

What is ALS?

An Introductory Resource Guide for Living with ALS



LIVING WITH ALS
RESOURCE GUIDE



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An Introductory Resource Guide for Living with ALS

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A NOTE TO THE READER: The ALS Association has developed the *Living with ALS* resource guides for informational and educational purposes only. The information contained in these guides is not intended to replace personalized medical assessment and management of ALS. Your doctor and other qualified health care providers must be consulted before beginning any treatment.



Introduction

After learning you or a loved one has amyotrophic lateral sclerosis (ALS) and processing this diagnosis, you can choose how much information about ALS you want to know and when you want to know it. Some people want to know as much as possible from the get-go, while others prefer to learn over time. This resource guide includes some of the basics you may want to learn now, beginning with how ALS is diagnosed, how it affects a person over time and how the disease can be managed as it progresses. When you are ready to learn more, there are several other resource guides on specific topics related to living with ALS published by The ALS Association.

In this resource guide we will cover some of the basics about:

- What “ALS” and motor neuron disease mean
- Facts about neurons and muscles involved in ALS
- Types of ALS
- Diagnosis, progression and treatment
- The ALS care team
- Clinical trial research

What Does Amyotrophic Lateral Sclerosis (ALS) and Motor Neuron Disease (MND) Mean?

The term “ALS” stands for “amyotrophic lateral sclerosis.”

Amyotrophic is the medical term for shrinkage of muscle. Lateral describes the area of the spinal cord, which shows damage in affected patients (the side).

The term sclerosis means hardening of the side.

As the first word implies, ALS causes weakness and wasting of all **voluntary muscles**; that is, the muscles we use to move, swallow, speak and breathe. However, the reason the muscles become wasted is not an illness of the muscle itself, but rather an illness of the nerve cells that send the signal to the muscles to fire.

Those nerve cells are called **motor neurons**, and therefore, ALS is often referred to as “**motor neuron disease**” (MND). That said, the terms ALS and MND should **not** be used interchangeably, because ALS is the most common form of motor neuron disease in adults, yet there are several other less common forms of MND that are not ALS.

The disease can start in different places in the body in different people. However, as time progresses the weakness worsens where the disease starts and then spreads to other parts of the body.

ALS causes weakness and wasting of all voluntary muscles; that is, the muscles we use to move, swallow, speak and breathe.

There are available treatments and many ways ALS specialists help people with their symptoms, but to date, ALS remains incurable. This means that there is no available treatment yet which will stop or reverse the progression of weakness.

“You have ALS” may be some of the most difficult words to hear. The ALS Association’s resource guides are meant to help you and your loved ones live fully with the diagnosis. Please know that your ALS healthcare providers are also available to help you navigate the challenges that this disease brings.

Why Is ALS Known as ‘Lou Gehrig’s Disease’?

As baseball fans know, Lou Gehrig was a powerful baseball player for the New York Yankees in the 1920s-30s. While still playing baseball, he noticed that he was becoming weak with no clear reason. He was evaluated at the Mayo Clinic and diagnosed with ALS. Gehrig gave his famous farewell speech on July 4, 1939, and even today, ALS is still commonly referred to as Lou Gehrig’s disease.

