



Tips for clinicians after ordering an Expanded Carrier Screening panel

NEGATIVE RESULTS

A Negative result: No clinically significant variants were identified. This is reassuring. Your patient is not a carrier of any of the conditions on the panel.

But remember, an expanded carrier screening panel does not screen for all genetic conditions. There is no test to guarantee a healthy baby.

Be sure that, in addition to the panel, your patient is also appropriately offered screening based on their ethnicity (e.g. alpha-thalassemia is not typically on expanded carrier screening panels, but is a condition for which certain ethnic populations have a higher carrier frequency) and their family history. See GECKO for Reproductive Genetic Carrier Screening in Canada point of care tools.

POSITIVE RESULTS

When screening for over 100 disorders, you are likely to receive at least one positive result. About 24-29% of individuals will be identified as a carrier of at least one disorder when screened by an expanded carrier screening panel.

A Positive result:

A) Your patient is found to be a **carrier** of one or more recessive genetic disorders:

There are usually no screening or medical management recommendations for an individual who is a carrier of a recessive condition as they are expected to be otherwise healthy. However, carrier status of recessive conditions is an important consideration for couples who are planning their family.

If your patient or patient's partner is pregnant or planning to become pregnant, consider suggesting your patient's partner have the same carrier screening panel. If both members of the couple are carriers of the same recessive disorder, consider offering referral for genetic counselling.

Remember:

- Family history-based risk assessment is still the gold standard in the initial assessment for heritable conditions.
- Genetic counselling is offered by many private genetic testing companies. Your patient may wish to have genetic counselling from the company where they purchased testing. This may require payment of an additional fee. Counselling should be provided by a board certified genetic counsellor (designated as Certified Genetic Counselor (CGC) or Canadian Certified Genetic Counsellor (CCGC)).
- Your patient inherited their carrier state(s) from one of their parents, who will also be a carrier of the recessive condition(s). Your patient's siblings are also at a 50% risk to be a carrier of the same recessive condition(s). You may wish to advise your patient to share this information with her/his adult family members.

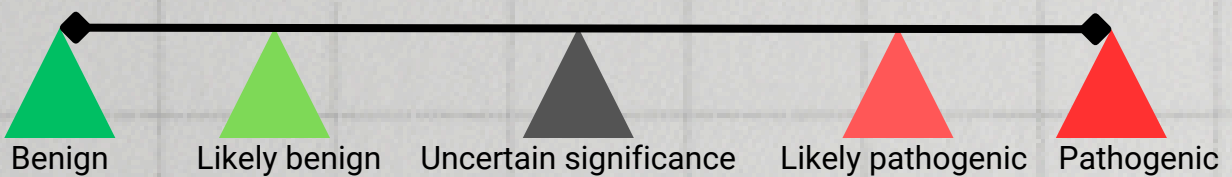
B) Your patient is found to have **one or more pathogenic genetic variants which may have health implications** e.g. familial hypercholesterolemia, hereditary hemochromatosis:

Consider appropriate screening, treatment, or offering referral to an appropriate specialist (e.g. geneticist, lipid specialist, hematologist).

VARIANT OF UNCERTAIN SIGNIFICANCE

A Variant of Uncertain Significance (VUS) result:

Most expanded carrier screening panels use next-generation sequencing to analyze patient samples. This testing method improves sensitivity of testing across ethnicities, however is limited in detecting some types of pathogenic genetic variants. NGS utilizes the human genome as a reference and compares that to a given patient sample to identify variation. Variations are then classified based on guidelines into one of five categories (below). More on genetic test results can be found here.



- Benign or likely benign variants are most often not reported (a negative test result).
- Pathogenic and likely pathogenic variants are known to or expected to cause disease by disrupting gene function (positive test result).
- A variant of uncertain significance (VUS) is a genetic variation that has not yet been classified as either benign or pathogenic. Variant interpretation is challenging. While most laboratories use standardized guidelines there is variability in which tools are used for interpretation. Additionally, as more information about the human genome is discovered, variants will be reclassified. Some laboratories will re-contact the ordering provider with this new information and some leave the onus on the provider and/or patient to seek out new information.

Follow-up on a reported VUS is generally case-by-case. Factors that may be considered are the gene, the disorder, family history, additional literature review, clinical interpretation. Consultation with a genetics specialist may be required. *Note that not every laboratory will report on VUSs.*