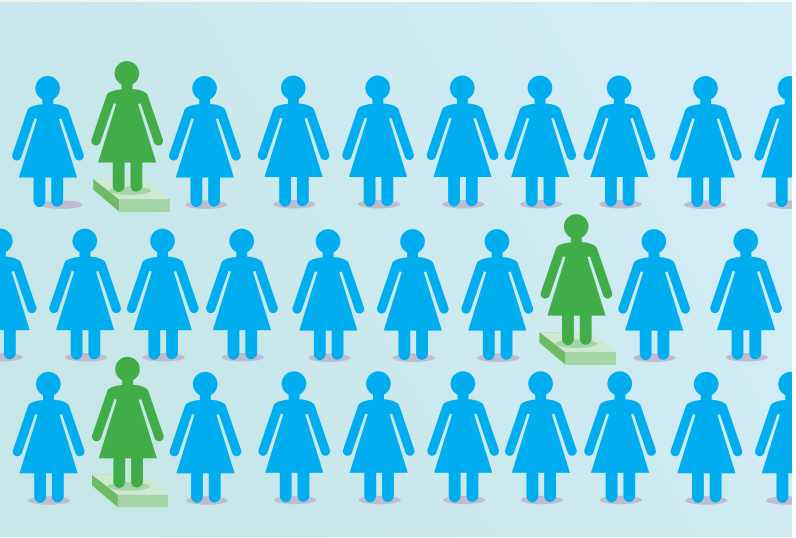

Prevention GENEration

The Importance of Genetic Testing for Hereditary Breast and Ovarian Cancer Syndrome (HBOC)

Israel Cancer Association

We thank
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Director, Prevention GENEration Program, the ICA and the NCF
Mrs. Miri Ziv
Director General, Israel Cancer Association
For their comments and guidance

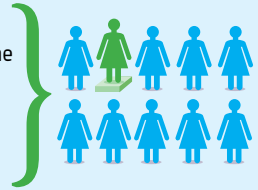
What is the "Prevention GENEration" program?

Many women who were diagnosed with breast or ovarian cancer are not aware that genetic testing is important for themselves and for their women relatives. As a result of this lack of awareness, they are not referred for genetic counseling or testing.
the presence of an inherited cancer predisposition is a **risk factor** for cancer, but if the cause is identified, it presents an **opportunity** for the prevention of additional cancers in the woman and in her relatives.
The "Prevention GENEration" program was established in order to raise awareness for the importance of genetic testing in women with breast cancer and ovarian cancer and to assist them in obtaining a genetics evaluation.
The program was established by the Israel Cancer Association (ICA) with the support of the Northern Charitable Foundation, Inc. (NCF), in collaboration with the The Israel Hereditary Breast and Ovarian Cancer Consortium, sponsored by the ICA

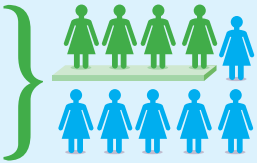
Genetic Risk Factors for Breast and Ovarian Cancer

Breast cancer is the most common cancer in Israeli women. Approximately 4,500 women are diagnosed with breast cancer every year. In 5-10% of women, breast cancer develops as a result of a hereditary predisposition, meaning that they have inherited (from one of their parents) a genetic change that makes them more susceptible to develop cancer. The most common cause of hereditary breast cancer is a genetic change (mutation) in one of two genes: BRCA1 and BRCA2 (see below for more detailed explanations about genetics and hereditary cancer). Changes in these genes are especially common in women of Ashkenazi origin, but they are found among women of all ethnic backgrounds.

Approximately **10%** of women diagnosed with breast cancer, became affected due to an inherited genetic change that also increases their risk of developing ovarian cancer and an additional breast cancer.



Approximately **40%** of ovarian cancer patients of Ashkenazi origin developed their cancers as a result of an inherited genetic change.

