ALZHEIMER'S RESEARCH UK FOR A CURE

GENES AND DEMENTIA

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INTRODUCTION

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. This booklet gives an overview of how the genes we might inherit from our parents are involved in the different diseases that cause dementia, along with information on genetic testing and current research.

The information here does not replace advice that doctors, pharmacists, or nurses may give you. If you are worried about your health, including memory and thinking problems, speak with your doctor as soon as possible.

This booklet was updated in September 2024 and is due to be reviewed in September 2026. It was written by Alzheimer's Research UK's Information Services team with input from lay and expert reviewers. Please get in touch using the contact details below if you'd like a version with references or in a different format.

ANY QUESTIONS

If you have questions about dementia or dementia research, or any feedback on this booklet, you can contact the Dementia Research Infoline on **0300 111 5111**. You can also email **infoline@alzheimersresearchuk.org** or write to us using the address on the back page.

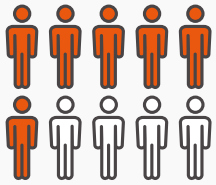
WHAT IS DEMENTIA?

Dementia is a word used to describe a group of symptoms, it is not a disease itself. This group of symptoms include:

- **memory loss**
- **confusion**
- **mood and behavioural changes**
- **movement problems**
- **and communication and language problems.**

Dementia is caused by different diseases that affect the brain. There are a number of different causes, including Alzheimer's disease, vascular dementia, dementia with Lewy bodies and frontotemporal dementia. Alzheimer's is the most common cause of dementia.

If you would like more information about these different types of dementia, please contact us using the details on the back page.



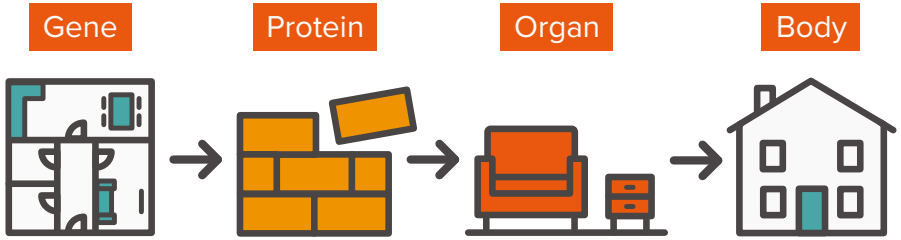
FOR EVERY 10 PEOPLE WITH DEMENTIA, SIX WILL HAVE ALZHEIMER'S DISEASE.

WHAT ARE GENES?

Genes determine our traits, such as our eye colour and height. In some cases, they can also determine whether we develop a disease, like Alzheimer's, or not. They are "passed on" or inherited from our parents.

Every cell in our body contains thousands of genes. Genes are the complex building instructions for each cell in our body. Proteins are the building blocks which make up every part of our body's cells.

These cells make up our organs, which are like rooms in a house where each has a different purpose. And all of these organs make up our body, which is the finished structure – like a house.



WHAT ROLE DO OUR GENES PLAY IN DEMENTIA?

There are two different types of genes which play a role in dementia: risk genes and faulty genes.

Dementia is common, so many of us have relatives with a disease like Alzheimer's. But this does not mean we will definitely develop it too.

99 out of 100 cases of dementia are not directly caused by genes we inherit from our parents. In most cases the likelihood of us developing dementia, is made up of a complex mixture of factors.

This includes our:

99 OUT OF 100 CASES OF DEMENTIA ARE NOT DIRECTLY INHERITED.

RISK GENES

The DNA code in our genes naturally varies from person to person. Often this variation has no effect on us. But sometimes our genes contain variations that alter the protein made by a particular gene, causing it to work differently.

This can change the way our cells work, which can increase (or sometimes decrease) our likelihood of developing a disease.

These variations are known as risk genes, and some are involved in the development of dementia. We might inherit risk genes from our parents, but this does not mean we will definitely get dementia. This is because our risk of developing dementia is usually a combination of our risk genes, lifestyle, environment and age.

MANY PEOPLE WHO INHERIT RISK GENES WILL NOT DEVELOP DEMENTIA. EQUALLY, PEOPLE WHO DO NOT HAVE RISK GENES MAY STILL DEVELOP DEMENTIA.

We cannot change our age or genes. But research has found that even if we do carry a risk gene, there are still things we can do to reduce our risk of developing dementia.

