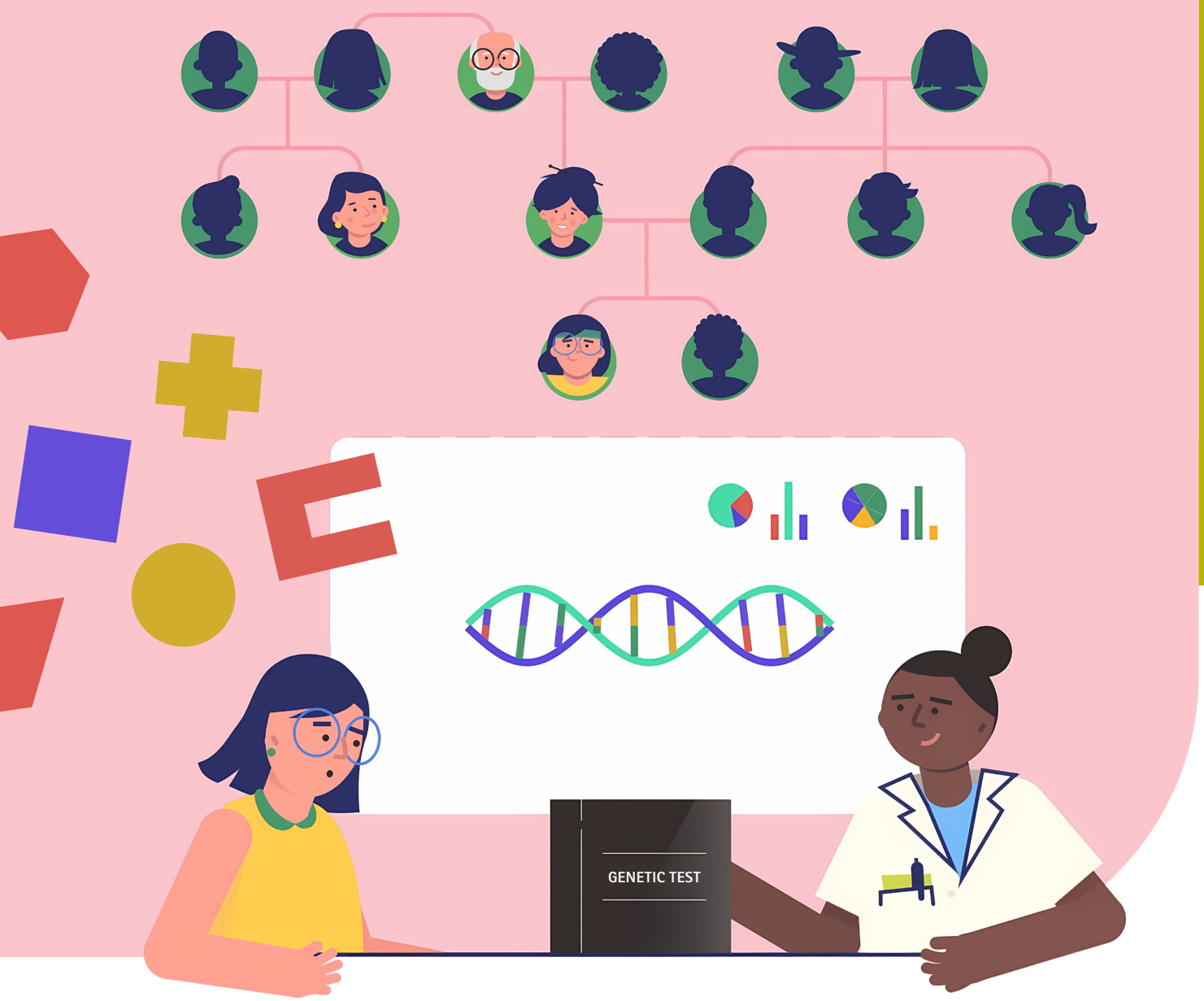
If you suspect a hereditary condition ...

