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Healthcare utilization at the end of life in people dying from amyotrophic lateral sclerosis: A retrospective cohort study using linked administrative data

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ABSTRACT

Background: ALS is an incurable neurodegenerative disorder, with the recommendation that symptom management and palliative care start immediately or soon after diagnosis. However, little is known about healthcare utilization at the end of life in this patient group.
Aim: To describe healthcare utilization at the end of life in patients who died from ALS.
Design: We performed a retrospective cohort study using population-level administrative databases. The description of healthcare utilization was based on (1) validated quality indicators for end-of-life care, and (2) the European Federation of Neurological Societies guidelines on the clinical management of ALS.
Setting: We included all people who died from ALS in Belgium between 2010 and 2015 (using ICD-10 code G12.2).
Results: 1636 people died from ALS in Belgium between 2010 and 2015. The mean age at death was 71 years (SD11.3), and 56% were men. Specialized palliative care was used by 44% at some point in the last two years of life. In the last month of life, 13% received tube feeding, 48% received diagnostic testing, 41% were admitted to a hospital, and 25% were admitted to an emergency department. Medications were used mainly to treat pain (43%), insomnia and fatigue (33%) and thrombosis (32%); 39% used riluzole. Non-invasive ventilation was used by 18%. 39% died at home.
Conclusion: Administrative data provide a valuable source to describe healthcare utilization in small populations such as ALS, but more clinical evidence is needed on the advantages and disadvantages initiating or terminating treatments at the end of life.

1. Background

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder with a highly predictable clinical course that is characterized by degeneration of the upper and lower motor pathways [1]. Patients who are diagnosed with ALS experience progressive muscle weakness involving all voluntary muscles, resulting in limb paralysis and difficulties with swallowing and breathing. Its prevalence is low, with about 6 persons afflicted per 100,000 and an incidence rate of between 1.5 and 2 per 100,000 per year [2]. In Belgium, more than 200 patients die of the disease each year, while an equal amount of new cases are diagnosed annually. Thus, a constant number of about 1000 patients (~ 8,7 persons per 100,000) suffers from the disease in Belgium [3]. In the most common clinical presentation of the disease, death usually occurs 2 to 3 years after diagnosis, due to spread of the disease to respiratory muscles, deglutition, global failure and inanition. The lack of curative treatment and the predictability of the disease's dismal course make its psychosocial and existential impact quite unique and suggests a role for palliative care immediately or soon after diagnosis [2,4], focusing mainly on the management of physical, psychosocial and existential issues and on maximizing the quality of life of patients in coping with this condition [5–7].

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As with all people suffering from chronic and life-threatening illnesses, the care needs of ALS patients change near the end of life, and the provision of appropriate care throughout the last months and weeks of life is of significant importance to promote a certain level of quality of life. Nevertheless, healthcare professionals are often trained to prolong and maintain life for as long as possible [6], conceivably resulting in inappropriate continuation of treatments or hospitalizations that are futile near the end of life and possibly threaten the quality of life of patients [8,9]. Literature has shown that palliative care is most often used by cancer patients, despite being also beneficial to patients with other, non-malignant life-threatening illnesses (such as ALS) [10,11].

However, due to the low prevalence of the disease [12] and the rapid physical decline of those with symptom onset [5], little is known about healthcare utilization at the end of life in this patient group. Only one previous study used population-level observational data to describe medication use in the last year of life, in a large cohort of older patients in Sweden who died of ALS between 2007 and 2013. It found that 37% of such patients were treated with ten or more drugs during the last month of life [13]. Other studies have described healthcare utilization in ALS using small-sample prospective designs in one hospital or hospice [14,15], a retrospective physician-reported questionnaire design [16], or death certificate data from one region (focusing on place of death) [17].

Using linked population-level administrative data, this study aims to describe the healthcare utilization at the end of life in all patients who died from ALS in Belgium between 2010 and 2015. Specifically, our research questions are:

- What is the appropriateness of end-of-life care in people who died from ALS in Belgium between 2010 and 2015 as measured by previously validated population-level quality indicators (QIs)?
- What proportion of people who died from ALS in Belgium between 2010 and 2015 received neuroprotective, symptom management, and respiratory treatments in the last 7, 14, 30, 90 and 180 days before death?

2. Methods

2.1. Study design and population

We conducted a retrospective cohort study, using linked data from eight administrative databases containing healthcare consumption and socio-demographic data for all deaths in Belgium between 2010 and 2015. The study was conducted for all those who were registered with a Belgian health insurance fund at time of death between 1 January 2010 and 31 December 2015 (98.8% of all deaths). We selected a population of people that died from ALS based on the registration of the underlying cause of death code G12.2, using the 10th revision of the International Classification of Diseases (ICD-10).

