Hereditary Amyloidosis (TTR-Related)

TTR-related hereditary amyloidosis is a genetic condition caused by the buildup of a protein called transthyretin (TTR) in the body's tissues and organs. This protein buildup, called amyloidosis, can damage the nerves, the heart, and other parts of the body. This test includes three of the most common genetic variants linked to TTR-related hereditary amyloidosis.

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Jamie, you have **one** of the three genetic variants we tested.

People with this variant have an increased risk of developing TTR-related hereditary amyloidosis over their lifetime. Other factors can also affect your risk.

How To Use This Test

This test does not diagnose TTR-related hereditary amyloidosis 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 three variants in the TTR gene linked to TTR-related hereditary amyloidosis.

Limitations

- Does **not** test for all possible variants linked to TTR-related hereditary amyloidosis.
- Does **not** test for variants in other genes linked to hereditary amyloidosis.
- Does **not** report if someone has two copies of the V36M variant or the T69A variant.

Ethnicity Considerations

The variants included in this test are three of the most common variants linked to TTR-related hereditary amyloidosis. Each variant is more common in people of certain ethnicities but can also be found in people of other ethnicities.

- **V122I:** Most common and best studied in **African Americans** and people of **West African** descent.
- **V36M:** Most common and best studied in people of **Portuguese**, **Northern Swedish**, and **Japanese** descent.
- **T69A:** Most common and best studied in people of **Irish** descent and also found in people of **British** descent.

You have an **increased risk** of developing TTR-related hereditary amyloidosis based on your genetic result.

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

We detected one copy of the V122I variant in the TTR gene.

See Scientific Details

People with this variant have an increased risk of developing heart and nerve damage due to TTR-related hereditary amyloidosis.

This heart and nerve damage is caused by the buildup of TTR protein in these organs and tissues. The heart is the most common site of TTR buildup for people with your result, but some people develop buildup of the TTR protein in the nerves and other parts of the body. In addition, symptoms can vary widely between people, and not everyone with this variant will develop symptoms.

See Scientific Details

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

At least one of your parents is also expected to have this variant. In addition, each of your children has a 50% chance of inheriting this variant from you, and each of your siblings has at least a 50% chance of having this variant.

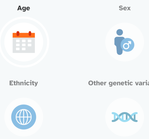
For people with a genetic variant, other factors can also influence the chances of developing TTR-related hereditary amyloidosis.

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

Age

TTR-related hereditary amyloidosis is an adult-onset condition. The risk of developing the condition increases as a person ages.

See Scientific Details for more information



About Hereditary Amyloidosis (TTR-Related)

Also known as: Hereditary transthyretin-mediated amyloidosis, hereditary ATTR (hATTR) amyloidosis, familial transthyretin amyloidosis, familial amyloid polyneuropathy (FAP), familial amyloid cardiomyopathy (FAC), familial amyloidosis, hereditary cardiac amyloidosis

When it develops

TTR-related hereditary amyloidosis typically develops in adulthood, but age of onset can vary widely. People with the V122I variant typically develop symptoms after the age of 69. People with the V36M variant can develop symptoms as early as their 20s or as late as their 90s, depending on ethnicity and family history. People with the T69A variant typically develop symptoms between 45 and 69 years of age.

How common is the condition?

It is estimated that about 1 in 28 African Americans, 1 in 67 people from Northern Sweden, 1 in 98 people from Northwest Ireland, and 1 in 625 people of Portuguese descent have one of the variants in this test. The exact fraction of people with one of these variants who go on to develop TTR-related hereditary amyloidosis is currently unknown.

Typical signs and symptoms

Symptoms can vary widely depending on which TTR variant a person has and the location(s) of TTR protein buildup. Symptoms can vary even among people with the same variant. People with TTR-related hereditary amyloidosis may experience:

- **Cardiomyopathy** (heart damage), characterized by thickening of the walls of the heart, which can lead to heart failure.
- **Peripheral neuropathy** (damage to the nerves that connect the spinal cord to the rest of the body, including the arms and legs), characterized by symptoms including carpal tunnel syndrome as well as tingling, numbness, or burning in the hands, legs, or feet.
- **Autonomic neuropathy** (damage to the nerves that help control the internal organs), characterized by symptoms including constipation, diarrhea, sexual dysfunction, and dizziness.

