Healthcare Resource Utilization (HCRU) by Disease Stage for People with Amyotrophic Lateral Sclerosis (pALS) in the French National Health Data System (SNDS)

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Objective

- The aim of this study was to analyze the healthcare resource use (HCRU) in pALS across disease stages and to compare HCRU between ALS and non-ALS populations in France between 2012 and 2019.

Conclusions

- HCRU burden persists across all stages of progression and increases with advanced disease, highlighting the potential value of delaying progression into a more resource-intensive stage.
- As the disease progresses, a decrease in the consumption of outpatient and ambulatory resources was seen in pALS in France, accompanied by a corresponding increase in in-patient health care use whether in short term institutions, aftercare and rehabilitation or home care. Our findings highlight the importance of alternative care settings and support services to manage the complex needs of pALS, especially in advanced stages.
- These real-world findings demonstrate a significant healthcare burden related to the management of pALS compared to the non-ALS population.

Introduction

- Amyotrophic lateral sclerosis (ALS) is a rare, fatal neurodegenerative disease characterized by progressive loss of upper and lower motor neurons.
- Therapeutic management of ALS requires multi-disciplinary care, resulting in extensive HCRU. To our knowledge, no studies have characterized HCRU in pALS in France, despite its high burden on patients, caregivers and the healthcare system.
- An ALS staging system can be beneficial to provide a proxy measure of disease evolution and to describe the required resources for each stage. There are two validated staging criteria in ALS; King's and MiToS. These are commonly used in clinical practice and rely on the patient reported outcome measure ALSFRS-R. Considering that this scale is not captured in medico-administrative claims databases, we developed a staging system to group individuals into 3 stages: early, middle and late-stage ALS, based on clinical input from ALS experts and survey data.

Methods

Study Design

- A retrospective longitudinal study was conducted among newly diagnosed pALS identified between 2012 and 2019 in the French National Health Data System, SNDS. pALS were identified as having at least 2 events (or 1 event in the case of death) within 6 months:
  - Reimbursement of riluzole (which is only approved for use in ALS) and/or
  - Diagnosis of MND (International Classification of Diseases, Tenth Revision code G12.2) recorded during a hospitalization or registration in the long-term illness list.
- People who had at least one diagnosis for Parkinson disease, Multiple sclerosis, and other conditions within G12 (spinal muscular atrophy and related syndromes), 6 months after the first ALS event were excluded.
- A symptom- and milestone-based algorithm was built using available information in the SNDS database to define progression stages in ALS: early, middle, and late (Table 1). Stage onset was determined by the first occurrence of an event defining that stage (from the 2-year pre-index date until the end of follow-up). Disease progression to a later stage was irreversible.
- HCRU was evaluated in incident pALS from the first recorded event and stratified by disease progression stage. HCRU was compared in pALS and their matched non-ALS controls (matching ratio 1:3 based on year of birth, age, sex, and region). Hospital health care consumption was retrieved from the national discharge database (*Programme de Médicalisation des Systèmes d'Information,* PMSI) which includes acute hospital stays (*Medicine, Surgery, Obstetrics,* MCO), Home Care (HAD), and Rehabilitation Care (SSR).
- Hospitalizations were analyzed in MCO as follows: all-cause hospitalizations were defined as any hospitalization occurring in MCO. ALS as the primary diagnosis was defined as any hospitalization occurring in MCO with MND as the primary diagnosis (ICD-10 code G12.2). One-day hospitalization was defined when admission date is equal to discharge date, as opposed to inpatient hospitalizations lasting at least 24 hours. Intensive care unit (ICU) hospitalizations admissions were defined as any admission occurring in an ICU department.
- Consultations correspond to outpatient (*Actes et consultations externes*, ACE) and ambulatory care. ACE does not cover one-day hospitalizations. In France, pALS can be seen during multidisciplinary consultations usually delivered in excellence centers. However, the granularity of SNDS does not allow to capture these type of encounters.
- Comparative statistical analyses were performed using Paired t-test and Chi-square exact test.

