PINK HOPE

A Guide to Hereditary Breast and Ovarian Cancer for *Jewish Families*

In collaboration with:

SHARSHERET®
Your Jewish Community Facing Breast Cancer

Sponsored by:

TERRACE TOWER GROUP

www.pinkhope.org.au | *www.sharsheret.org*

Content

Introduction

Pink Hope is Australia's only community designed to **inspire women to be proactive and vigilant with their breast and ovarian health,** while providing a safe haven for high-risk women to connect. **Sharsheret**, Hebrew for 'chain', is the only national United States organisation **supporting young Jewish women and families** facing breast cancer, including those at high- risk. Pink Hope and Sharsheret have joined forces to create a resource specifically designed to help the Australian Jewish community understand their risk. And if they are high-risk, the options available to them throughout their journey.

One in 40 people of Ashkenazi Jewish descent carry a gene mutation that increases their lifetime risk of developing breast and ovarian cancer. This means that individuals of Ashkenazi Jewish descent have a higher hereditary predisposition to breast and ovarian cancer than the general population, increasing the need for awareness and support for these families.

Hereditary predisposition to breast and ovarian cancer comes from specific mutations within the BRCA1 and BRCA2 genes. If you or someone you care about is of Ashkenazi Jewish decent, genetic counselling and testing may be helpful to determine whether a BRCA1 of BRCA2 gene mutation is carried within the family. **Knowing your risk can empower you to make informed decisions about your health.** This knowledge can also help identify the options you have to reduce your risk and increase early detection. By knowing you and your partner's genetic background, you can also make informed decisions and assess any potential for passing on gene mutations to the next generation.

Whether or not you decide on genetic counselling and testing, Sharsheret and the Pink Hope community are here to provide you with support through your journey.

The information contained in this booklet is intended to provide broad knowledge of available resources and should not be construed as an endorsement of any health care professional, organisation or program mentioned. All medical information should be discussed with a health care professional.

UNDERSTANDING THE *Risk*

of Breast & Ovarian Cancer in the Jewish Population

What are the BRCA1 and BRCA2 Genes?

All individuals carry the BRCA1 and BRCA2 genes, which belong to a class of genes known as tumour suppressors in breast and ovarian tissue. Everyone has two copies of each of these genes - one from each parent. In normal cells, BRCA1 and BRCA2 help ensure the stability of the cell's DNA and regulate the cycle of cell division. Mutations in these genes can lead to the deregulation of cell division, causing uncontrollable cell growth. Thus, BRCA1 and BRCA2 gene mutations are associated with an increased risk of hereditary breast and ovarian cancer.

It is important to note that while 90% of breast and ovarian cancer diagnoses are sporadic, approximately 5-10% of breast and ovarian cancer diagnoses are due to an inherited predisposition, associated with BRCA1 and BRCA2 gene mutations. In women, carrying a BRCA1 or BRCA2 mutation can increase the lifetime risk of breast cancer between 50% - 80%, and increase the lifetime risk of ovarian cancer between 10% - 45%. In men, carrying a BRCA1 or BRCA2 mutation can increase the lifetime risk of breast cancer between 1-10%, and increase the lifetime risk of prostate cancer between 15-25%. The BRCA1 and BRCA2 mutations have also been associated with pancreatic cancer and melanoma, as seen in the table below. In the general population, only 1 in 200 people carry a mutation in these genes, whereas in the Ashkenazi Jewish population, 1 in 40 people will carry the mutation. Having an inherited gene mutation on BRCA1 or BRCA2 does not mean a person is guaranteed to develop cancer, but the risks are significantly higher than for someone who does not have a gene mutation.

The following tables show how BRCA1 and BRCA2 gene mutations affect the lifetime risk of different cancers in men and women:

Table 1: Lifetime BRCA1 and BRCA2 Cancer Risks for Women

Type of Cancer	Women with BRCA1 mutation	Women with BRCA2 mutation	Average woman in US without mutation
Breast	60 - 80%	50 - 70%	13%
Ovarian	20 - 45%	10 - 20%	1 - 2%
Pancreatic	2 - 3%	3 - 5%	1%
Melanoma	-	3 - 5%	1 - 2%

Source: Abramson Cancer Center

Table 2: Lifetime BRCA1 and BRCA2 Cancer Risks for Men

Type of Cancer	Men with BRCA1 mutation	Men with BRCA2 mutation	Average man in US without mutation
Breast	1 - 5%	5 - 10%	0.1%
Prostrate	*	15 - 25%	16%
Pancreatic	2 - 3%	3 - 5%	1%
Melanoma	-	3 - 5%	1 - 2%

Source: Abramson Cancer Center

* There is no solid evidence of an overall increased risk of prostate cancer in BRCA1 mutation carriers, although this mutation may be associated with an earlier age of onset in prostate cancer in comparison with the general population.

