Genomics Education Programme

NHS
Health Education England

Returning results from the 100,000 Genomes Project: Rare Disease

Introduction

This document describes general guidance regarding the return of 'primary' results from the 100,000 Genomes Project that are of relevance to the participant's clinical presentation. It does not cover the return of results for 'additional looked-for findings'.

The document offers some general guidance, including advice from those participants who are taking part in the project, and should not replace your own clinical judgement.

SEE PAGE 2...
... for advice from participants on how best to deliver feedback

Does the participant now have a genetic diagnosis?

YES

What to do next for the participant and family?

In the report summary, it will state 'consistent with a genetic diagnosis of xxx' or 'genetic diagnosis of xxx'. In the technical section of the report, the variant will be classified as 'pathogenic' or 'likely pathogenic'.

What does this mean for the participant?
Further information about what this result means for the participant and their family may be included in the report. Further details about the condition may also be found at Genetics Home Reference: bit.ly/GenHomeRef, and Gene Reviews: bit.ly/GeneRev.

What to do now for the participant:

- Outline and explain the results and give the participant a copy of the report. Explain that results will be shared, with their consent, with other healthcare professionals, such as their GP.
- Determine management for the condition, make appropriate referrals and discuss the course of action with the participant and their family.
- Consider referral to Clinical Genetics for further discussion regarding the condition and/or to provide genetic counselling if appropriate.
- Provide information on patient support groups available for the condition. See the Genetic Alliance UK website: bit.ly/GenAllUK

What to do for the family:

- The results may be relevant for other family members, and the participant may need to share them with siblings, parents and other relatives.
- Ask about plans to extend the family. If anyone in the family plans to have children, consider a referral for genetic counselling.
- Consider whether anyone else in the family should be offered, or referred to Clinical Genetics for, genetic testing to determine affected, at-risk, or carrier status.
- Families where there are complex communication or social issues may need a referral for genetic counselling to help them manage the diagnosis within the family.

What is the inheritance pattern of the condition?
Terminology used in the report will indicate the inheritance pattern of the condition. See the Genomics Education Programme website for more information.

Dominant: described as a 'heterozygous pathogenic / likely pathogenic variant'.

Recessive: described as a 'homozygous pathogenic / likely pathogenic variant', or two 'compound heterozygous pathogenic / likely pathogenic variants'.

Variant on the X chromosome: described as a 'heterozygous pathogenic / likely pathogenic variant' in females, or a 'hemizygous pathogenic / likely pathogenic variant' in males.

De novo: described as '*de novo* in this participant', meaning the variant was not detected in the parents, but may have implications for the participant's existing and future siblings and children.

To find out more, visit
www.genomicseducation.hee.nhs.uk

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Does the participant now have a genetic diagnosis? cont.

UNCERTAIN — Is there further testing that should be done?

Results can be uncertain for different reasons. For example, a variant was detected, but there is not enough evidence to classify it as pathogenic / likely pathogenic. The result could also just be part of normal genetic variation in the population and not relevant to the participant's diagnosis.

Follow-up testing may be requested from relatives to clarify the results. There may also be a need for further clinical assessment, tests or information about the family history. Any actions that need to be taken will be outlined in the report. As with all outcomes, it is important to discuss the result with the participant.

NO — Should there be further follow-up?

If the result is negative:

A 'negative' test report does not mean the participant doesn't have a genetic condition. It just means that a (likely) pathogenic variant, or pair of variants for recessive disorders, has not yet been identified.

Reasons that a genomic test can be 'negative' include:

- The participant does not have one of the (likely) pathogenic variants in the gene(s) that were included in the virtual gene panel. However, there may be other genes or areas of the genome associated with the participant's condition that have not yet been included in the virtual gene panel.
- The (likely) pathogenic variant, or variant pair, was not detected by the current technology.
- The clinical information used to determine the appropriate analysis didn't include all the relevant information.
- Not all causative genes linked to this condition have been identified yet.
- The basis for the disease or condition is not genetic.

What to do if no variants were reported?

- Follow any actions outlined in the clinical report.
- Remind the participant and their family that their data will be held for research in the future (unless they opt out), and that if research identifies any relevant new information, they will be informed.
- **Remember:** Negative results are as important for the participant and their family as any other type of result, and should be handled with as much care and sensitivity as a 'positive' result.

BOTTOM LINE

- Follow any 'to do' actions that may be in the report.
- Contact the laboratory or Clinical Genetics if you have any queries.
- Provide an opportunity for discussion and questions from the participant and their family, both during and after the appointment.
- If in doubt, contact Clinical Genetics to advise whether a referral is indicated.
- With consent, provide the result to other clinicians involved in the participant's care, such as their GP.

ADVICE FROM PARTICIPANTS AND THEIR FAMILIES

Before contacting individuals about their results, please consider this advice from participants in the 100,000 Genomes Project.

Many participants and families have waited years for results. As such, the delivery of a result, whether positive or negative, may be a highly emotional time.

1. If possible, participants appreciate an initial call/ letter to let them know results are available, prior to receiving results. This allows time to prepare and consider any questions they may have. Be mindful that the time between initial contact and appointment should not be excessively long, as this could lead to increased anxiety. Please also be mindful when letters are posted, for example not arriving on a day when clinical departments are closed (and therefore unavailable for contact).
2. If telephoning, be mindful that the participant may not be able to speak freely. They may want to ensure they are in a quiet location, with time to ask any questions.
3. Please provide a named person that the participant can contact if they have any further questions. This should be someone in their clinical team who can support individuals after they receive their results. Be mindful that time is often needed for information to be understood and initial emotion to ease.

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