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Alpha-1 Antitrypsin Deficiency

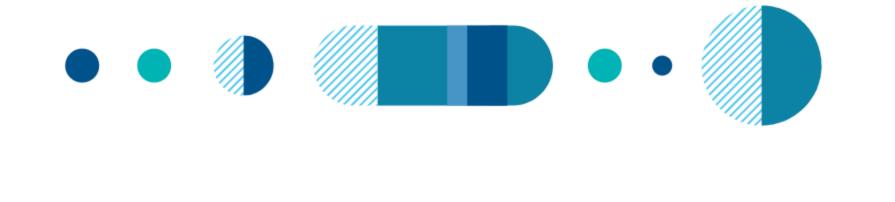
AAT deficiency is a genetic condition that can lead to lung and liver disease. It is caused by decreased levels of the alpha-1 antitrypsin (AAT) protein. This test includes the two most common variants linked to this deficiency.

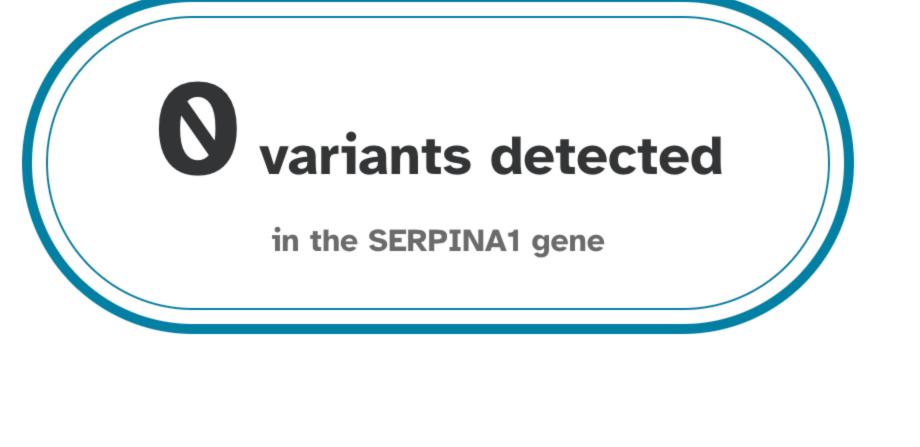
Overview

Scientific Details

Frequently Asked Questions

Jamie, you do not have the two genetic variants we tested. You could still have a variant not covered by this test.







any other health conditions.

See Scientific Details

How To Use This Test

Please talk to a healthcare professional if this

This test does not diagnose AAT deficiency or

condition runs in your family, you think you might have this condition, or you have any concerns about your results.

See Frequently Asked Questions

Review the Genetic Health Risk tutorial

Tests for the PI*Z and PI*S variants in the SERPINA1 gene linked to AAT

Intended Uses

deficiency. Limitations

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

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

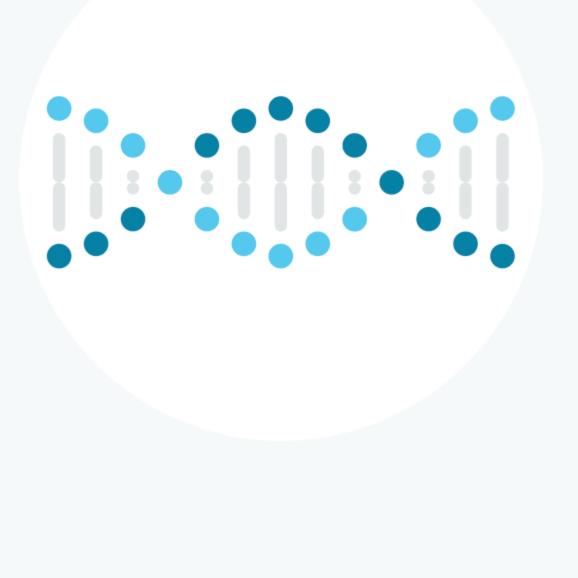
You are not likely at risk for AAT deficiency based on your

Ethnicity Considerations

to AAT deficiency.

Genetic variants are the only known risk factor for developing AAT deficiency.

genetic result.



