Recognizing *BRCA* gene mutation risk subsequent to breast cancer diagnosis in southwestern Ontario

Meredith Vanstone - Winsion Chow - Laura Lester - Peter Ainsworth - Jeff Nisker - Muriel Brackstone

**Abstract**

**Objective** To describe the population of women in southwestern Ontario who were diagnosed with potentially preventable *BRCA* mutation-related breast cancer.

**Design** Retrospective chart review.

**Setting** The Cancer Genetics Clinic of the London Regional Cancer Program in London, Ont.

**Participants** Patients younger than 52 years of age who were referred to the London Regional Cancer Program Cancer Genetics Clinic between 1997 and 2007 for *BRCA* testing after being diagnosed with breast cancer (N = 1017).

**Main outcome measures** The proportion of women with *BRCA1* or *BRCA2* gene mutations and the proportion of women who would have qualified, based on family cancer history, for referral for genetic counseling and testing before their breast cancer diagnoses.

**Results** Among the 1017 women referred for *BRCA* testing, 63 women younger than 52 years of age who had been diagnosed with breast cancer were found, subsequent to this diagnosis, to have *BRCA1* or *BRCA2* gene mutations. Of these, 41 (65%) had family cancer histories that would have qualified them for genetic counseling and testing, according to provincial criteria, before their own breast cancer diagnoses. Of the 63 women, most (81%) had been referred for *BRCA* gene mutation testing by their oncologists or surgeons.

**Conclusion** Our results suggest that the diagnosis of breast cancer could have been anticipated, and perhaps in some cases prevented, in up to two-thirds of high-risk women younger than 52 years of age in southwestern Ontario. If the high-risk status of these women had been recognized, they might have had the opportunity to choose genetic counseling, testing, more effective cancer surveillance, and potentially preventive options. The results of this study call for increased public and care provider awareness about hereditary breast cancer risk to promote women’s ability to choose to access genetic counseling.

**Editor’s Key Points**

- Breast cancer related to *BRCA1* or *BRCA2* gene mutation is an autosomal dominant inherited disease. These mutations confer a lifetime breast cancer risk of 45% to 87%. Women who have been made aware of familial high risk before cancer diagnosis can choose to access genetic counseling, testing, and preventive strategies. However, many identifiably high-risk women are not being referred for genetic counseling before being diagnosed with breast cancer.

- There are many structural constraints to providing genetic care in primary care, including lack of time; lack of clear clinical practice guidelines for referral to genetic counseling; difficulties in compiling, confirming, and regularly reviewing family cancer history information; and lack of up-to-date knowledge concerning genetic information and available genetic services.

- Women should have access to information that is publicly available to allow them to initiate a conversation about their personal genetic risks with their primary care providers.
Mise en évidence du risque inhérent à la mutation du gène BRCA chez des femmes du Sud-Ouest de l’Ontario qui ont déjà eu un diagnostic de cancer du sein

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Résumé

**Objectif** Décrire le groupe de femmes du Sud-Ouest de l’Ontario chez qui on a diagnostiqué un cancer du sein lié à une mutation du BRCA, qu’on aurait pu prévenir.

**Type d’étude** Revue rétrospective de dossiers.

**Contexte** La Cancer Genetics Clinic du London Regional Cancer Program à London, Ontario.

**Participants** Patientes de moins de 52 ans qui ont été dirigées à la Cancer Genetics Clinic du London Regional Cancer Program entre 1997 et 2007 pour un dépistage du BRCA après avoir eu un diagnostic de cancer du sein (N = 1017).

**Principaux paramètres à l’étude** La proportion de femmes porteuses de la mutation du gène BRCA1 ou BRCA2 et la proportion de celles qui, en fonction de l’histoire familiale de cancer, se seraient qualifiées pour être dirigées pour une consultation et des tests génétiques avant qu’on leur diagnostiquent un cancer du sein.

**Résultats** Sur les 1017 femmes qui ont été dirigées à la clinique pour un dépistage BRCA, on a observé que chez 63 patientes de moins de 52 ans qui avaient eu un diagnostic de cancer du sein, on a plus tard trouvé des mutations des gènes BRCA1 ou BRCA2. Parmi ces femmes, 41 (65%) avaient des histoires familiales de cancer qui, selon les critères provinciaux, les auraient qualifiées pour avoir une consultation et des tests génétiques avant le diagnostic de leur cancer du sein. La plupart de ces 63 femmes (81%) avaient été dirigées pour un dépistage de la mutation du gène BRCA par leur oncologiste ou leur chirurgien.