All About Motor Neurons and How We Move

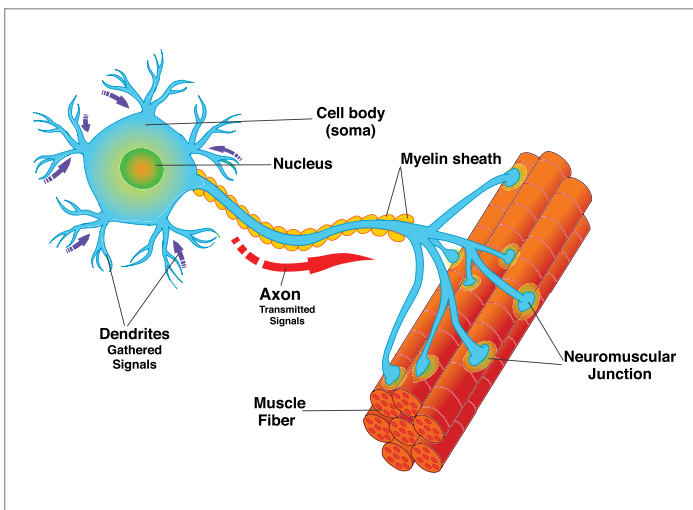


Figure 1: A motor neuron and its axon

Movement of the human body requires nerve cells in the brain and in the spinal cord called motor neurons. The brain sends signals to the correct cells in the spinal cord (pick up the glass, put your foot down), and these cells send messages to the muscles via a long nerve

fiber called an “axon.” (See Figure 1)

Without this signal, there is no way for a muscle to know what to do! It is a little like our TV sets: If they are not plugged in, there is no electricity and they can’t turn on. But motor neurons are more important than that: The muscle also needs this nerve axon connection to survive. There is a **symbiotic relationship** between every muscle in our body and a specific nerve axon (**that means they work together**). If the tie is severed, the muscle will shrink. So, not only does the muscle not get the signal of what to do (pick up the glass), it also will wither away without an axon. (See Figure 2)

So, in the disease called ALS, or any MND, if the nerve cell dies, then the axon is lost and the muscle it is communicating with will stop working and wither (medical term: atrophy). Therefore, in ALS or other MNDs, we cannot stimulate the nerve artificially (through a stimulator) to reverse the effects of the disease: The nerve axon must be intact for the muscle to remain healthy.

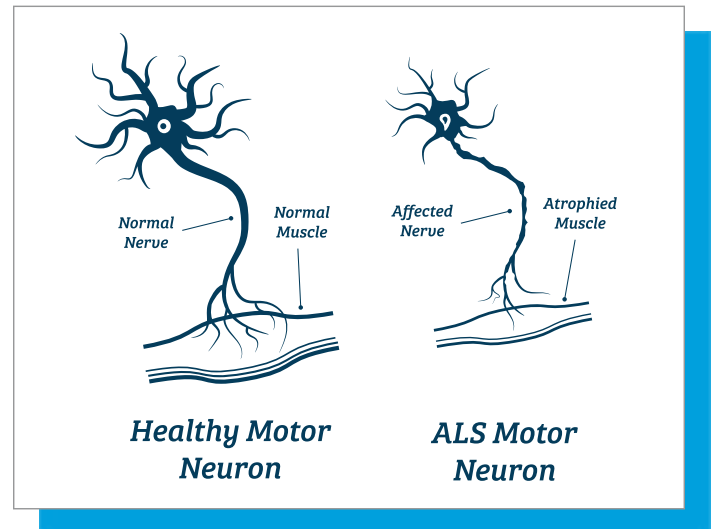


Figure 2: Muscle wasting as a result of motor neuron disease

Voluntary Movement (What’s Involved and What’s Not)

Earlier, we described the problems that people with ALS have: progressive loss of voluntary muscle activity. In our bodies, we have three types of muscle: striated, smooth and cardiac. In general, all striated muscle is “**voluntary**,” meaning we control movement.

Breathing is controlled by striated muscle (the main

breathing muscle is the diaphragm), but we do not have to think about breathing. Nevertheless, it is a striated muscle and is therefore affected in ALS.

The muscles that control eye movements (medical term: extraocular muscles) are affected very late or sometimes not at all in the disease. Smooth muscle, such as the food pipe (esophagus), is not affected. The heart muscle (cardiac) is also not affected.

Facts About ALS

When and How Likely Is It for ALS to Occur?

ALS usually occurs when people are in their mid-50s, but it can occur at much younger and older ages as well. Men are more likely affected than women. ALS affects about six in 100,000 people at a given time point (prevalence rate). The incidence, or new cases per year, is approximately two per 100,000.

What Causes ALS to Develop?