When can a genetic test be useful for you?



What is a genetic test?
What information can it provide?
When and how can you request one?

Find the answers in this free brochure.

Centrum voor
Medische Genetica

Before you start reading

This brochure is intended for young and old – for people who are new to genetics or already more familiar with the topic. In short, it's for anyone who's interested in finding out more. We've tried to present the essential information about genetic testing as clearly as possible for everyone. You'll find this **basic info** on the **left side** of the pages. And, if you want, you can often read **additional information** in **coloured boxes** on the **right side** of the pages.

We illustrate the information with the story of Anja, but that's just one example. Hereditary factors play a role in many different conditions, so the information in this brochure is broadly applicable and not just limited to Anja's disease.

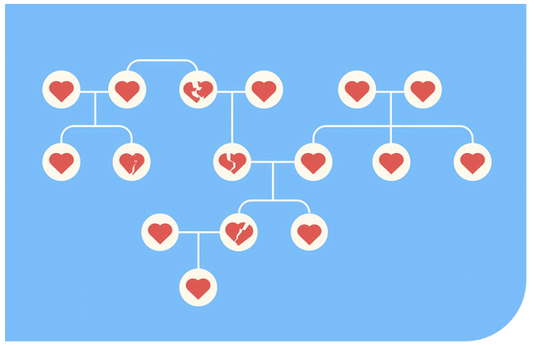
Contents

Introduction

This is Anja.

She loves playing football at the weekends. But it's not quite as straightforward as that – because **her heart doesn't always beat as it should**. And that means that taking part in sports comes with a risk for Anja.

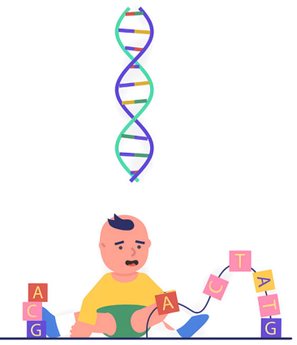
Anja found out about her heart condition by taking a genetic test. And she had good reason to do so – because her mother, grandfather and mother's cousin all had the same problem.



But thanks to the test, she now has certainty. So she can play football with peace of mind – under the supervision of her doctor. In this brochure, you may discover if genetic testing could also be sensible for you, and what you can expect.

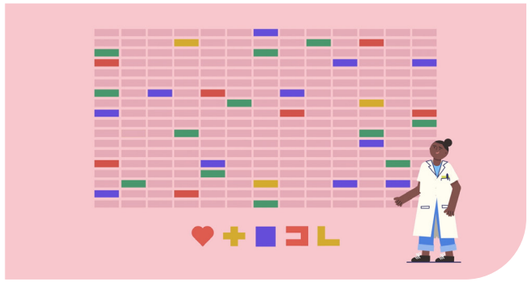
What is a genetic test?

Everyone has their own genetic baggage, received as a baby from their parents. What's in your genes is hereditary.



Genetic information is contained in **DNA**. This is a long 'molecule' made up of just four different building blocks, which we call 'nucleotides' and represent with the letters: **A, T, G and C**. The sequence of these four letters determines your genetic info, and all these letters together form your 'genome'.

A genetic test maps your DNA or a part of it. It shows whether you have a hereditary condition or a genetic abnormality that could cause such a condition later. So the test says something **about your current and sometimes future health**.



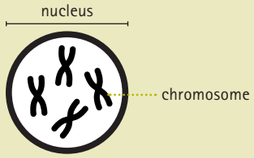
And, just like Anja, you can be tested for a hereditary disease. Or your doctor can use it to make a diagnosis when a disease emerges.

What are genes again?

Every human body is made up of billions of cells, each containing genetic (hereditary) information that ensures every part of our body functions properly.

This hereditary information is contained in DNA. Different names are given to various parts of our DNA.