How it's treated

TTR-related hereditary amyloidosis is often managed by treating the symptoms through medications or surgical intervention. However, some recently approved medications treat the underlying cause of the condition by making the TTR protein less likely to build up in the body's tissues and organs. In addition, most of the TTR protein is produced in the liver, and liver transplants have been beneficial for some patients. Scientists are currently working on other treatment options for this condition.

Read more at: GeneReviews® MedlinePlus® Genetic and Rare Diseases Information Center®

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

A healthcare professional may be able to help you understand if additional testing might be appropriate.

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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Hereditary Amyloidosis (TTR-Related)

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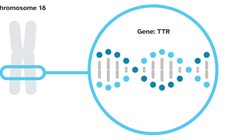
TTR-related hereditary amyloidosis is linked to variants in the TTR gene.

TTR

The TTR gene contains instructions for making a protein called transthyretin, which is produced primarily in the liver. Certain variants in the TTR gene make the protein less stable, which can cause it to fold incorrectly and clump together into abnormal structures called amyloid fibrils. These amyloid fibrils can then build up in the body's tissues and organs. This protein buildup, called amyloidosis, can damage the nerves, the heart, and other parts of the body.

Read more at MedlinePlus[+]



You have one of the three genetic variants we tested.

Variants Detected | View All Tested Markers

Marker Tested	Genotype*		Additional Information
V122I **Gene:** TTR **Marker:** rs76992529	**A** Variant copy from one of your parents	**G** Typical copy from your other parent	Biological explanation Typical vs. variant DNA sequence(s) Percent of 23andMe customers with variant References [3, 5, 11, 12, 15, 16, 18, 23, 25, 32] | 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 information about risk for TTR-related hereditary amyloidosis in people who have a variant included in this test.

Health Risk Estimates

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

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

References [5, 6, 10, 11, 12, 13, 22, 28]

Risk estimates

- The V122I variant is most commonly found in African Americans and in people of West African descent. About 3.5% of African Americans have the V122I variant. Most people with this variant have some amount of TTR protein buildup in the heart after the age of 69. However, not all of these people go on to develop cardiomyopathy (heart damage) due to TTR-related hereditary amyloidosis. For people with this variant who develop the condition, symptoms typically develop after the age of 69.
- The V30M variant is most commonly found in people of Portuguese, Northern Swedish, and Japanese descent. The fraction of people with this variant who go on to develop TTR-related hereditary amyloidosis is influenced by factors such as ethnicity. For example, about 58% of people of Northern Swedish descent with the V30M variant develop the condition by the age of 86, with symptoms typically appearing after the age of 69. By comparison, about 96% of people of Portuguese descent with the V30M variant develop the condition by the age of 86, with symptoms appearing as early as 29–39 years of age. People of Japanese descent with the V30M variant can develop symptoms as early as their 20s or as late as their 90s depending on family history.
- The T60A variant is most commonly found in people of Irish descent and can also be found in people of British descent. People with this variant typically develop symptoms between 45 and 80 years of age.

Other Factors

Only people with variants in the TTR gene are at risk of developing TTR-related hereditary amyloidosis. In these people, other factors can influence the chances of developing the condition.

This is not a complete list of other factors.

People with multiple risk factors may have a higher risk of developing TTR-related hereditary amyloidosis.

