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Communication and Technology in Genetic Counseling for Familial Cancer

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Abstract

When a cancer predisposing germline mutation is detected in an index case, the presence of the underlying syndrome is confirmed and the potential for predictive testing of at-risk relatives is established. However, the reporting of a positive family history does not routinely lead to communication of information about risk to close, much less distant relatives. This review summarizes information technology utilized to address penetration or “reach” of knowledge of risk within extended families, including the use of telephone and video counseling to reach distant patients, and anticipate novel internet-based processes for communication between investigators and relatives.

Keywords

colorectal cancer; familial cancer; genetic testing; genetic counseling; hereditary cancer; hereditary nonpolyposis colorectal cancer; information technology; Lynch syndrome

Introduction

A patient found to have cancer, especially if occurring at an early age and with similarly affected relatives, may be found to have an underlying germline mutation that predisposes to cancer,¹ confirming the presence of the suspected syndrome and serving as a foundation for predictive mutational testing for at-risk relatives. Pedigree inspection of a mutation-positive individual can readily identify relatives who would benefit from mutation testing. In reality, however, identifying collateral relatives and informing them of risk poses greater challenges. A variety of factors may account for this, such as: reluctance of the index patient to contact family members, lack of contact information, providers’ lack of resources to assist in tracking those at risk, and considerations of privacy and confidentiality.

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Conflict of Interest:

None of the authors have a potential conflict of interest.

The purpose of this paper will be to summarize advances in information technology that foster communication regarding inherited cancer risk. These will stress measures and challenges to facilitate the counseling process itself. In addition, we emphasize measures to render a more efficient process of identifying and reaching potentially at-risk collateral relatives, to overcome some of the challenges.

Methods

Sources included a comprehensive PubMed search for the terms distant relatives, extended family, family networks, and communication among family members in conjunction with HNPCC/LS, complemented by our own approaches at Creighton University and the University of Texas MD Anderson Cancer Center.

Current practice of genetic counseling

The prevailing model for genetic counseling involves a referral, within or between institutional providers. The counseling session would generally involve the patient, with or without a cancer diagnosis, a few family members (spouse, children, perhaps siblings or parents), a genetic counselor, and perhaps another cancer genetics professional such as a physician. The face to face encounter, much like any other clinical consultation, but emphasizing family history and with the goal of confirming a monogenic disorder, if present, identifying a mutation, and improving family management by predictive testing and coordination of clinical services. The patient with a positive mutation test is encouraged to communicate with his or her parents, children and siblings, in the hope that they will be seen for predictive mutation testing. The standard of care is to provide the patient with a detailed letter and/or information sheet to share with their family member covering the clinical features and management of the disorder in question, the findings from the mutation testing, and a description of how predictive testing works, including clinical implications of both positive and negative test results. The elements of genetic counseling of cancer risk have been nicely summarized by Ken Offit, including a list of principles underlying consent to have genetic testing.²

Genetic Counseling and Information Technologies

Shortcomings in the existing practice model

There are several limitations in the current genetic counseling model. Genetic counseling is quite time-consuming, and the counseling may be very poorly reimbursed, if at all. Although perhaps little can be done about reimbursement patterns at this time, there are measures that have been developed to make the counseling process more efficient.

Remote Capture of Family History

One of the most time-consuming chores of the genetic counselor is collection of family history information and construction of a family pedigree. For decades, this approach has been simplified by the patient completing a family history questionnaire. If the family is to be followed prospectively, this information is ideally transcribed into a database. Some databases maintained by academic centers are quite elaborate and essentially become

registries for the long-term follow-up of families, in some cases making it possible to gradually identify at-risk relatives to extend the pedigree. When a given patient and family are evaluated at a center offering more comprehensive services, there is a greater likelihood that a registry will have resources supporting outreach. In recent years, some centers have simplified the family history collection process by having patients enter information into an online questionnaire that populates a database. MD Anderson uses such a system, which manages appointments and serves as a confidential source of information about tests that have been performed. When a patient's initial genetic counseling appointment is created, the web-based kiosk can be accessed by the patient and a link is provided to a questionnaire that populates a database that can then be reviewed by the genetic counselor. Limitations include the need for a genetic counseling appointment, the need for the patient's ability to navigate the web, and sufficient time prior to the appointment for the patient to access and use the portal and for the genetic counselor to review the database. MD Anderson is currently moving toward a web-based platform for use by other family members. The Ohio State University Comprehensive Cancer Center enrolls relatives of index patients and provides a website where they enter information about themselves and receive a personalized prescription that includes screening recommendations. The participant can access a link to find local gastroenterologists. Half of the participants are randomly assigned a patient navigator who follows up after the online session.³

