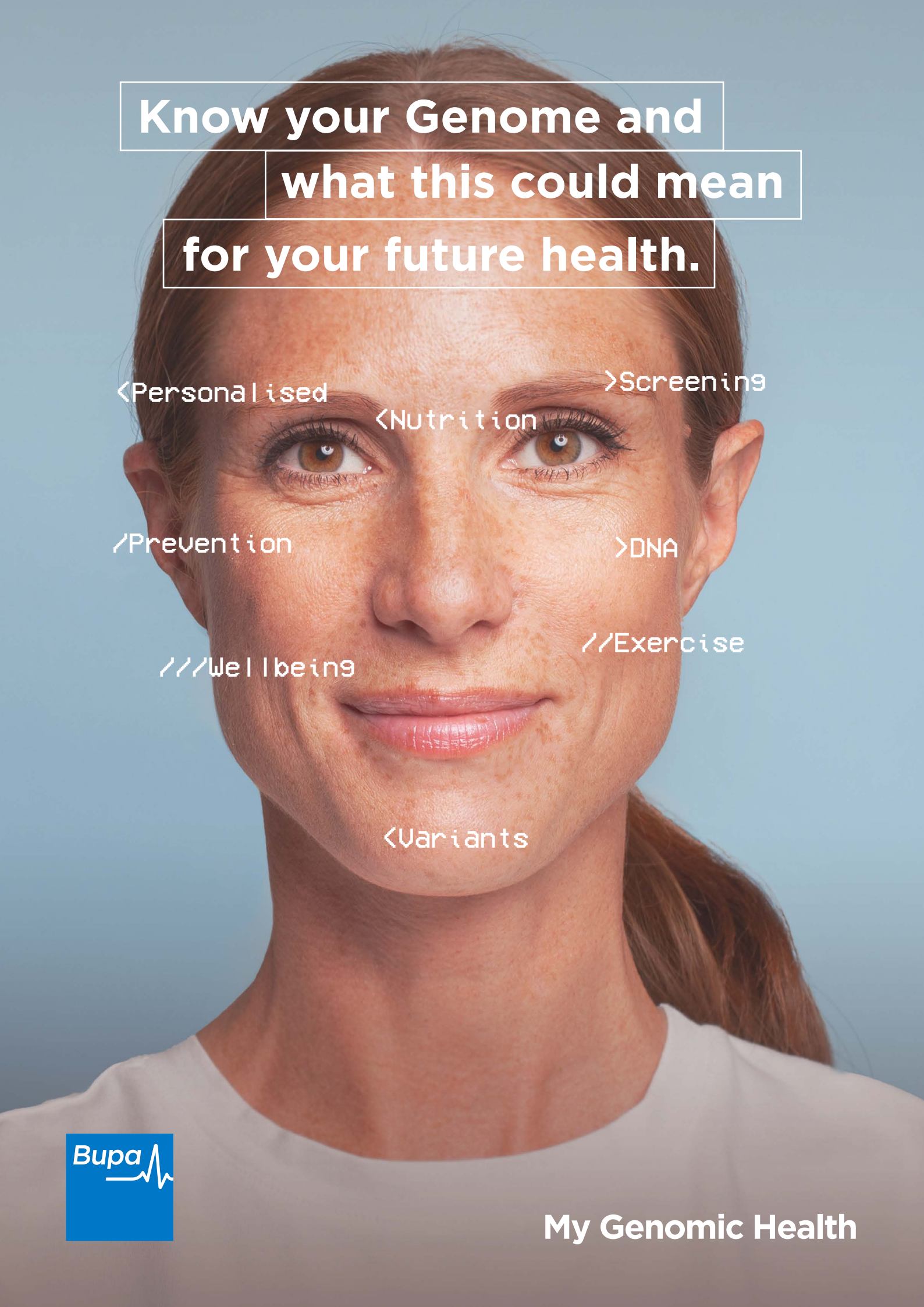
Know your Genome and
what this could mean
for your future health.
<Personalised
>Screening
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//Exercise
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Bupa
My Genomic Health

