CO121

Analysis of the Burden of Illness, Treatment, and Health Disparities in Amyotrophic Lateral Sclerosis

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BACKGROUND

- Amyotrophic lateral sclerosis (ALS), which is the most common form of motor neuron disease, is a neurodegenerative disorder characterised by the weakness of voluntary muscles due to the degeneration of motor neurons located in the brain, brainstem, and spinal cord.[1]
- Common ALS phenotypes include bulbar onset and spinal onset.
- There is no cure for ALS, and individuals typically die from respiratory failure within 2 to 4 years of diagnosis.[2]

OBJECTIVE

- To review the literature on burden of illness and treatment of ALS and to highlight disparities in the disease and management.

METHODS

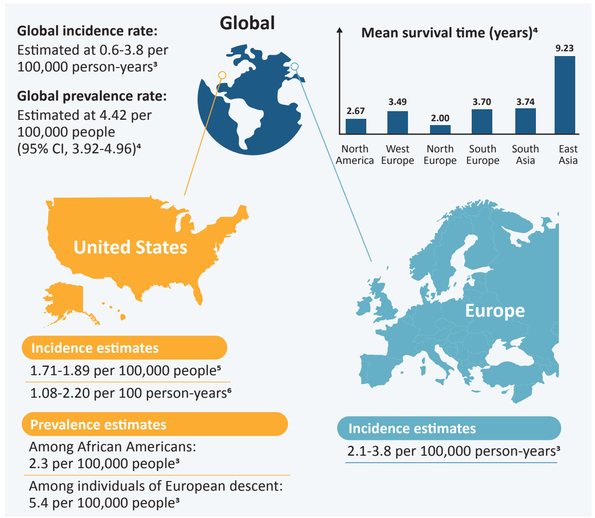
- A structured review of articles published between 9 May 2019 and 4 July 2024 was conducted, examining aspects such as disease description, epidemiology, humanistic and economic burden, treatment guidelines, treatment patterns, and health disparities.

RESULTS

Epidemiology

- Incidence and prevalence tend to be greater than global estimates in regions with high proportions of people of European descent, such as Europe and North America. In the United States (US), there is a greater prevalence of ALS among individuals of European descent compared with African Americans (**Figure 1**).

Figure 1. Global Incidence, Prevalence, and Survival Estimates



CI = confidence interval.
Sources: Longinetti and Fang[3]; Xu et al.[4]; Feldman et al.[5]; Wolfson et al.[6]

RESULTS (continued)

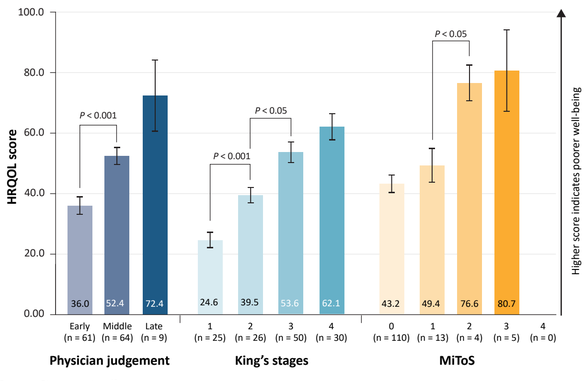
Clinical Burden

- The classical form of ALS is characterised by the impairment of upper motor neurons (UMNs) in the brain motor cortex and of lower motor neurons (LMNs) in the brainstem and spinal cord. The selective degeneration of UMNs and LMNs causes motor dysfunction in bulbar, cervical, thoracic, and lumbar segments, resulting in diverse ALS phenotypes.[1]
- Symptoms of disease progression include motor changes, which are associated with the loss of muscle strength, balance, and coordination and result in reduced exercise tolerance and increasing limitations in activities and self-care.[7,8]
- Fatigue is experienced by almost 50% of patients with ALS and is associated with lower functional status and poorer health-related quality of life (HRQOL).[8]
- ALS affects the motor neurons, causing loss of strength in the extremities, problems eating and speaking, and respiratory issues.[9]
- Patients with ALS are also at risk of increased prevalence of pain and depression.[9]
- The King's staging and ALS–Milano-Torino staging (MiToS) systems are used to monitor ALS patients' disease progression and survival (in both systems, higher scores indicate greater disease severity). Disease progression typically follows a sequential stage-by-stage pattern, with mortality risk escalating at each subsequent stage.[2]

Humanistic Burden

- The Amyotrophic Lateral Sclerosis Assessment Questionnaire–40 items (ALSAQ-40) and the shortened version, ALSAQ-5, are recommended and validated instruments for assessing HRQOL in people with ALS.[10]
- Functional status and anxiety have been shown to be the most important factors that negatively affect HRQOL.[11]
- Patients at later, more severe stages of ALS had worse well-being than those in earlier stages of the disease (**Figure 2**).[12]

Figure 2. HRQOL in Patients at Different Stages of ALS (ALSAQ-5)



