Short Communication

Predictors of Enrollment into a Familial Cancer Registry by Individuals at High Risk for *BRCA1/2*

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Abstract

Background: **Registries of individuals at risk for hereditary cancer syndromes are an invaluable resource for cancer research, yet little is known about the predictors of enrollment in hereditary cancer registries. We sought to identify the factors that characterize individuals who enroll versus those who decline participation in a Familial Cancer Registry (FCR). We also sought to identify the factors associated with provision of a blood sample to the FCR.**

Methods: **Participants (n = 549) had a 10% or greater prior probability of having a *BRCA1/2* mutation or were members of a family with a known *BRCA1/2* mutation.**

Results: **Of 549 participants, 81.1% (n = 445) enrolled in the FCR and 18.9% (n = 104) declined. Independent significant predictors of FCR participation included: lower anxiety (odds ratio$_{0.5\ SD}$, 0.83; 95% confidence interval, 0.73-0.95) and being unaffected with breast or ovarian cancer (odds ratio, 0.52; 95% confidence interval, 0.39-0.67). Of the 445 FCR participants, 80.4% provided a blood sample whereas 19.6% declined, with blood sample provision predicted by being employed full time (odds ratio, 1.68; 95% confidence interval, 1.31-2.16).**

Conclusion: **These findings have implications for the generalizability of results from research using hereditary cancer registry samples. Individuals who are affected with breast/ovarian cancer and have more anxiety are less likely to enroll in a hereditary cancer registry. Clinically, these results indicate that cancer registry enrollment strategies could benefit from the use of tailored approaches to increase the enrollment of individuals that are less likely to participate.** (Cancer Epidemiol Biomarkers Prev 2007;16(12):2763–7)

Introduction

Registries of individuals at high risk for hereditary cancer are an invaluable resource for cancer research. Hereditary registries, typically based on large kindreds with extensive family histories of cancer (1), were instrumental in initial linkage studies for discovery of the breast and ovarian cancer gene mutations, *BRCA1* and *BRCA2*. Several hereditary cancer registries remain active (2, 3), and other registries were developed as part of the National Cancer Institute's Cancer Genetics Network (CGN; ref. 4). We established the Familial Cancer Registry (FCR) at Georgetown University in concert with the development of a CGN site and as a means for long-term follow-up of patients at high risk.

Hereditary cancer registries, including the FCR, recruit participants through physician referral and/or high-risk cancer clinics (4), whereas CGN registries may invite individuals from the general population or from high-risk clinics. In this way, hereditary cancer registries allow researchers to easily identify and solicit individuals with a hereditary cancer history to participate in research (5).

Research derived from hereditary cancer registries span the cancer control spectrum, including, but not limited to, molecular epidemiology, genetics, clinical prevention, screening, treatment, behavioral, and health services research (6-12). To date, few studies have evaluated the individual characteristics that predict enrollment into hereditary cancer registries. Furthermore, we are not aware of research examining the factors associated with provision of a blood sample to hereditary cancer registries for future research purposes, although prior research has evaluated predictors of blood sample provision for genetic testing (13).

Characteristics related to registry enrollment may influence the outcomes of studies from the registry. For example, the underrepresentation of racial and ethnic minorities in hereditary cancer registries could limit the generalizability of study results (14-16). Moreover, self-selection into registries based on psychosocial factors may influence behavioral outcomes because distress is also associated with risk management behaviors such as prophylactic mastectomy (17). Age and/or education

Received 5/25/07; revised 8/17/07; accepted 9/19/07.

Grant support: National Cancer Institute P30-CA-51008 (C. Isaacs) and R01CA82346 (M.D. Schwartz), and the Jess and Mildred Fisher Center for Familial Cancer Research (M.D. Schwartz and C. Isaacs).

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Note: Portions of this paper were presented at the Frontiers of Cancer Prevention Research Meeting, American Association of Cancer Research, November 2006, Boston, MA.

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doi:10.1158/1055-9965.EPI-07-0469

may also vary among individuals who enroll in cancer genetics research (18, 19). Generalizability concerns are particularly relevant to research using data from hereditary cancer registries because outcomes associated with individual characteristics such as ethnicity, education, age, psychological functioning, and socioeconomic status may be overlooked.

A recent study comparing individuals who self-referred to a cancer genetics registry versus those who were actively recruited found that those who self-referred were better educated, reported higher anxiety and depression, were more likely to have a personal history of cancer, and were more likely to consider themselves a candidate for genetic testing (19). However, we are aware of no studies that have evaluated sociodemographic *and* psychological factors associated with enrollment in a high-risk hereditary cancer registry. Thus, in the present study, we sought to identify the sociodemographic and psychological factors that characterize individuals who enroll versus those who decline participation in our FCR. We also explored the factors associated with provision of a blood sample to the FCR.

