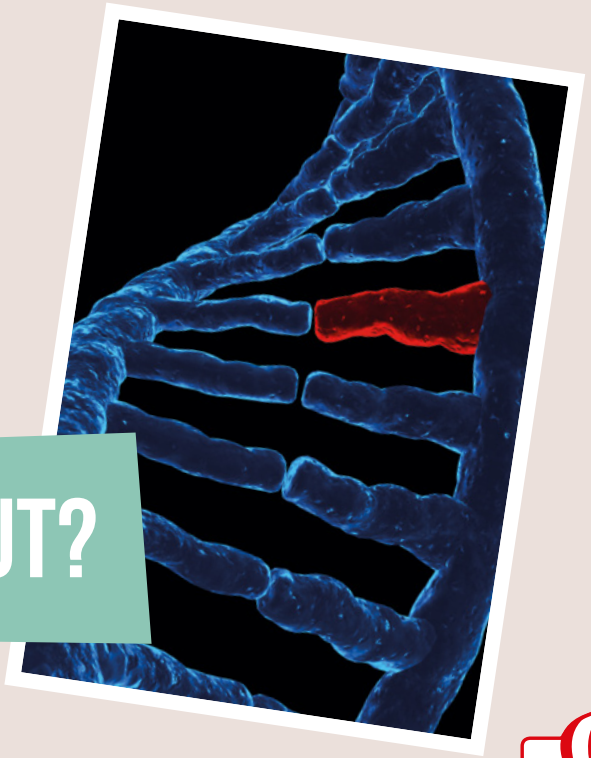
RECALL BY GENOTYPE

WHAT'S IT ALL ABOUT?



University of BRISTOL

Avon Longitudinal Study of Parents and Children

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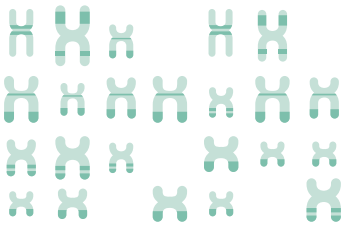
CHILDREN OF THE 90s

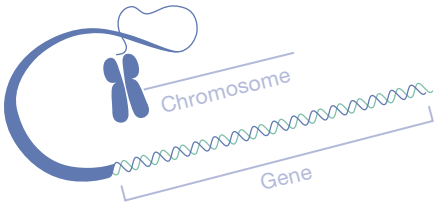
As a Children of the 90s participant you may be invited to take part in a **recall-by-genotype** study. Before you decide whether or not to take part, we'd like to explain exactly what a recall-by-genotype study is.

GENOME

Your genome or genetic code is your body's instruction manual, containing all the information needed to make and maintain you. It is the full set of your genes (about 19,000 in total) plus all the DNA between your genes, organised in chromosomes.



GENES



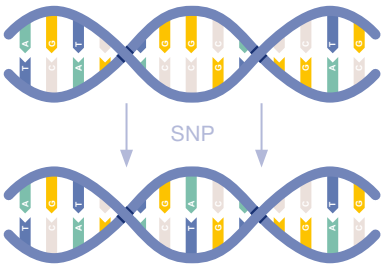
Genes are sections of genetic code that give your body instructions about your make-up, e.g. your blood group or hair colour. For example, the genes that 'code' for eye colour, could tell your body to have brown, blue, or green eyes. Genes are made up of DNA.

DNA

DNA stands for **D**eoxyribo**N**ucleic **A**cid. It is made up of four chemical building blocks represented by the letters A, T, C and G. There are about 3 billion of these letters in your genome.

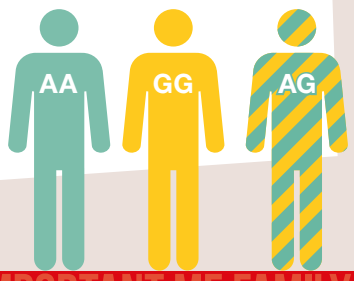
GENETIC VARIANTS

Much of the genetic code is the same in everyone but there are also some subtle differences. These differences are called genetic variants and they can occur in genes or elsewhere in the genome. Usually the difference is just a change in a single letter, e.g. from a C to an A, and these are called **SNPs** (**S**ingle **N**ucleotide **P**olymorphisms). These changes make us different from one other (e.g. hair and eye colour) and in some cases can contribute to illness.