Results

Population characteristics

- Between 2012 and 2019, we identified 18,289 incident cases in adults. There was a slight male predominance (56.1%) and the average age at diagnosis was 68.4 (standard deviation 12.5) years. The majority of pALS (73.6%) received treatment with riluzole, the only approved therapy to treat ALS in France.

HCRU across disease stage

- Over the study period, 11,215, 15,098, and 16,025 cases were identified in the early, middle, and late stages of ALS, respectively.
- For all cause and hospitalizations where ALS was the primary diagnosis, the proportion of patients having at least one event increased as the disease advances from early to mid stage and decreased from mid to late. The proportion of patients experiencing at least one inpatient hospitalization and admission to intensive care unit increased significantly as the disease progressed to the late stage ($p<0.01$) (Figure 1).
- Home care hospitalizations and admissions to rehabilitation centers were more prevalent in later stages compared to the early stage (Figure 1).
- The rates for MCO hospitalizations in patient-years (PY) are presented in Table 2 for early, middle, and late stages.
- The percentage of patients with at least one consultation with physicians (all specialties) remained high in the early and mid-stages, decreasing slightly in the late stage. Underutilization of outpatient and ambulatory care in late-stage ALS, including consultations with neurologists (Figure 2), may suggest a greater need for inpatient care. This can be seen through the increase of hospitalization rates in MCO as the disease the progresses, along with the increase on the proportion of patients having at least one admission in home care and rehabilitation.
- The rates of consultations in patient-years (PY) for early, middle, and late stages are presented in Table 3.

HCRU for ALS vs non-ALS population

- When comparing ALS to the non-ALS population, pALS were more likely to be hospitalized in MCO, across all types of hospitalizations. Home care and rehabilitation care were also more prevalent in ALS patients than non-ALS controls (Figure 3).
- In addition, the hospitalization rates were significantly higher for pALS ($p<0.01$) (Table 4).
- pALS were significantly more likely to have consultations than their matched controls (Figure 4). Also, patients with ALS exhibited significantly higher rates across all specialties, indicating their greater need for specialized medical attention ($p<0.01$) (Table 5).
- General practitioners seemed to play a prominent role in ALS care management, with higher consultation rates compared to neurologists (8.6 and 0.9 PY, respectively). These findings are consistent with previous research on multiple sclerosis in France using the SNDS database reporting more frequent consultations to general practitioners (9.6 and 0.9 PY, respectively)[3].

Limitations

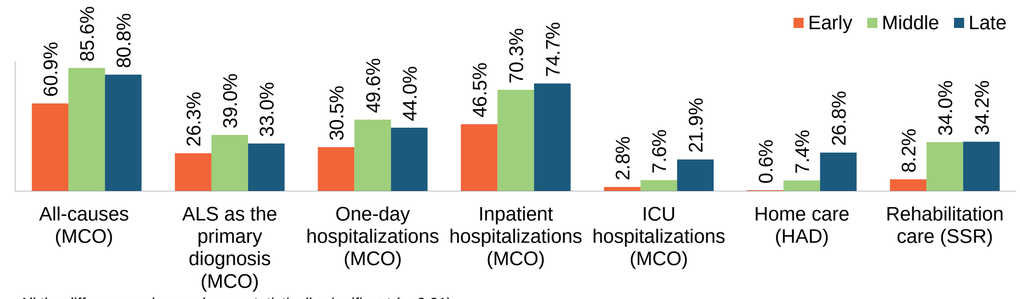
- For outpatient consultations (ACE), there is some uncertainty around the quality of coding for physician' specialties in SNDS, which is set by default as general medicine, when in reality it took place with neurologist or any other specialty, with no possibility of distinguishing them. Overall, the utilization of outpatient care is likely not comprehensively described due to multidisciplinary visits not being captured in SNDS.
- While statistically significant differences were observed across subgroups, the large sample size may have introduced a greater probability of Type II errors. No mathematical correction was made for multiple comparisons. Additional dedicated studies are needed to confirm the results.

