Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is a genetic condition associated with very high levels of cholesterol in the blood, specifically low-density lipoprotein (LDL), or "bad" cholesterol. High cholesterol due to FH increases the risk for early cardiovascular disease, which can lead to a heart attack. This test includes 24 genetic variants linked to FH.

Overview Scientific Details Frequently Asked Questions

Jamie, you have **one** of the genetic variants we tested linked to FH.

People with this result have an increased risk of having very high LDL cholesterol levels related to FH, which can lead to early heart disease if not appropriately treated.

Please share your result with a healthcare professional, such as a cardiologist or lipid specialist. It is important to discuss cholesterol screening and management.

How To Use This Test

This test does not diagnose familial hypercholesterolemia or any other health conditions.

Please talk to a healthcare professional if this condition runs in your family, you think you might have this condition, or you have any concerns about your results.

Review the Genetic Health Risk tutorial
See Scientific Details
See Frequently Asked Questions

Intended Uses

- Tests for one variant in the APOB gene and 23 variants in the LDLR gene. These variants are linked to having very high LDL cholesterol levels, which is associated with an increased risk for heart disease.

Limitations

- Does **not** test for all possible variants in the APOB and LDLR genes. More than 1,000 variants in these genes are linked to FH. Only 24 of those variants are included in this test.
- Does **not** test for variants in other genes linked to FH and other forms of inherited high cholesterol.
- Does **not** report if someone has two copies of a tested variant.

Ethnicity Considerations

- The majority of the variants included in this test are most commonly found in people of **European** and **Lebanese** descent, as well as in the **Old Order Amish**. In addition, some of these variants have also been found in other ethnicities.
- However, more than 1,000 variants have been linked to FH in people of European descent, as well as in people of other ethnicities. This test does not include the majority of those variants.

You are at **increased risk** of having very high LDL cholesterol related to FH based on your genetic result.

It is important to talk with a healthcare professional, such as a cardiologist or a lipid specialist, about cholesterol screening and management.

We detected the R3527Q variant in the APOB gene.

See Scientific Details

Most people with this variant are likely to have elevated LDL cholesterol levels.

High LDL cholesterol related to FH is associated with an increased risk for early heart disease. Overall heart disease risk is also influenced by family history and other factors.

See Scientific Details

Since you share DNA with your family members, they may also be interested in this result.

Your parents, siblings, and children each have a 50% chance of having the variant we detected. Genetic counselors can help your adult family members decide about genetic testing.

Lifestyle and other factors can also influence the chances of developing heart disease.

Consult with a healthcare professional before making any major lifestyle changes.

Family history

Parents, siblings, and children of an individual with early heart disease (younger than 55 years in men and younger than 65 years in women) have a higher chance of developing heart disease themselves.

See Scientific Details for more information

Family history
Age
High blood pressure
Smoking
Other genetic factors
Lifestyle

About Familial Hypercholesterolemia

Also known as: FH, familial hypercholesterolæmia, autosomal dominant hypercholesterolemia, hyperlipoproteinemia type IIA

When it develops

Because it is a genetic condition, FH is present at birth, meaning most people with this condition have high LDL cholesterol levels from a young age. Since many people with FH show no physical symptoms, this condition is typically diagnosed with a blood test for cholesterol. However, some people with FH may not be diagnosed until after experiencing symptoms related to early heart disease, including chest pain or heart attack.

Typical signs and symptoms

- Elevated total and LDL cholesterol levels
- Heart disease, heart attack, or chest pain
- In some cases, cholesterol deposits may build up in the skin or tendons (xanthomas), under the skin in the eyelids (xanthelasmas), or around the cornea of the eye (corneal arcus)

How common is this condition?

FH affects people of all ethnicities. About 1 in 200 to 1 in 250 people in the world have FH.

How it's treated

Early and active treatment of FH can substantially reduce the risk for heart disease. FH treatment focuses on lowering LDL cholesterol levels, and FH is usually treated with cholesterol-lowering medications. Lifestyle modifications, including diet, exercise, and weight control can help lower LDL cholesterol levels. But these changes are generally not enough to effectively manage the condition. In extreme cases of FH, LDL-apheresis, a procedure that filters cholesterol out of the blood, can be used when other treatments have failed.

