Canadian Breast Cancer Network
Réseau canadien du cancer du sein

BRCA and Beyond: Navigating Hereditary Breast Cancer

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Making Sense of Genetic Testing in Breast Cancer – Part 1: Understanding the Basics

Shelley Kennedy is a Board-Certified Genetic Counsellor with over 21 years of clinical experience. Over the course of her career, she has worked in Canada, Australia, Saudi Arabia, and Qatar. She is a strong advocate for patient health and believes that knowledge is essential for making informed decisions that are right for each individual.

By Shelley Kennedy, MS, CGC

Genetic testing has become an important tool in understanding breast cancer risk. Whether you've heard about BRCA1 and BRCA2 or are just beginning to learn about hereditary cancer, knowing the basics can help you and your family make informed choices. In this first part, we'll explore what genetic testing is, how it works, and why it matters for breast cancer.

What is genetic testing?

To answer this, we need to review a bit of biology you may not have thought about since high school. Inside each cell of your body is your DNA – half inherited from your mother, the other half from your father. Genes are pieces of DNA that tell your body how to work. Each gene has a specific job. Some are responsible for things like hair colour or eye colour. Other genes play an important role in preventing cancer. If there is a change (called a mutation or pathogenic variant) in one of these cancer genes, resulting in the gene not working

properly anymore, it can raise your risk of developing certain cancers.

Genetic testing can look at specific genes in your DNA for mutations. The two most common genes in cases of breast cancer are BRCA1 (BReast CAncer 1 Gene) and BRCA2 (BReast CAncer 2 Gene). In short, genetic testing can check to see if you were born with a change in a cancer-related gene that might affect your health or your family's health.

How is it done?
The actual process is fairly straightforward: usually a blood test or sometimes a saliva (spit) sample is taken.

What exactly is hereditary breast cancer?
Hereditary (or 'inherited') breast cancer occurs when a gene with a mutation in it causing an increased risk for cancer is passed from one generation to the next within a family. Individuals who inherit this non-working gene have a higher chance of developing breast cancer and certain other cancers than the general population does.

How common is hereditary breast cancer?
It is currently estimated that about 1 in 10 cases of breast cancer is linked to inherited gene changes. This also means that most breast cancer, about 90%, is not inherited. These cases of breast cancer are often referred to as 'sporadic' – meaning they are the result of a combination of events including lifestyle, environment, genetics, and chance.

Unfortunately, breast cancer is a common cancer in women, with 1 in 8 women developing breast cancer in their lifetime. The biggest risk factors for developing breast cancer are being born female and aging. Did you know? About 85% of women diagnosed with breast cancer have no family history of the condition, meaning they are the first person in their family to be diagnosed.

What factors make breast cancer more likely to be a hereditary form?
Both personal factors and family history play a role.

Personal factors:

1. Diagnosis of breast cancer at a young age
2. Diagnosis of certain types of breast cancer (for example: triple negative breast cancer, which is more likely to be caused by an inherited mutation)

Family history – occurrences in a family that are considered a 'red flag' for hereditary breast cancer include:

- Many relatives with breast or ovarian cancer on the same side of the family (either the mother's or the father's side)
- A family member diagnosed with breast cancer at a younger age, usually before the age of 40
- Relatives who have both breast and ovarian cancer
- A person with breast cancer in both breasts
- Breast cancer in a male relative
- A breast cancer which is said to be 'triple negative'.
- An ovarian cancer diagnosed before the age of 70 years
- Ashkenazi Jewish ancestry as mutations in the BRCA1 and BRCA2 breast cancer genes are more common in this population

How can genetic testing impact treatment for breast cancer?

If you have already been diagnosed with breast cancer, the results of

genetic testing may change your treatment plan. For example, certain gene changes, like BRCA1 or BRCA2, can make some chemotherapy or targeted medicines work better.

The results can also guide surgery choices — for example, some people may choose to remove both breasts (not just the one with cancer) and/or their ovaries and fallopian tubes, if testing shows a high inherited risk.

Others opt to have enhanced screening for cancer. If you don't have breast cancer, genetic testing can guide your prevention and screening options, like starting mammograms earlier, adding breast MRI scans, ultrasound or even considering risk-reducing surgery in advance of a cancer diagnosis.

What are some additional benefits of genetic testing?
If a mutation is found it can:

- Explain why you (or a family member) developed cancer
- Help identify which relatives may also be at risk — and which ones can be reassured they are not
- Sometimes provide information on risks for other types of cancer
- Understanding the basics of genetic testing is the first step in deciding if it is right for you.

But knowing what to expect before testing, how results are reported, and how to access testing can be just as important. In Part 2, we'll walk through the practical side of genetic testing: what the results mean, how to get testing in Canada, and how genetic counsellors can help guide you through the process.

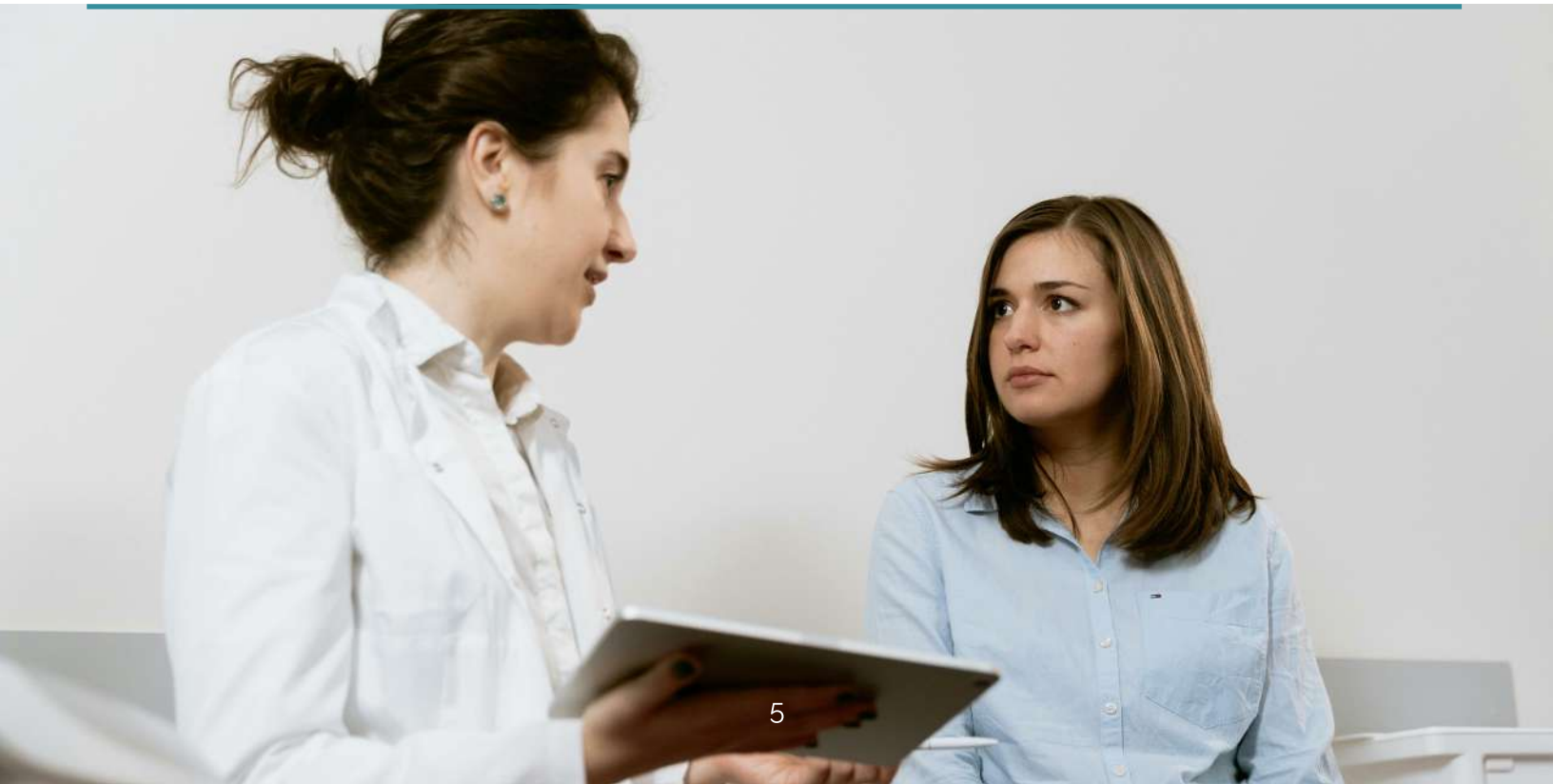
Important Note: This information is for general knowledge and does not constitute medical advice. If you have concerns about your risk of breast or ovarian cancer, consult with a healthcare professional for personalized guidance.

