Cancers related to genetic mutations

Important psychosocial issues for Canadian family physicians

Tara E. Power, LLB, PHD **John Robinson,** PHD, RPSYCH

ABSTRACT

OBJECTIVE To review psychosocial issues family physicians might wish to be aware of when discussing genetic testing for predisposition for cancer with their patients.

QUALITY OF EVIDENCE Articles from academic journals were reviewed. Studies provided level II and III evidence.

MAIN MESSAGE Family physicians should be prepared to explore their patients' decisions for or against genetic testing, as well as to discuss the possible outcomes of a decision to test. While genetic testing has many potential benefits, patients are at risk of having psychosocial problems at many stages in a genetic testing inquiry. To minimize these problems, family physicians should discuss motivation for testing and the potential psychosocial effect of both deciding to undergo and deciding to forgo genetic testing for cancer-related genes. Also important are deciding whether patients qualify for the tests; coping with the waiting period before testing can be done; and discussing positive, negative, and inconclusive outcomes of testing.

CONCLUSION Family physicians are likely in the best position to discuss genetic testing for predisposition for cancer with their patients given their knowledge of both the tests and their patients' ability to cope with testing.

RÉSUMÉ

OBJECTIF Faire le point sur les aspects psychosociaux que le médecin de famille pourrait désirer connaître lorsqu'il discute de tests génétiques pour la prédisposition au cancer avec un patient.

QUALITÉ DES PREUVES Des articles de revues scientifiques ont été consultés. Les preuves obtenues étaient de niveaux II et III.

PRINCIPAL MESSAGE Le médecin de famille devrait être en mesure d'examiner avec le patient sa décision de subir ou non un test génétique et de discuter avec lui des issues possibles s'il décide de subir les tests. Même si le dépistage génétique comporte plusieurs avantages éventuels, le patient risque de rencontrer des problèmes d'ordre psychosocial à plusieurs étapes du processus. Pour minimiser ces problèmes, le médecin devrait discuter des motivations à subir les tests et des effets psychosociaux potentiels de la décision de subir les tests pour les gènes associés au cancer ou d'y renoncer. Il est également important de vérifier si le patient se qualifie pour les tests; de tenir compte de la période d'attente avant que les tests puissent être faits; et de discuter des résultats positifs, négatif ou non concluants du dépistage.

CONCLUSION Le médecin de famille est probablement le mieux placé pour discuter des tests génétiques pour la prédisposition au cancer avec son patient, parce qu'il connaît les tests ainsi que la capacité du patient à faire face au dépistage.

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Genetic testing is becoming available for an increasing number of genes that predispose patients to cancer (**Table 1**[1-6]). Although patients might initially have learned about genetic testing for cancer from the media and might ultimately be referred to specialists, family physicians are often their primary source of information.[7,8] This paper outlines some of the psychosocial issues involved in genetic testing for cancer to assist family physicians in fully informing and advising patients about the benefits and limits of testing.

Quality of evidence

MEDLINE and PsychINFO were searched from January 1956 to December 2005 using the key words "genetic testing" in various combinations with "cancer," "psychological," "sociological," and "ethics." Original research articles and review articles pertaining to motivation for or against genetic testing and to the effects of genetic testing were chosen. Most studies offered levels II and III evidence.

Levels of evidence

Level I: At least one properly conducted randomized controlled trial, systematic review, or meta-analysis
Level II: Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than one study
Level III: Expert opinion or consensus statements

Dr Power *and* **Dr Robinson** *are researchers in the Department of Psychosocial Resources at the Tom Baker Cancer Centre in Calgary, Alta.* **Dr Robinson** *also teaches in the Department of Oncology and the Program in Clinical Psychology at the University of Calgary.*

Why psychosocial issues need to be addressed

With the growing availability of genetic tests for cancer, family physicians are increasingly called upon to discuss the physical and psychosocial aspects of testing.[9] They often have the initial duty of informing and advising their patients about the risks and benefits of knowing about a family history of cancer and of undergoing genetic testing.[7,9]

What drives interest in presymptomatic testing for cancer-related genetic mutations?