Read more at: National Human Genome Research Institute* GeneReviews* MedlinePlus* Family Heart Foundation*

It is important to discuss this result with a healthcare professional.

Consult with a healthcare professional, such as a cardiologist or a lipid specialist, about cholesterol screening and management, and to discuss other heart disease risk factors.

Print report

If you have questions about your results or how they might affect you or your family, a genetic counselor may be able to help.

Learn more

See our Frequently Asked Questions for more information.

FAQs

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Print

Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is a genetic condition associated with very high levels of cholesterol in the blood, specifically low-density lipoprotein (LDL), or "bad" cholesterol. This condition increases the risk for early cardiovascular disease, which can lead to a heart attack. This test includes 24 genetic variants linked to FH.

Overview | Scientific Details | Frequently Asked Questions

FH is linked to variants in multiple genes.

This report includes one variant in the APOB gene and 23 variants in the LDLR gene.

APOB | LDLR

The APOB gene provides instructions for making a protein called apolipoprotein B. This protein helps LDL cholesterol bind to LDL receptors on the surface of cells, particularly in the liver. Certain variants in this gene reduce the ability of LDL cholesterol to bind to its receptor, causing fewer LDL cholesterol particles to be removed from the blood.

Read more at Genetics Home Reference

You have one of the genetic variants we tested.

Variants Detected | View All Tested Markers

Marker Tested	Genotype*		Additional Information
R3527Q **Gene:** APOB **Marker:** **rs5742904**	**C** Typical copy from one of your parents	**T** Variant copy from your other parent	**Biological explanation** **Typical vs. variant DNA sequence(s)** **Percent of 23andMe customers with variant** **References [2, 15, 47, 165, 168]	Clinvar**

This test cannot distinguish which copy you received from which parent. This test also cannot determine whether multiple variants, if detected, were inherited from only one parent or from both parents. This may impact how these variants are passed down.

23andMe always reports genotypes based on the 'positive' strand of the human genome reference sequence (build 37). Other sources sometimes report genotypes using the opposite strand.

Test Interpretation

This report provides risk estimates for heart disease based on LDL cholesterol levels and the presence or absence of variants linked to FH. In most cases, these estimates represent a general risk for individuals with any variant linked to FH, not specific risk estimates associated with the 24 variants in this report.

For reference, LDL cholesterol ranges for adults are provided based on the classification by the National Heart, Lung, and Blood Institute.

Health Risk Estimates

Risk estimates are based on clinical studies that identify an association between a genotype and a health condition.

Numerical risk estimates are not available for people who have more than one variant linked to FH. An interpretation of "increased risk" is provided to people with these results, because it is likely that their risk is at least as high as the risk for people with just one variant.

Consider talking to a healthcare professional if you have any concerns about your results.

References [64, 80, 126]

Odds ratios | Likelihood ratios | LDL cholesterol ranges

An "odds ratio" estimates how strongly a genetic variant is associated with a condition. An odds ratio greater than 1 means that people with that variant are more likely to develop the condition, while an odds ratio less than 1 means that people with that variant are less likely to develop the condition, compared to people without the variant.

The table below shows the odds ratios for heart disease based on LDL cholesterol levels and the presence or absence of variants linked to FH.

LDL cholesterol level (mg/dL)	Without FH variant	With FH variant
<138	1	2.2
≥138-169	1.8	3.8
≥169-199	2.9	5.6
≥199-229	5.2	17.9
≥229	7.7	25.8

Other Factors

Many factors are known to influence the chances of developing heart disease. In general, people with variants linked to FH cannot remove cholesterol from the body properly and will likely need medical management to lower cholesterol levels and to reduce the risk for heart disease. With early treatment of FH, the risk for heart disease may be reduced to levels similar to that of the general population. However, other factors can also add to your risk for heart disease.

This is not a complete list of other factors.

People with multiple risk factors may have a higher chance of developing heart disease. Heart disease risk associated with FH variants varies from person to person. Overall risk depends on family history and other factors.

Keep in mind that in general, a healthy lifestyle (eating a healthy diet, maintaining a healthy weight, and exercising regularly) has been associated with many health benefits.

Consult with a healthcare professional before making any major lifestyle changes.

