

# Colon Cancer Screening Practices Following Genetic Testing for Hereditary Nonpolyposis Colon Cancer (HNPCC) Mutations

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**Background:** Although increased colonoscopic surveillance is recommended for hereditary nonpolyposis colon cancer (HNPCC) mutation carriers, limited information is available on adherence to colorectal cancer screening recommendations. This study investigated colonoscopy practices following genetic testing for HNPCC mutations.

**Methods:** This prospective cohort study was conducted between May 22, 1996, and November 13, 1999. Participants were 98 men and women without a personal history of colon cancer or colectomy who were identified from 11 extended HNPCC families. Colonoscopy use was evaluated by telephone before genetic counseling and was reassessed 1, 6, and 12 months following test results disclosure.

**Results:** During the 12 months following genetic counseling and testing, 73% (16/22) of HNPCC mutation carriers, 16% (8/49) of noncarriers, and 22% (6/27) of de-

cliners reported having a colonoscopy ( $\chi^2=23.97$ ,  $P<.001$ ). After controlling for clinical factors and pre-test screening practices, HNPCC mutation carriers were significantly more likely than test decliners to have a colonoscopy (odds ratio [OR], 12.12; 95% confidence interval [CI], 3.42-42.96;  $P<.001$ ). There were no differences in colonoscopy use between noncarriers and decliners (OR, 0.60; 95% CI, 0.28-1.29;  $P=.19$ ). Perceived control over developing colon cancer also had a significant effect on posttest colonoscopy use (OR, 2.19; 95% CI, 1.22-3.94;  $P=.01$ ).

**Conclusions:** Genetic testing may motivate increased colonoscopic screening among HNPCC mutation carriers. Increased efforts may be needed to assess patients' family histories of colon cancer and provide appropriate referrals for genetic counseling and testing to target colonoscopic screening to high-risk individuals.

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**H**EREDITARY NONPOLYPOSIS colon cancer (HNPCC) is the most common autosomal dominantly inherited cancer syndrome that predisposes to colorectal cancer (CRC).<sup>1,2</sup> Estimates of its frequency range from 2% to as much as 7% of the total CRC burden.<sup>2-5</sup> Colorectal cancer occurs at an early age (mean age, about 44 years), with right-sided predominance (approximately 70% of tumors are proximal to the splenic flexure)<sup>1,2,6</sup> and a significant occurrence of synchronous and metachronous lesions.<sup>2,7</sup> There is an excess of extracolonic cancers, the most common of which is carcinoma of the endometrium, followed by cancers of the ovary, stomach (particularly in Asian countries such as Japan and Korea), small bowel, pancreas, hepatobiliary tract, and brain, and transitional cell carcinoma of the upper uroepithelial tract.<sup>8,9</sup> Some families also have phenotypic manifestations such as se-

baceous adenomas or sebaceous carcinomas consistent with the Muir-Torre syndrome.<sup>2,10-16</sup> Profuse colonic adenomas consonant with classic familial adenomatous polyposis and its attenuated variant must be excluded in the medical evaluation of patients at high risk for HNPCC.<sup>1,2</sup>

Most HNPCC cases are attributable to mutations in 1 of 5 mismatch repair genes (*hMSH2*, *hMLH1*, *PMS1*, *PMS2*, and *hMSH6*).<sup>15,17-19</sup> Individuals who are found to carry HNPCC mutations have an 80% to 85% lifetime risk of developing colon cancer in the absence of CRC screening.<sup>1,20</sup> Screening recommendations for HNPCC mutation carriers include colonoscopy every 1 to 2 years starting at age 20 to 25 years, while noncarriers are advised to follow colon cancer screening guidelines for the general population.<sup>2,21-24</sup> There is emerging evidence that regular colonoscopic screening can reduce colon cancer risk and improve survival among at-risk individuals from HNPCC families.<sup>25-28</sup>

Genetic testing for inherited colon cancer risk is increasingly being offered in clinical settings to individuals who have a family history of cancer that is suggestive of HNPCC. Rates of genetic test acceptance in empirical investigations range from 43% to 75%.<sup>29,30</sup> Although as many as 95% of HNPCC mutation carriers report that they would consider lifetime screening as a risk management option,<sup>31</sup> empirical data on the effect of genetic testing on adoption of CRC screening are limited.