**Conclusion** Nos résultats laissent penser qu’on aurait pu anticiper le diagnostic de cancer du sein et, dans certains cas, le prévenir même chez près des deux-tiers des femmes de moins de 52 ans de l’Ontario du sud-ouest qui présentaient un risque élevé. Si on avait reconnu la présence d’un risque élevé chez ces femmes, elles auraient pu opter pour des conseils et des tests en génétique, pour une surveillance plus efficace et éventuellement pour des interventions préventives. Les résultats de cette étude demandent que des mesures soient entreprises pour que le public et les soignants soient davantage éveillés au risque de cancer du sein héréditaire, afin que les femmes soient plus en mesure de recourir aux consultations génétiques.

POINTS DE REPÈRE DU RÉDACTEUR
• Le cancer du sein associé à une mutation des gènes BRCA1 ou BRCA2 est une maladie héréditaire transmise sur un mode autosomique dominant. Ces mutations entraînent un risque à vie de cancer du sein dans une proportion de 45 à 87%. Les femmes qui ont été informées d’un risque familial élevé avant d’avoir un diagnostic de cancer peuvent décider de recourir à des consultations et des tests génétiques et à des stratégies préventives. Toutefois, plusieurs femmes qui pourraient être classées à haut risque ne sont pas dirigées vers des consultations génétiques avant qu’un diagnostic de cancer du sein soit posé.

• Il y a plusieurs obstacles structurels qui empêchent de fournir des soins génétiques en contexte de soins primaires, incluant les contraintes de temps; l’absence de directives cliniques claires concernant la prescription de consultations génétiques; les difficultés en rapport avec la compilation, la confirmation et la révision régulière des données sur l’histoire familiale de cancer; et le manque de mise à jour des connaissances au sujet de l’information génétique et des services de génétique disponibles.

• Les femmes devraient avoir accès à toute l’information qui est disponible au grand public afin d’être en mesure d’aborder avec leurs soignants de première ligne le sujet de leurs risques génétiques personnels.
Breast cancer is the predominant malignancy among women, affecting more than 23,000 Canadian women each year. Breast cancer related to BRCA gene mutation is an autosomal dominant inherited disease. The lifetime risk of breast cancer for those carrying BRCA mutation is 45% to 87%, although this appears to be increasing over time, suggesting a substantial environmental component in the presentation of the abnormal phenotype. The prevalence of BRCA mutations in the general population is not known, but risk models hypothesize that 1 in 300 to 1 in 500 unaffected (non-Jewish) women might carry BRCA1 or BRCA2 mutations. Hereditary breast cancer is thought to account for 5% to 10% of all cancer cases, although known mutations such as BRCA and other less common mutations are estimated to account for only 25% of hereditary breast cancer.

If a woman is identified as being at high risk of breast or ovarian cancer, she can choose to participate in genetic counseling to discuss surveillance and prevention strategies. Magnetic resonance imaging (MRI) has been shown to be 3 times more effective than mammogram for identifying invasive cancers in the breasts of young women. Bilateral mastectomy and reconstruction, while invasive, provide 85% to 100% protection depending on the procedure. Salpingo-oophorectomy might reduce the risk of breast cancer by approximately 50%. It also might provide about 80% protection from ovarian and fallopian tube cancer. Other options include tamoxifen, which affords approximately 50% protection against contralateral breast cancer.

In order to access genetic counseling and BRCA genetic testing in Ontario, women must have an identifiable risk based on personal and family history, as identified through the Ontario Ministry of Health testing criteria. The purpose of this study was to identify and describe the population of women in southwestern Ontario who were diagnosed with potentially preventable BRCA mutation-related breast cancer. By recognizing women who were at identifiably high risk before breast cancer diagnosis, but who might not have been offered access to genetic counseling, testing, surveillance, or preventative strategies, we can explore the obstacles to this identification and work to ameliorate this issue.

