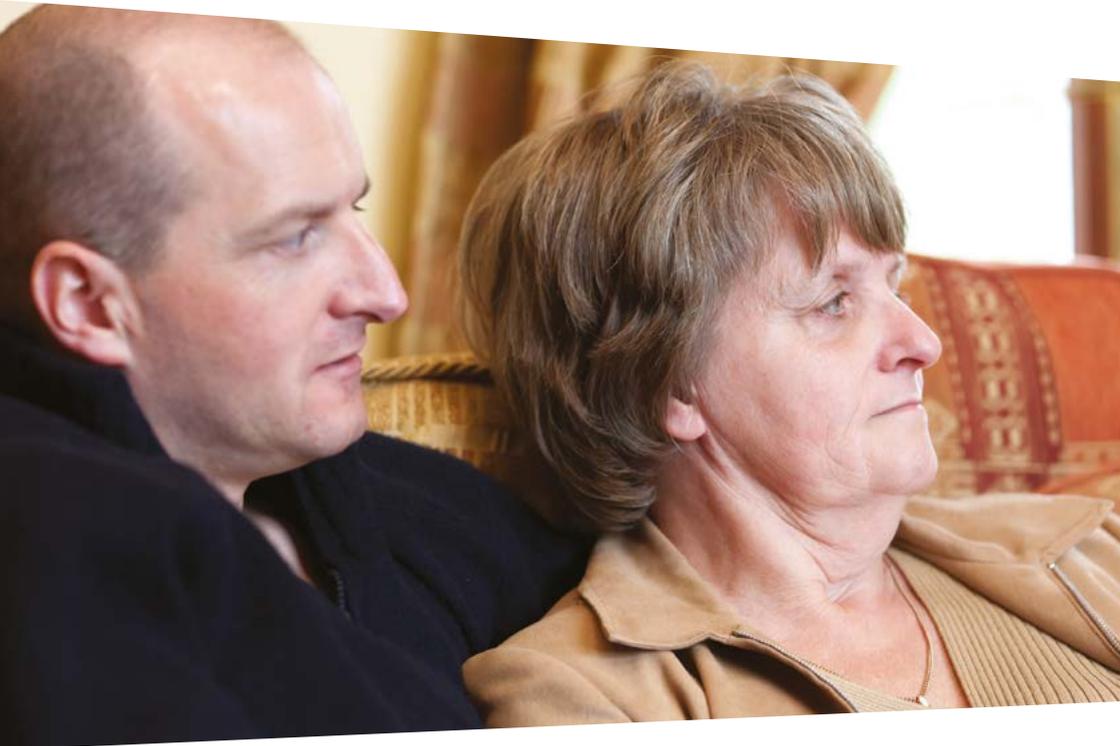


Genes and dementia



**Alzheimer's
Research
UK**

Make breakthroughs possible



This information is for anyone who wants to know more about the link between genes and dementia. This includes people living with dementia, their carers, friends and families.

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The booklet gives an overview of what genes are and how they are involved in the different diseases that cause dementia, along with information on genetic testing and current research.

The information here does not replace any advice that doctors, pharmacists or nurses may give you, but provides some background information which we hope you will find helpful.

This booklet was updated in November 2020 and is due to be reviewed in November 2022. Please contact us if you would like a version with references or in a different format.



What is dementia?

The word dementia describes a group of symptoms including memory loss, confusion, mood changes and difficulty with day-to-day tasks.

There are a number of different causes of dementia, including Alzheimer's disease, vascular dementia, dementia with Lewy bodies and frontotemporal dementia.

For more detailed information on dementia, ask for our booklet '**All about dementia**' or talk to your doctor.

What role do our genes play in dementia?

As dementia is so common, many of us will have a relative living with the condition – but this does not mean we will develop it too.

Dementia is caused by diseases that affect the brain, such as Alzheimer's disease. The likelihood of developing dementia will usually depend on a complex mix of factors like our age, medical history and lifestyle, as well as our genes. Most cases of dementia are not directly caused by genes we inherit from our parents.

