Published in final edited form as:
Cancer. 2009 September 15; 115(18): 4071–4079. doi:10.1002/cncr.24478.

Colon cancer screening practices and disclosure following receipt of positive or inconclusive genetic test results for Hereditary Non-Polyposis Colorectal Cancer

Anne D. Letocha Ersig, PhD[1,2,3], **Donald W. Hadley, MS**[1], and **Laura M. Koehly, PhD**[1]

[1] Social & Behavioral Research Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland [2] College of Nursing, University of Iowa, Iowa City, Iowa [3] National Institute of Nursing Research, National Institutes of Health, Bethesda, Maryland

Abstract

Background—People who receive conclusive genetic test results for hereditary non-polyposis colorectal cancer (HNPCC) tend to adopt appropriate colorectal cancer screening behaviors and disclose their test results. However, little is known about the disclosure processes or screening behaviors of individuals who receive inconclusive genetic test results. This study compared endoscopy use and disclosure between individuals with positive and inconclusive genetic test results, within a year after results were received.

Methods—Individuals with a personal history of cancer and suspected of having HNPCC participated in genetic education and counseling, underwent HNPCC testing, and received genetic test results (GCT) within a prospective cohort study. Demographic, psychosocial and behavioral data were obtained from questionnaires and interviews completed before and after GCT.

Results—Index cases with inconclusive genetic test results were less likely to screen within 12 months. Index cases who disclosed test results to children within 6 months were more likely to screen within 12 months, controlling for mutation status. Index cases with inconclusive genetic test results were less likely to share results with a health care provider within 6 months. Index cases who disclosed genetic test results to health care providers within 6 months were more likely to have endoscopy within 12 months.

Conclusions—Genetic test results and disclosure significantly affected colon cancer screening at 12-month follow-up. Interventions to improve adherence to colorectal cancer screening should consider increased education of those receiving inconclusive results and encourage disclosure to health care providers and family members

Keywords

hereditary non-polyposis colorectal cancer; health behavior; cancer screening

Corresponding Author'fs Contact Information: Donald W. Hadley, SBRB/NHGRI/NIH, Building 31, Room B1B37F, 31 Center Drive, MSC 2073, Bethesda, MD 20892-2073, 301-496-3980, dhadley@mail.nih.gov, FAX: 301-480-3108.

Disclaimer: The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Departments of the Navy, Defense, Health and Human Services, or the U.S. Government.

Introduction

Colorectal cancer (CRC) is the third most common cancer in the U.S., with almost 150,000 new cases diagnosed each year[1]. Some families are at risk for inherited forms of CRC, affecting multiple family members in several generations. Hereditary non-polyposis colorectal cancer (HNPCC) is an inherited cancer susceptibility syndrome that significantly increases risks for colorectal, endometrial, ovarian, stomach, and small intestine cancers, among others[2]. HNPCC has been associated with deleterious mutations in any one of four mismatch repair genes (*MSH2, MLH1, MSH6, PMS2)*[3]. Families at risk for HNPCC are identified through clinical, pathological, and family history criteria[4, 5]. Cancers associated with HNPCC typically develop at younger ages and progress more rapidly than cancers in the general population; on average, HNPCC-associated CRC is diagnosed about a decade earlier than CRC in the general population[6].

In a large prospective study, colonoscopy every 3 years in individuals at risk for HNPCC reduced the risk of developing CRC by 62% and prevented disease-related deaths. Colorectal cancers diagnosed in the study group were detected at earlier stages[7]. Persons known to carry a deleterious mutation in an associated mismatch repair gene, or strongly suspected of having HNPCC, should undergo CRC screening through colonoscopy at an earlier age (20-25 vs. 50) and more frequently (every 1-2 years vs. every 5-10 years) than the general population[6, 8].

Genetic testing is one way for at-risk individuals and families to clarify their risk for HNPCC-associated cancers. In families meeting criteria, genetic testing is first offered to a family member diagnosed with an HNPCC-associated cancer (index case). Identification of an HNPCC-associated mutation in the index case allows at-risk family members to consider focused testing for the mutation. This enables clarification of disease risk and targeted cancer screening; mutation carriers continue intensive screening, while noncarriers revert to the general population screening schedule.

