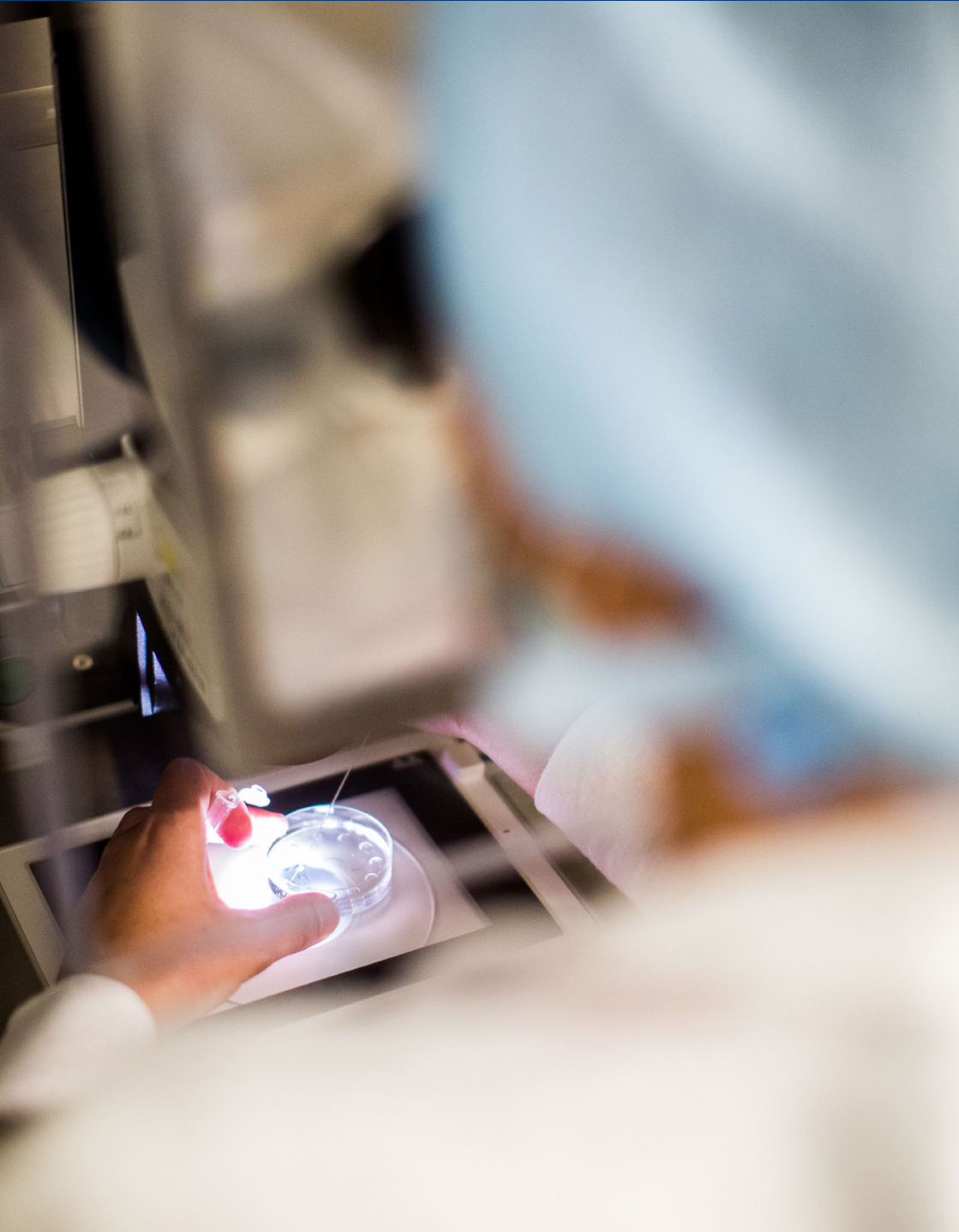


# Genetic carrier screening

BeGECS





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## Introduction

In this information leaflet you will find information about the genetic carrier screening test offered in all Belgian genetic centers.

## What is this test and who is it for?

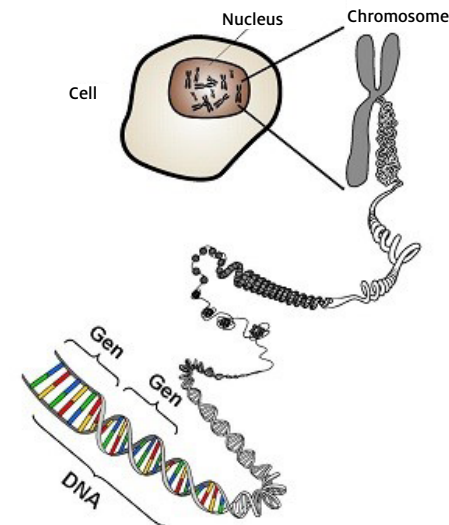
Carrier screening is intended specifically for couples considering having children in the future. The test is performed using a blood sample from both reproductive partners. The test determines if you, together with your partner, have an increased risk of having a child with one of the many serious genetic disorders included in this test. This information can provide you with the opportunity to make informed decisions when planning for a future pregnancy.

