Genetics inMedicine | ORIGINAL RESEARCH ARTICLE

Communication of genetic test results to family and health-care providers following disclosure of research results

Kristi D. Graves, PhD[1], Pamela S. Sinicrope, DrPH[2], Mary Jane Esplen, RN, PhD[3], Susan K. Peterson, PhD[4], Christi A. Patten, PhD[9], Jan Lowery, PhD, MPH[5], Frank A. Sinicrope, MD[10], Sandra K. Nigon[2], Joyce Borgen[2], Sherri Sheinfeld Gorin, PhD[6], Louise A. Keogh, PhD[7] and Noralane M. Lindor, MD[8]; for the Behavioral Working Group of the Colon Cancer Family Registry

Purpose: Few studies have examined methods to promote communication following the return of DNA mismatch repair genetic test results obtained during research. The purpose of the present study was to evaluate a telephone protocol for returning research results of DNA mismatch repair gene testing to identify Lynch syndrome.

Methods: We invited individuals with known DNA mismatch repair mutations in their family, who were enrolled in the Colon Cancer Family Registry at the Mayo Clinic, to participate in this study. Participants completed surveys before and 6 months after DNA mismatch repair test result disclosure.

Results: Among 107 participants, 79% opted to learn their DNA mismatch repair test results; of these, 44 (41%) carried DNA mismatch repair mutations. After disclosure, 54% reported screening for any type of cancer. Among carriers, >74% reported communicating results to family; communication was predicted by baseline confidence in coping with the genetic test result ($Z = 1.97$; $P = 0.04$). Result disclosure to a physician was predicted by greater perceived cancer risk ($Z = 2.08$; $P = 0.03$) and greater intention to share results with family ($Z = 3.07$; $P = 0.002$).

Conclusion: Research versus clinically based gene disclosure presents challenges. A telephone disclosure process for the return of research-based results among Lynch syndrome families led to high rates of result uptake and participant communication of results to providers and family members.

Genet Med advance online publication 3 October 2013

Key Words: communication; gene test disclosure; Lynch syndrome; research; telephone genetic education

INTRODUCTION

Individuals who carry a germline mutation in a DNA mismatch repair (MMR) gene (*hMSH2*, *hMLH1*, *hMSH6*, or *hPMS*) are at significantly increased risk for a number of cancers, often at young ages, specifically colorectal cancer (CRC), endometrial cancer, stomach cancer, ovarian cancer, small bowel cancer, urothelial cancers, and hepatobiliary tract cancer.[1] This autosomal-dominant cancer predisposition is termed Lynch syndrome.[1] Knowledge of MMR gene status can inform clinical decision making regarding screening and/or prophylactic surgery. For people who carry the MMR gene mutation, routine screening with colonoscopy appears to decrease CRC-related mortality by ~65%.[2] For people in families with a known MMR mutation who test negative for the family mutation, screening practices are the same as recommendations for individuals at average risk.

Research on the return of genetic test results to research participants has described approaches to disclosure and the costs involved,[3,4] as well as the subsequent ethical, legal, and social implications.[5] Although research participants are typically interested in receiving genetic results,[6–8] key issues identified in the literature include: (i) clinical utility of the information, (ii) mode of information delivery, (iii) development of educational materials, (iv) decisions about retesting samples within a CLIA-certified laboratory, and (v) facilitation of communication to family and providers. Facilitating communication among families and their health-care providers is especially important when the genetic results are not disclosed by a health-care provider, and the research team is not involved in postdisclosure clinical or communication decisions.[3,9] Although prior research has explored different modes of delivery for the disclosure of genetic test results and subsequent psychosocial support for clinical populations,[10,11] to our knowledge, no studies have yet examined the impact of an educational intervention to promote research participant communication following the return of MMR genetic test results. Likewise, few studies have explored telephone-based disclosure procedures for clinically relevant genetic test results obtained during research rather than clinical testing. Evaluating intervention approaches to disclosing test

[1]Department of Oncology, Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; [2]Department of Medical Genetics, Mayo Clinic College of Medicine, Rochester, Minnesota, USA; [3]Department of Psychiatry, University of Toronto University Health Network, Toronto, Ontario, Canada; [4]Department of Behavioral Science, Division of Cancer Prevention and Population Sciences, M. D. Anderson Cancer Center, University of Texas, Houston, Texas, USA; [5]Department of Epidemiology, Colorado School of Health University of Colorado, Aurora, Colorado, USA; [6]NCI (SAIC), Rockville, Maryland and New York Physicians Against Cancer (NYPAC), New York, New York, USA; [7]Melbourne School of Population and Global Health, University of Melbourne, Victoria, Australia; [8]Department of Health Science Research, Mayo Clinic Arizona, Scottsdale, Arizona, USA; [9]Department of Psychiatry and Psychology, Mayo Clinic College of Medicine, Rochester, Minnesota, USA; [10]Departments of Oncology and Gastroenterology, Mayo Clinic College of Medicine, Rochester, Minnesota, USA. Correspondence: Kristi D. Graves (kdg9@georgetown.edu)

Submitted 31 May 2013; accepted 29 July 2013; advance online publication 3 October 2013. doi:10.1038/gim.2013.137

results is particularly timely with the increasing identification of genetic and genomic risk markers, including clinically relevant results obtained through next-generation sequencing methods within the context of research studies.