Poor follow-through with referrals

In their landmark population study of hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome [LS]) frequency in Ohio, Hampel et al.⁴ were able, with the support of the NIH, to identify incident cases of colorectal cancer (CRC), screen the tumors for microsatellite instability (MSI), and work with the patient's local hospital in the interest of achieving near-universal germline testing of those with informative MSI studies and/or family history. When the study was completed, the proof of principle had been established for performance of MSI-driven mutational testing, including a testing algorithm that provides an excellent clinical approach. But when this team attempted to incorporate this algorithm into their clinical practice setting, some key challenges became evident, including the need for a referral from the clinical center to medical genetics. Whereas the follow-through with testing had been greater than 80% in the original study, it fell off to less than 25% when a referral and clinic appointment with medical genetics was required.⁵

One solution is to simply have the genetic counselor(s) housed in the clinical center that is considered “home” by the patient. Thus, at the MD Anderson Cancer Center, where genetic counselors see patients in the GI center, uptake of counseling and of testing consistently are at 80% or greater (PML, unpublished data). However, even these measures to facilitate the logistics of counseling/testing for the convenience of the patient continue to rely on the paradigm of face-to-face counseling.

Because of unusual questions posed by cancer susceptibility, such as risk to potentially numerous near and not-so-near relatives, a variety of novel approaches to counseling have been undertaken. At Creighton University, where large families are commonly encountered, the so-called “Family Information Session” or FIS,⁶ initiated through collaboration between

genetics unit staff and motivated family members, has involved a visit to a local community center, with a didactic teaching session in a small group counseling setting followed by private, individual counseling.. This approach has enabled the identification of at-risk relatives with limited knowledge of their susceptibility prior to the intervention. Those who attended an FIS were significantly more likely to undergo mutation testing, as discussed below.

Unlike these large, individual, mutation positive families involved in the Creighton programs, Ridge et al.⁷ addressed different resource and efficiency issues in British Columbia, Canada. Their solution to long delays for counseling appointments was to have consenting patients attend group counseling sessions with other women of comparable risk. In a fashion similar to Creighton's FIS, the efficiencies of scale had to do with the use of didactic teaching materials for those who shared a common problem. Overall satisfaction was good, with group dynamics largely viewed as an advantage. However, about one third of the women offered the group counseling declined for various reasons, such as desire for confidentiality. Among those attending the sessions, some complained of limited ability to adequately address individual concerns. About half required additional individual follow-up, but this was generally accomplished over the phone. Like Creighton's FIS, the British Columbia effort may not be an approach that can be readily adopted in the community practice setting or for small and dispersed families. Clearly, other creative approaches are warranted.

The traditional face-to-face counseling model faces many issues having to do with how counselors may most effectively utilize their time, including issues of interaction with physician providers and how billing for time is addressed.⁸

Technologies Used to Enhance Genetic Counseling

The studies described above for large-scale counseling of patients and families generally do still adhere to the traditional model of in-person counseling with its limitations.

In the interest of utilizing emerging information technologies to supplement or substitute for some of the more standard, repetitive elements of genetic counseling, a number of studies have described the use of telephone counseling, videoconferencing, and web-based strategies for communicating information about cancer-prone diseases such as HNPCC/LS, hereditary breast-ovarian cancer (HBOC), and other adult-onset cancer susceptibilities. This section will take these up in the order of progressively more “high-tech” approaches.

Telephone conferencing—The goals of telephone counseling, the most low-tech outreach, are mainly the convenience of the patient, meeting increasing demand, and reaching rural patients. The main issue is the equivalency or not of this most basic method of “remote communication.” One helpful example was from the Karolinska Hospital in Sweden.⁹ About 200 patients referred for counseling over one year received a letter proposing randomization to in-person or telephone counseling. Most consented, with pre- and post-intervention questionnaires completed by study participants. Regardless of counseling method, all patients were offered a follow-up visit with a medical provider. Virtually no differences were observed between the two groups according to measures of

expectations of and satisfaction with genetic counseling, nor for measures of cancer worry and quality of life. Telephone counseling was less time consuming and was shown to be a more cost-effective alternative.

