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Colorectal Cancer Cases and Relatives of Cases Indicate Similar Willingness to Receive and Disclose Genetic Information

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Abstract

Context—Recent developments in genetic testing allow us to detect individuals with inherited susceptibility to some cancers. Genetic testing to identify carriers of cancer-related mutations may help lower risk by encouraging preventive behaviors and surveillance. This study assessed willingness of colon cancer cases and relatives to receive genetic information that may indicate an increased risk for cancer, to whom they would disclose genetic information, and whether receiving genetic test results may influence future prevention behaviors among individuals enrolled in the Seattle Colorectal Cancer Family Registry.

Methods—Incident invasive colorectal cancer cases were identified from the Puget Sound Surveillance Epidemiology and End Results (SEER) registry. In 2007, a sequential sample of cases and relatives (n = 147) were asked to respond to a questionnaire addressing study aims. The questionnaire was administered during a baseline or 5-year follow-up interview.

Results—Patterns of response to each statement were similar between colorectal cancer cases and relatives. Both colorectal cases (95%) and relatives (95%) reported willingness to receive genetic information. Nearly all participants would tell their doctor the results of a genetic test (99% of cases; 98% of relatives), and all married participants would tell their spouses. Cases (96%) anticipated being slightly more likely than relatives (90%) to change their cancer screening behavior, but this difference was not statistically significant (p = 0.33).

Conclusions—A high percentage of both colorectal cancer cases and relatives sampled from the Seattle Colorectal Cancer Family Registry are interested in identifying their genetic status, discussing their genetic status with their family and doctor, and adopting behavioral changes that may reduce cancer risk.

Introduction

Developments in genetic testing provide opportunities for clinicians and researchers to identify individuals with some hereditary mutations that result in increased susceptibility to cancer. Genetic testing to identify those affected by mutations, such as Lynch syndrome (LS), may help lower risk of cancer by encouraging preventive behaviors and monitoring for early detection in those at high risk (Halbert *et al.*, 2004; Loader, Shields, and Rowley, 2005).

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Issues of privacy and confidentiality as well as questions surrounding the obligation to disseminate information about genetic status to potentially affected family members are at the forefront of ethical discussions about genetic testing for hereditary mutations (Codori, 1997; Kass *et al.*, 2004; Satia *et al.*, 2006; Hay *et al.*, 2007; Kohut *et al.*, 2007). Overall, studies have shown that there is high agreement among individuals with colorectal cancer that it is important to disclose results of genetic tests to family members, especially members of the immediate family (Smith and Croyle, 1995; Vernon *et al.*, 1999; Esplen *et al.*, 2007; Kohut *et al.*, 2007). In a recent study by Kohut *et al.* (2007), a cross-sectional analysis of 314 colorectal cancer patients enrolled in the population-based Ontario Familial Colon Cancer Registry expressed a strong sense of obligation to reveal results of their LS test to members of their immediate and often extended family. Over 90% of both mutation-positive and mutation-negative colon cancer cases indicated that they would inform at-risk family members (e.g., children and siblings) of a genetic mutation, if present, and encourage regular cancer screenings among at-risk family members.

In contrast, few studies have assessed the perspective of first-degree relatives of colorectal cancer cases with respect to their willingness to receive information regarding a genetic susceptibility to colon cancer and undergo genetic testing. These few studies have revealed mixed results (Lerman *et al.*, 1996; Glanz *et al.* 1999; Petersen *et al.*, 1999). Specifically, the intentions of participants to undergo genetic testing ranged 26-92%. Methodological differences in sample sizes, populations, and data collection procedures may have contributed to the wide range of responses.

The current study was designed to assess the desires of both colorectal cancer cases and relatives of colorectal cancer cases before either the case or relative is tested for hereditary mutations. Aims of the study were to assess (1) willingness of colon cancer cases and relatives to receive genetic information that may indicate an increased risk for cancer, (2) to whom they would disclose genetic information, and (3) whether receiving genetic test results may influence future prevention behaviors among a population-based sample of individuals enrolled in the Seattle Colorectal Cancer Family Registry (C-CFR).