With the exception of approximately 10% of ALS, which is inherited (**familial** ALS, see below), the short answer for the remaining 90% of ALS cases, known as "**sporadic**" ALS, is that we don't know. There is nothing that someone with ALS did or didn't do to cause ALS. Military service, smoking and possibly professional soccer or playing football, have been associated with a higher likelihood of getting ALS, but it is unclear if serving in the military, cigarettes or repetitive head injuries during contact sports actually caused ALS. A lot has been written about the role of "ALS triggers" or environmental toxins, and a lot of research is being done to figure out what factors in one's environment may influence the likelihood of getting the disease, but definitive answers are still lacking.

Sporadic vs. Familial ALS, and Relation to Dementia

Sporadic ALS means that an individual is the only one in the family with this diagnosis; parents were not affected and the likelihood of siblings or children getting the disease is very low. To diagnose a person with “sporadic” ALS a careful three-generation family history should be obtained.

In contrast, about 10% of people with ALS (**familial ALS**) have a positive family history of the disease, which means that it runs from generation to generation, e.g., from grandparent to parents, patient and their siblings. Because this trait has a high (up to 50%) likelihood of being passed to the children of the affected person, genetic testing, which is done in blood samples, is now commercially available and can be ordered after discussion with a physician or genetic counselor.

Until a few decades ago, physicians used to believe that people with ALS are cognitively normal until the very late stages of the disease. We now have realized this is not always true; about 10-20% of people with ALS have coexistent dementia, called frontotemporal dementia (FTD). Unlike the well-known Alzheimer’s disease, FTD does not present with forgetfulness and confusion; it usually starts as trouble with decision-making and behavior changes, such as talking too much or too little, saying inappropriate comments, not responding to someone’s needs, becoming obsessed with new habits or food tastes, etc. In addition, at least 30% of persons with ALS score below normal on standard cognitive testing, even if the cognitive dysfunction is not severe enough to label them “demented.” This can complicate making difficult decisions as the disease progresses.

The importance of the relationship between FTD and ALS is that the two conditions are genetically linked; a few of the genetic changes that can cause ALS can also cause FTD, sometimes within the same family.

The importance of the relationship between FTD and ALS is that the two conditions are genetically linked; a few of the genetic changes that can cause ALS can also cause FTD, sometimes within the same family. In the last decade, scientists realized that some of those genetic changes can be detected in 5-10% of people who were considered to have "sporadic" ALS, making the boundaries between "sporadic" and "familial" ALS less clear. This is one of the reasons that many ALS clinics now routinely include a certified genetic counselor who can explain those complex concepts to patients and their families and offer the option of testing.

Diagnosing ALS

More than 150 years after ALS was originally described by the French Neurologist Charcot in 1869, it remains a clinical diagnosis. There is still no single test that can confirm ALS, except perhaps for genetic tests for the 10% of cases that are familial. This is why

being evaluated by a specialist in neurology is so important. There are certain symptoms and variables that need to be seen together to confirm an ALS diagnosis and, just as important, rule out other possible conditions.

Most specialists will order various tests to seek evidence that supports the diagnosis and evaluate for any other condition that might be producing the same symptoms. Those tests include blood work, electromyogram/ nerve conduction study, MRI and occasionally a lumbar puncture (spinal tap):

however, none are required to make the diagnosis of ALS.