My Genetic Test Results Changed my Treatment Plans

Stacy Zelazny lives in a tiny town in Ontario, literally. She resides in a little-known place called Tiny, Ontario. Stacy describes herself as a mom of two amazing girls who is married to her best friend and winning the biggest fight of her life.

When Stacy first felt a lump in her breast, she dismissed it. She had no reason to worry; she was young and there was no history of breast cancer in her family. During one of her annual checkups with her family doctor, she brought up the lump she had felt earlier, still not too concerned. As a precaution, her family doctor ordered an ultrasound since she was too young for a mammogram. Her healthcare team was also not too concerned, assuming that it was nothing, probably just a cyst. Stacy was told to keep an eye on the lump, and should it change, she could give them a call back.

While her healthcare team was not concerned about the lump, she began to worry about it. So much so that once home, she received a call from her doctor asking her if she was okay since she seemed very concerned about it. And she was worried. At this point, the lump was



now 5cm across her chest. “There’s something there”, she told her doctor.

At that, her doctor referred her to get a biopsy done. The result from the biopsy came back in and in March 2021, Stacy was diagnosed with invasive ductal carcinoma at just 35 years old.

Stacy began her treatment process, meeting with a local general surgeon and the plan was to perform a lumpectomy. She was also to get genetic testing done, but because there was a queue, the timing of when that could be done was uncertain. Stacy had been speaking to a friend about her diagnosis and her friend recommended Dr. Renee Hanrahan, a breast specialist out of the Royal Victoria Regional Health Centre. Dr. Hanrahan told Stacy about a rapid genetic testing study that was being conducted by Women’s College Hospital and she suggested that Stacy join it in order to get the results of a genetic test quicker. The results from the test would help determine whether Stacy’s treatment should involve a double mastectomy or a lumpectomy.

Stacy joined the study and was sent a testing kit that required a simple saliva sample. She sent the sample in and received the results over the phone. She was a BRCA2 mutation carrier. The results meant that a lumpectomy was off the table and her treatment plan now included a double mastectomy and chemotherapy. The results also meant that other family members were tested to see who else was a carrier of the gene mutation. It turned out that both her father and her second eldest sister were carriers. It also means that her two daughters will also have to be eventually tested.

While being diagnosed with breast cancer was shocking, Stacy is grateful to have been involved in the study and that the cancers were found early enough that they hadn’t spread. She is also thankful that she advocated for herself after being told for 6 months that the lump was nothing. “Check those boobies, be proactive, and always ALWAYS advocate”, Stacy urges.

Making Sense of Genetic Testing in Breast Cancer - Part 2: What to Expect and How to Access Testing

By Shelley Kennedy, MS, CGC

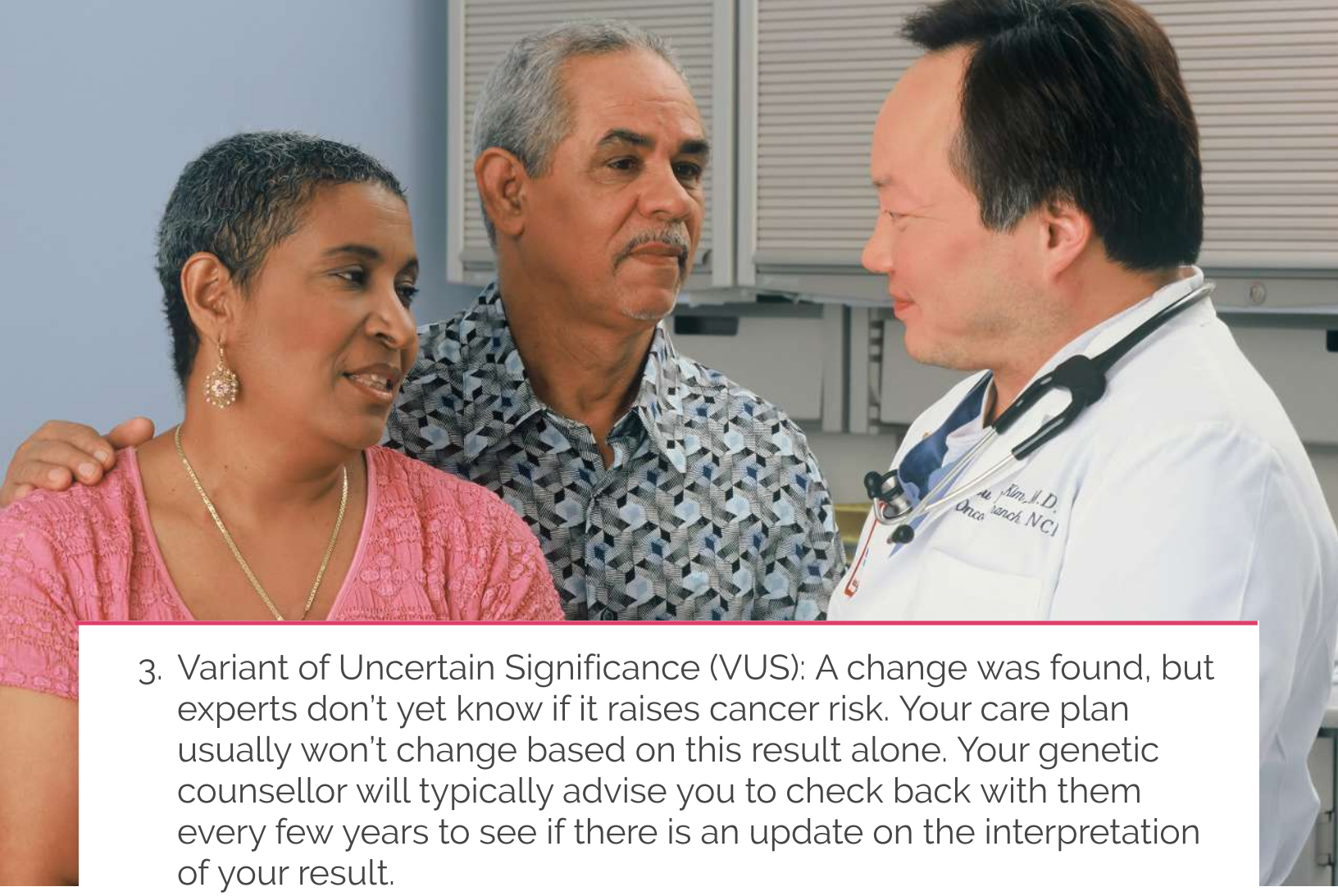
In Part 1, we looked at what genetic testing is and how it helps us understand breast cancer risk. Now let's turn to the practical side: what to consider before testing, the possible results, how to get tested, and the role of genetic counsellors.