Materials and Methods

Participants

Study cases were men (n = 25) and women (n = 20) from King, Snohomish, and Pierce counties in Washington State who had been diagnosed with invasive colorectal adenocarcinoma [International Classification of Disease for Oncology codes C18.0, C18.2-9, and C20.0.9 (18)] from October 1998-2006, as identified through the Puget Sound Surveillance Epidemiology and End Results (SEER) Program registry, aged 20-74 years at diagnosis. All cases were participants in the Seattle C-CFR. First-degree relatives of cases (men = 45; women = 57) identified through the population-based Seattle C-CFR were also contacted for participation in this study. This study was approved by the Institutional Review Board at Fred Hutchinson Cancer Research Center.

Procedures

Details about study recruitment are presented elsewhere (Newcomb *et al.*, 2007). Briefly, eligible cases were contacted via mail regarding the research study. During a 50 minute telephone interview cases were asked to provide demographic information and information regarding lifestyle factors. Cases were also asked to provide names and contact information for their first degree relatives. If informed consent was provided by the case, family members were contacted with an introductory study letter and a follow-up telephone call to initiate the interview. The sequential relative sample included individuals identified as

relatives of any case enrolled in the Seattle C-CFR, but were not otherwise linked to specific cases in the sample.

Data for the current study were collected at the end of either the baseline or 5-year follow-up phone interview in 2007. Both colorectal cancer cases and family members were asked questions from a 14-item survey, developed by the research team, which assessed three components of receiving genetic test results. The questions measured whether or not participants would want to know if a genetic test indicated that they or members of their immediate family were at increased risk for cancer; whom the participant would tell if a genetic test indicated that they or members of their immediate family were at increased risk for cancer; and how the participant perceived results of a genetic test indicating an increased risk of cancer would affect their cancer prevention behaviors and screening. Participants were asked to select one categorical answer (strongly disagree, disagree, agree, strongly agree, not applicable, do not know, and refuse to answer) for each of the 14 statements.

Statistical analysis

Percentage of cases and percentage of relatives of cases agreeing with questionnaire statements were compared using χ^2 or Fisher's exact test, as appropriate. Proportions presented in tables were standardized for the age and gender of the larger Seattle Colon Cancer Registry population. Potential confounders evaluated were age, gender, type of family member affected with colorectal cancer (parent, child, sibling, multiple members), education, income, and timing of data collection (baseline or 5-year follow-up). Significant factors were included as covariates in subsequent multinomial regression analyses in which the relationship of case type (colorectal cancer case vs. relative) and strength of agreement for each questionnaire statement was analyzed.

Gender, type of immediate family member affected by colorectal cancer, and time of data collection were not statistically significant predictors of outcomes. These variables were therefore not included in subsequent analyses. Age, education, and income were significantly associated with participant responses for several questions and were included in the final regression analyses (Tables 2a-c). To each statement, the majority of participants responded, "agree" or "strongly agree"; some categories (disagree, strongly agree) had few or no respondents. Therefore, to optimize the multinomial regression analysis, the category "strongly agree" was compared to an "other" (agree, disagree, strongly disagree) category. Additionally, according to the Theory of Planned Behavior (Ajzen, 1985), behavioral intention is a consistent predictor of future action, as intent is the precursor to action. Based on face valid measures, the research team concluded that the term "strongly agree" is representative of a strong behavioral intention to engage in a behavior. Therefore, for the purpose of statistical analysis, the *p*-value reports the difference between "strongly agree" vs. "other." However, the frequency and percent of participant responses for each of the primary categories (strongly agree, agree, disagree, strongly disagree) are presented in the tables.

One relative of a case reported a previous diagnosis of colon cancer and was excluded from the analysis. For some participants, some of the statements on the survey (i.e., "I would tell my parents" or "I would tell my children") did not apply to their current situation, and were therefore excluded from the final analyses.

Results

Study participants were approximately equally divided by gender, were predominantly Caucasian, and were of higher socioeconomic status compared to the U.S. population (Table 1). Cases (60 ± 12 years; range, 38-81) were older than relatives (52 ± 15; range, 23-86) ($p <$

0.01). Cases and relatives had an approximately equal proportion of individuals diagnosed with a cancer other than colon or colorectal cancer (i.e., skin cancer).