Some authors have suggested that one of the best ways to minimize psychological distress around discussing the risks of cancer and genetic testing is to fully explore patients' motivation for undergoing or forgoing testing.[10,11] Family physicians are in a unique position to understand their patients' motivations, as their ongoing relationships with them can give insight into what patients truly wish to obtain from testing.[12] This paper outlines some of the motivational forces for or against testing that family physicians might want to explore with their patients.

Table 2[13-33] lists reasons commonly given by patients for their interest in genetic testing. Additional, more subtle, influences might, however, need to be explored. These include the following:

- fear and worry,
- a need for certainty and control, and
- anticipated unpleasant emotions.

It appears that those who are most fearful of cancer and who believe (rationally or not) that they are at high risk of developing a hereditary cancer syndrome are

Table 1. Prevalence of hereditary cancer syndromes, risk, and options for surveillance and prophylaxis

HEREDITARY CANCER SYNDROME	RISK IN THE GENERAL POPULATION (%)	RISK AMONG THOSE WITH THE MUTATION (%)	SURVEILLANCE OPTIONS	PROPHYLACTIC OPTIONS
Hereditary breast and ovarian cancer: BRCA1 and BRCA2 mutations	Breast cancer: 11-14	Breast cancer: 50-85[1]	Mammography (or magnetic resonance imaging, where available); clinical breast examination; and breast self-examination	Bilateral mastectomy Salpingo-oophorectomy[3]
	Ovarian cancer: 1-2[1]	Ovarian cancer: 35-45[2]	Pelvic examination; CA125 test[3]	
Hereditary nonpolyposis colorectal cancer	Colon cancer: 2[4]	Colon cancer: 40-90[4]	Colonoscopy[5]	Colectomy[4]
Familial adenomatous polyposis	Colon cancer: 2[4]	Colon cancer: 60-100[4]	NA	Colectomy[4]
Hereditary prostate cancer	Prostate cancer: 11[4]	Prostate cancer: 22-88[4]	Regular digital examination; prostate-specific antigen testing[6]	Prostatectomy[6]

NA—not applicable.

Table 2. Reasons for and against undergoing genetic testing for predisposition for cancer

REASONS FOR TESTING
To learn about children's or other family members' risk [13-24]
To enable more active surveillance (possibly to help catch developing cancer early)[14,16,25] or to assess for prophylactic surgery[13,17,21,22,24,26,27]
For reassurance[16,18,19,25,27,28]
To plan for the future (ie, child-bearing decisions)[17,22,26,29,30]
To help advance research[18,23]
To please family members[19]
REASONS FOR NOT TESTING
Potential difficulties with insurance coverage[16,31]
Problems with accuracy of genetic tests[19]
Negative reactions from family[16]
Disapproval of family physician[31]
Not believing that knowing genetic status will assist in preventing cancer[31,32]
Inability to cope emotionally if test result is positive for the mutation[30-33]
Mistrust in medicine[32]

most likely to desire genetic testing.[13,26,31,34-40] A review of the psychosocial issues in cancer genetics suggests that "it is not so much objective risk of developing cancer, but subjective, perceived risk that is most strongly related to test uptake and also preventions such as risk reducing surgery."[41] The role of worry as a motivator should be explored. Patients who could benefit from increased screening or prophylaxis might avoid testing out of fear, while other patients who are fearful or worrying about being tested might be disappointed by how little their stress is reduced by testing.

