Health Behaviors in Patients and Families with Hereditary Colorectal Cancer

Allison M. Burton, Ph.D.¹ Shelly R. Hovick, Ph.D.¹ Susan K. Peterson, Ph.D., M.P.H.¹

¹Department of Behavioral Science, The University of Texas MD Anderson Cancer Center, Houston, Texas.

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Address for correspondence and reprint requests Allison M. Burton, Ph.D., The University of Texas MD Anderson Cancer Center, Department of Behavioral Science, Unit 1330, P.O. Box 301439, Houston, TX 77230-1439 (e-mail: aburton@mdanderson.org).

Abstract

It is estimated that 5 to 10% of all colorectal cancer (CRC) cases are attributed to a hereditary cause. The primary hereditary cancer syndromes that confer an increased risk for colorectal cancers are Lynch syndrome/hereditary nonpolyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP). Through genetic testing, health care providers can identify patients and families who carry gene mutations and subsequently are at a substantially greater risk for developing colorectal cancer than the general population. Genetic testing provides risk information not only about an individual patient, but also his or her biological relatives. A variety of risk-reduction behaviors (including screening, surgery, and health and lifestyle behaviors) have been examined in Lynch syndrome and FAP populations. The research indicates that screening behaviors are less than optimal, although the rates vary from study to study. Prophylactic colectomy is the primary course of treatment for individuals who test positive for a FAP mutation, but the results are inconclusive for cancer-unaffected Lynch syndrome mutation carriers. Although research suggests that the adoption of healthy lifestyles and behaviors (e.g., diet, physical activity, weight control, smoking cessation, limited alcohol consumption) could have a favorable impact on colon cancer burden, there is minimal data on how these behaviors may moderate cancer risk among those at risk of hereditary colon cancer. To date, we know very little about the actual health and lifestyle behaviors of those at risk of hereditary colon cancer. Genetic testing and counseling at risk individuals may resolve uncertainty about their personal and familial cancer risk and provide information to guide and personalize decisions about their future health care.

Keywords

- ▶ hereditary nonpolyposis colorectal cancer (HNPCC)
- ▶ Lynch syndrome
- ▶ familial adenomatous polyposis (FAP)
- ▶ genetic counseling and testing
- ▶ decision making

Objectives: On completion of this article, the reader should be able to summarize the current research findings on health behaviors in patients and families with hereditary colorectal cancer.

It is estimated that 5 to 10% of all colorectal cancer (CRC) cases are attributed to a hereditary cause.¹ The primary hereditary cancer syndromes that confer an increased risk for CRCs are Lynch syndrome/hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP). In addition, there are some rare syndromes that also confer increased risk for CRC, including Turcot, Muir-Torre,

Peutz-Jeghers, and juvenile polyposis syndromes. In this article, we focus on Lynch syndrome and FAP because they are the most prevalent and have received the greatest amount of attention in the literature.

Through genetic testing, health care providers can identify patients and families who carry gene mutations and subsequently are at a substantially greater risk for developing CRC than the general population. A primary benefit of genetic testing is the ability to offer targeted options for cancer risk reduction. Since genetic testing for hereditary cancers became clinically available, psychosocial and behavioral

research has investigated motivations and decisions regarding genetic testing as well as the impact of genetic testing results on patients and their families. Much research to date has focused on the psychological impact of genetic risk notification, effects on family and interpersonal relationships, and factors that influence the uptake of risk-reduction options (e.g., screening, risk-reducing surgery, or chemoprevention). However, there is a growing interest in lifestyle and health behaviors in hereditary cancer populations. We will discuss the relevant literature on these topics for hereditary CRC syndromes and the implications for clinical practice. Findings from these studies can guide clinicians in understanding the impact of genetic counseling and testing on hereditary CRC families, how families communicate genetic risk, and what risk reduction behaviors are being utilized in this population.