BRCA1 and BRCA2 mutations are currently one of the best indicators of an individual's hereditary breast and ovarian cancer risk. However, there are many families with extensive histories of breast and ovarian cancer who do not carry these mutations. This means BRCA1 and BRCA2 may not be the only gene mutations responsible for hereditary cancers, and researchers continue to search for other associated genes. A genetic counsellor can help you determine the appropriate genetic test for you and whether further testing is recommended.

Why are the Ashkenazi Jewish Population at a Higher Risk?

It is well established that some inherited diseases occur more commonly in some ethnic groups than in the general population. This can be explained by what is called the 'founder effect', which is seen in groups that have been isolated due to religious, geographical, or cultural reasons and have a small collection of common ancestors. Because of the small group of founding Ashkenazi Jews, there is a limited genetic lineage that has been passed down through the generations. This means that any disease-associated mutations present in the founding ancestors become common in the resulting population. In the case of breast and ovarian cancer, specific BRCA1 and BRCA2 mutations have been passed down more frequently in Ashkenazi Jews than in the general population. Research has indicated that the BRCA1 and BRCA2 mutations that are present in Ashkenazi Jews today originated in common ancestors roughly 600 years ago. It is important to remember that Jewish ancestry, and its influence on your risk, is based upon your genetic makeup and not on your spiritual connection to Judaism.

Ashkenazi Gene Mutations

Studies conducted on DNA samples of Ashkenazi Jews led to the discovery of a high prevalence of BRCA1 and BRCA2 gene mutations. On each of these genes, there are hundreds of possible mutations, though research has revealed the presence of three specific mutations that account for ~90% of Ashkenazi BRCA1 and BRCA2 gene mutations. Of these three gene mutations, two occur on the BRCA1 gene and one occurs on the BRCA2 gene.

185delAG BRCA1 mutation was the first to be linked to Ashkenazi Jews and is found in approximately 1% of the Ashkenazi population.

5382insC BRCA1 mutation is the least common Ashkenazi mutation, occurring in approximately 0.15% of Ashkenazi Jews.

6174delT BRCA2 mutation is the most common of the three BRCA1 and BRCA2 mutations found in Ashkenazi Jews, and is found in approximately 1.5% of such individuals.

Since these mutations have been identified as accountable for the majority of the BRCA1 and BRCA2 mutations in Ashkenazi Jews, it has made genetic testing more straightforward in this population. Testing can begin with just the three mutations, rather than the hundreds of other possible mutations on BRCA1 and BRCA2 that can be found in the general population. This can make testing more affordable and easier to interpret. If the results related to these three specific mutations test negative, then proceeding with a broader full sequence or rearrangement test should be considered to rule out the presence of other BRCA1 or BRCA2 mutations.

Frequency of Ashkenazi Gene Mutations

In the general population, approximately 1 in 200 people carry a BRCA1 or BRCA2 mutation, whereas around 1 in 40 individuals of Ashkenazi Jewish descent carry one of the three associated mutations. This means 2.65% of the Ashkenazi population carries one of these three mutations. Adding to this, if a person of Ashkenazi descent has a personal or familial history of breast or ovarian cancer, their chance of having one of these mutations is much higher.

- **21% of Ashkenazi Jews who have had breast cancer before the age of 40 have been found to carry a BRCA1 mutation.**
- **29% of people of Ashkenazi decent with a family history of two or more cases of breast cancer carry one of the BRCA1 or BRCA2 mutations.**
- **73% of Ashkenazi Jews with a family history of two or more cases of breast cancer and at least one case of ovarian cancer carry one of the BRCA1 or BRCA2 mutations.**

SO, IF I CARRY A MUTATION,
What Is My Risk of Developing Breast or Ovarian Cancer?