Although recent advances in genetic testing have improved rates of mutation detection[9], historically, up to 50% of index cases receive inconclusive genetic test results[2], further categorized as a variant of uncertain significance (VUS) or indeterminate. A VUS is a change in DNA sequence, compared to the reference sequence, whose functional meaning is not known or is not associated with disease in other HNPCC families[10]. Indeterminate genetic test results indicate a failure to detect changes in the DNA sequence of the genes under study[11], and include the possibility of true-negative and false-negative studies. A true-negative study reflects the true absence of an associated germ-line mutation. A false-negative study could result from 1) limitations of mutation detection technology, or 2) a limited number of genes under study[2].

Index cases receiving inconclusive genetic test results but still suspected of having HNPCC remain at high risk for HNPCC-associated cancers. They and their family members should continue recommended intensive screening. However, unlike biological relatives of mutation-positive index cases, family members of inconclusive index cases would not benefit from genetic testing for HNPCC.

In previous studies, HNPCC mutation carriers tend to follow screening recommendations, although adherence varies[12-14]. Colonoscopy use appropriately declines among non-carriers, although some continue with hyper-vigilant screening[12-14]. Little is known about CRC screening behaviors in families suspected of having HNPCC but without identified HNPCC mutations. Inconclusive genetic test results may be more difficult to interpret than mutation-positive test results, and their implications for cancer risk may be unclear[15, 16]. Inconclusive HNPCC genetic test results affect disclosure of test results[15] and emotional response to cancer risk[17], but their effect on health behaviors is unknown.

Relational factors, such as communication, encouragement, and support, could affect cancer screening. Discussions about CRC screening, encouragement to screen, and family support are positively associated with CRC screening among at-risk relatives of colon cancer patients[18-20]. Similarly, individuals who discuss their risks for HNPCC-associated cancers may be more likely to screen appropriately. Interactions with social network members can influence health behaviors, but additional study is needed[21, 22]. Family communication about HNPCC and cancer screening may be of particular importance in families without identified mutations. Since family members would not benefit from genetic testing, they are less likely to pursue genetic counseling. Communication may play an important role in informing family members of their risk for HNPCC-associated cancers, and the need for intensive cancer screening[23].

The purpose of this study was to examine colon cancer screening by endoscopy and disclosure of genetic test results among index cases at risk for HNPCC in the year after genetic test results were received. Of particular interest were the effects of mutation status (mutation-positive vs. inconclusive) and disclosure of the genetic test result to others on endoscopy completion.

Patients and Methods

Study Population and Procedures

The study population included adults, 18 years of age or older, with a personal history of at least one HNPCC-associated cancer, who met study criteria (Table 1). The protocol was approved by the Institutional Review Boards of the participating institutions (National Human Genome Research Institute [Protocol #95-HG-0165]; National Naval Medical Center [Protocol # NNMC.1995.0045]). All participants gave written informed consent. Index cases were referred to the research team through colon cancer clinics at the National Institutes of Health and National Naval Medical Center between November 1995 and December 2004. Following an initial consent process, a family cancer history was obtained and medical records were requested to confirm diagnoses. Tumor blocks were obtained for Microsatellite Instability (MSI) testing, to determine whether molecular testing for HNPCC was appropriate. Patients meeting study criteria were offered participation, including genetics education and counseling, and the option of genetic testing. Participants completed a baseline assessment and a scripted genetics education session including comprehensive information about HNPCC, recommendations for cancer screening, and a discussion about the potential risks and benefits of genetic testing. A client-centered counseling session occurred to facilitate decisions about genetic testing. To ensure consistency, members of one research team enacted all study procedures. Those who pursued genetic testing had a blood sample drawn, with sequencing of the MMR genes *MLH1* and *MSH2* completed by a Clinical Laboratories Improvement Act (CLIA)-approved laboratory. Index cases received test results in-person, 2 to 6 months after collection, accompanied by a support person of their choice. Index cases received verbal and written recommendations for cancer screening, based upon published guidelines[24]. Following completion of study procedures, participants returned to the care of their primary health care providers. Research team members encouraged discussion of cancer screening recommendations with primary health care providers. Participants received a supportive telephone call 1 to 2 weeks after provision of results. Follow-up telephone assessments occurred 6 and 12 months after genetic test results were received.