For HNPCC genetic testing to translate into reduced CRC morbidity and mortality, individuals identified as mutation carriers must adopt more intensive CRC surveillance. Although prior studies<sup>26,27</sup> have evaluated the efficacy of colonoscopy in reducing colon cancer mortality in HNPCC families, few empirical studies have documented rates of adherence to CRC screening recommendations following genetic testing for HNPCC. Therefore, the present study evaluated whether genetic testing for HNPCC mutations and receipt of positive test results have an effect on the use of colonoscopy. A secondary aim was to identify factors associated with adherence to identify potential barriers to patient compliance.

## METHODS

### STUDY POPULATION

Eligible participants included men and women identified from 11 extended families in which a risk-conferring HNPCC mutation had been identified. The mean family size was 8.9 members, and most families (7 [64%]) resided in the Midwest. These individuals were participants in an HNPCC genetic counseling and testing research study. Eligible participants had a 25% risk of having the HNPCC gene alteration that had been identified in their family. Participants were enrolled in this study from May 22, 1996, through November 13, 1999. As part of this study, participants received education and counseling about hereditary colon cancer and were provided with recommendations for colon cancer screening. Individuals affected with colon cancer or with a history of colectomy were excluded.

### PROCEDURES

This research was completed at Creighton University and Georgetown University Medical Center, Washington, DC, and all procedures were approved by the institutional review boards at both centers. As described in a previous report,<sup>29</sup> all family members who were at 25% risk for having an HNPCC mutation identified in their family were invited by mail to participate in genetic counseling and testing provided through a family information session. Those who agreed to participate in the study were contacted by a professional telephone interviewer from the Georgetown University Medical Center to obtain oral consent to participate in a structured baseline telephone survey. This interview evaluated sociodemographic factors, perceptions about screening, and screening behaviors and was conducted approximately 4 weeks before the education session. The baseline interview took about 40 minutes to complete. All subjects were informed that completing the survey did not obligate them to participate in the family information session, obtain genetic testing, or receive HNPCC test results. Specific information about the family information session was mailed to all family members about 2 weeks after the introductory letter.

Each family information session was conducted on a family basis in a centrally located area. These 1- to 2-hour semi-structured sessions were conducted by a medical oncologist (H.L.) and an oncology nurse. After obtaining written informed consent, subjects received information about (1) the inheritance of cancer susceptibility in HNPCC families; (2) background information on linkage analysis, gene identification, and the meaning of mutation test results; (3) the potential benefits, limitations, and risks of genetic testing; and (4) information about options for risk reduction and surveillance (ie, regular screening could potentially increase early detection of premalignant lesions among mutation carriers) and the limitations of different screening modalities. Specifically, individuals were informed that, for high-risk individuals with an unknown mutation status, colonoscopy should begin between the ages of 20 and 25 years and should be obtained every other year until age 35, and then annually. Individuals identified as mutation carriers were told that annual colonoscopy should be performed beginning at age 25. Noncarriers were advised to follow the screening recommendations for individuals in the general population, which include colonoscopy every 10 years starting at age 50.

The potential benefits of other screening tests (endometrial aspiration biopsy) and risk-reduction options (subtotal colectomy and prophylactic total abdominal hysterectomy) were also discussed; however, the lack of data regarding the efficacy of these options was acknowledged. After the education session, an oncology nurse collected blood samples from subjects who wished to receive testing. Written informed consent was obtained before collecting blood samples. Some subjects had participated in an earlier study that was conducted to determine linkage to one of the HNPCC-associated genes. However, individual mutation analysis was not performed in the prior study, and none of these subjects received genetic test results before the present study.

