ELECTRONIC LETTER

# Experience of discharge from colonoscopy of mutation negative HNPCC family members

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Hereditary non-polyposis colorectal cancer (HNPCC or Lynch syndrome) is an autosomal dominant predisposition for early onset colorectal cancer and other tumours. The mean age at diagnosis of colorectal cancer is about 44 years.[1] At least five genes have been associated with errors in DNA mismatch repair, the genetic basis of HNPCC. A large proportion of HNPCC families (50%–60%) harbour changes in one of two genes, *hMSH2* and *hMLH1*.[2] Genetic testing for HNPCC has been possible since 1993/4.[3] In HNPCC, two important goals of genetic testing are (1) to identify those with a high risk (mutation positive) to promote preventive strategies and reduce morbidity and mortality; and (2) to reduce unnecessary worry among those with a low risk of cancer (mutation negative).[4] In mutation positive families, predictive testing can determine who is a carrier of a known mutation in the family, and who is not. Carriers of an HNPCC mutation are estimated to have a lifetime risk of developing colorectal cancer of about 80%.[5] These carriers are advised to adhere to a lifelong screening programme for early detection of colorectal polyps. The screening programme currently includes a colonoscopy every one to two years,[1 6 7] and should be initiated when the patient is between the ages of 20 and 25.[1] Regular screening reduces substantially the morbidity and mortality from colorectal cancer.[8] Those found not to be carriers of the mutation that runs in their family, "HNPCC mutation negative family members", are discharged from this burdensome, lifelong surveillance programme. Their risk and that of their children of developing colorectal cancer reverts to that of the general population (5%). In The Netherlands, there is currently no colorectal surveillance programme for the general population aged 50 years and over, as is the case in some other countries.

Aktan-Collan *et al*[9] reported that HNPCC mutation negative subjects were less anxious than mutation positive subjects immediately after disclosure of their predictive genetic test results, but these differences were no longer present after one and 12 months of follow up. However, neither this nor other studies have investigated the impact of negative test results on attitudes toward discharge from colon screening or actual surveillance behaviour in HNPCC families.[10] Although it is generally assumed that discharge from screening will be experienced as a relief, this assumption has yet to be confirmed empirically. A recent study of another hereditary colorectal cancer syndrome, familial adenomatous polyposis (FAP), found that 42% of those who had received a negative predictive genetic test result intended to (continue to) undergo colon screening in the future despite the fact that it was no longer necessary to do so.[11] Whether such continued vigilance is also prevalent among those found to be non-carriers of an HNPCC mutation is unknown.

## METHODS

As part of a larger, retrospective study of the experience of those counselled for the familial occurrence of colorectal cancer, we investigated the psychosocial impact of receiving a negative DNA test result. The study comprised all those counselled for the familial occurrence of colorectal cancer at three family cancer clinics in Amsterdam during the period 1986–98. Both asymptomatic subjects and those ever treated for cancer were invited to participate in the study. The study was approved by the institutional ethics committees of the three participating hospitals.

Of the 214 counsellees eligible for the overall study, 178 returned a completed questionnaire (83%). Among the 178 respondents, 25 were established to be non-carriers of the pathogenic mutation detected in their families (response within non-carriers 83%), and 31 were found to be carriers of a pathogenic HNPCC mutation (response within carriers 84%). The remaining 122 counsellees received a risk estimation and screening advice based on their family history only, either because DNA testing was not available or performed at the time they were counselled (n=108) or because the DNA test yielded inconclusive results (n=14). In this letter, we report data on the HNPCC mutation negative and positive counsellees.

As part of a self-report questionnaire assessing a wide range of psychosocial issues, three questions adapted from Lerman *et al*[12] were posed about the prevalence of cancer worries: "During the past year, how frequently did you worry about the risk

### Key points

- The purpose of the study was to investigate the experience of discharge from colonoscopy of mutation negative HNPCC family members.
- As part of a larger, retrospective study, 25 established non-carriers and 31 carriers of a pathogenic HNPCC mutation completed a questionnaire.
- None of the non-carriers reported being often worried about their own cancer risk, compared to 19% of the carriers. Only 3% of the non-carriers and 4% of the carriers reported that concerns about cancer had a significant impact on their daily functioning during the past year. Of the non-carriers, 82% were pleased that they no longer needed to undergo screening. However, 32% were concerned with their discharge from screening, suggesting conflicting positive and negative feelings among some subjects.
- Most non-carriers are pleased that colonoscopies are no longer necessary, but about one third have some concerns about stopping surveillance. These concerns should be addressed during the final consultation with the geneticist or gastroenterologist.