Measures

Outcome variable—The outcome variable of interest was endoscopic CRC screening in the year after genetic test results were received. Recommendations for persons at risk for HNPCC include complete examination of the colon[1] through endoscopy. Endoscopy screening was assessed by asking two questions: “Have you had a colonoscopy (flexible sigmoidoscopy) done

in the past 6/12 months?" on the 6- and 12-month surveys, respectively. Response options were yes or no. A variable for cumulative screening was created, which accounted for affirmative answers at either time point.

Predictor variables—Mutation status and communication of the genetic test result were selected as predictor variables, to determine whether they significantly affected CRC screening in the year after HNPCC genetic test results were received.

Mutation status was defined by the index case's genetic test results. Mutation positive referred to the identification of a deleterious mutation in either MMR gene. Inconclusive referred to either no detectable sequence alteration or the identification of a genetic variant of uncertain significance.

Communication of genetic test results was assessed at 6-month follow-up. Index cases were asked, "Have you shared your genetic test results with your (spouse/parents/children/siblings/friends/health care provider) since your last contact with us?" For each relation, response options were yes, no, and does not apply. Analyses controlled for living family members within each group.

Covariates—Covariates were selected due to their potential effect on CRC screening, as demonstrated in previous studies[25-27]. Sex, marital status, and number of first-degree relatives (FDRs) with cancer were assessed via self-report and included as covariates in all analyses. Cancer diagnoses in family members were confirmed through review of medical records when available and permitted. The final covariate was screening in the year before genetic test results were received. This identified participants who adhered to the recommended screening interval (every 1-2 years). Prior year screening was assessed at baseline by asking, "When was your last colonoscopy (flexible sigmoidoscopy) done?" Response options were within the past year, between 1 and 3 years ago, more than 3 years ago, and never. Responses were collapsed into endoscopy within the past year and no endoscopy within the past year.

Analyses

We hypothesized that CRC screening practices in the year after genetic test results were received would differ based on mutation status. We also examined whether communication of test results to others within 6 months differed based on mutation status, and whether communication affected endoscopy use at 12-month follow-up.

Descriptive statistics were constructed for all variables, and were compared between groups (mutation-positive vs. inconclusive) using a chi-squared test. Logistic regression models were fitted to examine whether mutation status was associated with screening 12 months after receipt of test results, controlling for covariates. Logistic regression models were also fitted to examine whether disclosure of results within 6 months was associated with screening one year after genetic testing, controlling for covariates. Disclosure analyses were first completed without consideration of mutation status, then repeated, controlling for mutation status. Analyses were conducted in SPSS version 14.0 for Windows (Chicago, IL: SPSS, Inc.). P-values < .05 were considered significant.

[1]Colonoscopy is recommended; however, in persons with less than 60 cm of colon remaining following resection, flexible sigmoidoscopy provides complete surveillance of the remaining colon. The term "endoscopy", as used here, represents complete examination of the colon through either procedure.

Results

Sample characteristics

Sixty-nine individuals participated (59.4% male; 91.3% Caucasian; 76.8% married). Their mean age was 47.75 ± 10.97 years (range, 25-74 years), and the mean number of FDRs with cancer was 1.97 ± 1.30. Just over half (55.1%, n=38) received mutation-positive genetic test results; the remaining 44.9% (n=31) received inconclusive genetic test results. Demographic data according to test result are presented in Table 2.

CRC Screening

Of the 69 index cases, 33.3% (n=23; 16 mutation-positive) completed CRC screening by endoscopy in the year before they received their genetic test results. In the year after receipt of genetic test results, 69.6% (n=48; 30 mutation-positive) of index cases had an endoscopy. Screening participation for the year before and the year after receipt of genetic test results was compared between groups. As expected, there was no significant difference between mutation-positive vs. inconclusive index cases for screening the year before test results were received ($p = 0.26$). However, in the year after receiving genetic test results, index cases who received inconclusive genetic test results were significantly less likely to have an endoscopy than mutation-positive index cases (OR=0.19; p=0.01; Table 3).