Table 1. Definition of early, mid, and late ALS stages

Early	Middle	Late
Initiation of oral form riluzole	Initiation of liquid form riluzole	Communication aids devices
First MND diagnosis	Initiation of anti-cholinergic drugs	Parenteral nutrition use
First consultation with Neurologist	Initiation of spasticity drugs	Admission to palliative care
Electromyography	Reimbursement of positioning splints/ orthoses, walking sticks, wheeled walkers and manual wheelchair	Reimbursement of electric wheelchair
Measurement of conduction velocities	Enteral nutrition use, Placement of gastrostomy	Respiratory failure
Signs and symptoms (Cramps and spasms, Fasciculations, Unspecified abnormal involuntary movements, Abnormalities of gait and mobility, lack of coordination, Abnormal reflex, Malaise and fatigue, Dysarthria, Mild malnutrition)	Signs and symptoms (Dysphagia, Disturbances of salivary secretion, Dyspnea, Moderate to severe malnutrition)	Non-invasive ventilation > 12 hours Invasive ventilation Tracheostomy Tracheal suction
AND not having the events defining mid- and late-stage ALS	Non-invasive ventilation < 12 hours Pneumonia	Death
	AND not having the events defining late-stage ALS	

Stage definitions were developed with involvement with disease experts and adapted from Adelphi ALS Disease-Specific Programme™[1]
Information available in SNDS were leveraged to build this staging system such as outpatient reimbursed healthcare expenditures including consultations with healthcare professionals (diagnosis or reason of consultation not available), medications, registration in Long Term Disease regimen for chronic diseases, procedure codes, medical devices, reasons for hospital admissions using ICD-10 diagnoses codes.

Figure 1. Hospitalization (MCO/ HAD/ SSR) by disease stage



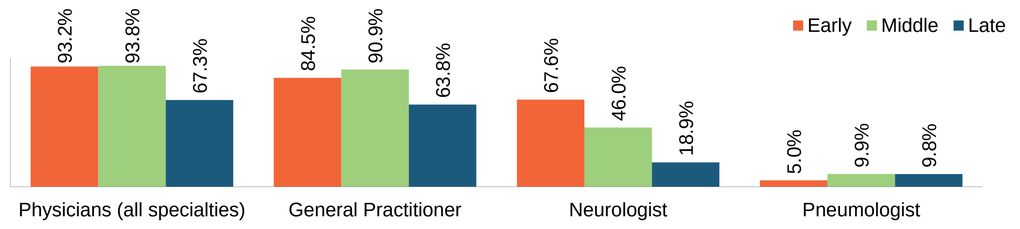
All the differences observed were statistically significant ($p<0.01$)

Table 2. Hospitalization rate in patient-years (MCO) by disease stage

	Early	Middle	Late
All-cause hospitalizations (rate in PY)	1.46	1.66	2.82
ALS as the primary diagnosis (rate in PY)	0.38	0.34	0.44
One-day hospitalization (rate in PY)	0.57	0.61	0.98
Inpatient hospitalization (rate in PY)	0.88	1.05	1.83
ICU hospitalization (rate in PY)	0.04	0.06	0.33

All the differences observed were statistically significant ($p<0.01$)

Figure 2. Consultations (ambulatory and outpatient) to specialties by disease stage



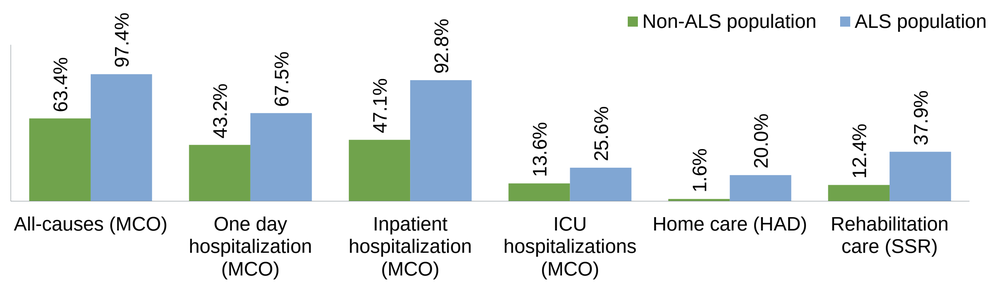
All the differences observed were statistically significant ($p<0.01$)
Physicians (all specialties) include general practitioner (GP), neurologist, pneumologist, ophthalmologist, neurosurgeon, psychiatrist, occupational therapy, geneticist, and other