Graves et al.¹⁰ performed a prospective randomized study involving 90 BRCA1/2 mutation carriers. They investigated the effect of psychosocial telephone counseling (PTC) following standard genetic counseling (SGC). Anxiety, depression, and genetic testing distress were measured. At 6 months, PTC reduced depressive symptoms, genetic testing distress, and clinically significant anxiety compared with SGC. There were no significant differences between the methods at the 12-month follow-up. PTC as an adjunct to SGC appears to offer modest short-term benefits for distress and anxiety. (Note that this study did not compare stand-alone telephone counseling with standard genetic counseling, but looked at it only as an adjunct to standard counseling.) Telephone counseling was investigated by Sutphen et al.,¹¹ who found that it increased knowledge of cancer risk, increased intention to change health-related behaviors, and was found to be highly satisfactory by participants. However, long-term effects were not studied.

Halbert et al.¹² determined that while most *BRCA1/2* mutation carriers were likely to complete a psychosocial telephone counseling intervention, those with a personal history of breast or ovarian cancer were less likely to complete the intervention, while those with higher cancer-specific distress and those with greater perceptions of social support were more likely to complete the process.

Videoconferencing—Coelho et al.¹³ focused on 37 at-risk familial breast-ovary cancer subjects from outlying centers several hours' travel from the counseling center. They were offered face-to-face videoconferencing. PowerPoint presentations were used by counselors in both instances. A knowledge and satisfaction survey was completed by all evaluable subjects. Overall, scores on pre- and post-test counseling improved by a similar magnitude in each group and no significant differences in satisfaction with the counselors or overall experience were found. The basis for selecting subjects for face-to-face versus videoconferencing was not described, and it did not appear that there was randomization to the counseling arm. It appears that the videoconferencing was conducted with subjects physically present at the outlying clinics, rather than from their homes, decreasing the potential for hardware and software challenges, but still requiring modest travel on the part of the subjects.

A significant concern arising from this study and likely others is that of "sustainability" or continuation of the program once proof of principle is established. Correspondence with a senior author of this study indicates that the videoconferencing program was not continued substantially beyond the period of the study in question.

Zilliaccus et al.¹⁴ undertook a similar approach in Australia. Women residing near the counseling center were recruited for in-person counseling, while those near more remote sites were offered videoconferencing. For essentially all measures, the outcomes were comparable, and the teleconferencees actually scored higher on the measure of perceived personal control. Notably, in the case of remote subjects, a local genetic counselor was

present in the remote site clinic with the patient; only the counseling physician was teleconferenced to the patient. Conversely, a counselor was not always present for the in-person visits, so the effect of the counselor, potentially very significant, could not be altogether controlled.

As opposed to these studies, in which the teleconference was held at a central counseling center, Meropol and colleagues¹⁵ at the Fox-Chase Cancer Center in Philadelphia sent webcams to the homes of consenting subjects that had been identified as being at risk of *BRCA* mutations. Most of the approximately 30 participating subjects were satisfied with the content and tone of the remote-access genetic counseling session. There were fairly common technical glitches that will likely be resolved with continued improvement in consumer-based telecommunication.

It would seem that the primary goal of remote counseling is the delivery of counseling to patients in distant and often rural areas without local access to genetic counselors. When this is done by videoconference, ideally in the patient's own home, it opens up new opportunities for the further use of information technology, including videos and narrated slide presentations. Reliance on such supplemental materials offers the potential for more efficient use of the genetic counselors time.

Web-based strategies—The combination of remote web-based access and pre-packaged content means that more and more of the traditional content-oriented materials made available by providers will have already been reviewed by the patient on-line. Several studies have shown that from the standpoint of content, CD-ROM and similar materials provide learning that is on a par with that provided by counselors in person.¹⁶⁻¹⁹ So our initial step for the patient from a family with a known mutation may be to simply achieve an efficient assessment of the patient's need for information, and the available resources to meet their informational needs.