Communication Patterns

There were no significant differences between groups regarding disclosure of genetic test results to spouses, parents, siblings, children, or friends at 6 months (data not shown). In large part, index cases disclosed their genetic test results to their living parents (92.1%), living siblings (96.6%), and, if married, spouses (90.6%). The majority of index cases with children (78.6%) shared their test results with their offspring, while approximately 78.3% shared their test results with a friend. There was a significant difference in disclosure of genetic test results to health care providers. Index cases who received inconclusive genetic test results were significantly less likely to disclose their results to a health care provider within 6 months, compared to mutation-positive index cases (67.7% vs. 89.5%, respectively; p=0.01).

Due to the lack of variability in disclosure to parents, siblings, and spouses, analyses of the association between disclosure and screening focused on disclosure to friends, children, and health care providers. Disclosure to friends was not significantly associated with screening. In analyses that did not control for mutation status, disclosure of genetic test results to children was not significantly associated with endoscopy (OR=4.76, p=0.06), but disclosure of test results to health care providers was (OR=4.32, p=0.03). When controlling for test result, disclosure to children was significantly associated with endoscopy (OR=5.20; p=0.05), but disclosure to a health care provider was not (OR=2.76; p=0.15).

Discussion

We found that index case mutation status was significantly associated with CRC screening behavior and disclosure of genetic test results to health care providers. Index cases with inconclusive genetic test results were significantly less likely to have endoscopy in the year after genetic test results were received, compared to mutation-positive index cases. Index cases with inconclusive genetic test results were also significantly less likely to share their results with a health care provider within six months. Disclosure of genetic test results was significantly associated with CRC screening behaviors. The effect of disclosure to a health care provider on endoscopy was significant in analyses that did not control for mutation status: index cases who disclosed their genetic test results to a health care provider within six months were more likely to have endoscopy within a year. When controlling for mutation status, index

cases who disclosed genetic test results to their children within 6 months were significantly more likely to have endoscopy within a year, compared to index cases who did not share their test results with their children.

Although previous studies have demonstrated the emotional impact of inconclusive genetic test results[17], this study is among the first to demonstrate their behavioral impact. One possible explanation for lower rates of screening among inconclusive index cases might be misinterpretation of their results as truly negative, with an associated decrease in perceived risk for cancer and decline in cancer screening[28]. This false reassurance hypothesis has not been examined in families at risk for HNPCC. Misinterpretation of inconclusive genetic test results could result in a decline in screening similar to that seen among confirmed noncarriers[12-14]. Alternatively, avoidance of screening behaviors could be one possible response to the emotional impact of inconclusive genetic test results[17]. Among siblings of CRC patients, increased cancer-related distress led to a decrease in screening intentions[29]. The difference in endoscopy completion is particularly interesting since the analysis controlled for family history, and all participants had a personal history of at least one HNPCC-associated cancer. Additionally, the same study team provided genetic counseling and education, using the same protocol. This highlights the importance of the test result and its interpretation for screening behavior.

Genetic test results also have the potential to affect communication choices[15, 30]. In the current study, index cases with inconclusive genetic test results were significantly less likely to share their results with health care providers within 6 months, compared to mutation-positive index cases. Again, this could be due to misinterpretation of inconclusive genetic test results; index cases might assume that the lack of an identified mutation is not essential to share with their health care providers. Alternatively, index cases with inconclusive results are typically counseled that a causative mutation could still be found as technology improves and the number of genes under study increases[16]. They may be waiting for conclusive genetic test results to share with their health care providers. Index cases with inconclusive results may also be concerned that their health care providers will misinterpret their results and limit access to CRC screening.

