

Purpose of the Test + Genetic**Counselling**

Analysis of BRCA1 and BRCA2 genes (BRCA1/2) looks for changes in your DNA called mutations. Certain mutations within the BRCA1/2 genes can make it more likely that you could develop certain cancers, such as breast, ovarian, fallopian tube, peritoneal, melanoma, pancreatic and/or prostate cancer. Individuals with BRCA 1/2 mutations are more likely to develop cancer at a younger age and have high grade (aggressive) tumours. Among those who develop cancer, variable age at diagnosis and type of cancer is observed, even within the same family. If you have a family history of a BRCA1/2 mutation, you should inform the LifeLabs Genetics team of the specific gene mutation(s) present in your family. Private pay BRCA 1/2 analysis offered through LifeLabs includes next-generation sequencing and dosage analysis of BRCA1/2, in addition to a 30 minute pre-test telephone session with a board certified genetic counsellor prior to the start of the analysis and an optional 15-30 minute post-test counselling session. LifeLabs will make two attempts to contact you to schedule your pre-test counselling session once you submit your blood sample.

During the pre-test counselling session, the genetic counsellor will:

- Review your family history of cancer. Please inquire with relatives as to specific diagnosis and age of onset.
- Discuss the benefits, limitations and risks of genetic testing
 - You will have the option to decline further genetic testing once reviewing the benefits, limitations and risks.
- Review the possible outcomes of genetic testing (positive, true negative, uninformative negative and variants of unknown significance)
- Discuss possible implications to insurability
 - A positive genetic test result may affect an individual's eligibility for insurance such as (although not limited to) private medical, life, disability and travel insurance.
- Send a summary letter of the pre-test counselling session to you and your ordering physician

Benefits

You may use the results of genetic testing to help guide surveillance, prevention and medical management decisions in regards to cancer. This information can also affect your family members. In the two copies of our genes, only one copy needs to have a mutation for a person to be more likely to develop the cancers listed above. This is called autosomal dominant inheritance. If an individual is found to have a BRCA1/2 mutation, there is a 50% chance that their child could inherit the mutation as well, which means there is also a 50% chance that an individual's siblings and parents have the same mutation.

Risks

Genetic testing may reveal sensitive information about your health or that of your relatives. Test results may reveal incidental, unsought information, such as discovering that a man is not the father of a child (non-paternity). Results of genetic testing can create emotional burdens (feeling guilty, sad, worried, angry), which can impact yourself and family members. It can also potentially have negative impacts when applying for insurance, although the current data is uncertain when assessing genetic risks and insurance premiums.

Test Results

Once your blood is taken, your sample will be sent to our partner laboratory, Centogene, in Germany. **Your pre-test counselling session will be set up concurrently to your sample being sent to and processed by Centogene.** Testing will take 4-6 weeks from when Centogene receives the sample. Urgent results (7-15 business days) are available for an additional fee of \$250. Results will be sent to the ordering physician and to the patient if the physician has consented to release the results on the requisition.

Possible results:

Positive: A disease-causing mutation was identified. This individual has an increased risk for specific types of cancer. Family members are at increased risk of carrying the same mutation.

True Negative: This individual tested negative for a mutation previously identified in the family. This individual's risk for cancer is not expected to be increased above the general population risk.

Uninformative negative: No disease-causing mutation was identified. If an individual has a personal or family history of cancer, the exact cause of the cancers in the family remains unknown. This individual's risk for cancer remains increased based on family history assessment. If applicable, testing affected family members could be considered.

Variant of Unknown Significance (VUS): A VUS indicates that the pathogenicity (whether a mutation causes a predisposition to cancer) of the variant identified cannot be established. Testing other family members may help clarify the clinical significance. Over time, variants may be reclassified as pathogenic or non-pathogenic (eg, disease causing or not associated with disease).

Test Limitations

The genetic consultation provided with the purchase of BRCA1/2 genetic testing is not a substitute for a full genetic evaluation. Specialized care providers have or can obtain access to clinical records, which LifeLabs Genetics cannot. The focus of the pre and post-test counselling session is on the benefits and limitations of genetic testing for BRCA1 and BRCA2 specifically and implications of results. There are genes other than BRCA1/2 related to inherited breast and ovarian cancer and there remain many uncertainties, including the effects of as yet unknown genes, which may impact on the prevalence of breast/ovarian and other cancers. Although a pedigree (also known as a family tree, documenting family history related to cancer) will be drawn up for use by your healthcare provider, it will not be assessed to determine if other genes or conditions are appropriate for testing or the likelihood of developing cancer. Genetic counsellors at LifeLabs will rely on information provided by the patient and will not seek to confirm or disprove clinical information provided by requesting medical records.

Medical information and technology change constantly, and therefore we encourage you to review the recommendations from the LifeLabs genetics consultation regularly with your healthcare provider to ensure that they are still aligned with current practice. LifeLabs Genetics bases their clinical management recommendations on "The Canadian Consensus Guidelines [Horsman et al: JOGC 28(1): 45-60 (2007)]" and NCCN guidelines.

Alternatives to privately paying for BRCA1/2 testing

The ordering physician may consider referring a patient to a local cancer genetics clinic, which can be found through <https://www.cagc-accg.ca>. Provincial Ministry of Health funding in Canada for genetic testing for BRCA1/2 and counselling may be available for individuals with a personal and/or family history of breast, ovarian, fallopian tube, peritoneal, melanoma, pancreatic and/or prostate cancer. Wait times vary per clinic, and can range from 2 months to 2 years.

Who should have BRCA1/2 testing?

There are certain individuals who are considered to be at a higher risk of having a BRCA1/2 mutation:

- Breast cancer diagnosed at age 50 or younger
- Multiple primary breast cancers either in the same breast or opposite breast
- Triple-negative breast cancer at age 60 or younger (ER-, PR- and HER2/neu -)
- Ovarian cancer, fallopian tube or primary peritoneal cancer at any age
- Both breast and ovarian cancer
- Pancreatic cancer with breast or ovarian cancer in the same individual or on the same side of the family
- A previously identified BRCA1 or BRCA2 pathogenic mutation in the family
- Two or more relatives with breast cancer, one under age 50
- Three or more relatives with breast, ovarian, pancreatic, and/or aggressive prostate cancer
- Ashkenazi Jewish ancestry with history of breast, ovarian or pancreatic cancer
- Male breast cancer at any age

Some individuals who do not meet the above criteria above may still choose elect to pursue BRCA1/2 genetic testing to find out more information about their susceptibility risk for to cancer, even though the chance of finding a BRCA1/2 mutation might be low.

Cancellation of Samples

You can withdraw your consent to the analysis at any time in full or in part without stating reasons. You have the right not to be informed about test results (right not to know), to stop the testing processes that have been started at any time up to being given the results and to request the destruction of all test material and all results collected up to that time. If a test is cancelled after the pre-test counselling session, you will be refunded less the amount of \$200, which is incurred for processing and counselling. Once testing is initiated, the full price of the analysis will be