall bias on the results.

We also found that, unlike women, anxiety levels had a significant negative impact on family cohesion for men 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) might account for the remaining variance among men as regards cohesion declines over time. However, the fact that there was no relationship between anxiety levels and change in cohesion among the women might be further evidence that *BRCA1* genetic testing may not be a significant stressor event for women who already know or suspect that they are at higher risk for breast and ovarian cancer.

Selection bias may also be playing a role in anxiety's effect 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 (26) or genetic testing (27). Among the men in this sample, higher amounts of family coping strategies prior to 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 that cope by reframing or redefining stressful life events in order 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. However, the psychosocial stress perspective and the Resiliency Model underscore the notion that the types and amount of coping strategies prior to 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 a 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. We found that men with a history of cancer reported greater rates of declining family adaptability and cohesion up to one 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. It is possible, however, that having a carrier sister may create an atmosphere in families in which they appreciate the relative risk of cancer for a maternal relative. This appreciation may translate into greater connectedness and a willingness to adjust to changing life circumstances in light of the carrier's cancer risk and the demands it might place on extended family members. Previous research, however, may point to a reverse relationship between the

carrier status of a sibling and family cohesion (28, 29). That is, more cohesive families are more likely to discuss genetic testing and genetic counseling, which may lead to the subsequent participation of untested sisters. Since we did not consider the timing in which family members were tested and given genetic test results, there is no way of knowing whether the cohesive families in this study were affected by the carrier status of tested sisters or if the 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 faster 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 several caveats to our findings. First, appraisal assessments were not made and therefore not accounted for in the analysis. A recent 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* non-carrier). 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 populatons.

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 which 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. If individuals and families are interested in genetic testing, the informed consent process must be as comprehensive as possible. This might include disclosure of the potential familial effects of both genetic knowledge and the genetic testing experience. Counselors may need to consider the gender of the parent undergoing testing in order to target key risk and protective factors. They may also benefit from gathering information as regards familial coping resources and strategies or whether the individual/family is experiencing high levels of strain associated with family, work or care giving demands or high levels of anxiety associated with genetic testing overall. Knowing where individuals and families stand in terms of their life course may alert counselors to the possibility that families or individuals may be preoccupied with other, more immediate concerns and events. If the counselor finds that there is a pile-up of stress and strain 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, he or she may advise the individual to postpone testing or recommend other cancer-prevention strategies to the individual and their family.

