Journal of Clinical Research, Reports and Trails (JCRRT)

OLITES PUBLISHERS
A Global Approach For Research

Open Access

Research paper

# Beyond the Dying Motor Neuron: Amyotrophic Lateral Sclerosis in the Era of Precision Medicine

**Weimer F, Cawson H, Chipika W, Burton T, Labrunie J, Claypool L**
Department of Neurology, Israel
***Corresponding Author:** Cawson H, Department of Gastroenterology, Belgium
**Citation:** Cawson H (2026). Beyond the Dying Motor Neuron: Amyotrophic Lateral Sclerosis in the Era of Precision Medicine V2 (1)

**Received date:** February 10 2026**: Accepted date:** February 25, 2026**: Published date:** March 02,2026

**Keywords:** Amyotrophic Lateral Sclerosis, ALS, Motor Neuron Disease, Neurodegeneration, Precision Medicine, Gene Therapy, Biomarkers, Riluzole, Edaravone

## Abstract

**Background:** Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disorder characterized by the degeneration of upper and lower motor neurons, leading to muscle weakness, paralysis, and respiratory failure. Despite significant advances in neuroscience, ALS remains an incurable disease with complex genetic and environmental etiologies.

**Objective:** This article provides a comprehensive overview of ALS, including its epidemiology, pathophysiology, risk factors, clinical manifestations, diagnostic approaches, treatment strategies, and emerging therapeutic developments.

**Methods:** A narrative review was developed using current scientific knowledge from peer-reviewed literature, clinical practice guidelines, and recent advances in molecular biology and precision medicine

**Results:** ALS affects approximately 2–3 individuals per 100,000 population annually, with both sporadic and familial forms contributing to disease burden. Advances in genetic testing have identified several disease-associated genes, including *C9orf72*, *SOD1*, *TARDBP*, and *FUS*. Although disease-modifying therapies remain limited, newer targeted treatments, gene therapies, stem cell research, and biomarker discoveries have expanded the therapeutic landscape.

**Conclusion:** Early diagnosis, multidisciplinary care, personalized treatment strategies, and continued research into disease mechanisms are essential for improving survival and quality of life in individuals with ALS. Future precision medicine approaches hold promise for transforming ALS management

## Introduction

Amyotrophic Lateral Sclerosis (ALS), commonly known as Lou Gehrig's disease, is a rapidly progressive neurodegenerative disorder that selectively affects upper motor neurons in the cerebral cortex and lower motor neurons located in the brainstem and spinal cord. Progressive degeneration of these neurons disrupts voluntary muscle control, resulting in weakness, muscle wasting, fasciculations, dysarthria, dysphagia, and respiratory insufficiency.

ALS is one of the most devastating neurological diseases due to its relentless progression and limited treatment options. The median survival following diagnosis ranges from 2 to 5 years, although a small proportion of patients survive for more than a decade. Increasing knowledge of molecular genetics and neurobiology has revolutionized the understanding of ALS, creating opportunities for personalized therapeutic interventions

## Epidemiology

ALS occurs worldwide with relatively consistent incidence.

- Annual incidence: 1.5–2.5 cases per 100,000 people
- Prevalence: 5–8 cases per 100,000 population
- Peak onset: 55–75 years
- Men are affected slightly more frequently than women.
- Approximately 90–95% of cases are sporadic.
- About 5–10% are familial with inherited genetic mutations.

Improved diagnostic awareness and longer survival have contributed to increasing prevalence in many countries.

Pathophysiology

ALS involves multiple interconnected pathogenic mechanisms

## Motor Neuron Degeneration

Journal of Clinical Research, Reports and Trails (JCRRT)

Loss of upper and lower motor neurons produces progressive muscle weakness and paralysis.

### Protein Misfolding

Abnormal accumulation of proteins such as:

- TDP-43
- SOD1
- FUS

results in neuronal dysfunction and cell death.

### Glutamate Excitotoxicity

Excess glutamate overstimulates neurons, increasing intracellular calcium and triggering apoptosis.

### Oxidative Stress

Free radicals damage DNA, proteins, lipids, and mitochondria, accelerating neuronal degeneration.

### Neuroinflammation

Activated microglia and astrocytes release inflammatory cytokines that contribute to neuronal injury.

### Mitochondrial Dysfunction

Impaired energy production reduces neuronal survival and promotes oxidative damage.

Diagnosis

There is no single diagnostic test for ALS.