This test is aimed at couples who have no family or personal history for genetic diseases. If you or your partner are aware of a genetic disease in your families, this test may not be appropriate for you. In case of known personal or family history for genetic diseases, please contact a genetic center to discuss your testing options.

## A healthy carrier of a genetic disorder

### Genetic material

Genetic material, or DNA, is located in the nucleus of every cell. Genes are the units of genetic material, coding for all our hereditary traits. For example, they determine the color of our hair and eyes. For each gene, we inherit two copies, one copy from our mother and one copy from our father. A change, or a mutation in a gene can affect the normal functioning of the gene, which may result in a disease.

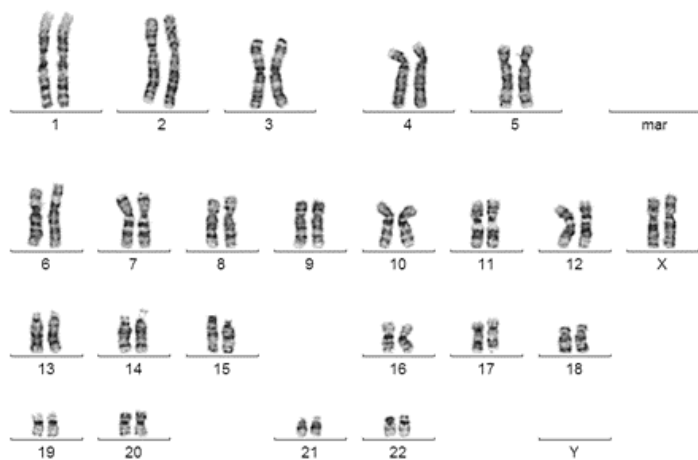


### Carrier

We are all healthy carriers of multiple changes in our genes which could possibly cause disease within our children. This is called carrier status for a genetic disorder. Most people are not aware of their carrier status because it usually has no consequences for your own health.

## Chromosomes

Genes are located on chromosomes. Chromosomes can be autosomes (non-sex chromosomes) and sex chromosomes. The sex chromosomes determine gender: men have an X and a Y chromosome, women have two X chromosomes.



## Monogenic disease

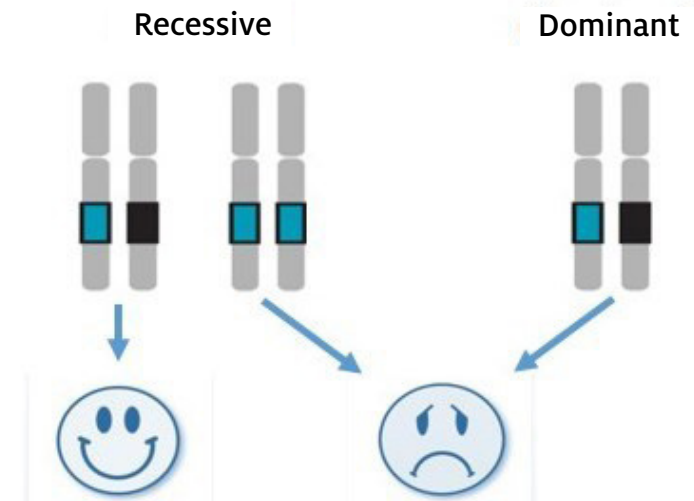
Diseases caused by a mutation in one single gene are called monogenic diseases. Monogenic diseases can be autosomal or X-linked, wherein autosomal stands for genes that are located on one of the 22 pairs of non-sex chromosomes.

## Dominant or recessive

The inheritance pattern of monogenic diseases can be dominant or recessive.

- In dominant diseases, a mutation in one of the two copies of the gene results in the disease.

