

It is 2024 and Heather and her husband Charlie want to start a family. They both decide to get genotyped so that they can find out whether they are carrying any genetic conditions that might affect their future children. Heather has an identical twin, Holly, who is firmly against the test. Holly does not wish to know what the future holds and has warned her sister that she doesn't want to hear the results, whether they are good or bad. When the test results come back, Heather and Charlie are shocked to discover that she is at increased risk of developing Alzheimer's disease in later life (since she has two copies of the gene variant *ApoE-e4*).

As they share the same genetic makeup, Heather knows that her twin (and her parents) must also be at increased risk of developing the condition. Heather is faced with a dilemma. Should she tell her family or should she keep the news to herself?

## Should Heather tell her sister and parents about her results?

I know Holly didn't want Heather to take the test but that was before we found out about this Alzheimer's risk. It affects the whole family. They have a right to know. In fact, they need to know!

**Charlie**  
(Heather's husband)

It doesn't make any difference to me. I don't know if I would want to know myself but I can see why Heather wanted to be tested; that way she can be prepared. It's up to her; it's her body, her life. It doesn't affect anyone else does it?

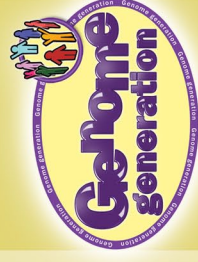
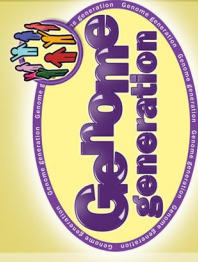
**Jean**  
(Heather & Holly's mum)



**Heather**

**Holly**  
(Heather's twin)

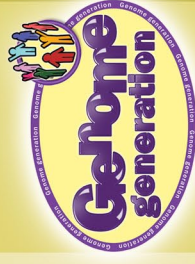
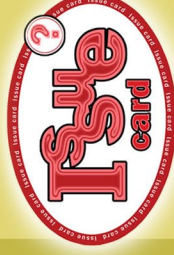
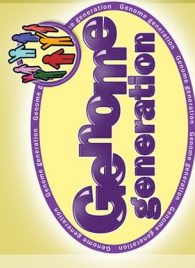
I don't understand why Heather wanted to be tested. Why would you want to know about things that you can do nothing about? I'd drive myself mad thinking about them. Whatever the results say, she can just keep them to herself!



With a condition like Alzheimer's disease, for which there is no cure, is it better to find out now or to find out when symptoms occur?

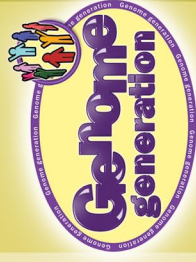
How might the information change a person's behaviour? Would they become resigned to their fate or would they take positive actions, such as changing to a healthier lifestyle?





If Heather decides not to tell her family, should they have the right to access the results? If one of her parents falls ill with the condition, the family may realise that she kept the news a secret.

Should Heather tell her sister and parents the results? What will be the impact on the family if she does share the news?



What can, or should, Heather do now that she has discovered that she has a predisposition to Alzheimer's disease? Does the information give her an advantage over her sister?

Is your genotype really yours? Considering that Heather is an identical twin, and therefore has the same genetic makeup as her sister, is it fair to reveal the results to anyone without informing her sister (or getting her sister's permission)?



## Our genes

Most of the DNA in human cells is packaged into 46 chromosomes, in 23 pairs. Our genes are arranged along these chromosomes and carry the instructions to make molecules, such as proteins. To function properly, each cell depends on thousands of proteins doing the right job, in the right place, at the right time. Our complete set of DNA, containing all the instructions required to make us, is called a genome.

[yourgenome.org](http://yourgenome.org)

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## 'Maybe' genes & 'definitely' genes

There are two types of genes associated with Alzheimer's disease. These are: 'deterministic genes' and 'risk genes':

- **Deterministic genes** guarantee that anyone who inherits them will **definitely** develop the condition at some point. There are three known deterministic genes for Alzheimer's disease.
- **Risk genes** indicate that a person has an increased risk of developing the disease but there is no guarantee that they will. There is one known risk gene for Alzheimer's disease, called *ApoE-e4*.