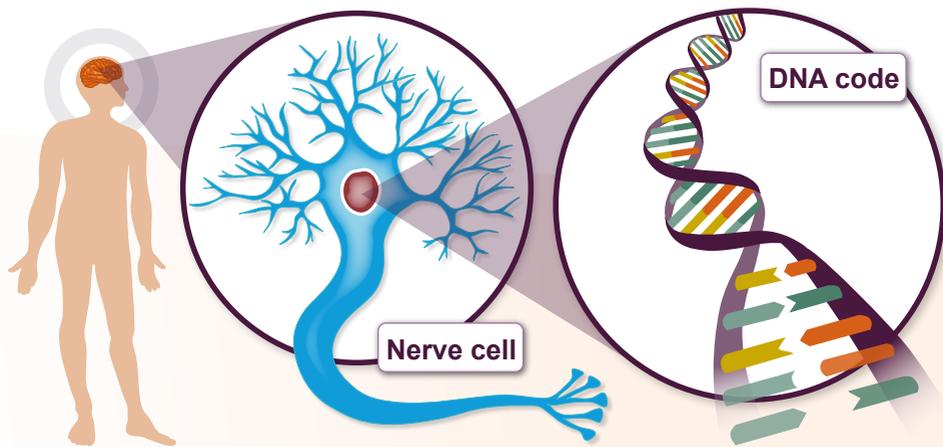
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What are genes?

Genes determine our traits, such as our eye colour and height. In some cases, they can determine whether we will develop a disease or not. They are “passed on” or inherited from our parents.

Every cell in our body contains thousands of genes. Each gene is a portion of DNA ‘code’, which holds the information our cells need to make a specific protein. These proteins are the building blocks of life. They make up our tissues and organs, and many have specific functions, like carrying messages between our nerve cells.



Risk genes

The DNA code in our genes naturally varies from person to person. Often this variation has no effect on us, but sometimes the DNA code can contain changes that increase our likelihood of getting a disease. These are known as risk genes.

If a person inherits a risk gene from their parents, it does not mean they will definitely get dementia. Your individual risk of developing dementia is a combination of your genes, lifestyle and age. We cannot change our age or genes, but some research has found that even if you carry a risk gene, there are still things you can do to reduce your risk. You can find out how to reduce your risk of developing dementia in our booklet **‘Reducing your risk of dementia’**.

Faulty genes

In very rare cases, a person may inherit a gene that does not work properly from one of their parents. This faulty gene, sometimes called a gene mutation, can cause a person to develop a disease no matter what other risk factors they have. Rare types of Alzheimer’s disease and some cases of frontotemporal dementia can be caused by faulty genes and passed down in families. Having one of these rare mutations makes someone extremely likely to develop the disease during their lifetime.