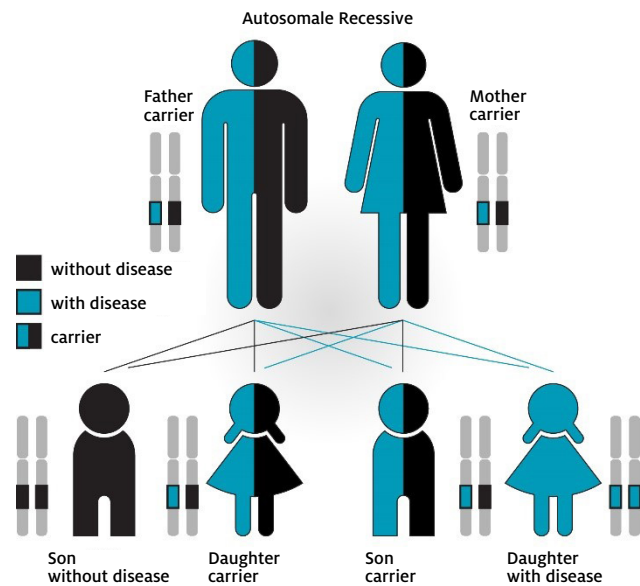
- In recessive diseases, a mutation is present in both copies of the gene. A person who carries only one mutation in one of the two copies of a recessive gene is a healthy carrier.



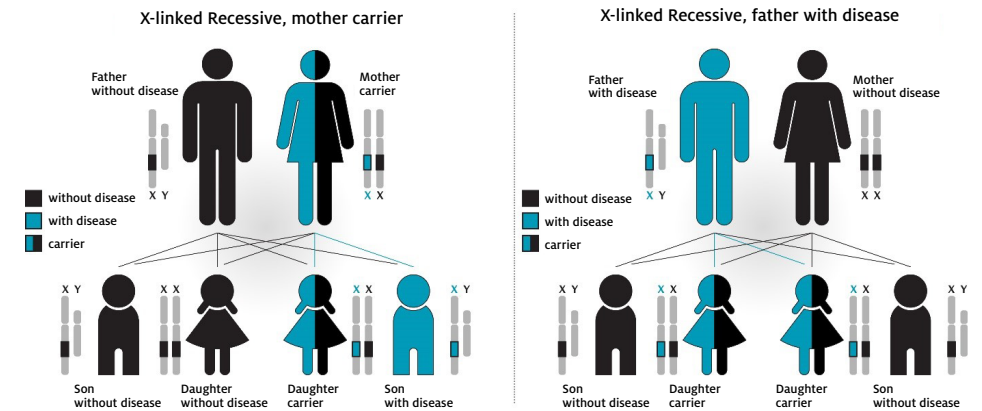
This carrier screening test only looks for mutations that give rise to recessive diseases. Recessive diseases can be caused by mutations in a gene located on an autosome (autosomal recessive diseases), or the X chromosome (X-linked recessive diseases).

## Autosomal recessive diseases

If both parents are carriers of a mutation in the same autosomal recessive gene, they have a 25% chance of having an affected child in each pregnancy. Both parents are healthy carriers of the disorder.



## X-linked recessive inheritance



Female carriers of X-linked disorders have one X chromosome with a faulty/mutated copy of a gene and one X chromosome with a normal functioning copy of the gene. These female carriers are usually healthy, but in some cases they may show milder symptoms of the disease. Should a female carrier of an X-linked disorder pass the X chromosome with a mutated copy to her son, the son will develop the disease, since he has only one X chromosome.

There are more than 7000 monogenic disorders, or disorders caused by a mutation in a single gene. Approximately one-third of these disorders are inherited in an autosomal recessive manner. It is estimated that every individual is a healthy carrier of several serious recessive disorders. X-linked recessive disorders are less frequent than autosomal recessive disorders.

## Which hereditary diseases ?

The carrier screening test includes more than 1000 genes associated with multiple hereditary diseases. The majority of these diseases are autosomal recessive. This means that both partners must be carriers to have an increased risk of having a child with the disease. The test also includes some disorders inherited in the X-linked recessive manner. In these diseases, only the woman has to be a carrier for the couple to be at risk.

Disorders included in this test have different clinical characteristics. Some of them impair intellectual development, while others mainly result in a physical disability. Furthermore, some disorders are associated with shorter lifespan, while others severely limit the daily functioning of affected individuals. For certain disorders included in the BeGECS test, there are treatment options available, such as lifelong medication and adhering to a specific diet. Finally, some diseases may manifest in variable forms, ranging from mild to very severe.

For each included disorder, the BeGECS test identifies main changes or mutations in the genes that are currently known to cause the disease. If the test result indicates that these mutations are absent, the chance of being a carrier of these disorders is reduced, but never fully eliminated.

A normal couple result means that the couple's chance of having a child with one of the tested genetic disorders is very small, but not zero. In addition, there still remains a chance that the couple conceives a child with a genetic disorder that was not included in the BeGECS test, or a disorder that is not genetically inherited. Sometimes a disease is the result of a combination of genetic and non-genetic factors.

## Where can I have this test?

You can request this test at one of the 8 Belgian genetic centers or through your doctor. The test is performed before pregnancy, so request the test before you want to become pregnant.