Materials and Methods

Participants. Participants (n = 549) self-referred to the clinical genetic counseling research program at the Lombardi Comprehensive Cancer Center. Participants were eligible if they had a personal history of breast or ovarian cancer and approximately ≤10% prior probability of having a *BRCA1/2* mutation (n = 330) or were members of a family with a known *BRCA1/2* mutation (n = 219). All data were collected through a telephone interview prior to genetic counseling.

Procedure. Potential participants were drawn from individuals who were enrolled in the Lombardi Comprehensive Cancer Center Cancer Assessment and Risk Evaluation clinical research program. All Cancer Assessment and Risk Evaluation participants provided verbal consent prior to completing a baseline telephone interview to collect information on demographics, personal and family cancer history, and psychological distress. Following the baseline interview, participants were scheduled for their initial genetic counseling session. Immediately prior to the initial genetic counseling session, participants were informed about the availability and purpose of the FCR by a genetic counselor. Potentially interested individuals were informed that participation in the FCR involved completion of a health history questionnaire, annual updates of medical and family history information, and an optional blood sample for DNA banking. Participants were also informed that participation in any additional studies was independent of their decision to consent/decline FCR enrollment. Although not the focus of the present study, most participants were also invited to participate in the CGN. All participants who elected to enroll in the FCR signed an Institutional Review Board–approved consent form that detailed the purpose and procedures related to registry participation. Several weeks *after* participants decided to enroll or decline participation in the FCR, individuals who received positive *BRCA1/2* results were invited to participate in a randomized clinical trial separate from the present study.

Measures

Sociodemographics. We collected information during the baseline telephone interview, with variables dichotomized for analysis: age (<50 versus ≥50), race (Caucasian versus other), marital status (married versus other), education (high school graduate versus some college or beyond), employment (employed full time versus other), insurance status (yes versus no), religion (Jewish versus other), and annual income (≤$75,000 versus >$75,000). We dichotomized income using these cut-points as they represented the two bimodal distributions of annual income in our sample.

Medical. Participants self-reported family cancer history, personal medical history (cancer diagnosis, screening, surgery, other treatment), and prior genetic testing in the family.

Distress. Participants completed the Impact of Event Scale (20), a 15-item measure that assesses cancer-specific distress through two subscales of avoidant and intrusive thoughts. Items are scored on a weighted four-point scale (0 = not at all, 1 = rarely, 3 = sometimes, 5 = often). Internal consistency for the total Impact of Event Scale score in the present study was α = 0.88. Participants also completed the anxiety and depression subscales of the Brief Symptom Inventory (21) to measure general distress. Each subscale consists of six items on a four-point scale (1 = not at all, 4 = extremely). Internal consistency in the present study was α = 0.83 and α = 0.79 for the anxiety and depression subscales, respectively.

Statistical Analyses. We generated descriptive statistics to characterize sociodemographic, medical, and distress variables. To evaluate bivariate predictors of enrollment and provision of a blood sample, we used χ^2 tests and t tests. To determine which variables were independently associated with our outcomes, we conducted logistic regression analyses using generalized estimating equations to account for familial clustering. We included all variables with bivariate associations of $P < 0.10$ to each outcome (FCR participation and blood sample provision) in the initial models. Because of the almost complete overlap between proband status (being the first person in the family to seek genetic testing) and being affected with breast or ovarian cancer (Fisher exact test, n = 549: $P < 0.00001$), we opted to enter affected status into the regression equation and did not include proband status.

Results

Sample Characteristics. Participants had a mean age of 48 years (SD = 12; range, 19-86; see Table 1). Most were Caucasian (91%), married (73%), attended some college or beyond (94%), had health insurance (98%), and about half were employed full time (55%). Fifty-five percent (n = 301) of the participants reported a personal history of breast cancer and 7.8% (n = 43) reported a personal history of ovarian cancer. The majority of participants (70.5%) were also invited to participate in the CGN (n = 387). No demographic differences were evident between individuals who were and were not approached to participate in the CGN.

