

A Study of Familial Cancer in Jewish Women

Background

About 5% of women in Canada with breast cancer and about 12% of women with ovarian cancer are born with an inherited genetic predisposition to cancer. In many cases, these women will have a strong family history of breast and/or ovarian cancer. In families with hereditary cancer there may be several individuals affected with breast cancer and/or ovarian cancer, in more than one generation of the family. The genetic susceptibility to develop breast and ovarian cancer in these families is passed from one generation to another, through both women and men. On average, individuals in cancer families develop cancer at a younger age than the general population and they may develop cancer in both breasts (bilateral breast cancer). Many of these family clusters of cancer are caused by inherited mutations in the BRCA1 or BRCA2 genes. If individuals are known to have a genetic predisposition to cancer, many management options are available to them to reduce the risk of developing cancer or to detect cancer at an early stage.

In some populations, there are more hereditary breast/ovarian cancers than in others. This is true for the Jewish population. Both Ashkenazi and Sephardi Jews may inherit a mutation, but mutations are more common in Ashkenazis (Jews of Eastern European origin). In this group, about 1 in 45 men or women carry a genetic predisposition to breast and ovarian cancer. We can test for this genetic tendency to get cancer by a simple saliva test. Currently the test is offered in Ontario to selected women, based on their personal history of cancer, or their family history of cancer. We are now offering this test (as part of a research study) to all adult Jewish women in Ontario who wish to know their mutation status, including those without a personal or family history of cancer.

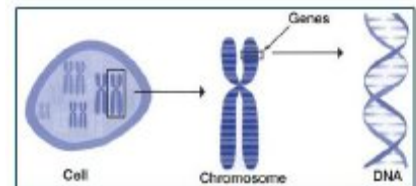
Why are we doing this study?

We are currently offering genetic testing for BRCA1 and BRCA2 genes to all Jewish women in Ontario. We would like to evaluate the interest in genetic testing for BRCA1 and BRCA2 in the Jewish community. We would like to know how common mutations are among the Jewish population. We would like to know if we are able to identify women with a genetic predisposition to developing cancer who otherwise might not come to the attention of the medical community and receive the preventive care and screening that might benefit them. We would like to know if women are satisfied with the genetic testing process or if there are ways that it could be improved.

This following information may help you decide whether or not you wish to participate and have this genetic test.

Genetics of Hereditary Breast/Ovarian Cancer

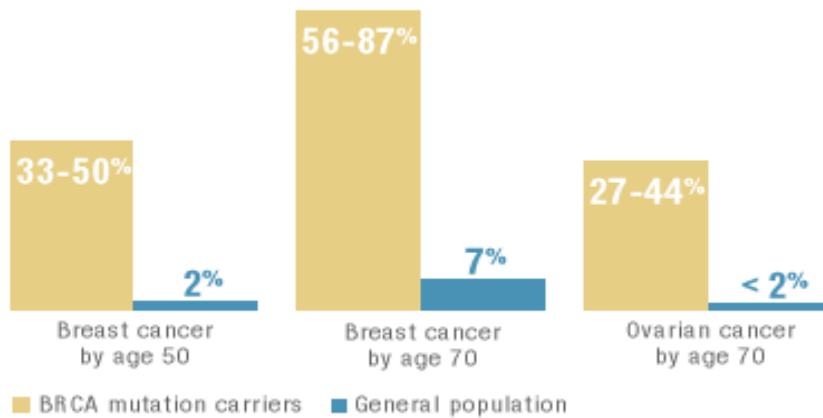
We get our genetic information from both our parents. The individual pieces of genetic information are coded in our genes. Each person has two copies of about 25,000 genes. Sometimes a change occurs in a gene, which stops the gene from working properly. Such a change is called a “mutation”. We know some genes function to protect our body from developing cancer. If a person has a mutation in a cancer-protection gene, that gene does not work properly and the person has a higher chance of developing cancer. This is genetic susceptibility to cancer.



There are two genes, which, when mutated, cause women to have a high chance of developing breast or ovarian cancer. The first gene was identified in 1994 and is called BRCA1 (BREast CAncer 1), the second gene was identified in 1995 and is called BRCA2. A person who has a mutation in the BRCA1

gene is referred to as a BRCA1 mutation carrier; a person who has a mutation in the BRCA2 gene, a BRCA2 mutation carrier. Both female and male carriers have a 1 in 2 (50%) chance of passing on the gene mutation to each of their children.