What are some things to think about before having genetic testing?
Learning that you have inherited a gene that increases your risk of cancer can be an emotional experience. Sharing results with family isn't always easy, especially if relationships are complicated. A genetic counsellor can assist you in this process.

What results are possible on a genetic test?
There are three main possible results that could be reported by the laboratory:

1. Mutation (pathogenic variant) found: You have a gene change that increases your cancer risk. The actual risk for cancer and recommended screening depends on which gene is involved, as well as personal and family history factors. Your family members can be offered testing. It is important to note that not every individual with an inherited breast cancer gene will develop breast cancer. The risk is increased but it is not a 100% chance.

2. No mutation found: No changes were detected. Your cancer risk is now determined based on your family history of cancer and other personal factors. A "negative" result does not rule out the possibility of developing cancer in the future. Speaking with a genetic counsellor can determine your personalized residual risk.



3. Variant of Uncertain Significance (VUS): A change was found, but experts don't yet know if it raises cancer risk. Your care plan usually won't change based on this result alone. Your genetic counsellor will typically advise you to check back with them every few years to see if there is an update on the interpretation of your result.

How can someone get genetic testing?
Women recently diagnosed with breast or ovarian cancer can be referred to a genetics clinic in their region by their oncologist or primary health care provider. Some clinics accept self-referrals.

Note: People recently diagnosed with breast or ovarian cancer may be offered genetic testing directly by their treating oncologist as the result may impact treatment decisions.

People who do not have breast and/or ovarian cancer but are worried because of their family history can ask for a referral to a genetics clinic by their family doctor.

Individuals in both scenarios listed above also have the option of pursuing private testing.

A listing of Genetic Clinics in Canada can be found at the Canadian Association of Genetic Counsellors (CAGC) or Genetics Education Canada: Knowledge Organization (GECKO).

Who is eligible for genetic testing (Public vs Private testing)?
In Canada, each province and territory has its own guidelines for who qualifies for free, publicly funded testing. For a listing of all breast screening programs by province and territory in Canada visit GECKO. Factors that influence whether you qualify for testing include: your age at diagnosis, the type of breast cancer, your family history of breast cancer, whether your family is from a higher risk ethnic group (e.g. Ashkenazi Jewish), a diagnosis of ovarian cancer, a diagnosis of male breast cancer.

Public testing: This testing is usually arranged through a genetics clinic and requires a referral by a primary care provider. A list of genetics clinics in Canada can be found at CAGC or GECKO.

These testing criteria aim to identify individuals at the highest likelihood of having or developing an inherited form of breast cancer.

Private testing: If you don't meet the current criteria, you can pay out of pocket. This is not typically coordinated through a genetics clinic. Some companies require a doctor's involvement; others offer the test directly to the patient (direct-to-consumer testing).

A few things to consider if choosing a private company/laboratory:

- Does the laboratory hold appropriate certifications standards for patient testing? e.g., Clinical Laboratory Improvement Amendments (CLIA) certification or appropriate provincial licensure bodies for laboratories, board-certification of genetic counsellors and geneticists.
- Does the test look at the right gene(s)? Is the correct type of testing done? The number of genes tested for can vary by laboratory and regularly change. It is the role of the genetic counsellor and geneticist to determine what genes are the correct ones for you. It is important to understand which genes are being tested and what type of testing is used. There have been cases where individuals received a 'negative' result, only to later discover—through a different laboratory—that they carried a breast cancer gene that was not included in their original test.

- Does the company provide genetic counselling to help explain the results?
- How will the company protect your privacy? How long will they keep your DNA?
- There is also the option of participating in The Screen Project, a Canadian National initiative to make BRCA1 and BRCA2 screening available to all Canadians over 18 years of age at an accessible price.

How can a genetic counsellor help in this process?

A genetic counsellor is a health professional with specialized training in explaining genetics and helping individuals adjust to genetic information that not only impacts them, but their family.

Genetic counsellors work as part of a healthcare team with geneticists and oncologists to advise you of your individual cancer risk and help develop a personalized screening and prevention plan for you.

Genetic counsellors can help with:

- Deciding if genetic testing is right for you/your family
- Determining who the best person is in a family to have genetic testing to provide an informative result

- Explaining what your result means
- Talking about how results affect your relatives and how to share the information
- If you test positive for a cancer-related gene change, your close relatives (brothers, sisters, children, and parents) have a 50% chance of having the same change. If they decide to have testing and are found to have the same non-working gene, they can take steps to reduce their risk or undergo screening to try and catch their cancer earlier.

It is important to highlight that testing negative for an inherited breast cancer mutation does not guarantee that you will be cancer free for the rest of your life. Your remaining (residual) cancer risk will be based on your personal and family history. As part of your genetic counselling appointment, you will also have the opportunity to discuss patient support resources and options for participating in research studies.

For some people, genetic testing can feel overwhelming, but you do not have to navigate it alone. Speaking with a genetic counsellor and your healthcare team can help you understand your options and create a plan that fits your personal and family situation. Whether or not you qualify for public testing, knowing the facts can help you make decisions that support your health and peace of mind.

Important Note: This information is for general knowledge and does not constitute medical advice. If you have concerns about your risk of breast or ovarian cancer, consult with a healthcare professional for personalized guidance.

Resources:

- GECKO
- Canadian Association of Genetic Counsellors
- National Cancer Institute
- The Screen Project

Navigating the Stop Signs: A Story of Genetic Testing

By Quinn Obrigewitch

My mother was diagnosed with triple negative breast cancer at the age of 30, both of which are strong indicators of a genetic mutation. Triple negative breast cancer is a more aggressive and lesser-seen subtype of breast cancer that disproportionately targets young women and has fewer treatment options, often resulting in a more aggressive therapy process. This is all due to the unfortunate circumstance that triple negative breast cancer can be a hereditary pathology, commonly known as the Breast Cancer 1 (BRCA1) or BRCA2 mutations. Typically, mutations are not something to be wary of. In fact, they are a rather good thing. They are what make you different from your neighbour, or what has given you your beautifully coloured eyes, or what might be protecting you from a certain disease. Life requires genetic mutations to progress; the world adapts, and then we adapt, and the world adapts again in harmonious flux. However, people born with the BRCA1 or BRCA2 mutations are at a disadvantage against their environment.

The BRCA genes are tumour suppressor genes and can be thought of as the traffic officers of the body. In each hand, they hold one stop sign, which signals to replicating cells that they have fulfilled their duty and can stop dividing. Sometimes, the environment gets too harsh, and a stop sign is lost. This is to be expected, which is why there are two; BRCA1 and BRCA2 will still

function normally following the loss of one stop sign. The mutation causes the loss of function of one stop sign in utero, meaning those possessing the BRCA mutations are only equipped with one stop sign. Once that is lost, cells lose their guidance signal and begin to divide uncontrollably, thus resulting in a difficult-to-treat cancer, which often occurs earlier in life.

With this knowledge, it is easy to understand the essential role genetic testing has in cancer diagnosis and prevention. In fact, genetic testing is what I consider having saved my life. My mother was quick to expose my sisters and me to the danger we may face in young adulthood following her diagnosis. She was never shy to tell us that we need to be vigilant, and our 18th birthdays were marked with the exciting milestone of now being legally old enough to request genetic testing for the BRCA mutation, as per the province of Alberta's cancer screening guidelines. I attended my older sister's appointment with her and had the opportunity to listen to the genetic counsellor speak. My sister and I were met with a warm, safe, and comfortable environment where we drew our family tree and learned all about BRCA, what it does, and why the mutation is bad. The appointment only lasted one hour but we left with a wealth of new information, feeling both scared of what our bodies could do yet relieved that we had the opportunity to act before the cancer. I was so excited to tell my friends about their stop signs.