Interactions with others can also affect cancer screening behaviors[19, 20]. In this study, index cases who shared their genetic test results with their children within 6 months, regardless of the specific genetic test result, were significantly more likely to have endoscopy within one year. Parents may share genetic test results with children for multiple reasons, including raising children's awareness of their own risks for disease[31]. This could positively affect children's cancer screening behaviors. By sharing genetic test results and information about disease risk, parents may feel accountable to their children for their actions. Parents may also strive to act as role models in demonstrating appropriate screening behavior. Part of the genetic legacy of women with cancer includes the hope that their diagnosis will impress on their children the need for cancer screening and early diagnosis[32]. This is viewed as a generally positive outcome of a negative health legacy, with affected parents hopeful that early and regular cancer screening by their at-risk children[32] will mitigate their risk. In families without identified HNPCC mutations, parental role modeling may be an effective way to educate younger family members about the need for screening. The number of cases analyzed in the present study did not allow examination of the effect of gender on modeling screening behavior, which should be pursued in future research.

Without controlling for test result, index cases who disclosed their genetic test results to their health care providers within 6 months were more likely to have endoscopy within a year. Health care providers may be important motivators of cancer screening. Women at risk for HNPCC who share their genetic test results with their physicians are significantly more likely to have

endometrial cancer screening than women who do not share their genetic test results with their physicians[33]. Encouragement to screen for colon cancer from a health care provider significantly impacts colon cancer screening among relatives of patients with colon cancer[19, 20]. In the general population, simply having a primary health care provider is associated with having a colonoscopy[34]. Providers who are aware of a patient's mutation status and risk for disease may be more likely to encourage screening. Under many health insurance plans, referrals from a primary health care provider are necessary in order to obtain specialized care, including screening exams. Health care provider referrals may be of particular importance in families at risk for HNPCC, since CRC screening should begin at a young age. Primary health care providers must recognize the importance of a family history of CRC, understand the need for early, frequent screening, and refer patients for colonoscopy. Providing the genetic test result to the health care provider may be one way at-risk individuals ensure that this awareness among their health care providers. It is essential that health care providers understand the implications of inconclusive genetic test results in the context of a significant family history of disease.

Limitations

Several characteristics of the current study have the potential to limit the generalizability of the findings. First, index cases all participated in the same research study. This can be a threat to the external validity of the findings[35]. Replication of these findings would provide additional evidence that they are not a function of the current study protocol or sample. This study also provided genetic education, counseling, and testing away from participants' usual sources of medical care (e.g., oncologists, primary care providers), and relied on participants to share genetic test results with their primary clinicians. The processes described here might differ if genetic testing were requested by an oncologist or primary care physician in a clinical setting; in that case, the test results would be returned to the patient's clinician. Whether the clinician obtains the genetic test results directly from the laboratory, or from the patient, what is important is that the clinician can appropriately interpret the information and is knowledgeable about current screening guidelines. Second, the study sample lacked ethnic diversity: most subjects self-identified as Caucasian. HNPCC affects persons of all races and ethnic groups, although the exact phenotype may vary slightly[36]. Future studies should attempt to increase the ethnic diversity of participants. Data not included in this analysis could also affect screening behaviors, such as elapsed time since cancer diagnosis.

Conclusions

These findings reveal some important differences between mutation-positive and inconclusive index cases. The genetic test result affected CRC screening behaviors and disclosure of the results to a health care provider. Disclosure of mutation status to children and health care providers was important for endoscopy completion. Additional research could expand on these findings. Exploring interpretation of inconclusive genetic test results would provide additional insight. Evaluating reasons for screening decisions could help determine why index cases with inconclusive genetic test results were less likely to screen. Assessing reasons for or against test results disclosure could provide additional insight, particularly since participants were encouraged to share their genetic test results with their health care providers. Knowing more about these reasons could help in the development of interventions designed to maximize disclosure to health care providers and other essential social network members.

These findings have implications for clinical care of individuals at risk for hereditary cancer syndromes. To ensure appropriate cancer screening among at-risk populations, health care providers should receive comprehensive education regarding risk factors for hereditary cancer syndromes, genetic testing, and recognizing family histories that warrant more intensive screening than the recommendations put forward for the general population, or for persons

with an affected first-degree relative. Developing interventions to facilitate disclosure of genetic test results to health care providers and children could also have a significant impact on cancer screening behaviors and, ultimately, the health of those at risk for HNPCC.