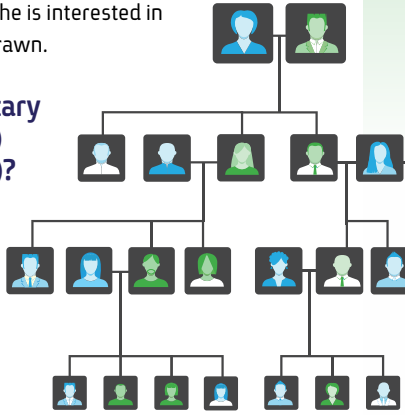


How can we tell if a woman developed breast or ovarian cancer as a result of an inherited risk factor?

Genetic changes can be identified in a simple blood test. However, genetic counseling is required prior to testing.

What is genetic counseling?

Genetic counseling is a consultation with a genetic counselor or a clinical geneticist (physician). The genetic counseling session includes the preparation/drawing of a family pedigree based on the medical information provided by the patient about herself and her relatives. The counselor also explains the appropriate options for genetic testing, including the advantages and disadvantages of testing, and the implications of the test results to the patient and her relatives. If the patient decides that she is interested in pursuing genetic testing, a blood sample is drawn.



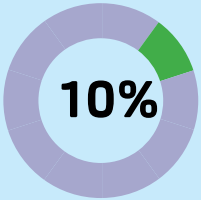
What is the genetic test for Hereditary Breast and Ovarian Cancer (HBOC) Syndrome - BRCA (BReast CAncer)?

The most common causes of hereditary breast and ovarian cancer syndrome are genetic changes in the BRCA1 or BRCA2 genes. In certain ethnic groups in Israel there is a high frequency of specific genetic changes in these genes. Genetic testing will often start by testing these

common changes. For example, in women of Ashkenazi origin, there are three common mutations in BRCA1 and BRCA2 and other mutations in these genes are rare. In women of other ethnic origins, different BRCA1 and BRCA2 mutations have been described. Beyond testing for specific mutations, there is a comprehensive test called "sequencing", which examines the entire sequence of both genes. In special cases, even more extensive testing is possible and can include the sequencing of different genes associated with hereditary cancer syndromes.

Mutations (genetic changes) in the BRCA1 or BRCA2 genes are the most common hereditary causes of breast or ovarian cancer.

If there is at least a **10%** chance that a mutation will be identified (as estimated by a genetic counselor/geneticist), BRCA1 and BRCA2 sequencing is included in the Israeli "Health Basket" (universal health coverage for Israeli citizens).



How are genetic test results delivered?

Test results are given in a follow-up genetic counseling session. The significance of the results and their implications for surveillance and prevention are discussed during this session, as well as recommendations for relatives.

Why is it important to know if you developed cancer because of an inherited predisposition?

The importance of genetic testing in women who had cancer

• A woman who was affected with breast cancer may be at increased risk of developing ovarian cancer or additional breast cancer. If a genetic risk factor is identified, there are specific measures for the prevention and early detection of these cancers. Mutation carriers are entitled to these measures within the Health Basket.

• Knowing that the cancer developed as the result of an inherited predisposition may affect treatment decisions . In particular, it may suggest experimental therapies that are targeted to the genetic basis of the tumor.

The importance of genetic evaluation for relatives

- If a mutation is identified in the family, relatives can be tested for this mutation. Relatives who inherited the mutation have increased risk for cancer, whereas relatives who did not inherit it are not at an increased risk.
- **Taking Action.** Family members who are found to be at an increased risk receive recommendations for special surveillance and prevention measures which have been shown to reduce the risk of developing cancer.
- If a mutation if not identified - a genetics evaluation is still important for family members, because this evaluation includes recommendations for appropriate surveillance and prevention.

What can be done if a genetic change (mutation) is found?

• When a genetic change (mutation) in the BRCA1 or BRCA2 genes is identified, there are several ways to reduce the risk of developing ovarian cancer and additional breast cancers.