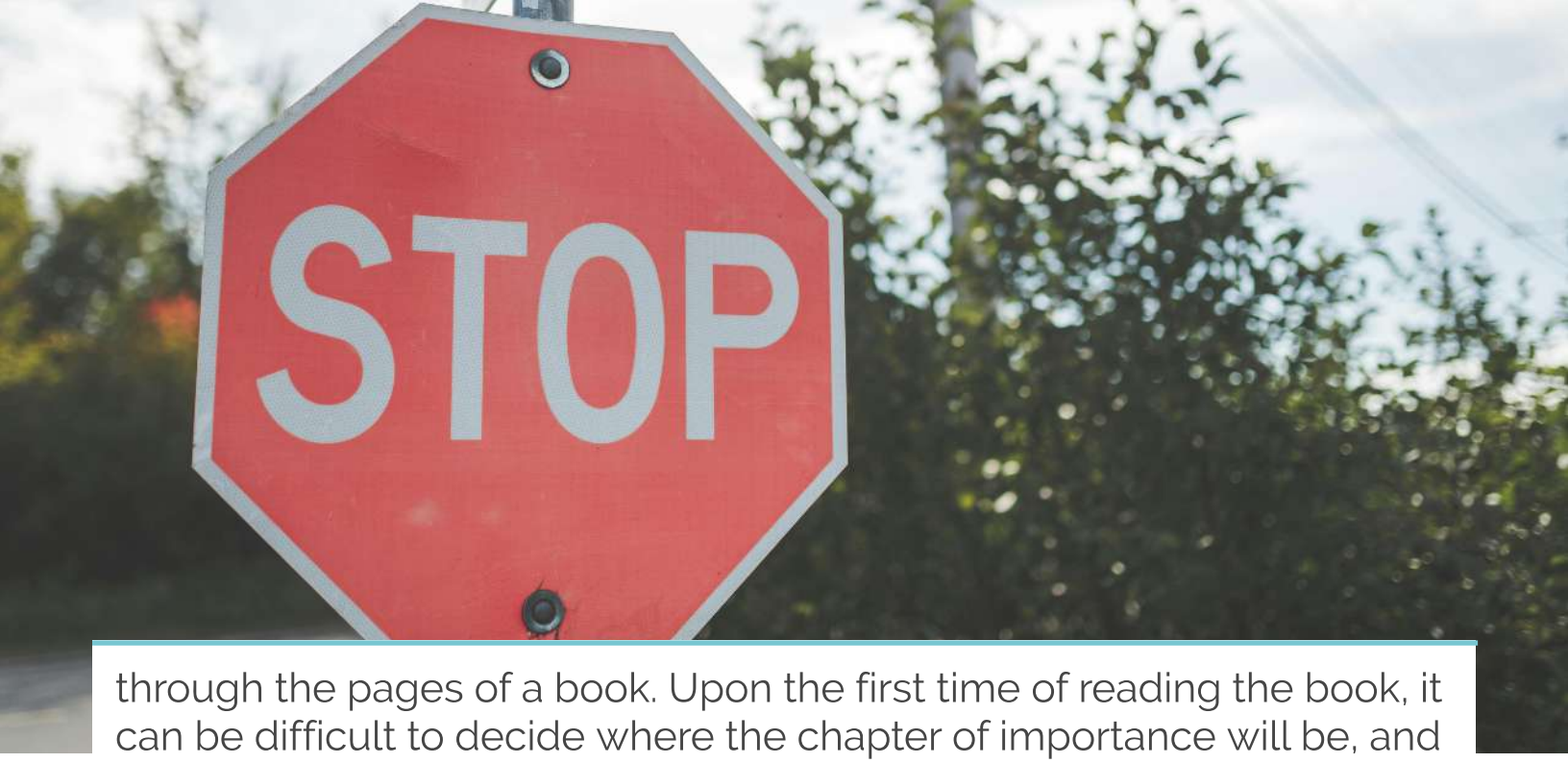
I had my 18th birthday in May of 2018 and had booked myself an appointment to see my family doctor the following week. I remember feeling excited, rather than scared, to request my genetic testing. I had enjoyed everything I learned at my sister's appointment a few years prior so much that I began actively volunteering with the local genetic counsellor, which mostly involved helping her organize her files. Nevertheless, I was looking forward to having her on my team and knew I could put my full trust in her to read my genetic background. My usual family doctor was on maternity leave at the time of my appointment, so I spoke with one who was standing in for her. I come from a relatively small town where everyone is quite well known to each other, so my mother's diagnosis, battle with cancer, and subsequent health advocacy beginning about a decade prior were no

secret. I was in for quite a surprise when I went to speak with the interim doctor and not only had to regurgitate my entire family history of breast cancer and other cancers, but was also met with resistance; “Who is this 'genetic counsellor' you keep asking for? I have never heard of her; we don’t normally have people requesting for genetic testing”. I explained once again the breadth of my family history, my sister’s referral, and how much I needed this test. I walked out of that health clinic with a newfound confidence in advocating for myself, a smile on my face, and a referral in hand.

My appointment was booked two weeks later and fell at the beginning of June. I met with the counsellor whom I had seen 100 times prior, yet I was incredibly nervous. I was so well versed in how these appointments go that at this point I could have recited it myself, but this whole situation was beginning to feel much more real. She asked me how I was feeling, to which I responded honestly, and I was sent away for my bloodwork. Genetic testing is typically done through blood sample analysis; however, it can be done through saliva samples or a cheek swab.

The human genome can be thought of as chapters in a book, with every individual lineage holding its own unique story. Searching for one gene in the entire genome is like sorting

I walked out of that health clinic with a newfound confidence in advocating for myself, a smile on my face, and a referral in hand.



through the pages of a book. Upon the first time of reading the book, it can be difficult to decide where the chapter of importance will be, and so the length of the book must be read carefully and thoroughly. Once the book has been read and understood, a bookmark can be inserted into the desired chapter to make future searches easier and take less time.

My mother was the first one in my family to undergo genetic testing and patiently waited over the course of a year while her book was carefully read. My sister and I were graced with the fortune of my mother's bookmark, and my results were delivered to me, by phone call, three months after my blood test, in September 2018. My genetic counsellor was the one to deliver the news, where she kindly asked me how I was feeling and if I would like any resources including BRCA1 support groups. I politely declined, as I felt the best people for me in that moment were my mother and sister, and that was the end of my journey with my genetic counsellor.

The following years were marked by routine cancer screening and decision making. I opted for prophylactic removal of my breast tissue to reduce my risk of breast cancer, and four years later I am happy to be living freely under normal-population cancer screening guidelines. Genetic testing offered me a brief window into my future by telling me I was missing a stop sign, where I was able to take action to keep myself as healthy as possible, for as long as possible, for the sake of myself, my friends, and my family. Two surgeries in exchange for more certainty, and all because of a silly little stop sign.

History of the BRCA 1 & 2 Genes

Before it was known that genes could be linked to various cancers, 1970s research focused largely on viruses and their role in the development of cancer. With the knowledge that family history had an impact on cancer risk, Mary-Claire King, an American geneticist, began to theorize possibilities beyond viruses and started her mission in identifying the cause of breast cancer running in families.