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Stroup, Figure 1

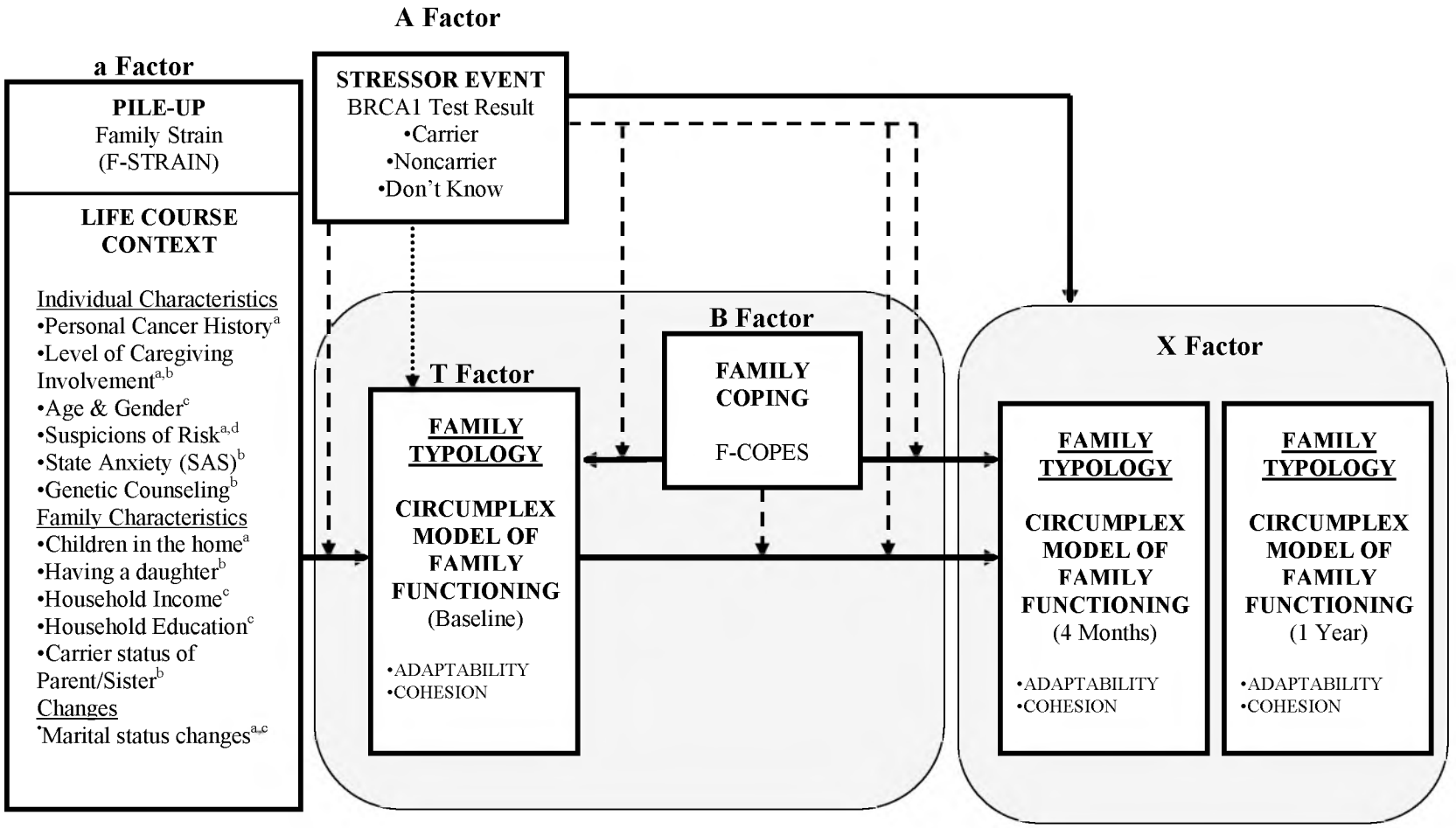

FIGURE 1: Genetic Testing, Family Stress, and Family Functioning Model

TABLE 1. Participant Characteristics by Sex[a] (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 yr	100.0	93.2
Stayed Single by 1 yr	0.0	4.5
Married at baseline/Single by 1 yr	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 months	18.9	18.2
Sister carrier at baseline	6.7	3.0
Sister carrier at 4 months	32.2	20.5
Received genetic counseling	86.7**	77.3**
Median household income (1000s)	42.5	42.5
Mean household education (in years)	15.06	15.08
Mean age at baseline	44.86	43.21
Mean SAS[b]	29.88*	31.77*
Mean F-STRAIN[c]	6.43*	8.04*
Mean F-COPES[d]	86.4***	93.7***
Family Functioning Outcomes[e]		
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

*** p<.01 ** p<.05 * p<.10

[a] Frequency percentages reported, unless otherwise noted. P-values refer to chi-square analyses with Fisher's Exact Tests (right-tailed) between men and women.

[b] SAS: Chronbach's Alpha for internal consistency calculated at 0.92.

[c] F-STRAIN: Chronbach's Alpha for internal consistency calculated at 0.69.

[d] F-COPES: Chronbach's Alpha for internal consistency calculated at 0.82, subscales range 0.32-0.83.

[e] FACES: Chronbach's Alpha for internal consistency calculated at 0.88, 0.89, 0.87 at baseline, 4 months, and 1 year, respectively. Males ranged from 0.87-0.90 and females ranged from 0.87-0.89 for all three time periods.

TABLE 2. Multilevel Unconditional Model of Initial (Baseline) Family Cohesion and Adaptability and Subsequent Changes (Slope) 1-Year after *BRCA1* Genetic Risk Notification by Sex

	Cohesion		Adaptability	
Estimation of Fixed and Random Effects	**Men** Coefficient (Std Error)	**Women** Coefficient (Std Error)	**Men** Coefficient (Std Error)	**Women** Coefficient (Std Error)
Baseline Intercept, β_{00}	65.43*** (0.61)	66.59*** (0.56)	56.73*** (0.67)	57.00*** (0.62)
Slope, β_{10}	-0.19*** (0.05)	-0.23*** (0.04)	-0.04 (0.05)	-0.06 (0.05)
Residual Variance: Intercept, r_{0i}	23.73***	29.73***	31.93***	37.72***
Residual Variance: Month Slope, r_{1i}	0.003	0.049***	0.005	0.058**
Random Error, Level-1, e_{ti}	13.34	15.54	13.43	17.56

*** p<.01 ** p<.05 * p<.10

$\boldsymbol{\beta_{00}}$ = Mean FACES II score prior to genetic testing (baseline).

$\boldsymbol{\beta_{10}}$ = Mean rate of change in FACES II scores per month among tested parents.

$\mathbf{r}_{0i}$ = Residual random effect in mean FACES II scores prior to genetic testing (baseline).

$\mathbf{r}_{1i}$ = Residual random effect in mean rates of change in FACES II scores among tested parents.

$\mathbf{e}_{ti}$ = Random error for person *i* at time *t*.