2.2. Data sources

The data used involved eight administrative databases, linked at an individual level using a unique identifier by a third party responsible for data protection and linkage in Belgium. The linked data included person-level inpatient and outpatient reimbursed healthcare use in the last two years of life (recorded as nomenclature codes for all reimbursed healthcare use and Anatomical Therapeutic Chemical (ATC) classification system codes for all dispensed drugs in both the hospital and the public pharmacy). The exact date of delivery (coded as number of days before death) is recorded for all healthcare data. Additionally, the data includes demographic data, fiscal data, and death certificate data [18]. The data linkage process and content is described in detail elsewhere [19].

2.3. Healthcare measures

To describe the healthcare use at the end of life in people dying from ALS, we used two main sources to determine our list of variables.

Firstly, we used a set of 14 quality indicators of appropriateness of end-of-life care that can be measured using routinely collected administrative data [20]. The quality indicators provide population-level evidence on an aggregated level, and appropriateness or inappropriateness of care should not be extrapolated to the individual level (e.g. a high rate of end-of-life hospital use in the entire population of people who died from ALS suggests inappropriate care at the population level, but does not suggest that a particular hospitalization was inappropriate). The set was developed and validated using the RAND/UCLA appropriateness method, based on literature and a consensus process consisting of a multidisciplinary expert panel of 12 physicians and nurses [21]. Only those indicators that were deemed valid across different pathologies (i.e. not specifically for one pathology such as Alzheimer's disease, COPD, or cancer) were retained in the final set. The selected set of quality indicators and details about operationalization are provided in Supplementary Table S1 (for the complete set of indicators, development and validation process, see De Schreye et al. [20]).

Secondly, we used the 2012 European Federation of Neurological Societies (EFNS) guidelines on the clinical management of ALS [22] to create a list of medications and other healthcare use relevant to the end-of-life phase in ALS (see Supplementary Table S2 for the full list). All recommendations that provided clear information for which we had a nomenclature or ATC codes (e.g. exact drug names or interventions) were operationalized (this method excluded the operationalization of recommendations concerning diagnosis, communication, caregivers, unproven therapies, genetic testing and counselling, and cognitive testing). The search strategy, methods, and full list of recommendations are available in the guidelines publication [22].

All variables were measured at time intervals between the time of death and 7, 14, 30, 90, and 180 days before death, except when the periods for a specific indicator were not validated by the expert panel.

2.4. Statistical analyses

We used descriptive statistics to describe the characteristics of our cohort of people who died from ALS. We report counts and overall proportions for all socio-demographic characteristics, use of medications and of healthcare interventions, and report the mean number of primary caregiver contacts. All analyses were performed using SAS Enterprise Guide V.7.1.

3. Results

3.1. Study population characteristics

A total of 1636 people died from ALS in Belgium between 2010 and 2015 (an average of 273 annually), of whom 56% were men (Table 1). The mean age at death was 70.7 years (SD: 11.3; data not shown). 63% were married, and 20% lived in a single person household. 54% had attained a secondary education level or higher. The most common immediate causes of death were respiratory arrest (35%), respiratory failure (24%) and cardiac arrest (8%).

3.2. Healthcare utilization indicating appropriate end-of-life care

Of all the people who died from ALS in Belgium between 2010 and 2015, 43.8% received specialized palliative care (inpatient palliative care unit or multidisciplinary palliative home care) at some time in the last two years of life; for 22.3% of this group, specialized palliative care was initiated in the last 14 days of life (Table 2). On average, they had 3 primary caregiver (i.e. general practitioner or home nursing) contacts

Table 1
Characteristics of the study population of people dying from amyotrophic lateral sclerosis in Belgium between 2010 and 2015 (n = 1636).

	People who died from ALS	
	Number	Percent
All deaths	1636	100.0
Age		
0–64	506	31.0
65–84	1018	62.3
85 and older	111	6.8
Gender		
Male	909	55.6
Female	727	44.4
Immediate cause of death (top 3)		
Respiratory arrest (R09)	418	35.0
Respiratory failure (J96)	282	23.6
Cardiac arrest (I46)	97	8.1
Highest attained level of education		
Higher education	228	13.9
Secondary education	656	40.1
Primary education	283	17.3
No education	69	4.2
Unknown	400	24.5
Region		
Flanders	1079	66.3
Wallonia	445	27.3
Brussels	104	6.4
Household composition		
Married	1031	63.1
Single person	329	20.1
Living together	71	4.3
Collective household	115	7.0
Other	88	5.8

Missing datas for age (n = 1), immediate cause of death (n = 409), region (n = 8), household composition (n = 2).

per week during the last three months of life; 39.4% died at home.

3.3. Healthcare utilization indicating inappropriate end-of-life care

12.6% received tube feeding or intravenous feeding and 47.6% received diagnostic testing in the last month of life. In the last month of life, 48.7% were admitted to a hospital, 31.3% were admitted to an emergency department (ED), and 9.1% of those residing in a nursing home had an ICU admission.