In the 1970s, King discovered, through a study analyzing the connection between birth control pills and cancer, that an autosomal dominant gene likely explained the multiple incidences of breast cancer within families. This revelation pushed her to identify this gene, and in 1990 she discovered the BRCA1 gene; the first gene known to be linked to breast cancer. Later in 1995, another lab discovered the BRCA2 gene. It was not until the late 1990s that genetic testing was made available for these mutations to the public.

Having a mutation in one of these genes increases a woman's susceptibility to being diagnosed with breast and ovarian cancers. According to US statistics, 55-72% of women with the BRCA 1 and 45-69% with the BRCA 2 mutation will develop breast cancer by 70-80 years of age – this is compared to 13% in the general population.

What are the BRCA genes?

BRCA1 and BRCA2 are genes that create proteins that help with repairing damaged DNA. Everyone has two copies of each, inheriting one from each parent. When one of these genes mutates, the individual has an increased risk of developing breast or ovarian cancer. It is considered autosomal dominant, meaning only one mutated copy needs to be passed down from one parent to cause the increased cancer risk. Having the gene doesn't mean one will definitively develop cancer, and it cannot skip generations.

What is the PALB2 gene?

The PALB2 gene stands for partner and localizer of BRCA2 – this gene

works with the BRCA2 gene to repair DNA that has been damaged. Less is known about the PALB2 genes' connection to breast cancer than the BRCA genes, but research published in 2014 shows indications that having a mutation on this gene increases your risk for breast cancer. It is estimated that by age 50, a woman with the PALB2 mutation will have a 14% risk of breast cancer — this number increases to 35% by age 70. If a 70-year-old woman has two first-degree relatives diagnosed with breast cancer prior to age 50, her risk increases from 33% to 58%.

Who should get tested?
Testing for the BRCA1 and BRCA2 mutations is a personal choice; however, the following factors may increase the chances of having a mutation:

- Having a parent with a positive BRCA1 or BRCA2 result – there is a 50% chance that they passed the mutation on to you
- Being of Ashkenazi Jewish descent
- Family history of:
  - Male breast cancer
  - Young adult breast cancer (breast cancer diagnosed in an individual under the age of 50)
  - Multiple immediate relatives on the same side diagnosed with breast cancer

Options for those with a mutated BRCA or PALB2 gene
Finding out you carry a BRCA mutation can be difficult, and decisions regarding what to do with this information vary and are personal to each family.

Some options include:

- Screening for breast cancer at a younger age and more often
- Prophylactic surgery: removal of breast tissue to reduce risk
- Using chemo preventative drugs which reduce the risk of breast cancer in women at increased risk

After doing a genetic test, it is best to speak with the genetic counsellor who did your testing to decide on the best next steps for you.

Reducing the Risk of Hereditary Breast and Ovarian Cancer: One Woman's Story

In October 2013, Allegra Kawa of Edmonton had surgery to remove both her breasts. She's also considering surgery to remove her ovaries and uterus.

She didn't have cancer and she is perfectly healthy. However, a strong family history of breast and ovarian cancer had led her to get genetic testing, which revealed she had a BRCA1 gene mutation, putting her at high risk for these cancers.

She had seen her cousin die at age 30 from metastatic breast cancer. Her maternal grandmother had ovarian cancer at age 40 and died at age 46. Her mother had breast cancer at age 35.

She says that normally, a prophylactic surgery is performed at age 25 or later. But her risk was so strong that she had hers at age 23.

Her surgery involved a cut underneath the breast, sparing the nipple. The breast tissue was scooped out and a tissue expander inserted behind the pectoral muscle.

Over six weeks, more and more saline was gradually injected into the tissue expander to increase the volume of skin. Then in May 2014, the tissue expander was removed, and implants were inserted.

During the skin stretching, "There was so much pressure applied to the nipple that the areola actually lost its colour and was misshaped," says Allegra. She had her areola tattooed to restore the colour.

That was not the end of her breast surgery. When she later fell and injured her breast, the surgeons tried to repair it. They were concerned

about the possibility of lymphoma, and so they took extra tissue out and sent it to a laboratory for analysis.

The results were negative for lymphoma, but Allegra was left with a breast that was "kind of droopy, not looking quite so pretty." She felt very self-conscious and wanted to hide her appearance from her husband.

"It put me in a bit of depression, thinking `Oh, he's not going to think I'm beautiful anymore.' That kind of hindered our physical relationship."

Another surgery restored a somewhat better appearance. "They tried to fix it and it wasn't quite fixed. But I thought, I'm just going to move on with the rest of my life," says Allegra.

In 2017, Allegra and her husband were having difficulties in their marriage, and they separated.

One month later, Allegra gave birth to a son who is the joy of her life. She couldn't breastfeed, and she got "very annoyed" with people asking why she was using formula. "If you breastfeed in public, you get a look. And if you don't breastfeed, you get a look, too. You're doomed if you do, doomed if you don't!"

While Allegra's risk of breast cancer is greatly reduced, her risk for ovarian cancer remains high. At age 34, she will start screening for ovarian cancer. She also needs to decide whether to have surgery to remove her ovaries and uterus.

"Ideally they would like me to make the decision before I turn 40 because that is when my risk is at its highest. So that decision is probably the scariest for me because as a nurse, I know how impactful estrogen and the ovaries are to a woman's health, especially heart health and bone health."

Allegra is considering hormone replacement therapy because, she says, "Surgical menopause would kick in right away without a natural progression through your lifetime. So it is a very big shock to the body." She has a lowered risk of breast cancer because of her mastectomies, so HRT is less risky for her than for other women.

This is not a journey that you have to do by yourself. Surround yourself with your family. Surround yourself with the people you love.

Allegra says she had "great care" from the general surgeon and plastic surgeon who performed her mastectomies and reconstruction. However, she lacked information designed specifically for a prophylactic mastectomy. Most of the information she received was aimed at breast cancer patients.

She would have liked to know more about how her breasts would feel post-mastectomy and what the process was for surgery and recovery. She also didn't know what items to pack for her hospital stay. In addition, she wanted more support for her husband.

She says that her breasts now have decreased sensation. "Your chest will get very cold quickly and you won't notice," she says.

She recommends a lanyard to hold wound drains while showering (wound drains are plastic tubes that are attached to the surgical site to drain fluids; they are removed a few weeks after surgery).

She also recommends asking lots of questions of the medical team and of other patients who have been through the same experience. She says that Breast Reconstruction Awareness Day, or BRA Day, held in October each year, and the Hereditary Breast and Ovarian Cancer Foundation are good sources of information.

To other patients embarking on a similar journey to hers, Allegra says, "This is not a journey that you have to do by yourself. Surround yourself with your family. Surround yourself with the people you love. Don't isolate yourself. You have the opportunity to make a decision for you. Don't allow anyone else to make that decision for you. If screening is the way you want to go, just do a screening. If you change your mind, that's okay, too. You are the master of your own body."

What Are the Other Breast Cancer Genes?

Awareness of the various genetic mutations that can lead to breast cancer is necessary in understanding the risk factors for the disease, particularly when it comes to hereditary forms. While mutations in the BRCA1 and BRCA2 genes are now well-publicized, there are other, lesser-known genetic mutations which can significantly increase the likelihood of developing breast cancer as well. Understanding these genetic risks allows individuals to make informed decisions about their health, from preventive measures to early detection strategies. Here, we discuss the lesser-known genetic mutations that can also impact the risk of developing breast cancer.