We aimed to evaluate a telephone counseling protocol for returning MMR genetic test research results to participants at the Mayo Clinic site of the Colon Cancer Family Registry (CFR).[12,13] Guided by principles from a shared decision-making framework,[14] we examined psychological, communication, and behavioral outcomes following an offer to learn MMR results. We were particularly interested in participants' communication with their family members and health-care providers.[15,16] We qualitatively explored the experiences of the professionals involved in the delivery of research results to Colon CFR participants.

MATERIALS AND METHODS

Using a prospective single-group pre–post study design, we evaluated psychosocial, communication, and behavioral variables before and 6 months following telephone disclosure of MMR results to Colon CFR participants (**Figure 1**).

Study population

The study was conducted with Mayo Clinic Colon CFR participants. Briefly, Mayo is one of the six international Colon CFR centers that facilitate population- and clinic-based interdisciplinary research on the genetic and molecular epidemiology of CRC and its behavioral implications.[1,13] The Colon CFR has information and biospecimens on 41,000 individuals (14,500 families). To date, the Mayo site has enrolled 4,800 individuals among 1,250 families.[12,17] Upon enrollment in the Colon CFR study, all participants signed an informed consent document that stated they would be given the option to learn of clinically meaningful results if such results were found. Individuals eligible for the present study included 373 men and women who were from families with an identified mutation in an MMR gene (*hMSH2*, *hMLH1*, *hMSH6*, and *hPMS2*).

Procedures

Procedures were approved by the Mayo Clinic institutional review board. Study invitation letters were sent from the Mayo Colon CFR principal investigator (N.M.L.). Participants were informed that their blood had been tested for an MMR gene

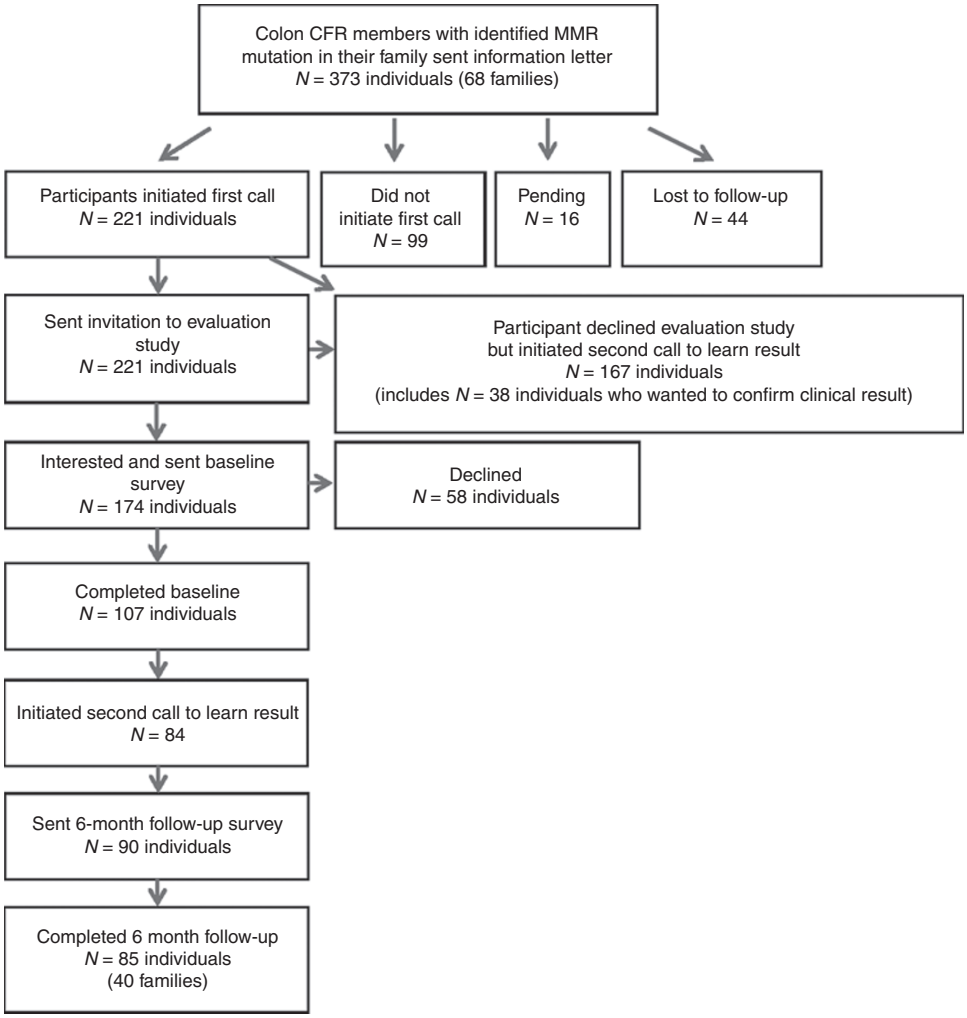

Figure 1 Study flow. CFR, Cancer Family Registry; MMR, mismatch repair. MMR, mismatch repair.

mutation and that potentially clinically meaningful results were available. The letter did not indicate whether results were positive or negative. This letter briefly explained Lynch syndrome, MMR gene testing, the pros and cons of learning genetic test results, and the required two-step process for learning results (described below). The letter also explained the current study, although study involvement was not required to receive genetic test results. Letters were mailed simultaneously to all probands (first person in the family to be tested) and relatives who also had been tested for a family mutation. We resent letters two times if we did not receive a response.