Acknowledgments

This research was supported by the Intramural Research Programs of the National Human Genome Research Institute and the National Cancer Institute at the National Institutes of Health, Bethesda, Maryland. The data were collected through a protocol monitored by the Institutional Review Boards at the National Human Genome Research Institute (Protocol #95-HG-0165) and the National Naval Medical Center (NNMC.1995.0045). Dr. Ersig was supported by a Graduate Partnerships Program fellowship from the National Institute of Nursing Research, National Institutes of Health.

References

1. American Cancer Society. Cancer facts & figures 2006. Atlanta: American Cancer Society; 2006.
2. Vasen, HFA.; Boland, CR. Progress in genetic testing, classification, and identification of Lynch syndrome; Journal of the American Medical Association. 2005. p. 2028-30.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15855438
3. Kohlmann, WK.; Gruber, SB. Hereditary Non-Polyposis Colorectal Cancer GeneReviews. Vol. 2008. National Institutes of Health; 2006.
4. Vasen, HFA.; Watson, P.; Mecklin, JP.; Lynch, HT. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC; Gastroenterology. 1999. p. 1453-6.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10348829
5. Umar, A.; Boland, CR.; Terdiman, JP.; Syngal, S.; de la Chapelle, A.; Ruschoff, J., et al. Revised Bethesda guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability; Journal of the National Cancer Institute. 2004. p. 261-8.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14970275
6. Lindor, NM.; Petersen, GM.; Hadley, DW.; Kinney, AY.; Miesfeldt, S.; Lu, KH., et al. Recommendations for the care of individuals with an inherited predisposition to Lynch syndrome: a systematic review; Journal of the American Medical Association. 2006. p. 1507-17.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17003399
7. Jarvinen, HJ.; Aarnio, M.; Mustonen, H.; Aktan-Collan, K.; Aaltonen, LA.; Peltomaki, P., et al. Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer; Gastroenterology. 2000. p. 829-34.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=10784581
8. Burke, W.; Petersen, G.; Lynch, P.; Botkin, J.; Daly, M.; Garber, J., et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer II BRCA1 and BRCA2 Cancer Genetics Studies Consortium; Journal of the American Medical Association. 1997. p. 997-1003.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9091675
9. EGAPP Working Group. Recommendations from the EGAPP Working Group: genetic testing strategies in newly diagnosed individuals with colorectal cancer aimed at reducing morbidity and mortality from Lynch syndrome in relatives. Genetics in Medicine 2009;11(1)
10. Stopfer JE. Genetic counseling and clinical cancer genetics services. Seminars in Surgical Oncology 2000;18:347–57. [PubMed: 10805957]
11. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian Practice Guidelines in Oncology. Vol. 2006. National Comprehensive Cancer Network; 2006.

12. Claes, E.; Denayer, L.; Evers-Kiebooms, G.; Boogaerts, A.; Philippe, K.; Tejpar, S., et al. Predictive testing for hereditary nonpolyposis colorectal cancer: subjective perception regarding colorectal and endometrial cancer, distress, and health-related behavior at one year post-test; Genetic Testing. 2005. p. 54-65.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15857188

13. Collins V, Meiser B, Gaff C, St John DJB, Halliday J. Screening and preventive behaviors one year after predictive genetic testing for hereditary nonpolyposis colorectal carcinoma. Cancer 2005;104:273–78. [PubMed: 15948171]

14. Hadley, DW.; Jenkins, JF.; Dimond, E.; de Carvalho, M.; Kirsch, I.; Palmer, CGC. Colon cancer screening practices after genetic counseling and testing for hereditary nonpolyposis colorectal cancer; Journal of Clinical Oncology. 2004. p. 39-44.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=14701766

15. Stoffel EM, Ford B, Mercado RC, Punglia D, Kohlmann W, Conrad P, et al. Sharing Genetic Test Results in Lynch Syndrome: Communication With Close and Distant Relatives. Clinical Gastroenterology and Hepatology 2008;6 ePub ahead of print.