Introduction

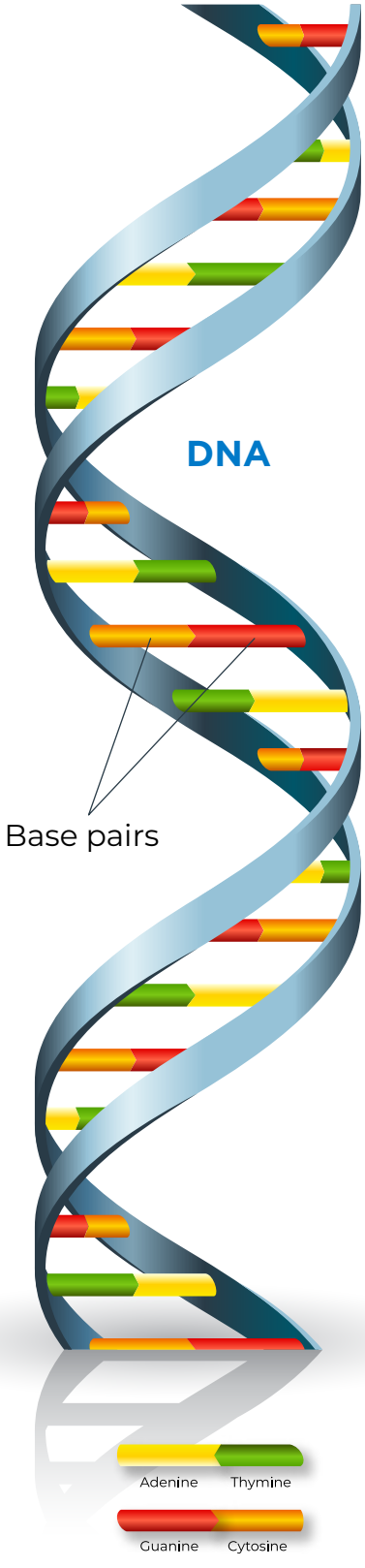
Your DNA contains a genetic code that's unique to you. This code not only defines your physical characteristics (traits), but it can also indicate whether you're at risk of developing certain health conditions.

That's why we've introduced My Genomic Health. In this new health and wellbeing programme, we'll use a method called Whole Genome Sequencing to analyse your DNA. We'll help you understand your risk of developing certain diseases and support you to help manage your health – now and in the future.

Contents

[1]

What is **the genome?**



Put simply, your genome is the blueprint that defines who you are.

It contains all of your genetic material, including your genes. Genes are sequences of DNA. You have two copies of each gene – one that you've inherited from your mother, and one from your father.

DNA is made up of pairs of four chemical bases, represented by four letters: adenine (A), guanine (G), cytosine (C), and thymine (T). Human DNA consists of about three billion bases. The order (sequence) of these bases acts like instructions, much like letters of the alphabet form words and sentences in a certain order. The cells that make up your body follow these instructions to function.

On a genetic level, people are more alike than you might think – more than 99.9 per cent of our DNA bases are the same. But there are variations in the remaining 0.1 per cent. Genes that have an alteration in their DNA sequence are known as variants. Variants are what define our different physical traits, like eye colour and height. Some variants don't seem to make any obvious difference. But other variants may lead some people to develop certain health conditions.

Genetic testing is done to identify these disease-related variants. The results can be used to assist doctors in providing healthcare advice that's tailored to your genetic risk.

Key points

- The genome is your body's set of genetic instructions
- It's made up of your DNA, which carries the genetic code your body follows to function
- Genes are small sections of DNA inherited from your parents
- Genetic testing identifies genes linked to different types of disease
- Doctors can use this information to give you personalised healthcare advice

[2]

What is **Whole Genome Sequencing?**

Whole Genome Sequencing is a process that looks at your whole genome – including all of your genes. The human genome contains around 20,000 genes. Other parts of the genome don't contain genes and are known as non-coding regions. But alterations in these regions may still affect our health. Whole Genome Sequencing looks at these regions, too.

Whole Genome Sequencing determines the order of bases (letters) that make up your DNA. This information can then be used by clinicians to assess:

- your health risks
- your response to medication
- your traits - characteristics that can be influenced by your genes and environment, such as blood pressure
- whether you carry certain variants (carrier testing).

Health risks

Your risk of developing certain health conditions can be based on changes in one gene (single-gene variants), or multiple genes (multiple-gene variants). Some diseases are caused by a combination of your genes and environment. Your health risks are assessed by testing for the following.

- **Single-gene variants –** also known as monogenic variants. These are variants of a single gene that are associated with a condition. For example, the BRCA1 and BRCA2 variants that put you at increased risk of breast cancer
- **Polygenic risk score (PRS)** - This score is calculated by comparing your DNA to that of people who've developed a certain condition and looking for similarities in your genes. The more of these variations you have, the higher your risk of developing that condition. You'll have different polygenic risk scores for different conditions. For example, combinations of certain variants could increase your risk of type 2 diabetes. This would be presented as a polygenic risk score for diabetes
- **Multifactorial diseases** – are diseases associated with both genetic and environmental factors (for example, lactose intolerance). The risk of developing these diseases can be modified by lifestyle changes

Response to medication

Whole Genome Sequencing uses pharmacogenomics to help predict how well how you might respond to medications.