The burning question is always going to be about how relevant this information is, and in this case, how many carriers of the mutation will actually develop the associated disease. A recent population based study of Ashkenazi Jews who carry the BRCA1 and BRCA2 mutations has shown that 56% of such individuals will develop breast cancer and 16% will develop ovarian cancer in their lifetime. This study also found that the presence of the same mutations increase the risk of prostate cancer in men, with 16% of male mutation carriers developing the disease by age 70. See how this compares to the general population in the table below.

Table 3: Lifetime Risk of Breast and Ovarian Cancer in General Population and Ashkenazi Jewish Mutation Carriers

Type of Cancer	% of General Population That Will Develop the Disease	% of Ashkenazi Jewish Mutation Carriers That Will Develop the Disease
Breast	12%	56%
Ovarian	1.4%	16%

ASSESING YOUR *Individual Risk*

Every individual is different and your risk is determined by a combination of factors, including family history and genetics. It is important to investigate your risk so as to understand and be proactive about your breast and ovarian health. Knowing your risk and understanding your options can help you determine the best way to manage your health.

Investigate Your Family History

5-10% of breast and ovarian cancer cases are due to an inherited predisposition to the disease. Your family history is a good indicator of your risk, so it is important to gather information on the cancer history of both your mother's and father's relatives. Sometimes this can be difficult to discuss, but Judaism urges us to protect our health, and investigating family history is in the best interest of health preservation. So make some calls, or take the opportunity on the next Jewish holiday to ask your relatives about your family cancer history. In some Ashkenazi Jewish families there can be a lack of information about family history due to the Holocaust. Additionally, for some of Ashkenazi Jewish descent, there is a taboo surrounding cancer topics, and cancer diagnoses may not be discussed within a family.

This can make it difficult to compile accurate information about the health history of past generations and further research may be required. Reach out to all living family members, and consider trying online genealogies to source relatives and information.

Your family history can suggest whether or not you are likely to inherit an increased risk of hereditary cancer. This in turn can indicate whether you are likely to carry the BRCA1 or BRCA2 gene mutations, and may highlight whether you should look into genetic counselling and testing.

Consider Genetic Testing

If you uncover a family history of cancer, you should alert your doctor to the relevant information. Based on this, they may suggest genetic counselling and testing o determine whether you carry a gene mutation associated with breast or ovarian cancer. A series of health care professionals will guide you through this process if you chose to go forward with it.

On the next page are a few **FAQ´s** in regards to genetic testing.

FAQ´s

What are the BRCA1 and BRCA2 Genes?

The BRCA mutation genetic test involves collecting a DNA sample, which can be done through a blood test or a mouthwash. As explained above, three specific mutations have been identified as accounting for ~90% of Ashkenazi BRCA1 and BRCA2 gene mutations. Because of this, genetic testing can begin with just the three mutations rather than the hundreds of other possible mutations on BRCA1 and BRCA2 that can be found in the general population. If the result of these three mutations is negative, then proceeding with a broader full sequence test or rearrangement may be recommended to assess whether other mutations are responsible for your family history.

After your test, your doctor or genetic counsellor will contact you with the results. Your health professional will interpret the results and take into consideration other factors about your family history and lifestyle to explain your risk. Once you understand this, your health care team can help you develop strategies to lower your risk.

The results of a genetic test may help you to better understand your risk, though interpreting the results is not a clear-cut process. While the risk is elevated, not all people who carry a BRCA1 or BRCA2 mutation will develop breast or ovarian cancer. Furthermore, if you do not carry a BRCA1 or BRCA2 gene mutation, but your family has a high incidence of cancer, you may still be considered high risk. It is also important to note that not all children of those with a BRCA1 or BRCA2 mutation will inherit the gene mutation. Your genetic counsellor will help you determine if further testing should be considered.

Due to the many factors that influence your risk, it is essential to involve medical professionals in this process. Consult your doctor, family cancer clinic or genetic counsellor in reference to how you are impacted by your family history and your genetics. In doing so you can accurately understand your risk, and make informed decisions about your health and risk reduction.

Should men also be tested for BRCA1 and BRCA2 mutations?