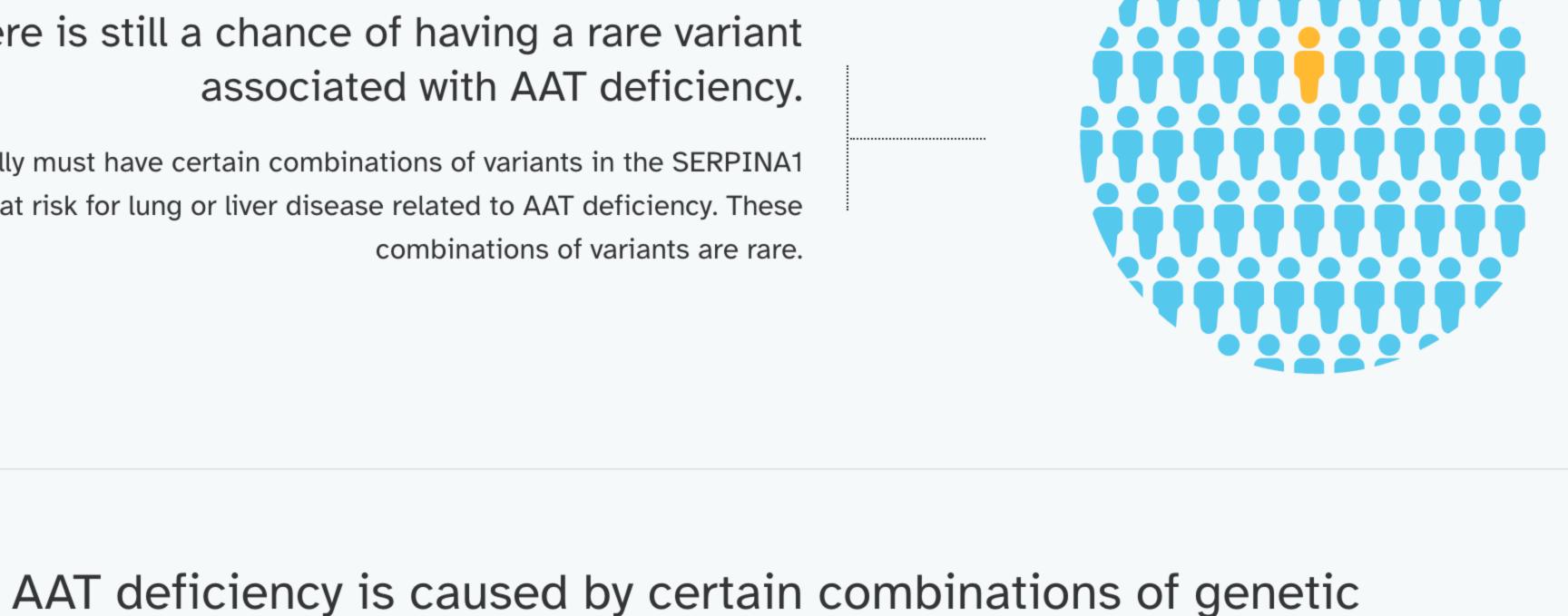
These variants are most commonly found in people of **European** descent. **See Scientific Details**

You do not have the two most common variants linked

A person typically must have certain combinations of variants in the SERPINA1 gene to be at risk for lung or liver disease related to AAT deficiency. These combinations of variants are rare.

There is still a chance of having a rare variant

associated with AAT deficiency.