GENOTYPE

You have two sets of genes – one from your mother, one from your father. This means that where there are genetic variants, you could have two letters the same (e.g. GG), or two different (e.g. GA). We call this your genotype.



WHY ARE RECALL-BY-GENOTYPE STUDIES IMPORTANT?

Complex diseases like cancer, depression and type 2 diabetes occur when lots of genes combine with lifestyle choices like diet, exercise and work patterns to influence the risk of developing a disease. Many genetic variants have been linked to disease but in most cases researchers have little idea how they work. Recall-by-genotype studies in healthy people, like Children of the 90's participants, can help us figure out the relationship between the genetic variant and the disease.

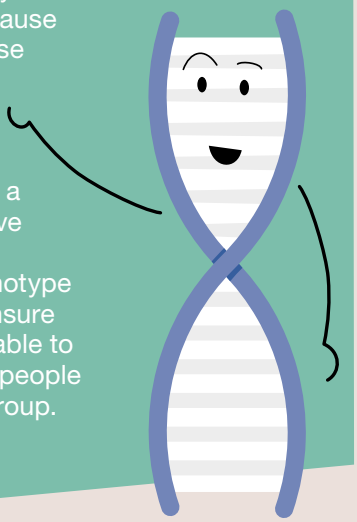
WHAT TYPES OF RECALL-BY-GENOTYPE STUDIES ARE THERE?

Type 1 studies look at single genetic variants, one at a time.

Type 2 studies look at the overall effect of lots of genetic variants, all at the same time.

WHY DO YOU DO THEM?

- They enable us to look at the role of genetic variants that occur naturally in healthy people. This avoids complications caused by a disease or the medicine used to treat it.
- They are very efficient because they maximise differences between participants.
- We can pick a representative sample from different genotype groups to ensure that we are able to see enough people from each group.



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RECALL BY GENOTYPE AND GENETIC RISK

In recall-by-genotype studies, participants are invited to take part on the basis of their genotype.

WHAT IS GENETIC RISK?

Genetic risk is the contribution our genes play in the chance we have of developing certain illnesses or diseases. Researchers are increasingly using genetic knowledge to predict the likelihood of developing different illnesses, from cystic fibrosis to mental illness.

Some genetic variants, called risk variants, can increase your risk for developing a disease. Other genetic variants can decrease your risk for developing a certain disease. How much a genetic variant tells us about an individual's chance of developing a disorder is not always clear.

RISK IS HARDER TO PREDICT FOR COMPLEX DISEASES

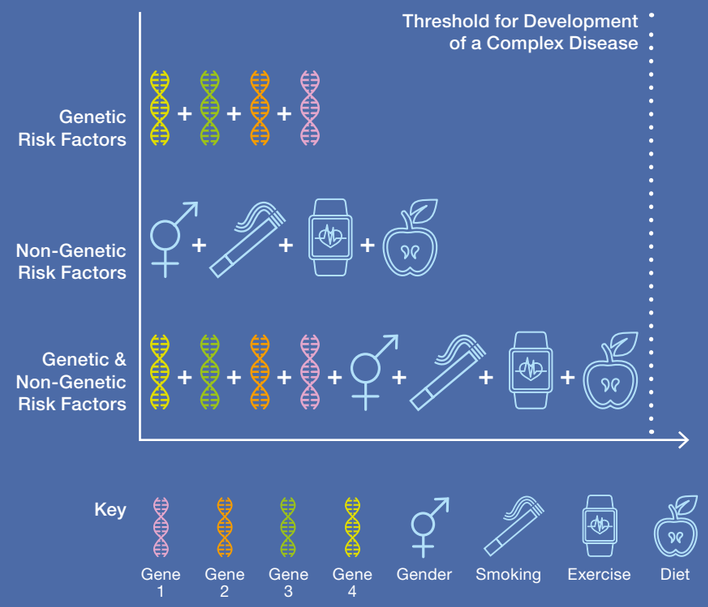
Complex diseases are caused by a combination of changes in genes and environmental factors such as exercise and nutrition. There may be many genetic variants that contribute to a disease. The number and combination of variants in a person's genome, along with environmental and lifestyle factors, determine his or her overall risk of disease.