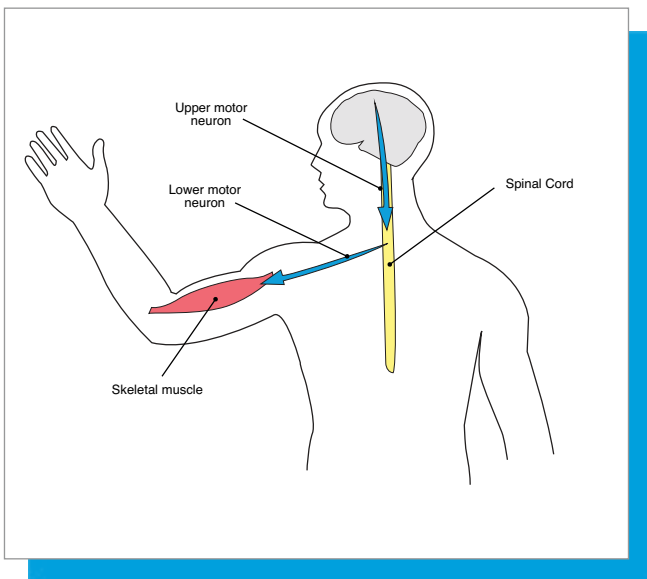


Figure 3: Upper and lower motor neurons are affected in ALS

ALS is diagnosed when a person has clinical signs indicating loss of motor neurons in different places in the body. What does this mean?

Upper motor neurons (UMN) are nerve cells that travel from the brain to the spinal cord to control movement. When they are lost, you have stiffness of the limb (spasticity), brisk reflexes (hyperreflexia), slow movements of the hands and legs (bradykinesia) that may appear as weakness and slow movements of the muscles producing your voice and speech which leads to a strained, effortful speech quality.

In addition, as we mentioned earlier, you will have loss of motor neurons in the spinal cord (the lower motor neuron). These are the nerves that run from the spinal cord to the muscle. Loss of the **lower motor neuron (LMN)** causes weakness, muscle wasting (medical term: **amyotrophy**) and muscle twitching (**fasciculations**). (See Figure 3)

Fasciculations are spontaneous twitches or movements of parts of a muscle, not the entire muscle. It is not a jerk, but a painless fluttering within the muscle. There are many causes for fasciculations (fatigue, exercise) and not all fasciculations are due to ALS. They are only one of the symptoms used to diagnosis the disease. Fasciculations are not harmful. They are simply a sign of irritation of the lower motor neuron.

ALS specialists divide the body in four regions based on the way the nerves that attach to muscles are wired: the face and tongue (**brainstem or bulbar**), the arms (**cervical**), the trunk (**thoracic**) and the legs (**lumbar**). The neurologist looks for signs of upper motor and lower motor neuron loss in each one of

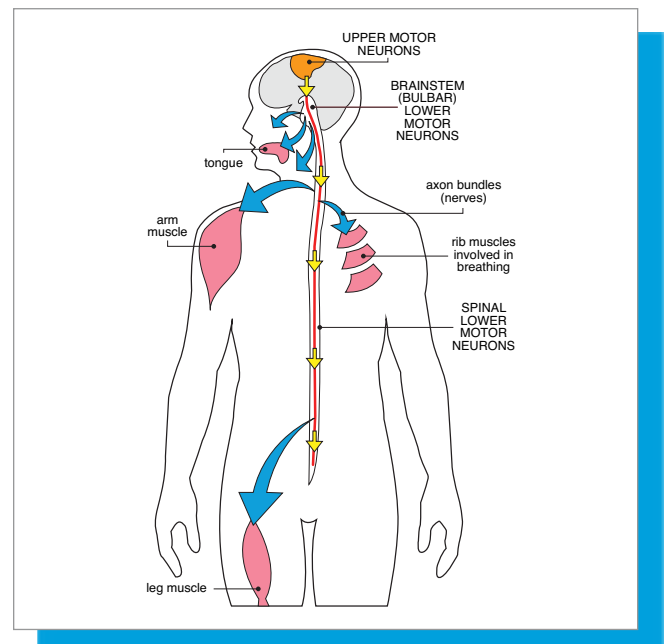


Figure 4: Upper and lower motor neuron connections in the bulbar (face and tongue), cervical (arms), thoracic (trunk) and lumbar (leg) region

these four regions of the body (see Figure 4) to determine if a patient has ALS. Ideally, a neurologist should identify those signs in at least one region to make the diagnosis.

It is not unusual to seek a second opinion after you have been given the diagnosis. Many doctors will refer you to a specialized clinical center to make sure nothing was missed.