BRCA gene mutations are associated with increased risk of breast and ovarian cancer. Obviously the latter is not relevant for men, but you must remember – men also have breast tissue. Although the risk of breast cancer is higher in women than men, males account for approximately 1% of all breast cancer cases. A genetic link for the disease has also been observed in men, with studies showing that men who carry a BRCA2 mutation have a one in 15 chance of developing breast cancer before age 70.

Often men and their doctors wouldn't think to routinely examine their breasts, so it is important to know if they are at high risk so as to increase screening and preventative behaviour. BRCA mutations are also associated with an increased risk of prostate cancer. If you are male, knowing your BRCA status can inform whether you should undergo early screening processes for this type of cancer.

Additionally, it is important to remember that if a man carries a mutation, he has 50% chance of passing it on to his children, so investigating this information can be valuable for future generations.

Are BRCA1 and BRCA2 mutations associated with other cancers?

BRCA gene mutations are predominantly associated with breast and ovarian cancer risk. However, because the BRCA genes are responsible for tumour suppression, mutations may negatively affect other cell types. Depending on the gene involved, there have been small links to increased risk of melanoma, prostate, pancreatic and colon cancers. See table 1 and 2 in section 2 for more information.

How are BRCA1 and BRCA2 mutations inherited?

An individual who carries a BRCA1 or BRCA2 mutation has a 50% chance of passing it on to their children. This chance is the same regardless of the parent or child's sex. This means that not all carriers will pass on the gene mutation to their children. It is also important to understand that not all carriers will actually develop breast or ovarian cancer, though they will have an increased risk.

I have had cancer, what would be the benefit of genetic testing?

If you have already been diagnosed with cancer, the results of a genetic test may guide and focus your surgery and treatment options. Knowing your genetic profile may also assist in determining ongoing screening methods, preventative behaviour, and risks for other cancers.

Finding out you carry a gene mutation can also help your family to better understand their risk. If you carry a gene mutation, it may have been inherited from one or both of your parents, and may have also been passed on to your siblings or throughout other members of your family. Identifying the presence of a gene mutation in one individual can help other family members be proactive in understanding their options for screening and prevention. Knowing your BRCA1 and BRCA2 status can also help you understand whether you may pass on a genetic risk of breast or ovarian cancer to the next generation.

Are there other considerations in genetic testing?

Many individuals are concerned about the possible ramifications of a genetic test. Information on how it can impact your insurance policy in Australia can be found on the Pink Hope website. If you have queries about how genetic testing is seen under Jewish law, please contact Sharsheret, other Jewish organisations, or speak to your Rabbi.

If you decide not to be tested, you can work with your doctor to develop a plan to lower your risk and establish a frequent screening regime.

Remember, you are not alone in this process. Countless other women are on this journey. Pink Hope and Sharsheret are here to help you navigate your journey, through community support and information.

I CARRY A BRCA MUTATION, *what now?*

Risk Reduction and Surveillance

Knowing that you have a mutation gives you the advantage of being aware of your risk and the opportunity to be proactive about preserving your health. A medical professional is the best person to help you plan risk-lowering strategies that are specific and relevant to you. You may also seek the counsel of a Rabbi or spiritual leader to understand how medical suggestions can fit into Jewish lifestyle and religious practice. These are some of the options you may consider if you test positive:

- Increased screening - **being closely monitored for signs of breast and ovarian cancer. This can mean being screened more frequently, thoroughly, and at a younger age than the general population. Screening can be in the form of mammograms, MRIs, sonograms, ultrasounds, physical breast examinations by a doctor and self-breast checks for breast cancer. Although there is no reliable screening method for ovarian cancer, there are symptoms that you can look for (more information on symptoms are available on the Pink Hope website).**

- Risk reducing surgery - **opting for the removal of the breasts (mastectomy) or ovaries (oopherectomy) so as to reduce the cancer risk.**

- Chemoprevention - **the use of natural or synthetic medication to reduce the risk of cancer or its return.**

As always, consultation with a medical professional is the best way to determine which options are appropriate for you. More information on risk reduction and surveillance is available on the Pink Hope website.

How Pink Hope Can Help

Pink Hope's website provides information, support and inspiration about hereditary breast and ovarian cancer to empower you with the knowledge you need to be proactive with your health.