Table 1. Characteristics of samples according to FCR participation status

Characteristic	FCR (n = 445)	Non-FCR (n = 104)	All (n = 549)
Mean age (SD)*	48.3 (12.5)	48.9 (11.5)	48.4 (12.3)
Mean cancer-specific distress (SD)	18.4 (14.8)	23.5 (17.2)	19.4 (15.4)
Mean anxiety (SD) †	8.8 (3.1)	10.5 (4.1)	9.1 (3.4)
Mean depression (SD) ‡	8.0 (2.6)	8.8 (3.0)	8.1 (2.7)
Breast cancer–affected status*			
Affected with breast cancer	229 (51.5)	72 (69.2)	301 (54.8)
Unaffected with breast cancer	216 (48.5)	32 (30.8)	248 (45.2)
Proband status*			
Proband	215 (48.3)	71 (68.3)	301 (54.8)
Relative	230 (51.7)	33 (31.7)	248 (45.2)
Marital status			
Married (%)	115 (25.8)	73 (70.2)	403 (73.4)
Unmarried (%)	330 (74.2)	31 (29.8)	249 (45.6)
Education			
No college (%)	24 (5.4)	6 (5.8)	30 (5.5)
Some college/degree (%)	421 (94.6)	98 (94.2)	519 (94.5)
Employed			
Full time (%)	239 (53.7)	61 (58.7)	300 (54.6)
<Full time (%) ‡	206 (46.3)	43 (41.3)	249 (45.4)
Annual income ‡			
<75,000 (%)	182 (40.9)	30 (28.8)	212 (38.6)
≥75,000 (%)	263 (59.1)	74 (71.2)	337 (61.4)
Race			
White (%)	406 (91.2)	95 (91.3)	501 (91.3)
Other (%)	39 (8.8)	9 (8.6)	48 (8.7)
Ethnicity*			
Jewish (%)	139 (31.2)	47 (45.2)	186 (33.9)
Non-Jewish (%)	306 (68.7)	57 (54.8)	363 (66.1)
First-degree relatives with breast cancer ‡			
<2 (%)	325 (73.0)	84 (80.8)	409 (74.5)
≥2 (%)	120 (27.0)	20 (19.2)	140 (25.5)
Gender§			
Male	57 (12.1)	7 (6.7)	64 (11.6)
Female	388 (87.9)	97 (93.3)	485 (88.3)

*Significant bivariate relationships with FCR enrollment ($P < 0.01$).
†Significant bivariate relationships with FCR enrollment ($P < 0.001$).
‡Significant bivariate relationships with FCR enrollment ($P < 0.05$).
§Significant bivariate relationships with FCR enrollment ($P < 0.10$).

Predictors of FCR Participation. Of 549 participants, 81.1% (n = 445) enrolled in the FCR and 18.9% (n = 104) declined. Bivariate predictors of FCR participation were: less cancer-specific distress [t (df, 547) = 2.70, P = 0.006], lower anxiety [t (df, 547) = 3.86, $P < 0.001$], less depression [t (df, 547) = 2.71, P = 0.0069], more affected first-degree relatives [t (df, 547) = −1.62, P = 0.10], lower annual household income [χ^2_1 (n = 549) = 5.16, P = 0.023], *not* having a personal history of breast or ovarian cancer [χ^2_1 (n = 549) = 10.75, P = 0.001], male gender [χ^2_1 (n = 549) = 3.02, P = 0.08], and being non-Jewish [χ^2_1 (n = 549) = 7.33, 7.33, P = 0.007].

As displayed in Table 2, the final multivariate generalized estimating equations model predicting FCR participation revealed that lower anxiety (odds ratio$_{0.5\ SD}$, 0.83; 95% confidence interval, 0.73-0.95) and being unaffected with breast or ovarian cancer (odds ratio, 0.52; 95% confidence interval, 0.39-0.67) predicted FCR enrollment. Being of non-Jewish descent approached statistical significance (Z = −1.90, P = 0.06).

Predictors of Provision of a Blood Sample for DNA Banking. Of 445 FCR participants, 80.4% (n = 358) provided a blood sample and 19.6% (n = 87) declined to provide a blood sample. Bivariate predictors of blood sample provision were: less cancer-specific distress [t (df, 443) = 2.50, P = 0.013], less depression [t (df, 443) = 1.73, P = 0.09], more first-degree relatives with breast or ovarian cancer [t (df, 443) = −2.55, P = 0.01], being employed full time [χ^2_1 (n = 445) = 5.44, P = 0.012], being male [χ^2_1 (n = 445) = 4.83, P = 0.028], and being non-Jewish [χ^2_1 (n = 445) = 3.10, P = 0.08]. Of note, almost all (98%) of the people who provided a blood sample for banking also pursued genetic testing in the parent study.