Hereditary Colorectal Cancer Syndromes and Their Risks

Lynch Syndrome

Lynch syndrome is an autosomal dominant condition characterized by a predisposition to several adult-onset cancers, most commonly CRC. Lynch syndrome is caused by mutations in DNA mismatch repair (MMR) genes (MLH1, MSH2, MSH6, and PMS2) that can be identified through clinical genetic testing.²⁻⁶ Genetic testing for Lynch syndrome optimally begins with preliminary screening of tumor tissue using microsatellite instability (MSI) testing and/or immunohistochemistry (IHC) to identify candidates for diagnostic testing.⁷ Among those with a MMR gene mutation, the lifetime risk for CRC is ~60% for men and 30% for women, and women have a 40 to 60% risk of endometrial cancer. Lynch syndrome confers modestly increased lifetime risks for other malignancies, including ovarian, stomach, small bowel, hepatobiliary tract, pancreatic, urinary tract, brain, and skin cancers.^{8,9} Consequently, individuals with Lynch syndrome are advised to follow high-risk management recommendations including annual colonoscopy (often initiated at 20 to 25 years of age) and screening for endometrial cancer and other cancers associated with the syndrome.⁸ Data support the efficacy of prophylactic hysterectomy and oophorectomy for gynecological cancer risk reduction.¹⁰

Familial Adenomatous Polyposis

FAP is an autosomal dominant condition characterized clinically by having multiple adenomatous polyps in the colon and rectum that typically begin to develop before puberty. In classic FAP, the colonic polyp burden is greater than 100. A less common form of FAP, known as attenuated FAP (AFAP), does not show this same polyp density. Both forms of FAP are caused by mutations of the APC gene on chromosome 5q21 and can be identified through clinical genetic testing.¹¹ For individuals with classic FAP, the risk for developing CRC is 75% by age 20 and 90% by age 45; for AFAP, the risk is ~70% by age 80.¹²⁻¹⁵ FAP confers an increased risk for other extracolonic manifestations, such as desmoids and other cancers.¹¹ As a result of these increased risks, particularly for individuals

with classic FAP that present at very young ages, surveillance includes annual sigmoidoscopy beginning around puberty, which guides the timing of a preventive colectomy.^{14,16}

Genetic Counseling and Testing for Hereditary Colorectal Cancers

Understanding individuals' motivations to undergo genetic testing, as well as reasons for declining testing, is critical to maximizing the usefulness of genetic testing in clinical practice. Much of our knowledge regarding the utilization of MMR mutation testing for Lynch syndrome is based on studies that offered genetic counseling and testing through research protocols that often included no-cost or low-cost testing. In these studies, testing rates ranged from 14% to 59%.¹⁷⁻²¹ Studies that offered free genetic counseling and testing as part of a research protocol reported the highest proportion of persons who underwent testing (i.e., 36 to 59%). Persons who underwent genetic testing were more likely to have had a personal history of cancer themselves and also to have had a greater number of cancer-affected relatives.²⁰ Other personal factors that have been associated with utilization of MMR mutation testing include having a greater perceived risk of developing CRC and having frequent thoughts or worries about CRC risk.^{18,20,21} Persons who underwent testing in these studies also were likely to be employed and to have higher educational levels compared with those who did not have testing, suggesting that use of genetic testing may vary based on socioeconomic status.²¹ Greater perceived social support has also been correlated with participation in genetic counseling to learn about Lynch syndrome-associated cancer risk,²² and the belief that testing will help family members may be a motivating factor in the desire to learn about one's mutation status.²³ Less attention has been given to uptake of tumor screening using MSI and/or IHC. One study that evaluated the impact of a CD-ROM intervention to educate patients at risk of LS about MSI and IHC testing found that patients who were randomized to receive a brief education session plus the CD-ROM reported greater knowledge about tumor screening, greater preparation to make a decision about testing, lower decisional conflict and greater decisional self-efficacy, compared with those who received a brief education session only.²⁴ In studies that offered genetic counseling and testing for Lynch syndrome to high-risk families, those who declined testing were more likely to report depressive symptoms, were less likely to have had prior CRC screening, and were more likely to report having a lower perceived ability to cope with mutation-positive test results.^{18,19,21,25} Other reasons cited for not seeking genetic counseling or testing have included concerns about potential insurance discrimination, how genetic testing would affect one's family, and emotional reactions to genetic test results.²¹ It is important to understand reasons why individuals choose not to undergo genetic testing for Lynch syndrome to develop targeted efforts to increase the awareness and perceived importance of testing for patients, their families, and their health care providers. For example, although the perceived risk for health insurance discrimination

has been cited across many studies as a barrier to genetic testing for hereditary cancers, efforts to increase awareness of protection offered by the 2008 Federal Genetic Information Nondiscrimination Act, or GINA, may help allay this particular concern.²⁶

