

PRESYMPTOMATIC GENETIC TESTING FOR CANCER

A guide to counselling patients about their risks

Tara E. Power, LLB, PhD and John Robinson, PhD, RPsych



Top-line summary

People facing the decision of whether or not to undergo presymptomatic genetic testing for cancer gene mutations often begin their quest for knowledge with their primary care practitioner — who is accustomed to helping patients who need information about all aspects of a medical decision. Here, *Oncology Exchange* describes the psychosocial, ethical and legal issues facing those considering this question, prior to seeking more indepth information from specialists and genetic counsellors. The article introduces the drivers of patient interest in testing and suggests ways to help them appreciate the limitations of genetic testing for satisfying these drives. The potential legal and psychosocial outcomes of testing are then outlined, to guide practitioners in fully informing patients of the possible harms and benefits of choosing or foregoing these investigations. While intended primarily for primary care practitioners, this information is also relevant to oncologists and other members of the oncology team when counselling patients and families about options for close relatives of people with cancer.

From the time of Hippocrates, the medical practitioner's credo to has been *primum non nocere*: do no harm. Recognizing that some medical treatments may do harm, and that the patient should be the one who decides whether the potential harm of a treatment is worth the potential benefit, the ethical principle of informed consent has become a standard in medicine. To be fully informed, the patient needs to understand both the physical and psychosocial aspects of the situation.

WHY ADDRESS PSYCHOSOCIAL, ETHICAL AND LEGAL ISSUES?

Deciding whether or not to undergo genetic testing for cancer gene mutations carries the same imperatives as any medical genetic testing. Ethically, patients need to be fully aware of all of the potential pitfalls and outcomes of the testing. Further, patients will likely gain greater satisfaction with their testing decision — thereby maintaining a positive alliance with the medical practitioner — if the practitioner recognizes and addresses the motives behind the decision. As with many medical decisions, it is difficult to characterize a “good” or “right” decision and to know what influences a good decision. Evidence as to the most effective interventions in assisting an individual to make a good decision is sparse. Medical decision-making research suggests, however, that in good decisions, the patient:¹

- has full knowledge of the options and the potential impact of each
- experiences minimal anxiety and decision conflict
- is fully involved in the decision process

Addressing a patient's reasons or drives for wanting to be tested — and whether the test result can fulfill these drives — can avoid later patient dissatisfaction and disappointment. Fully-informed consent requires exploration of all of the possible reasons a patient may be making a decision, outlining them explicitly, and then deciding what is important.

Tara E. Power, LLB, PhD is a clinical psychologist and former practicing lawyer. She is currently a Canadian Cancer Society research fellow (funded through the National Cancer Institute of Canada) with the Department of Psychosocial Resources, Tom Baker Cancer Centre, Calgary AB.

John Robinson, PhD, RPsych is a clinical psychologist associated with the Department of Psychosocial Resources, Tom Baker Cancer Centre and the Department of Oncology and Program in Clinical Psychology, University of Calgary. *Address for correspondence:* Dr. Tara Power, Dept of Psychosocial Resources, TBCC—Holy Cross Site, 2202 Second Street SW, Calgary, AB T2S 3C1; Tel: (403) 355-3225; Fax: (403) 355-3206; email: tarapowe@cancerboard.ab.ca

DRIVERS OF INTEREST IN PRESYMPTOMATIC GENETIC TESTING

Certainty and control

Few studies have investigated what drives the desire to undergo or forego genetic testing specifically for cancer-related mutations. Studies on the full gamut of genetic disorders for which testing is available suggest that individuals seek testing in order to gain certainty and a sense of control over their health. Issues for which people desire certainty may range from their own future health to their children's genetic status.² Individuals' targets of control also appear to vary, from control over preventive measures that can be taken, to surveillance, to treatment planning.^{3,4} A sense of control is essential to successfully coping with a health threat.⁵⁻¹⁰

Examination of the uptake rates of testing across the genetic disorders studied confirms that certainty and control play a major role in interest in genetic testing (Table 1). A test's ability to tell an individual that they have a 100% chance of developing a disorder provides certainty. For example, a positive test for Huntington's Disease

provides psychologic certainty as to one's future health and death. The availability of a prophylactic treatment option provides a sense of control over one's health, as with a colectomy done as a result of a positive test for familial adenomatous polyposis (FAP).