Source: Stenson et al.[12]

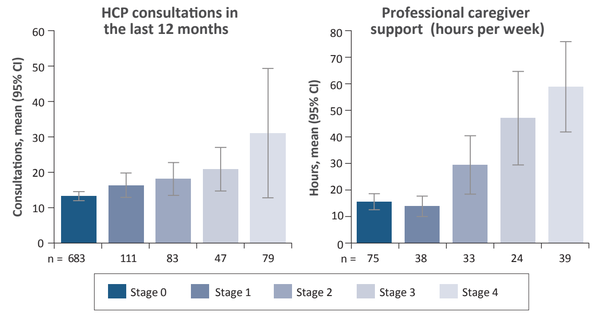
- Caregivers of people with ALS experience significant burden. In a European survey study of 82 caregivers, 37% reported a change to their working arrangements; 50% of this group had either reduced hours or stopped work.[13]

Economic Burden

Healthcare Resource Use (HCRU)

- A survey in the US and Europe found that ALS patients with higher MiToS stages (≥ 1) and faster disease progression had increased HCRU **(Figure 3)**.[14]

Figure 3. HCRU by MiToS Stage in the Overall Population

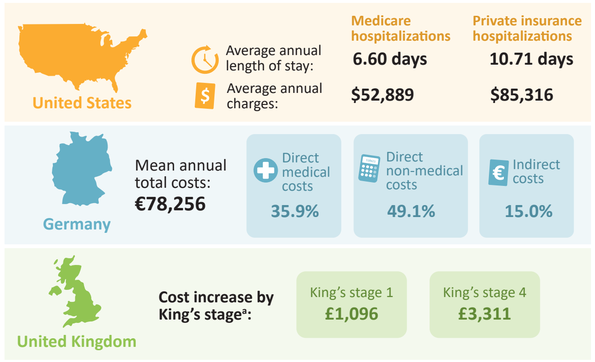


HCP = healthcare professional.
Source: Gebrehiwet et al.[14]

HCRU and Costs (Figure 4)

- Private insurance had higher hospital costs and longer stays than Medicare, suggesting possible Medicare undertreatment (US study, 2016 National Inpatient Sample data).[15]
- In a United Kingdom (UK) study[16]:
  - Costs increased between King's stages from £1,096 in stage 1 to £3,311 in stage 4 over a 3-month period.
  - MiToS staging showed unclear cost association, with stage 0 patients having the lowest cost of £1,115 (95% CI, £937-£1,130) and stages 1 to 4 incurring higher costs.
  - Secondary care costs were higher than primary care costs in all health states except for those in MiToS stage 4.
  - Patients with bulbar-onset ALS had higher costs in every cost category compared with other onset types.

Figure 4. HCRU and Costs for US, UK, and Germany



[a]Estimates at 3 months.
Sources: Aggarwal et al.[15]; Moore et al.[16]; Schönfelder et al.[17]

Indirect Costs (Figure 5)

Figure 5. ALS-Associated Average Annual Costs in the US and Germany

Sources: Schönfelder et al.[17]; Gautam et al.[18]

Racial and Ethnic Differences

- Significant differences were found in HCRU among patients with ALS in different racial/ethnic groups.[19]
- Significant diagnostic delays are common and have been reported to be longer for Black versus non-Hispanic White patients.

Treatments

Table 1. Summary of Treatments Approved for ALS

Drug molecules (brand name)	Indication	US (FDA approval)	EU (EMA approval)
Riluzole oral tablets (Rilutek)	Treatment of ALS	✓	✓
Quinidine sulfate and dextromethorphan hydrobromide (Nuedexta)	Treatment of ALS and its associated symptoms	✓	✗
Edaravone (Radicava)	Treatment of ALS	✓	✗
Riluzole oral suspension (Tiglutik)	Treatment of ALS and its associated symptoms	✓	✗
Riluzole oral film (Exservan)	Treatment of ALS and its associated symptoms	✓	✗
Riluzole oral film (Zentiva)	Treatment of ALS to extend life or the time to mechanical ventilation	✗	✓
Sodium phenylbutyrate and tauroursodeoxycholic acid or AMX0035 (Relyvrio)	Treatment of ALS in adult patients (withdrawn in US in April 2024)	✓	✗
Tofersen (Qalsody)	Treatment of ALS caused by *SOD1* gene mutations	✓	✓

Sources: Exservan PI[20]; Li and Bedlack[21]; Nguyen[22]; Qalsody SmPC[23]; Rilutek SmPC[24]; Riluzole SmPC[25]; Saini and Chawla[26]; Sun et al.[27]; Makam et al.[28]

CONCLUSIONS

- ALS continues to present a substantial clinical, humanistic, and economic burden. Despite recent treatment developments, significant unmet needs and disparities remain, warranting further research and innovation.
- None of the available treatments can cure ALS or stop disease progression, and they only have modest effects on prolonging median survival or reducing the rate of disease progression.

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