



# Amyotrophic Lateral Sclerosis

ALS is a rare neurodegenerative disease characterized by the progressive deterioration of nerve cells (motor neurons) that initiate and control muscle movement. As these cells die, the muscles they stimulate deteriorate, weaken, and eventually lose normal function

## Risk Factors



**Genetic Factors**



**Environmental Factors**



**Lifestyle Factors**



**Brain Injuries**

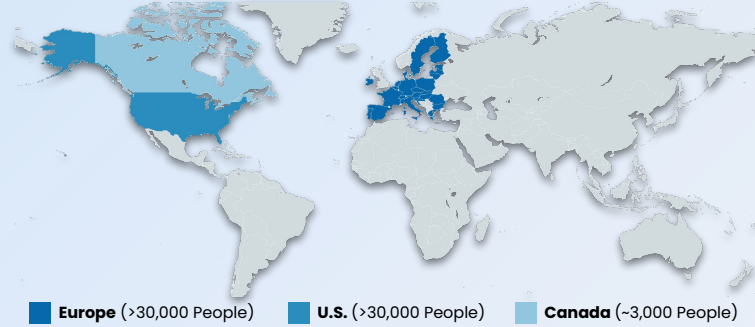


**Spinal Cord Injuries**



**Smoking**

## Global Prevalence Of ALS



**Projected living persons/cases (≥18 years) with ALS in the US in 2026**

## Types Of ALS

### Familial ALS

- At least one family member with ALS
- 10% of all ALS cases
- 60% of cases have a known disease-causing mutation

### Sporadic ALS

- No known family history of ALS
- 90% of all ALS cases
- 10% of cases have a known ALS-related mutation

## ALS Gene Mutations

### C9orf72

- Most common genetic cause of ALS
- Familial ALS: Accounts for 25 to 40% cases
- Sporadic ALS: ~6% of cases

### SOD1

- Second most common cause of familial ALS
- Familial ALS: 10 to 20% of cases
- Sporadic ALS: 1 to 2% of cases

### TARDBP

- Familial ALS: 4% of cases
- Sporadic ALS: ~1% of cases

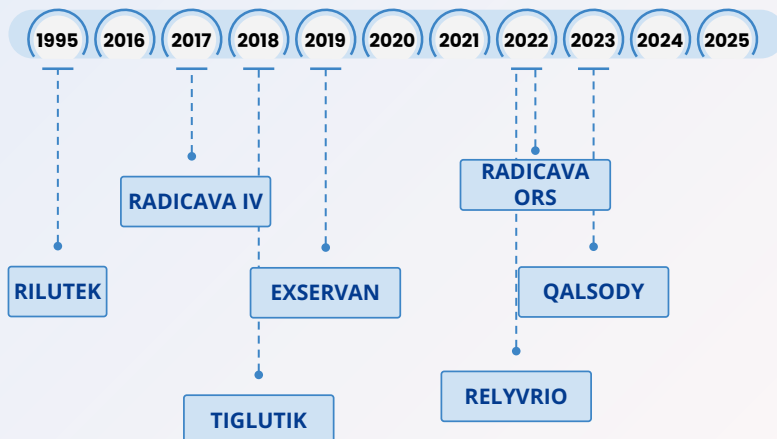
### FUS

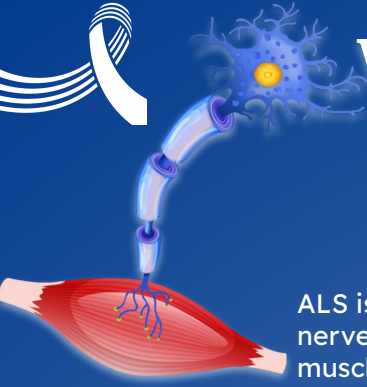
- Familial ALS: ~5% of cases
- Sporadic ALS: ~1% of cases

## Pathophysiological Differences In Familial ALS

	SOD1	TARDBP	FUS	C9orf72
Protein misfolding	✓	✓	✓	✓
Protein aggregates	✓	✓	✓	✓
Sequestration of physiological proteins	✓	✓	✓	✓
Proteasome impairment	✓	✓	✓	✓
Autophagy impairment	✓	✓	✓	✓
Hexanucleotide repeat	✗	✗	✗	✓
Dipeptide repeat	✗	✗	✗	✓
RAN translation	✗	✗	✗	✓
RNA mis-splicing	?	✓	✓	✓