TP53 (tumour Protein 53)

Li-Fraumeni syndrome (LFS) is linked to mutations in the TP53 gene, called a tumour suppressor gene, which normally acts as a safeguard to stop cells from growing and dividing too quickly. When this gene is mutated, the protein it produces becomes inactive, causing tumor cells to lose their protection against genetic changes. As a result, people with LFS have a very high risk—up to 90%—of developing one or more types of cancer by age 60, with many facing cancer before

they turn 40. For women with LFS, breast cancer is the most common type, and many are diagnosed before the age of 40. Breast cancers in women with a TP53 mutation are more likely to be hormone receptor-positive (HR+) and/or HER2-positive.

PTEN (phosphatase and TENsin homolog)
The PTEN gene is another important tumor suppressor, and mutations in this gene are most commonly linked to Cowden syndrome. This condition increases the risk of developing benign tumors, but also raises the likelihood of certain cancers, including breast cancer. PTEN mutations are not only associated with breast cancer but also with endometrial, thyroid, kidney, and colorectal cancers. PTEN mutations are often found in more aggressive subtypes of breast cancer, and loss of PTEN function has been linked to poorer responses to trastuzumab (Herceptin), a drug used to treat HER2-positive breast cancer.

CDH1 (cadherin 1)
The CDH1 gene is linked to an increased risk of two types of cancer: diffuse gastric cancer and invasive lobular carcinoma (ILC), a form of breast cancer. The CDH1 gene provides instructions for making a protein called E-cadherin, which is crucial for holding cells together. When this gene is mutated, it disrupts cell bonding, which can lead to the development of cancer. Around 6% of new cases of ILC are linked to genetic mutations, including those in the CDH1 gene. Changes in this gene have been linked to a 55% lifetime risk of developing ILC. Genetic testing for CDH1 mutations is especially recommended for people with early-onset ILC (under age 45), bilateral ILC (both breasts affected, especially in those over 70), or a strong family history of ILC. Provincial genetic testing criteria may not reflect these recommendations, so we encourage a discussion with your doctor to explore your eligibility.

STK11 (serine/threonine kinase 11)
STK11 is another important tumor suppressor gene, and mutations in this gene are linked to Peutz-Jeghers syndrome (PJS). PJS can show early signs during childhood, such as darker skin spots around the mouth, lips, fingers, and toes, and some people may also develop freckling inside the mouth. One of the main features of PJS is the

growth of hamartomatous polyps, which are non-cancerous lumps in the gastrointestinal tract. While most cancers related to PJS occur in the digestive system, individuals with STK11 gene mutations are also at a higher risk of developing breast cancer, especially as they age.

PALB2 (partner and localizer of BRCA2)
PALB2 is a tumour suppressor gene that works closely with BRCA2 to help prevent healthy cells from becoming cancerous. PALB2 mutations are associated with a high risk of breast cancer and moderately high risk of ovarian and pancreatic cancer. Subtypes associated with the PALB2 mutation are most often estrogen receptor positive (ER+) but have also been linked to triple negative as well. People with this mutation are also more often diagnosed at a younger age.

CHEK2 (checkpoint kinase 2)
The CHEK2 gene helps repair damaged DNA and control cell growth. People with a CHEK2 mutation are more likely to develop breast cancer, often before age 50, and are more likely to develop invasive ductal carcinoma (IDC) or ductal carcinoma in situ than other types of breast cancer. Some studies suggest that individuals with CHEK2 mutations could be at an increased risk of breast cancer recurrence over a 10-year period.

ATM (ataxia telangiectasia-mutated)
Mutations in the ATM gene cause Ataxia Telangiectasia, a rare inherited disorder that affects the nervous system and increases the risk of breast cancer. ATM-mutated breast cancers are more commonly ER+, and may be more aggressive and harder to treat.

Genetic testing is the only way to positively confirm the presence of a genetic mutation associated with cancer. Hereditary cancer risk assessment is a process used to estimate the likelihood of inheriting mutations in cancer-related genes, based on both personal and family medical histories. This assessment includes genetic counseling, testing, and managing individuals who may be at risk, helping them make informed decisions about cancer surveillance, preventive surgeries, and the use of medications or other treatments to lower cancer risk.

A proper hereditary cancer risk assessment is essential for understanding both personal and family risks for breast cancer and other cancers. To help guide these decisions, individuals are encouraged to discuss key questions with their doctors, and they can refer to our Hereditary Breast Cancer Syndrome factsheet for more information on genetic testing and personalized cancer screening and care.

Genetic testing is the only way to positively confirm the presence of a genetic mutation associated with cancer.

Why Men Should Consider Genetic Testing for BRCA Genes

Both men and women have breast tissue, and while men don't have the ability to produce milk, their breast cells can still develop into cancer. About 1 in 5 men with breast cancer have a close relative —male or female—who also had the disease. Research indicates that biological males make up half of the U.S. population carrying a BRCA1 or BRCA2 mutation, genes commonly linked to breast cancer in women.

Men with a BRCA mutation have up to an 8% lifetime risk of developing breast cancer, compared to 0.1% for the general male population. Additionally, men with BRCA mutations are at an increased risk of developing prostate, pancreatic, and other cancers throughout their lives. This makes it important for men with a family history of breast cancer to consider genetic testing. If a man carries the BRCA mutation, it's important to inform family members, such as sisters or daughters, as they may also carry the gene mutation. This gives them the option to also undergo genetic testing, which can lead to personalized screening protocols that detect cancers early and improve treatment outcomes.

Men are typically diagnosed after the age of 60 and may exhibit many of the same symptoms as women with breast cancer, such as:

- A lump in the breasts (usually painless to the touch)
- Nipple discharge
- Swollen and/or sore breasts
- Nipple retraction or an inverted nipple
- Rash on or near the nipple
- Lumps under the arm
- Redness of the nipple or of skin near the breasts

However, due to a lower awareness of breast cancer in men, they often delay seeing their healthcare provider. Treatment for male breast cancer is similar to treatment for women as well, which may involve surgery to remove breast tissue, chemotherapy and radiation therapy. This delay can result in a diagnosis at a more advanced stage, leading to poorer health outcomes.

While men with the BRCA mutation are at a higher risk of developing breast cancer compared to the average man, carrying the gene mutation does not guarantee that they will develop the disease. There are other risk factors that, when combined with the BRCA mutation, can increase the likelihood of developing breast cancer. These include elevated estrogen levels, which may occur if you:

- Have long-term liver damage, such as cirrhosis
- Are overweight or obese
- Have Klinefelter syndrome, a condition where a genetic male has an extra X chromosome
- Were assigned male at birth and have received estrogen hormone therapy for more than 2 years as part of gender-affirming care