Other Factors	References
Family history People with a variant linked to FH also have had a first-degree relative (with early heart disease (younger than 55 years in men and younger than 65 years in women) have a higher chance of developing heart disease themselves. This may be primarily explained by genetic factors, but could also be explained by family members sharing a similar lifestyle and environment.	[23, 47, 67, 182, 133]
Age In general, the risk for heart disease increases as a person gets older. With age, blood vessels become less flexible, which can impede blood flow to the heart. Also, deposits called plaques can build up over time along blood vessels and restrict blood flow to the heart. Men with a variant linked to FH who are 39 years or older and women with a variant linked to FH who are 45 years or older, or postmenopausal, have an even greater risk of developing heart disease. Individuals with unrelated FH who have two variants linked to FH have an increased risk of developing heart disease before 29 years of age.	[23, 38, 65, 67, 190]
Smoking Smoking increases the risk for heart disease, especially in people with a variant linked to FH. The chemicals found in tobacco smoke can damage the inner lining of blood vessel walls, increase heart rate, and cause irregularities in the timing of heartbeats, making a person more susceptible to having heart disease. Smoking also interacts with other risk factors for heart disease, including high blood pressure, high cholesterol, and obesity, to increase the risk for heart disease even more. Exposure to secondhand smoke, including smoke from a burning cigarette and smoke exhaled by smokers, also increases the risk for heart disease since it contains many of the same harmful substances found in the smoke inhaled by smokers.	[7, 23, 133, 134]
Sex Men are generally at higher risk than women for developing heart disease earlier in life, but women's risk increases after menopause. Certain risk factors around the time of menopause, including weight gain and high blood pressure, increase a woman's risk for heart disease.	[7, 23, 65, 81, 87, 190]
High blood pressure Chronic high blood pressure increases the risk for heart disease. High blood pressure puts excess strain and increased workload on the heart and blood vessels, which can damage them over time. Damaged blood vessels are more vulnerable to plaque deposits, which can limit blood flow to the heart. This can lead to chest pain or heart attack.	[23, 45, 58, 65, 190, 188, 133, 134]
Diet In general, a diet high in saturated fat, trans fat, dietary cholesterol, and added sugars is associated with increased heart disease risk. In contrast, studies have found foods rich in soluble fiber such as fruits, vegetables, and legumes are associated with reduced heart disease risk.	[35, 41, 45, 59, 63, 133, 134]
Physical activity In general, being physically active can help reduce the risk for heart disease by lowering a person's LDL cholesterol levels and blood pressure. Current U.S. guidelines recommend that adults should get at least 150 minutes a week of moderate-intensity activity or 75 minutes a week of vigorous-intensity activity for a healthier life. Learn more from the **American Heart Association**	[5, 35, 45, 59, 63, 121, 133, 134]
Obesity In general, being overweight increases a person's risk of developing heart disease. In addition, excess weight typically worsens other risk factors for heart disease, including high blood pressure and diabetes.	[36, 45, 58, 63, 190, 133, 134]
Other genetic factors Other genetic variants may influence heart disease risk in people with a variant linked to FH. In combination, these other variants may increase or decrease a person's risk for heart disease compared to the people with a variant linked to FH. Scientists are still working to understand how these other variants modify heart disease risk.	[97]
Diabetes Having diabetes, especially type 2 diabetes, increases a person's risk for heart disease. The risk is greater in women than in men. High blood sugar can damage blood vessels, so it is important to control blood sugar levels and manage other modifiable risk factors, such as obesity and physical activity, to minimize risk for heart disease.	[23, 36, 58, 62, 65, 96, 186, 133, 134]
High lipoprotein(a) levels Lipoprotein(a), also called Lp(a), is a lipoprotein similar to LDL. High Lp(a) in the blood is associated with an increased risk for heart disease. Lp(a) may deposit in blood vessels and contribute to plaque buildup, which may reduce blood supply to the heart. Lp(a) levels are primarily determined by inherited genetic factors.	[4, 19, 23, 65, 108]

Cholesterol Screening and FH Management Guidelines

Cholesterol screening and FH management can help reduce your risk for heart disease. The guidelines below may help you and your doctor create a screening plan that's right for you.