**METHODS**

**Study design and participants**

The study protocol received full ethics approval from the University of Western Ontario Health Science Research Ethics Board for the London Regional Cancer Program (LRCP). The London Health Sciences Centre Molecular Diagnostics Laboratory is 1 of 7 provincially recognized molecular laboratories that provides BRCA genetic testing in Ontario. It is located in a region with a few small cities (London, Windsor, and Sarnia) and a large rural population.

The chart review identified 1017 women who had personal histories of breast cancer and who were tested for BRCA mutations at the LRCP between 1997 and 2008. Results of the BRCA test were not available for 14 women. Of the remaining women, 122 received a diagnosis of a BRCA1 or BRCA2 mutation. This population was narrowed to a final study population of 63 women based on the following criteria:

- diagnosed with breast cancer after 1997;
- diagnosed with cancer before the age of 52;
- subsequently identified as a BRCA1 or BRCA2 mutation carrier.

**Figure 1** illustrates the chart review process. The age of 52 has been identified as the average age of menopause, and BRCA gene mutation-related breast cancer is more likely to occur before menopause. Testing for BRCA mutation has been publicly funded in Ontario since 2000, but has been available in Ontario since 1995 through research studies. The year 1997 was chosen as a cutoff as it represents the year in which BRCA testing was widely available through the Cancer Genetics Clinic at the LRCP.

**Data collection and analysis**

Comprehensive patient demographic characteristics, as well as medical and family histories, were obtained by genetic counselors during initial consultations with patients at the LRCP; this information, including information on the source of referral to the genetics clinic, was extracted from each of the 122 charts (by M.V. and W.C.) using a data collection tool developed for this process. Family histories were used to categorize patients into groups within the Ontario Ministry of Health’s (MOH’s) classification system. The abstractors independently categorized patients into MOH groups. When a patient qualified for more than one MOH group, she was placed in the group with the highest positivity rate. Lists were compared for discrepancies, and consensus was achieved on the categorization of each patient.

Positivity rates reported here are internally calculated figures used to establish benchmarks for local clinicians to use when counseling about risk. Positivity rates are continuously updated as the LRCP performs more tests. The positivity rates reported in this study are based on the test results of 1270 probands, from the years 1997 to 2008. A **proband** is an individual being studied or reported on. A proband is usually the first affected individual in a family who brings a genetic disorder to the attention of the medical community. For an example of positivity rates in a larger population, see the prevalence tables published by Myriad Genetics.

We evaluated whether each woman would have been eligible for testing before her own breast...
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RESULTS

Table 1 outlines the standards for genetic testing, as developed by the Ontario MOH and used at the LRCP Cancer Genetics Clinic. Within this classification system, patients were grouped according to their family histories obtained by genetic counselors during the initial consultation. Sixty-five percent of the patients in the study population presented with family histories that would have qualified them for genetic testing before their own breast cancer diagnoses. As illustrated in Table 1, the family histories of 41 patients would have been sufficient to warrant genetic testing before personal cancer diagnosis. Ontario MOH policy instructs that, when possible, the highest-risk affected individual in a family should be tested first, to maximize detection rates. This is known as the principle of best to test. However, any woman who meets MOH risk criteria can access genetic counseling when the best-to-test family member is not available or does not wish to be tested.

Figure 2 illustrates the source of referrals for genetic testing. As expected when examining a population of women who had already been diagnosed with cancer, by far most referrals for genetic counseling and genetic testing (81%) were made by local oncologists or surgeons.

DISCUSSION

Sixty-three patients of the LRCP diagnosed with breast cancer between 1997 and 2007, before the age of 52, might not have been offered genetic counseling or BRCA
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Table 1. Number of women who were eligible (according to Ontario Ministry of Health criteria) for BRCA testing before being diagnosed with breast cancer, based on family history