The three survey items assessing willingness to receive genetic information indicated that between 96% and 98% of cases and between 94% and 97% of relatives agreed or strongly agreed that they would be willing to receive genetic testing (Table 2a). When those that responded strongly agree were compared to all other categories, no statistically significant differences were present between cases and relatives, regardless if the willingness to receive genetic information referred to the potential increased risk for cancer of the participant themselves ($p = 0.19$), their children ($p = 0.30$), or their brothers and sisters ($p = 0.71$).

Between 89% and 100% of cases and between 94% and 99% relatives agreed or strongly agreed that they would discuss the results of a test revealing the presence of a genetic mutation with family or their physician (Table 2b). There were no statistically significant differences between the number of cases and relatives who strongly agreed that they would disclose results of genetic tests to their spouse ($p = 0.84$), parents ($p = 0.78$), children ($p = 0.63$), siblings ($p = 0.51$), or physician ($p = 0.95$). While 89% of participants indicated agreement with disclosing results to their parents about the presence of a genetic mutation, all participants would discuss results of the genetic test with their spouse, siblings, and children.

Statements discussing the effect of having a positive test result on the promotion of cancer prevention and screening behaviors revealed that between 96% and 100% of cases and between 90% and 99% of relatives agreed or strongly agreed with each statement (Table 2c). This reflects an anticipated improvement in prevention and screening behaviors as a consequence of a positive test result. Similar percentages of cases and relatives reported that they strongly agreed with statements reflecting changes in their own prevention behavior ($p = 0.33$), openness to learning about prevention techniques [learning new behaviors ($p = 0.24$); making changes in diet/exercise ($p = 0.19$)], and encouraging family members to seek both genetic testing ($p = 0.82$) and cancer screening ($p = 0.34$).

Discussion

Our overall findings from this study suggest that both colon cancer cases and relatives of cancer patients would like to know if they or a member of their immediate family is a carrier of a genetic mutation for cancer. Further, the sample population would most likely inform their spouse, parents, siblings, and children. Over 90% of both cases and relatives anticipated that their practice and promotion of cancer prevention behaviors (i.e., diet, exercise, and screening) would change if a genetic test showed that they themselves or their family members were at increased risk for cancer.

Overall, these data are consistent with the findings of Petersen and colleagues (1999), who reported that over 90% of relatives agreed that they would be interested in receiving information about their genetic susceptibility to cancer. Although Peterson and colleagues did report a positive association between the strength of family history for colon cancer (i.e., number of family members diagnosed with colon cancer) and perception of risk, similar to our study, family history was not related to willingness to undergo testing. Although retrospective studies have reported some barriers to communication during disclosure among colon cancer cases (Kohut *et al.*, 2007), they have also revealed a strong willingness and a sense of obligation to disclose both positive and negative genetic test results to relatives (Peterson *et al.*, 2003; Kohut *et al.*, 2007). The willingness to disclose information in these studies was largely equivalent to the levels identified in the current investigation. Recognizing that relatives have similar concerns and interests as do colon cancer cases to

learn about genetic status and disclosure provides preliminary evidence that the topic of genetic testing is an acceptable option for many with a family history of colon cancer.

However, multiple studies have shown that disclosure and dissemination of genetic information needs to be considered on a case-by-case basis (Esplen *et al.*, 2001; Koehly *et al.*, 2003; Pentz *et al.*, 2005; Gilbar, 2007). While identifying genetic susceptibility to cancer provides an opportunity for preventive behavior, including improvement in diet, exercise, and screening practices, negative consequences are also possible. For example, a recent paper by Lynch *et al.* (2007) noted the potential emotional distress that may occur following identification of a genetic susceptibility to cancer, as well as the distress that those who have negative or ambiguous results can experience. These findings highlight the importance of evaluating participant willingness *a priori* to receive such information and discussing implications of results. Several authors (Bookman *et al.*, 2006; Burke and Press, 2006) have drafted guidelines regarding the selection of individuals for genetic testing and a program of individualized assessments to discuss testing and dissemination. Our study, which assessed the opinions of a subset of individuals from the Seattle C-CFR, was conducted as an initial step in this process of disclosure for participants enrolled in the cancer registry.