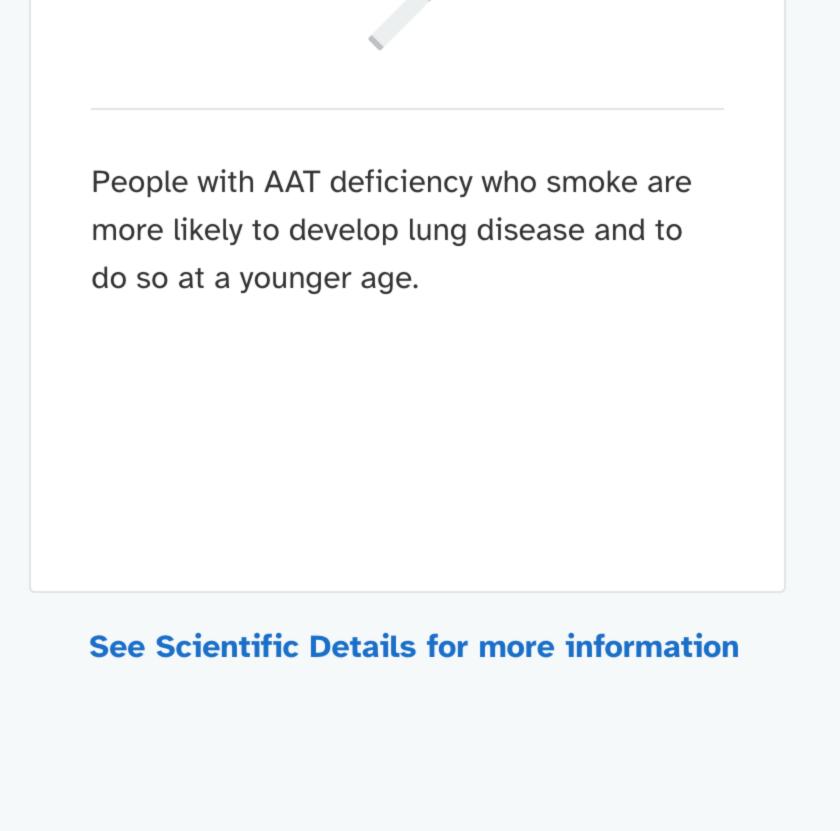


People with your genetic result are not at risk for AAT deficiency.

variants, and only some combinations increase risk for lung and

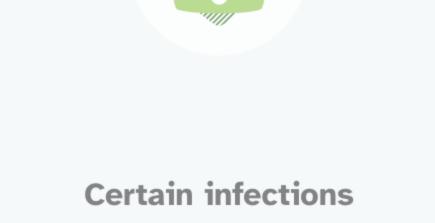
liver disease.

Smoking



Smoking





Occupational and other

exposures

Excessive alcohol





consumption

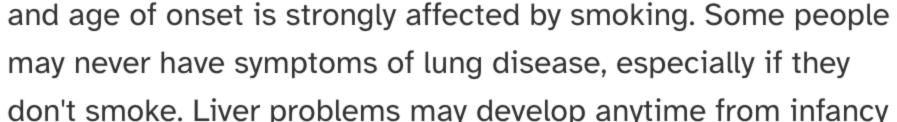


How common is the condition?

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 AAT deficiency is most common in people of Northern



may never have symptoms of lung disease, especially if they don't smoke. Liver problems may develop anytime from infancy to adulthood.

 Shortness of breath and wheezing Chronic cough

Potential signs and symptoms

birth. Symptoms of lung disease usually appear later in life,

• Lung disease, including emphysema Liver disease, including cirrhosis

Recurrent lung infections

How it's treated There is currently no known cure. People with AAT deficiency

this condition.

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.

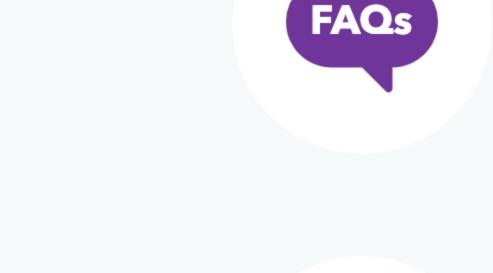
Lung and liver transplants may be beneficial in some cases.

European descent. In the U.S., 1 in 3,000-5,000 people has

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

Learn more about AAT deficiency.

See our Frequently Asked Questions for more information.



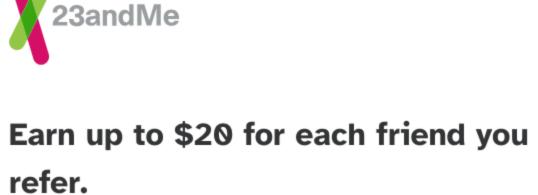
If you have a personal or family history of lung or liver disease, consult with a

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Print report

healthcare professional.

FAQs



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Traits

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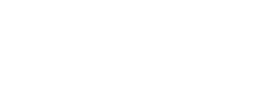
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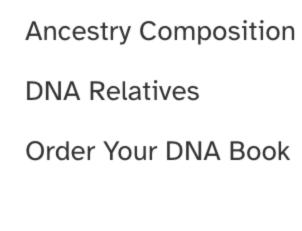
View all DNA Relatives Family Tree **Your Connections** GrandTree Advanced DNA Comparison

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RESEARCH

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Frequently Asked Questions

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Health > Health Predisposition

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.

Scientific Details

SERPINA1

AAT deficiency is caused by variants in the SERPINA1 gene.