TABLE 3. Multivariate-Multilevel Estimation of Initial (Baseline) Family Cohesion and Adaptability and Subsequent Changes (Slope) 1-Year after *BRCA1* Genetic Risk Notification[a] by Sex

	Cohesion		Adaptability	
Final Estimation of Fixed and Random Effects	**Men** Coefficient (Std Error)	**Women** Coefficient (Std Error)	**Men** Coefficient (Std Error)	**Women** Coefficient (Std Error)
Baseline Intercept, β_{00}	65.43*** (0.46)	66.59*** (0.42)	56.73*** (0.50)	57.00*** (0.49)
Slope, β_{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** (110 *df*)	0.002 (71 *df*)	0.04** (110 *df*)
Random Error, Level-1, e_{ti}	13.33	15.53	12.83	17.53

*** p<.01 ** p<.05 * p<.10

[a] 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.

$\boldsymbol{\beta_{00}}$ = Mean FACES II score prior to genetic testing (baseline).

$\boldsymbol{\beta_{10}}$ = Mean rate of change in FACES II scores per month among tested parents.

$\mathbf{r}_{0i}$ = Residual random effect in mean FACES II scores prior to genetic testing (baseline).

$\mathbf{r}_{1i}$ = Residual random effect in mean rates of change in FACES II scores among tested parents.

$\mathbf{e}_{ti}$ = Random error for person *i* at time *t*.

TABLE 4. Significant Factors Associated with Initial (Baseline) Family Cohesion and Adaptability and Subsequent Changes (Slope) 1-Year after *BRCA1* Genetic Risk Notification: Men

	Cohesion		Adaptability	
Final Estimation of Fixed Effects	**Intercept** Coefficient (Std Error)	**Slope** Coefficient (Std Error)	**Intercept** Coefficient (Std Error)	**Slope** Coefficient (Std Error)
Carrier	-2.13	0.16	-2.64	0.21*
	(1.50)	(0.13)	(1.64)	(0.13)
Don't know carrier status	-2.81	0.02	-4.26	-0.05
	(2.83)	(0.28)	(3.10)	(0.27)
Age 18-40	2.06*	-0.10	1.72	-0.16
	(1.44)	(0.11)	(1.25)	(0.11)
No children living in home	-0.37	-0.03	0.45	-0.07
	(1.17)	(0.11)	(1.28)	(0.11)
Household Education	0.41	-0.02	0.32	-0.02
	(0.29)	(0.03)	(0.32)	(0.03)
Household Income	-0.02	-0.00	-0.03	-0.00
	(0.02)	(0.00)	(0.02)	(0.00)
Married to Single	-------	-------	-------	-------
Stayed Single	-------	-------	-------	-------
Suspect higher risk	-0.14	-0.02	-1.77	0.07
	(1.17)	(0.11)	(1.27)	(0.11)
Attended genetic counseling	-3.09	0.01	-5.37**	0.01
	(2.24)	(0.22)	(2.45)	(0.22)
Cancer History	0.57	-0.27*	-0.02	-0.34**
	(1.52)	(0.15)	(1.66)	(0.15)
Has a daughter	-------	-------	-------	-------
Parent Carrier	-0.09	-0.11	-1.55	-0.13
	(1.97)	(0.14)	(2.16)	(0.14)
Sister Carrier	0.43	-0.04	3.47*	0.07
	(1.89)	(0.12)	(2.08)	(0.12)
No caregiving	2.40*	-0.05	2.43	-0.13
	(1.43)	(0.14)	(1.57)	(0.14)
Some caregiving	0.76	-0.05	-1.19	-0.19
	(1.36)	(0.14)	(1.49)	(0.14)
A Great Deal of caregiving	3.37**	-0.02	3.72**	-0.29*
	(1.65)	(0.18)	(1.81)	(0.17)
Carrier x Suspect	-0.74	0.10	-1.65	0.29
	(2.50)	(0.24)	(2.77)	(0.24)
SAS	-0.14**	-0.01**	-0.24***	-0.01
	(0.07)	(0.01)	(0.07)	(0.01)
F-STRAIN	-0.31***	0.00	-0.24***	0.01
	(0.08)	(0.01)	(0.08)	(0.01)
F-COPES	0.18***	-0.01***	0.17***	-0.01***
	(0.04)	(0.00)	(0.05)	(0.00)

*** $p<.01$ ** $p<.05$ * $p<.10$

TABLE 5. Significant Factors Associated with Initial (Baseline) Family Cohesion and Adaptability and Subsequent Changes (Slope) 1-Year after *BRCA1* Genetic Risk Notification: Women

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

*** $p<.01$ ** $p<.05$ * $p<.10$

Figure 1 Legend:

Direct Effect

Interaction Effect

Effect for Unobservable Heterogeneity

[a] Timing-Sequencing Context

[b] Linked-Lives Context

[c] Position in the Social Structure

[d] Anticipated Event Mechanism