A sense of control and a sense of certainty have been found to be essential in successfully coping with health threats.[42-47] With presymptomatic genetic testing, the target of the desire for certainty[48] could range from certainty over future health to certainty about their children's genetic status.[14] A desire for control can vary from control over prevention (through prophylactic measures) to control of treatment planning.[15,32] If a family physician finds that these targets are indeed motivating patients' interest in genetic testing, the degree to which testing can provide control and certainty ought to be addressed. For example, the genetic test for hereditary nonpolyposis colorectal cancer (HNPCC) can offer a high degree of certainty that a patient will develop colon cancer, but this certainty is not 100%, nor is it certain as to the age at which a patient will develop it.[49] In contrast, a complete mastectomy, as a result of a BRCA1 or BRCA2 carrier testing result, might provide patients with a sense of control over the disease, but their risk of ovarian cancer remains uncontrolled without a prophylactic oophorectomy.

Patients might also need help from their family physicians in managing their anticipated emotional reactions to all the possible outcomes of such genetic testing. It appears that the decision to undergo or forgo genetic testing is as influenced by a desire to regulate emotional reactions in the future (ie, to avoid future regret, guilt, or worry about being at increased risk of developing cancer) as by the desire to deal with the potential physical health threat.[50]

Demographic influences

Family physicians discussing genetic testing with patients might consider potential demographic influences on the testing decision also. These include the following.

- Patients with a family history of cancer might be less interested in testing than those without such a history.[15,26,32,39,40,51,52]
- Education level might affect a patient's willingness to consider genetic testing. Although few studies support this hypothesis, some suggest that patients with less education are more likely to be interested in testing for HNPCC,[16] hereditary polyposis colon cancer,[53] and BRCA1 and BRCA2.[14] Family physicians might wish to consider their patients' education levels to ensure that decisions are based on a firm understanding of genetic testing.
- Age might increase the likelihood of seeking testing,[15,35,52] but it might also decrease it.[29,31,51]

Who qualifies for provincially funded testing?

The rules on who qualifies for provincially funded cancer genetic testing vary among provinces. **Table 3** lists websites and contact information for genetics clinics in each region of Canada. Patients often are eligible for genetic counseling, which involves reviewing family history of cancer and analyzing patients' risk, but do not qualify for genetic testing itself.[54] Family physicians might wish to ensure that patients are aware of the possibility of not qualifying for testing. Patients not qualifying might require extra counseling and support, as it has been suggested that patients who do not qualify for testing experience high levels of anxiety and worry as a result of not having their uncertainties addressed.[55]

Are patients prepared for the wait?

Patients need to know how long they will have to wait for test results, and family physicians should assess patients' ability to cope with anxiety during the wait. It is not unusual to wait between 1 and 2 years for full genetic sequencing and test results in Canada. Patients might require psychological support from family physicians during the wait, because that time can be most distressing, even more distressing than discovery of a positive mutation.[56]

Table 3. Information about cancer genetic testing: *For general information, see* **http://www.cancercare.on.ca/index_researchgenetics.htm**

REGION	ADDRESS OR WEBSITE
Newfoundland and Labrador	Provincial Medical Genetics Program, Health Sciences Centre, Room 2088, 300 Prince Philip Dr, St John's, NF A1B 3V6; telephone 709 777-4363; fax 709 777-4190
Maritime Provinces	Maritime Medical Genetics Service, IWK Health Centre, 5850/5980 University Ave, PO Box 3070, Halifax, NS B3J 3G9; telephone 902 470-8754; fax 902 470-8709
Quebec	Montreal: Clinique des cancers familiaux, Centre hospitalier de l'Université de Montréal, Pavillon Masson de l'Hôtel-Dieu, 3850 St-Urbain, Montréal, QC H2W 1T7; telephone 514 890-8104; fax 514 412-7131 Quebec city: Département de génétique humaine, Centre hospitalier de l'Université de Laval, 2705 boulevard Laurier, Québec, QC G1V 4G2; telephone 418 654-2103; fax 418 654-2748
Ontario	Cancer Care Ontario, 620 University Ave, Toronto, ON M5G 2L7; telephone 416 971-9800; fax 416 971-6888; website **http://www.cancercare.on.ca/index_researchgenetics.htm**
Manitoba	Clinical Genetics Health Sciences Centre, Children's Hospital, 685 William Ave, Winnipeg, MB R3E 0Z2; telephone 204 787-2494; fax 204 787-1419
Saskatchewan	Royal University Hospital, 103 Hospital Dr, Saskatoon, SK S7N 0W8; telephone 306 655-1692; fax 306 655-1736
Alberta	Calgary: Dr R. Brian, Lowry Clinical Genetics Unit, Alberta Children's Hospital, 1820 Richmond Rd SW, Calgary, AB T2T 5C7; telephone 403 943-7373; fax 403 543-9100 Edmonton: Medical Genetics Clinic, 853 Medical Sciences Bldg, University of Alberta Hospital, Edmonton, AB T6G 2H7; telephone 780 407-7333; fax 780 407-6845
British Columbia	Hereditary Cancer Program, BC Cancer Agency, 200–601 West Broadway Ave, Vancouver, BC V5Z 4C2; telephone 604 877-6000, extension 2198; fax 604 707-5931