Colon CFR participants interested in proceeding with result disclosure were scheduled for a telephone education session with a certified genetic counselor or medical geneticist. Individuals who expressed interest in the current study were mailed the baseline survey, informed consent documents, and a postage-paid return envelope. Individuals who did not return the baseline survey within 4 weeks received up to two reminder telephone calls. Study participants completed and returned the baseline survey and consent documents prior to learning their genetic test results.

Telephone disclosure process

The first telephone call with the certified genetic counselor or medical geneticist was a predisclosure education session to review the information participants could learn, including positive or negative MMR mutation carrier status, the impact of the test result on cancer risk/risk management, and the implications for family members. Variants of uncertain significance were not communicated as the informed consent document indicated that only results of medical significance would be reported back. Clinical management is not impacted by the discovery of variants of uncertain significance.[18]

Participants were counseled that if they received a negative test result, it could not be fully interpreted unless there was a known mutation carrier in the family. They were also informed that the study team could not indicate whether there was a known positive result in their family. Rather, confirmation of a known mutation in the family would need to come from family members. Participants were also advised in advance that any result disclosed would need to be confirmed in a clinical laboratory. If participants elected to learn their research results, they were scheduled for a second disclosure telephone call with the same genetic counselor/medical geneticist. To encourage and allow time for intrafamilial communication of information, the research team attempted to schedule the disclosure telephone calls with individuals with positive mutations before the calls to relatives without mutations.

On the second call, the genetics professional disclosed the MMR genetic test result (specifying the exact mutation) and discussed implications for the participant and family members, along with specific recommendations regarding medical risk management. Participants were mailed a letter detailing their MMR genetic test result and risk management recommendations. They also received a separate letter they could share with a health-care provider that reviewed published screening guidelines, how to find a genetic counselor or how to order a confirmatory test in a clinical laboratory. Six months after disclosure, participants were mailed the follow-up survey. We also administered a semistructured questionnaire to the two genetics professionals involved with the result disclosure process to aid in the interpretation of the survey findings.

Measures

Participant demographics and clinical variables. We used Colon CFR data on participants' age, sex, education, marital status, race and ethnicity, personal/family history of cancer, and the MMR gene test results.

Psychological measures

Perceived CRC risk was assessed at baseline and follow-up using two validated items.[19] First, we asked "How likely do you think it is that you will get CRC?" with responses made on a 4-point Likert scale. We then asked participants to compare their lifetime risk of CRC to others of the same age, sex, and race with responses on a 5-point Likert scale.[19] For individuals with a prior CRC diagnosis, items reflected perceived risk of being diagnosed with CRC again.

CRC worry was assessed at baseline and follow-up using two items from prior research related to the frequency of thoughts about getting CRC and the impact of those thoughts on mood.[20] Participants responded on a 4-point Likert scale.

Hereditary CRC knowledge was assessed at baseline and follow-up via a 12-item measure[21] consistent with a similarly validated scale in the literature.[22] A sample item was, "People who carry the gene for hereditary CRC will definitely develop cancer at some time in their lives." Response options were true, false, or not sure.

Decision making about learning research results was assessed at baseline with 10 items to capture participants' preparation for decision making around receipt of MMR results.[23] Constructs included: decisional needs, decision quality, and decision support. Responses were scored on a 5-point Likert scale.

Motivation for receiving results was assessed at baseline via a 9-point checklist of face-valid items about motivation for receiving a result using a 5-point Likert scale ranging from "not at all important" to "very important." Sample motivation items included: having risk management information for children, family members, or insurance purposes.

Self-efficacy for communicating and coping with test results was assessed at baseline with three items about confidence in communicating with both immediate and extended family members and confidence in clearly explaining the meaning of the test result. Likewise, we used one item to assess participants' confidence in their ability to meet with their regular health-care provider to discuss the result. Responses were made on a 4-point Likert scale ranging. We also used a visual analog scale (from 0 to 100%) to assess participants' confidence in their ability to cope if they were to learn that they carried a gene that put them at risk for CRC.

Well-being was assessed at baseline and follow-up by asking participants to indicate their overall well-being on a scale from 1 ("not very well at all") to 10 ("extremely well").[24]

Satisfaction with disclosure process was assessed at the 6-month follow-up as satisfaction with the (i) care received from their regular health-care provider (two items) and (ii) telephone counseling process (eight items). At follow-up, we also measured decisional regret related to the participant's choice of whether or not to learn about their genetic test result (five items).[25] For all satisfaction items, we used a 5-point Likert scale.

Communication measures

Result communication. At baseline, we assessed participants' intentions to tell their family or physician their MMR test results. At 6 months, we assessed whether participants had communicated results to a list of immediate and extended family and close friends. We also assessed topics discussed, including whether participants talked about how the results affect their own risk, risk to other family members and children, or the impact on insurance. For communication with health-care providers, we assessed whether participants discussed how their test results would change cancer-screening recommendations.