Use of Technology to Identify Those at Risk

Moving on from counseling of the index patient, with or without cancer, but typically with a germline mutation detected, one is confronted with the challenge of identifying and testing at-risk relatives. This has been termed “cascade” testing.²⁰ When characterized, the number of at-risk relatives undergoing testing appears to be quite variable^{4,21-23} (Table 1). Studies in familial breast-ovarian cancer (FBOC) and HNPCC/LS indicate that, on average, no more than about half the evaluated at-risk relatives of mutation carriers underwent predictive testing themselves. Additionally, these figures are generally limited to siblings and offspring, with values amongst extended relatives being virtually unknown. One can infer that the lack of data on testing in distant relatives relates to the difficulty in simply collecting that information in the first place. If the efforts of the index case are relied upon, there will necessarily be significant biases; only the most motivated patients and families will contribute any data. If the investigator initiates contact, concerns about privacy and confidentiality at the institutional review board (IRB) level may preclude the effort getting under way. Even if the investigator initiates all contact with distant relatives, such relatives

cannot be contacted without the index case having provided at least some contact information, again raising some degree of responder-bias.

It does appear that a substantial proportion of patients want help from their providers in communicating with relatives. Mesters et al.²³ in conducting qualitative interviews with Dutch LS patients, found there to be "...a tendency to rely on medical care/experts for more technical information". Further, "a disappointing contact in the early dissemination process concerning the hereditary information seemed to increase the chance that the index patient would give up". This was echoed in the qualitative work in LS by Peterson et al.²² Among these families, spread of risk information, to an unspecified degree of kinship, was by "word of mouth," that is, individual conversations that had not been planned, scripted or organized in any particular fashion. But it appeared that communication to distant relatives was quite limited, in that communication seemed to be limited to the nuclear family.

Given the vagaries and limitations of patient initiated and patient/family propagated communication, what measures might be employed to provide more structure for the communication process, or to even "take over" the communication process when desired by the patient? If the index patient wants help in contacting relatives, he or she could routinely provide consent for the provider to initiate such contact. This should avoid any violation of HIPAA and related institutional, state, or federal policies. This typically would follow some initial notification by the index case to the relative that such a communication was in the offing, though such notification is not something that any policy necessarily requires.

The problem with this apparently reasonable approach is that it simply is not how the process has ever really worked. Direct communication with relatives, even with the consent and encouragement of the patient before us, is generally considered beyond the scope or "boundary" of customary patient care. In the U.S., reimbursement for genetic counseling, even of the index cancer patient, is variable, with little or no provision made for the time devoted to counseling of more distant relatives.

If evaluation of extended families and the members at risk is not something that is a routine part of medical practice, how does it get accomplished? Many academic centers have registries of sorts that are supported through funded research and/or philanthropic resources. However, these are highly variable, with most programs struggling on a day-to-day basis to accomplish any sort of outreach to at-risk relatives. As such, the overall matter of communicating risk information to extended families is simply an unmet need in most instances. In other words, there seems to be a divide between the modestly encouraging uptake of genetic testing in siblings and children of mutation carriers on the one hand, and the more disappointing penetration of testing into more distant relatives, some of whom appear to be obligate mutation carriers. Most people are in frequent contact with their siblings and children and are highly motivated to seek their welfare. They often have less-frequent communication with cousins and more distant relatives and do not hold the same stake in their health maintenance.

The few examples in which efforts to communicate with extended family members have occurred are worth examining in a bit of detail.

Myers et al.²⁴ developed Kintalk.org which is a novel communication-based tool for LS families that is yet to be validated in regards to efficacy and utility among families. This tool was developed to address the failure of many families to share their genetic information. The advantage of Kintalk.org's system is that it is designed to allow patients to share their genetic information through an email invitation the patient generates in Kintalk.

Aktan-Collan et al.²⁵ in 2007 undertook a study to contact relatives of mutation carriers in 101 Finnish LS families with known mutations and in which considerable genetic counseling had already been undertaken. Pedigrees had already been constructed utilizing population-based and cancer registries, with 286 at-risk relatives identified, apparently without having to engage in significant information-gathering from index-cases. Relatives were contacted by letter, which included a return that contained a consent form which, if signed, agreed to being called by phone with further information about genetic counseling and testing. The letter did not refer to the specific fact that LS was known to exist in the recipient's family. A survey collected demographic information, the recipient's sense of the presence of family cancer history, worries about personal cancer risk, history of screening, and attitude toward being directly contacted by providers about such a health matter.