Genetic testing for FAP has been considered standard management for this condition as a means of confirming a clinical diagnosis of multiple polyps, and to identify young persons in an FAP-affected family who do not have an APC mutation and thus can be relieved of the burden of annual surveillance.¹¹ Given the early age of polyp onset, at risk individuals often undergo APC mutation testing when they are minors. Parents with FAP have cited the need for early detection and management, reduction in parental anxiety and uncertainty, and help with decision making regarding surveillance as reasons for having their children undergo genetic testing. The cost of testing and concerns about possible insurance discrimination were reported as reasons for not having children tested.²⁷

Psychological Effects of Undergoing Genetic Counseling and Testing

A primary concern among clinicians and researchers has been whether undergoing genetic testing for hereditary colorectal cancer poses a risk for psychological distress and diminished quality of life. Longitudinal studies of psychological outcomes after genetic testing for Lynch syndrome have shown that, in most cases, those found to have a MMR gene mutation experienced increased levels of distress shortly after receiving test results; however, distress levels subsided during the course of the year after disclosure^{28,29} and did not differ from pretest distress levels at one year postdisclosure.³⁰ Findings from these studies also indicate that those who tested negative for an MMR gene mutation may derive psychological benefit from testing, as they experienced a reduction or no change in distress up to a year following results disclosure.^{29–31} Less is known about the longer-term psychological impact of Lynch syndrome genetic counseling and testing. However, subgroups of individuals may be at higher risk of psychological distress following disclosure of test results, including those who present with relatively higher scores on measures of general or cancer-specific distress before undergoing testing.^{22,29} Predictors of higher levels of distress from 1 to 6 months postdisclosure include (1) a prior history of major or minor depression, (2) higher pretest levels of cancer-specific distress, (3) having a greater number of cancer-affected first-degree relatives, and (4) greater grief reactions.²⁹ These findings underscore the importance of genetic counseling both before and after MMR mutation testing, as counseling can help individuals anticipate their emotional responses to testing and in turn identify means of coping with testing outcomes.

For individuals undergoing genetic testing for FAP, the research indicates that some individuals, particularly mutation carriers, may be at risk for experiencing increased distress.³² More specifically, mutation carriers report higher levels of state anxiety and anxiousness compared with non-carriers. Factors associated with higher anxiety included

lower optimism and lower self-esteem. Factors associated with more state anxiety included FAP-related distress, perceived seriousness of FAP, and belief in the accuracy of genetic testing.^{33,34} The current research suggests that factors associated with higher FAP-related distress include greater perceived risk of developing cancer, higher levels of discussion about FAP with family or friends, and having no children; factors associated with cancer-specific worries included being female, poorer family functioning, higher levels of actual or desired discussions about FAP with family or friends, greater perceived cancer risk, poorer general health perceptions, and having been a caregiver for a family member with cancer.³⁵ As previously stated, genetic testing is often conducted in children from families affected by FAP, therefore the psychological impact of testing in such a young population is of particular concern. To date, the research suggests that most children do not experience significant distress as a result of genetic testing.³²

Communication of Genetic Risk within the Family

Genetic testing for inherited cancer risk provides risk information not only about the individual who undergoes testing, but also his or her biological relatives. Persons who undergo genetic testing for Lynch syndrome or FAP, particularly index cases (i.e., the first person tested in the family), often serve as the gatekeepers for genetic information and may determine whether and how risk information reaches family members.^{36,37} In general, persons who undergo genetic testing are willing to share test results with at least some of their relatives, often within a few weeks after receiving results. People are also more likely to share test results with first-degree relatives than more distant relatives.^{38–40}

Motivations for disclosing genetic risk information include a perceived moral obligation, a responsibility to help others, a desire for emotional support, and to increase family awareness of health care options and predictive genetic testing.^{38,39,41,42} Reasons for nondisclosure include not being close to family members, not wanting family members to worry, and having concerns that family members might not understand test results.⁴² Disclosure may be less likely when at risk family members are considered too young to receive the information (i.e., children), when it is perceived relatives would be uninterested, when family members are on bad terms, or when the information might cause new or old conflicts to erupt.^{38,39,41,43} Proband may feel particularly obliged to inform family members about a hereditary cancer risk³⁹ and may be strong advocates for genetic counseling and testing.⁴⁰ In the case of Lynch syndrome, positive mutation carrier status is also associated with disclosure to family members.^{42,43}

In regard to disclosure of genetic risk information within families, several models of communication are cited including face-to-face communication, telephone and written contact.^{38–40} Lynch syndrome-related mutation informants have suggested that the information should be delivered in a way that underscores its seriousness, but provides hope and

support for cancer prevention.⁴¹ Recommendations and support by health care providers to inform relatives may encourage communication and help overcome barriers in communicating information to family members.^{39,44} Communication aids (e.g., educational booklet or letter) are also considered helpful in the communication process, but are not perceived as necessary.³⁸