Subjects requesting genetic testing were notified by letter when mutation results became available. Those who were interested in obtaining their HNPCC test results contacted Creighton University to make arrangements for test results disclosure. Written informed consent was obtained again before test results disclosure. The HNPCC test results were disclosed during a standardized, supportive counseling session in which subjects discussed expectations about their test result and were provided with cancer risk estimates. Plans for communicating HNPCC test results to family members were also discussed as part of the disclosure session, and subjects were provided with a toll-free telephone number to contact the medical oncologist or oncology nurse if any additional information was needed. Subjects could also defer their decision about receiving their HNPCC test results; in these cases, genetic test results were disclosed at any point during the study after obtaining written informed consent.

Following disclosure of HNPCC test results, subjects were contacted for follow-up telephone interviews to reassess screening behaviors. These interviews were completed 1, 6, and 12 months following the disclosure session. Screening recommendations were not provided to participants during the follow-up interviews.

## MEASURES

### Predictor Variables

**HNPCC Test Results.** HNPCC genetic test results were obtained from study records, and subjects were categorized as mutation carriers, noncarriers, or test decliners.

**Sociodemographics.** Sex, age, marital status, education level, and employment status were obtained during the baseline telephone interview.

**Prior Study Participation.** Participation in the linkage analysis study was determined from registry records.

**Knowledge About Risk Status.** Knowledge about one's increased risk of developing cancer was assessed at baseline using a binary item. Specifically, subjects were asked if they had ever been told by a health care provider that they might be at high risk for cancer. The number of years since they had been informed about their increased risk was recorded for those who had received this information.

**Pretest Screening Practices.** Use of colonoscopy before genetic testing was evaluated during the baseline telephone interview using a binary item. Specifically, subjects were asked, "Have you ever had a colonoscopy, which is a test where a tube with a light on the end is inserted into the rectum? This test is given after the administration of colon preparations and intravenous sedatives and after a special diet." The month and year of the most recent colonoscopy were recorded. Those who reported having a colonoscopy within 2 years before the baseline telephone interview were categorized as prior test users. Those who reported that they had never had a colonoscopy or that their last colonoscopy was received 3 or more years before the baseline survey were categorized as nonusers.

**Perceptions About Screening.** Two Likert-style items were used to evaluate perceptions about colon cancer screening tests during the 1-month follow-up telephone interview. Specifically, subjects were asked to indicate how much control they had over developing colon cancer (1, none at all; 2, a little; 3, a moderate amount; or 4, a lot) and to indicate their perceptions of the effectiveness of colon cancer screening tests for finding cancer in its early stages (1, not at all effective; 2, a little effective; 3, moderately effective; or 4, very effective). These items were developed and validated among men in the general population<sup>32</sup> and have been shown to predict colon cancer screening intentions.<sup>33</sup> We recoded these items into binary variables (none at all, a little vs moderately, or very much) for statistical analysis.

#### Outcome Variables

Use of colonoscopy was assessed by self-report during the 1-, 6-, and 12-month follow-up telephone interviews. As with the pretest screening measure, subjects were asked, "Have you had a colonoscopy, which is a test where a tube is inserted into the rectum and is usually given after taking tranquilizers and after a special diet?" The month and year that this test was received were recorded. Specific recommendations for colon cancer screening tests were not provided during follow-up interviews. Subjects who reported having a colonoscopy at any of the follow-up assessments were categorized as colonoscopy users, and those who reported that they had not obtained screening during the 1-, 6-, and 12-month follow-up interviews were categorized as nonusers.

#### STATISTICAL ANALYSIS

We first generated descriptive statistics to characterize the sample in terms of study retention, sociodemographic factors, perceptions about screening, and HNPCC test results. Next,  $\chi^2$  tests of association were used to evaluate the association between predictor variables and colonoscopy practices. McNemar tests were also used to compare changes in screening use rates from baseline to posttest in test result groups. We then conducted logistic regression analysis using generalized estimating equations to identify factors having independent associations with colonoscopy use, while adjusting for correlations among fam-

ily members (intrafamilial correlation,  $-0.03$ ). Because our outcome (colonoscopy use) was a binary variable, we used a logit link to estimate the odds of having a colonoscopy during the year following genetic counseling and testing. Variables significantly associated with study retention and those that had significant bivariate association ( $P < .10$ ) with colonoscopy use were included in the general estimating equation model. Dummy variables were used to test for study group effects, using decliners as the reference group.