Common Reactions to the Diagnosis

Anyone who is diagnosed with a rare, incurable disease will experience shock and disbelief. This is normal. No one expects to have a disease like this. Please discuss your concerns and fears with your neurology specialist and your ALS care team. Some individuals with ALS also find comfort in a support group setting; it can be helpful to meet other people dealing with the same illness.

How Does ALS Progress?



After the initial shock of the diagnosis, many people will want to know: "How bad is my ALS?" "How quickly is it progressing?"

This is another difficult aspect of this disease: **no two presentations are the same.** Some people have severe involvement in one area before it spreads; other persons show progression throughout the body right away. In some individuals, the disease progresses very slowly, and for others, it progresses quickly.

In general, persons with ALS live about three years after diagnosis. This is a generalization based on averages, not individuals. Individuals can live anywhere from a few months to decades depending on disease changes and the types of medical care people choose.

Research over the past two decades has allowed doctors to identify some factors that predict a worse prognosis and shorter life expectancy for persons with ALS. Those factors include older age at onset (>75), major delay in diagnosis, low body weight, bulbar onset (i.e., first symptoms being trouble talking or swallowing), presence of dementia or breathing problems at onset and certain genetic changes. Those data have led to the development of online tools and algorithms that may help predict the expected survival for each person; however, no single prediction tool is perfect, so doctors will often refrain from giving prognostic “numbers” to people with a new diagnosis of ALS unless they follow them in clinic for a sufficient amount of time to allow a better understanding of each individual’s rate of progression.

Symptoms

A person with ALS will eventually develop **weakness** (medical term: **paralysis**) of all muscles in the arms and legs and the muscles of breathing, swallowing and speaking; however, every patient is different. Some patients will have severe paralysis of one area, but little in others (e.g., unable to swallow but still able to walk and drive). Other individuals get a similar degree of involvement of different areas within a short time frame. Currently, **clinicians have no way to predict in what order a person’s ALS will progress; therefore, they follow the patient and assess symptoms periodically.**

Symptoms do not begin all at once or suddenly, even though it may feel to patients or family members as if there has been a sudden change. This is most often because we attempt to compensate for a problem until our bodies are eventually too

weak to keep it up. It is important to take notice of any small changes as they will progress over time. Discuss them early with your ALS specialists because they may be able to minimize the symptoms and can help you prepare for upcoming changes.

Eventually, you will need help with all movements: getting out of bed, moving onto a chair, getting dressed and showering. This is due to the loss of the spinal motor neurons, causing paralysis. People lose **muscle mass** and, as a result, **body weight**. Weight loss is also due in part to decreased ability to eat adequately because of eating and swallowing difficulties.

Some of the symptoms you may experience include:

- Muscle cramps or twitching
- Fatigue
- Trouble with stairs
- Trouble getting up from a chair
- Occasional falls
- Difficulty lifting items or holding a pen
- Choking on liquids or trouble swallowing certain foods
- Drooling or trouble clearing phlegm
- Poor sleep
- Shortness of breath with activity or laying down
- Changes in speech or getting tired when speaking
- Trouble with decision-making or forgetfulness
- A tendency to cry or laugh too much (medical term: **pseudobulbar affect**)

All of these symptoms are explained in more detail in other resource guides published by The ALS Association. What has been introduced in this guide is an important way of approaching ALS after diagnosis. It's essential to remember:

- Do not hesitate to make notes about any problem you notice and discuss them with your ALS care team specialists. No problem is too small to bring up.
- ALS symptoms do not change suddenly, but problems grow with time. It is much better to acknowledge a slight problem and address it right away.

Treatment and Care for ALS

Drugs

Although there is currently no cure for ALS, researchers across the globe are working diligently to find effective treatments to extend life expectancy and minimize the impact of symptoms.

There are two FDA approved drugs available for patients with ALS: riluzole (trade name: Rilutek®) and **edaravone** (trade name: Radicava®).