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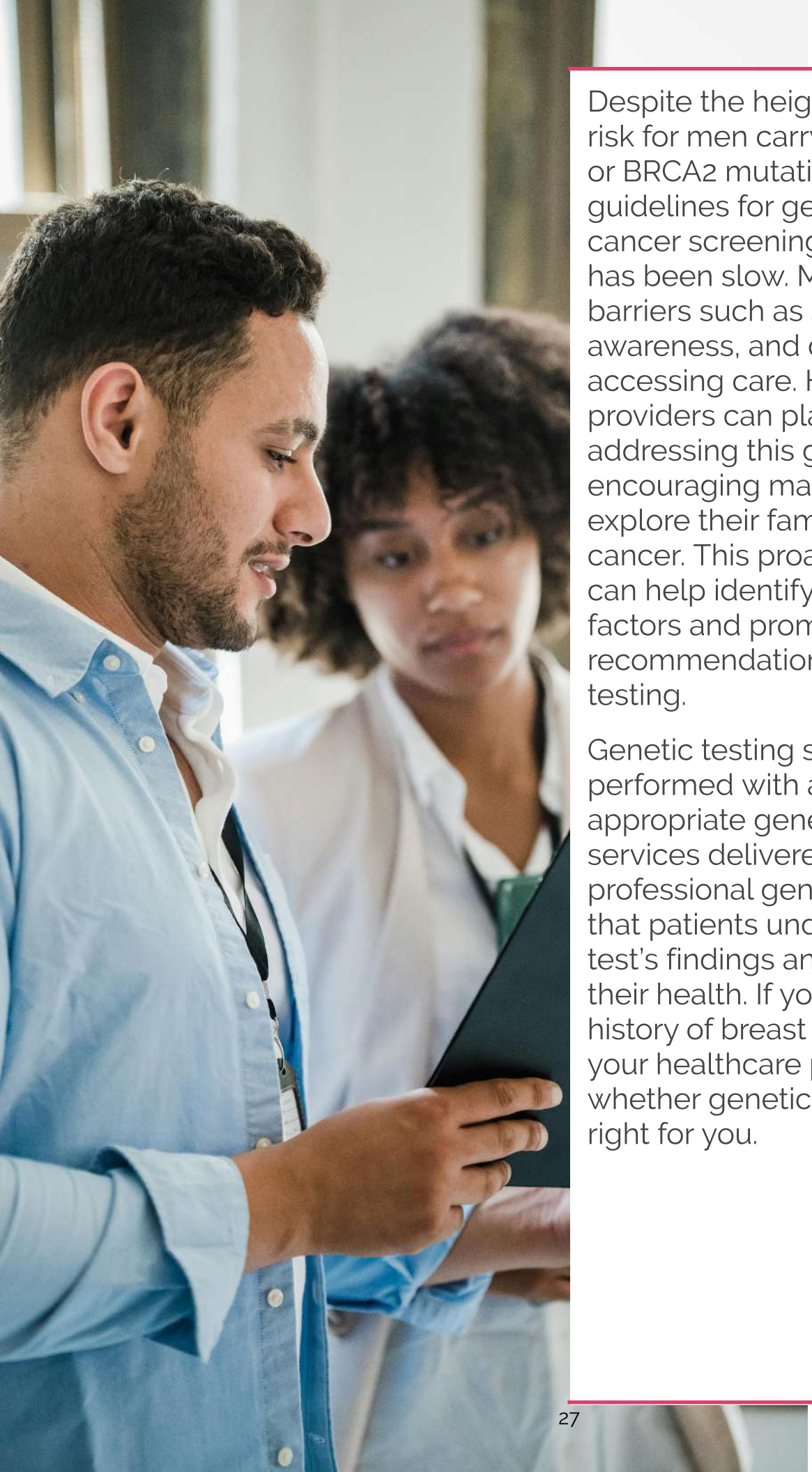


Despite the heightened cancer risk for men carrying the BRCA1 or BRCA2 mutations, progress for guidelines for genetic testing and cancer screening for this group has been slow. Men often face barriers such as stigma, lack of awareness, and difficulty accessing care. Healthcare providers can play a crucial role in addressing this gap by encouraging male patients to explore their family history of cancer. This proactive approach can help identify potential risk factors and prompt recommendations for genetic testing.

Genetic testing should be performed with access to appropriate genetic counselling services delivered by a certified professional genetic counselor, so that patients understand the test's findings and implications for their health. If you have a family history of breast cancer, talk to your healthcare provider about whether genetic testing might be right for you.

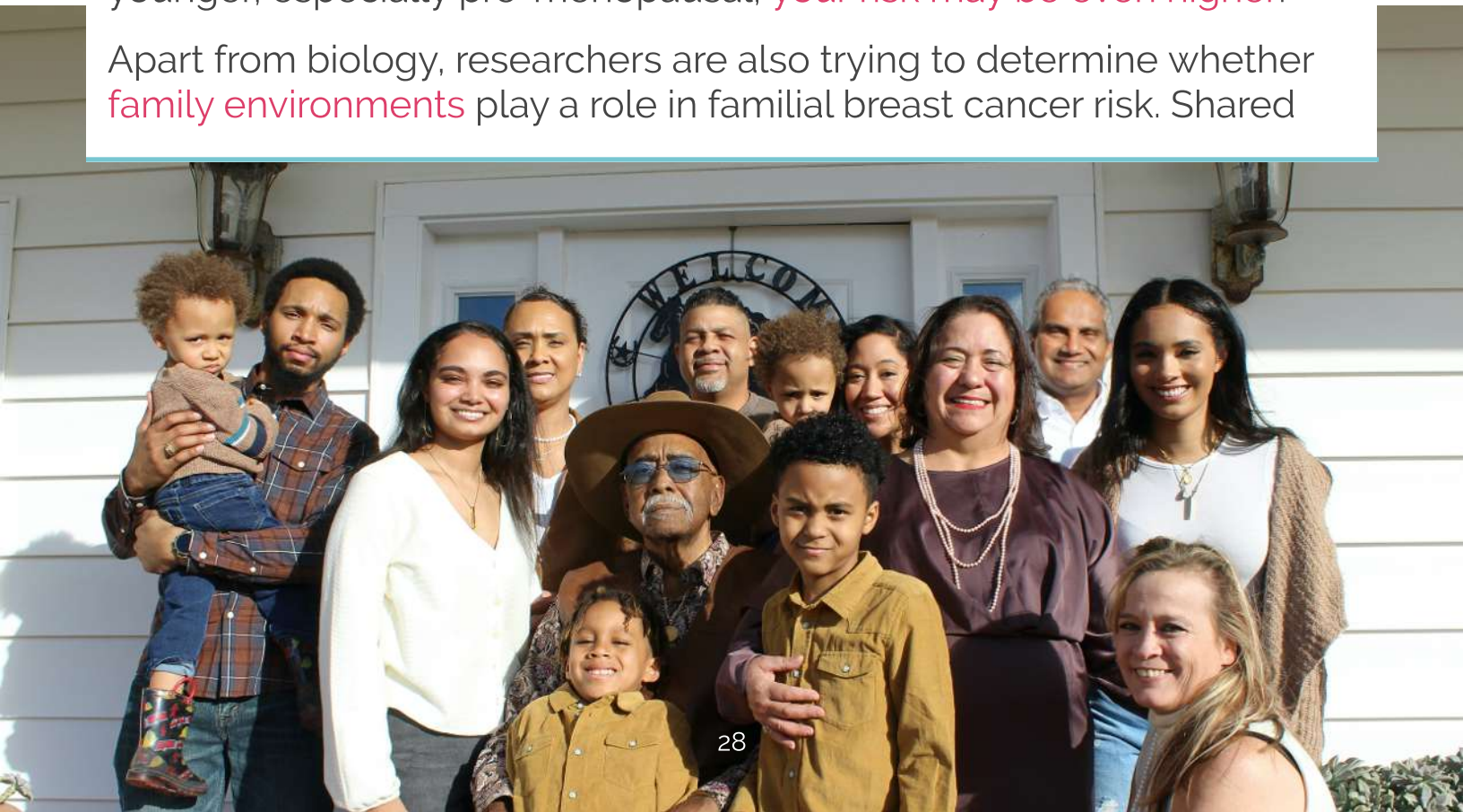
Familial vs Hereditary Breast Cancer: What's the Difference?

About 5% to 10% of breast cancer cases are passed down through families. These are caused by changes (commonly known as mutations) in certain genes, like the BRCA1 and BRCA2 genes, that are inherited from a parent. This is hereditary breast cancer. However, most people who get breast cancer do not have one of these inherited gene changes.

Sometimes, several people in a family may have breast or other types of cancer, even if no specific gene mutation is found. This is called familial breast cancer. Having a family history can raise your risk, but it doesn't always mean the cancer is genetic.