This study had many strengths, including the population-based nature of the sample. The wide age and gender distribution enhance the generalizability of study results to the larger Seattle C-CFR population. This encourages further work into the interest and disclosure of genetic status among individuals enrolled in the C-CFR and their relatives, as well as colorectal cancer families in the population.

Some limitations should be considered, however. First, the sample size was limited, and the relative group was not an independent series. Caution should be taken in generalizing these findings to other populations. Second, participants enrolled in the C-CFR may be more willing than the general population to discuss factors that may contribute to increased risk of cancer. Third, our participants were predominantly Caucasian, of higher education, and of higher income compared to national averages (Buckner, 2004, May 10; U.S. Census Bureau, 2006). This feature is generally similar to individuals enrolled in the larger Seattle C-CFR, the population from which our participants arose, and Seattle in general. Previous research studies have found mixed results with regard to education and income effects on interest and intent to undergo genetic screening for cancer susceptibility (Lerman *et al.*, 1996; Petersen *et al.*, 1999; Satia *et al.*, 2006). For example, in contrast to the current study, studies with similar educational distributions to ours showed no relationship between education and willingness to undergo genetic screening (Glanz *et al.*, 1999; Petersen *et al.*, 1999; Kinney *et al.*, 2001). While age, education, and income were significant predictors of participant response in this study, the inclusion of these variables in the multiple regression analysis did not significantly affect differences (or lack of differences) between cases and relatives.

Future studies can address the potential limitations of C-CFR participation, education, and income by including a true unaffected population-based control group. Factors, such as age, that may have influenced the difference between cases and relatives in personal cancer screening behaviors should also be investigated to determine if the difference is because of increased awareness or a reduced sense of urgency among our younger relatives. Finally, although the assessment tool did elicit responses regarding a wide range of issues in genetic testing, it should be expanded to include more comprehensive questioning about the issue of genetic testing for colorectal cancer specifically, and for LS status in particular.

In summary, much of the discussion around genetic testing has involved concern about the effect of disclosure on colorectal cancer cases and their relatives. This study was an initial attempt at evaluating the interest and willingness of colorectal cancer cases and relatives

enrolled in the population-based registry to receive genetic testing. These findings suggest that relatives of registered cases are as interested in receiving genetic information about cancer risk for them and their family as individuals already diagnosed with colon cancer. Study results suggest that a high percentage of both colorectal cancer cases and relatives are interested in learning the results of genetic tests, disclosing information about their status, and encouraging behavioral changes that may reduce cancer risk.

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Table 1

Selected Characteristics of Colorectal Cancer Cases and Relatives in the Seattle Colon Cancer Family Registry

	Cases **n (%)**	***Relatives*** **n (%)**
Gender		
Men	25 (56)	45 (44)
Women	20 (44)	57 (56)
Race		
Caucasian	40 (89)	96 (94)
Other	5 (11)	6 (6)
Education		
8-11 years	2 (4)	10 (10)
High school graduate	9 (20)	21 (21)
Some college	12 (27)	35 (34)
College/graduate degree	22 (49)	36 (35)
Household income		
Less than $30,000	7 (16)	23 (23)
$30,000-69,999	17 (38)	45 (44)
$70,000+	21 (47)	34 (33)

Table 2a

Willingness to Receive Results of Genetic Test: Distribution of Responses among Cases and Relatives of Cases

	Case type		
	***Cases* n (%)**	***Relatives* n (%)**	**p-*value***
I would want to know if the test showed that . . . I have an increased risk for cancer			
Strongly agree	34 (77)	66 (64)	0.19
Agree	8 (18)	30 (31)	
Disagree	3 (4)	5 (5)	
Strongly disagree	0 (0)	0 (0)	
my children might have an increased risk for cancer			
Strongly agree	32 (80)	66 (68)	0.30
Agree	8 (18)	26 (29)	
Disagree	1 (2)	2 (2)	
Strongly disagree	0 (0)	1 (1)	
my brothers and sisters might have increased risk for cancer			
Strongly agree	29 (64)	62 (62)	0.71
Agree	14 (34)	31 (32)	
Disagree	2 (3)	6 (5)	
Strongly disagree	0 (0)	1 (1)	

