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 do not have the genetic variants we tested.

However, this test does not include the majority of variants linked to FH, so **you could still have a variant not included in this test**.

If you have a personal or family history of high cholesterol or early heart disease, you should talk to a healthcare professional about cholesterol screening options.

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.

Important Ethnicities

- 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 **do not have** the genetic variants we tested linked to FH.

People without these variants are still at risk for high cholesterol and heart disease due to other factors, including lifestyle, family history, and other genetic factors.

There is still a chance of having a variant linked to FH.

More than 1,000 variants are linked to FH and are known to be associated with very high LDL cholesterol levels. This test only includes 24 of those variants.

See Scientific Details

In the U.S., about 30% of people who are 20 years and older have high LDL cholesterol levels.

Most cases of high LDL cholesterol are not caused by the genetic variants in this report. Your risk is influenced by many other factors, including lifestyle, family history, and other genetic factors.

If you have a personal or family history of high cholesterol or early heart disease, it's important to talk to a healthcare professional about your cholesterol screening options.

A healthcare professional can help you assess your overall heart disease risk. Learn more from the American Heart Association^.

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^

Learn more about FH.

See our Frequently Asked Questions for more information.

FAQs

If you have a personal or family history of high cholesterol or early heart disease, consult with a healthcare professional.

Print report

Learn more about cholesterol screening to help you and your doctor create a screening plan that's right for you.

Learn more

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Familial Hypercholesterolemia

Familial hypercholesterolemia (FH) is a genetic condition associated with very high levels of cholesterol in the blood and increased risk for heart disease. In the US, FH affects about 1 in 250 people and is most common in people who identify as Ashkenazi Jewish, particularly in the Dutch Jewish population, in the Lebanese population, and in the Quebec population. FH is caused by variants in three genes, causing lower LDL cholesterol (particularly in the Lebanese population), causing higher LDL cholesterol (particularly in the Ashkenazi Jewish population).

Read more at Genetic Home Reference!

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-100. This protein plays a crucial role in the body's ability to take up, process, and distribute fats and cholesterol. It also plays a key role in the process that allows fats to be stored in the body. Mutations in the APOB gene cause familial hypercholesterolemia, causing lower LDL cholesterol (particularly in the Lebanese population).

You do not have the genetic variants we tested.

View All Tested Markers

Variants Detected				
Marker Name	Your Genotype	Allele	Additional Information
rs121912754 Gene: APOB Position: 21152284	A	C	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 76, 87], 100, 118	Clinvar
c.1706+4A>T Gene: LDLR Position: 21229664	A	T	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 76, 87], 100, 118	Clinvar
R87Q Gene: LDLR Position: 21229665	T	T	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 40-44, 71, 77, 79, 114, 119, 125, 127	Clinvar
D98G Gene: LDLR Position: 21229666	A	A	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 27, 53, 73, 74, 93, 127	Clinvar
E181K Gene: LDLR Position: 21229739	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 41, 71-74, 77, 79, 119, 125, 128	Clinvar
G171S Gene: LDLR Position: 21229806	C	C	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 74, 77, 79, 119	Clinvar
C164Y Gene: LDLR Position: 21229869	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 16, 29, 37, 41, 44, 71, 73, 119, 125, 127	Clinvar
G279Ins4 Gene: LDLR Position: 21229882	TGG	TGG	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 16, 29, 37, 44, 71, 73, 125, 127	Clinvar
E224K Gene: LDLR Position: 21229963	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 44, 48, 71, 77, 107, 125, 127	Clinvar
E230G Gene: LDLR Position: 21229965	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 44, 48, 71, 77, 107, 125, 127	Clinvar
S245R Gene: LDLR Position: 21229997	T	T	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 44, 71, 77, 107, 125	Clinvar
G287D Gene: LDLR Position: 21230022	A	A	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 44, 71, 77, 107, 125	Clinvar
C246R Gene: LDLR Position: 21230027	C	C	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 44, 71, 77, 107, 125	Clinvar
G415S Gene: LDLR Position: 21230088	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 44, 71, 77, 107, 125	Clinvar
E490G Gene: LDLR Position: 21230283	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 29, 44, 71, 77, 107, 125	Clinvar
V519M Gene: LDLR Position: 21230478	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 44, 71, 77, 107, 125	Clinvar
D542N Gene: LDLR Position: 21230543	G	G	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 44, 71, 77, 107, 125	Clinvar
W556S Gene: LDLR Position: 21230733	T	T	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 44, 71, 77, 107, 125	Clinvar
G592E Gene: LDLR Position: 21230794	A	A	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 44, 71, 77, 107, 125	Clinvar
W577C Gene: LDLR Position: 21230734	T	T	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 44, 71, 77, 107, 125	Clinvar
C681X Gene: LDLR Position: 21231044	C	C	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 44, 71, 77, 107, 125	Clinvar
P664L Gene: LDLR Position: 21231045	C	C	Typical copy from one parent	• **Biological relationship** • **Typical or rare (RAA sequencing)** • **Percent of (Classified) customers with variant** • **References** [1, 6], 44, 71, 77, 107, 125	Clinvar