You can find out how to reduce your risk of developing dementia by asking us for our **'Reducing your risk of dementia'** information using the contact details on the back of this booklet.

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 mutated gene, can cause a person to develop a disease no matter what other risk factors they have.

Around one in 100 cases of dementia are caused by faulty genes. People who carry these faulty genes normally develop dementia at a younger age, before they are 65.

Rare types of Alzheimer's disease, and some cases of frontotemporal dementia, can be caused by faulty genes which may be passed down from an affected parent. Someone who inherits one of these rare genes is extremely likely to develop the disease during their lifetime.

If people with these faulty genes have children, there's a one in two chance of passing the faulty gene to their child. If a child of a parent with the faulty gene doesn't inherit it, they will not carry the gene or pass it on to their own children – these faulty genes don't skip generations.

"In these rare families a mutation in one of these genes causes dementia, often at an early age. These are single gene disorders. The rest of us have changes in many genes that contribute a small amount to our overall risk."

Professor Nick Fox
Director of the Dementia Research Centre at UCL

GENES AND ALZHEIMER'S DISEASE

LATE ONSET ALZHEIMER'S

Late onset Alzheimer's disease affects people over the age of 65. It is caused by a combination of risk factors including our age, lifestyle, environment and risk genes. It is not caused by our genes alone.

Scientists have found versions of over 75 different risk genes that can affect someone's likelihood of developing late onset Alzheimer's disease. Scientists are working hard to understand more about these genes and their role in the development of Alzheimer's.

The best understood risk gene, with the largest effect on Alzheimer's risk, is called APOE. Everyone carries two copies of the gene, one inherited from each parent. This gene makes a protein that helps keep our brain cells healthy.

There are three different versions of it:

APOE2 APOE3 APOE4

Because we all carry two copies of APOE, there are six possible combinations we could have - for example, APOE2/APOE2 or APOE2/APOE3.

APOE2 is thought to decrease our risk of developing Alzheimer's disease. People may still develop Alzheimer's disease with this version due to other contributing risk factors. But they are more likely to develop it much later in life than those with the APOE4 version.

APOE3 is the most common version of this gene. Research shows that it doesn't have an effect on our risk of developing Alzheimer's disease.

People who inherit one copy of APOE4 (roughly one in four people) are around three times more likely to develop late onset Alzheimer's disease.

About one in 50 people inherit two copies of APOE4 – one from each parent. They may be up to 15 times more likely to develop Alzheimer's. People with two copies of APOE4 who develop Alzheimer's disease are also more likely to experience symptoms much younger than those with one or no copies of this version of the gene.

However, due to other contributing factors, such as age and lifestyle, people who inherit APOE4 – from one or both parents - may still never develop the disease. People without APOE4 can also develop late onset Alzheimer's. This is because late onset Alzheimer's is not directly inherited through faulty genes.

YOUNG ONSET ALZHEIMER'S

Around one in 30 people with Alzheimer's disease develop the condition at a younger age, usually in their 40s, 50s or early 60s. For many cases of young onset Alzheimer's, the cause is still unclear but is likely due to a complex interaction of genes and lifestyle.

Some cases of young onset Alzheimer's are caused by a faulty gene passed down in families. This is called 'familial Alzheimer's disease' or 'young onset inherited Alzheimer's'. It usually affects many members of the same family in every generation, typically in their 40s, 50s or 60s.

People who carry one of these faulty genes will develop Alzheimer's, usually in their 40s or 50s. It is important to know that faulty versions of these genes are rare and account for between one and five in every 100 cases of Alzheimer's disease.

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

amyloid precursor protein (APP)

presenilin 1 (PSEN1)

presenilin 2 (PSEN2)

These genes are involved in how our cells produce a protein called amyloid. If the gene is faulty it causes an abnormal build-up of amyloid in the brain, which forms clumps or 'plaques'. These plaques damage brain cells and are part of how Alzheimer's disease develops. If you would like more detailed information about amyloid, please get in touch using the contact details on the back.

The **Familial Alzheimer's Disease (FAD) Support** Group helps families affected by faults in the PSEN1, PSEN2 or APP genes. More information can be found at **raredementiasupport.org/familial-alzheimers-disease** You can also email **contact@raredementiasupport.org** or call on **020 3318 0243**.