BRCA Mutation Increases the Risk of Cancer



BRCA1: Among women who are BRCA1 mutation carriers, ~70% will develop breast cancer by age 70 (compared to 7% of women in the general population); approximately 40% will develop ovarian cancer by age 70 (compared to 1.5% of women in the general population).

BRCA2: For individuals in HBOC families who have a mutation identified in the breast cancer susceptibility gene BRCA2, both women and men have a genetic susceptibility to develop breast cancer. Among women who are BRCA2 mutation carriers ~70% will develop breast cancer by age 70. We estimate that women who have a BRCA2 mutation are at increased risk of developing ovarian cancer, approximately 15-20% by age 70. Men have an increased risk of developing prostate cancer. Both men and women have a slightly higher chance of developing pancreatic cancer, melanoma, stomach cancer and possibly colon cancer.

Management Options for BRCA1 and BRCA2 Mutation Carriers

For women who are BRCA1 or BRCA2 mutation carriers, a range of options is available (depending on the wishes of the individual). Current options include screening, preventive surgery and taking medications to prevent cancer. We are also now investigating the use of dietary supplements to reduce cancer risk.

Breast screening options include monthly breast self-exams, breast exams by a specialist every 6 months, and yearly mammograms. In Ontario, annual breast screening by MRI (magnetic resonance imaging) is recommended. Ovarian screening options include pelvic exams, transvaginal ultrasounds and a CA-125 blood test.

Preventive drug therapies can also be used. Taking a medication called Tamoxifen for 5 years is believed to lower the chances of developing breast cancer for women at risk of developing breast cancer. Oral contraceptives can reduce the chance of developing ovarian cancer in women with BRCA1/2 mutations (as well as in the general population). Preventive surgeries include preventive removal of the breast(s) (prophylactic mastectomy) and preventive removal of the ovaries (prophylactic oophorectomy). These surgeries have been shown to be very effective at reducing cancer risk, for women who choose this option.

Testing in the Ashkenazi Jewish Population

It is estimated that over 80% of families with hereditary breast/ovarian cancer have a mutation in either BRCA1 or BRCA2. In the general population, mutations can occur anywhere in the genes (there have been over 3500 mutations that have been identified). However, in the Jewish population it is usually in one of the three specific spots. Two of these mutations are in BRCA1, and one is in BRCA2. These three mutations account for the majority of the hereditary breast/ovarian cancer families in the Ashkenazi Jewish population. In this study, participants will only be tested for these three mutations.

Rarely, Jewish individuals can carry other BRCA1/2 mutations that would be missed by our test. This would usually be in people who have a very strong family history of breast and/or ovarian cancer. In some cases, women with a strong family history of cancer, but who are negative for the test will be referred to a Cancer Genetics Clinic for risk assessment and possibly for other genetic testing.

Results

There are two different possible results of this genetic test for the three common Ashkenazi Jewish BRCA1/2 mutations. Either the test will be normal, meaning none of these three mutations was found, or it will be positive, meaning one of the three BRCA1/2 mutations was found.

Normal Test result:

This means that the person tested was not found to carry any of the three BRCA1/2 mutations that are more common in the Ashkenazi Jewish population. This does not mean that the person tested will not get breast cancer, ovarian cancer or any other type of cancer. Cancer is common in the general population and population cancer screening guidelines should be followed. In the absence of a family history, a normal test result implies that the woman is at average risk of breast cancer.

In some cases, if a woman has a family history of cancer and a normal test result, her breast cancer risk may still be high, depending on her family history. She may still need additional screening as recommended by her family doctor. If you have any concerns about your family history, you should talk to your family doctor. All participants who have a normal test result will be sent a letter stating their result. In addition, participants with a strong family history of cancer will receive a telephone call.

Positive Test Result:

This means that the person tested was found to carry either a BRCA1 mutation or a BRCA2 mutation and is at increased risk of cancer. Participants who have a positive test result will be phoned to arrange a genetic counselling clinic appointment. At this appointment the participant will be given individualized information about their cancer risks (dependent on their age, medical & surgical history and their personal cancer history). Also, all the management options will be thoroughly reviewed and any necessary referrals will be organized. Being positive could mean that participants can get screening that they weren't eligible for beforehand. After this appointment, a summary letter will be written detailing all the information, options and our recommendations. Participants can decide at the clinic appointment if they wish to have this information shared with their doctors.

