Genetic Insights: quick reference guide for healthcare providers

This guide is intended to facilitate a discussion between a provider and their patient.

Genetic Insights test results: **Familial hypercholesterolemia**

Key results

A pathogenic or likely pathogenic variant associated with familial hypercholesterolemia was found in the *PCSK9* gene.

People with familial hypercholesterolemia have very high levels of LDL cholesterol which leads to an increased risk of cardiovascular disease.

Next steps

Clinical recommendations	Resources
Genetic Insights is a screening test and not intended for diagnosis. *A cholesterol test to check for elevated LDL and total cholesterol levels for correlation of this result is indicated.* *Follow-up genetic testing may also be indicated if medical management would be impacted.*	**Ready to order?** Check with your institution and/or patient's insurance about the preferred testing laboratory. Quest Diagnostics® offers cholesterol testing through your EHR or from the Quest online Test Directory Blueprint Genetics® offers familial hypercholesterolemia genetic testing. To confirm this test result, targeted variant testing for the variant identified is available. You can order a confirmation test here: **Blueprint Genetics/TVT** **Have questions?** Call **1.866.GENE.INFO** (1.866.436.3463) to speak to a specialized Quest genetic counselor or geneticist available to healthcare providers to discuss test selection and results.
Refer your patient to a genetic counselor specializing in familial hypercholesterolemia. *Genetic counselors can provide counseling on the implications of this test result and next steps for your patient.*	Your patient can schedule a 1-on-1 remote genetic counseling session through their online Genetic Insights Familial Hypercholesterolemia Report at no additional cost. To find a genetic counselor with expertise in familial hypercholesterolemia practicing in your patient's area for an in-person session, please visit FindAGeneticCounselor.NSGC.org

Patient conversation starters:

Patient conversation starters summarize the preceding information in plain language to support meaningful conversations between you and your patient.

FindAGeneticCounselor.NSGC.org

Your Genetic Insights test is a screening test. The next step is to confirm your result with a second test, such as a cholesterol test to see if your cholesterol level is high.

It's also important that you talk with a genetic counselor. Genetic counselors are experts in genetics and can help you understand this result and potential next steps.

You can access a genetic counselor through your Genetic Insights dashboard at no additional cost to you, and we can discuss a referral to a local genetic counselor.

Visit QuestDiagnostics.com/Genetic-Health-Screening for more information about this test.

What is familial hypercholesterolemia?

Familial hypercholesterolemia (FH) is a genetic condition characterized by LDL-C cholesterol levels typically above 190 mg/dL and/or total cholesterol greater than 310 mg/dL.[1,2] This is associated with an increased risk for premature coronary artery disease and heart attack.[1,2]

Males with FH who are untreated have about a 50% risk for a coronary event by age 50. Females with untreated FH are at a 30% risk for the same by age 60.[2]

Treatment is based on LDL cholesterol levels including aggressive pharmacological management.[1,2]

See the Management options section for more detail.

Patient conversation starters:

Familial hypercholesterolemia (called FH for short) causes very high levels of the form of cholesterol called LDL cholesterol. Left untreated, these high levels increase the chance of having a heart attack or other serious heart problems.

Most of the time for people with FH, diet and lifestyle changes are not enough to lower cholesterol levels. Most people need to take medication to help stay healthy.

What this result means for family members

Family members may have the same DNA variant. The DNA variant was most likely inherited from a parent.

Full siblings and children have a 50% chance of having this variant.

In people with a confirmed DNA variant associated with FH, cascade genetic testing for other family members may help inform their risks and screening protocols.

A genetic counselor can help determine the most appropriate testing options. Therefore, it is strongly recommended that people share their results with their biological relatives.

Patient conversation starters:

FH runs in families.

That means the DNA variants that cause FH can be inherited or passed down from parents to their children. Your close relatives—like your parents, full siblings, and children—have a 50% (or 1 in 2) chance of having the same DNA variant.

Other relatives might also have the same DNA variant.

Sharing these results with your family is important so family members can decide if they want to have genetic testing for FH.

Management options

There are options for management for people with FH. Clinical guidelines from the American Heart Association[1] include:

For adults with FH

For individuals with increased cholesterol, high-intensity statin therapy to achieve LDL cholesterol reduction of greater than or equal to 50% is critical

Individuals with FH require treatment of associated cardiovascular risk factors, including obesity, hypertension, diabetes mellitus, and tobacco use

Cascade lipid screening of first-degree relatives should be offered; genetic testing for a known familial DNA variant associated with FH can clarify the necessity for accelerated screening recommendations

Other clinical, treatment, and management considerations are required for:

- Children
- Women of childbearing age or who are pregnant
- Individuals nonresponsive to statins or where statins are contraindicated
- Individuals who may be candidates for LDL apheresis

Patient conversation starters:

People with FH need to get the right treatment. Most of the time, people with FH need to take medication to lower their cholesterol levels and help prevent a heart attack. It's important to work with the right FH specialist to make a treatment plan.

Refer to current guidelines for complete recommendations. Guidelines and recommendations may change over time.
Local centers for excellence in FH should be consulted for further clinical management. Search the FH Foundation's website and locate a specialist for your patient.

Additional resources

The following advocacy groups have additional information and resources about FH:

The FH Foundation: TheFHFoundation.org
The American Heart Association: Heart.org

References

1. Gidding SS, Champagne MA, et al. The Agenda for Familial Hypercholesterolemia: A Scientific Statement From the American Heart Association. *Circulation.* 2015;132(22):2167-2192. https://www.ncbi.nlm.nih.gov/pubmed/26510694
2. Ison HE, Clarke SL, Knowles JW. Familial Hypercholesterolemia. January 2, 2014. Updated July 7, 2022. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews®. University of Washington, Seattle; 1993-2023. https://www.ncbi.nlm.nih.gov/books/NBK174884