Living with ALS

Guide for Researchers and Research Funders

Congress requested that the National Academies of Sciences, Engineering, and Medicine convene a committee of experts to recommend actions public, private, and nonprofit sectors should undertake to make amyotrophic lateral sclerosis (ALS) a livable disease within 10 years. This included considering pathways for developing more effective and meaningful treatments as well as a cure; identifying the type and range of care and services people with ALS and their families need; and ensuring equitable access to comprehensive care to improve quality of life.

The committee recognizes that researchers and research funders play a critical role in building a more comprehensive system of care for ALS; therefore, the committee's report makes recommendations specifically for this audience as follows:

EXPAND ALS TRANSLATIONAL RESEARCH

Researchers have identified a wide range of potential therapeutic pathways, drug targets, and genes associated with ALS, many of which are currently being pursued. However, the heterogeneity and complex biological pathways of ALS have slowed the translation of this research into safe, effective drugs for people living with ALS.

It is important that researchers and research funders aim to increase understanding of how ALS develops within the body over time by identifying better biomarkers, indicating potential pathophysiological targets, and allowing for better measurement of the development of ALS. Programs currently in development under the Accelerating Access to Critical Therapies for ALS Act (ACT for ALS) are an opportunity for researchers and research funders from academia, government, and the private sector to set a research agenda aimed at making ALS a more livable disease.

The ALS-focused, public–private partnerships created under ACT for ALS should consider additional translational research priorities that would accelerate therapeutic developments in ALS (see Recommendation 5-2 in the report). These topics could include:

- **Disease staging, especially the preclinical and prodromal stages**
- **A comprehensive, robust, and indefinitely ongoing natural history study across diverse patient populations, disease stages, and ALS phenotypes**
- **Biomarker development**
- **New therapeutic targets derived from a better understanding of sporadic ALS**
- **Plateaus in ALS progression**

- **Novel drug delivery methods and ALS patient-friendly formulations**
- **Trade-offs between earlier access and safer, more effective drug development**
- **Improvement in the expanded access pathway**

FUND RESEARCH TO YIELD NEAR-TERM GAINS IN QUALITY OF LIFE

Nonpharmacologic interventions can help treat secondary symptoms of ALS that often go overlooked or untreated, including the effects of ALS on mental health and well-being. Technical advances have introduced many new tools that may also provide support for persons with ALS and their families, while improving quality of life at home. Investing in research to understand what works best of the currently available ALS interventions is important.

Opportunities also exist for participatory research that includes people with ALS, their caregivers, and their families to inform larger ALS research efforts. Development of new technologies, outcome measures, and other emerging tools can engage people with ALS while prioritizing equity and privacy.

The National Institutes of Health (NIH), the National Institute of Neurological Disorders and Stroke (NINDS), the Agency for Healthcare Research and Quality, and other ALS research funders should prioritize research to learn what works best in ALS care and increase support for other critical areas of ALS research that are currently neglected but would yield near-term gains in quality of life for persons with ALS (see Recommendation 5-4 in the report). These topics could include:

- **Health services research**
- **Rehabilitative therapy; physical therapy; speech and language, respiratory, and other nonpharmacologic interventions**
- **Social and behavioral research, especially into the intersection of clinical care and social connections**
- **ALS risk and protective factors related to disease progression and trajectory**
- **Development of ALS following trauma**
- **Clinical outcome measures for function, survival, and quality of life**
- **Emerging technologies focused on at-home end user needs**
- **Diagnostic artificial intelligence in electronic medical records and medical search engines**

CREATE AN ALS CLINICAL TRIALS NETWORK

The ALS therapeutic development space is characterized by many cross-sector collaborations including stakeholders in industry, academia, the federal government, and nonprofit organizations. Each ALS research initiative or network is uniquely structured and funded to meet its mission.

While every cooperative endeavor provides a useful resource, the differences among them make it difficult to integrate results and to maximize any individual trial. Fragmentation also keeps data siloed and hampers the development of the ALS clinical trial workforce. A centralized ALS clinical trials network led by NIH would build on current networks while improving data sharing, research infrastructure, equity in enrollment, community engagement, governance, and the diffusion of innovative techniques. Similarly structured networks for cancer, for example, have benefited from NIH leadership.

NINDS should ensure the existence of a dedicated ALS clinical trials network distributed across diverse geographic regions in the United States, coordinated and funded by NIH (see Recommendation 5-1 in the report).

To access the full report and supporting materials, visit https://nationalacademies.org/Living-with-ALS.

Health and Medicine Division