Family communication about cancer was assessed at baseline with six items from a validated instrument to capture participants' perceptions of how their family communicates about cancer.[26]

Behavioral measures

Health behaviors. At the 6-month follow-up, we assessed whether participants had engaged in the following health behaviors: making an appointment to discuss screening with a health-care provider, making an appointment for cancer screening, having CRC or other cancer screening since learning the genetic test result, and an open-ended question about other life changes due to learning the test result.

Analyses

We characterized the sociodemographic characteristics of the sample by calculating means, SDs, and frequencies of study variables. We used Pearson and Spearman correlations, *t*-tests, and χ^2-tests to examine relationships between the variables in bivariate analyses. Variables associated with the psychosocial (communication, well-being, and satisfaction) and health behavior (cancer screening) outcomes at the bivariate level of $\alpha < 0.05$ were included in multivariate analyses. The independent impact of genetic test results, demographic and clinical characteristics, and the selected psychosocial and health behavior predictor variables were evaluated using generalized estimating equations to control for intrafamilial correlations.

Finally, we explored the experiences of the genetics professionals who disclosed results to the participants by analyzing written responses to the open-ended, structured questions.[27] Items assessed impressions of the disclosure process, protocol logistics (e.g., scheduling disclosure sessions with family members), and participants' responses to being encouraged to communicate results to family members and health-care providers.

RESULTS

Sample characteristics

Of 373 invitation letters sent to eligible Mayo Clinic Colon CFR participants, we received responses from 329 individuals (from 68 families; 88%); 44 either did not receive the mailing or failed to respond after repeated mailing attempts. Of the 329, 59 (18%) declined participation because they already knew their results from clinical testing, and 40 (15%) of the remaining 270 individuals declined because they were not interested in receiving results. A total of 221 individuals (67.2% of total invitees; 82% of the respondents) indicated that they wanted to learn their MMR gene test result, of whom 38 (17%) wanted to confirm test results that they had already obtained through clinical testing (**Figure 1**). Of the 174 participants who expressed interest in participating in the present study, 107 completed the baseline survey, and 85 completed the 6-month follow-up survey. Participants had a mean age of 61.2 years (SD: 14.9 years; range: 28–98 years), and nearly one-third (30%) had a previous diagnosis of CRC. Of the 107 participants who completed the baseline survey, 84 (79%) opted to learn their genetic test result. Participants who declined to learn their genetic test results were younger (M = 52 years; SD: 14.6 years) than participants who chose to receive their test results (M = 63.3 years; SD: 14.3 years; t = −3.11; P = 0.003). Decision to receive gene test results did not differ by sex or by perceived risk of CRC. A total of 44 individuals were positive for an MMR gene mutation (41% of study participants; **Table 1**).

Predisclosure: motivation, preparation, and confidence

Figure 2 shows the most common reasons for electing to learn test results, including the desire to learn if their children were at risk (79%) and to benefit research (72%). Participants reported that they felt moderately well prepared to make an informed decision about whether to learn their test result (M = 28.6; SD: 7.6; range: 8 (not at all prepared) to 50 (prepared a great deal)). Before disclosure, many participants felt confident in their ability to cope with their test results (M = 91 of 100, where 100 indicates the highest possible confidence in coping with test results) and in their ability to communicate results to family and health-care providers. Participants reported moderate-to-high perceived risk of CRC (M = 6.7; SD: 2.1; range: 0–10).

Postdisclosure: satisfaction with the disclosure process

Overall, satisfaction with the two-step telephone disclosure process was high. Specifically, participants reported feeling satisfied with the process of telephone counseling to receive their results (M = 29.5; SD: 4.4; range 8 (not at all satisfied) to 40 (extremely satisfied)) and with their discussion with a genetics professional before disclosure (M = 31.4; SD: 4.0; range:

Table 1 Participant characteristics (n = 107)

Mean (SD)	*n* (%)
Age in years (range: 27–97) 61.8 (14.3)	
<50 years	26 (24.3%)
≥50 years	81 (75.7%)
Sex[a]	
Men	48 (46.6%)
Women	55 (53.4%)
Education level[b]	
≤High school	24 (23.8%)
>High school	77 (76.2%)
Race[c]	
Caucasian	96 (96.8%)
Non-Caucasian	3 (3.2%)
MMR status	
MMR positive	44 (41.1%)
MMR negative	63 (58.9%)
CRC	
Affected	32 (29.9%)
Unaffected	75 (70.1%)
Children	
Had children	94 (87.9%)
Did not have children	13 (12.1%)

CRC, colorectal cancer; MMR, mismatch repair.

[a]Missing sex data on four participants. [b]Missing education data on six participants. [c]Missing race data on eight participants.