Pharmacogenomics is the study of how your genes affect your response to different medicines. The name pharmacogenomics comes from two words:

- **pharmacology** is the study of drugs and how they affect your body
- **genomics** is the study of genes and their functions

Many current medicines are 'one size fits all', but they don't work the same way for everyone.

It can be difficult to predict who'll benefit from medicine, who'll not respond at all, and who'll experience negative side-effects.

Traits

Traits are personal characteristics that are influenced by multiple genetic and environmental factors. Some of these characteristics - for example, weight and muscle mass - can be modified by lifestyle changes, such as exercise and diet. Others, such as eye colour and height, can't be changed.

Carrier testing

Whole Genome Sequencing can identify variants that, if inherited from both you and a partner, could result in your child being affected by a condition. These variants won't affect your health, but they could affect the health of your child. This is known as carrier testing because it's a test to see if you 'carry' a variant. It can be helpful to understand these potential genetic risks if you're planning a family or already have children.

What **My Genomic Health** can tell you

When you visit your doctor, they often ask you about your medical history. This includes your family's medical history. This is because they want to understand if a health condition could genetically run in your family. My Genomic Health does something similar, but rather than asking you questions, it looks at your genome for answers.

The goal of My Genomic Health is to help you understand your risk of developing certain health conditions in the future. This includes conditions such as breast cancer, prostate cancer, high blood pressure, and type 2 diabetes (see full list on page 16). We'll also give you advice on what you can do to reduce your risk.

Although we'll be sequencing your whole genome, we will only be reporting on a subset of genes. These genes are associated with conditions for which some preventative action can be taken. These conditions are 'actionable'.

'Actionable' means that you can do something positive to potentially improve your health, such as:

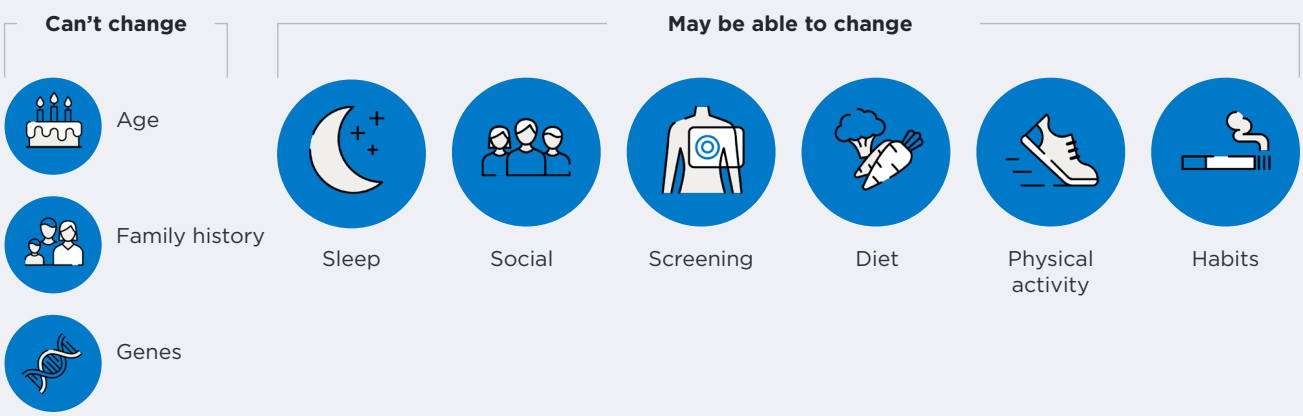
- test for the condition
- enter into screening for the condition
- introduce lifestyle measures that may reduce your risk of developing the condition

Need to know:

Whole Genome Sequencing can't definitively predict whether you'll develop a condition or not. For example, you might have a gene variant that significantly increases your risk of a condition, but never develop it. And it can't be guaranteed that Whole Genome Sequencing will identify all actionable diseases.

Can I change my risk of developing a health condition?

Many factors affect our risk of disease. Some, we can't change – for example, our age, our family history, and our genes. But others we can, such as our diet, activity levels, and lifestyle habits. Making changes like these can help lower our risk of several health conditions.



[4]

Understanding **your health**

As part of My Genomic Health, you may receive information that affects your understanding of your health, and the health of your family. These are some of the things you should think about before agreeing to genome sequencing.

Mental health

Discovering that you may be at an increased risk of certain health conditions can be challenging. It's essential to prioritise your mental wellbeing and make informed decisions about whether this test is right for you. If you have active mental health issues, it's really important to consider how Whole Genome Sequencing might affect your mental health.