Table 3
Healthcare utilization for the clinical management of ALS, within the total population of people dying from amyotrophic lateral sclerosis in Belgium, 2010–2015 (n = 1636).

	Time period (number of days before death until death)[a]				
	7	14	30	90	180
Neuroprotective treatment					
Riluzole use	10.6	21.9	39.3	57.2	61.4
Symptom management					
Pain	29.4	35.8	42.5	49.1	53.6
Insomnia and fatigue[b]	20.0	26.8	33.2	41.2	46.4
Venous thrombosis[b]	14.8	24.4	32.0	44.4	54.0
Depression and anxiety[b]	10.4	14.8	19.2	25.2	30.0
Bronchial secretions[b]	7.2	14.0	19.6	31.6	37.6
Pseudobulbar affect (pathological laughing or crying)[b]	5.2	8.4	12.4	17.6	21.2
Sialorrhea (hypersalivation)	3.1	5.0	8.4	15.3	18.7
Spasticity	1.3	3.0	5.6	8.4	8.9
Fasciculations and muscle cramps[b]	0.4	0.4	1.2	1.2	1.2
Respiratory management					
Non-invasive ventilation[c]	–	–	17.5	–	–
Oxygen therapy[c]	–	–	5.9	–	–
Invasive ventilation[c]	–	–	3.6	–	–

[a] The time intervals presented here refer to the last 0–7, 0–14, 0–30, 0–90, 0–180 days before death.
[b] Percentages were only available for 2012 (n = 250).
[c] Percentages were only available in the last 0–30 days before death (n = 1636).

3.4. Healthcare utilization for the clinical management of ALS

In the last six months of life, 61.4% of those who died from ALS used riluzole; 10.6% received riluzole in the last week of life. In the last month of life, 17.5% used non-invasive ventilation, 5.9% received oxygen therapy, and 3.6% used invasive ventilation (Table 3). In the last week of life, medications were used mainly to treat symptoms related to pain (29.4%), insomnia and fatigue (20.0%), and venous thrombosis (14.8%). Medications to treat symptoms of depression and anxiety (10.4%), bronchial secretions (7.2%), pseudobulbar affect (5.2%), sialorrhea (3.1%), spasticity (1.3%) and fasciculations and muscle cramps (0.4%) were used less frequently in the last week of life.

Table 2
Quality indicators for appropriateness of end-of-life care, within the total population of people dying from amyotrophic lateral sclerosis in Belgium, 2010–2015 (presented as % of n = 1636).

	Time period (number of days before death until death)[a]					
	No time specification	7	14	30	90	180
Indicators of appropriate end-of-life care						
Specialized palliative care	43.8					
Palliative care status	39.8					
Home death	39.4					
Increased contact with family doctor		40.8	56.2	58.4		
Average number of primary caregiver contacts per week[b]		3.2	3.1	3.1	3.0	
Indicators of inappropriate end-of-life care						
Hospital admission		33.0	40.9	48.7	59.8	69.1
Diagnostic testing		31.2	38.0	47.6		
ED admission		18.9	25.2	31.3	41.6	49.0
Late initiation of palliative care		6.9	9.8			
ICU admission from nursing home		5.4	7.6	9.1		
Tube feeding or intravenous feeding		3.3	5.9	12.6		

All indicators with a prevalence rate of less than 5% were excluded from the table (surgery, blood transfusion, port-a-cath instalment).
[a] The time intervals presented here refer to the last 0–7, 0–14, 0–30, 0–90, 0–180 days before death.
[b] This indicator represents the average number of contacts per week across the population during the indicated period, and is not presented as a percentage.

4. Discussion

4.1. Summary of main findings

Using administrative data, this study described healthcare utilization at the end of life among all patients who died from ALS over 6 years in Belgium. Specialized palliative care was used by 44% of patients who died from ALS, but for 10% of patients it was initiated only in the last two weeks of life. Nearly half of all patients who died from ALS were hospitalized or underwent diagnostic testing in the last month of life. Healthcare utilization for the clinical management of the disease mainly involved medications to treat symptoms of insomnia or fatigue, venous thrombosis or pain. About 18% received non-invasive ventilation in the last month of life, and 13% received tube feeding or intravenous feeding in the last month of life. Thirty-nine percent of patients died at home.

4.2. Strengths and weaknesses

This was the first study to include the entire population of those who had died from ALS over a period of 6 years in one country. This allowed avoiding common biases due to small sample sizes, which is particularly relevant in rare disease populations such as ALS (e.g. by including only patients that were treated in a specialized ALS centre). While some authors have raised concerns about the validity of using mortality data to study ALS [23] in Belgium, the causes of death on the death certificates are thoroughly checked by the regional health authority and a number of additional error checks are made (e.g. controls for unlikely information on record level or sampled controls by the civil registrar), thus guaranteeing a good quality of data [24].