Diagnosis relies on clinical evaluation combined with exclusion of other neurological disorders

Clinical Criteria

- Progressive motor weakness
- Upper motor neuron signs
- Lower motor neuron signs
- Spread of symptoms to multiple body regions

Investigations

### Electromyography (EMG)

Demonstrates widespread denervation and reinnervation.

### Nerve Conduction Studies

Help exclude peripheral neuropathies.

### Magnetic Resonance Imaging (MRI)

Rules out cervical myelopathy, tumors, and multiple sclerosis.

### Genetic Testing

Recommended for familial ALS and selected sporadic cases.

### Pulmonary Function Tests

Evaluate respiratory muscle strength.

### Supportive Management

Comprehensive multidisciplinary care significantly improves outcomes.

### Physical Therapy

Maintains mobility and reduces contractures.

### Occupational Therapy

Promotes independence through adaptive equipment.

### Speech Therapy

Supports communication and swallowing.

### Nutritional Support

High-calorie nutrition delays weight loss.

Percutaneous endoscopic gastrostomy (PEG) may become necessary.

### Respiratory Care

Non-invasive ventilation improves survival and quality of life.

Emerging Therapies

Several promising approaches are under investigation.

### Stem Cell Therapy

Mesenchymal stem cells may provide neuroprotection and reduce inflammation.

### Gene Editing

CRISPR-based technologies aim to correct pathogenic mutations.

### Biomarker Development

Blood and cerebrospinal fluid biomarkers such as neurofilament light chain (NfL) facilitate early diagnosis and disease monitoring.

## Artificial Intelligence

Machine learning models are increasingly being used for:

- Early diagnosis
- Disease progression prediction
- Clinical trial optimization
- Imaging analysis

## Future Perspectives

Recent advances suggest that ALS management is entering a precision medicine era. Personalized genetic therapies, biomarker-guided treatment selection, stem cell interventions, and artificial intelligence-assisted diagnostics are expected to transform clinical practice. Earlier diagnosis through molecular biomarkers and improved understanding of disease heterogeneity may enable interventions before irreversible neuronal loss occurs.

## Conclusion

Amyotrophic Lateral Sclerosis remains one of the most challenging neurodegenerative disorders due to its rapid progression and limited therapeutic options. Advances in molecular genetics have significantly expanded our understanding of disease mechanisms, paving the way for personalized medicine. While current treatments primarily slow disease progression and improve symptom management, emerging gene-targeted therapies, stem cell research, biomarker discovery, and artificial intelligence offer hope for more effective interventions. Continued investment in multidisciplinary care, early diagnosis, and translational research is essential to improve survival, enhance quality of life, and ultimately achieve disease-modifying or curative therapies for individuals living with ALS.

## References

1. Atassi N, Berry J, Shui A, Zach N, Sherman A, Sinani E, et al. The PRO-ACT database: design, initial analyses, and predictive features. Neurology. 2014;83(19):1719–25.
2. Belosludtseva, N.V.; Dubinin, M.V.; Belosludtsev, K.N. Pore-Forming VDAC Proteins of the Outer Mitochondrial Membrane: Regulation and Pathophysiological Role. Biochemistry 2024, 89, 1061–1078.
3. Hsiao, Y.H.; Chen, Y.T.; Tseng, C.M.; Wu, L.A.; Perng, D.W.; Chen, Y.M.; Chen, T.J.; Chang, S.C.; Chou, K.T. Sleep disorders and an increased risk of Parkinson's disease in individuals with non-apnea sleep disorders: A population-based cohort study. J. Sleep. Res. 2017, 26, 623–628.
4. Quaranta, V.N.; Carratù, P.; Damiani, M.F.; Dragonieri, S.; Capozzolo, A.; Cassano, A.; Resta, O. The Prognostic Role of Obstructive Sleep Apnea at the Onset of Amyotrophic Lateral Sclerosis. Neurodegener. Dis. 2017, 17, 14–21
5. Gunnarsson, L.-G.; Bodin, L. Amyotrophic Lateral Sclerosis and Occupational Exposures: A Systematic Literature Review and Meta-Analyses. Int. J. Environ. Res. Public Health 2018, 15, 2371.
6. Niccolai, E.; Pedone, M.; Martinelli, I.; Nannini, G.; Baldi, S.; Simonini, C.; Di Gloria, L.; Zucchi, E.; Ramazzotti, M.; Spezia, P.G.; et al. Amyotrophic Lateral Sclerosis Stratification: Unveiling Patterns with Virome, Inflammation, and Metabolism Molecules. J. Neurol. 2024, 271, 4310–4325.

Journal of Clinical Research, Reports and Trails (JCRRT)


DOI:10/JCRRT/2026/012