Alpha-1 Antitrypsin Deficiency

AAT deficiency is a genetic condition that can lead to lung and liver disease. It is caused by decreased levels of the alpha-1 antitrypsin (AAT) protein. This test includes the two most common variants linked to this deficiency.

Overview Scientific Details Frequently Asked Questions

Jamie, you have **two copies** of a genetic variant linked to AAT deficiency.

People with this result have an increased risk of developing lung and liver disease related to AAT deficiency. Smoking, drinking excessive amounts of alcohol, and other factors can also affect your risk.

How To Use This Test

This test does not diagnose AAT deficiency 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 the **PI*Z** and **PI*S** variants in the SERPINA1 gene linked to AAT deficiency.

Limitations

- Does **not** test for all possible variants linked to AAT deficiency.

Ethnicity Considerations

- The variants included in this test are most common and best studied in people of **European** descent.

You have an **increased risk** of developing lung and liver disease related to AAT deficiency based on your genetic result.

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

We detected two copies of a variant called PI*Z.

You inherited one copy of this variant from each of your parents.

See Scientific Details

Most people with this result develop emphysema, a serious lung disease. Some people with this result will also develop liver disease.

However, some people with this result do not develop lung or liver disease. Smoking, drinking excessive amounts of alcohol, and other factors can also influence your risk.

You will likely pass down a variant to each of your children.

If your partner has a variant linked to AAT deficiency, your children could inherit a combination of variants that may put them at risk of developing lung or liver disease.

The chances of developing lung and liver disease related to AAT deficiency also depend on lifestyle, environment, and other factors.

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

Smoking

People with AAT deficiency who smoke are more likely to develop lung disease and to do so at a younger age.

See Scientific Details for more information

About Alpha-1 Antitrypsin Deficiency

Also known as: Alpha-1 antitrypsin deficiency, AATD, A1AT deficiency, Alpha-1, A1AD, α1

When it develops

Because it is a genetic condition, AAT deficiency is present at birth. Symptoms of lung disease usually appear later in life, and age of onset is strongly affected by smoking. Some people may never have symptoms of lung disease, especially if they don't smoke. Liver problems may develop anytime from infancy to adulthood.

Potential signs and symptoms

- Shortness of breath and wheezing
- Chronic cough
- Recurrent lung infections
- Lung disease, including emphysema
- Liver disease, including cirrhosis

How common is the condition?

AAT deficiency is most common in people of Northern European descent. In the U.S., 1 in 3,000–5,000 people has this condition.

How it's treated

There is currently no known cure. People with AAT deficiency are encouraged to avoid smoking, limit alcohol consumption, and consider getting certain vaccinations. For those with symptoms, treatment focuses on management of lung and liver problems. Direct replacement of the AAT protein into the blood may be used to slow the progression of lung disease. Lung and liver transplants may be beneficial in some cases.

Read more at: National Heart, Lung, and Blood Institute› GeneReviews› MedlinePlus›

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

If you have a personal or family history of lung or liver disease, consult with a healthcare professional.

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

Alpha-1 Antitrypsin Deficiency

AAT deficiency is a genetic condition that can lead to lung and liver disease. It is caused by decreased levels of the alpha-1 antitrypsin (AAT) protein. This test includes the two most common variants linked to this deficiency.

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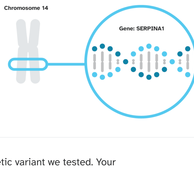
AAT deficiency is caused by variants in the SERPINA1 gene.

SERPINA1

The SERPINA1 gene contains instructions for making a protein called alpha-1 antitrypsin (AAT). This protein is made in the liver, but is transported to the lungs where it has a protective function. Certain variants in SERPINA1 result in too little AAT protein getting transported to the lungs, and more AAT protein getting trapped in the liver. As a result, the lungs are less protected from damage, and the liver can become damaged as well.

Read more at MedlinePlus*

Chromosome 14



You have two copies of a genetic variant we tested. Your genotype is PI*ZZ.