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>FAMILY HISTORY TESTING CRITERIA*</th>
<th>NO. OF PATIENTS WHO WOULD HAVE QUALIFIED FOR TESTING BEFORE DIAGNOSIS (TOTAL = 41)</th>
<th>POSITIVITY RATE IN LRCP DATABASE, FOR ALL TESTED PROBANDS, 1997-2008† (N = 1270), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>Ashkenazi Jewish AND breast cancer at age &lt; 50 y OR ovarian cancer at any age</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Group 2</td>
<td>Breast cancer at age &lt; 35 y</td>
<td>4</td>
<td>7.7</td>
</tr>
<tr>
<td>Group 3</td>
<td>Male breast cancer at any age</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Group 4</td>
<td>Invasive serous ovarian cancer at any age</td>
<td>0</td>
<td>8.5</td>
</tr>
<tr>
<td>Group 5</td>
<td>Breast cancer at age &lt; 60 y AND first- or second-degree relative with ovarian cancer OR male breast cancer at any age</td>
<td>4</td>
<td>13.3</td>
</tr>
<tr>
<td>Group 6</td>
<td>Breast and ovarian cancer in same individual OR bilateral breast cancer with first case at age &lt; 50 y</td>
<td>9</td>
<td>15.4</td>
</tr>
<tr>
<td>Group 7</td>
<td>Two cases of breast cancer in first- or second-degree relatives at age &lt; 50 y</td>
<td>4</td>
<td>15.1</td>
</tr>
<tr>
<td>Group 8</td>
<td>Two cases of ovarian cancer, at any age, in first- or second-degree relatives</td>
<td>0</td>
<td>15.8</td>
</tr>
<tr>
<td>Group 9</td>
<td>Ashkenazi Jewish with breast cancer at any age and family history of breast or ovarian cancer</td>
<td>0</td>
<td>11.8</td>
</tr>
<tr>
<td>Group 10</td>
<td>Three or more cases of breast or ovarian cancer</td>
<td>24</td>
<td>12.3</td>
</tr>
</tbody>
</table>

LRCP—London Regional Cancer Program.
*Data from the Predictive Cancer Genetics Steering Committee, 2001.28
†Positivity rate data are LRCP internal data for probands tested between 1997 and 2008. A proband is an individual being studied or reported on. A proband is usually the first affected individual in a family who brings a genetic disorder to the attention of the medical community.35

Figure 2. Source of patient referral to genetic counseling

Genetic testing before their cancer diagnoses. Forty-one of the 63 patients (65%) presented with family histories that would have qualified them for genetic testing before their own breast cancer diagnoses. Therefore, two-thirds of these patients could have been identified as being at increased risk of developing breast or ovarian cancer and, if so identified, would have had the opportunity to access genetic counseling and possibly testing, surveillance, and preventive strategies before they developed breast cancer.

Women might have low levels of knowledge about hereditary breast cancer, even if they are from high-risk families.38 Common misconceptions include the belief that paternal family history does not confer substantial risk39,40 or thinking that sharing physical attributes with a family member makes it more likely that other genetic attributes are also shared.41,42 Without public education, women must rely on their health care practitioners to recognize their risk and provide appropriate referral for genetic counseling or testing. Canadian women have enthusiastically voiced their support for public education,43,44 fearing that their primary care providers might not have the necessary time or knowledge to educate them about these topics. Canadian primary care providers have also expressed interest in increased educational and information tools for women, and for themselves.45
In addition to the need for increased genetic education for primary care providers and the public, our data might also reflect the well-understood problem of many patients not having access to primary care providers or having to rely on walk-in clinics, where the focus might be on acute issues and where full family histories are not always elicited.

**Barriers to genetic services in primary care**

As genetic testing becomes increasingly prevalent, the direct involvement of primary care providers will be necessary to ensure access for as many Canadians as possible. However, high-risk women might not be receiving referrals for genetic services because they might not have primary care providers or their primary care providers might have incomplete knowledge of, might have forgotten, or might only have access to out-of-date family histories. Primary care providers might struggle with time constraints that impede their ability to assemble family cancer histories, or they might not have adequate knowledge of new genetic information and services. Primary care providers might not know where to refer patients for genetic counseling, even if they are aware of the existence of such services. Considerable constraints on the provision of predictive genetic services in primary care make it unreasonable for women to be solely dependent on their primary care providers for recognition of the need for and provision of genetic testing services. As Miller and colleagues point out, these barriers to genetic services in primary care might constrain all but the most resourceful or persistent patients.

Miller and colleagues and Carroll and colleagues have found that oncologists refer 2 to 5 times as many patients to genetic counseling as primary care providers do. This is congruent with our finding that most women (81%) in our study were referred for genetic counseling by their oncologists or surgeons. Lower numbers of referrals from primary care providers have been linked to unrecognized risk in certain groups of patients, such as patients with moderate levels of risk, risk from the maternal side, or risk related to ovarian cancer history.

