

Return Results

Negative and/or VUS results

Understanding what these genetic test results mean and exploring next steps

- Even when genetic testing is negative, genetic factors may still contribute to autism and other neurodevelopmental conditions. Many cases involve a complex interaction between genetic and environmental factors. A helpful counselling tool is the **"Jar Model"** of multifactorial inheritance developed by **Dr. Jehannine Austin's team**: [Figure - PMC \(nih.gov\)](#)[1]
- **A Variant of Uncertain Significance (VUS)** is a genetic change for which there is insufficient or conflicting evidence to determine whether it is associated with disease. A VUS may or may not be related to the patient's phenotype and should not be used to guide medical management. Its classification may change over time and should be periodically re-evaluated.
- **For either a negative or VUS result**, discussion with the family should convey **that no genetic diagnosis has been made by tests performed**, however this **can not rule out all possible genetic conditions**. For example, most single-gene disorders would not be detected by chromosomal microarray.
- **Consider referral to genetic services** for coordination of further testing if any of the below criteria are met.
 - **Multi-system involvement** (e.g. presence of congenital anomalies or significant physical health concerns)
 - **Multiple family members similarly affected**
 - **Parents of the affected individual are consanguineous** (related by blood)
 - **Family is highly interested in pursuing further testing** (e.g. for reproductive risk assessment for other family members) and patient has moderate to severe functional impact

Letter / Consult Note Template for Return of Negative Results

Template is written to be saved as a **Connect Care smart phrase**. Please feel free to adapt and modify to suit your practice. This letter is to summarize genetic testing completed to date for @NAME@. Genetic testing was offered due to their diagnosis of *** and these investigations have now been completed. The results of genetic testing completed for @FNAME@ are summarized below:

- **Chromosomal Microarray**: No clinically significant gains or losses identified.

We discussed that these results **greatly reduce the likelihood of a genetic diagnosis** for @FNAME@ but **cannot rule out a genetic cause beyond the detection limits of available testing**. In the absence of a genetic diagnosis, *** (diagnosis) is thought to be of **multifactorial etiology**. Multifactorial disorders result from an interaction of several genes with environmental factors. Recurrence risks are estimated from empiric evidence as well as the number of affected individuals in the family, and how they are related. **Management should continue to be based on @FNAME@'s presenting symptoms**.

Letter / Consult Note Template for Return of VUS Results

Template is written to be saved as a **Connect Care smart phrase**. Please feel free to adapt and modify to suit your practice. This letter is to summarize genetic testing completed to date for @NAME@. Genetic testing was offered due to their diagnosis of *** and these investigations have now been completed. The results of genetic testing completed for @FNAME@ are summarized below:

- **Chromosomal Microarray:** A VUS, namely _____, was identified that has not been previously described in literature. The **clinical significance of this copy number variant is unknown** at this time, **does not alter immediate medical management. Re-evaluation of this finding with ordering laboratory is recommended every two years.**

We discussed that these results **greatly reduce the likelihood of a genetic diagnosis** for @FNAME@ but **cannot rule out a genetic cause beyond the detection limits of available testing**. In the absence of a genetic diagnosis, *** (diagnosis) is thought to be of **multifactorial etiology**. Multifactorial disorders result from an interaction of several genes with environmental factors. Recurrence risks are estimated from empiric evidence as well as the number of affected individuals in the family, and how they are related. **Management should continue to be based on @FNAME@'s presenting symptoms.**

Return of Pathogenic Results

- A "pathogenic" or "likely pathogenic" result means a genetic change was found that is medically relevant, and could impact a person's health or development.
- This result might provide an explanation for symptoms your patient already has, and it may be associated with other health problems.
- The lab report will provide some information about the genetic change found. Some genetic conditions are well studied with large amounts of information available about symptoms, progression, and management. Some genetic conditions are extremely rare or newly discovered, and less information may be available.
- Share the result with your patient, and let them know that they will be referred to a genetics specialist to review these results in more detail.