Variants Detected | View All Tested Markers

Marker Tested	Genotype*		Additional Information
PI*Z **Gene:** SERPINA1 **Marker:** rs28929474	T Variant 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, 3, 5, 6, 11, 15, 16, 17, 19, 20, 23] | 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 the risk of developing lung and liver disease in people of European descent who have the variants included in this test. Estimates for other ethnicities are not currently available. Keep in mind that other risk factors — including smoking, drinking excessive amounts of alcohol, and having nonalcoholic fatty liver disease (NAFLD) — can increase the risk of developing lung and severe liver disease, regardless of genetics.

Health Risk Estimates

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

For certain genotypes, quantitative risk estimates may not be available.

Variants in the SERPINA1 gene can affect AAT protein levels differently. Severe AAT deficiency is defined by AAT levels below 11 µM/L. Lung diseases such as emphysema and COPD are most commonly associated with AAT levels below this protective threshold. This table provides AAT protein levels associated with each genotype for informational purposes only, and does not indicate a person's actual protein levels.

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

References [1, 16, 20]

Risk estimates for developing lung and liver disease in people of European descent

Genotype	Average serum AAT levels, µM/L (5th to 95th %ile)	Lung Disease	Liver Disease
PI*M5	33 (18–52)	Not likely at increased risk of developing COPD, including emphysema, due to AAT deficiency.	Not likely at increased risk of developing severe liver disease, including cirrhosis, due to AAT deficiency.
PI*S5	28 (26–48)	Not likely at increased risk of developing COPD, including emphysema, due to AAT deficiency.	Not likely at increased risk of developing severe liver disease, including cirrhosis, due to AAT deficiency.
PI*MZ	25.4 (15–42)	Not likely at increased risk of developing COPD, including emphysema, due to AAT deficiency. However, smokers with this genotype have an increased risk.	Not likely at increased risk of developing severe liver disease, including cirrhosis, due to AAT deficiency. However, excessive alcohol consumption and having nonalcoholic fatty liver disease (NAFLD) can increase risk.
PI*SZ	16.5 (10–23)	Not likely at increased risk of developing COPD, including emphysema, due to AAT deficiency. However, scientists estimate that 29–56% of smokers with this genotype will develop signs of emphysema during their lifetime.	Not likely at increased risk of developing severe liver disease, including cirrhosis, due to AAT deficiency. However, excessive alcohol consumption and having nonalcoholic fatty liver disease (NAFLD) may increase risk.
PI*ZZ	5.3 (3.4–7.9)	Increased risk of developing COPD, including emphysema, due to AAT deficiency. Scientists estimate that greater than 89% of people with this genotype will develop signs of emphysema during their lifetime.	Increased risk of developing severe liver disease due to AAT deficiency. Scientists estimate that people with this genotype have a 39–46% chance of developing cirrhosis after the age of 56.

Other Factors

AAT deficiency is a genetic condition. People with this condition have a higher risk of developing lung and liver disease, but their risk is also influenced by other factors.

This is not a complete list of other factors.

The factors described here include the most common and well-established risk factors associated with lung or liver disease in people with AAT deficiency. Other factors not listed here may also influence risk for lung or liver disease in people with the condition.