**Abbreviations:** FAP, familial adenomatous polyposis; HNPCC, hereditary non-polyposis colorectal cancer

**Table 1** Cancer worries during the past year: percentage of non-carriers (n=25) and carriers (n=31)

| | Almost never (%) | Sometimes (%) | Often/almost always (%) |
|---|---|---|---|
| Worries about own cancer risk: | | | |
| Non-carriers | 68 | 32 | 0 |
| Carriers | 52 | 29 | 19 |
| Worries had impact on daily functioning: | | | |
| Non-carriers | 88 | 8 | 4 |
| Carriers | 87 | 10 | 3 |
| Worries about cancer risk in relatives: | | | |
| Non-carriers | 32 | 56 | 12 |
| Carriers | 43 | 43 | 13 |

of developing cancer", "During the past year, how frequently did your worries about cancer have an impact on your daily functioning?", and "During the past year, how frequently did you worry about the risk of cancer in members of your family". Response categories included "almost never", "sometimes", "often", and "almost always". Those found to be HNPCC mutation negative were also asked to answer the following questions: "When were you told that colonoscopies were no longer necessary?", "Did you undergo colon screening before this date?", "Did you undergo colon screening after this date?", "Are you pleased that colon screening is no longer necessary?", and "Are you concerned about having been discharged from colon screening?". The questionnaire was sent, on average, four years (SD 2 years, median 3 years) after they had received their final counselling session during which, if tested, personal DNA test results were discussed.

## RESULTS

The HNPCC mutation negative counsellees comprised 12 men and 13 women with a mean age of 48 years at the time of completion of the questionnaire (SD 9 years, range 29–63 years). Of these 25 counsellees, three had been treated for benign polyps in the past; the remaining 22 had no personal history of polyps or cancer. The mean age of 31 mutation positive counsellees was 42 years (SD 10 years, range 26–58 years). Of the 18 male and 13 female carriers, 10 had been treated for polyps or colorectal cancer in the past.

As shown in table 1, none of the non-carriers reported being "often", or "almost always" worried about their own cancer risk, compared to 19% of the carriers (p=0.06). Only a small percentage of the non-carriers and carriers (3% and 4%, respectively) reported that concerns about cancer had had a significant impact on their daily functioning during the past year. Relatively few respondents reported being frequently concerned about the risk of cancer for other family members (12% and 13% for the non-carriers and carriers, respectively).

Of the 25 non-carriers, one had never had a colonoscopy, 10 had undergone one colonoscopy, six had had two colonoscopies, and eight had had three or more colonoscopies. Of the 22 counsellees who responded to the questions about discharge, most (82%) were pleased with the fact that they no longer needed to undergo screening. However, of the 22 respondents, seven (32%) reported that they were concerned with their discharge from screening. Of these seven, three had also reported that they were pleased that the screening was no longer required, suggesting the presence of conflicting feelings. Only one counsellee reported having undergone a colonoscopy about one year after having been discharged from the surveillance programme. This woman had been under surveillance since 1975 and had no personal history of polyps or cancer. Her motives for undergoing colonoscopy after having been discharged were unclear.

## DISCUSSION

These results suggest that, although worries about developing colorectal cancer are infrequent and most non-carriers are pleased that colonoscopies are no longer necessary, about one-third of non-carriers have some concerns about stopping surveillance. The reasons for these concerns are unclear. It might be that, as in the study by Michie *et al*,[11] some people doubt the accuracy of the genetic test results. This issue should be investigated in future studies, preferably with larger samples and using a prospective design. Although it is generally accepted that discharge from surveillance is one of the greatest benefits of genetic counselling for colorectal cancer, clinical geneticists and gastroenterologists need to be aware of the fact that, for some HNPCC mutation negative family members, concerns remain. During the final consultation with the geneticist or gastroenterologist, these concerns should be addressed and, depending on local guidelines, participation in a general population surveillance programme might be recommended.

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