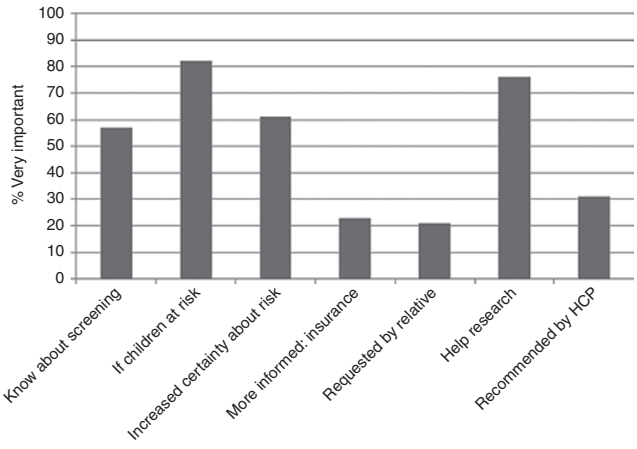

Figure 2 Common reasons for learning gene test result. HCP, health-care provider.

0–40). Overall satisfaction with the decision to learn their genetic test result was also high (M = 12.8; SD: 0.1; range: 5–16). Satisfaction outcomes did not differ by participants' gene test results or whether they had been personally affected by CRC.

Postdisclosure: psychosocial, communication, and behavioral outcomes

Psychosocial outcomes. Participants reported high levels of well-being at the 6-month follow-up (M = 8.4; SD: 1.4; range: 0–10). Well-being did not significantly differ by gene test result (t = −0.61; P value is not significant) or CRC-affected status (t = -0.75; P value is not significant). Perceived risk about CRC and concerns about CRC also did not differ based on the gene test result or affected status.

Communication. By 6 months postdisclosure, most participants had shared their MMR genetic test result with their spouse/partner (86%), children (74%), extended family members (80%), and close friends (64%). Predominant discussion topics included how the result affected their own cancer risk (67%), family members' cancer risk (80%), or their children's risk (76%). In bivariate analyses, baseline knowledge of hereditary CRC (r = 0.31; P = 0.005) and baseline confidence coping with the genetic test result (r = 0.26; P = 0.03) were positively related to communication of genetic test results to family members at 6 months. In a generalized estimating equations multiple linear regression model, baseline knowledge (Z = 1.91; P = 0.056) no longer remained statistically significant, whereas baseline confidence in coping with the result (Z = 1.97; P = 0.04) remained an independent predictor of result communication to family at 6 months (**Table 2**).

We also evaluated factors related to discussion of genetic test results with a health-care provider. In bivariate analyses, intentions to share results with family members (r = 0.27; P = 0.02), number of first-degree relatives affected with CRC (r = 0.22; P = 0.04), baseline-perceived risk of CRC (r = 0.21; P = 0.06), having a personal history of CRC (t = 2.39; P = 0.02), and receipt of a positive MMR genetic test result (t = 2.27; P = 0.03) were each associated with greater likelihood of discussion of test results with a health-care provider. In a generalized estimating equations multiple linear regression model, intentions to share results with family members (Z = 3.07; P = 0.002) and baseline-perceived risk of CRC (Z = 2.08; P = 0.03) remained independent predictors of communication of results to a health-care provider (**Table 2**).

Across both affected and unaffected participants, individuals who received a positive MMR result were significantly more likely to have discussed how their result would impact cancer screening (χ^2 = 5.13; P = 0.02) and to have made an appointment to discuss screening recommendations with their doctor (χ^2 = 4.74; P = 0.03) as compared with individuals who received negative MMR test results.

Among individuals unaffected with colon cancer, those who were MMR positive were significantly more likely to discuss their result with their health-care provider as compared with the unaffected individuals who were MMR negative (F = 4.3 (df = 3.75); P = 0.007).

Health behaviors. Before test result disclosure, 87% of the participants reported having undergone prior CRC screening. At 6 months, 97% of the participants reported ever receiving screening for CRC, and 44 individuals (54%) had received any type of cancer screening since learning their genetic test result. Screening behavior was not significantly impacted by test result: 64% of the individuals with a positive MMR result and 51% of

the individuals with a negative MMR result reported any type of cancer screening since learning their test result (*P* value is not significant).

Impressions of genetics professionals. The genetic counselor and the medical geneticist who provided the telephone education and counseling reported feeling satisfied with the two-step process. On average, the first call took 25 min. The second call averaged 35 min to disclose positive results and 15 min to when true-negative results could be disclosed. The genetics professionals noted that the protocol allowed participants to make informed decisions about whether to learn about their MMR gene test results (**Table 3**).

DISCUSSION

Knowledge of genetic testing results for Lynch syndrome has important implications for medical management among those who do and do not carry a deleterious mutation.[2] Despite compelling reasons to provide this information to research participants, limited resources and distance to genetics professionals support the importance of telephone-based approaches.[28] Tailored telephone approaches have been successful in increasing other health behaviors, including screening mammography and CRC screening; more recently, to return genetic test findings in clinical settings.[29,30] The often slow translation of research findings into clinical practice underscores the need to make relevant and clinically actionable research results available to interested research participants, and if appropriate, their families and health-care providers.