Medical practitioners can help patients articulate the extent to which desire for certainty and control drives them to undergo genetic testing. The degree to which these desires are likely to be satisfied then needs to be clarified. It is important that the practitioner be able to explicitly inform the patient how much the test they seek will answer their desire for certainty and control. For example, the genetic test for hereditary nonpolyposis colorectal cancer (HNPCC) offers a fair degree of certainty, but not 100%, that a patient will develop colon cancer — but the age at which cancer will develop is unknown. Regarding the drive for control, surveillance via colonoscopy rather than colectomy is currently recommended for those who test positive. Surveillance allows disease to be discovered at an earlier stage, in turn leading to better prognosis, but does not provide control over

the development of the disease. The test for the *BRCA1* and *BRCA2* genes that indicate predisposition for premenopausal breast and ovarian cancer carries even greater uncertainty and less control. Since as many as 80% of breast and ovarian cancer cases are unrelated to these gene mutations,¹¹ their absence is no safeguard. The degree to which prophylactic surgery prevents the development of these cancers is also uncertain. While bilateral mastectomy and oophorectomy offer the greatest potential to prevent breast and ovarian cancer, many women opt only for mastectomy or increased surveillance after finding that a gene mutation makes them vulnerable to developing these cancers.

Anticipated psychologic outcomes

Besides certainty and control over their health, people may also take their anticipated emotional reactions into account when deciding whether to undergo genetic testing. Anticipated emotional reactions to the results of testing may influence the decision as much as the anticipated factual outcomes. One

TABLE 1. Comparison of uptake rates (weighted averages) across genetic disorders for those with a family history of selected diseases

Disease	uptake rate	average diagnosticity*	prevention†	severity‡
Huntington's Disease	14%	~100%	no	fatal
Cystic Fibrosis	30%	~100%	no	fatal
Hemochromatosis	36.3%	75%	no	severe but easily treated
Alzheimer's Disease	8.4%	35%	no	fatal
HPC	unknown	55%	no	75% 10-year survival§
HNPCC	58%	65%	no	75% 5-year survival§
FAP	unknown	80%	yes (surgery)	75% 5-year survival§
<i>BRCA1/2</i> -related breast cancer — in Ashkenazi Jewish women	38.5%	61% 85%	yes (surgery)	80% 5-year survival§

* **diagnosticity:** the degree to which a positive genetic test means the disease will develop

† **prevention:** the availability of treatments to prevent development of the disease

‡ **severity:** the "treatability" of the disease and resulting life expectancy if no preventive treatments are undertaken

§ Based on early-stage (Stage I or II) diagnosis¹²

STATUS REPORT

study found that individuals were as likely to factor their anticipated regret at not having been tested and then developing cancer as much as the ability to prevent the disease through prophylaxis.¹³ Besides regret, other emotional-psychologic states that appeared to influence the decision to undergo or forego genetic testing included the idea of living with uncertainty vs certainty, living in a state of fear, anticipated worry and anticipated guilt.

Education

Education level has been found to play a role in some cancer-related genetic testing decisions, but not in others. In an exploration of the decision of first-degree relatives to undergo testing for *BRCA1/2*, education level did not correlate with the testing decision.¹⁴⁻¹⁷ In other studies, however, less education was associated with greater expressed intention of people with a family history of HNPCC,¹⁸ hereditary prostate cancer (HPC)¹⁹ and *BRCA1/2*² to undergo testing. A community study that approached women in a medical waiting room and asked if they were interested in testing found a lower educational level to be associated with the hypothetical intention to undergo *BRCA1/2* testing.²⁰

Practitioners need to be aware of a patient's education level and the potential impact it may have on the decision to undergo genetic testing. It is important that the decision be based on a firm understanding of the tests' meaning. Further, as those with lower education may be more highly influenced by physicians,²¹⁻²³ it is essential to determine whether someone is making an autonomous decision or blindly following a physician's suggestions.

POTENTIAL NEGATIVE OUTCOMES

Qualifying for provincially-funded testing

In most Canadian provinces, patients referred for cancer mutation genetic testing first see a genetic counsellor who helps them understand their probability of having a mutation.²⁴ Testing is offered only if provincial health care rules deem the probability or susceptibility to be significant. Patients need to be informed of possible delays and barriers in this process:

- **The rules vary by province.** Some provinces take into account the fact that women of Eastern European (Ashkenazi) Jewish heritage have a higher probability of having the *BRCA1/2* gene, as well as a greater likelihood of not knowing their genetic history due to the Holocaust. Thus, these provinces consider ethnicity as an additional risk factor. Other provinces do not, leaving many higher-risk individuals ineligible for testing.²⁵
- **Access to testing varies.** Many provinces lack referral mechanisms, giving primary care medical practitioners nowhere to refer patients for more indepth information, counselling and testing. Although not documented, there is concern amongst public health advocates that numerous high-risk Canadians are obtaining testing in the U.S. at a cost of over \$2000^{26,27} — an option available only to those with the financial means to pursue it. Those who seek testing but do not qualify may experience poor psychologic outcome, e.g. increased distress as a result

of not having their uncertainties addressed.²⁸ Practitioners should inform patients before referral that they may not qualify, ensure that they are aware of the potential negative impact if this happens, and be prepared to provide subsequent counselling and support.