Risk perception

We all have different attitudes to risk. This will affect how you interpret the results of Whole Genome Sequencing. Some people will find the information motivating and take proactive steps. Others may feel anxious if they learn they may be at increased risk of a condition. Understanding your perception of risk can help you make informed decisions about how to approach your results. By considering how you may react, you can better prepare yourself to take positive action around your health and wellbeing.

Uncertainty

This test is designed to help you understand your genetic risk of disease. But it can't predict with certainty that you'll develop any condition. While it may be challenging to live with uncertainty, knowing your potential risks allows you to make informed decisions and take preventive measures.

Implications for your family

Understanding your genetic risk can provide valuable insights for your family members because they may share the same risks. But there are particular things to consider if:

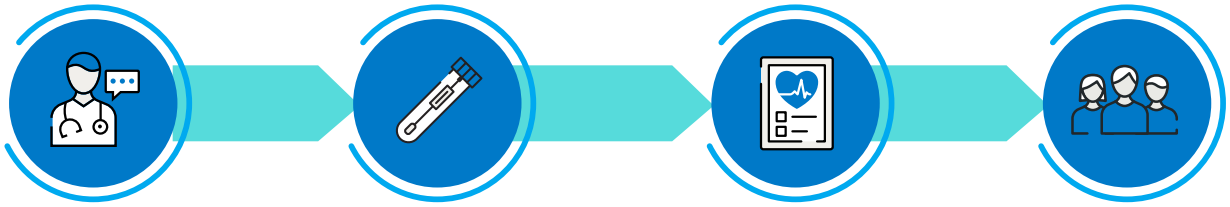
- You're an identical twin: it's important to obtain consent from both twins, as sequencing one twin essentially sequences the other. This ensures that both individuals are informed and can make decisions together.
- You're pregnant: pregnancy can be a stressful time, and receiving information about potential genetic risks might not be ideal during this period. It's important to consider the timing and how this information may affect your wellbeing.
- You have a family history: if there's a strong family history of a specific genetic condition, such as bowel cancer, Whole Genome Sequencing might not be the most appropriate test. In these cases, other tests may provide more relevant and targeted information.

If any of these family circumstances are relevant to you, or you have health anxiety, we strongly recommend that you have a pre-test counselling appointment. This meeting is a great opportunity to ask any questions you have about the test, including the risks and benefits, and decide if you would like to take part.

How **My Genomic Health** works

We work with a range of experts to offer Whole Genome Sequencing and offer support both before and after testing.

As part of My Genomic Health, you will:



1. Complete a questionnaire about your health and family history, and choose if you'd like to speak to a genetic counsellor before taking part in the pilot.
2. Visit one of our genomic health centres to provide a blood sample.
3. You'll receive your results up to 10 weeks later in a full digital report.
4. If necessary, you'll receive appropriate onward clinical support as needed based on your results.

Code on Genetic Testing and Insurance

As a member of the Association of British Insurers, Bupa Insurance is signed up to the Code on Genetic Testing and Insurance.

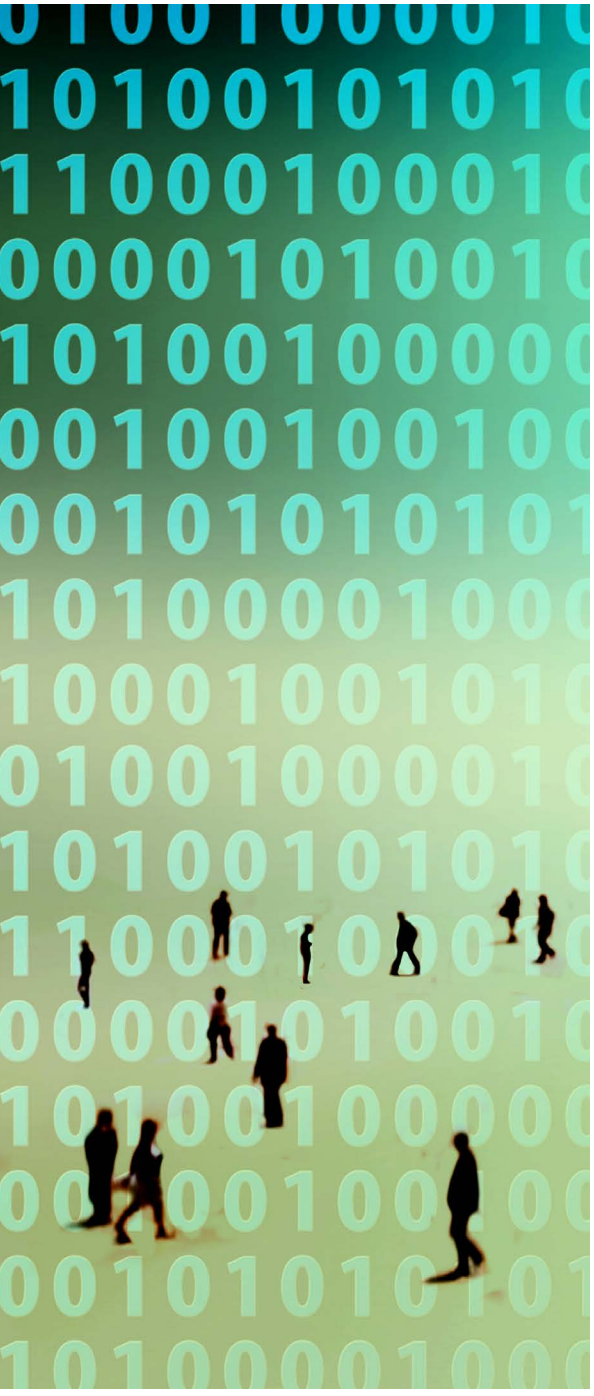
This means:

- Bupa Insurance does not require or pressure you to have a predictive or diagnostic genetic test
- Bupa Insurance won't ask for, or take into account the result of, a predictive genetic test. This includes for existing insurance policies
- if you have a condition which is symptomatic and you claim for support or treatment under your health insurance policy, your policy terms and conditions will apply, including in relation to the impact of that claim

You should be aware that:

- if you apply for life insurance over £500,000 and you've had a predictive genetic test for Huntington's disease, an insurer may look at this test result as part of your application. We won't report on the Huntington's gene as part of My Genomic Health
- The Code on Genetic Testing and Insurance only applies to ABI members and other signatories and doesn't apply if you live or plan to live outside of the UK. If you live or plan to live outside of the UK or apply for insurance with an insurer who isn't bound by the Code you may be asked to disclose the results of any genetic testing you've had and you may be asked to comply with other requirements imposed by the codes of practice that may be applicable in the country where you live.

Who can take part?



To use My Genomic Health, you must:

- **Be the main policyholder/main beneficiary or a named dependent of that policyholder or beneficiary, under a Bupa provided private medical insurance policy or health trust**
- **Be over 18 years or older and living in the UK**
- **Travel to London for any follow up care, if required**
- **Agree to the terms and conditions of My Genomic Health**
- **Provide your consent to participate**

After the test

Your results will be in the form of a report. Once it's been created, this report will be reviewed by our Clinical Geneticist, a Specialist Consultant (for example, for cardiovascular disease), a GP, or a Genetic Counsellor. You'll be offered an appointment to discuss the results. In many cases, you won't need further clinical support.

We'll then discuss next steps that are best for you to take. These could include enhanced screening, wellbeing and lifestyle changes, and, in some cases, surgery. You'll be involved in all decision making; no decision will be made without your knowledge.

If we detect a gene that is directly linked to a disease (monogenic variant), your results will be reviewed by a team of experts before our recommendations are discussed with you. This team will include a Consultant Clinical Geneticist and experts in the relevant field of medicine. For example, if we detect a BRCA variant, the team would include a breast cancer specialist.

Please note that in all instances, we'll only provide access to this support for two years from the date of your blood test. We may fund extra screening or medical interventions if they're suitable. See section 9 for more information.

Case study

Your results will show your risk of a range of different conditions. Here's an example of the advice you may receive based on your test results.

Sarah's experience

Sarah meets with a Genetic Counsellor to discuss her medical and family history. After asking questions about My Genomic Health, she decides to undergo Whole Genome Sequencing to learn more about her health. She provides a blood sample, which is sequenced in the laboratory. Her results show she's at increased risk of hypertension (high blood pressure) and breast cancer.

Sarah discusses these results with the Genetic Counsellor. They recommend that Sarah considers annual screening for hypertension and breast cancer.

After this, Sarah decides to book her Bupa health assessment, where she has a mammogram. Before now, she waited a few years between mammograms but now she has one every year as part of her health assessment package.

Her blood pressure and lipid profile are also checked as part of her health assessment. She has slightly raised blood pressure (hypertension). She speaks with the GP about breast health, self-examination, and what symptoms to look for.

Her lifestyle action plan now feels more relevant to her. She's seen her mother struggle with hypertension for years. Now she knows that staying active is the best thing she could do to prevent hypertension.

She's also committed to getting her health checked annually, whereas she hadn't thought of it as a priority in the past. She knows it's especially important to keep an eye on her blood pressure, to be aware of breast changes, and to have regular mammograms.