## RESULTS

### SAMPLE CHARACTERISTICS

The sample consisted of 222 eligible subjects who completed a baseline telephone interview. Of these, 134 (60%) completed all 3 of the follow-up assessments (1, 6, and 12 months after genetic testing). The retention rate was 67% (45/67) for mutation carriers and 70% (56/80) for noncarriers, compared with 44% (33/75) for test decliners ( $\chi^2 = 12.79$ ,  $P = .002$ ). We compared subjects who were lost to follow-up (ie, could not be reached for follow-up surveys or declined to complete these interviews) with those who were retained in terms of sociodemographic characteristics and prior colonoscopy practices. Men ( $\chi^2 = 8.82$ ,  $P = .003$ ) and subjects who were younger than 40 ( $\chi^2 = 12.92$ ,  $P = .001$ ) were significantly more likely to be lost to follow-up. Subjects who were employed ( $\chi^2 = 4.11$ ,  $P = .04$ ) and those who had not participated in the prior linkage analysis study ( $\chi^2 = 7.48$ ,  $P = .006$ ) were also significantly more likely to be lost to follow-up. Subjects who had not been informed about their cancer risk ( $\chi^2 = 3.42$ ,  $P = .06$ ) and those who had never had a colonoscopy or who were screened more than 3 years before the baseline interview ( $\chi^2 = 3.01$ ,  $P = .08$ ) were less likely to be retained in the study, but these differences were not statistically significant. Marital status, education level, and health insurance status were not significantly associated with being lost to follow-up.

Of the 134 subjects who were retained in the study, we excluded those who reported a prior history of colectomy or colon cancer at baseline ( $n = 25$ ) or who developed colon cancer during the study ( $n = 2$ ). Subjects who received genetic test results during the follow-up period ( $n = 9$ ) were also excluded from the analysis. Therefore, the final sample included 98 men and women. **Table 1** shows that 22% ( $n = 22$ ) were mutation carriers, 50% ( $n = 49$ ) were noncarriers, and 28% ( $n = 27$ ) declined genetic testing. Most subjects were female (67 [68%]), married (71 [72%]), had some college education (55 [56%]), were employed (68 [69%]), and had health insurance (93 [95%]). Forty-nine (50%) subjects participated in the prior linkage analysis study, and 44 (45%) had been informed that they were at increased risk for developing cancer by a health care professional. Among those who had been informed about their increased risk of developing cancer, the mean  $\pm$  SD amount of time for having this information was  $15.0 \pm 9.5$  years. The mean  $\pm$  SD age of the subjects was  $49.3 \pm 14.9$  years. Noncarriers were older than mutation carriers and decliners (mean  $\pm$  SD age of carriers,  $43.2 \pm 12.2$  years; noncarriers,  $52.1 \pm 14.6$  years; and decliners,  $49.1 \pm 16.3$  years;  $F = 2.83$ ,  $P = .06$ ).

**Table 1. Sample Characteristics\***

Variable	All Subjects (N = 98)	Carriers (n = 22)	Noncarriers (n = 49)	Decliners (n = 27)
Sex				
Female	67 (68)	13 (59)	36 (74)	18 (67)
Male	31 (32)	9 (41)	13 (27)	9 (33)
Age, y				
≥40	67 (68)	11 (50)	37 (76)	19 (70)
<40	31 (32)	11 (50)	12 (24)	8 (30)
Marital status				
Married	71 (72)	17 (77)	36 (73)	18 (67)
Not married	27 (28)	5 (23)	13 (27)	9 (33)
Education level				
>High school	55 (56)	13 (59)	27 (55)	15 (56)
≤High school	43 (44)	9 (41)	22 (45)	12 (44)
Employment status				
Employed	68 (69)	19 (86)	31 (63)	18 (67)
Not employed	30 (31)	3 (14)	18 (37)	9 (33)
Prior study participation				
Yes	49 (50)	12 (55)	29 (59)	8 (30)
No	49 (50)	10 (46)	20 (41)	19 (70)