Implications of Genetic Testing

If a participant is found to carry a BRCA1 or BRCA2 gene mutation, this means that she is at increased risk of cancer. The level of risk will depend on a number of different factors (age, personal medical history, etc). If an individual is found to carry a BRCA1/2 mutation, she will have to make decisions about how she would like to manage this increased risk of cancer. She will be seen for a personal appointment to discuss her risks, management and any necessary referrals will be organized.

If a participant is found to carry a BRCA1 or BRCA2 mutation, this will also have implications for family members. Any children or siblings (brothers or sisters) of the participant will have a 50/50 chance of carrying the same genetic predisposition to cancer. However, this does not mean that they will get cancer. It also means that one of the parents of the participant must have carried the same BRCA1 or BRCA2 mutation, as may some of their relatives. Finding out there is a genetic predisposition in the family can be hard on family members and can raise conflict, mixed emotions and guilt. We strongly encourage participants who carry a BRCA1/2 mutation to inform all their at-risk relatives about the mutation. We can help with this by providing a letter that can be given to family members. Predictive genetic testing is available to all adult at-risk family members, either through our unit or through a local genetics clinic. We do not test children, as there are no risks to them until they are adults.

It is important to be aware of potential non-medical implications of your genetic result. Currently, there are no guidelines or laws regarding the use of genetic information by insurance companies. It is possible that if you are found to carry a BRCA1 or BRCA2 mutation, then such information in your medical records may be used to determine your eligibility for obtaining future insurance policies (such as life insurance or critical care insurance). Genetic testing should not affect any insurance policies you already have in place. Also, if your test is normal this should have no effect on your current or future insurance policies.

Who is Eligible to Participate

In order to be eligible to participate in this study you must be Jewish (Ashkenazi or Sephardi), between the ages of 20 and 70 years old, be a resident of Ontario and not had previous genetic testing for the BRCA1/2 genes. You also must be willing to attend our centre in Toronto to give a saliva sample.

What You Will Have to Do to Participate

If you are interested in participating in this study, you can sign up online or by phone (See ***How Can You Join the Study/Contact Us?*** Section). The study coordinator will contact you to explain the study further. You will then be offered the option of scheduling a clinic appointment and arrangements will be made to send you the study package (either by mail or through our online system). The study package will include a consent form, a study booklet about BRCA1 and BRCA2 testing, and three brief questionnaires.

Before your appointment

You should review the study package and complete the questionnaires and consent form prior to your scheduled appointment if you wish to participate in the study. If you received the package by mail, please bring all completed forms to your appointment. If you prefer to complete the forms online, you may visit the study website at www.womensresearch.ca/jewishstudy/forms.php

If the forms were completed online, you may bring in only your read and/or signed consent form to your scheduled appointment. Your appointment will take place in our study centre on the seventh floor of 790 Bay Street. It will take approximately 20 minutes. **Appointments will begin in March 2010.**

At your appointment

The study co-ordinator will ensure that the relevant background forms and questionnaires have been completed, including the consent form. A saliva sample will be taken and will be sent to the laboratory for genetic testing.

After your appointment

Upon completion of genetic testing, the genetic test result will be made available to you. **It might take up to one year to receive your results after your clinic appointment.** If you have a negative (normal) genetic test result, the information will be given to you in a letter or you may receive a telephone call to give you your results (it will depend on your family history of cancer).

In the event that you test “positive” for a genetic mutation, you will be given an appointment to visit the study centre for further genetic counselling. This appointment will include discussion of the results, and follow-up referrals will be completed. Positive results will be confirmed by a second test.

One year following enrolment in the study, we will mail you one additional questionnaire to complete. This questionnaire will ask you about your experience with genetic testing and your satisfaction with the process.

Participation is voluntary and study participants are allowed to withdraw from the study at any time, without prejudice or loss to their medical care.

Study Risks and Benefits

Benefits

You will receive (at no charge) a genetic test for an inherited predisposition to breast and ovarian cancer. The research team will be available to provide the most current information regarding genetic risk assessment and will provide a referral to screening centres for breast and ovarian cancer if requested. Carriers identified through the study will receive personal genetic counselling and be given individualized cancer risks and management options. Being identified as a carrier can mean access to additional screening (such as breast MRIs) that may not otherwise be available, and referrals requested by the carriers will be arranged.

Risks

Any potential risks of this testing are primarily of a psychological nature, in particular for women with a positive test result. An increased risk of cancer can lead to serious psychological consequences including feelings of depression, futility, despair and stress, or have unpredicted implications for obtaining insurance. Counselling will be provided to help adjust to the information given to you.