In all, 51% of those contacted agreed to participate further in the study, 39% simply did not reply, and 10% actively refused further participation, with older and unmarried most likely to actively decline. About three-fourths of consenting subjects did follow through with genetic predisposition testing. A full 97% of those contacted expressed approval of direct contact by health-care providers, though it is predicted that the 49% not responding at all or who had refused participation would likely have scored lower in this regard. Considering that all contacted subjects were already known by the investigators to be at 50% risk of mutation carriage, it should perhaps not be surprising that 74% considered cancer risk in their family to be increased. Among those perceiving an increased cancer risk, about half expressed worry and about a third had sought any sort of counseling, but only 21% had ever had a colonoscopy.

Several elements of this study are a bit unsettling. It may have been disingenuous to have failed to note the known presence of LS or the source of information that had targeted the recipient for communication. This does underscore the authors' appreciation for the sensitive nature of family risk information and frames for the future a possible debate over just how to best alert family members as to their risk. It is also noteworthy that no follow-up was provided for in the case of relatives that did not respond to the initial letter, out of a stated concern that the appearance of harassment be avoided.

In their discussion, Aktan-Collan and colleagues emphasized that in countries with national cancer and death registries, such as Finland and Denmark, identifying those at risk can be very much facilitated by such a registry. They concede that in countries without such registries, such as the US, the identity of at-risk relatives can only come about through information volunteered by the index case or other helpful relatives.

Recent Measures Employed to Communicate with Relatives

There are surprisingly few studies that have attempted to evaluate the extent of communication within cancer prone families. Fewer still have assessed interventions intended to increase uptake of information about risk and/or to encourage predisposition testing. The following studies have shed some important light on the current state of the art.

Current Status of Family Studies

Modern genetic counseling for generally adult-onset disorders, including cancer susceptibility, stresses the ability of mutation testing to clarify risk for offspring of affected relatives, however distant from the proband they may appear to be. Supportive and positive patterns of communication within families tend to be associated with sophistication at the level of health awareness/preventive screening adherence and with having health insurance that covers costs of such services, including genetic testing.^{26,27} Conversely, poor communications predict suboptimal levels of health maintenance and low likelihood of good protective health insurance. As is so often the case, those families needing the greatest intervention to overcome disabilities are also the families least likely to receive such services. Most U.S. health insurers will pay for DNA testing for those relatives clearly at 50% risk in the setting of a known mutation.²⁷ Most group insurance is employment-related and few of us work for the same company as our parents, siblings, or children. Consequently, individual insurance companies have no interest in, much less any mechanism for, investigations to identify those relatives that might benefit from mutation testing. Even if they did, patient fears of self-interested motivations such as cancellation of insurance or loss of employment would impede such undertakings.

The question of how genetic testing can alter the cancer risk status of other family members was partially answered by Watson et al.²⁸ By studying Creighton's LS and HBOC families with deleterious mutations, they showed that testing for cancer-associated mutations in relatives could, on a fairly large scale, reclassify hereditary cancer risk status from uncertain to certain. Although degree of kinship to the index case was not specified in this report, the high number of patients reclassified from 50% *a priori* risk to "non-carrier" harbored significance for their screening and for the reclassification of all their descendants as noncarriers. The converse of reclassification from high risk to carrier status was also observed. Importantly, 60% of persons with a carrier risk status change were not themselves tested; their risk status changed because of a relative's test result. Figure 3 is a pedigree which depicts this phenomenon of use of LS mutation to track family cancer risk. Pedigrees with this much detail are rarely performed in the clinical genetic setting. It gives many examples of how the presence and/or absence of the deleterious MMR germline mutation can be highly informative in identifying individuals at increased risk or at general population risk.

BRCA Mutation-prone Families: Limited Contact with Distant Relatives

Among hereditary cancer syndromes, the literature on family study dynamics is most abundant in regard to the HBOC syndrome (*BRCA1/2* germline mutations).