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

Other Factors	References
Smoking People with at least one copy of the PI*Z variant are more likely to develop lung disease if they smoke. People with AAT deficiency who smoke typically have a worse progression of lung disease between 40 and 59 years of age. In contrast, non-smokers with AAT deficiency may not experience symptoms until their 60s, and some non-smokers will never develop the symptoms of lung disease.	[1, 12, 20]
Occupational and other exposures A small number of research studies — mostly looking at men working in construction or farming — suggests that prolonged occupational exposure to industrial gases, metal fumes, and mineral dust may lead to a faster decline in lung function in people with AAT deficiency. Exposure to pollutants from kerosene heaters on a regular basis may also increase the chances of developing lung disease related to AAT deficiency. The effects of occupational and other exposures on symptoms of lung disease in people with AAT deficiency are still not fully understood.	[1, 10]
Personal or family history of lung disease People with AAT deficiency who have a personal history of lung problems such as asthma or wheezing are more likely to develop severe lung disease later in life. The risk of lung disease can also depend on family history. People with AAT deficiency who have a family history of lung disease are more likely to develop lung disease themselves. This may be due to genetic and/or environmental factors.	[1]
Certain infections Diseases like the flu can damage the lungs, and diseases like hepatitis A and B can damage the liver. Yearly immunization against Influenza (a virus that causes the flu) and immunization against pneumococcus (a bacterium that causes respiratory infections) are generally recommended for people with AAT deficiency. This can prevent lung disease from getting worse. Immunizations against the viruses hepatitis A and B, which cause liver disease, may also be recommended by a healthcare professional.	[1, 9]
Excessive alcohol consumption People with at least one copy of the PI*Z variant are more likely to develop severe liver disease if they drink excessive amounts of alcohol.	[7, 21]
Certain health conditions People with at least one copy of the PI*Z variant are more likely to develop severe liver disease if they also have nonalcoholic fatty liver disease (NAFLD). This means reducing risk for NAFLD may help lower the chances of developing cirrhosis. Factors like maintaining a healthy weight and keeping blood sugar and cholesterol levels in the healthy range can help reduce the risk for NAFLD.	[4, 7, 21]

Test Details

Indications for Use

The 23andMe PGS Genetic Health Risk Report for Alpha-1 Antitrypsin Deficiency is indicated for reporting of the PI*Z and PI*S variants in the SERPINA1 gene. This report describes if a person has variants associated with AAT deficiency and a higher risk for lung or liver disease, but it does not describe a person's overall risk of developing lung or liver disease. This report is most relevant for people of European descent.

Special Considerations

- Testing for genetic variants associated with AAT deficiency is recommended under certain circumstances by several health professional organizations, including the American Thoracic Society.

Test Performance Summary

Clinical Performance [1]

More than 95% of all cases of AAT deficiency are caused by the PI*Z and PI*S variants in the SERPINA1 gene.

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. American Thoracic Society, et al. (2003). "American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency." Am J Respir Crit Care Med. 168(7):818-900. ^
2. Blanco I et al. (2017). "Alpha-1 antitrypsin PI*SZ genotype: estimated prevalence and number of SZ subjects worldwide." Int J Chron Obstruct Pulmon Dis. 12:1563-1694. ^
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4. Chalasani N et al. (2018). "The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases." Hepatology. 67(1):328-357. ^
5. Dahl M et al. (2005). "The protease inhibitor PI*S allele and COPD: a meta-analysis." Eur Respir J. 26(1):67-76. ^
6. Fregonese L et al. (2008). "Hereditary alpha-1-antitrypsin deficiency and its clinical consequences." Orphanet J Rare Dis. 3:16. ^
7. Hamesch K et al. (2020). "Non-Invasive Assessment and Management of Liver Involvement in Adults With Alpha-1 Antitrypsin Deficiency." Chronic Obstr Pulm Dis. 7(3):260-271. ^
8. Hersh CP et al. (2004). "Chronic obstructive pulmonary disease in alpha1-antitrypsin PI MZ heterozygotes: a meta-analysis." Thorax. 59(10):843-9. ^
9. Köhnlein T et al. (2010). "Diagnostic delay and clinical modifiers in alpha-1 antitrypsin deficiency." Ther Adv Respir Dis. 4(5):279-87. ^
10. Lieberman J et al. (1986). "Alpha 1-antitrypsin Pi-types in 965 COPD patients." Chest. 89(3):370-3. ^

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 liver disease risk was updated for people with certain genotypes.
April 17, 2017	Alpha-1 Antitrypsin Deficiency report created.

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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 people of **European** descent. What if I'm not of European descent?

Where can I learn more about alpha-1 antitrypsin deficiency, support groups, and other resources?

My report says **two copies of a variant** called **PI*Z** were detected. What does this mean?

What does **increased risk** mean?

My report says **two copies of a variant** called **PI*Z** were 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.**