Through the Members section of the website (it is free and easy to join) you can find other women who have had cancer, or are at high- risk, who are willing to share their personal and medical experiences, and answer any questions you may have. It helps to connect with others who have shared similar experiences. Pink Hope also has closed state support groups on Facebook that you are welcome to join.

For kits, resources and support
visit *www.pinkhope.org.au*

HOW SHARSHERET *can help*

Sharsheret supports young Jewish women and families facing breast cancer at every stage — before, during, and after diagnosis. We help women and families connect to our community in the way that feels most comfortable, taking into consideration their stage of life, diagnosis, or treatment, as well as their connection to Judaism. We also provide educational resources, offer specialized support to those facing ovarian cancer or at high risk of developing cancer, and create programs for women and families to improve their quality of life.

Women who are at high risk of developing cancer can speak with our staff genetic counsellor, connect with a peer supporter, or learn more about genetics through our free health care symposia.

Learn more about our services and programs at *www.sharsheret.org*

STORIES FROM THE *Jewish Community*

Heidi's Story

My story is a somewhat long one and has taken me ages to write despite being a member of Pink Hope for quite a while. I am 42 years old with an 11 year old son and 6 year old daughter and have my own private practice as a Clinical Psychologist. I am of Ashkenazi descent and am BRCA2 positive, with a6417delT mutation. I underwent bilateral prophylactic mastectomy with immediate reconstruction on 11 July 2012.

BRCA2 has impacted many members of my family. My father's oldest sister passed away from ovarian cancer and carried the gene fault. Over 8 years ago, two of my first cousins living in South Africa (daughters of my father's youngest sister) were diagnosed with breast cancer ages 39 and 41, within a few years of each other. They both had mastectomies, chemo, radiation and thankfully today are well. They too tested were BRCA2 positive. When I heard that BRCA2 was "in my family" I ensured that I had regular ultrasounds and mammograms.

I often had the odd pain in the right breast and the thought would always cross my mind: is this it, have I got breast cancer? But I chose not to get formally tested for a few years, I focused on my children, husband and work. It was obvious that I was not emotionally ready to go down the testing path and contend with the possibility of also being BRCA2 positive.

At the end of 2009 I had a nagging pain in the right breast and my GP sent me off to the breast surgeon. When he heard about my two cousins, and that I was of Ashkenazi descent he recommended that I have genetic testing. It took me a few months to finally book the appointment at St Vincent's Hereditary Cancer Clinic but I knew I now had to be tested. I knew in my heart that I would be positive, and so when I received the result, I was not that surprised. But the emotions were huge, my husband was shocked, but I was adamant that surgery would be my only option. In my mind my breasts were dangerous, my enemies that could cause havoc if I did not have surgery. This decision was strengthened while I watched my father dying in hospice, I knew that I never wanted my children to see me struggle with cancer and that it would be the easier and only option to lose my breasts and ovaries than wait for cancer to develop.

My doctors encouraged me to first work though my grief and loss once my dad died, they highlighted that I had to be in the right emotional space when I had the surgery. Initially I had decided that I would have the oophorectomy because surveillance is so unreliable, it was all booked and then I got cold feet. I was worried about all the side effects, not just being catapulted into menopause and having hot flushes but also the bone density, cardiac and cognitive changes that can present with surgical menopause. So I decided that if I had the mastectomy first. I would have more options in terms of having HRT after the oophorectomy. I had prepared my kids for the surgery, my son is very mature and understood exactly what the surgery was for and would entail. I told my daughter I was having an operation on my chest "to keep mummy healthy", she still does not know exactly what the surgery was and I will only explain this to her when she is an older adolescent as I do not want her to have any anxieties or qualms about her body.

The morning of the surgery was surreal. The day had arrived, there was no going back. It was time to say goodbye to my breasts that I loved, that my husband loved, that had fed my children. But these breasts could potentially make me sick so my attachment to my breasts at this time was indifference. I had had months to process losing them, and did not feel a sense of loss. But I still felt like I had no control, my thinking was that I was being forced to have surgery but I knew that if I didn't that I would have to live with ongoing anxiety every time I got a pain in my breasts and that I would never forgive myself if I got cancer and hadn't had surgery. I used to often read through the comments on the Pink Hope forum while I was recovering and it helped normalise my own experience.