Our test of a telephone counseling protocol with research registry participants evaluated the psychosocial, communication, and behavioral outcomes following MMR gene test disclosure. The two-step telephone delivery process used to educate and then disclose MMR gene test results was well received by participants. The participants who declined to receive their results following the first phone call were younger than those who opted to learn their results. Perhaps younger individuals have yet to complete their families, have more competing time

Table 2 General estimating equation multiple regression analysis of 6-month communication outcomes (n = 85)[a]

Dependant variable	Predictor variables	Parameter estimate	*Z* value
Communication with family about result	Baseline CRC knowledge	0.12	1.91
	Baseline confidence in coping with genetic test result	0.01	1.97[a]
Communication with physician about result	Genetic test result	0.2	1.27
	Affected status	–0.38	–1.18
	Of FDR with CRC	0.1	0.86
	Baseline perceived CRC risk	0.1	2.08[a]
	Baseline intentions to share results with family	0.8	3.07[b]

Affected status: affected versus unaffected with CRC.

CRC, colorectal cancer; FDR, first-degree relative.

[a]Because of a small amount of missing data for outcome variables, not all models have the same sample size indicated above. [a]$P < 0.05$; [b]$P < 0.01$.

Table 3 Experiences of genetics professionals in research result disclosure by telephone

Topic area	Representative quote
Satisfaction with process	"I am satisfied that the disclosure process we have outlined walks the line pretty well in terms of allowing people to get or reject getting their research results, and gives enough information to allow them to make a decision they are comfortable with."
Telephone delivery	"I try to make a bit of small talk with the patients and get to know their families, situations, and specific needs. It takes a bit of extra time in the phone conversation but allows me to feel more comfortable in sharing such sensitive information with them." "I find the counseling much more challenging than a face to face interaction and have had to adjust my typical counseling in order ensure that the patient is understanding the information—I ask A LOT more questions during the phone interview than I would in person, so that I can assess their understanding."
Constraints of disclosure within the research context when multiple family members are participating	"… Family dynamics are complicated and not all families share this information openly. …If I am speaking to someone whose test result is negative and they do not know that a family member has been identified to have a genetic mutation, and I cannot disclose this information … I must counsel them somewhat ambiguously (challenging)." "I try to tell all the negative people up front that if there is a mutation in the family and their relative has chosen not to tell them about, then neither can I, and in that case a negative result to them will not be interpretable… but if relatives are communicating, then their result, positive or negative, will be interpretable."
Need for visual aids	"I wonder if it would be helpful to send them some additional materials on Lynch syndrome before our telephone conversation, so that they may reference pictures of autosomal-dominant inheritance, a chart of cancer-related risks, may be a worksheet asking them to outline their personal risks versus benefits of receiving their genetic testing results. I rely a lot on visual aids during our counseling session and am missing this during the phone interaction."

demands, or have greater concerns about insurance discrimination. Of note, among individuals who opted to learn their results, many participants communicated their MMR test result to family members and to a health-care professional. Receipt of a positive MMR test result did not appear to cause distress among participants, consistent with previous research among women who undergo *BRCA1/2* genetic counseling and testing.[31] Individuals unaffected with CRC who had MMR positive results were more likely to share their results with their physicians than unaffected individuals who were not MMR mutation carriers. Increased engagement with a health-care provider by those at greatest risk is an important and desired outcome of our protocol. Since a negative MMR result can indicate a return to average risk recommendations for CRC screening, exploring why those who tested negative for an MMR mutation were less likely to share results with their health-care providers requires further study. Perhaps the 6-month follow-up timeline was too short to capture communication between unaffected individuals with a negative MMR result and their health-care providers. Given that both the MMR-positive and MMR-negative groups reported cancer screening (including colonoscopy) after the disclosure of results, further investigation is needed to understand if the additional screening followed risk-relevant guidelines and the role of the participant, family, and health-care provider in decisions about screening. Individuals at moderate- to high-risk based on family history or among people with evidence of a hereditary cancer syndrome differ in their adherence to cancer screening guidelines over time.[32,33] These behaviors may also be influenced by the context of disclosure, whether in clinical practice or through participation in a research study.

Of note, MMR gene test results did not change the perceived risk of CRC. Perhaps individuals from families with a significant family history of cancer still perceived themselves at higher risk, even if they received negative MMR results. Future work can explore whether genetic test result disclosure in the context of a research study yields different perceptions of disease risk as compared with genetic test result disclosure in a clinical context.

Our findings have important implications for the process of disclosure of clinically meaningful genetic test results through research. Our findings also have implications for the future delivery of clinical information as genomic-based information is integrated into clinical care.[34] First, a thorough explanation using both written materials and telephone discussion of the risks and benefits of learning about one's genetic test result led to high levels of satisfaction. The written information and telephone education also led to reports of informed decisions by both participants and clinicians. Second, the challenges inherent to the disclosure and interpretation of negative test results with respect to confidentiality constraints required careful and nuanced explanations by the genetics professionals. Continual emphasis on the importance of family communication, along with the attempts to schedule the disclosures so that family members with positive results were informed before family members with negative results, helped ease these challenges.

As the field of genomics evolves with next-generation whole-exome or whole-genome sequencing, many ethical, legal, and social issues remain regarding the return of genetic test results to research participants. The protocol used in the present study attempted to address two of these challenges. First, questions remain regarding what genetic information to include in health records. Participants in the present study were provided with a "Dear Doctor" letter that detailed their MMR gene test results that they could opt to share with their physicians. Second, recent recommendations indicate that only validated genomic data[35] obtained from credentialed clinical laboratories should be included in health records.[36] Accordingly, individuals with positive MMR results in the present study were strongly advised to have their test results confirmed in a CLIA-certified laboratory.[37] We did not collect data on whether participants confirmed their research results; future research can address the extent to which participants confirm their research results through a CLIA-certified laboratory.