Risk-Reduction Behaviors

Screening Behaviors

Lynch Syndrome

CRC screening prior to genetic counseling and testing may be less than optimal among persons at risk for Lynch syndrome. Among cancer-unaffected persons over age 18 participating in research protocols offering genetic testing and counseling for Lynch syndrome, between 52% and 73% reported ever having had a colonoscopy prior to testing or study enrollment.^{45–50} Among cancer-unaffected persons at risk for Lynch syndrome, adherence to CRC screening recommendations prior to genetic testing has ranged from 11 to 47%.^{45,51}

Several longitudinal studies have examined colonoscopy screening prior to and up to one year after testing in persons who had undergone genetic testing for Lynch syndrome MMR gene mutations. MMR gene mutation carriers were more likely to have had a colonoscopy following genetic testing, compared with noncarriers and those who declined testing (73% vs 16% vs 22%), and their colonoscopy use increased from 36 to 73% in the year following disclosure of test results.⁴⁶ One study in Belgium showed adherence to colonoscopy to be as high as 100% during the same period.⁴⁵ Other studies have shown no significant increase in colonoscopy uptake among carriers and decreases among noncarriers.^{52,53} Those most likely to have had screening endoscopy within 1 year after genetic testing were patients who tested positive for a MMR gene mutation,^{52–54} expressed greater perceived control over CRC,⁴⁶ were older,⁵³ and had disclosed genetic testing results to a health care provider.⁵⁵

Studies assessing screening beyond one year postdisclosure of genetic test results suggest that improvements in colorectal screening behaviors among carriers may be maintained over time. Adherence to colorectal screening ranged from 73 to 100% among persons with a genetic or clinical diagnosis of Lynch syndrome in studies with follow-up periods from 1 to 18 years after genetic testing and/or counseling.^{31,56,57} Although the majority of carriers believe screening using a colonoscopy is safe and effective, many reported beliefs that it was an invasive and burdensome technique.⁵⁷ However, future screening intention has been reported to be high among MMR gene mutation carriers, with 94% intending to have annual or biannual colonoscopy, versus 34% of noncarriers intending to have a future colonoscopy.⁴⁵

These findings suggest that genetic testing may motivate individuals to maintain or improve recommended CRC screening for Lynch syndrome. Further research is needed to identify barriers to screening and to evaluate interventions that aim to increase colonoscopy use among those who are

nonadherent to screening recommendations. These results suggest particular attention should be given to counseling noncarriers about appropriate screening.⁴⁵ Risk communication and encouragement from family members is associated with colonoscopy uptake, thus interventions also may want to focus on the family.⁵⁸

Additionally, research suggests health professionals should pay attention to hypervigilant persons who undergo CRC screening more frequently than recommended. Excessive screening may result in higher health care costs, overutilization of health care resources, and unnecessary risks to patients.⁵⁹ Hadley et al⁵³ reported that 35% of MMR gene mutation carriers and 13% of noncarriers were nonadherent to colorectal screening recommendations one year after testing and, of those, about half were hypervigilant. This behavior may be attributed to inappropriate screening advice or persistent worry about CRC risk.

Familial Adenomatous Polyposis

There is limited data on uptake of colorectal screening among persons at risk for or affected with FAP. One study of individuals age 17 years or older, with a family history of FAP who were offered participation in a genetic counseling and testing protocol, found that although all asymptomatic persons had undergone at least one screening endoscopy before the study, only one-third continued screening at the recommended intervals.⁶⁰ Additionally, the study found that nearly all FAP-affected persons (92%) who had a colectomy were adherent to recommended colorectal surveillance.

A cross-sectional study of patients with a clinical or genetic diagnosis of FAP or attenuated FAP, and relatives at greater risk, found that the use of endoscopic screening was low among those affected by FAP (52%) and their at risk relatives (46%), as well as among those with attenuated FAP (58%) and their at risk relatives (33%).⁶¹ Additionally, results show nonuse of CRC surveillance tests to be associated with not receiving screening recommendations from a health care provider, not having health insurance or insurance reimbursement for endoscopic colorectal surveillance tests, and having lower CRC risk perceptions. In terms of participant opinions toward sigmoidoscopy and colonoscopy, participants most commonly described it as a “necessary evil” (19%) or reported they disliked the bowel preparation (18%) or the pain and discomfort from the procedure (14%). The desire to avoid endoscopic screening has been suggested as a motivating factor to undergo APC genetic testing,⁶² although many continue to screen after testing. One study showed that 42% of people who had undergone APC mutation testing expected to continue endoscopic surveillance, despite the fact that their genetic test result was mutation-negative, due to doubts about the accuracy of genetic testing.³⁴

