RiskBRCA Basic

Non-invasive saliva test to detect all BRCA1 and BRCA2 associated Hereditary Breast and Ovarian Cancer (HBOC) syndrome, as the most common inherited Breast Cancer and Ovarian Cancer predisposition (the reported cancer risks associated with HBOC are up to a 60% to 80% risk for Breast Cancer and up to a 40% risk of Ovarian Cancer)

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BREAST AND OVARIAN CANCERS STATISTICS

Every year more than 1,500,000 new cases of Breast Cancer and more than 240,000 of Ovarian Cancer are diagnosed worldwide, being hereditary between the 5-10% of Breast Cancer cases and approximately the 20% of Ovarian Cancer cases.

These cases of hereditary cancer are frequently associated with mutations in the BRCA1 and BRCA2 genes, both of which are tumor suppressor genes involved in the maintenance of DNA integrity.

WHAT ARE BRCA1 AND BRCA2?

BRCA1 and BRCA2 are human genes that produce tumor suppressor proteins. These proteins help to repair the damaged DNA and, therefore, have the role of ensuring the stability of the genetic material of each of the cells.

When any of these genes have a mutation, or alteration, in such way that their protein is no longer produced or is not working properly, the DNA damage can not be repaired properly.

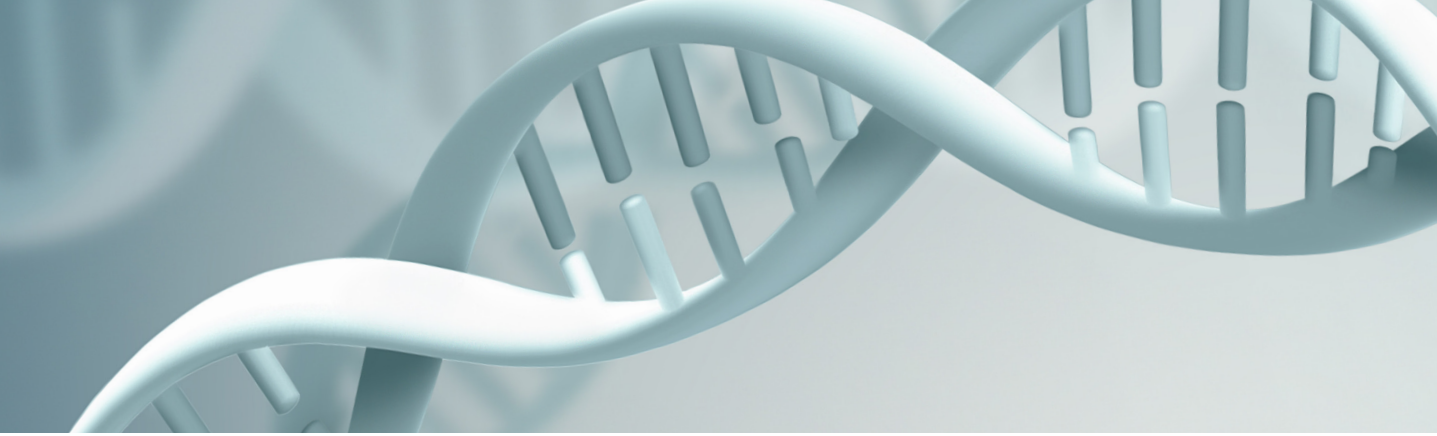
The specific mutations that are inherited in BRCA1 and in BRCA2 especially increase the risk of Breast and Ovarian Cancers in women.

In addition, women who have inherited mutations in BRCA1 and BRCA2 tend to have Breast and Ovarian Cancers at younger ages than those without these mutations.

HISTORY OF BRCA1 AND BRCA2

Clinical genetic testing of BRCA1 and BRCA2 began in the mid-1990s, but was mainly limited to one laboratory in the United States (US) and a small number of laboratories in Australia and Europe.

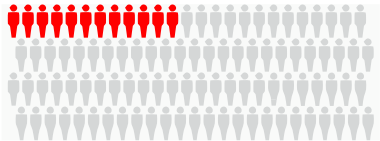
Twenty-five years later the number and types of patients being offered BRCA1 and BRCA2 testing has changed dramatically due in part to changes in patent laws and increased recognition of potential benefits of testing. Additionally, advances in highthroughput sequencing technology have enabled laboratories to offer less expensive tests than older ones and feature shorter turn-around times (TAT).



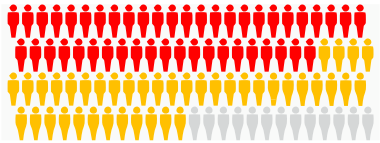
BREAST CANCER ACCUMULATED RISK THROUGHOUT LIFE

The Breast Cancer Accumulated Risk throughout Life increases from a 12% for general population to a 46-87% when BRCA1 mutation occurs and up to 38-84% when BRCA2 mutation occurs.

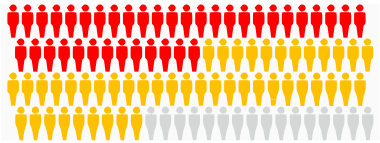
General Population



BRCA1 Mutation



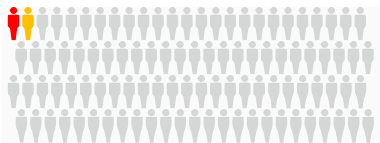
BRCA2 Mutation



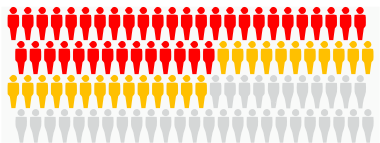
OVARIAN CANCER ACCUMULATED RISK THROUGHOUT LIFE

The Ovarian Cancer Accumulated Risk throughout Life increases from a 1-2% for general population to a 39-63% when BRCA1 mutation occurs and up to 16-27% when BRCA2 mutation occurs.