The study had some limitations. Although participants were heterogeneous in terms of age and education level, our sample lacked racial and ethnic diversity, therefore limiting the generalizability of our results. A sizeable subset of the Colon CFR participants invited to enroll in the present study had already received their MMR results in a clinical setting; these people may differ from those in the registry who had not yet sought out genetic counseling and testing for genetic mutations associated with Lynch syndrome. We were unable to compare participants and study decliners by their psychosocial functioning or perceived risk, and our measure of well-being was not specific to genetic testing–related distress. We also did not assess whether individuals with negative results confirmed they were true negatives by communicating with family members, nor how confirmation of having a true-negative result impacted health behaviors. Finally, we did not obtain medical records to confirm self-reported CRC screening procedures among participants, although studies indicate that self-reported cancer screening, including colonoscopies, are reasonably accurate.[38]

Building upon the present findings, future work can include a controlled experiment of disclosure processes, such as comparisons between telephone, the internet, or other modes. Next steps could also include the development and testing of print or interactive decision tools to facilitate telephone counseling before and after test disclosure using the extant literature as a guide.[28,30] Our finding that predisclosure confidence in coping with genetic test results was related to result disclosure to family members points to specific intervention targets. Findings from this study suggest that telephone counseling to return MMR test results is feasible within a research context, that many participants choose to disclose MMR results to family members, and that those at greatest risk report sharing results with a health-care professional. Disclosure of clinically meaningful gene test results is an important part of the process to reduce the cancer burden faced by families with Lynch syndrome.[16]

ACKNOWLEDGMENTS

This work was supported by the National Cancer Institute, National Institutes of Health, under RFA #CA-95-011 and through cooperative agreements with the members of the Colon Cancer Family Registry and principal investigators. This work was further supported by NCI CAK07131172-5 (K.D.G.) and NCI P30CA051008. Portions of this work were presented at the 32nd Annual Meeting and Scientific Sessions of the Society of Behavioral Medicine, Washington, DC, April 2011. We thank the Colon Cancer Family Registry participants for their involvement in the study.

The content of this article does not necessarily reflect the views or policies of the National Cancer Institute, the National Institutes of Health, or any of the collaborating centers in the CFRs, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government or the CFR.

DISCLOSURE

The authors declare no conflict of interest.