- DNA in the cell nucleus is packed into small rod-shaped structures: **chromosomes**. We have 23 pairs of chromosomes (so 46 in total), with 23 coming from the egg and 23 from the sperm. Under a microscope, a chromosome looks like an X (or H, if you prefer).



- The complete DNA content of the 23 chromosome pairs in the cell nucleus is called the **genome**. Half of the genome comes from the sperm, the other half from the egg.
  Each half is made from 3 billion combinations of the letters A (adenine), C (cytosine), G (guanine) and T (thymine).
- A small piece of DNA, whose letter combinations together contain the code to build a certain protein, is called a **gene**. We have about 20,000 genes in our genome. Proteins are the building blocks of our body, but also messengers. Our body uses these messengers to communicate from one organ to another, but also from one cell to another cell within an organ. An example of such a messenger is insulin, a protein that regulates blood sugar levels.

Why might genetic testing be sensible?

- Genetic testing may (or can) indicate whether you have a genetic abnormality or not. A test can't remove that abnormality, of course, but it can be very useful to know about it if you have one.

Many hereditary conditions can be **managed**, and some can be **treated**, especially if caught early. Sometimes we can even **prevent** a genetic abnormality from leading to real health problems.

In Anja's case, this knowledge means that she, thanks to tailored medical supervision, can do almost everything she enjoys. And that includes playing football – even though her heart sometimes beats irregularly.

Furthermore, if Anja has children later in life, she can give them the **same chances** for good health – with their own genetic test.

Anja could also choose not to pass on the hereditary condition to her children, by doing a genetic test before or during pregnancy.

What types of genome abnormalities or mutations exist?

The sequences of letters in our DNA differ slightly from those of others. And it's these differences that make us unique – think of our hair or eye colour, for example. But it's also possible that these variations in the correct sequence of the letters A, C, G and T lead to genetic conditions, because the change in the DNA code results in a changing or absent protein.

We can identify different types of genetic changes.

- One of the letters A, C, G or T may have changed into another letter (a so-called 'point mutation').
- A number of letters may have disappeared ('deletion') or doubled ('duplication'), possibly leading to a shift in the DNA reading frame ('frameshift mutation').
- Smaller parts may be abnormally repeated.
- Extra letter sequences may appear in the wrong place ('insertion') or be reversed in a chromosome ('inversion').
- Pieces of chromosome may have been exchanged between two different chromosomes ('translocation'), possibly with a loss or gain of genetic material.

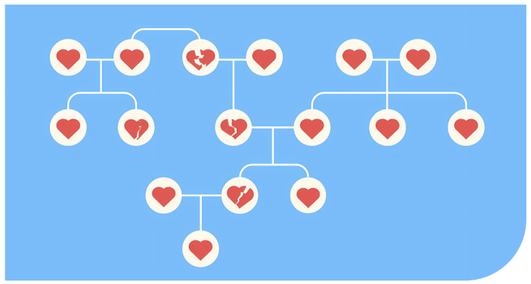
Do you want to avoid passing a hereditary condition on to your child? Then there are several options.

For some hereditary conditions, you can choose to have a genetic test of the unborn child during pregnancy ('prenatal testing').

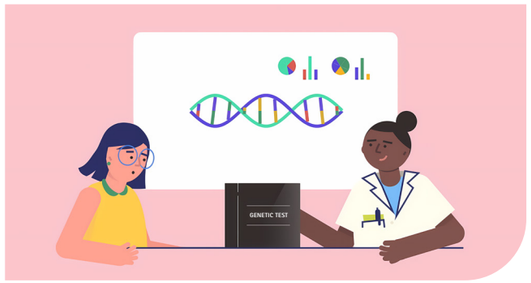
With IVF treatment, you can even request a genetic test for some hereditary diseases before the embryo is returned in the womb ('pre-implantation test').

Additionally, you can choose a sperm or egg donor if you or your partner carry a certain gene and you want to be sure not to pass it on to your offspring.

How does it work?