What will Bupa fund as part of this pilot?

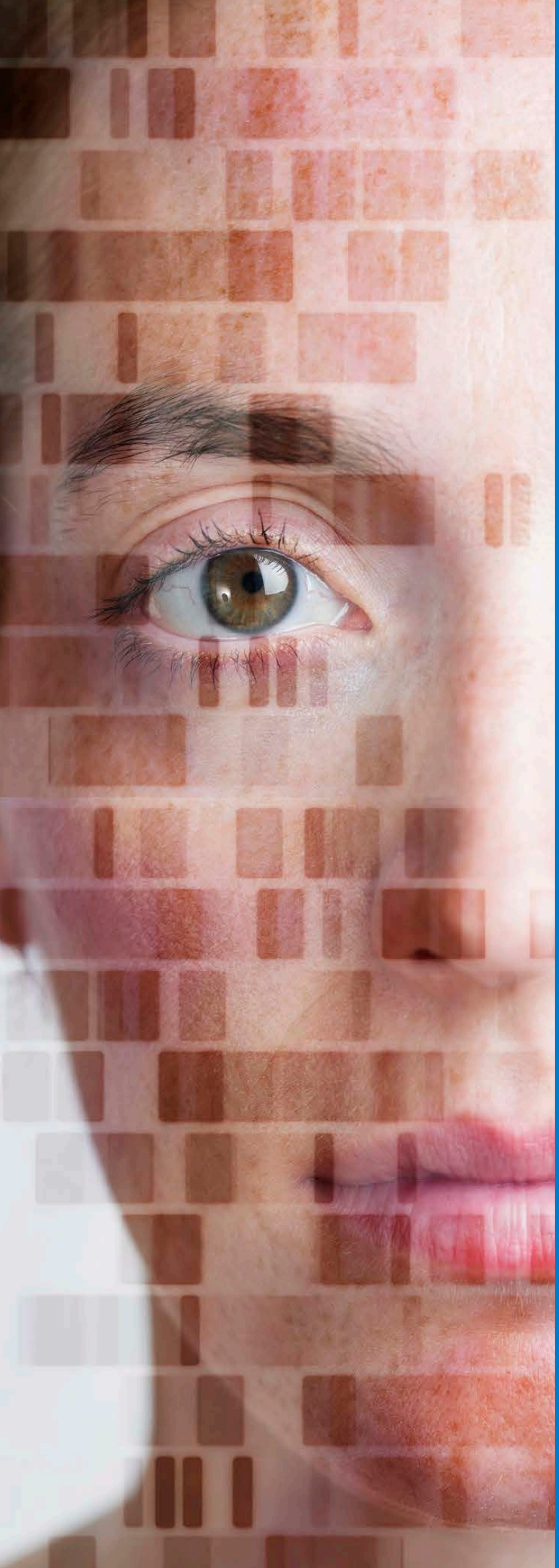
We'll cover all costs of the My Genomic Health pilot for two years. This includes:

- **Genetic counselling**
- **Taking your blood sample and extracting DNA from it to sequence in the laboratory**
- **Analysing and reviewing your findings**
- **Any follow-up appointments with our doctors based on your My Genomic Health findings**
- **We may fund additional screening or medical interventions if we believe they are suitable**

Need to know: what isn't included

If our doctors believe you have symptoms of a disease and need treatment for it, the pilot won't cover the costs of this. This is because My Genomic Health is designed to help prevent diseases from developing, not to treat them.

If this happens, you'll need to decide whether to obtain treatment through your Bupa private medical insurance policy or Bupa health trust, where eligibility rules and terms and conditions (including in relation to the impact of claims), will apply. In the event your medical insurance doesn't cover the condition, you may need to consider approaching your GP for an NHS referral. You should also be aware that the NHS may not recognise the preventative health report you have received from us.



[10]

What happens after I take part in My Genomic Health?

We'll ask you to fill in surveys over the course of the two years to track your health and wellbeing after Whole Genome Sequencing.

This is to understand if you've changed how you manage your health following the test, and the impact it's had.

We'll keep your clinical data for up to 20 years, in line with our medical data retention policy. We may contact you in the future to understand how your health and wellbeing has progressed.