"The morning of the surgery was surreal. The day had arrived, there was no going back. It was time to say goodbye to my breasts."

So it is almost nine months since my surgery, it took about 10 weeks for me to feel like my old self. My recovery was initially slow, as I am allergic to many medications, so I could only take panadol for pain but got through it with the support of my amazing husband. I had to learn to be patient with myself and not expect myself to feel 100% in the first few weeks. The pathology results showed that there were no precancerous cells, what a relief, but for a second I did think, what a waste, cutting healthy parts off my body. But then I remembered that that was why I had opted for the surgery because I never wanted to be in a position where there would be any cancerous cells. I still have to have the oophorectomy, and am planning to do so mid next year.

Every day I am grateful that I was given an option, a choice to do something to protect myself and my family from my potentially getting ill. I never wanted my having BRCA2 to define me or my life, many people who hear my story say "you are so brave" , but I think more than anything I was sensible, I had the knowledge and I had the choice to use it. Hopefully, by the time my children will be tested, there will be many more options available to them. But in mean time, I believe I have to be proactive and help educate as many others, particularly in the Ashkenazi community about heritable cancers.

"I believe I have to be proactive and help educate as many others, particularly in the Ashkenazi community about heritable cancers."

Sarah's Story

I was diagnosed with breast cancer in August 2006 when I was 29 years old. It was a big shock as I have no other family members who have had breast or ovarian cancer so it was assumed that my cancer was just unlucky not genetic. I had a grade 3 triple negative 1.2cm tumour. I was lucky enough not to have any lymph nodes involved but because of my age and the aggressiveness of the tumour I was advised to undergo chemo and radiotherapy. I finished chemo in January 2007 just after my 30th birthday and finished radiotherapy in March 2007.

I started to think about whether I had a genetic mutation. I did some research and found out that triple negative cancer is common in women with BRCA1 mutations and families with Ashkenazi Jewish backgrounds are also prone to have BRCA1 mutations. My grandmother on my Dad's side was Jewish from Lithuania. I called Peter MacCallum and they sent me all the forms to fill out. Peter Mac called me almost straight away to come in for counselling and testing. It wasn't a surprise that I had a BRCA1 mutation. We believe the reason I am the first one in my family to show any signs of the mutation is due to my Dad's family being very small and my Dad's siblings never having their own children. I am literally the first women (except my Aunt who had MS) to be born since my Grandmother. We also think that one of my Grandmother's sisters may have had breast cancer but it's very hard to get any information now as there is no one to ask.

I found out about my mutation in December 2008 yet it took until I had a check up in August 2009 to realise that I am just a ticking time bomb. With my odds of getting breast cancer again as high as 40-60%, I was crazy to think that screening is adequate. At that check up they found a lump they wanted to biopsy and while I was waiting for the results I made my mind up to get a mastectomy. Thankfully that lump was benign. I had my bilateral mastectomy and reconstruction in May 2010.

> *"Even though I have had breast cancer... I feel like I am now in a position to help and support other high-risk women..."*

Since I am also at high risk of ovarian cancer we decided to try for another baby so I can start thinking about removing my fallopian tubes and ovaries. We tried for a few months and then decided to see a fertility specialist. We did some tests including an AMH test, which gave me a very poor result. We then decided to use one of our 5 embryos we stored before chemo. Unfortunately when we did we ended up using 3 of our 5 embryos, as 2 did not survive he thawing process. I found out on Christmas eve that the embryo did not work and started to lose hope. However at the end of January last year I found out I was pregnant, and it happened naturally! My son Jackson was born in October last year is now 8 months old. A few weeks ago I had my fallopian tubes removed to help reduce my risk of ovarian cancer and when I'm 40 I'll have my ovaries removed. I'm currently 36 years old.

I feel lucky that even though I have had breast cancer, I have still managed to have 2 children and my life has turned out pretty much the way I would have imagined. I have a very supportive husband who has always been there for me and has helped me through 7 surgeries in the past 7 years. I have no family here in Australia, my Dad passed away when I was 20 and my Mum died a couple of months ago from Lymphoma. My brother and sister live in London. Being involved with Pink Hope has been a really positive experience for me as I feel like I am now in a position to help and support other high risk women and sharing my story may help others feel not so alone.

Sources

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