By looking at the biological differences between healthy individuals with high and low genetic risk for a particular disease relative to the population as a whole, researchers can better understand disease processes relevant for treatment and prevention. Researchers therefore select individuals with particular genetic variants to take part in recall by genotype studies.

EXAMPLE: HEART DISEASE

There are likely to be hundreds of genetic variants that affect a person's risk of getting heart disease. Nutrition, exercise and smoking also play a big role in determining a person's risk of heart disease.

If you have gene variants associated with an increased risk of heart disease, it does not mean that you definitely will develop heart disease. The opposite is also true. If you do not have variants associated with an increased risk of heart disease, it is still possible that you could develop heart disease.



EXAMPLE: TYPE 1 DIABETES

Some diseases cause the body's immune system to attack itself by mistake. These are called auto-immune diseases and there are more than 80 of them, including type 1 diabetes.

In type 1 diabetes, cells called T-cells don't work properly and damage the pancreas. Researchers wanted to find out if a specific gene called IL2RA was involved in causing the damage.

The researchers found that the genotype linked to type 1 diabetes also affected the T-cells in healthy people. This discovery helps to explain why the genetic variant studied is linked to type 1 diabetes. We hope this will help scientists develop new treatments for the disease and prevent some people developing it in the future.

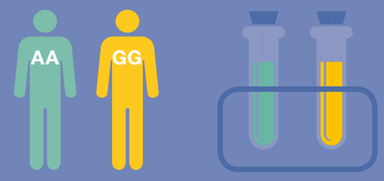
1 INVITATION

Researchers invited participants in a project (like Children of the 90s) to take part based on their genotype at a location that they knew was linked to type 1 diabetes and that affected the function of the gene*.

2 RESEARCH

The researchers invited an equal number of people from two genotype groups.

3 TESTS



Each participant gave a blood sample and had their T-cell function tested in the laboratory.

4 RESULTS

Researchers compared T-cell function in participants from the two different genotype groups.

* this study was conducted by researchers from King's College London and the University of Cambridge.

FAQS

Q Will Children of the 90s staff know my genotype?

A No, neither you, Children of the 90s staff, or the researchers conducting the study will know which group you are in.

Q If I am asked to take part in a RBG study looking at a particular disease, does that mean I have the gene for that disease?

A With a few rare exceptions, we all carry the same set of genes, so there is no such thing as having a 'disease' gene. It's the changes in our genes that can cause us to have a disease, not the genes themselves. Because we select people from more than one genotype group for recall-by-genotype studies, you won't be able to tell which group you are in.

Q If I am invited to participate in a study does it mean I am at increased risk of developing a disease?

A No. To understand the role our genes play, these studies invite people with different genotypes or 'risk genes'. We will never invite only individuals in high- or low-risk groups. If you are invited to a recall-by-genotype study it will mean you could have a high, low or 'neutral' risk gene that is being studied. The diseases we are investigating involve many interacting genes in addition to possible lifestyle and environmental factors. It is therefore usually impossible for researchers to infer anything about your overall risk based on these genotypes alone and you should not be concerned if you are invited to one of these studies.

DID YOU KNOW?

- In some cases, having a particular genetic variant that increases your risk of developing one disease, could reduce your risk of developing others.
- Although genetic variants can increase or decrease our risk of developing various diseases, the change in the amount of risk for each variant is usually very small. This means that our research can't predict what will happen to your health but it does help us understand what the pattern is likely to be for Children of the 90s as a whole.
- Researchers have found 97 genetic variants that may contribute to people having a high body mass index (BMI). But, overall, these variants explain less than 3 percent of variation in BMI. There are lots of other factors that affect it too, like your lifestyle and diet. This means that we can't predict your personal BMI but we can predict the pattern for Children of the 90s as a group.

WHAT SHOULD I THINK ABOUT BEFORE I AGREE TO TAKE PART?

Everyone's perception of risk, including genetic risk, is different and depends on individual circumstances. Before agreeing to take part in a recall-by-genotype study, you might want to consider whether, when combined with other information (for example, your own family history), the knowledge that you carry either an increased or decreased risk of disease will be of concern to you. If you think you might be concerned about being invited to a recall-by-genotype study for any reason, you can opt-out of this type of study by contacting us to let us know.

If you have any more questions, not answered here, please get in touch:

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