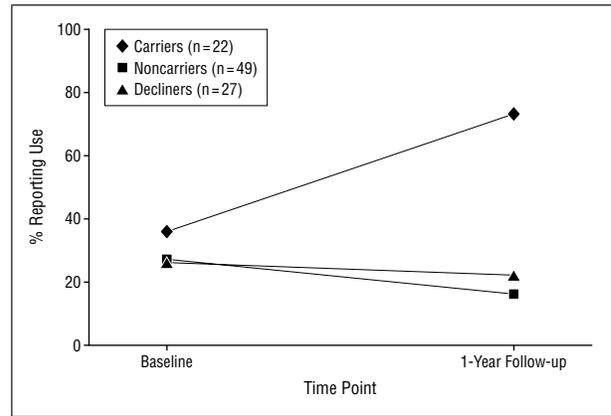
\*Data are given as number (percentage).

### COLON CANCER SCREENING PRACTICES BEFORE GENETIC COUNSELING AND TESTING

Overall, 37 (38%) subjects reported that they had never had a colonoscopy, and 61 (62%) subjects reported having a colonoscopy before genetic counseling and testing. However, of those who reported having had a colonoscopy, 33 (54%) received this test 3 or more years before the baseline survey, 18 (30%) received screening 2 years before the baseline survey, and 10 (16%) received screening 1 year before the baseline survey. Colonoscopy use rates before genetic counseling were not significantly different between test result groups; 36% (8/22) of carriers, 27% (13/49) of noncarriers, and 26% (7/27) of decliners ( $\chi^2=0.85, P=.65$ ) had a colonoscopy within 2 years of the baseline survey. Age, sex, marital status, employment status, and health insurance status were not significantly associated with colonoscopy use at baseline; however, participants with greater education (36% [20/55] vs 19% [8/43];  $\chi^2=3.73, P=.05$ ) and those who had been informed of their increased risk for developing cancer (44% [19/43] vs 17% [9/54];  $\chi^2=8.83, P=.003$ ) were significantly more likely to have a colonoscopy before genetic counseling and testing.

### BIVARIATE ANALYSES OF COLON CANCER SCREENING PRACTICES AFTER GENETIC TESTING

During the 12 months following genetic testing, 73% (16/22) of mutation carriers, 16% (8/49) of noncarriers, and 22% (6/27) of decliners reported having a colonoscopy ( $\chi^2=23.97, P<.001$ ). We reran these analyses excluding subjects who reported having had a colonoscopy in the year before the baseline survey; the results were unchanged. Mutation carriers were significantly more likely than noncarriers and decliners to have a colonoscopy fol-



Changes in colonoscopy use following HNPCC testing.

lowing genetic counseling and testing ( $\chi^2=18.91, P<.001$ ). Sex, age, marital status, education level, employment status, prior study participation, and knowledge of cancer risk were not significantly associated with postcounseling colonoscopy use.

With regard to screening perceptions, only perceived control over developing colon cancer 1 month following genetic counseling and testing was significantly associated with colonoscopy use. Subjects who reported that they had at least a moderate amount of control over developing colon cancer were significantly more likely to report having a colonoscopy compared with subjects who reported little or no control (42% [18/43] vs 22% [12/54];  $\chi^2=4.32, P=.04$ ). Perceived effectiveness of colon cancer screening was not associated with colonoscopy use during the year following genetic testing.

### CHANGES IN COLON CANCER SCREENING PRACTICES

We conducted McNemar analyses to evaluate whether colonoscopy practices changed from baseline to follow-up in test result groups. As shown in the **Figure**, mutation carriers reported significantly increased use of colonoscopy following genetic testing (McNemar statistic, 5.33;  $P=.02$ ). There were no significant changes in colonoscopy use among noncarriers (McNemar statistic, 1.19;  $P=.28$ ) or decliners (McNemar statistic, 0.11;  $P=.73$ ). Similar results were obtained when subjects who had a colonoscopy 1 year before genetic testing were excluded from the analysis.