Family histories provided to primary care providers are not always as detailed as those provided to genetic counselors after breast cancer has been diagnosed. There is evidence that patients do not always share available family history information with their physicians, perhaps because they do not understand the importance of the information. A systematic review found that patients with personal diagnoses of cancer were more likely to provide accurate family history information than control patients were. This recall bias is a challenge to primary care providers trying to gather comprehensive family histories.

The time needed to regularly collect and review family history information is a key barrier in completing and maintaining comprehensive family histories. The barriers to collection and regular review of family history information might be ameliorated by the use of patient-generated family history tools, the use of other health care professionals to collect and maintain family history information, or reevaluation of the current fee-for-service structure. Family history tools have been shown to result in an increased number of referrals to cancer genetics specialists and might assist in improving the likelihood of a referral to genetic counseling before a cancer diagnosis. Patient-generated computerized family history tools, such as the Web-based tool introduced by the US Surgeon General (www.hhs.gov/familyhistory), have been rated by family physicians and specialists as being able to provide more useful information than it is possible to collect in a traditional patient-provider visit.

A lack of adequate knowledge of the specific criteria for referral to genetic counseling and testing might be another factor that is impeding referrals in primary care. Vig and colleagues found that primary care providers affiliated with teaching hospitals were more likely to refer patients to cancer genetics clinics. Additionally, physicians with access to genetic counselors were more likely to refer patients for such counseling, and lack of physician access to genetic counseling professionals was cited frequently as a barrier to referral.

**Improving access to genetic counseling services**

Improved access for primary care providers to genetic counselors might alleviate the difficulty in finding clinical policy and practice guidelines in this area. Although attempts have been made to provide primary care providers with the information they require to determine which patients are at high risk of hereditary breast cancer and to offer referral to genetic counseling, primary care providers report that they wish to receive more information about this topic. The Ontario MOH testing criteria used in this study are no longer readily available online to either health professionals or the public, as the original task force, assembled to generate guidelines, principles, and broad criteria for referrals for genetic testing has been dissolved. Ontario physicians can access information about managing women at risk of hereditary breast cancer by using bulletins from the Ontario Health Insurance Plan (OHIP), the Canadian Cancer Society risk triage and management recommendations, or an article from the original task force published in the *Ontario Medical Review*. However, to use these resources, physicians must be able to recognize the risk factors for hereditary breast cancer. In some cases, a substantial search must be made to access these clinical resources. For example, the OHIP bulletins are not available from the main OHIP bulletin site, and the original task force article published in the *Ontario Medical Review* is not currently available.
online. There might be guidelines more readily available to physicians in other provinces through their own provincial medical associations.

Patients and physicians alike would greatly benefit from updated, comprehensive, easy-to-use evidence-based guidelines disseminated publicly, and physicians have indicated interest in more provider and patient education.\(^{57}\) There has been a recent move toward educating primary care providers about genetics issues (eg, the GenetiKit research project\(^ {59,60}\)), and increased education should increase early access to genetic counseling services.

The issues of physician time and education are secondary to a more important ethical issue, that women should not have to rely on their primary care providers (if indeed they have primary care providers), given the current constraints on practice. It is important that women have access to publicly available information so that they can identify their own risk and choose to bring this to the attention of their primary care providers. Public information about the type of family histories that can indicate risk would enable many women to assess their personal risk and begin conversations with their primary care providers.

Bearing an inherited gene mutation is a lifelong condition; personal risk information is not just relevant to women at risk of BRCA mutation–related breast cancer, such as those in our study population. Women who have family histories of breast or ovarian cancer where BRCA1 or BRCA2 gene mutations have not been identified would also benefit from counseling about risks and surveillance strategies,\(^ {70,71}\) as they are clearly at above-average risk of breast or ovarian cancer.\(^ {72}\) The BRCA1 and BRCA2 mutations are associated with 10% to 15% of ovarian cancer cases.\(^ {73,75}\)

Primary care providers should consider that not all women with family histories of breast or ovarian cancer will wish to know their genetic status.\(^ {76}\) A systematic review of studies examining women with high-risk family histories found a mean of 63% chose to be tested for BRCA gene mutations, although a range of uptake rates has been reported in the literature (24% to 93%).\(^ {77}\) Among women who choose to get tested, positivity rates for BRCA gene mutations will vary considerably, depending on background and family history.\(^ {78}\) If a woman belongs to a family which has an autosomal dominant inheritance pattern but in which no woman with breast cancer has tested positive for a BRCA gene mutation, she might still be at increased risk of breast cancer, even after testing negative for a BRCA gene mutation herself.\(^ {12,13,79,80}\) There are several non-BRCA gene mutations that have been identified,\(^ {13}\) and considering that BRCA gene mutations account for only an estimated 25% of hereditary breast cancers,\(^ {14}\) there will surely be more gene mutations identified in the future.