GENES AND FRONTOTEMPORAL DEMENTIA

Frontotemporal dementia (FTD), sometimes called Pick's disease, is a rarer type of dementia mostly affecting people under the age of 65. The symptoms of FTD can include changes to behaviour, communication and language.

Some people with FTD have a family history and the condition may be inherited. In a particular form called 'behavioural variant' FTD, a third to half of people affected may have a family history. This figure is thought to be much lower for other types of FTD.

Several genes have been found to cause inherited types of FTD, including:
Faults in the MAPT gene can cause the protein it makes,

MAPT GRN C9orf72

called tau, to behave abnormally, forming toxic clumps that can damage brain cells. Researchers are less certain about how faults in GRN and C9orf72 cause the disease. Faults in 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 these faulty genes, researchers are still studying which risk factors might be involved in the development of the disease.

There are different types of FTD that have different underlying causes. To find out more information about FTD, please ask us for our booklet **'What is frontotemporal dementia?'**. Contact and order details can be found on the back of this booklet.

THREE IN 10 CASES OF FTD ARE THOUGHT TO BE CAUSED BY FAULTY GENES.

GENES AND OTHER DEMENTIAS

VASCULAR DEMENTIA

Vascular dementia is caused by reduced blood flow to the brain which damages 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.

However there are risk genes that affect a person's chances of having a stroke, heart disease, high blood pressure or high cholesterol which can all contribute to vascular dementia. But age and lifestyle factors - such as smoking, lack of exercise, regularly drinking alcohol over the recommended limits, and an unhealthy diet - also increase someone's risk.

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

To find out more about vascular dementia, you can ask for our booklet **'What is vascular dementia?'** using the contact details on the back page.

DEMENTIA WITH LEWY BODIES

Dementia with Lewy bodies (DLB) is caused by a build-up of an abnormal protein called alpha-synuclein, which clumps together to form Lewy bodies in the brain. It can have symptoms similar to those seen in people with Parkinson's disease. Age is currently the biggest known risk factor for DLB, but several risk genes may also be involved.

These risk genes include:

- APOE
- GBA.

One variation of the APOE gene, called APOE4, increases the risk of developing DLB. This risk gene is also associated with an increased risk of Alzheimer's disease. Research is ongoing to understand the link between this variation and an increased risk of developing DLB.

Variations of the GBA gene are thought to affect how alpha-synuclein is disposed of in the brain. Certain variations can increase the risk of alpha-synuclein clumping together into Lewy bodies.

Research has shown that faulty genes can also directly cause dementia with Lewy bodies. These genes are called SNCA and SNCB, and can cause alpha synuclein protein to clump together.

To find out more about dementia with Lewy bodies, you can ask for our booklet **'What is dementia with Lewy bodies?'**.

DEMENTIA AND DOWN'S SYNDROME

People with Down's syndrome are born with an extra piece of DNA in all their cells. This means they have an extra copy of the APP (amyloid precursor protein) gene. This leads to the build-up of amyloid protein in the brain, which plays a role in the development of Alzheimer's disease.

While not everyone with Down's 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 in their brains. It is estimated that about half of people with Down's syndrome develop symptoms like memory loss, usually in their 50s and 60s.

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

GENETIC TESTING

Genetic tests can be used to tell whether someone has inherited a gene linked to a particular disease, and to estimate their chances of developing that disease later in life.

GENETIC TESTING FOR RISK GENES

Genetic testing for dementia risk genes is not currently available on the NHS. This is because most of the genes discovered so far only have a relatively small effect on someone's overall risk of developing a condition like late onset Alzheimer's disease. Many people who inherit these genes will not develop dementia and equally, people who do not have risk genes can still develop it.

People who may benefit from new Alzheimer's treatments will have a genetic test to screen for which variations of the APOE gene they have. This is because people with two copies of APOE4 have an increased likelihood of experiencing more severe side effects when taking these treatments.

For the most up to date information about new Alzheimer's treatments visit **alzres.uk/treatment** or contact us using the details on the back of this booklet.

GENETIC TESTING FOR FAULTY GENES

Having a test to look for a faulty gene that causes dementia is only appropriate in certain circumstances. This is because directly inherited dementia is rare.

If you are worried that you have a strong family history of young onset 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. Some 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.

If a test is appropriate, your doctor should 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.
- What will be involved.
- Where the results will be kept.
- Who they will be shared with.