Riluzole is a pill, 50 mg, taken twice a day. It can be taken at any point in the disease and **has been shown to slow disease progression and prolong life by three months, on average.** Most people tolerate it well, although a minority may experience a feeling of dizziness, fatigue, nausea, loss of appetite and uncommonly abnormal liver function; for that reason, lab work may need to be done periodically.

Edaravone is available as an oral medication or an intravenous infusion. Both are administered 14 days per month for the first two months, and 10 days per month thereafter. It has been shown to

slow disease progression by about 30% in selected patients with early disease, meaning less than 2 years from symptom onset, and good functional status, i.e., able to carry out activities such as eating, walking, and toileting, without help. It is also tolerated well overall, and can be added to riluzole. 10% or more of persons taking it have reported bruising, headache, or unsteady walking.

What does this mean? This means that in large, randomized clinical trials, patients who took the medicines either lived **on average** three months longer (riluzole) or their disease progressed **on average** about 30% slower (edaravone) than those who did not take them. It does not mean those benefits are guaranteed for every person who receives the medications, because each person will respond to them differently. Neither of the two medications will make patients feel stronger or stop the disease from getting worse over time.

Some patients may say, “Why take medicine with so little effect?” Many people want to do everything possible to fight the disease and live longer with it. This is a personal decision influenced by each person’s preferences and values; it should be discussed with your doctor.

Research is being carried out with the participation of patients to look for ways of improving ALS treatments (medical term: **clinical trials**). Not all trials are available to every patient and not all trials are available at every medical center. This is a good topic to discuss with your ALS physician at an appointment. Some patients may wish to be involved, but others do not. Please know that even if you are using the drugs riluzole and/or edaravone to slow down the progression of ALS, you most likely will still be able to enroll in a clinical trial.

As of this printing, there are several promising new drugs in the pipeline, including targeted personalized-medicine approaches for persons with a particular genetic form of ALS, but no other

treatments besides riluzole and edaravone have shown enough data to convince regulatory agencies, such as the FDA, that they work for ALS. The situation is likely to change in the near future and we encourage you to stay updated on latest developments by contacting your neurologist, The ALS Association and support groups. Well-meaning friends and family may hear of someone who was “cured” by a special treatment that was found on the Internet or required traveling abroad. These are, unfortunately, just rumors. A good website for verifying if these claims are true is **ALS Untangled** at <http://www.alsuntangled.com>.

The Care Team

It takes a village to care for and help you manage ALS. Accepting help and care can be difficult at first. It is not something we are used to doing and being dependent—or worse, the fear of becoming a burden to others—are very common thoughts. However, it truly makes a difference if you are not left to tackle ALS alone. A team that works together and supports each other makes the biggest impact every step of the way.

The most important member of the care team is YOU, the person with ALS, who sets the priorities and makes all the decisions.

Your care team includes caregivers such as spouses, parents or children. It may include other relatives, friends, neighbors and other members of the community. There is usually one person who is considered the main caregiver due to being more intimately involved and in charge of the day-to-day activities and planning.

The medical care team includes many specialists. **Ideally, the person with ALS has access to a Certified Treatment Center of Excellence, a Recognized Treatment Center or clinic with expertise in ALS.** The benefit of having a professional interdisciplinary team like this lies in getting coordinated care. The members of the team communicate to make sure everybody is on the same page and work toward the same goals and priorities that the person with ALS has set forward.

