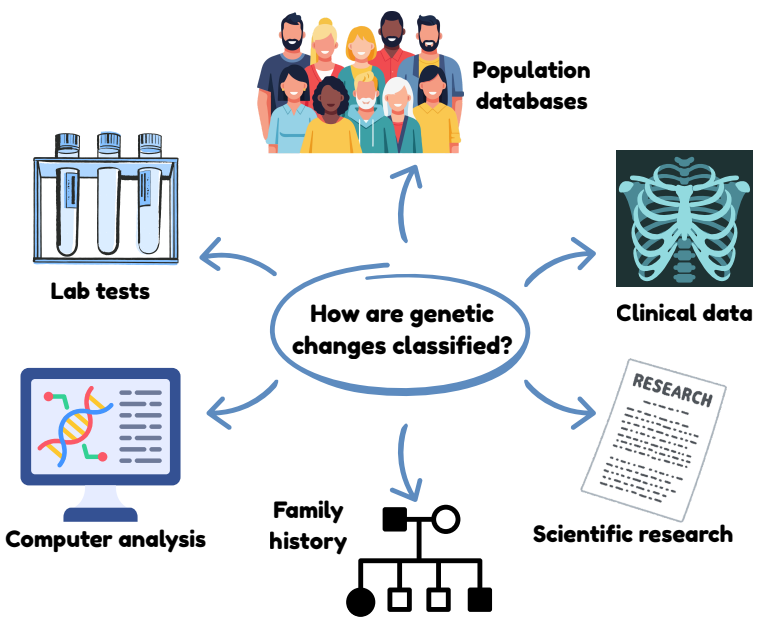
VARIANTS OF UNCERTAIN SIGNIFICANCE

This summarises our information sheet on **Variants of Uncertain Significance (or VUS) in congenital hyperinsulinism (shortened to HI)**. For more on different types of genetic changes, check out our information sheets available from the link here!

HOW DO WE KNOW WHICH GENETIC CHANGES CAUSE A CONDITION?

It is important to understand if a genetic change **causes congenital HI** or is just part of **normal genetic variation**. When a genetic change is found, the laboratory will **review all the evidence** and decide **how likely it is to cause congenital HI.**



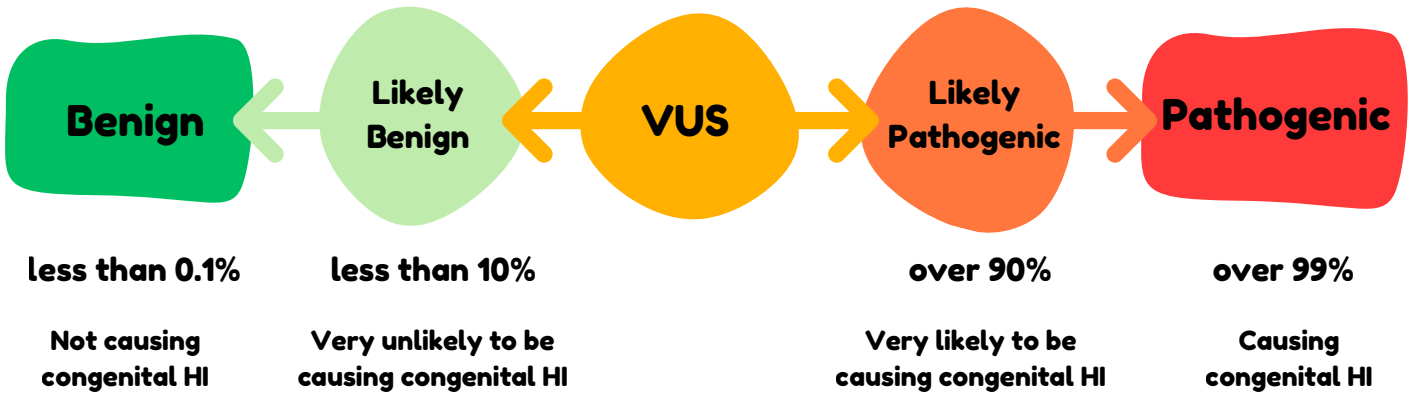
KEY MESSAGES:

- **Genetic changes** are put into **categories** based on **how likely they are to cause a condition**
- When we **don't know** if the genetic change is **causing congenital HI** or if it's part of our **normal genetic variation**, it is called a **Variant of Uncertain Significance** or **VUS**
- A VUS **should not be used to make medical decisions** so your doctor will decide how best to manage the HI **based on your symptoms**
- Some laboratories **may continue to research the VUS** and give an **updated report** once they find enough information, but it is important to **keep talking to your doctor too**
- This means the **VUS could eventually be reclassified** to confirm if **it is or is not the cause of the congenital HI**

- If there is lots of evidence that the genetic change **causes congenital HI**, it will be classified as a **pathogenic or likely pathogenic variant**
- If there is **evidence** that a genetic change is **not a cause of congenital HI** and it is part of our **normal genetic variation** it will be classified as a **benign or likely benign variant**

But sometimes there is **not enough evidence to be confident** that the genetic change causes HI or is part of our normal variation. These are called **Variants of Uncertain Significance** (or **VUS**).

How likely is a variant to cause congenital HI?



WHAT HAPPENS IF I GET A VUS RESULT?

As a VUS is **uncertain**, they **should not be used to make decisions** on treatment or management Instead, your **doctor will decide what the best options** are going forward **based on your symptoms**.

Some laboratories **may continue to research the VUS** and give an **updated report** once they find enough information. This means that the **VUS could be reclassified** and be used to **diagnose or rule out the genetic change as the cause of the congenital HI.** The time it takes for this to happen is different for each VUS and could take up to **months or years.**

HOW OFTEN SHOULD I ASK ABOUT MY GENETIC DIAGNOSIS?

It is good to keep **asking your doctor** if there is any **new information** available that could **change your diagnosis**. Your doctor may also suggest testing other family members which could help them to better understand the VUS.

It's important to remember that it **isn't unusual to have a VUS** on a genetic report, and as we get better at understanding our genes, we hope that there will be **fewer reports with a VUS in the future.**