This rare variant (genotyped using proprietary technology) has been reported in the literature in individuals affecting the trait or condition, but may also be found in healthy individuals. You may want to keep these versions as a reminder.

23andMe stores raw genetic data for a number of the human genome reference build 37 (hg19) variants genotyped, plus 500 other variants important for quality control and ancestry inference. This report includes all genotyped SNPs in the APOB and LDLR genes, plus other variants in these genes that are known to be associated with Familial Hypercholesterolemia.

Test Interpretation

The genetic variants in this report are linked to FH and associated with an increased risk for heart disease. However, some factors beyond genetics may affect your risk or influence your chances of developing heart disease.

Health Risk Estimates

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

Nonetheless risk estimates are not available for people who have more than one variant linked to the same condition, because there is not enough evidence to provide accurate risk estimates. 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.

Risk Estimates	
Relative Risk	**Lifetime Risk**
2.2	2.2
1.0	3.6
2.9	5.0
5.2	17.8
7.1	25.6

This is not a complete list of other factors.

People with multiple risk factors may have a higher risk of developing heart disease. Consult with a healthcare professional for more information.

Keep in mind that in general, a healthy lifestyle (eating a healthy diet, maintaining a healthy weight, and avoiding tobacco) can help reduce the risk associated with many health conditions.

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

Other Factors

Other Factors	References
Family History First-degree relatives of an individual with early heart disease (younger than 55 years for men and younger than 65 years for women) are at higher risk of developing heart disease sooner. This may primarily apparently be genetic factors, but could also be explained by family members sharing a similar lifestyle.	[39, 87, 97]
Age In general, the risk for heart disease increases as a person gets older. With this a clinical research study from Framingham Heart Study, which is a long-term study of factors that increase your risk for heart disease, data, depends called pooled cohorts risk score (ASCVD) estimates that a person who is 40 years old and has a greater risk of developing heart disease than a person who is 20 years old.	[31, 34, 87, 108]
Smoking Smoking increases the risk for heart disease. The chemicals found in tobacco smoke damage the heart and blood vessels. Nicotine raises blood pressure and causes irregularities in the beating of heartbeats, making a person more susceptible to having heart disease. Smoking also interacts with other risk factors to increase the risk for heart disease. Smoking increases blood clotting, to increase the risk for heart disease, and decreases the amount of beneficial cholesterol, including those from a burning cigarette and smoke from other people's cigarettes. Secondhand smoke is a major cause of the same harmful substances found in the smoke inhaled by smokers.	[87, 97, 108, 120]
Sex Men are generally at higher risk that women for developing heart disease. Although women are at increased risk for developing heart disease as they approach the time of menopause. Including weight gain and high blood pressure, increase a woman's risk for heart disease.	[10, 87, 108]
Blood pressure Chronic high blood pressure increases the risk for heart disease. High blood pressure and cholesterol are considered as the heart and blood vessels, which can damage them over time. Damaged blood vessels are more susceptible to blockage and narrowing. Blood pressure, in the long run, can lead to stiff heart or heart attack.	[10, 87, 97, 110, 108, 109, 120, 124]
Diet A diet high in saturated fat (some fat), cholesterol, and added sugars is associated with increased heart disease risk. In contrast, studies have found that a diet high in fruits, vegetables, and legumes are associated with reduced heart disease risk.	[7, 10, 41, 49, 50, 87, 108]
Physical activity In general, being physically active can help reduce the risk for heart disease and improve cardiovascular fitness. Physical activity can improve blood pressure and improve blood sugar, which can lead to heart disease. Regular exercise is a major factor in reducing risk for heart disease. Exercise helps control the risk of developing heart disease.	[7, 10, 41, 49, 87, 123, 124]
Obesity Being overweight increases a person's risk of developing heart disease. In addition, being overweight increases other risk factors for heart disease, including high blood pressure and diabetes.	[38, 108, 87, 109, 124]
Other genetic factors Other genetic factors (more than 1,000 SNPs) linked to FH and associated with an increased risk for heart disease. These variants are in the LDLR and APOB genes, as well as other genes known to increase risk for heart disease. Some of these genes are known to increase risk for heart disease through other mechanisms, such as blood pressure and cholesterol levels. However, most of these variants are other rare or have only a small effect on risk.	[38, 98, 75]
Diabetes Having diabetes, especially type 2 diabetes, increases a person's risk for developing heart disease. Diabetes increases the risk for heart disease by drying from heart disease that people without diabetes. The risk is greater in people who have diabetes and other risk factors for heart disease. People with diabetes are at much higher risk for developing other conditions that affect factors, such as obesity and physical activity, to minimize risk for heart disease.	[7, 10, 50, 52, 70, 124]
High Sensitivity tests Lipoprotein(a), also called Lpa, is a lipoprotein similar to LDL. High Lpa in the blood is associated with an increased risk for heart disease. Lpa may also increase blood clotting and inflammation in the blood vessels, which could lead to the heart. Lpa levels are primarily determined by inherited genetic factors.	[19, 50]