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## ApoE inheritance

Everyone inherits a pair of genes which code for apolipoprotein E (ApoE) – one from each of their parents. There are three forms of the gene: *ApoE-e2*, *ApoE-e3* and *ApoE-e4*.

*ApoE-e3* is the most common form. The one with the strongest influence on developing Alzheimer's disease in later life is *ApoE-e4*. People who inherit *ApoE-e4* from both parents have an even higher risk of getting the disease.

### Approximate distribution of E2, E3, and E4 in the human population

Gene combination	Percent of population	Chance of developing Alzheimer's disease
E2/E2	1-2%	Decreased
E2/E3	15%	Decreased
E3/E3	55%	Normal (baseline)
E2/E4	1-2%	Normal (baseline)
E3/E4	25%	3 to 5 times greater
E4/E4	1-2%	15 times greater

Source: National Institutes of Health Office of Science Education



## *ApoE-e4* and Alzheimer's disease – what is the risk?

65% of all confirmed Alzheimer's disease patients carry at least one *ApoE-e4* allele. 12-15% of these have two *ApoE-e4* alleles. The average risk of contracting Alzheimer's disease at the age of 65 is approximately 15% but for those with an *ApoE-e4* allele the risk increases to 30%.





## Not a guarantee

*ApoE-e4* is linked to 20-25% of Alzheimer's disease cases. However, people with the risk gene *ApoE-e4* are NOT guaranteed to develop the disease.

People who do not have the risk gene *ApoE-e4* are at a decreased risk but they CAN still develop Alzheimer's disease.

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## The current situation

There are tests available for the 'deterministic genes' which guarantee that a person will develop Alzheimer's disease. These are usually carried out after lengthy discussion with a genetic counsellor.

Tests for 'risk genes' such as *ApoE-e4* are controversial. They are not routinely offered through health services but testing sometimes takes place during research studies.

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## What can we do to prevent it?

There is no known cure for Alzheimer's disease but certain lifestyle choices may reduce the risk of developing the disease. These include:

- maintaining an active and healthy lifestyle
- protecting our heads – researchers have made links between head trauma and Alzheimer's disease in later life.
- keeping a healthy heart – there are correlations between heart health and brain health.

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## Identical twins, identical genes

Identical twins (also known as monozygotic twins) develop from a single fertilised egg, which splits into two around the time it becomes implanted in the womb. This means that identical twins share 100% of their genes.

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## Changes to our DNA

Even though identical twins share the same DNA, 'epigenetic' changes (chemical changes to DNA) can occur in the course of their lifetime. Factors that lead to these changes can include diet, physical activity, chemical exposure (e.g. smoking) and ageing. This can mean that even identical twins will change as they grow older and may be susceptible to different diseases.

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## Our DNA

Our bodies are made up of around 50 trillion cells. Most of these cells contain a person's genetic information within a long molecule called DNA (deoxyribonucleic acid). This DNA contains the genetic information that we inherit from our parents.

DNA is made up of specific sequences of letters or bases that encode instructions on how to make proteins. These bases [Adenine (A), Guanine (G), Cytosine (C) and, Thymine (T)] are lined up along two strands of DNA. The DNA is coiled into a double helix structure that resembles a twisted ladder.

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## Gene mutations

A mutation is a permanent change in the DNA sequence. Mutations come in a number of different forms and can change the functioning of our genes. Some mutations may lead to a difference in the amount, or structure, of a protein produced by specific genes. Some mutations may switch genes on at the wrong time, preventing a protein from doing its job, or changing the way it does its job.

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## What is Alzheimer's disease?

Alzheimer's disease is the most common form of dementia, affecting over 465,000 people in the UK. Dementia is not a single illness but a group of illnesses caused by damage to the brain. Symptoms of Alzheimer's disease include memory loss, mood changes and problems with communicating and reasoning. These symptoms occur in Alzheimer's disease because of damage to brain cells caused by the build-up of protein "plaques" and "tangles" in the brain.

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