About the Women’s College Research Institute (WCRI) and the Familial Breast Cancer Research Unit

The Women’s College Hospital’s WCRI has an interdisciplinary faculty of clinical and academic scientists studying women’s health with the goal to improve women’s care. Within the WCRI is the Familial Breast Cancer Research Unit, a team dedicated to studying the causes and prevention of breast cancer. Of particular interest to the group is hereditary breast cancer (when cancer runs in families) and the genes involved. The main genes known to be associated with hereditary breast cancer are BRCA1 and BRCA2. At the research unit we have collected information on more than 10,000 women who carry either a BRCA1 or BRCA2 mutation. This information is being used to improve our understanding of the cancer risks to these women and how best we can reduce these risks. This information is shared with the scientific community and directly with the women through research articles, presentations, meetings, education strategies, and through our genetics clinic. Genetic counsellors at the unit offer information and support to women and their families about their cancer risks, management options and new developments in the field.

About the Research Team

Dr Steven Narod, MD, FRCP:

Dr Steven Narod is the Director of the Familial Breast Cancer Research Unit at the Women's College Research Institute (WCRI). He is a medical doctor who has specialized in the genetics and epidemiology of breast cancer. He has been working in the field for over 20 years and helped to discover the BRCA1 gene in 1994. He was appointed to the prestigious Canada Research Chair in Breast Cancer and created the Familial Breast Cancer Research Unit at Women's College Hospital. He heads up numerous breast cancer research studies, looking into the genes involved, population specific testing, cancer risks, modifiers of risk, management options and novel therapies. He has published extensively on the subject and is the most cited scientist in the world in the field of breast cancer. Dr Narod is also a Professor in the Department of Public Health Sciences at the University of Toronto.

Dr Kelly Metcalfe, RN, PhD:

Dr Kelly Metcalfe is a Research Scientist at the WCRI and an Associate Professor at the Faculty of Nursing, University of Toronto. Dr Metcalfe's research focuses on the prevention and treatment of hereditary breast cancer. She has published extensively on the implications of various preventive options, including prophylactic mastectomy. Dr. Metcalfe has led international studies reporting on the uptake rates of the various cancer preventive options in women with a BRCA1 or BRCA2 mutation. She has also recently designed a decision aid to help women make decisions about breast cancer prevention.

Sonia Nanda, MSc, CGC, CCGC:

Sonia Nanda is a Certified Genetic Counsellor working in the Familial Breast Cancer Clinic, under the direction of Dr Narod. She has over 6 years of experience in the field. She does risk assessments of cancer family histories and sees patients to discuss risks, genetic testing and management of hereditary breast/ovarian cancer. She is also closely involved with the ongoing clinical research and has an active role in numerous studies at the Familial Breast Cancer Research Unit.

How Can You Join the Study/Contact Us?

Please note that if you wish to participate in this study, there are only two ways in which you can enroll. We wish to assure you that ALL interested individuals will be contacted and an appointment will be arranged sometime over the duration of one year. Interested individuals must sign up independently, so please do not attempt to sign up on someone else's behalf. And, under no circumstances will walk-in enrollment and appointments be accepted.

Please note that if you wish to participate in this study, there are only two ways in which you can enrol. Please choose only ONE of these two enrolment options, as signing up more than once will delay the booking process:

1. In order to facilitate the study, we wish to encourage you to enroll online through our website at: www.womensresearch.ca/jewishstudy
2. If you do not have internet access, you may provide your contact information at the study's voicemail at 416-351-3795. Please note that due to the large volume of calls, this is the only phone number dedicated to the study. If you wish to speak to someone, please leave a message and the study coordinator will return your call.

Once you enroll by providing all the requested information, the study coordinator will contact you to book an appointment within 3 months of your initial sign up date. Please note that clinic appointments will begin on March 1st, 2010.