Test results: positive, negative, or inconclusive?

As well as reviewing motivation for testing, family physicians should discuss the outcomes of testing with their patients.

Positive for mutation

Adverse psychological effects[57]: Although results of early research suggested patients might suffer great distress as a result of presymptomatic genetic testing,[58,59] recent studies have shown that carriers suffer little regret[60] and little psychiatric dysfunction,[61] and only a few report feeling distressed.[57] In fact, there is some suggestion that those at high risk of familial cancer who decline testing are actually at increased risk of depression.[62]

Certain characteristics, however, do make some patients more likely to be upset by a positive result. Patients with little social support who are initially highly distressed[63] or who have unreasonable expectations of the outcomes of genetic testing[64] can become depressed or anxious when results are positive. Support and services need to be available for patients traumatized by positive results,[54] and finding these services might fall to family physicians.

Insurance discrimination: In discussing genetic testing, patients might express concern about being able to get extended health or life insurance if results of a genetic test are positive. Although no case has yet tested the issue in the Canadian courts, the Canadian federal and various provincial governments have instigated legislation to protect patients' private medical information, including their genetic status. It is unclear how these statutes will hold up against the Canadian Institute of Actuaries, the Canadian Life Insurance Medical Officers Association, and the Canadian Life and Health Insurance Association's view that results of genetic testing should be available to insurance companies as part of insured patients' health history.[65] Currently, the Canadian Genetics and Life Insurance Task Force is attempting to develop a fair policy on integrating genetic information in the underwriting process.[66]

Disclosure of results: Another point of discussion should include disclosure of test results. In families with strained relationships, decisions about whom to inform and how to inform them could be difficult for patients.[60] Patients might also require support from their physicians when they disclose positive test results to children.

Further decisions: Patients should also be prepared to make further decisions should they be found to be carriers of the cancer-predisposing genetic mutation. Discovery of a positive test result might lead to more uncertainty about future health because the preventive treatment options are limited or life-altering. This is the case with bilateral mastectomy and oophorectomy to prevent breast or ovarian cancer.[67] On the other hand, discovery of a genetic mutation might give patients psychological reassurance if they have

opportunities for more intense surveillance strategies or even risk-reducing surgery.

Negative for mutation

Distress: Patients with a strong family history of cancer, might not be reassured by finding out they do not have a gene mutation.[60,68] "Survivor guilt," or guilty feelings at not having the mutation in a family where some members do, can cause distress.[69,70]

Future surveillance: Negative test results sometimes give patients such a sense of security that they fail to continue with recommended surveillance.[17,71] Physicians need to remind these patients that those who test negative carry at least the same risk of cancer as the general population and that it remains important for them to have regular cancer screening.