Cardiovascular Disease Risk Assessment and Cholesterol Screening Guidelines

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

The American Heart Association and American College of Cardiology recommend that adults 20 years of age and older, who are free from cardiovascular disease, should have their cholesterol levels checked every 4 to 6 years. Cholesterol screening may be done additionally, guidelines recommend that people should talk to their healthcare provider about heart disease risk factors, such as family history, blood pressure, and lifestyle management. Learn more from the **American Heart Association**.

Consider talking to a doctor if you have a personal or family history of high cholesterol or heart disease. Your doctor may have specific screening recommendations for you.

Note that guidelines from different healthcare professional organizations may differ slightly in their recommendations.

Keep in mind that you could still have a gene or the APOB gene or other genes not included in this report that could affect your risk for heart disease. In that case, different screening and actions may be recommended. Consult with a healthcare professional to learn more.

Test Details

Indications for Use

This genetic test is intended for Genetic Health Risk Assessment for Familial Hypercholesterolemia to indicate for reporting of one gene in the APOB gene and 23 variants in the LDLR gene. The results are intended for use in a genetic counselor or other genetic professional. The genetic result is associated with an increased risk of having very high LDL cholesterol, which can lead to heart disease. The genetic test is not intended to be used as a stand-alone test. The genetic test is not intended to be used as a screening test for the general population. The genetic test is not intended to be used for diagnosis of Familial Hypercholesterolemia. The clinicality of the variants in this report are found in and have been more clinical research and/or clinical practice than other variants, as well as in the LDLR Gene Report.

Gene Specific Considerations

- Genetic testing for FH is first generation population is not currently recommended by any healthcare professional organizations.
- However, the U.S. CDC recommends screening using cholesterol testing with a lipid profile (lipid analysis) should be conducted on relatives of people with Familial Hypercholesterolemia.
- 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, 6, 16, 21, 29, 41, 52, 64, 76, 78, 82, 109, 117, 122, 127]

Data analysis is based on 75 the report genotyped variants in the APOB and LDLR genes. Of these, 23 variants are associated with increased risk for heart disease. Around 1 in 100 people with high LDL cholesterol carry FH.

- Approximately 90-95% of people of European descent with a genetic variant linked to FH have one of the 23 variants included in this test.
- Approximately 70-75% of people of Ashkenazi Jewish ancestry with a genetic variant linked to FH have one of the 23 variants included in this test.
- For people who have a genetic variant linked to FH, people who are not of European descent, or people who are not Ashkenazi Jewish, the 23 variants in this report are not as common.
- About 90% of the Dot 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 our results were correct. While similarly, this test may provide false positive or false negative results. For more details on the analytical performance of this test, refer to the genotyping report.

References

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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. 28, 2017	Familial Hypercholesterolemia report created

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.

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 **zero variants** were detected. What does this mean?

My report says **zero variants** were detected. Does this mean I'm not at risk of having high LDL cholesterol?

My report says **zero variants** were detected, but I have a personal or family history of high cholesterol or early heart disease. What does this mean for me?

My report says **zero variants** were detected. What are some things I could do?

Have more questions? **Check out our Customer Care Help Center.**

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