Risks associated with a familial breast cancer can vary depending on certain factors. Your risk can almost double if you have a first-degree blood relative, like a mother, sister, or daughter who has had breast cancer. The more first-degree blood relatives affected, the higher your risk. It also matters how old they were when diagnosed; if they were younger, especially pre-menopausal, your risk may be even higher.

Apart from biology, researchers are also trying to determine whether family environments play a role in familial breast cancer risk. Shared



If you have a strong family history of breast cancer, you may need to be screened more often... Your doctor can create a screening plan just for you.

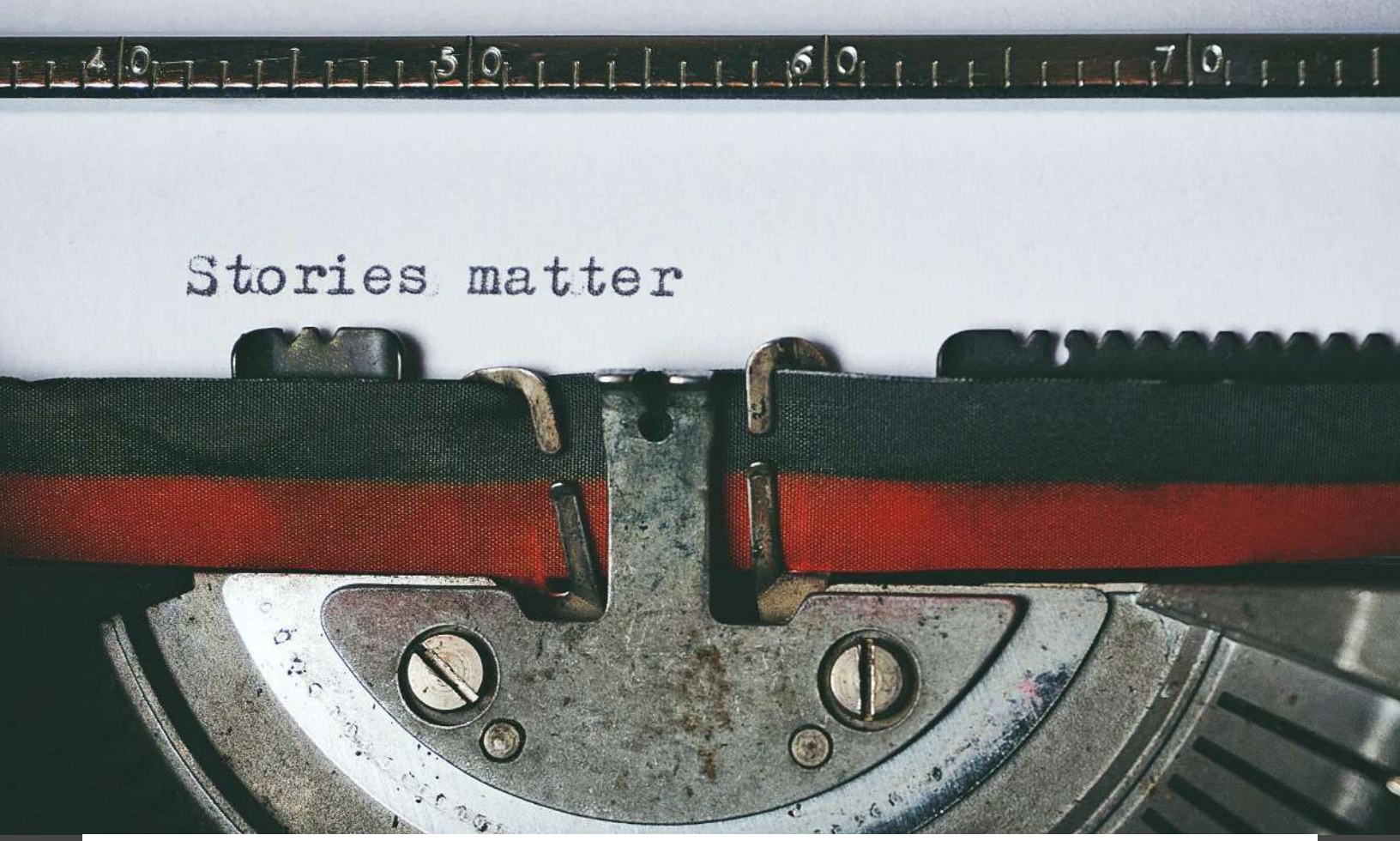
lifestyles, diets, and where you live could also affect the chances of cancer clustering in families.

If You Have Familial Breast Cancer
If you have a strong family history of breast cancer, you may need to be screened more often than someone without that history. Your doctor can create a screening plan just for you, which might include having a mammogram every year. Other tests, like an MRI or ultrasound, may also be suggested. These tests give clearer images of the breast, especially if your breast tissue is dense.

You might also need to start screening sooner than normal. Most provincial health organizations recommend getting your first mammogram at age 40, but if you're at high risk of breast cancer, you may benefit from starting to screen at a younger age.

In addition to screening, consider your family's shared lifestyle habits. Regular physical activity, a well-balanced diet, and avoiding smoking and alcohol can not only help reduce the risk of breast cancer, but also improve overall health and wellbeing.

What If It Is Hereditary?
If you have a strong family history of breast cancer but are unsure if there's a genetic connection, you can look into genetic testing to determine if you carry a mutation of one of the breast cancer genes. Speak to your doctor to discuss your options for genetic testing and getting a referral for a genetic counsellor.



Our Voices is a place for breast cancer patients to share their experiences in their own words and to inspire others. The best stories focus on one specific aspect of the cancer journey. For example, you may want to talk about tips for dealing with cognitive difficulties that come from chemotherapy, or organizing a team of friends and family to support you during treatment. The choice of topics is yours and the length can be as short as one page.

Before you start writing, send a brief description of your story idea to us at cbcn@cbcn.ca, and we'll give you some more specific writing guidelines. Interested in sharing your story but don't know how to get started? Use our submission template and we'll put your story together for you.

The breast cancer community will look forward to reading your story!

Canadian Breast Cancer Network
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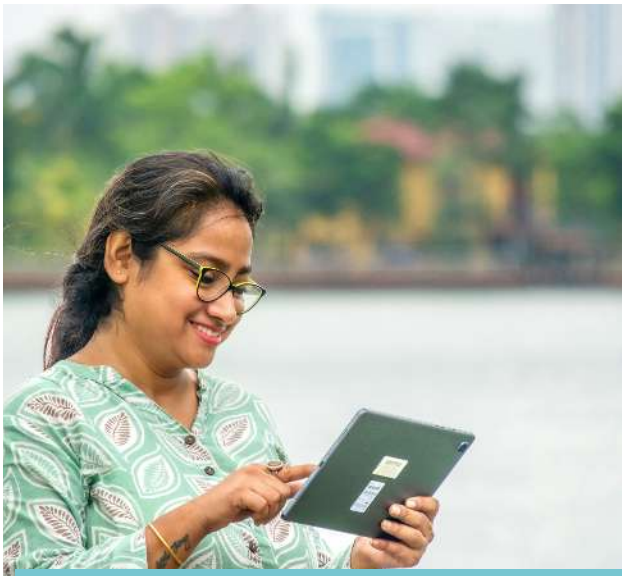
Order Our Resources

Finding reliable information on breast cancer can be overwhelming. We have produced various reports to help you understand your breast cancer diagnosis better. These resources are available online.

Explore our resources today!



Subscribe to Our Newsletter

CBCN Connected is our monthly digital newsletter which gives updates on our activities, educational events, and resources. We also give updates on metastatic breast cancer with our mBC Connected newsletter.

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