### MULTIVARIATE ANALYSES OF SCREENING USE

As shown in **Table 2**, none of the clinical characteristics or sociodemographic factors were significantly associated with colonoscopy use during the 12 months following genetic counseling and testing. The addition of HNPCC test results and perceptions of control over developing cancer improved the fit of the overall model (likelihood ratio test, 29.44;  $P=.001$ ); however, for test results, only the effect for the comparison of carriers with decliners was significant (odds ratio, 12.12; 95% confi-

dence interval, 3.42-42.96;  $P < .001$ ). The effect for perceived control over developing colon cancer was also significant (odds ratio, 2.19; 95% confidence interval, 1.22-3.94;  $P = .01$ ).

### COMMENT

To our knowledge, this is one of the first empirical studies to evaluate colon cancer screening practices following genetic testing for HNPCC mutations. HNPCC mutation carriers reported significantly higher rates of colonoscopy during the year following genetic testing. Before genetic testing, 36% (8/22) of mutation carriers reported having a colonoscopy, whereas 73% (16/22) of mutation carriers reported having a colonoscopy after genetic testing. This compares with national colonoscopy or sigmoidoscopy rates of 37.2% reported in the Behavioral Risk Factor Surveillance study for 2002 and 59% of first-degree relatives of colon cancer patients who reported that they had ever had endoscopic screening of the colon.<sup>34,35</sup> Subjects who perceived that they had at least a moderate amount of control over developing colon cancer were about twice as likely as those with less perceived control to have a colonoscopy during the year following genetic testing. Surprisingly, colonoscopy use did not decrease among noncarriers, who were advised to follow screening guidelines for individuals in the general population. This could be because of lack of reassurance.<sup>36</sup> Some noncarriers reported that they would continue with more frequent screening during the test results disclosure session.

Available data suggest that surveillance can improve colon cancer survival and reduce incidence among high-risk individuals.<sup>37</sup> Colon cancer screening at 3-year intervals was associated with a 62% risk reduction among individuals at risk for HNPCC mutations,<sup>26</sup> and these effects were maintained among HNPCC mutation carriers after 15 years of follow-up.<sup>27</sup> Furthermore, among high-risk families, the 10-year survival rate for colon cancer detected through screening was 93% compared with 68% among cases not detected through screening.<sup>28</sup>

Despite promising data on the benefits of colon cancer screening, the optimal screening interval for mutation carriers is a subject of debate.<sup>22,38</sup> Because HNPCC gene alterations are associated with accelerated carcinogenesis,<sup>39</sup> it is now recommended that HNPCC mutation carriers have a colonoscopy every 1 to 2 years until age 40, and annually after age 40.<sup>1,2,21,22,40</sup> The results of the present study are encouraging in that they suggest that most HNPCC carriers will adhere to these guidelines within the year after receiving test results. However, one-time use of screening tests has significant limitations in this population; colonoscopy is recommended at more frequent intervals for HNPCC mutation carriers because of the aggressive nature of the disease.<sup>2,21-24</sup> Therefore, long-term studies are needed to determine whether the levels of compliance with screening observed in this study will be maintained over time.

Although genetic testing for HNPCC mutations may increase compliance with colon cancer screening recommendations, low rates of participation in genetic coun-

**Table 2. Logistic Regression Analysis of Colonoscopy Use**

Variable	Odds Ratio (95% Confidence Interval)	P Value
Prior screening use		
Yes	0.60 (0.07-0.47)	.41
No		
Sex		
Female	0.90 (0.18-2.03)	.83
Male		
Age, y		
$\geq 40$	2.20 (0.33-2.43)	.13
$< 40$		
Employment status		
Employed	0.73 (0.80-6.05)	.54
Not employed		
Prior study participation		
Yes	0.92 (0.26-2.00)	.82
No		
Risk knowledge		
Yes	1.20 (0.41-2.02)	.66
No		
HNPCC test result		
Carrier vs decliner	12.12 (3.42-42.96)	$< .001$
Noncarrier vs decliner	0.60 (0.28-1.29)	.19
Perceived control		
Moderate amount or a lot vs none or a little	2.19 (1.22-3.94)	.01