The SERPINA1 gene contains instructions for making a protein called alpha-1 **Chromosome 14** antitrypsin (AAT). This protein is made in the liver, but is transported to the lungs

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'

Variants Detected

Your Genotype*

C

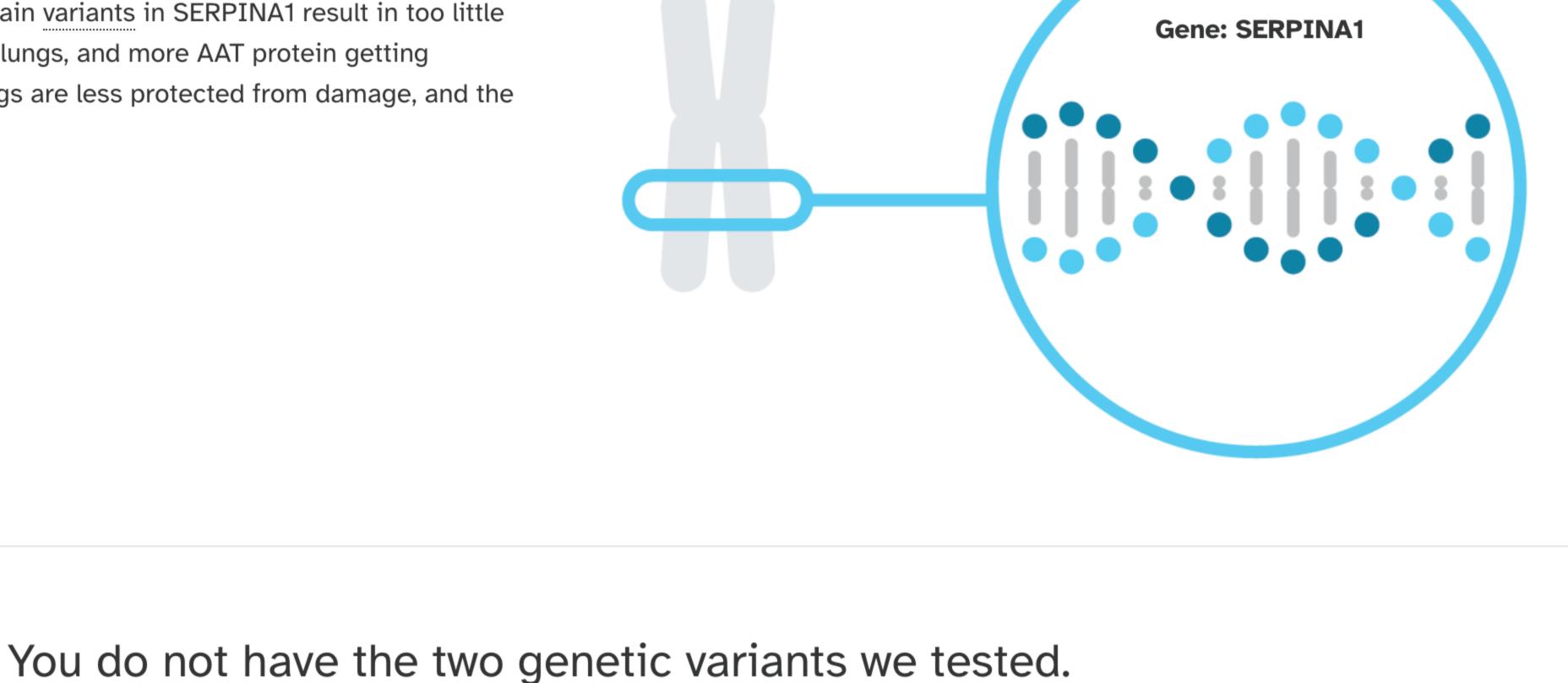
Health Risk Estimates

Risk estimates are based on clinical studies that

where it has a protective function. Certain variants in SERPINA1 result in too little

Marker Tested

PI*Z



View All Tested Markers

C **Biological explanation**

Additional Information

Gene: SERPINA1 Marker: rs28929474	Typical copy from one of your parents	Typical copy from your other parent	 Typical vs. variant DNA sequence(s) Percent of 23andMe customers with variant References [2, 3, 5, 8, 11, 15, 16, 17, 19, 20, 23] ClinVar
PI*S Gene: SERPINA1 Marker: rs17580	T Typical copy from one of your parents	T Typical copy from your other parent	 Biological explanation Typical vs. variant DNA sequence(s) Percent of 23andMe customers with variant References [2, 5, 10, 14, 20, 22] ClinVar
oth parents. This may impac	t how these variants are passed dov	wn.	t determine whether multiple <u>variants</u> , if detected, were inherited from only one parent or from ence sequence (build 37). Other sources sometimes report genotypes using the opposite strand.