If you suspect a genetic predisposition in your family, you can visit a centre for medical genetics for an **exploratory conversation**, just like Anja.



A doctor and/or genetic counsellor will start by explaining to you during an initial conversation how genetic testing is carried out.

We also explain that we sometimes come across information about other diseases. And that's important. Because you can choose **which results** you want to know more about after the genetic test. You can read more about this on pages 8 and 9 of this brochure.

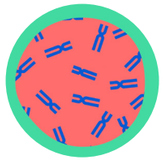
What do we need for a genetic test?

1) The test can be performed on various body materials such as blood (10ml), cheek mucosa, or a skin or muscle biopsy. We take a sample from you and sometimes also from your first-degree relatives, e.g. your parents and possibly a sibling with the same condition.

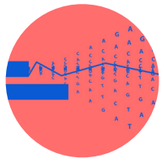
2) We also need your consent to perform the analysis and a signed 'informed consent' to discuss the results (more about this on page 10). For minors or those who are incapacitated, we ask for the consent of the parents or guardian.

To validate the test results, other samples may be requested at a later date with your consent.

The testing itself begins with a **sample collection**, usually a small amount of blood. Although sometimes we need a different type of sample, such as a bit of cheek mucosa or a small piece of skin or muscle.



The cells from your sample contain your DNA (just like most cells in your body). As mentioned before, you can compare this DNA to a long text of billions of letters. This 'library' (your genome) contains information about all your genes – these are the books in your library.



As soon as we receive your sample, we start to scrutinise the letters. Depending on the disease, we sometimes look at specific books, a larger part of the library, or immediately the entire library.

What are the possibilities and limitations?

Of the approximately four million letters that make you truly unique, we filter out a lot because we think they have nothing to do with your disease. The search in what remains is still a very complex task and requires the necessary time.

It eventually gives us a **list of suspect letters**. And we discuss that list with our multidisciplinary team of doctors and laboratory workers.

Sometimes we find no clear genetic cause. In that case, we may carry out **additional tests** to reach a conclusion. And sometimes the testing stops there because – with our current knowledge and techniques – we can't find out anything more.

It's quite possible that future techniques will allow a diagnosis so we store the genetic code in our **digital vault** after the test.

Multidisciplinary discussion

Some consultations are approached with a multi-disciplinary team, i.e. with several medical specialists. So you speak not only with the medical geneticist, but also with another specialist, genetic counsellor, psychologist or social nurse.

We always discuss rare diseases with a multi-disciplinary team. And the clinical team and laboratory specialists also consult with each other about the results.

What if we don't find anything?

Genetics is a field that evolves rapidly. New functions of genes are regularly discovered worldwide, or we learn more about the impact of specific mutations. And the techniques that allow us to analyse the genome are also becoming increasingly refined all the time.

When there's uncertainty about the initial test results, it's possible that we will reanalyse your DNA later when new scientific knowledge becomes available. A certain DNA variant may be found in the future in more people with the same condition, for example, or the variant is found to be more common in healthy individuals..

Or sometimes we can investigate other molecules, such as RNA or proteins, to get a better under-standing of the consequences of a certain DNA variant.

Is your genetic data safe with us?

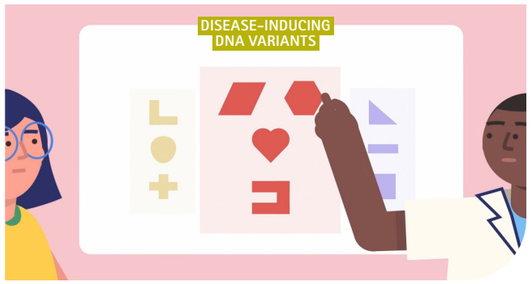
Your DNA is strictly personal. Not just physically but also legally. Privacy legislation therefore applies. It is still possible, however, that we share your results with other experts due to the complexity of the analysis of genome data. But this is done in an encrypted way so that no access is given to your personal data – such as name, address or date of birth – and only to your clinical and genetic data.