HBOC studies reported a high degree of DNA testing uptake and of communication of test results to family members. However, most of these studies looked at only first-degree relatives of probands,²⁹⁻³² and presumably involved uniformly dedicated investigators and predominantly well-motivated subjects. Those studies including second- and third-degree relatives³³⁻³⁵ showed first-degree relatives to be significantly more likely to be informed of the proband's test result and to undergo genetic testing. However, in a study by Finlay et al.,³³ although disclosure to first-degree relatives was higher than to second- and third-degree relatives among relatives informed of the results, the difference in testing uptake between first-degree and second/third-degree relatives was nonsignificant. This suggests, optimistically, that once effective counseling as to nature and extent of risk is accomplished, relatives can be brought to appreciate that risk of mutation remains high (due to affectedness of one's own parent) even when degree of kinship to index case is low.

Koehly et al.³⁶ reviewed a total of 5466 personal network members of 183 female participants from 124 families with known *BRCA1/2* germline mutations who were in the Breast Imaging Study. Significant findings (all $p < 0.001$) showed that those information gatherers were more often female, parents, and emotional support providers, while disseminators of information were more likely female first- and second-degree relatives, family members in the older or same generation as the participant, those with a cancer history, and providers of emotional or tangible support. Blockers tended to be spouses or partners and male, first-degree relatives. These findings give understanding regarding how family members can effectively gather risk information and disseminate it widely, thereby encouraging additional discussions regarding shared family risk. Because of the gender-specific implications of *BRCA1/2* results, it is unclear to what degree the male vs female results would transfer to other disorders such as LS.

HNPCC/LS Families

Although the literature regarding HBOC is more plentiful, similar results have been seen in preliminary work with LS.

Burton-Chase et al.³⁷ examined colonoscopy adherence and patient attitudes toward CRC colonoscopic screening in patients who underwent genetic counseling and DNA testing for LS and concluded that genetic counseling and testing improved adherence to the risk-appropriate colonoscopy guidelines for CRC. Increasingly positive attitudes toward CRC screening followed mutation-positive findings, thereby potentially reinforcing long-term colonoscopy adherence. Hughes Halbert et al.³⁸ evaluated adherence to CRC screening recommendations following genetic testing for LS in 98 men and women without a personal history of CRC or colectomy who were identified from 11 extended LS families. After controlling for clinical factors and pre-test screening practices, mutation carriers were still more likely than test decliners to participate in the colonoscopy preventive strategy; in fact, the difference in colonoscopy use between noncarriers and decliners was insignificant.

Peterson et al.²² investigated knowledge about how genetic counseling and testing information is communicated within LS families. In all, 39 adults from 5 families with LS germline MMR mutations were queried as to how information from genetic counseling and testing was disseminated within their families, and the manner in which family members

reacted to and acted upon this information. This included family members who had been diagnosed with a LS cancer, unaffecteds who were at 50% risk of harboring a mutation, as well as their spouses. Participants included those who had or had not undergone testing. All index cases had shared the news about the LS mutation with at least some at-risk relatives. In communication about LS genetic counseling and testing, mutation noncarriers, “nontesters,” and those who were not biological relatives showed less interest in discussing genetic counseling and testing. They perceived these processes as being less relevant to them. While family members were often willing to share educational preventive information, probands and mutation carriers were especially more likely to inform extended family members, and encourage other family members to seek counseling followed by DNA testing. Furthermore, those family members who had been persuaded by the proband to seek these preventive activities were found to be more likely to seek counseling and testing and, indeed, they sought these services sooner.

Codori et al.³⁹ measured uptake of genetic testing for LS among first-degree relatives of CRC patients. They compared 77 test acceptors and 181 test decliners, controlling for distance from the testing center. Significant predictors of test uptake were higher perception of increased risk, greater perception of ability to cope with unfavorable genetic information, more frequent cancer thoughts, and a personal history of at least one colonoscopy.