Certified Center Program

The ALS Association has a Certified Treatment Center of Excellence Program that helps provide care for patients and families with ALS. A Certified Center has all the required medical professionals available to provide the best care possible including:

- **Neurologist** (Medical doctor who specializes in diseases of the muscles and nerves and committed to treating ALS)
- **Nurse or nurse practitioner**
- **Respiratory therapist (RT)**
- **Physical therapist (PT)**
- **Occupational therapist (OT)**
- **Speech-language pathologist (SLP)**
- **Dietitian (RD)**
- **Social worker (SW)**
- **Mental health professional**
- **ALS Association liaison**

Many centers offer the services of a **pulmonologist** (doctor specializing in respiratory system), **gastroenterologist** (specializing in the digestive system), **palliative care physician** (specializing in supportive care and pain management), **physiatrist** (specializing in physical and rehabilitative medicine), **psychologist and other mental health professionals.**

Instead of traveling and making separate appointments for all services needed, all of the specialists can be seen in a single clinic visit. The clinic visit may be long and tiring, but it is usually worthwhile and productive. Many patients will

bring family members and friends to these visits so everybody can ask questions and learn from all the care providers.

It has been shown that getting care in an interdisciplinary ALS specialty setting allows for extended or better quality of life.

Clinical Trials

Clinical trials are research trials with people. **Clinical trials try to answer specific scientific questions to find better ways to prevent, detect or treat ALS, or to improve care for people with ALS.** Clinical trials are geared to finding better treatments and usually occur after preliminary work is done with animals or other laboratory methods.

Once a treatment is to be tested in people, the testing is usually done in several stages:

1. A **Phase 1** study, which only involves a small number of participants, determines how a drug may affect the human body and what dose may be used.
2. A **Phase 2** study focuses on if the drug is safe and tolerated and gets a better sense of dosing and possible effects.
3. A **Phase 3** study, which usually involves a large group of participants, determines if the new treatment is working and if it is indeed better than any of the known and available treatments.

Clinical trials follow a recipe or a blueprint called a **study protocol**. It outlines the purpose of the study, how many people will participate, who is able to participate, what will be done and what information will be gathered about participants.

One of the most important parts of this recipe is **eligibility**. Eligibility criteria outline the attributes a participant must have to qualify for the study. They are worded as criteria for inclusion as well as criteria for exclusion. Usually, there must be a reasonable suspicion that a person indeed has ALS and they must be able to understand and agree to be part of research. **Having advanced**

stages of ALS, using a ventilator or living far away from the research center often make a patient not eligible to participate in a trial.

The same clinical trial is usually carried out by teams of researchers at many different places throughout the country and world. The main researcher who designed the study and oversees the research is referred to as the **principal investigator**.

Most clinical trials are done in what is called a double-blind placebo-controlled way. "Placebo-controlled" means that volunteers are divided randomly into two groups. One group will receive the actual intervention (like a new drug or invention). The other group will be given something that tastes and looks similar, but does not have any effect. "Double-blind" means that neither the researchers nor the participants know what the participant is getting until the study is concluded and the results are analyzed.

It is important that everybody who is affected by ALS considers helping with research efforts. This can be as easy as registering through the national registry and filling out questionnaires or as complicated as getting a medical device implanted. There are opportunities for research that include caregivers and other members of the care team.

The best place to look for up-to-date information on trials is www.clinicaltrials.gov. You can select ALS as the target disease and then narrow the search by geography by entering a zip code or by type of trial and recruitment status. You will find a detailed description of the trial and contact information to see if you can be considered. You may also visit The ALS Association website to look for listings of ongoing trials or research results. The Northeast ALS Consortium (NEALS) is another source of good information (www.alsconsortium.org).

Summary Statement

There is much to know about ALS, and now you have read some of the basics facts about diagnosis, progression, treatment and the role you can play in research. Some people want to know everything they can soon after diagnosis. Others prefer to learn about different aspects of living with ALS as time goes by. You get to choose your pace. Remember, there is excellent information available through The ALS Association and your ALS clinical team of experts. Use these supports—they are here to help you. Knowledge is power. It will help you understand what to expect and how to manage living with ALS as best as possible. The goal is to prevent crises and maximize quality of life.



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About The ALS Association

The ALS Association is the largest philanthropic funder of ALS research in the world. The Association funds global research collaborations, assists people with ALS and their families through its nationwide network of care and certified clinical care centers, and advocates for better public policies for people with ALS. The ALS Association is working to make ALS a livable disease while urgently searching for new treatments and a cure.