

VARIANT OF UNCERTAIN SIGNIFICANCE (VUS)

When a genomic (DNA) test does not provide a clear answer



Key points

- When a change in a person's DNA (genetic variant) is identified but it is not known whether the variant is involved in causing the health condition for which the test was done, it is called a **variant of uncertain significance (VUS)**
- Testing other family members may help work out whether the variant caused the health condition



Why was genomic testing done?

Genomic (DNA) tests are performed to work out whether a particular health condition is caused by a change in a person's **genome**. Our genome is found in every cell in our body and is like an instruction manual for our bodies. The 'sentences' in this instruction manual are called **genes**, and each gives a different instruction to the body. Genes work together to tell our bodies how to grow, develop and function.

Changes in our genes are known as **variants**. These may be harmful (pathogenic) or harmless (benign). Every person has thousands of benign variants that do not cause health conditions.

Sometimes having a pathogenic variant in a gene can affect our health, learning or physical development. Health conditions that are caused by variants in genes are called **genetic conditions**.

The results of genomic testing may be positive (i.e. a pathogenic variant is found that causes a health condition) or negative/uninformative (i.e. no pathogenic variant found that is known to cause a health condition). Occasionally a variant of uncertain significance (VUS) is identified.



Will the significance always be uncertain?

The significance of the variant can sometimes be worked out by checking whether other members of the family with or without the same condition also have the variant. Family members would require testing, or permit access to their own genomic testing results. The laboratory may also do further research/testing. In some cases, referral to the local clinical genetics service may be helpful.

Sometimes a clear answer may not be possible even after further testing. As technology improves and more is known about the identified gene, the role of the variant in the health condition may become clearer. The VUS may then be re-classified as either pathogenic or benign. It may also be possible to re-analyse the genomic data again in the future.

When a change in a gene (variant) is found but it is not known whether the variant is involved in causing the health condition for which the test was done, it is called a **variant of uncertain significance (VUS)**

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What happens now?

We recommend that you keep in touch with your managing doctor to revisit this again in the future, especially if you are planning to have a baby, and/or a genetic diagnosis may be helpful to you. You may also wish to be referred to a clinical genetics service if you are not already in touch with one.

The genetic health professionals at a clinical genetics service can provide further information, advice and support, including genetic counselling. Details of local clinical genetics services can be found at the NSW Centre for Genetic Education.

Sometimes it is possible to participate in research studies or patient registries. More information about these may be available from the support services below or the doctor who ordered the test for you.



Support

- Genetic Alliance Australia
- Syndromes Without a Name (SWAN)
- Rare Voices Australia

To print more copies of this fact sheet and access links to the underlined topics, go to www.genetics.edu.au/VUS

This fact sheet should not replace a consultation with a specialist healthcare professional.