Genes and Alzheimer's disease

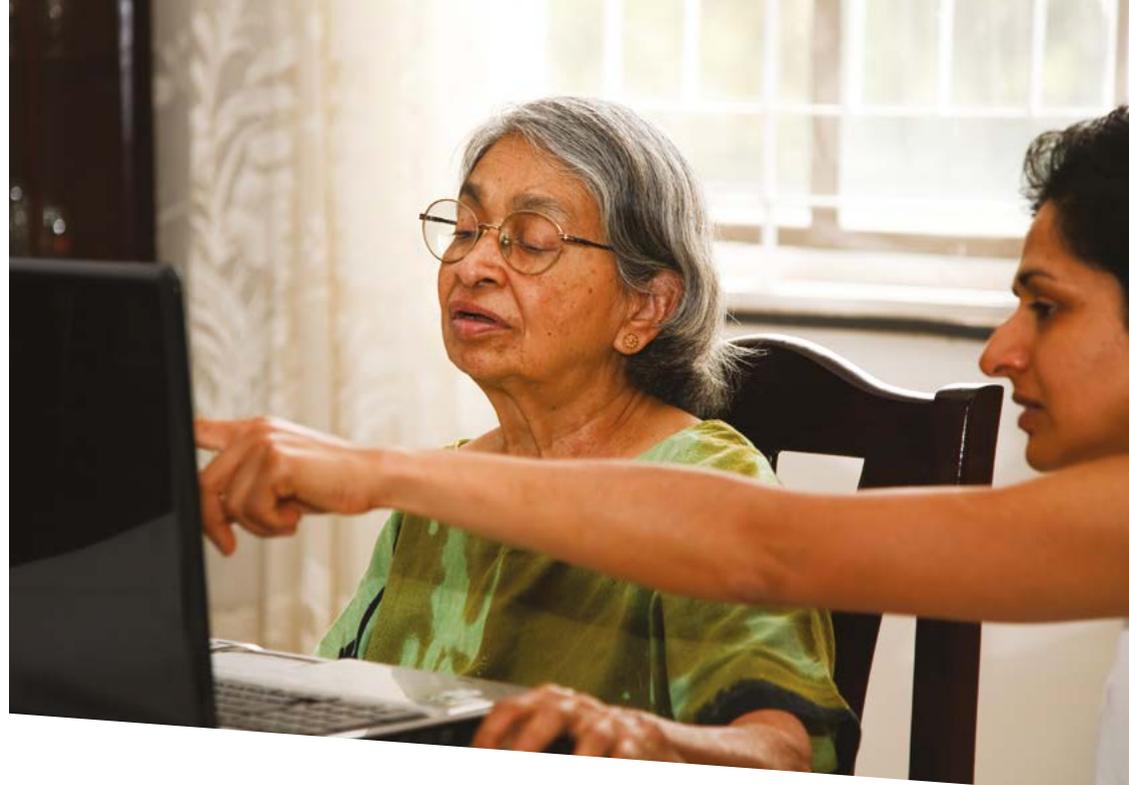
Late-onset Alzheimer's

Late-onset Alzheimer's disease affects people over the age of 65. It is the most common type of Alzheimer's and is likely to be caused by a combination of risk factors including our age and lifestyle. Our genetics also play a part.

To date, scientists have found versions of over twenty different genes that are associated with an altered risk of developing Alzheimer's disease. However, having one of these versions may only have a small effect on our total risk. There is still a lot to be understood about these genes and their role in the development of late-onset Alzheimer's.

The most well-known gene with the largest effect on our risk is called APOE. This gene makes a protein that helps keep our brain cells healthy. There are three different versions of it – APOE2, APOE3 and APOE4 – and we inherit one version of the APOE gene from each parent.

People who inherit one copy of APOE4 (roughly one in four people) are around three times more likely to develop Alzheimer's disease. About one in fifty people inherit two copies of APOE4 – one from each parent. They may be more than eight times more likely to develop Alzheimer's. However, due to other contributing factors, such as age and lifestyle, people who inherit APOE4 still may never develop the disease.



Is genetic testing available for late-onset Alzheimer's?

Genetic tests can be used to tell us whether we have inherited a gene linked to a particular disease, and to predict whether we will develop a disease later in life. Most of the genes discovered so far only have a relatively small effect on the risk of developing late-onset Alzheimer's disease, and many people who have these genes will not develop it. Equally, people who do not have these genes may still develop the disease. For that reason, genetic testing for late-onset Alzheimer's is not currently available on the NHS.

Early-onset Alzheimer's disease

Around one in 20 people with Alzheimer's disease develop the condition at a younger age, usually in their 50s or early 60s. For many cases of early-onset Alzheimer's, the cause is still unclear but is likely due to a complex interaction of genes and lifestyle.

A very small number of early-onset Alzheimer's disease cases are caused by a faulty gene passed down in families. This can be called 'familial' or 'early-onset inherited' Alzheimer's. It usually affects many members of the same family, typically in their 30s, 40s or 50s, but occasionally symptoms can start at a later age. The faulty gene can only be passed down directly from an affected parent, it does not skip generations.

So far three genes have been linked to early-onset inherited Alzheimer's disease. These genes are called:

amyloid precursor protein (APP)

presenilin 1 (PSEN1)