As displayed in Table 3, the final generalized estimating equations model revealed that being employed full time (odds ratio, 1.68; 95% confidence interval, 1.31-2.16) was the only variable independently associated with the provision of a blood sample. Lower cancer-specific distress (Z = −1.62, P = 0.10) and having more first-degree

Table 2. Generalized estimating equation logistic regression model of participation in a FCR

Variable*	Odds ratio (95% confidence interval)
Anxiety (0.5 SD)	0.83 (0.73-0.95)
Being unaffected with breast or ovarian cancer	0.52 (0.39-0.67)

*Variables removed from the model: cancer-specific distress (Z = −0.04, P = 0.97), Jewish heritage (Z = −1.90, P = 0.06), annual household income (Z = −1.03, P = 0.30), number of first-degree relatives (Z = −0.04, P = 0.96), and gender (Z = 0.11, P = 0.91).

Table 3. Generalized estimating equations logistic regression model of provision of a blood sample for FCR participants

Variable*	Odds ratio (95% confidence interval)
Being employed full time	1.68 (1.31-2.16)

*Variables removed from the model: cancer-specific distress ($Z = -1.62$, $P = 0.10$), depression ($Z = -0.76$, $P = 0.44$), total number of first-degree relatives with breast or ovarian cancer ($Z = 1.90$, $P = 0.06$), Jewish heritage ($Z = -1.10$, $P = 0.27$), and gender ($Z = -1.21$, $P = 0.23$).

relatives with breast or ovarian cancer ($Z = 1.90$, $P = 0.06$) were marginally associated with blood sample provision.

Discussion

The overall rate of enrollment into the FCR was quite high, suggesting that within a sample of individuals seeking genetic counseling and testing, active recruitment strategies yield excellent participation. Enrollment rates were lower for women previously diagnosed with breast or ovarian cancer, a group for whom future risk prevention strategies may be useful. Perhaps women affected with breast or ovarian cancer enrolled at lower rates because of the perceived burden of completing health history surveys and annual updates in addition to treatment and/or regular health surveillance appointments with their oncology team.

We did not find differences in registry enrollment between African Americans and Caucasians; however, these results, although encouraging, warrant replication due to the small overall proportion of minorities in our sample. Given the overall low rate of minority participation in genetic testing (14), it is possible that African American participants in the Cancer Assessment and Risk Evaluation program may have been particularly motivated to, or perceived fewer barriers toward, enrolling in the FCR. Minority recruitment and enrollment into hereditary cancer registries is critical so that the conclusions and practical implications drawn from registry-based research can be applied across diverse groups (14).

The relationship between lower anxiety and greater likelihood of FCR participation suggests that individuals experiencing distress may be the least likely to participate in registries. This could have significant implications for psychosocial research using registry-based samples; intervention studies that recruit via a registry may be systematically excluding those individuals most in need of psychosocial intervention. Similarly, to the extent that distress is associated with risk management behaviors (17), individuals enrolled in registries may differ from decliners on outcomes such as screening and prophylactic surgery.

The relationship between employment status and provision of a blood sample is interesting. Given the high degree of overlap between provision of a blood sample for the FCR and the receipt of genetic testing results, we examined the possibility that the association between employment and blood provision could be due to other variables known to predict genetic testing decisions. Surprisingly, age, insurance status, and annual income were not directly related to FCR blood sample provision. Still, it is possible that employment status serves as a proxy for some combination of these variables. Future research could replicate and further explore this result.

Results should be interpreted in the context of the study's limitations. Specifically, all participants were recruited from a single site (Lombardi Comprehensive Cancer Center), were seeking *BRCA1/2* genetic counseling, and had previously consented to participate in research. Moreover, we did not have reliable data related to the source of referral to the program. In addition, we did not measure constructs such as cancer fatalism or medical mistrust that may be important predictors of registry enrollment. As a largely descriptive study, we did not evaluate our results within a specific theoretical framework; however, our results seem to be consistent with a cognitive-behavioral approach (22). For example, having anxious thoughts may lead one to engage in behaviors to reduce or avoid anxiety, such as declining to enroll in a registry that requests completion of annual updates about health and well-being. Finally, our sample was primarily Caucasian, well educated, affluent, and insured, limiting our ability to make generalizations regarding these potentially important variables.

Clinically, these results suggest that cancer registry recruitment strategies could benefit from tailored approaches to increase the enrollment of individuals less likely to participate. Tailored recruitment efforts could consist of targeted outreach and support to distressed individuals. For example, education and resources provided to registry enrollment personnel, such as genetic counselors or clinic staff, may be useful. Registry personnel may be less likely to discuss the possibility of enrollment with distressed individuals; however, with appropriate training and/or support, information about registry participation could be presented to minimize any increase in distress. Just as the results from randomized clinical trials of cancer therapies may have limited generalizability due to self-selection of participants (23), researchers recruiting participants from hereditary cancer registries are encouraged to consider the generalizability of their results, as the present data suggests that individuals who enroll in these registries may be less distressed and less likely to have been personally affected with breast or ovarian cancer.

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