[11] Conditions included in **My Genomic Health**

Here are some of the conditions screened for in My Genomic Health:

Monogenic variants that determine risk of:

- **Colorectal cancer** also known as bowel cancer. This cancer starts in your large bowel (colon) or inside your back passage (rectum). It's one of the most common types of cancer in the UK; more than 40,000 people get bowel cancer each year.
- **Gastric cancer** also known as stomach cancer. Around 6500 people get stomach cancer in the UK each year.
- **Breast cancer** is the most common cancer in the world. In the UK, one woman is diagnosed with breast cancer every 10 minutes.
- **Neurofibromatosis** describes three different conditions caused by gene variants. These variants lead to an increased risk of tumours growing in the brain and spinal cord (the nervous system).
- **Retinoblastoma** a type of childhood eye cancer but can be a carrier of a germline mutation that can affect one or both eyes, retinoblastoma is caused by a variant of the retinoblastoma gene.
- **Thyroid cancer** develops in the thyroid gland. This gland produces thyroid hormones, which control your metabolism.
- **Hereditary endocrine cancer syndromes** affect hormone-producing (endocrine) glands and are often caused by gene variants. Examples include multiple endocrine neoplasia and von Hippel-Lindau disease.
- **Non-melanoma skin cancer, and melanoma skin cancer** are the two main types of skin cancer: Most skin cancers are non-melanomas. These usually start in areas of skin that are regularly exposed to the sun. Melanoma skin cancers often start from a mole.
- **Leukaemia, lymphoma, and myeloma** are the most common types of blood cancer.
- **Cardiomyopathy** is when the walls of your heart thicken or become stiff, this is known as cardiomyopathy. You might inherit this condition, or develop it because of other factors, such as high blood pressure.
- **Cardiac arrhythmias** is when your heartbeat is irregular. This might be because of an inherited condition, such as long QT syndrome. Lifestyle factors, such as smoking, alcohol, and caffeine, can also affect your heartbeat.
- **Marfan's syndrome** affects connective tissues, which support your body and your organs. It's a genetic disorder, which means it's inherited. Marfan syndrome can affect the eyes, heart, blood vessels, lungs, and bones.
- **Ehlers-Danlos syndromes** are inherited conditions that affect connective tissue. They can lead to hyper-mobile joints and long-term (chronic) pain.
- **Hereditary haemochromatosis** is a genetic condition where your body absorbs too much iron from food, leading to iron buildup in organs like the liver, joints, heart, and pancreas. This can cause damage over time, but if picked up early and treated properly with regular blood removal this can help manage iron levels and prevent complications.
- **Wilson's disease** is when people have too much copper in their body. It builds up in the liver, brain, and eyes, amongst other organs. Wilson's disease is a genetic condition.
- **Inborn errors of metabolism** is the way in which our bodies break down the nutrients we eat into the energy we need. Inborn errors of metabolism are a group of genetic conditions that affect these pathways.
- **Hereditary Haemorrhagic Telangiectasia** (HHT) is an inherited genetic disorder that affects the blood vessels. It's also known as Osler-Weber-Rendu syndrome. People with HHT have some blood vessels that have not developed properly and sometimes cause bleeding, known as arteriovenous malformations (AVMs).

- **Familial Hypercholesterolaemia** (FH) a genetic disease which results in the reduced clearance of atherogenic LDL-cholesterol ("bad cholesterol") in the blood, and an increased risk of early heart disease.

- **Maturity Onset Diabetes of the Young** (MODY) is a rare form of diabetes which is different from both type 1 and type 2 diabetes and runs strongly in families. It is caused by a mutation (or change) in a single gene. The key features of MODY are: Being diagnosed with diabetes under the age of 25, having a parent with diabetes, with diabetes in two or more generations, not necessarily needing insulin.

- **Malignant Hyperthermia** is a severe reaction to certain drugs used for anaesthesia. This severe reaction typically includes a dangerously high body temperature, rigid muscles or spasms, a rapid heart rate, and other symptoms.

- **Polycystic Kidney Disease** (PKD) is a genetically inherited condition that causes cysts to form in the kidneys and sometimes other organs, including the liver. Over time, PKD can cause complications such as high blood pressure and reduced kidney function.

Multifactorial diseases, susceptibility to:

- **Malignant Melanoma** is a kind of skin cancer that starts in the melanocytes. Melanocytes are cells that make the pigment that gives skin its colour. The pigment is called melanin. Melanoma typically starts on skin that's often exposed to the sun.

- **Long QT Syndrome** (LQTS) is a heart rhythm disorder that causes fast, chaotic heartbeats. The irregular heartbeats can be life-threatening. LQTS affects the electrical signals that travel through the heart and cause it to beat.

- **Venous Thromboembolic Disease** is having a blood clot that blocks the flow of blood through your veins. A Venous Thromboembolism (VTE) can be stuck in the deep veins of the legs or arms (Deep Vein Thrombosis) or travel though the veins to the lungs (Pulmonary Embolism).