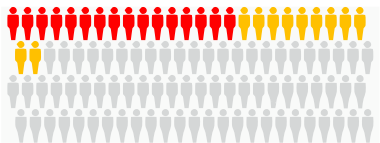
General Population



BRCA1 Mutation



BRCA2 Mutation



WHY CHOOSE BIOPROGNOS' RISKBRCA BASIC TEST?

Tranquility

Sense of relief about the future risk of cancer, knowing that one's children are not at risk of inheriting the predisposition to cancer.

A positive test result can also provide relief by resolving uncertainty about the future risk of cancer and may allow the person to make decisions based on information about their future health care, including taking steps to reduce their risk of cancer.

In addition, people who have a positive test result can choose to participate in medical research that could, in the long run, help reduce deaths from hereditary Breast and Ovarian Cancer.

Non-invasive

Test based on a simple saliva test.

Accurate

RiskBRCA Basic captures and sequences all of the exons and intron-exon transition of both genes, so all Single Nucleotide Polymorphism (SNPs) located in these regions will be identified, rather than other available BRCA1 and BRCA2 tests that only check for few SNPs.

Most advanced

RiskBRCA Basic sequencing is performed using Next-Generation Sequencing (NGS) technology with an Illumina NextSeq 500 device, capturing the genes through a proprietary assay produced by Roche-Nimblegen.

Already validated

CE Declaration of Conformity achieved (According to In Vitro Diagnostics Directive 98/79/EEC).

FOR WHOM IS IT INTENDED?

- Women with a family history of Breast Cancer (female or male) and/or Ovarian Cancer.
- Women who suffer from Breast or Ovarian Cancer to know their possible hereditary character.
- Women over 30 years of age with no Breast or Ovarian Cancer family history, to know the genetic risk of hereditary Breast and Ovarian Cancer and be able to evaluate the different preventive and screening options.

INTERPRETATION OF RESULTS

Once the saliva sample is analyzed, a final report with BRCA1 and BRCA2 mutations is generated. This report can give several possible outcomes: positive, negative, or an ambiguous or uncertain outcome.

The meaning of these outcomes is:

Positive result

A positive test result indicates that a person has inherited known deleterious mutation in the BRCA1 gene or BRCA2 and, therefore, has a higher risk of developing Breast or Ovarian Cancer.

Negative result

A negative result of the test may be more difficult to understand than a positive result because the meaning of the result depends in part on the individual's family history of cancer and whether a mutation in BRCA1 or BRCA2 has been identified in a blood of relative or not.

If a close relative (first or second degree) of the person who was tested is known to be a carrier of a deleterious mutation in BRCA1 or BRCA2, a negative result of the test is clear: it means that the person it is not a carrier of the harmful mutation responsible for the risk of cancer in your family and, therefore, can not pass it on to your children. Said test result is said true negative. A person with such a test result is currently considered to have the same cancer risk as any person in the general population.

If the tested person has a family history suggesting the possibility of having a deleterious mutation in BRCA1 or BRCA2, but a complete genetic test does not identify that mutation in the family, a negative result is less clear. The probability that the genetic test does not detect a known deleterious mutation in BRCA1 or BRCA2 is very low, but it can happen. In addition, scientists continue to discover new mutations of BRCA1 and BRCA2 and have not yet identified all those that may be harmful.

Because of this, it is possible that a person in this scenario with a "negative" result of the test may, in fact, have a harmful mutation in the BRCA1 or in the BRCA2 that has not been previously identified.

Ambiguous or uncertain result

Sometimes, a genetic test finds a change in BRCA1 or BRCA2 that previously had not been associated with cancer. This type of test result can be described as "ambiguous" (which is often referred to as "a genetic variant of undetermined significance").

Fortunately, only 1% of women who undergo the mutation tests in BRCA1 and BRCA2 will present this kind of ambiguous result.

AND FINALLY, WHAT TO DO IN CASE OF MUTATIONS?

Intensified screening

Some women who have positive mutations in BRCA1 and BRCA2 can choose to start Breast Cancer screening at 25 to 35 years of age or get more frequent screenings than women who have a risk of average Breast Cancer. Intensive screening can increase the chance of detecting Breast Cancer at an early stage, when it may be better to treat it successfully.

Besides, BIOPROGNOS has developed two innovative tests —OncoBREAST Dx and ScreenBREAST Sx— for the confirmation of the diagnosis (which allows to avoid up to 90% of unnecessary biopsies), as well as for the screening of Breast Cancer, respectively, both based on a simple blood test and with diagnostic capabilities superior to 93%. If you would like to have more information, please visit **www.bioprognos.com**.

Prophylactic surgery (for risk reduction)

Prophylactic surgery involves removing as much risky tissue as possible (both breast as well as ovarian and fallopian tubes to reduce the risk of Breast and Ovarian Cancer, respectively. Besides, removing the ovaries can also reduce the risk of Breast Cancer in premenopausal women by eliminating a source of hormones that fuel the growth of some types of Breast Cancer. Unfortunately, prophylactic surgery does not guarantee that the cancer will not occur because it is not possible to remove all the risky tissue with these procedures.

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BIOPROGNOS TESTS FOR BREAST & OVARIAN CANCER RISK

BIOPROGNOS' BRCA tests are composed by RiskBRCA Basic and RiskBRCA Advanced. If you would like to have more information about these tests, as well as which one suits better for you, please visit **www.bioprognos.com**.

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