REFERENCES

1. Win AK, Young JP, Lindor NM, et al. Colorectal and other cancer risks for carriers and noncarriers from families with a DNA mismatch repair gene mutation: a prospective cohort study. *J Clin Oncol* 2012;30:958–964.
2. Järvinen HJ, Aarnio M, Mustonen H, et al. Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. *Gastroenterology* 2000;118:829–834.
3. Roberts JS, Shalowitz DI, Christensen KD, et al. Returning individual research results: development of a cancer genetics education and risk communication protocol. *J Empir Res Hum Res Ethics* 2010;5:17–30.
4. Roberts JS, Christensen KD, Green RC. Using Alzheimer's disease as a model for genetic risk disclosure: implications for personal genomics. *Clin Genet* 2011;80:407–414.
5. Heaney C, Tindall G, Lucas J, Haga SB. Researcher practices on returning genetic research results. *Genet Test Mol Biomarkers* 2010;14:821–827.
6. Fong M, Braun KL, Chang RM. Native Hawaiian preferences for informed consent and disclosure of results from research using stored biological specimens. *Pac Health Dialog* 2004;11:154–159.
7. Moutel G, Duchange N, Raffi F, et al.; APROCO-COPILOTE Study Group. Communication of pharmacogenetic research results to HIV-infected treated patients: standpoints of professionals and patients. *Eur J Hum Genet* 2005;13:1055–1062.
8. Murphy J, Scott J, Kaufman D, Geller G, LeRoy L, Hudson K. Public expectations for return of results from large-cohort genetic research. *Am J Bioeth* 2008;8:36–43.
9. Peterson SK. The role of the family in genetic testing: theoretical perspectives, current knowledge, and future directions. *Health Educ Behav* 2005;32:627–639.
10. Bradbury AR, Patrick-Miller L, Fetzer D, et al. Genetic counselor opinions of, and experiences with telephone communication of *BRCA1/2* test results. *Clin Genet* 2011;79:125–131.
11. Graves KD, Wenzel L, Schwartz MD, et al. Randomized controlled trial of a psychosocial telephone counseling intervention in *BRCA1* and *BRCA2* mutation carriers. *Cancer Epidemiol Biomarkers Prev* 2010;19:648–654.
12. National Cancer Institute. About Colon CFR. http://epi.grants.cancer.gov/CFR/about_colon.html Accessed 23 July, 2013.
13. Newcomb PA, Baron J, Cotterchio M, et al.; Colon Cancer Family Registry. Colon Cancer Family Registry: an international resource for studies of the genetic epidemiology of colon cancer. *Cancer Epidemiol Biomarkers Prev* 2007;16:2331–2343.
14. O'Connor AM, Tugwell P, Wells GA, et al. A decision aid for women considering hormone therapy after menopause: decision support framework and evaluation. *Patient Educ Couns* 1998;33:267–279.
15. Bartuma K, Nilbert M, Carlsson C. Family perspectives in lynch syndrome becoming a family at risk, patterns of communication and influence on relations. *Hered Cancer Clin Pract* 2012;10:6.
16. Ishii N, Arai M, Koyama Y, et al. Factors affecting encouragement of relatives among families with Lynch syndrome to seek medical assessment. *Fam Cancer* 2011;10:649–654.
17. Mayo Clinic. Colon Cancer Family Registry. http://mayoresearch.mayo.edu/mayo/research/c-cfr/ Accessed 23 July, 2013.
18. Plon SE, Eccles DM, Easton D, et al.; IARC Unclassified Genetic Variants Working Group. Sequence variant classification and reporting: recommendations for improving the interpretation of cancer susceptibility genetic test results. *Hum Mutat* 2008;29:1282–1291.
19. Lipkus IM, Lyna PR, Rimer BK. Colorectal cancer risk perceptions and screening intentions in a minority population. *J Natl Med Assoc* 2000;92:492–500.
20. Armstrong K, Weiner J, Weber B, Asch DA. Early adoption of BRCA1/2 testing: who and why. *Genet Med* 2003;5:92–98.
21. Esplen MJ, Aronson M, Rothenmund H, et al. Hereditary colon cancer knowledge level among high risk colorectal cancer patients undergoing genetic testing. Abstract presented at the 2nd Biennial Scientific Meeting of the International Society of Gastrointestinal Hereditary Tumours (InSIGHT), Yokohama, Japan, 2007.
22. Domanska K, Carlsson C, Bendahl PO, Nilbert M. Knowledge about hereditary nonpolyposis colorectal cancer; mutation carriers and physicians at equal levels. *BMC Med Genet* 2009;10:30.
23. O'Connor AM. Validation of a decisional conflict scale. *Med Decis Making* 1995;15:25–30.
24. Locke DE, Decker PA, Sloan JA, et al. Validation of single-item linear analog scale assessment of quality of life in neuro-oncology patients. *J Pain Symptom Manage* 2007;34:628–638.
25. O'Connor AM. *User Manual - Decision Regret Scale*. Ottawa Hospital Research Institute: Ottawa, 1996 [modifield 2003]. http://decisionaid.ohri.ca/docs/develop/User_Manuals/UM_Regret_Scale.pdf. Accessed 2 April 2013.
26. Sinicrope PS, Vernon SW, Diamond PM, et al. Development and preliminary validation of the cancer family impact scale for colorectal cancer. *Genet Test* 2008;12:161–169.
27. Krippendorff K. *Content Analysis: An Introduction to Its Methodology*. 2nd edn. Sage Publications: Thousand Oaks, CA, 2004.
28. Peshkin BN, Demarco TA, Graves KD, et al. Telephone genetic counseling for high-risk women undergoing BRCA1 and BRCA2 testing: rationale and development of a randomized controlled trial. *Genet Test* 2008;12:37–52.
29. Costanza ME, Stoddard AM, Luckmann R, White MJ, Spitz Avrunin J, Clemow L. Promoting mammography: results of a randomized trial of telephone counseling and a medical practice intervention. *Am J Prev Med* 2000;19:39–46.
30. Graves KD, Leventhal KG, Nusbaum R, et al. Behavioral and psychosocial responses to genomic testing for colorectal cancer risk. *Genomics* 2013;102:123–130.
31. Graves KD, Vegella P, Poggi EA, et al. Long-term psychosocial outcomes of BRCA1/BRCA2 testing: differences across affected status and risk-reducing surgery choice. *Cancer Epidemiol Biomarkers Prev* 2012;21:445–455.
32. Hadley DW, Jenkins JF, Dimond E, de Carvalho M, Kirsch I, Palmer CG. Colon cancer screening practices after genetic counseling and testing for hereditary nonpolyposis colorectal cancer. *J Clin Oncol* 2004;22:39–44.
33. Rubinstein WS, Acheson LS, O'Neill SM, et al.; Family Healthware Impact Trial (FHITr) Group. Clinical utility of family history for cancer screening and referral in primary care: a report from the Family Healthware Impact Trial. *Genet Med* 2011;13:956–965.
34. Feero WG. Genomics in medicine: maturation, but not maturity. *JAMA* 2013;309:1522–1524.
35. Incidental benefits. [Editorial]. *Nature* 2012;483:373.
36. Tran B, Dancey JE, Kamel-Reid S, et al. Cancer genomics: technology, discovery, and translation. *J Clin Oncol* 2012;30:647–660.
37. Goldenberg AJ, Sharp RR. The ethical hazards and programmatic challenges of genomic newborn screening. *JAMA* 2012;307:461–462.
38. Eberth JM, Vernon SW, White A, Abotchie PN, Coan SP. Accuracy of self-reported reason for colorectal cancer testing. *Cancer Epidemiol Biomarkers Prev* 2010;19:196–200.