## How is the test performed?

In Belgium, the test is done exclusively through the accredited (i.e. internationally recognized) laboratories of the Belgian genetic centers. To perform the test, a blood sample will be taken from both partners.

The DNA needed to perform the BeGECS test will be extracted from the white blood cells. The DNA is then analyzed using a technique called 'massive parallel sequencing', which determine the exact sequence of the genetic building blocks (DNA sequence) in all the genes included in the test. Subsequently, the test examines whether there are disease-causing changes (mutations) in these DNA sequences.

Sometimes, it is unclear whether a specific mutation found in a gene is disease-causing. In such cases, the mutation is not taken into account and will not be reported. If the test finds a mutation that is clearly disease-causing, this is considered a relevant finding and will be incorporated in the test results. The lists with the pathogenic genes of both partners are then compared with each other.

### No increased risk

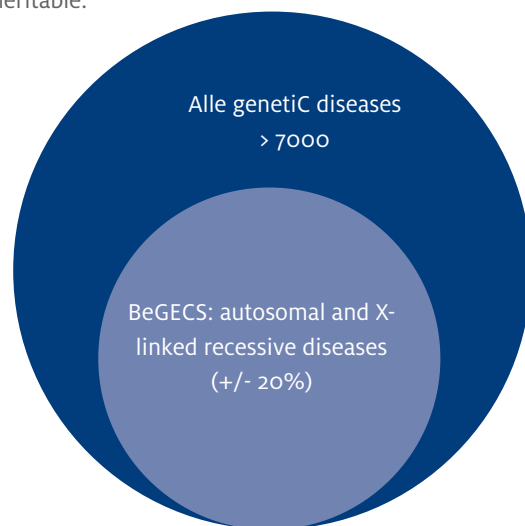
If we do not identify mutations in the same gene in both partners and the woman is not a carrier of a mutation located on the X chromosome, the report will state that there is no increased risk of having a child with a disorder.

### Increased risk

If both partners carry a disease-causing mutation in the same gene, their report will indicate that they have an increased risk of having an affected child with that condition (see below). The couple then receives a report with detailing these results.

## (Residual) Risk following a normal test result?

What is the risk of a child with a genetic disease following a normal test result? This test screens for recessive disorders that are severe and manifest in early childhood. However, the disorders included in this test comprise only a subset of all recessive disorders, which means that there are other recessive disorders that are not included in this test. Moreover, in addition to recessive disorders, there are many other genetic diseases or disorders inherited in a non-recessive manner, which are also not included in this test. Finally, some diseases that can arise in offspring are not genetically heritable.



## For whom is this test not appropriate?

This test is not available to couples who are already pregnant. This also applies to couples in which one of the partners has previously undergone a bone marrow transplantation. If there is already a known genetic disorder in your family, this test may not be sufficient. In these situations, genetic counseling is highly recommended.

## What results can you expect?

It is estimated that in the general population, approximately 1% of couples are at risk of having a child with a recessive genetic disorder.

### Increased risk

An abnormal couple test result means that there is a high risk of having a child with one of the genetic diseases screened for. When both reproductive partners are carriers of the same autosomal recessive disease, the couple has a 25% chance of conceiving an affected child with that disease in each pregnancy. There is also a 50% chance that the couple's child will be a healthy carrier of the disease, just like the parents, and a 25% chance that the child will be neither affected nor a carrier. When a woman is a carrier of a disorder located on the X chromosome, the couple has in each pregnancy a 50% chance of having either a son with the disorder or a daughter who is a carrier and shows no or mild symptoms of the disease.

### No increased risk

A normal couple result means that there is no demonstrably increased risk that the couple may have a child with any of the diseases tested for, but the risk is not zero.

If only one partner is identified as a carrier of one of the recessive diseases, or if both partners are identified as carriers of different autosomal recessive diseases, this has no consequences for the health of future children. Furthermore, for most disorders, this information also has no implications for the carrier individual's own health.

In order for a carrier screening test to provide accurate risk assessment, it is essential that test results for both reproductive partners are known. The test results only apply to the combination of both partners that were tested. Should you decide to have children with a different partner in the future, a new carrier screening test will be required, and your results may be different.

In exceptional cases, carrier screening may reveal a finding that has medical consequences for the tested individual. If this is the case, medically relevant information will also be reported.

## How will you learn your test results?

Your medical doctor, who orders the test on your behalf, will receive a report from the genetic center. The results report will report on the recessive disorders for which both partners carry a mutation in the same gene.

The results will be communicated approximately four months following the sample collection

## Contact details Belgian genetic centers

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[http://www.chu.ulg.ac.be/jcms/c\\_11417/genetique](http://www.chu.ulg.ac.be/jcms/c_11417/genetique)

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