16. Vadaparampil ST, Wey JP, Kinney AY. Psychosocial aspects of genetic counseling and testing. Seminars in Oncology Nursing 2004;20(3):186–95. [PubMed: 15491028]

17. Shiloh S, Koehly LM, Jenkins J, Martin J, Hadley DW. Monitoring coping style moderates emotional reactions to genetic testing for hereditary non-polyposis colorectal cancer: A longitudinal study. Psycho-Oncology. 2008

18. Rees G, Martin PR, Macrae FA. Screening participation in individuals with a family history of colorectal cancer: a review. European Journal of Cancer Care 2008;17:221–32. [PubMed: 18419625]

19. Madlensky L, Esplen MJ, Gallinger S, McLaughlin JR, Goel V. Relatives of colorectal cancer patients: Factors associated with screening behavior. American Journal of Preventive Medicine 2003;25(3): 187–94. [PubMed: 14507524]

20. Manne SL, Meropol NJ, Rakowski W, Markowitz A, Winawer S, Haller D, et al. Correlates of colorectal cancer screening compliance and stages of adoption among siblings of individuals with early onset colorectal cancer. Health Psychology 2002;21(1):3–15. [PubMed: 11846342]

21. Welch Cline, RJ. Everyday interpersonal communication and health. In: Thomspon, TL.; Dorsey, AM.; Miller, KI.; Parrott, R., editors. Handbook of Health Communication. Mahwah, NJ: Lawrence Erlbaum Associates; 2003.

22. Albrecht, TL.; Goldsmith, DJ. Social support, social networks, and health. In: Thomspon, TL.; Dorsey, AM.; Miller, KI.; Parrott, R., editors. Handbook of Health Communication. Mahwah, NJ: Lawrence Erlbaum Associates; 2003.

23. Lewis MA, McBride CM, Pollack KI, Puleo E, Butterfield RM, Emmons KM. Understanding health behavior change among couples: An interdependence and communal coping approach. Social Science & Medicine 2006;62:1369–80. [PubMed: 16146666]

24. Burke W, Petersen G, Lynch P, Botkin J, Daly M, Garber J, et al. Recommendations for follow-up care of individuals with an inherited predisposition to cancer. I. Hereditary nonpolyposis colon cancer. Cancer Genetics Studies Consortium. Journal of the American Medical Association 1997;277 (11):915–19. [PubMed: 9062331]

25. Wee CC, McCarthy EP, Phillips RS. Factors associated with colon cancer screening: the role of patient factors and physician counseling. Preventive Medicine 2005;41(1):23–29. [PubMed: 15916989]

26. Slattery ML, Kinney AY, Levin TR. Factors associated with colorectal cancer screening in a population-based study: the impact of gender, health care source, and time. Preventive Medicine 2004;38(3):276–83. [PubMed: 14766109]

27. van Jaarsveld CHM, Miles A, Edwards R, Wardle J. Marriage and cancer prevention: does marital status and inviting both spouses together influence colorectal cancer screening participation? Journal of Medical Screening 2006;13(4):172–76. [PubMed: 17217605]

28. Lerman C, Marshall J, Audrain J, Gomez-Caminero A. Genetic testing for colon cancer susceptibility: Anticipated reactions of patients and challenges to providers. International Journal of Cancer (Predictive Oncology) 1996;69:58–61. [PubMed: 8600064]

29. Manne SL, Markowitz A, Winawer S, Guillem J, Meropol NJ, Haller D, et al. Understanding intention to undergo colonoscopy among intermediate-risk siblings of colorectal cancer patients: a test of a mediational model. Preventive Medicine 2003;36(1):71–84. [PubMed: 12473427]

30. Koehly, LM.; Peterson, SK.; Watts, BG.; Kempf, KK.; Vernon, SW.; Gritz, ER. A social network analysis of communication about hereditary nonpolyposis colorectal cancer genetic testing and family functioning; Cancer Epidemiology, Biomarkers & Prevention. 2003. p. 304-13.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12692104