For people found to have a genetic mutation that causes directly inherited dementia, these discussions will also cover the options available if you are considering starting a family.

It is also important to note that not all faulty genes that cause dementia have been identified. Some families may have many affected members, but no mutation can be found. Therefore, a negative genetic test result cannot always rule out a genetic cause of a disease.

Within one family, any blood relative who may be at risk of inherited dementia can be offered genetic counselling. Several months of genetic counselling are required before someone can undergo genetic testing. This allows time to discuss what a potential test result may mean, considering things like finances, insurance and family planning. Genetic testing is not the right decision for everyone, and you can still choose to decline testing after a period of genetic counselling.

“ My mum died with frontotemporal dementia (FTD) caused by the faulty MAPT gene, which I had a 50 per cent chance of inheriting. Unfortunately, I discovered that I had inherited the gene, so will go on to develop FTD.

When I got my test result, it was an incredibly tough thing to hear, but there was also a massive sense of relief. Not knowing was a burden I could not live with. At least I now feel I know what the shape of my life will be. I can make plans and make choices to live a fulfilled life. I feel like the diagnosis is actually a licence to live.”

Jordan Adams
who decided to take a genetic test because of his strong family history of young onset frontotemporal dementia.

Some examples of faulty genes that a genetic test may look for, and the type of dementia they cause, can be seen in the table below.

Gene	Associated disease
APP	Alzheimer’s disease
PSEN1	Alzheimer’s disease
PSEN2	Alzheimer’s disease
MAPT	frontotemporal dementia
GRN	frontotemporal dementia
C9ORF72	frontotemporal dementia
NOTCH3	CADASIL and vascular dementia
SNCA	dementia with Lewy bodies
SNCB	dementia with Lewy bodies

To find out more about genetic testing and what support is available you can visit the **Rare Dementia Support** website at **raredementiasupport.org**, or contact them on **020 3318 0243**.

HOW CAN I REDUCE MY RISK OF DEMENTIA?

For the majority of people, genes are only one of many factors that affect their risk of dementia. Other factors that affect our dementia risk include our age, lifestyle and environment.

While we cannot change our age or genes, research has suggested that almost half of dementia cases are linked to factors we have some control over.

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

You can also explore your brain healthy habits and discover more tips to look after your brain via our **thinkbrainhealth.org.uk** website.

For good brain health, and to help lower your risk of developing dementia:

If you have diabetes, ensure your condition is managed well

Keep physically and socially active

Don't smoke

Maintain a healthy weight

Eat a healthy balanced diet

Only drink alcohol within the recommended limits

Keep high cholesterol and blood pressure under control

Stay socially connected and challenge your brain

Have your hearing and eyesight checked regularly

TAKING PART IN RESEARCH

Our scientists are working hard to change the lives of people affected by dementia. But they need your help.

People with and without dementia can take part in dementia research, to help us understand more about how our genes are linked to dementia. You can register to take part at **joindementiaresearch.nihr.ac.uk** or by calling **0300 111 5111**.

Join dementia research

SHARE YOUR STORY

If you have been diagnosed with dementia and would like to share your story to inspire others and to help shape our work please get in touch via **stories@alzheimersresearchuk.org**

RESEARCH

Alzheimer's Research UK have funded more than £8.5 million of pioneering projects focused on understanding the genetic basis of dementia.

Discovering new genes and understanding how they work provides vital clues about the causes of diseases like Alzheimer's, taking researchers closer to developing new treatments.

Researchers have already discovered over 75 risk genes for Alzheimer's disease. In 2012 our researchers discovered that changes to a gene called TREM2 were linked to Alzheimer's, opening the door to new treatments now being tested in trials.

Another project is aiming to understand how different versions of a gene called APOE interact with our environment and affect our risk of developing Alzheimer's disease. The researchers at the University of Exeter are analysing large amounts of information gathered from individuals including which version of the APOE gene they have. This research will provide new insights that could help inform new treatments and ways to prevent Alzheimer's disease.

But we will not stop there. With your support, we will continue to fund many more studies into the genetics of dementia and lead the search for a cure.

We are Alzheimer's Research UK.
We exist for a cure.

Alzheimer's Research UK is the UK's leading dementia research charity. We provide free dementia health information, like this booklet and others.

If you or your loved one have been diagnosed with dementia in the last two years and would like to share your experience to help shape our work visit alzres.uk/MCV

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