What information can it provide?

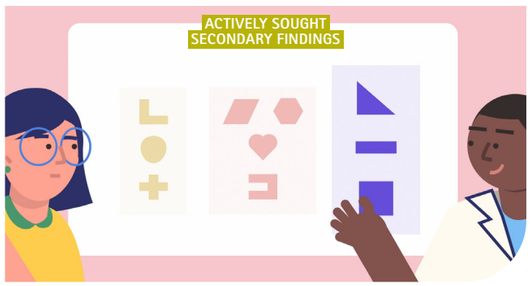
A lot of personal genetic information can be collected in a test.

We learn more about the genes you came to us for. But we also often find information about genes related to entirely different conditions.

You discuss in advance with your doctor what you want to know about. You can choose, for example, to only find out about results where follow-up, treatment or prevention is possible.

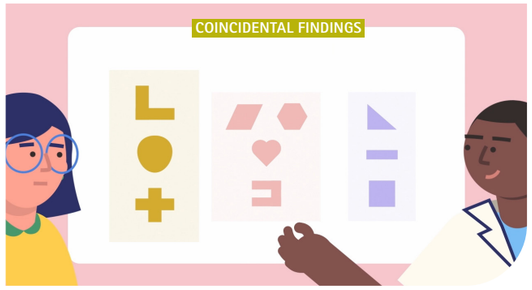


We distinguish three groups of possible variants in the DNA to help you with this. The first group includes variants that we **know**, or strongly suspect, to be related to the hereditary disease in your family. We always discuss these with you.



Secondly, we can **actively search** for other known **DNA variants** that are important for your future health, such as a hereditary predisposition to cancer, for example.

Sometimes, we can also see if medication for certain diseases would work and what the optimal dose would be for you.



And sometimes we find variants **by chance** that indicate **other diseases** for which guidance or treatment is possible, or that we can even prevent.

DNA variants from both the second and third groups can be confronting – because they can have significant implications for the health and life of you and your family. Maybe you don't want to know that at all, or maybe you do. It's not an easy choice, but you're **not alone**, of course.

We distinguish three groups of DNA variants

1) Primary variants
These are the variants that we know, or strongly suspect, are related to the hereditary disease for which you initially had the test.

2) Secondary variants
These are DNA variants known in genetics to cause certain conditions, e.g. a hereditary predisposition to cancer. Because they are known, we can actively search for them, even if it's not a problem you or your family have encountered.

3) Incidental findings
The third group consists of variants that we stumble upon by chance. This doesn't happen often, but it can. Sometimes we can link this DNA abnormality to a certain condition, and sometimes the effects are (still) unknown.

Secondary and incidental findings

A genetic test provides a lot of information about your hereditary material. Sometimes we find information unrelated to the condition you came for. It could be about carrier status for another hereditary condition, or an increased risk of a condition later in life, such as breast cancer.

If such an abnormal combination of letters in the genes can cause a condition that is important for the health of you or your family members, e.g. because treatment or the possibility of prevention exists, then you can choose to discuss this.

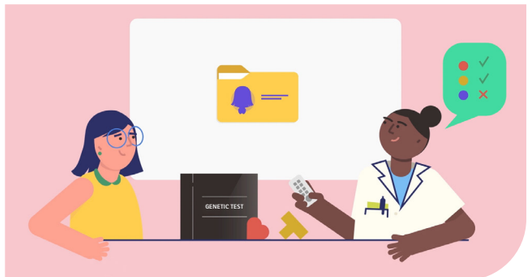
What about secondary or incidental findings about diseases for which no treatment exists?

It is also possible that a hereditary predisposition to a currently untreatable disease is discovered, e.g. a neurodegenerative condition such as Alzheimer's disease. When you are of age, you can choose to also learn this type of information. This knowledge could be important for you to make certain decisions in your life.