The long wait

Besides waiting often a year or longer for testing by provincially-funded genetic counsellors, people can wait as long as 3 years for their results in some provinces. For someone seeking certainty and control, the anxiety provoked by waiting can be more distressing than learning of a positive mutation.²⁹

Negative aspects of a positive result

Although early research in the field suggested a great deal of distress due to genetic testing,^{30,31} recent studies show that those who undergo testing suffer little regret³² and little psychiatric dysfunction.³³ Only a small number of people who undergo genetic testing for *BRCA1/2* report feeling distressed.²⁹ A 1998 study suggested that those at high risk who decline testing may actually be at increased risk for depression.³⁴ The researchers suggested that failure to address cancer-related stress and worry through the avoidance of testing might be the cause of the depressive symptoms. While most people do not appear to be traumatized by testing positive for a genetic mutation, support and services must be available for the few who are traumatized.²⁴ Recent data suggest that Supportive-Expressive group work can provide effective support.³⁵

Genetic testing can also have legal implications. Although Canadian courts have not yet addressed the issue, the use of genetic testing information by insurance companies is a concern. The federal and some provincial governments have instigated legislation to protect individuals' private medical information. It is unclear, however, whether such legislation would prevail over the views of the Canadian Institute of Actuaries, The Canadian Life Insurance Medical Officers Association and the Canadian Life and Health Insurance Association that genetic testing results should be available to insurance companies as part of the insured's health history.³⁶ The Canadian Genetics and Life Insurance Task Force is currently attempting to devise a fair policy for integrating genetic information into the underwriting process.

Patients need to know in advance that a positive test for a cancer gene mutation leads to other difficult decisions. Prophylactic treatment options may be limited or life-altering, e.g. bilateral mastectomy and oophorectomy to prevent breast and ovarian cancer, leading to more uncertainty about one's future health. Patients who test positive must decide whether to inform siblings, parents and children of the results. In families with strained interpersonal relationships these decisions may be even more difficult than the decision about undergoing testing.³² Telling children, including determining the best way and at what age, can be extremely distressing and overwhelming.

continued on page 22

A negative test may not be positive

For some people a negative finding may be as distressing as a positive one. Those with a strong family history of cancer appear to have too great a belief in their risk to be reassured by a negative genetic test.³⁷ Researchers are exploring why a negative test result does not decrease some individuals' feeling of risk — meanwhile, it is important not to assume that all patients will feel relieved by a negative test result.


Another concern requiring discussion is recommendations for surveillance after testing negative. A negative test finding appears to give some people such a sense of security that they fail to continue with normal recommended surveillance. For example, some women with a family history of breast cancer have been found to forego monthly breast self-exams and regular mammography after a finding of no gene mutation — despite the fact that most breast cancers are not linked to *BRCA1* and *BRCA2*. Physicians therefore need to emphasize that those who test negative carry at least the same cancer risk as the general population and that regular cancer screening remains important.

Inconclusive results

Patients need to be made aware that genetic testing sometimes produces equivocal results, that is, within the current parameters of the testing situation the test may be inconclusive. After making the decision to be tested and waiting a year with uncertainty and perhaps fear, to finally be told that the test was not a certain yes or no can engender enormous psychologic distress — in fact, the greatest psychologic morbidity may associated with patients who receive inconclusive results.^{38,39}

IMPLICATIONS FOR PHYSICIANS:

primum non nocere

Research has revealed a number of psychosocial issues faced by patients considering genetic testing for cancer gene mutations. For patients to make a “good” decision about whether to seek testing, they must be informed of — and have the opportunity to explore the potential driver behind — their interest in testing, and to develop insight into whether such testing will, in the end, address these drives. They must also be informed in advance of the possible outcomes and psychosociologic pitfalls — independent of the actual test finding — that may arise as a result of genetic testing. The primary care medical practitioner or member of the oncology team, who often initially addresses a person's interest in genetic testing, has an ethical duty to inform and address psychologic and legal issues. 

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