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

Other Factors	References
Age The risk of developing TTR-related hereditary amyloidosis increases as a person ages. The age of onset can vary depending on the variant and a person's ethnicity. For example, people with the V122I variant typically develop symptoms after the age of 66. People of Northern Swedish descent with the V30M variant typically develop symptoms after the age of 69, whereas people of Portuguese descent with the same variant can develop symptoms as early as their 20s. People of Japanese descent with the V30M variant can develop symptoms as early as their 20s or as late as their 90s depending on family history. People with the T60A variant typically develop symptoms between 45 and 80 years of age.	[8, 10, 12, 22, 26, 29, 30]
Sex In some ethnicities, studies have found that men with a TTR variant may be more likely than women to develop symptoms of TTR-related hereditary amyloidosis. The reason for this difference between the sexes is unknown.	[22, 27]
Ethnicity Studies have found that for certain TTR variants, ethnicity can impact the fraction of people with a variant who go on to develop TTR-related hereditary amyloidosis, as well as the age at which people develop symptoms of the condition. For example, about 58% of people of Northern Swedish descent with the V30M variant develop the condition by the age of 86, with symptoms typically appearing after the age of 69. By comparison, about 96% of people of Portuguese descent with the V30M variant develop the condition by the age of 86, with symptoms appearing as early as 29–39 years of age.	[10, 22]
Other genetic variants For people with a TTR variant, other genetic variants not included in this test may influence the risk of developing TTR-related hereditary amyloidosis. For example, some variants can stabilize the abnormal TTR protein, which can keep it from building up in the body's organs and tissues.	[9, 29]

Test Details

Indications for Use

The 23andMe PGS Genetic Health Risk Report for Hereditary Amyloidosis (TTR-Related) is indicated for reporting of the V122I, V30M, and T60A variants in the TTR gene. This report describes if a person has variants linked to TTR-related hereditary amyloidosis, but it does not describe a person's overall risk of developing the condition. This report is most relevant for African Americans, and for people of West African, Portuguese, Northern Swedish, Japanese, Irish, and British descent.

Special Considerations

- Genetic testing for TTR-related hereditary amyloidosis in the general population is not currently recommended by any healthcare professional organizations.

Test Performance Summary

Clinical Performance [4, 7, 8, 26, 31]

- In most studied populations, approximately 59–99% of TTR-related hereditary amyloidosis cases are caused by the three variants included in this test.
- Approximately 16% of African Americans over the age of 68 with congestive heart failure are expected to carry the V122I variant.

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.*
- 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

1. **Adams D et al. (2021). "Expert consensus recommendations to improve diagnosis of ATTR amyloidosis with polyneuropathy." J Neurol. 268(6):2109-2122.** +
2. **Ando Y et al. (2005). "Transthyretin-related familial amyloidotic polyneuropathy." Arch Neurol. 62(7):1057-62.** +
3. **Bourgault S et al. (2011). "Mechanisms of transthyretin cardiomyocyte toxicity inhibition by resveratrol analogs." Biochem Biophys Res Commun. 410(4):707-13.** +
4. **Buxbaum J et al. (2006). "Transthyretin V122I in African Americans with congestive heart failure." J Am Coll Cardiol. 47(8):1724-5.** +
5. **Buxbaum J et al. (2010). "Significance of the amyloidogenic transthyretin Val 122 Ile allele in African Americans in the Arteriosclerosis Risk in Communities (ARIC) and Cardiovascular Health (CHS) Studies." Am Heart J. 159(5):864-70.** +
6. **Buxbaum JN et al. (2017). "Transthyretin V122I (pV142I)* cardiac amyloidosis: an age-dependent autosomal dominant cardiomyopathy too common to be overlooked as a cause of significant heart disease in elderly African Americans." Genet Med. 19(7):733-742.** +
7. **Damy T et al. (2019). "Transthyretin cardiac amyloidosis in continental Western Europe: an insight through the Transthyretin Amyloidosis Outcomes Survey (THAOS)." Eur Heart J.** +
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9. **Hammarström P et al. (2001). "Trans-suppression of misfolding in an amyloid disease." Science. 293(5539):2459-62.** +
10. **Hellman U et al. (2008). "Heterogeneity of penetrance in familial amyloid polyneuropathy, ATTR Val30Met, in the Swedish population." Amyloid. 15(3):181-6.** +

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
Nov. 3, 2021	Information about the clinical performance of the test was updated.
April 9, 2019	Hereditary Amyloidosis (TTR-Related) report created.

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Hereditary Amyloidosis (TTR-Related)

What does this test do?

What does this test **not** do?

The report says the variants included in this test are most common and best studied in certain ethnicities. What does this mean?

Where can I learn more about TTR-related hereditary amyloidosis, support groups, and other resources?

My report says **one variant** called **V122I** was detected. What does this mean?

What does **increased risk** mean?

My report says **one variant** called **V122I** was detected. What are some things I could do?

How could my result affect my family?

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

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