A Guide for Individuals and Families

Genetic Testing Options for Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is a progressive neuromuscular disease that destroys muscle-controlling nerve cells called motor neurons.

In ALS, motor neurons in the brain and spinal cord are affected. As these nerve cells deteriorate and are lost, they stop sending signals to muscles. Without those signals, the muscles become weak and then stop working.

Types of ALS

Scientists are still learning why ALS occurs. Cases in which two or more family members have been diagnosed with ALS are classified as familial ALS (fALS). This accounts for at least 10% of all ALS cases, and approximately two-thirds of these cases can be traced to an underlying genetic cause.

The majority of ALS cases occur in individuals with no known family history and may be called sporadic, simplex, or non-familial ALS. A genetic cause may still be responsible in these cases, but less frequently. Having a family history of other possibly related diagnoses, like frontotemporal dementia, may result in a higher chance to have an identifiable genetic cause.

Variations in about 30 different genes have been associated with increased risk for developing ALS and/or other neurologic conditions with overlapping symptoms.

MDA Care Centers provide expert care from clinicians specializing in neuromuscular diseases. To find an MDA Care Center near you, visit mda.org/care/mda-care-centers.

Receiving an ALS diagnosis

An ALS diagnosis is based on a detailed history of symptoms, the signs a doctor observes during a physical examination, and a series of tests meant to rule out other diseases that can mimic ALS. There is no single test that can provide a definitive ALS diagnosis.

If your doctor suspects you have ALS, it is important to have a neurologist who specializes in ALS confirm your diagnosis because ALS is a progressive condition. While there currently is no cure for ALS, an early diagnosis is essential to starting treatments that may slow the disease course, as well as therapies that can help control symptoms, prevent complications, and make living with the disease easier.

Once you have a confirmed diagnosis of ALS, you can discuss treatment options and medical management recommendations with your care team. A multidisciplinary approach to medical care is important because of the numerous body systems that can be involved in ALS.

Benefits of genetic testing

Genetic testing is available for most of the genes commonly associated with ALS (see Genes and ALS on page 4). Genetic testing is important because it can shed more light on why the condition has occurred and provide additional information that may be helpful to your care team and beneficial to you and your family.

There are several reasons why genetic testing may be beneficial:

- Identifying a genetic cause of ALS may allow your care team to provide individualized, gene-specific treatments that aim to address the cause of the disease. Currently, some gene-specific therapies are available through clinical trials, but they are not available for all possible genetic causes of ALS. More options may be available in the future.
- Having genetic test results may allow you to participate in certain clinical research studies and disease registries. This can help the ALS community by expanding knowledge on the condition.
- Genetic testing results can be informative for family members. If a genetic risk for ALS is identified, other family members may have inherited it.

If you are interested in genetic testing for ALS, speak with your healthcare provider. Often genetic testing is coordinated by a geneticist or genetic counselor who will ask detailed questions about your personal and family history to help assess the most appropriate test to order and provide guidance in interpreting the final report.

Genetic test results can be complicated, so it's important to work with a healthcare professional who is comfortable with interpreting the results or can refer you to another provider if needed. You can locate a genetic counselor at **findageneticcounselor.nsgc.org**.

Genetic testing FAQs

Will genetic testing tell me what caused my ALS?

Genetic testing is expected to identify a cause in about 10%-15% of individuals with ALS. A genetic cause may be identified more frequently in an individual with early onset or a family history of ALS, but individuals with apparently sporadic ALS can also have a genetic cause identified.

What if a genetic test didn't find a cause for my ALS?

Talk with your care team and genetic counselor about whether analysis of additional genes should be considered based on the initial test completed. Additionally, as genetic understanding grows over time, there may be opportunities for further genetic testing in the future. Some families may want to consider DNA banking, where DNA collected from a blood or saliva sample can be stored and used for genetic testing in the future, even after an individual has passed away.

Should a person who has not been diagnosed with ALS but has a family history have a genetic test?

There are important potential risks a person who is not experiencing symptoms should be aware of before completing genetic testing. Learning they have an increased risk for ALS could be psychologically damaging. They should consider including a mental healthcare provider and genetic counselor in the testing process. Importantly, if an inherited risk for ALS is identified, it cannot inform on when an individual will develop symptoms and how exactly they will be affected. Even individuals within the same family can be affected differently by the same genetic risk factor.

Separately, there is a risk for genetic discrimination following a positive genetic test result. A US federal law called the Genetic Information Nondiscrimination Act provides some protection from health insurance or employment discrimination, but the law does not provide protection against discrimination for long-term care, life, or disability insurance. Individual states may have additional protections.

Genes and ALS

Variations in about 30 genes have been discovered to have possible association with ALS and/or similar neurologic conditions. This chart shows the most common associated genes.

Gene	% fALS cases	% non-familial ALS cases
C9orf72	39%-45%	3%-7%
SOD1	15%-20%	3%
FUS	~4%-8%	Very rare
TARDBP	1%-4%	Very rare; also called *TDP-43*

Siddique N, Siddique T. Amyotrophic Lateral Sclerosis Overview. 2001 Mar 23 [Updated 2021 Sep 30]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022.

Here are a few things to know about genetic testing for ALS genes:

- The technology used to analyze the *C9orf72* gene is different than the process for other associated genes, like *SOD1*, *FUS*, and *TARDBP*.
- Some laboratories may offer testing for *C9orf72* and other associated genes separately, so confirmation that both tests were ordered may be needed. Other genes have been associated with genetic ALS less frequently and may or may not be included in testing ordered.
- If the initial genetic test ordered does not find a gene variation associated with ALS, a healthcare provider may recommend additional testing.

Cost of genetic testing

Usually, genetic testing for ALS is performed for a fee, and the exact cost varies based on the specific test, laboratory, and insurance coverage.

Currently, one sponsored genetic testing program is available for ALS, called **ALS Identified**. A sponsored program means a company sponsors the test, so it is free of charge to the individual. There may be eligibility requirements for sponsored testing. You can work with your healthcare provider and your insurance company to determine potential costs and/or eligibility for sponsored genetic testing, including what information is shared with the sponsor.

Sponsored genetic testing program:

ALS Identified
ptcg.insideals.com/en-us/home/no-charge-genetic-testing.html

MDA also can provide more information on no-cost or low-cost genetic testing options. Contact the MDA Resource Center at **833-ASK-MDA1** or email **resourcecenter@mdausa.org**.

Images: iStock.com/koto_feja; FatCamera; Pogonici

To learn more about ALS, visit mda.org/disease/amyotrophic-lateral-sclerosis, or download our ALS Disease Fact Sheet at mda.org/education. For more information on genetic testing, contact the MDA Resource Center at 833-ASK-MDA1 or resourcecenter@mdausa.org.

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