Other Resources for Information:

About our Familial Breast Cancer Research Unit: <http://www.womensresearch.ca/familialbreastcancer>

About testing for BRCA1 and BRCA2 mutations:

<http://www.myriadtests.com/>

and a **video** about Testing and Management of HBOC including personal stories of women who tested positive for BRCA mutation and their choices:

<http://www.myriadtests.com/breast-cancer-patient-video.htm>

About risks and management options for BRCA1 and BRCA2 mutation carriers:

<http://www.facingourrisk.org/>

About the Hereditary Breast Ovarian Cancer Foundation:

<http://www.hboc.ca>

About breast cancer: <http://www.breastcancer.org/>

Breast cancer society of Canada: <http://www.bcsc.ca/>

Young women with breast cancer: <http://www.youngsurvival.org/>

About health care provider and patient information about types of cancer including screening, treatment and genetics:

Canadian Cancer Society: http://www.cancer.ca/ccs/internet/frontdoor/0,,3543__langId-en,00.html

National Cancer Institute: <http://www.cancer.gov/>

About cancer genetics:

<http://www.mtsinai.on.ca/FamMedGen/cancer.htm>

About standards/guidelines, prevention/screening treatment and research:

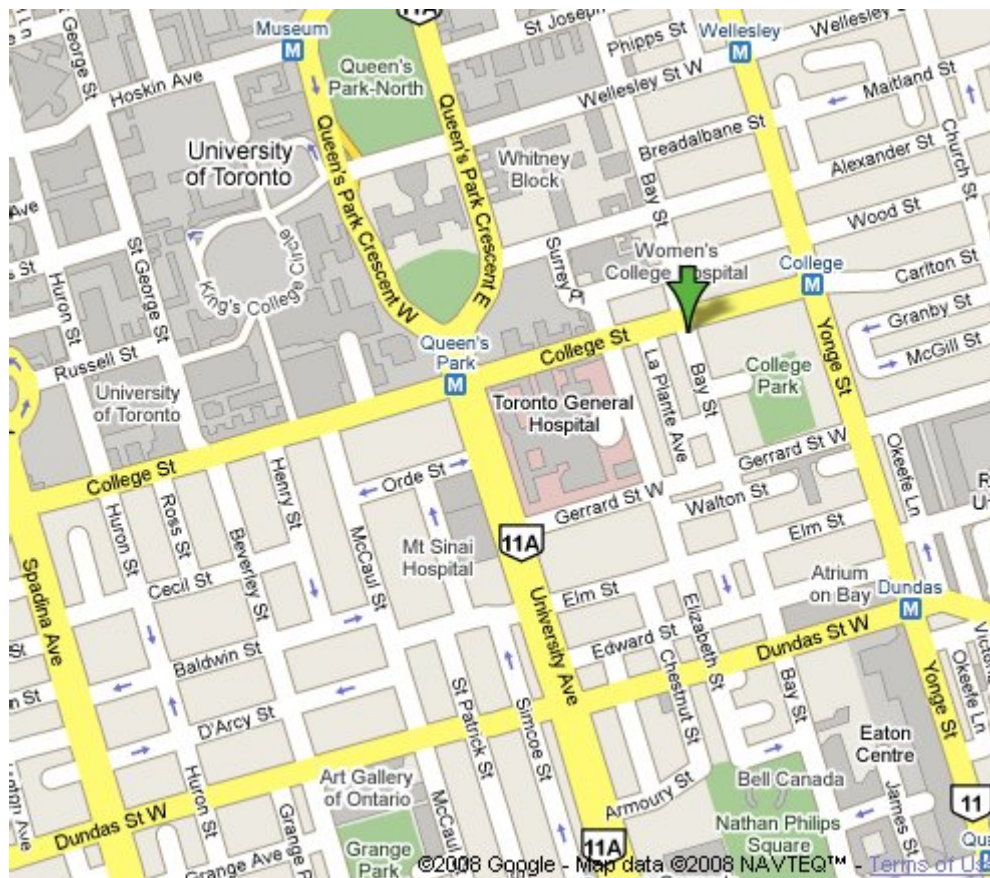
<http://www.cancercare.on.ca/english/home/>

About cancer genetic clinic locations in Canada:

http://www.cagc-accg.ca/component/option,com_sobi2/Itemid,30/

How to get to our study centre:

We are located at **790 Bay Street**, on the southwest corner of College Street and Bay Street. Our study centre is on the **7th FLOOR**. After exiting the elevator, please look for the large poster boards directing you where to go. **We are not located at Women's College Hospital.**



Public Transit

From College Subway Station: Exit the station and walk one block west to Bay Street.

From Bay Subway Station: Transfer onto a southbound Bay bus (Routes 6, 6A or 6B), and exit the bus at College Street.

From Queen's Park Subway Station: Exit the station and walk three blocks east on College Street to Bay Street.

Parking

If you are driving, parking is available but limited. There is an underground parking lot beneath College Park, and the entrance is located at 777 Bay Street. There is also a car parkade behind our building, located on Elizabeth Street, just west of Bay Street.