This report provides information about the risk of developing lung and liver disease in people of European

Test Interpretation

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.

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

Lung Disease

Liver Disease

References

[1, 12, 20]

[1, 18]

[1]

[**1**, **9**]

[**7**, **21**]

[4, 7, 21]

Genotype (1) **Average serum AAT** levels, µM/L (5th to

identify an association between a genotype and 95th %ile) 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	PI*MS	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.			
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	PI*SS	28 (20-48)	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.			
levels. Consider talking to a healthcare professional if you have any concerns about your results. References [1, 16, 20]	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 20–50% 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 (3.4–7.0)	Increased risk of developing COPD, including emphysema, due to AAT deficiency. Scientists estimate that greater than 80% 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 30–40% chance of developing cirrhosis after the age of 50.			
Other Factors							

Occupational and other exposures A small number of research studies — mostly looking at men working in

symptoms of lung disease.

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.

Other Factors

Smoking

This is not a complete list of other factors.

The factors described here include the most

associated with lung or liver disease in people

with AAT deficiency. Other factors not listed

here may also influence risk for lung or liver

Consult with a healthcare professional before

disease in people with the condition.

making any major lifestyle changes.

common and well-established risk factors

occupational and other exposures on symptoms of lung disease in people with AAT deficiency are still not fully understood. 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 whose siblings suffer from lung disease are more likely to

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

Immunizations against the viruses hepatitis A and B, which cause liver

AAT deficiency. This can prevent lung disease from getting worse.

disease, may also be recommended by a healthcare professional.

develop lung disease themselves. This may be due to genetic and/or

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

start to experience the symptoms of lung disease between 40 and 50 years

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

of age. In contrast, non-smokers with AAT deficiency may not experience

symptoms until their 60s, and some non-smokers will never develop the

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.

Certain health conditions

environmental factors.

Certain infections

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.

People with at least one copy of the PI*Z variant are more likely to develop

This means reducing risk for NAFLD may help lower the chances of

severe liver disease if they also have nonalcoholic fatty liver disease (NAFLD).

Test Details

Analytical Performance Accuracy was determined by comparing results from this test with results from sequencing. Greater than

Dis. 12:1683-1694. \

12:561-569.

Test Performance Summary

Indications for Use

Special Considerations

Clinical Performance

descent.

gene.

References

management of individuals with alpha-1 antitrypsin deficiency." Am J Respir Crit Care Med. 168(7):818-900.

The 23andMe PGS Genetic Health Risk Report for Alpha-1 Antitrypsin Deficiency is indicated for reporting

person's overall risk of developing lung or liver disease. This report is most relevant for people of European

circumstances by several health professional organizations, including the American Thoracic Society.

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

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.

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

• Testing for genetic variants associated with AAT deficiency is recommended under certain

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 3. Blanco I et al. (2017). "Alpha-1 antitrypsin Pi*Z gene frequency and Pi*ZZ genotype numbers worldwide: an update." Int J Chron Obstruct Pulmon Dis.

[1]

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.

1. American Thoracic Society. et al. (2003). "American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and

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.

revisions to this report.

Change Log

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

genotypes. Alpha-1 Antitrypsin Deficiency report created.

Information about liver disease risk was updated for people with certain

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conditions. Share results with your healthcare professional for any medical purposes.

and performance of this test.

may not pass our testing standards.

cause this condition.*

Warnings and Limitations

This test does not diagnose any health

If you are concerned about your results,

consult with a healthcare professional.

See the **Package Insert** for more details on use

* Variants not included in this test may be very rare,

may not be available on our genotyping platform, or

This test does not cover all variants that could

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Alpha-1 Antitrypsin Deficiency

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Overview

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Frequently Asked Questions

Alpha-1 Antitrypsin Deficiency

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 zero variants were detected. What does this mean?	~
What does not likely at risk for AAT deficiency mean?	~
My report says zero variants were detected. What are some things I could do?	~

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