Risk-Reduction Surgery

For Lynch syndrome, there is a lack of evidence for or against the recommendation of preventive colectomy among persons unaffected by cancer. Studies show low uptake of prophylactic colectomy among those at risk both 1 year and 3 years following genetic testing.^{50,63} Additionally, little is known

about the decision-making process or psychological impact of undergoing risk-reducing colectomy.⁵⁹ Among people receiving positive MMR gene mutation results, 67% expressed interest in risk-reducing colectomy, but the study did not assess actual surgical decisions.¹⁷

For FAP, prevention of CRC can be achieved only through prophylactic colectomy, which is offered when polyps become too numerous to manage endoscopically. Some studies measuring quality of life after risk-reducing colectomy have shown it be within normal ranges following surgery and most have reported no negative impact on body image.^{64,65} However, other studies have shown that quality of life may be negatively impacted by problems with bowel function following surgery, such as increased stool frequency, occasional liquid soiling, and worries about incontinence.^{66,67}

Health and Lifestyle Behaviors

Although research suggests that the adoption of healthy lifestyles and behaviors (e.g., diet, physical activity, weight control, smoking cessation, limited alcohol consumption) could have a favorable impact on colon cancer burden,^{68–70} there is minimal data on how these behaviors may moderate cancer risk among those at risk of hereditary colon cancer. Nevertheless, it is recommended health professionals offer a balanced discussion of the potential benefits of dietary and lifestyle modifications (in the case of Lynch syndrome) and follow general guidelines for preventive behaviors to maintain overall health and quality of life for those at risk of hereditary colon cancer.^{71–74}

To date, we know very little about the actual health and lifestyle behaviors of those at risk of hereditary colon cancer. Within Lynch syndrome families, one study showed that people unaffected by cancer exhibited more risk behaviors than patients with CRC, as well as those who were male, less educated, and under the age of 50.⁷⁵ Additionally, research evaluating anticipated behavioral reactions to genetic testing for Lynch syndrome shows those anticipating a high risk result from genetic testing were more likely to adopt a healthier lifestyle than those anticipating a low risk result.⁷⁶ People with a cancer history and a higher level of genetic knowledge were also more likely to endorse a link between cancer and diet.⁷⁷ Thus, even in the absence of genetic testing, people not previously diagnosed with cancer who perceive themselves to be a high risk for hereditary CRCs, are more likely to engage in health protective behaviors and perceive greater benefits.

Implications for Clinical Practice

Although a small percentage of total CRC cases are attributable to heredity, people with hereditary cancer syndromes such as Lynch syndrome and FAP have a much higher lifetime risk than the general population. Predictive genetic testing can be useful in clinical practice to identify those with inherited CRC susceptibility and results can be used to offer targeted options for cancer risk reduction and risk management. Through genetic testing and counseling, at risk individuals may resolve uncertainty about their personal and

familial cancer risk and obtain information to guide and personalize decisions about their future health care. However, as our review shows, decisions to undergo testing are difficult and complex and may affect not only the individual but the family. Given this complexity, health professionals may be called on to facilitate education and decision making about inherited cancer risk, genetic testing, and disclosure of testing results. This may be particularly true in the case of FAP where genetic testing and screening are common in children and young adults.

For those who are mutation-positive, research suggests surgery is effective for the prevention of CRC for FAP only. Thus, health behaviors, particularly screening, are important for those at risk of hereditary colon cancer. Given that colorectal screening rates are still less than optimal, more work must be done to influence uptake of colonoscopy screening and risk reduction behaviors at the individual and family level. Research suggests genetic testing for hereditary cancer syndromes may motivate individuals to screen, but is often most effective with positive-mutation carriers. Therefore, health professionals must pay particular attention to nonmutation or unidentified carriers to educate them about appropriate screening behaviors and counteract negative opinions of screening. Future research is also needed to more clearly identify screening barriers and to evaluate interventions (particularly at the family level) that encourage colonoscopy use. Whether or not individuals engage in the recommended strategies to reduce or manage their CRC risk is critical to the translation of genetic information into reductions in cancer morbidity and mortality.

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