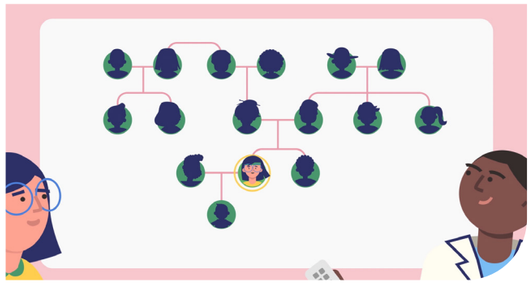
What information will we discuss with you?

You need to indicate what you want to know about your test results on a form that we call **'informed consent'**.

You don't have to decide immediately at the first conversation – you can **think about** it for a while and **talk about** it with your doctor, your family, or even a psychologist. Ultimately, you decide for yourself – well-informed and entirely according to your wishes – which information you want to receive.



We take your wishes into account when we discuss the results with you. This includes not only the possible **impact on your life** but also on the life of **your family**.



You will, of course, have ample opportunity to ask **questions**. Because the future of your health is important.

Difficult to decide what you do or don't want to know?

At the Centre for Medical Genetics, you can talk to a psychologist or genetic counsellor. They are specialised in these issues and can help you think about the various possible implications of your choices. They can't decide for you, but they will guide you so that you can make the best choice for yourself.

Can you change your mind later?

If you want to revisit your decision later, this can be discussed again during a genetic consultation.

How do we communicate the results?

When test results are known, we invite you to the Centre for Medical Genetics for a conversation ('genetic counselling').
Sometimes this is just a preliminary result, due to the complex nature of these types of tests. As soon as we have additional information or more complete results, we will contact you again.

When and how can you request a test?

If your GP or a specialist suspects a hereditary condition, they will **refer** you to a centre for medical genetics for an exploratory conversation. They might even make an appointment for you.

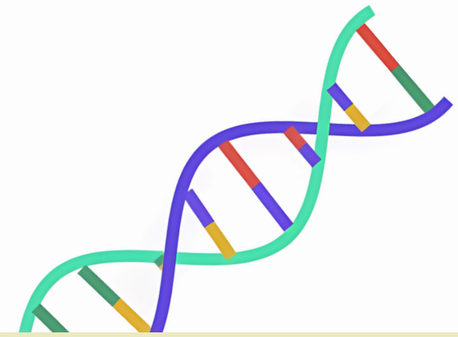
But you can also **take the initiative yourself** to contact such a centre if you suspect a genetic predisposition in your family. Please be aware, however, that you always need to make an appointment. If you're coming as a child and parent or as a couple, and you both want to be tested, then you both need to register in advance.

It's also best to bring as much important information as possible about your own and your family's medical history, and any previous genetic tests, to the consultation.

Is a complete screening of your genome possible?

You cannot yet go to a genetic centre for an analysis of your complete DNA (genome) without a medical reason.

How much does it cost?



Genetic testings are expensive, but the majority of these tests and the associated advisory consultations are **reimbursed** by social security for patients with Belgian or European health insurance. So you only have to pay the co-payment.

How much does a genetic test cost?

For most genetic tests, the National Institute for Health and Disability Insurance (RIZIV/INAMI) intervenes. More information about the rates can be found at www.uzbrussel.be/web/centrum-voor-medische-genetica/tarieven-en-riziv-tussenkomsten.

In exceptional cases, your test may not be eligible for reimbursement by the RIZIV/INAMI, and the costs can be significant.

This is discussed in detail with you in advance at the Centre for Medical Genetics, so you won't face any surprises.

If your health insurance is not set up yet, or you're uncertain, make sure to discuss this with the doctor before you start any genetic testing. You can still decide not to proceed with a genetic test at the end of this conversation.

Where can you ask questions?

Do you want more information about genetic testing after reading this brochure? Are you unsure about the 'informed consent' and the use of your test results? Or would you prefer to share some opinions and ideas first?

If so, you can discuss your questions with your doctor. You are always welcome to make an appointment for a genetic consultation.

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