• **Increased surveillance:** Carriers undergo more frequent surveillance for breast cancer. Surveillance includes a breast MRI in addition to a mammography and breast ultrasound, which are all covered by the Health Basket. Increased survillance for ovarian cancer is also recommended.

• **Prevention:** Surveillance for ovarian cancer has limited efficacy, so risk reducing salpingo-oophorectomy (surgical removal of the ovaries and the fallopian tubes) is recommended for carriers (upon completion of childbearing). In addition to reducing the risk for ovarian cancer, risk-reducing salpingo-oophorectomy also reduces the risk of future breast cancer. Another means of breast cancer prevention is the surgical removal of the breast(s) (risk reducing mastectomy), which significantly reduces the risk of additional breast cancer.

Is there a reason to be concerned about a genetics evaluation?

Possible psychological concerns are addressed during the course of the genetics evaluation. Some women are afraid to find out that they developed cancer as a result of a genetic change. A woman may be more anxious about her own health if testing reveals that she is at risk to develop additional cancers. Furthermore, she may be concerned about the consequences of this information for family members and the potential impact the results could have on her relationship with her relatives.

It is important to remember, that regardless of these concerns, we do not determine our genetic constitution, nor that of our relatives. Determining the genetic status can help to prevent cancer in people found to be at risk and can allay fears and prevent unnecessary procedures in those persons who are not at risk.

"We cannot change the genetic constitution with which we were born, but we can influence its outcome"

Limitations of genetic testing

Even when there is a strong suspicion that cancers observed in a family are due to a hereditary predisposition, the underlying genetic cause cannot always be identified. This is particularly true for women who are not of Ashkenazi of Iraqi origin.

How can you receive genetic counseling?

In order to receive a referral and coverage for genetic counseling, you should request a referral from the physician treating you for your cancer (surgeon or oncologist) or from your family physician. The initial genetic counseling session is often funded by Kupat Cholim (your Health Fund).

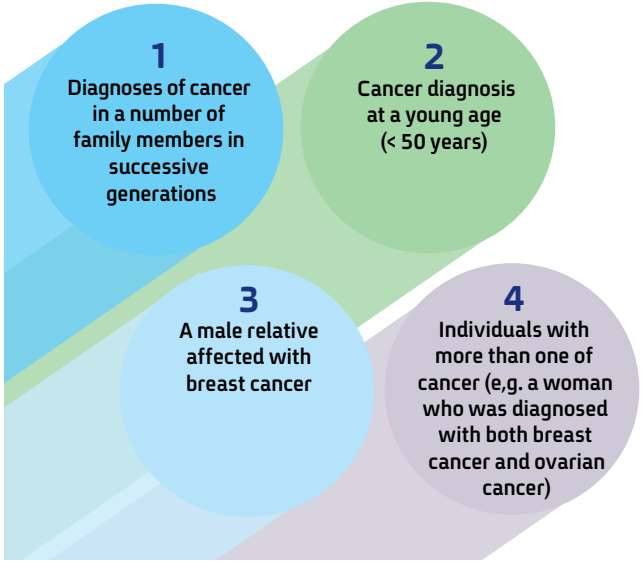
In order to facilitate the referral process and to help you arrive prepared for your genetic counseling, we recommended filling out a form about your personal and family history. This can be done using the interactive family history questionnaire found on the ICA (Israel Cancer Association) website. This interactive family history questionnaire can be filled out and printed, and will assist your physician in referring you for genetic counseling.

The list of genetics institutes providing genetic counseling and the interactive questionnaire can be found on the ICA's website:
www.cancer.org.il/prev-gene
You can also contact the Prevention GENEration coordinator by email or telephone. E-mail: prev-gene@szmc.org.il, Tel: 02-5645217

Want to know more?

When do we suspect an inherited cancer predisposition?