## Treatment





World

# Amyotrophic Lateral Sclerosis



Day - 2026

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Environmental factors

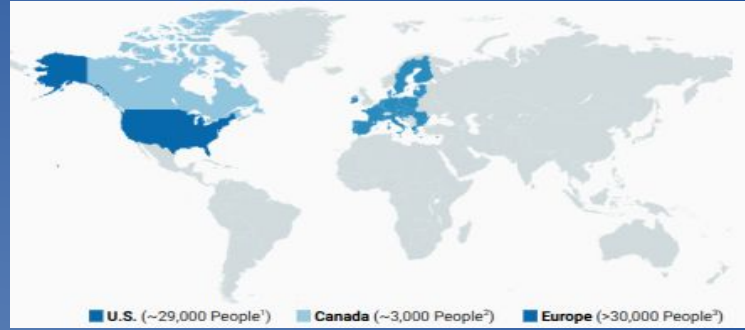
Lifestyle Factors

Brain Injury

Spinal Cord Injuries

Smoking

## Global Prevalence Of Hypertension



Projected living persons/cases (≥18 years) with ALS in the US in 2026

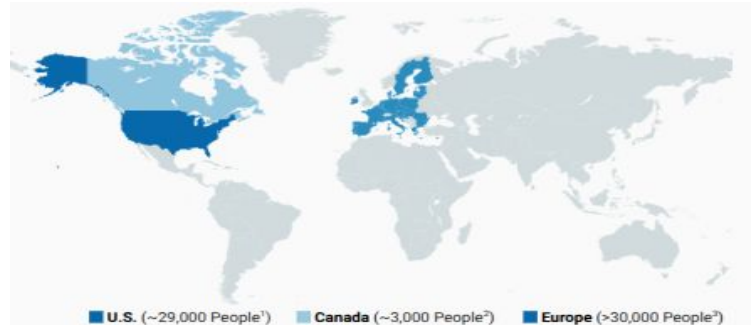
# World Amyotrophic Lateral Sclerosis Day - 2026

**DEFINITION:** ALS is a rare neurodegenerative disease that is characterized by the progressive deterioration of nerve cells (motor neurons) that initiate and control muscle movement. As these cells die, the muscles they stimulate deteriorate, weaken, and eventually lose normal function

## RISK FACTORS

- Genetic Factors
- Environmental factors
- Lifestyle Factors
- Brain Injury
- Spinal Cord Injuries
- Smoking

## GLOBAL PREVALENCE



Projected living persons/cases ( $\geq 18$  years) with ALS in the US in 2026

## TYPES OF ALS

	Definition	Prevalence	Causes
Familial ALS	<p>At least one family member with ALS</p>	Roughly 10% of all ALS cases	About 60% of cases have a known disease-causing mutation.
Sporadic ALS	<p>No known family history of ALS</p>	Around 90% of all ALS cases	Environmental and lifestyle factors play a larger role. Only 10% of cases have a known ALS-related mutation.

## SYMPTOMS

- Muscle twitches in the arm, leg, shoulder, or tongue
- Muscle cramps
- Tight and stiff muscles (spasticity)
- Muscle weakness affecting an arm, a leg, or the neck
- Slurred and nasal speech
- Difficulty chewing or swallowing



## TREATMENT

- Qalsody (tofersen)
- Radicava (edaravone)
- Riluzole (Rilutek, Tiglutik, and Exservan )
- Nuedexta (dextromethorphan HBr and quinidine sulfate)

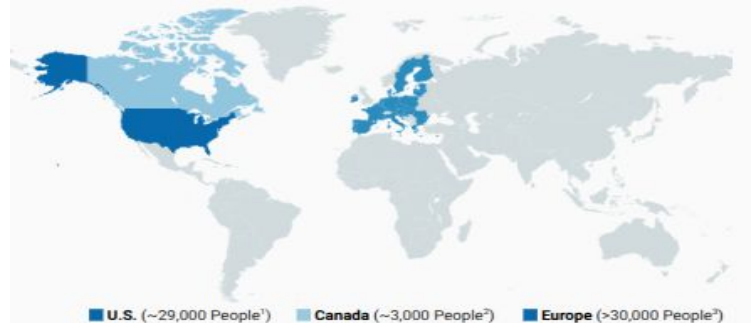
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## PATHOPHYSIOLOGICAL DIFFERENCES AMONG DIFFERENT FAMILIAL ALS

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Protein aggregates				
Sequestration of physiological proteins				
Proteasome impairment				
Autophagy impairment				
Hexanucleotide repeat				
Dipeptide repeat				
RAN translation				
RNA mis-splicing				

## TREATMENT