Abbreviation: HNPCC, hereditary nonpolyposis colon cancer.

seling and testing may pose a significant barrier.<sup>29</sup> Genetic testing for HNPCC mutations should be offered to individuals who have a high probability of having a risk-conferring alteration based on their personal and family history of disease.<sup>24,41</sup> This includes individuals with family histories of cancer that meet the Amsterdam criteria,<sup>42</sup> the modified Amsterdam criteria,<sup>43</sup> or the Bethesda guidelines.<sup>44</sup> Although primary care physicians and specialists can play an important role in the identification and management of HNPCC, their awareness of guidelines for genetic counseling and testing may be limited. For example, in a prior study,<sup>45</sup> only about one third of gastroenterologists knew about the availability of genetic testing for HNPCC mutations, and 16% recommended appropriate screening for a patient in a hypothetical HNPCC clinical scenario. Furthermore, in another study,<sup>46</sup> primary care physicians were significantly less likely than gastroenterologists to assess family history of colon cancer, refer high-risk patients to genetic testing, and identify colonoscopy as the preferred screening modality for high-risk patients. The linchpin for successful clinical translation for all matters regarding management of HNPCC will be physicians who are knowledgeable about hereditary cancer syndrome diagnosis, its differential diagnosis, and the disorder's natural history, so that this knowledge can be melded to the best posits available for surveillance and management of high-risk individuals. Therefore, additional research is needed to understand physician knowledge about HNPCC and barriers to referral for genetic counseling and testing for inherited colon cancer risk and to understand the effect of physician recommendation on colon cancer screening be-

aviors in HNPCC mutation carriers. Future studies are also needed regarding communication of HNPCC test results to physicians, because awareness of HNPCC test results is likely to influence physician recommendations about colon cancer screening.

In considering the findings of the present study, several limitations should be noted. First, subjects in this study were members of 11 HNPCC families who were enrolled in a familial cancer registry, and some had participated in prior linkage analysis research. All study participants were white and 31% (n=30) of the overall sample reported having a colonoscopy during the 12 months following genetic counseling and testing. However, individual mutation testing was not performed as part of the linkage analysis study, and none of these subjects received genetic test results before the present study. Moreover, participation in linkage analysis was not significantly associated with colonoscopy use. Second, only 134 (61%) eligible subjects were retained in the study during the year following genetic testing. However, retention rates were higher (101 [69%] of 147) among mutation carriers and noncarriers, suggesting that the degree of bias in screening rates in these groups was minimal. Another possible limitation is that screening data were based on self-reports, rather than confirmed through medical records. However, previous research has shown that self-reports of colon cancer screening are accurate.<sup>47</sup> Furthermore, if evaluated using carefully worded items that describe the procedure, as was done in this study, self-reported CRC screening behaviors are highly concordant with medical record data.<sup>48</sup> It is also possible that the high rates of compliance observed among mutation carriers in this study were because of the intensive pretest and posttest education about colon cancer screening recommendations that was provided as part of the protocol for this study. Although the small sample size, the structured setting in which counseling and testing were provided, and the ethnic homogeneity of the study sample may limit the generalizability of the study results, it is standard practice to provide pretest education about the benefits, limitations, and risks of testing to facilitate informed decisions about whether to have testing and posttest counseling to provide screening recommendations.<sup>41</sup> Therefore, the methods that were used to provide counseling and testing are consistent with those recommended for clinical genetic testing for inherited cancer risk.

Despite these potential limitations, our results demonstrate that genetic testing for HNPCC mutations may motivate use of colon cancer screening tests among individuals identified as mutation carriers. As genetic testing moves from research to clinical settings,<sup>49</sup> health care providers will increasingly influence patients' access to testing and adoption of screening practices. The results of the present study underscore the potential importance of assessing patients' family histories of cancer and providing appropriate referrals for genetic counseling and CRC screening. Moreover, these data suggest that, during clinical encounters with high-risk patients, greater provider emphasis on the potential for screening to reduce colon cancer risk and mortality could increase the likelihood of patient compliance.

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