A hereditary predisposition for breast or ovarian cancer is suspected if your personal or family history includes:

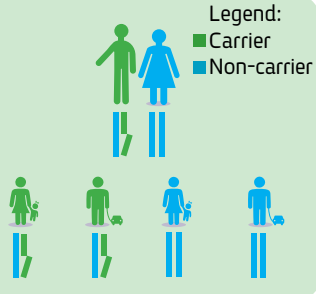


However, many people who have an inherited predisposition to cancer do not have a significant family history. This is particularly common if the family is small, or if family history information is incomplete (e.g. families of Holocaust survivors).

The mode of inheritance for inherited predisposition to cancer

Most hereditary cancer syndromes are inherited in what is called an autosomal dominant manner. We have two copies of each gene in our bodies: one inherited from our mother and one from our father. In cases of autosomal dominant inheritance, a defect in one of the two copies of the gene is sufficient to lead to an increased risk to develop cancer. A carrier is a person who has one malfunctioning copy of the gene, meaning that there is a change (mutation) in the gene. The inherited mutation is present in every cell of the body, and its existence increases the risk to develop cancers. Therefore, a carrier has a higher risk of developing cancer than a non-carrier. The specific types of cancers differ from syndrome to syndrome, and may also be gender dependent. For example, men who are carriers of mutations associated with breast/ovarian cancer have a much lower risk of developing breast cancer than women carriers of the same mutation. However, male carriers can pass the mutation on to their daughters.

*If a mutation is identified in the family, relatives have a 50% chance that they inherited the mutation, and a 50% chance that they did not inherit the mutation.



Summary

- If you had breast or ovarian cancer, of if these malignancies occurred in your relatives, it is important to find out if these cancers were a result of an inherited predisposition.
- The presence of Hereditary Breast and Ovarian Cancer (HBOC) syndrome in a family increases the risk that family members will develop breast and ovarian cancer.
- Mutations in BRCA1 and BRCA2 are the most common cause of Hereditary Breast and Ovarian Cancer (HBOC).
- Detecting a mutation in women who have had breast or ovarian cancer and subsequent identification of carriers in the family is important for making significant treatment decisions and planning more effective follow up care and various risk-reducing preventive measures.
- Even if follow-up surveillance and treatment entail difficulties, they can prevent cancer in relatives and save lives.
- Family members who do not carry the familial mutation will know that they are not at an increased risk to develop cancer and can avoid the frequent surveillance tests.

Knowing your genetic risk is also an opportunity for Prevention GENEration

For additional information, and to receive the ICA's (Israel Cancer Association) handbook: "Everything you wanted to know about Genetics and Cancer" (in Hebrew), call the ICA Tele-Meida (tele-info) at 1-800-599-995. Additional assistance can be found in the internet forum "BRCA carriers and women at high risk for breast and ovarian cancer" on the ICA's website: www.cancer.org.il
The interactive questionnaire can be found on the ICA's website at: www.cancer.org.il/prev-gene

For women coping with breast cancer

'Yad Lehachlama' (Reach to Recovery) breast cancer survivor volunteers group: 1-800-36-07-07

Or click on the pink button on the Israel Cancer Association website at:

www.cancer.org.il

For further information and informational materials on different types of cancers, cancer treatment, prevention and diagnosis, as well as patients' rights, please contact the Israel Cancer Association toll free at:

Telemeida® teleinformation service in Hebrew at: 1-800-599-995

Telemeida® teleinformation service in Russian at: 1-800-34-33-34

Telemeida® teleinformation service in Arabic at: 1-800-36-36-55

For advanced information services please contact:

The Israel Cancer Association Information Center at: info@cancer.org.il

or call: 03-5721608

For more information about the Prevention GENEration program please contact the Program Coordinator at: prev-gene@szmc.org.il or call 02-5645217

For a list of the genetic institutes, gene carrier and breast cancer care forums, and more detailed information - please visit the Israel Cancer Association website at: www.cancer.org.il