Our group has further shown a difference between testing uptake by nonprobands depending on whether the family of the proband has participated in an FIS, in which expert providers and counselors met in person with multiple family members in a convenient geographical location, providing information about LS risk and an opportunity for testing for the family's MMR mutation. Ninety-seven families with a known MMR mutation were studied. The difference between the FIS and non-FIS families in proportion of family members tested was statistically significant ($p=0.003$) and this difference was more pronounced in family members whose relationship to the proband was beyond first-degree ($p<0.0001$). In families that participated in an FIS, of the at-risk individuals, 20% were tested vs 13% in non-FIS families (confidence interval 16-25% and 10-15.5%, respectively). Thus, an opportunity for the family to meet with a provider and genetic counselor made a difference in testing uptake, particularly for non-first-degree relatives.⁴⁰

Aktan-Collan et al.²⁵ stress that identification of patients'/families' hereditary cancer predisposition may be of limited significance if there is a failure to inform family members, test them when appropriate, and enter them into a targeted cancer prevention program, a concern that has been expressed by others. The active recruitment of potential high-risk patients who could benefit from education, testing, screening, and management, is a novel approach. It does, however, raise the ethical questions of respect for autonomy and privacy (the right to be left alone) vs. beneficence (duty to warn one of a danger, the existence of which the reasonable person would want to know).

Aktan-Collan et al.²⁵ note that based on their early experience involving their predictive genetic testing program,⁴¹ family members who had not applied for genetic counseling and who developed colon cancer, without exception, expressed disappointment that their relatives had not warned them of their cancer risk. In addition, their large-scale genetic-

testing program “...had been encouraging, confirming high levels of satisfaction and no serious psychological side-effects related to testing.⁴¹⁻⁴³ These results have since been confirmed by other studies showing similar trends.⁴⁴⁻⁴⁶”

Several groups have proposed that the duty to warn patients may help waive the requirement for confidentiality in cases of life-threatening disease where prevention exists⁴⁷⁻⁵¹...” In their survey of the literature, Aktan-Collan et al. found studies that acknowledged that in the interest of preventing harm when serious immanent or treatable conditions are present,⁵² confidentiality can be breached. “...Thus, the resolution of the conflict between confidentiality and the duty to warn is not unambiguous.”²⁵

There has been a recent call for genetic testing for LS, using MSI and IHC, of all CRC patients.^{4,53,54} This is supported by research that shows it to be a cost-effective method of cancer control.⁵⁵⁻⁵⁷ The U.S. Department of Health and Human Services, through its Healthy People 2020 initiative⁵⁴ has deemed communication of risk to be a priority, stating that “...Screening interventions could potentially reduce the risk of colorectal cancer among men and women with Lynch syndrome by 60 percent.⁵⁸” The efficacy, however, depends on dissemination of risk status information to relatives of the patient, making this effort even more essential.

Menko et al.⁵⁹ advised predisposed family members with MMR mutation diagnosis to advise their at-risk relatives relevant to the options of predictive DNA testing and preventive measures. Findings have disclosed that more than half of these relatives fail to receive the necessary information. Barriers to information transmission involve communication problems in concert with variable attitudes and practice among clinical geneticists where both medical and psychological and ethical judicial aspects have been identified. Resolution of the problem will involve clinical geneticists playing a more active role with the aim being improving procedures to inform family members of their LS status.

Conclusion

Our experience, coupled with a comprehensive literature review, indicates an unmet need for better access to counseling/testing and better identification of those at risk in extended families of mutation carriers. There is both a need and a desire for providers to contact at-risk family members, and to inform them directly of their risk and invite them to participate in genetic counseling and testing. However, the processes by which this might occur are only dimly seen at this time. The ethical and legal balance between confidentiality and the duty to warn need to be reassessed. The technical advances cited are merely tools, but hopefully tools that can enable a more efficient and focused view of the content to be communicated.

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Figure 1.

This is an extended pedigree wherein DNA testing yielded useful clinical genetic information about risk status as in the case of the proband (III-1) with three CRCs starting at a young age and whose daughter (IV-1) was found to be a carrier of the deleterious mutation while her son (IV-2) was negative.

Table 1**Penetration Within Affected Families of Mutation Testing for Cancer Susceptibility**

<u>Author</u>	<u>Disease</u>	<u>#tested/mutation</u>	<u>Comments</u>
Hampel ⁴	LS	500	---
Brooks ²¹	BRCA	(34-45%)	Counselees "encouraged to contact relatives"
Peterson ²²	LS	(57-64%)	Mainly qualitative
Mesters ²³	LS	---	Qualitative, noted high variability in family communication
Landsbergen ⁶⁰	BRCA	36%	High between family variation
Finlay ³³	BRCA	61% FDR 47% SDR	>90% disclosure to relatives
Cheung ³²	BRCA	---	75% with at least 1 relative tested

FDR = first-degree relatives

SDR = second-degree relatives