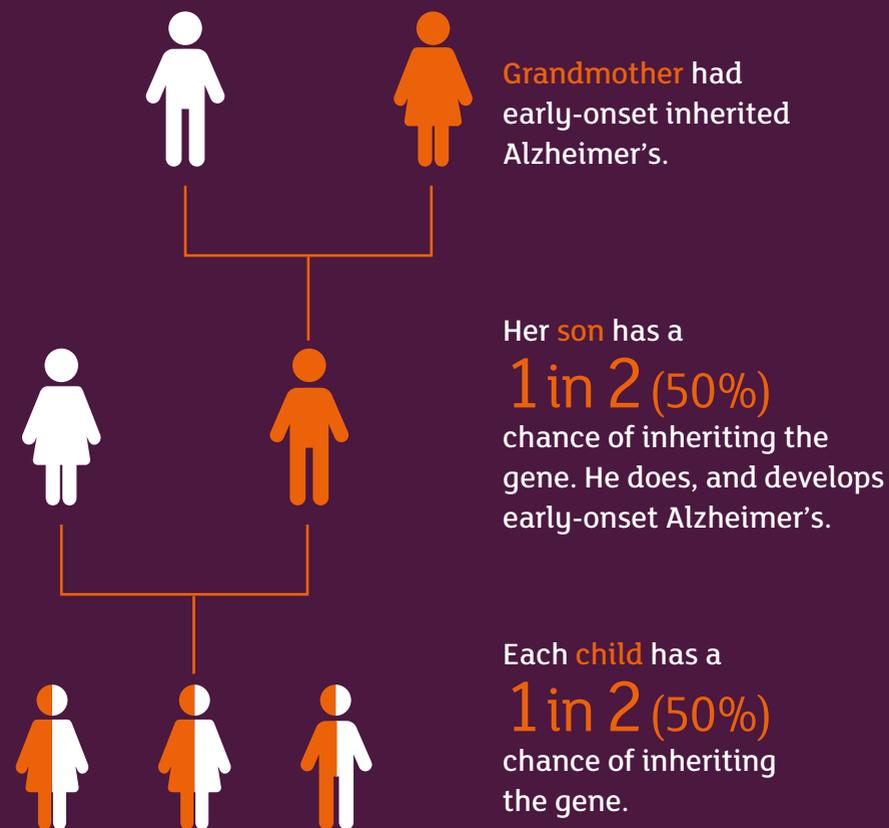
presenilin 2 (PSEN2).

These genes are involved in the production of a protein called amyloid. If the gene is faulty, there can be an abnormal build-up of amyloid in the brain that causes clumps or 'plaques', a characteristic feature of Alzheimer's disease.

People who carry one of these faulty genes will develop Alzheimer's disease, and their children have a 50% (one in two) chance of inheriting the gene and developing the disease too. It is important to stress that faulty versions of these genes are very rare and only account for a small number of cases of the disease.

Is genetic testing available for early-onset Alzheimer's?

If someone has a strong family history of Alzheimer's at a young age, genetic testing may be available on the NHS. A blood test is used to confirm a mutation in the PSEN1, PSEN2 or APP genes. This is known as diagnostic genetic testing. More information about genetic testing can be found on page 16 of this booklet.



Genes and frontotemporal dementia

Frontotemporal dementia (FTD), originally called Pick's disease, is a rarer type of dementia mostly affecting people under the age of 65 years. The symptoms of FTD can be quite varied but include changes that mostly affect behaviour or language. There are different types of FTD, and these are likely to have different causes. To find out more detailed information about FTD, please see our booklet '**What is frontotemporal dementia?**'.

Some people with FTD have a family history of dementia and the condition may be inherited in some of these families. For behavioural variant FTD, a third to half of people could have a family history. This figure is thought to be much lower for other types of FTD.

Overall, around one in ten cases of FTD are thought to be caused by a faulty gene passed down in families. Several genes have been found that can cause these inherited types of FTD, including:

tau (MAPT)

progranulin (GRN)

C9ORF72.

Mutations in the MAPT gene can cause the tau protein to behave abnormally, forming toxic clumps that can damage brain cells. We still need to understand more about how mutations in progranulin and C9ORF72 cause the disease.



The C9ORF72 gene can cause people to develop motor neurone disease, FTD or both conditions, and may affect members of the same family differently.

In cases of FTD that are not caused by faulty genes, the risk factors are not yet fully understood, and research is ongoing.

Is genetic testing available for frontotemporal dementia?

If there is a strong history of frontotemporal dementia, genetic testing is available on the NHS, to look for the faulty genes known to cause the condition. You can talk to your doctor if you are concerned about a strong family history of frontotemporal dementia. More information about genetic testing can be found on page 16 of this booklet.

Genes and other dementias

Vascular dementia

Vascular dementia is caused when blood flow to the brain is reduced, damaging nerve cells. This can happen as a result of a stroke or damage to blood vessels deep in the brain. The majority of cases of vascular dementia are not caused by faulty genes.

We may carry genes that affect our risk of stroke, heart disease or other diseases that may contribute to vascular dementia. However, lifestyle factors such as smoking, lack of exercise, obesity, drinking alcohol over the recommended limits, and an unbalanced diet can also affect our risk. To find out more about how to reduce your risk of dementia, please see our booklet '**Reducing your risk of dementia**'.

There are rare genetic disorders that can cause vascular dementia by damaging blood vessels in the brain. One is called CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) and can be passed down through families. CADASIL only affects around 1,000 people in the UK.