Current U.S. guidelines recommend that everyone should get their cholesterol levels measured. People with a variant linked to FH should talk to their healthcare provider, a cardiologist, or a lipid specialist as early as possible about ways to reduce cholesterol levels, including lifestyle modifications and therapeutic management of cholesterol levels. Additionally, other heart disease risk factors, including lipoprotein(a) and family or personal history of heart disease, should be assessed. Women who are pregnant or are considering pregnancy are recommended to ask their healthcare provider about how to best control their cholesterol before and during pregnancy. Learn more from the **National Lipid Association**

The guidelines above cover screening recommendations for people with a variant linked to FH. Note that guidelines from different healthcare professional organizations may differ slightly in their recommendations.

Test Details

Indications for Use

The 23andME PGS Genetic Health Risk Report for Familial Hypercholesterolemia is indicated for reporting of one variant in the APOB gene and 23 variants in the LDLR gene. This report describes if a person's genetic result is associated with an increased risk of having high LDL cholesterol, which can lead to heart disease. This test does not describe a person's overall risk of developing heart disease, and the absence of a variant tested does not rule out the presence of other variants that may be linked to familial hypercholesterolemia. The majority of the variants in this report are found in and have been most studied in people of European and Lebanese descent, as well as in the Old Order Amish.

Special Considerations

- Genetic testing for FH in the general population is not currently recommended by any healthcare professional organizations.
- However, the U.S. CDC recommends that screening using cholesterol testing with or without DNA analysis should be conducted on relatives of people with familial high cholesterol.
- Heart disease risk associated with FH variants varies from person to person. Overall risk depends on family history and other factors.

Test Performance Summary

Clinical Performance [1, 2, 10, 13, 21, 49, 52, 64, 78, 82, 105, 117, 122, 127]

The variants included in this report represent a small subset of all those linked to FH. Over 1,990 variants have been linked to FH. The 24 variants included in this test are linked to having very high LDL cholesterol, which is associated with an increased risk for heart disease. About 1 in 58 people with high LDL cholesterol have FH.

- Approximately 39-35% of people of European descent with a genetic variant linked to FH have one of the 24 variants included in this test.
- Approximately 15-28% of people of Hispanic/Latino or East Asian descent with a genetic variant linked to FH have one of the 24 variants included in this test.
- For people of Lebanese descent, the test covers about 89% of people who have a variant linked to FH.
- About 16% of the Old Order Amish have the APOB R3527Q variant linked to FH.

Analytical Performance

Accuracy was determined by comparing results from this test with results from sequencing. Greater than 99% of test results were correct. While unlikely, this test may provide false positive or false negative results. For more details on the analytical performance of this test, refer to the package insert.

Warnings and Limitations

- This test does not cover all variants that could cause this condition.* The absence of a variant tested does not rule out the presence of other genetic variants that are linked to FH.
- This test does not diagnose any health conditions.
- Share results with your healthcare professional for any medical purposes.
- If you are concerned about your results, consult with a healthcare professional.

See the **Package Insert** for more details on use and performance of this test.

* Variants not included in this test may be very rare, may not be available on our genotyping platform, or may not pass our testing standards.

References

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4. **Alonso R et al. (2014). "Lipoprotein(a) levels in familial hypercholesterolemia: an important predictor of cardiovascular disease independent of the type of LDL receptor mutation." J Am Coll Cardiol, 63(19):1982-6.**
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7. **American Heart Association. "Understand Your Risks to Prevent a Heart Attack." Retrieved Nov 30, 2016, from https://www.heart.org/en/health-topics/heart-attack/understand-your-risks-to-prevent-a-heart-attack**
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See all references

Change Log

Your report may occasionally be updated based on new information. This Change Log describes updates and revisions to this report.

Date	Change
Feb. 20, 2019	Familial Hypercholesterolemia report created.

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Familial Hypercholesterolemia

- How is familial hypercholesterolemia (FH) different from typical high cholesterol?
- What does this test do?
- What does this test **not** do?
- The report says the variants included in this test are most common in certain ethnicities. What does that mean?
- Where can I learn more about FH, support groups, and other resources?
- My report says **one variant** was detected. What does this mean?
- What does **increased risk** mean?
- My report says **one variant** was detected. What are some things I could do?
- How could my result affect my family?

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