Table 3. Consultations (ambulatory and outpatient) rates in patient-years by disease stage

	Early	Middle	Late
Physicians (all specialties) (rate in PY)	13.8	13.8	11.1
General Practitioner (rate in PY)	7.9	9.1	8.1
Neurologist (rate in PY)	1.9	0.8	0.4
Pneumologist (rate in PY)	0.1	0.2	0.3

All the differences observed were statistically significant ($p<0.01$)

Figure 3. Hospitalization (MCO/ HAD/ SSR) for ALS vs non-ALS population



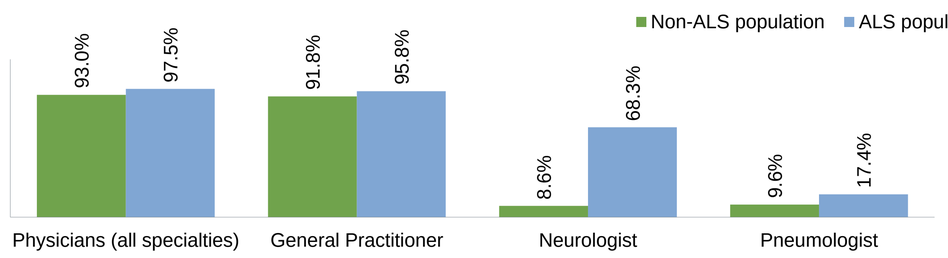
All the differences observed were statistically significant ($p<0.01$)

Table 4. Hospitalization (MCO) rates in patient-years for ALS vs non-ALS population

	Non-ALS population	ALS population
All-cause hospitalizations (rate in PY)	0.45	1.98
One-day hospitalization (rate in PY)	0.16	0.69
Inpatient hospitalization (rate in PY)	0.28	1.29
ICU hospitalization (rate in PY)	0.04	0.16

All the differences observed were statistically significant ($p<0.01$)

Figure 4. Consultations (ambulatory and outpatient) to specialties for ALS vs non-ALS population



All the differences observed were statistically significant ($p<0.01$)
Physicians (all specialties) include general practitioner (GP), neurologist, pneumologist, ophthalmologist, neurosurgeon, psychiatrist, occupational therapy, geneticist, and other

Table 5. Consultations (ambulatory and outpatient) rates in patient years for ALS vs non-ALS population

	Non-ALS population	ALS population
Physicians (all specialties) (rate in PY)	8.7	13.0
General Practitioner (rate in PY)	5.9	8.6
Neurologist (rate in PY)	0.05	0.9
Pneumologist (rate in PY)	0.1	0.2

All the differences observed were statistically significant ($p<0.01$)

References: 1. Stenson K, O'Callaghan L, Mellor J, et al. Healthcare resource utilization at different stages of amyotrophic lateral sclerosis: Results from a real-world survey. Journal of the Neurological Sciences. Available from: https://www.jns-journal.com/article/S0022-510X(23)00225-3/fulltext 2. PNDS. Protocole National de Diagnostic et de Soins (PNDS) Sclérose Latérale Amyotrophique Haute Autorité de Santé; 2021 Available from: https://www.has-sante.fr/upload/docs/application/pdf/2021-12/pnds_genetique_sla_10_2021_final.pdf 3. Roux J. Parcours de soins des patients atteints de sclérose en plaques à partir des données médico-administratives en France. Université de Rennes; 2018 Available from: https://theses.hal.science/tel-02379451
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