Genetic counseling can still be beneficial to a woman without a mutation diagnosis because it can help her understand her individual level of risk and inform her of available surveillance strategies such as MRI or more frequent breast examinations.

Not all women who test positive for BRCA gene mutations will wish to pursue preventative pharmaceutical or surgical treatment; uptake rates for preventative strategies vary by country, age, access to care, cost, and psychosocial factors\(^ {81}\) and are strongly influenced by a woman’s emotional response to previous cancer experiences and other psychosocial factors.\(^ {82,84}\) Women who do not wish to pursue pharmaceutical or surgical risk reduction procedures might still wish to increase their surveillance through a combination of more regular breast examinations (either self-examination or examination by primary care providers), MRI, or mammograms.

**Limitations**

This study represents the experiences of women referred for genetic counseling and BRCA genetic testing subsequent to their diagnosis of premenopausal breast cancer in southwestern Ontario, and it reflects the geographic nature of our study population (smaller cities, rural areas). This study protocol needs to be applied in other regions to relate these findings to particular regional populations.

The starting date of 1997 was chosen to reflect the policies and procedures in place for testing in southwestern Ontario at the LRCP. Data collection beginning in 1997 is a clear limitation to the generalizability of the study in relation to other centres, as the policies and funding mechanisms in other regions of Ontario might not have been put in place until 2000. In other regions, access to BRCA gene mutation testing might have been confined to research studies that might have excluded some of the patients in our study. This time frame was chosen to illustrate the scope of the issue, not to imply that family physicians in this area should have been referring the patients in this study during this time.

As our study reviewed charts from a genetics clinic, it was not possible to determine how many women were offered referrals to genetic counseling and declined. While we know the source of referral to the genetics clinic, it was not possible to determine how many patients had primary care providers before diagnosis; this information is not in each chart, as patients are given the choice to release their genetic status to their primary care providers or withhold it.

**Conclusion**

Public information and education will prove to be fundamental to the detection of individuals who have hereditary breast cancer syndrome. Sixty-five percent of the patients with BRCA mutations in our study
population experienced breast cancer that might have been preventable, as they were eligible for genetic counseling, testing, surveillance and preventive care before their cancer diagnoses. As a result of this finding, we recommend that a number of measures be taken to ensure that at-risk individuals are afforded the opportunity to pursue effective screening and preventive options. Both patients and physicians would benefit from increased education and knowledge about genetic services. While increased physician education and a change in the way family history information is collected and used at the primary care level are important for various genetic services, they are not sufficient. Publicly available information is essential, so that women are able to assess their own potential for risk and choose to speak to their physicians about the issue. It is essential that women are empowered to make decisions about their own health, and they have a right to have ready access to the information necessary to do so.

Ms Vanstone is a doctoral candidate in Health Professional Education in the Faculty of Health Sciences at the University of Western Ontario (UWO) in London. Mr Chow was a medical student at the Schulich School of Medicine and Dentistry at UWO at the time of this research. Ms Lester was an undergraduate student in the Faculty of Science at UWO at the time of this research. Dr Ainsworth is Director of the Molecular Diagnostic Laboratory of the London Health Sciences Center for the London Regional Cancer Program and Adjunct Professor in the Department of Biochemistry at UWO. Dr Nisker is Co-ordinator of the Health Ethics and Humanities program at the Schulich School of Medicine and Dentistry at UWO. Dr Brackstone is affiliated with the London Health Sciences Center of the London Regional Cancer Program, and she is a doctoral candidate in the Department of Pathology at UWO.

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Contributors

All authors contributed to the concept and design of the study; data gathering, analysis, and interpretation, and preparing the manuscript for submission.

 Competing interests

None declared

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