- **Chronic Kidney Disease** is a long-term condition where the kidneys do not work as well as they should. In the early stages it is asymptomatic and may only be diagnosed by a blood test.

- **Non-alcoholic Fatty Liver Disease** (NAFLD) is the term for a range of conditions caused by a build-up of fat in the liver. It's usually seen in people who are overweight or obese. Early-stage NAFLD does not usually cause any harm, but it can lead to serious liver damage, including cirrhosis, if it gets worse.

- **Pulmonary fibrosis** is a lung disease that occurs when lung tissue becomes damaged and scarred. This thickened, stiff tissue makes it harder for the lungs to work properly.

- **Hereditary haemochromatosis** is a genetic condition where your body absorbs too much iron from food, leading to iron buildup in organs like the liver, joints, heart, and pancreas. This can cause damage over time, but if picked up early and treated properly with regular blood removal this can help manage iron levels and prevent complications.

- **Pancreatitis** is inflammation of the pancreas. Inflammation is immune system activity that can cause swelling, pain, and changes in how an organ or tissues work.

- **Lactose intolerance** is when you get symptoms, such as stomach pain, after eating food containing lactose, a sugar found in dairy products. The symptoms can be prevented by eating smaller portions of foods that contain lactose or avoiding them completely.

- **Coeliac disease** is an autoimmune condition triggered by eating gluten, a protein found in certain foods such as bread, cereals, and pasta. This causes damage to the lining of the small bowel which leads to a variety of symptoms including abdominal pain, diarrhoea, bloating, and fatigue. The only treatment for coeliac disease is a lifelong gluten-free diet.

Polygenic Risk Scores (PRS) for:

- **Breast cancer.** PRS scores for breast cancer – can help identify those at higher risk of breast cancer and can be used to guide breast screening.
- **Prostate cancer.** Similar to breast cancer, polygenic risk scores for prostate cancer can help guide screening efforts.
- **Coronary artery disease**. Often referred to as heart disease, this is when fat builds up inside the blood vessels that carry blood to your heart (arteries). This increases your risk of chest pain (angina) and heart attacks.
- **Polygenic hypercholesterolaemia** is a genetic condition that causes high cholesterol. It's caused by several gene variants, which is why it's 'polygenic'.
- **Hypo-HDL cholesterolaemia** means you have low levels of high-density lipoprotein (HDL), which is a 'good' cholesterol. HDL gets rid of excess cholesterol in your body. Low HDL levels may increase your risk of heart disease.
- **Triglyceridaemia** are a type of fat found in your blood. Your body stores these for energy. If you have high triglyceride levels, this can increase your risk of heart disease and other cardiovascular conditions.
- **Hypertension.** Also known as high blood pressure, hypertension can increase your risk of conditions such as heart disease, stroke, and kidney disease.
- **Atrial fibrillation** causes your heart to beat irregularly. It's not life-threatening but it can increase your risk of stroke.
- **Type 2 diabetes** means your body can't control the amount of sugar (glucose) in your blood. As a result, your glucose levels become too high and this can lead to conditions such as kidney disease, heart disease, and stroke.

Glossary

We understand that a lot of the language used in this guide may be new. Here's a list of the terms we've used.

Term	Definition
DNA	deoxyribonucleic acid. DNA contains the instructions your body needs to function.
Gene	a sequence of DNA that you inherit from your parents. You have two copies of each gene. A gene that has a change in its DNA sequence is known as a variant. These variants are what make us different from one another.
Genetic	relating to genes. Genetics is the study of genes and how they are inherited.
Genome	a complete set of DNA, including all genes.
Genomics	the study of the genes and their functions
Monogenic	relating to a single gene. In genetic terms, this means a single gene is responsible for a trait or condition. For example, cystic fibrosis is caused by variants in the CFTR gene. Cystic fibrosis is therefore a monogenic disease. Some monogenic variants may be associated with a high risk of certain diseases. For example, variants of the BRCA1 and BRCA2 genes have been linked with breast cancer.
Pharmacogenomics	a combination of the words pharmacology (the study of drugs and their effects) and genomics. Pharmacogenomics studies how your genes affect your response to different medicines.
Polygenic	relating to multiple genes. Polygenic risk scores are a way of measuring your risk of disease, based on the variants you have of each gene linked to that disease. A polygenic risk score for coronary artery disease, for example, will be calculated using multiple gene variants that have been associated with that condition.
Variant	in genetics, a variant is an alteration in a DNA sequence. This alteration may have no effect, it may lead to a harmless difference, or it could cause disease.
Whole Genome Sequencing	a process used to determine the entire DNA sequence.

My Genomic Health

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