Percentages are adjusted to the age and gender of the larger SCCR population. Percentages and χ^2 analyses do not include “do not know,” “refuse,” and “not applicable” responses. χ^2 tests the differences between cases and relatives, and *p*-values represent “strongly agree” responses vs. “all other” response categories.

Table 2b

Anticipated Disclosure Following Genetic Testing: Distribution of Responses among Cases and Relatives of Cases

	Case type		
	***Cases* n (%)**	***Relatives* n (%)**	**p-*value***
If a genetic test showed that I or my family had an increased risk for cancer, I would . . . tell my spouse			
Strongly agree	28 (80)	62 (69)	0.84
Agree	6 (20)	20 (31)	
Disagree	0 (0)	0 (0)	
Strongly disagree	0 (0)	0 (0)	
tell my parents			
Strongly agree	17 (73)	42 (68)	0.78
Agree	5 (16)	14 (29)	
Disagree	2 (7)	3 (3)	
Strongly disagree	1 (4)	0 (0)	
tell my brothers and sisters			
Strongly agree	31 (76)	68 (65)	0.63
Agree	13 (24)	27 (28)	
Disagree	0 (0)	5 (5)	
Strongly disagree	0 (0)	1 (1)	
tell my children			
Strongly agree	31 (82)	56 (68)	0.51
Agree	8 (18)	25 (30)	
Disagree	0 (0)	0 (0)	
Strongly disagree	0 (0)	1 (1)	
tell my family doctor			
Strongly agree	34 (81)	72 (73)	0.95
Agree	10 (18)	24 (25)	
Disagree	0 (0)	1 (1)	
Strongly disagree	1 (1)	1 (1)	

Percentages are adjusted to the age and gender of the larger SCCR population. Percentages and χ^2 analyses do not include “do not know,” “refuse,” and “not applicable” responses. χ^2 tests the differences between cases and relatives, and *p*-values represent “strongly agree” responses vs. “all other” response categories.

Table 2c

Anticipated Changes in Practice and Promotion of Cancer Prevention Behaviors: Distribution of Responses among Cases and Relatives of Cases

	Case type		
	***Cases* n (%)**	***Relatives* n (%)**	**p-*value***
If a genetic test showed that I or my family had an increased risk for cancer, I would . . . change my cancer screening behavior			
Strongly agree	23 (65)	58 (56)	0.33
Agree	11 (31)	31 (34)	
Disagree	1 (4)	11 (10)	
Strongly disagree	0 (0)	0 (0)	
learn about ways to prevent cancer			
Strongly agree	32 (76)	68 (67)	0.24
Agree	12 (24)	32 (33)	
Disagree	0 (0)	1 (1)	
Strongly disagree	0 (0)	0 (0)	
try to lower my risk by changing my diet and/or exercise			
Strongly agree	31 (71)	61 (58)	0.19
Agree	13 (29)	39 (42)	
Disagree	0 (0)	1 (1)	
Strongly disagree	0 (0)	0 (0)	
encourage my family members to get genetic testing			
Strongly agree	26 (63)	59 (59)	0.82
Agree	17 (35)	36 (37)	
Disagree	1 (1)	4 (4)	
Strongly disagree	0 (0)	0 (0)	
encourage my children/brothers/sisters to increase their cancer screening			
Strongly agree	28 (68)	62 (60)	0.34
Agree	13 (28)	35 (36)	
Disagree	2 (4)	4 (5)	
Strongly disagree	0 (0)	0 (0)	

Percentages are adjusted to the age and gender of the larger SCCR population. Percentages and χ^2 analyses do not include “do not know,” “refuse,” and “not applicable” responses. χ^2 tests the differences between cases and relatives, and *p*-values represent “strongly agree” responses vs. “all other” response categories.