Inconclusive test results. Unfortunately, genetic testing sometimes produces inconclusive results. Because only a small proportion of mutations on cancer-related genes have been proven to be linked to development of cancer, these are the mutations for which genetic testing is done. The role of many mutations, however, is unclear, and they might in fact be related to predisposition for cancer. Genetic testing results are said to be inconclusive in these situations. As many as 75% of genetic tests for cancer gene mutations are estimated to result in inconclusive findings.[72] The greatest psychological morbidity is associated with patients who receive inconclusive results.[73,74] Although largely not studied, it could be that patients would cope better with such findings if they were prepared ahead of time for such a possibility.[11]

Conclusion

Family physicians might be called upon to assist their patients with the psychosocial issues that accompany genetic testing for cancer. Physicians should be prepared to explore their patients' motivation for undergoing or forgoing genetic testing as well as to discuss the outcomes of testing decisions. Such discussion should cover who is qualified for testing and why patients might not qualify; coping with waiting for results; and the ramifications of having positive, negative, or inconclusive results of the tests.

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Competing interests

None declared

Correspondence to: **Dr Tara Power,** *Department of Psychosocial Resources, TBCC-Holy Cross Site, 2202 Second St SW, Calgary, AB T2S 3C1; e-mail* **Tarapowe@cancerboard.ab.ca**

EDITOR'S KEY POINTS

- Genetic testing for predisposition for hereditary cancers is becoming increasing available, and more tests are coming in the future. While specialists will be involved, family doctors will still be an integral part of the counseling team, given their long-term relationships with their patients.
- Counseling should first explore patients' motives for testing. There are both positive and negative reasons for choosing to test, including fear, worry, and wanting a sense of certainty and control.
- Family doctors also need to discuss whether their patients qualify for testing and what positive, negative, or inconclusive test results mean.
- The potential outcomes of a decision to test, whether active surgical intervention, heightened surveillance, or something else, need to be explored before testing is carried out.

POINTS DE REPÈRE DU RÉDACTEUR

- Il existe de plus en plus de tests génétiques pour la prédisposition aux cancers héréditaires et l'avenir nous en réserve bien davantage. Les spécialistes auront toujours un rôle important, mais le médecin de famille participera aussi à l'équipe conseil en raison de sa meilleure connaissance du patient.
- Le médecin devrait d'abord vérifier pourquoi le patient désire subir les tests. Il existe des raisons positives et négatives pour prendre cette décision, y compris la peur, l'inquiétude, et la soif de certitude et de contrôle.
- Le médecin de famille doit aussi s'assurer que le patient se qualifie pour les tests et discuter avec lui de la signification d'un résultat positif, négatif ou non concluant.
- Avant les tests comme tels, il y a lieu d'en examiner les issues potentielles, qu'il s'agisse d'une intervention chirurgicale active, d'une surveillance accrue ou d'autres conséquences.

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When the thoughtful historian gets far enough away from the nineteenth century to see it as a whole, no single feature will stand out with greater distinctness than the fulfilment of the prophecy of Descartes that we could be freed from an infinity of maladies both of body and mind if we had sufficient knowledge of their causes and of all the remedies with which nature has provided us. Sanitation takes its place among the great modern revolutions—political, social and intellectual. Great Britain deserves the credit for the first practical recognition of the maxim salus populi suprema lex. In the middle and latter part of the century, a remarkable group of men, Southwood Smith, Chadwick, Budd, Murchison, Simon, Acland, Buchanan, J.W. Russell and Benjamin Ward Richardson, put practical sanitation on a scientific basis. Even before the full demonstration of the germ theory, they had grasped the conception that the battle had to be fought against a living contagion which found in poverty, filth and wretched homes the conditions for its existence. One terrible disease was practically wiped out in twenty-five years of hard work. It is difficult to realize that within the memory of men now living, typhus fever was one of the great scourges of our large cities, and broke out in terrible epidemics—the most fatal of all to the medical profession. In the severe epidemic in Ireland in the forties of the last century, one fifth of all the doctors in the island died of typhus.

Sir William Osler (1849-1919)

The Evolution of Modern Medicine

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