To find out more about vascular dementia, please see our booklet '**What is vascular dementia?**'

Dementia with Lewy bodies

Dementia with Lewy bodies is caused by a build-up of abnormal proteins in the brain and may have symptoms similar to those seen in Parkinson's disease. Age is currently the biggest known risk factor for dementia with Lewy bodies, although research is underway to find out whether genes may also play a role.

To find out more about dementia with Lewy bodies, please see our booklet '**What is dementia with Lewy bodies?**'.

Dementia and Down syndrome

People with Down syndrome are born with an extra piece of DNA. This means they also have an extra copy of the APP gene. This leads to the build-up of amyloid plaques in the brain, which play a role in the development of Alzheimer's disease. While not everyone with Down syndrome will go on to develop symptoms of Alzheimer's, most people with the condition over the age of 40 will have amyloid build-up. It is estimated that about 50% of people with Down syndrome develop symptoms like memory loss, usually in their 50's and 60's.

To find out more about Down syndrome and dementia you can contact **Down's Syndrome Association** helpline on **0333 1212 300**, or visit their website **www.downs-syndrome.org.uk**.

Information about genetic testing

Having a test to look for a faulty gene that causes dementia is only appropriate for a very small number of people. This is because inherited dementia is rare.

If you are worried that you have a strong history family of early-onset Alzheimer's disease or frontotemporal dementia, you can speak to your doctor about this.

Deciding to take a genetic test to see if you have an inherited type of dementia is a big decision and needs very careful thought. Many people may not wish to know if they carry a faulty gene that causes dementia. Others may feel it would help them and their families to plan for the future.

Not all gene mutations that cause dementia have been identified, meaning that some families may have many affected members, but no mutation can be found. Therefore, a negative test result cannot always rule out a genetic cause of a disease.

If a test is appropriate, your doctor should be able to refer you to a genetic counsellor or specialist. This could be a cognitive neurologist or memory clinic psychiatrist. They will discuss with you the pros and cons of taking a test and what will be involved. They will also tell you where the results will be kept, who they will be shared with, and what the next steps would be. For people found to have a genetic mutation that causes dementia, these discussions will also cover the options available if you are considering starting a family.

Within a family, any blood relative who may be at risk of inherited dementia will be offered genetic counselling. Several months of genetic counselling are required before someone can undergo genetic testing. This allows them to discuss what a potential test result may mean, considering things like finances, insurance and family planning. Predictive genetic testing is not the right decision for everyone, and you can still choose to decline testing after a period of genetic counselling. To find out more about genetic testing and what support is available you can visit the **Rare Dementia Support** website at www.raredementiasupport.org, or contact them directly at contact@raredementiasupport.org.



How can I reduce my risk of dementia?

For the vast majority of people, our genes are only one factor affecting our risk of dementia. There are many other factors involved, such as age and lifestyle. While we cannot change our age or genes, research has suggested that up to a third of all cases of dementia could be avoided through lifestyle changes.

There are simple things we can do that may help lower our risk:



Do not smoke.



Drink fewer than 14 units of alcohol per week.



Control high blood pressure.



Keep cholesterol at a healthy level.



Keep active and exercise regularly.



Maintain a healthy weight.



Eat a healthy balanced diet.

For more detailed information about how you can reduce your risk of dementia, contact us for our free booklet '**Reducing your risk of dementia**', or speak to your doctor.

Research into genetics

Alzheimer's Research UK has funded more than **£7.3 million** of research projects focused on understanding the genetic basis of dementia.



Discovering new genes and understanding how they work provides vital clues about the cause of diseases like Alzheimer's, taking researchers closer to developing new treatments. Our researchers have already discovered over twenty risk genes for diseases like Alzheimer's. We are helping them to build on these discoveries to develop effective new treatments for these diseases.

Through research we will bring about breakthroughs that will change lives. Thanks to the generosity of our supporters, we will continue to fund many more studies into the genetics of dementia.

Find out more

If you have questions about dementia research or want to find out more about how to get involved in research, contact our **Dementia Research Infoline** on **0300 111 5 111** or email **infoline@alzheimersresearchuk.org**

The Infoline operates 9.00-5.00pm Monday to Friday. Calls cost no more than national rate calls to 01 or 02 numbers and should be included in any free call packages.



We are the UK's leading dementia research charity dedicated to making life-changing breakthroughs in diagnosis, prevention, treatment and cure.

We welcome your comments to help us produce the best information for you. You can let us know what you think about this booklet by contacting us using the details below.



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