31. Metcalfe A, Coad J, Plumridge GM, Gill P, Farndon P. Family communication between children and their parents about inherited genetic conditions: a meta-synthesis of the research. European Journal of Human Genetics. 2008

32. Hunter EG. The legacy of cancer: The importance of passing on beliefs, values, and positive health behaviors for women with cancer. Journal of Psychosocial Oncology 2008;26(1):101–21. [PubMed: 18077265]

33. Hadley DW, Jenkins JF, Steinberg SM, Liewehr DJ, Moller S, Martin JC, et al. Perceptions of cancer risks and predictors of colon and endometrial cancer screening in women undergoing genetic testing for Lynch syndrome. Journal of Clinical Oncology 2008;26(6):948–54. [PubMed: 18281669]

34. Geiger TM, Miedema BW, Geana MV, Thaler K, Rangnekar NJ, Cameron GT. Improving rates for screening colonoscopy: Analysis of the health information national trends survey (HINTS I) data. Surgical Endoscopy 2008;22:527–33. [PubMed: 18074184]

35. Green LW, Glasgow RE. Evaluating the relevance, generalization, and applicability of research: Issues in external validation and translation methodology. Evaluation & the Health Professions 2006;29(1):126–53.

36. Abdel-Rahman, WM.; Ollikainen, M.; Kariola, R.; Jarvinen, HJ.; Mecklin, JP.; Nystrom-Lahti, M., et al. Comprehensive characterization of HNPCC-related colorectal cancers reveals striking molecular features in families with no germline mismatch repair gene mutations; Oncogene. 2005. p. 1542-51.Available from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=15674332

Table 1

Criteria for study entry

Personal history of colon (or HNPCC associated) cancer[•] and at least one of the following family or medical history criteria

Family history criteria

1 Family history meeting Amsterdam criteria (I or II)

- At least 3 relatives with histologically proven colorectal cancer (AC I) or HNPCC-associated cancer (AC II) with 1 being a first-degree relative of the other 2
- At least 2 successive generations affected
- Colorectal (or HNPCC-associated) cancer diagnosed under age 50 in at least 1 relative

2 Family history suggestive of HNPCC

- 1 second-degree (or closer) and 1 third-degree (or closer) relative with a HNPCC-associated cancer
- 1 affected family member must have one of the following:

  Right-sided colon cancer

  Multiple primary HNPCC-associated cancers

  Diagnosis of cancer prior to age 51

Medical history criteria

3. Multiple primary HNPCC-associated cancers

4. Diagnosis of colorectal (HNPCC associated) cancer at <40 years of age

[•] In all cases, tumor blocks were requested for microsatellite instability (MSI) studies. Tumors were classified as MSI-high, MSI-low, and MS-stable based on the number of positive markers in the assay. Persons whose tumors were MSI-low or MS-stable were excluded from our analyses.

Table 2

Index case Demographics

Mutation Status	Age	% female	% Caucasian	% married	No. FDRs[a] with cancer[b]	Type of cancer (%)	
Mutation-positive	47.05 ± 10.56	52.6	89.5	78.9	2.26 ± 1.2	Colorectal	60.5%
						Kidney (NOS)	2.6%
						Multiple cancers	36.8%
Inconclusive	48.61 ± 11.57	67.7	93.5	74.2	1.61 ± 1.35	Colorectal	71%
						Ovarian	6.5%
						Endometrial	3.2%
						Multiple cancers	19.4%

[a] FDRs = first-degree relatives

[b] Significant difference between groups, p=0.039

Table 3

Logistic regression results: mutation status and screening practices at 12-month follow-up

	OR	95% CI
Covariates		
Screening year prior to genetic testing	1.48	(0.42; 5.23)
Married	2.01	(0.51; 7.96)
Male	.512	(0.15; 1.77)
# FDRs with cancer	.475***	(0.27; 0.82)
Variable of Interest		
Test Result (Inconclusive)	0.203**	(0.06; 0.74)

* $p < .10$;

** $p < .05$;

*** $p < .01$