Another strength of this study is that we used a previously validated set of quality indicators for end-of-life care. These indicators were rigorously developed and validated for specific use with administrative data. It remains true that particular attention should be paid to the special needs of this patient population. Although access to and evaluation of administrative data offer a very informative picture of healthcare resource utilization, it does not allow a complete operationalization of the guideline recommendations, as some aspects of end-of-life care were not captured in the data (e.g. recommendations concerning communication of the diagnosis to the patient).

4.3. Interpretation of results and comparison with previous research

Few previous studies have described end-of-life healthcare utilization in a population of people who died from ALS, and none have done so in Belgium, thus impeding a valid comparison with our findings. Two previous studies using similar quality indicators allow for comparison with people who died from cancer or COPD. Our findings show that considerably more people who died from ALS received specialized palliative care (43.8%) those who died from COPD (12%) [25], and about the same proportion of people who died from cancer (47%) [26]. Patients who died from ALS more often died at home (39.4%) than those who died from cancer (29.5%) or COPD (28.2%), and on average they had more contacts with a primary caregiver (mean number of 3.2 contacts in the last week of life versus 1.1 for COPD and 2.4 for cancer). However, the use of potentially inappropriate end-of-life care was also high among people who died from ALS, compared to the other two disease groups. Compared to people who died from COPD and cancer, people who died from ALS had similar rates of hospital and ICU admissions at the end of life. The rates of ED admissions among ALS patients were lower at one month before death (31.3% versus 33.8% (cancer) and 40.5% (COPD)), but higher in the last week of life (18.9% versus 12.9% (cancer) and 16.1% (COPD)) [25,26], a pattern that was also found in a retrospective cross-sectional study from Australia that compared hospital and emergency department use in the last year of life between people dying from cancer and people dying from other conditions where death was expected [27]. This might indicate that patients and caregivers are potentially less prepared to handle crisis situations at the end of life in ALS, compared to end of life situations in other serious illnesses.

Internationally, one prospective study from France analyzed the utilization of healthcare in 302 patients who died from ALS using physician-reported questionnaires [16], and one retrospective cohort in Sweden reported the use of prescription drugs over the course of the last year of life in 1603 older adults who died with ALS between 2007 and 2013 [13]. In the last month of life, rates of opioid use were highest in Belgium (43% in Belgium, 38% in France, 31% in Sweden), but rates of anxiolytic use (19% in Belgium, 45% in France, 38% in Sweden), antidepressant use (19% in Belgium, 26% in France, 42% in Sweden), anticoagulant use (32% in Belgium, 20% in France, 37% in Sweden), and riluzole use (39% in Belgium, 55% in France, 45% in Sweden) were higher in France or Sweden. However, one-to-one comparison between the studies is difficult due to differences in the design and selected population – e.g. the Swedish study only included patients who were 65 years or older at time of death [16].

Hitherto, there is little evidence of good practices with regard to end-of-life care of ALS patients. The current guidelines on the clinical management of patients with ALS often remain vague about whether or when to initiate or terminate a certain intervention. For example, the document states that “riluzole may have little effect in late-stage ALS, and it is not clear whether and when treatment should be terminated” [22]. Riluzole is currently the only drug with quality evidence of effectively slowing the course of the disease, with few to no known severe side-effects [28]. Considering the uncertainty about its effectiveness in late-stage ALS, its high cost, and the fact that polypharmacy is already highly prevalent in the last year of life of people with ALS [13], it is important to investigate further when the discontinuation of the drug is advised. This current study was therefore only able to describe healthcare utilization for the clinical management of ALS, lacking the evidence to interpret the findings as possibly appropriate or inappropriate care at the end of life.

The prevalence of home death was described in the prospective study from France [16] and in three other, retrospective studies, covering Spain [17], the USA and Canada [29], Germany [14] and the UK [14]. Reported rates of home death varied between 30% (Spain) and 62% (USA/Canada) (in Belgium, the rate of home deaths was 39%).

Some healthcare interventions have been found to improve patients' survival and quality of life [30–32], while this remains debatable for other interventions such as invasive mechanical ventilation [33]. Our study found that 13% of people dying from ALS received tube feeding or intravenous feeding in the last month of life, whereas 17.5% and 3.6% respectively received non-invasive ventilation (NIV) or invasive mechanical ventilation (IMV). Strikingly, only three previous studies have measured the prevalence of tube feeding or ventilation at the end of life in a cohort of people who died from ALS. A small-sample study conducted in the UK and Ireland on 62 patients from 6 hospices, reported that 32% of patients had a gastrostomy installed [15], and Gil and colleagues found that 37% of 302 French patients had received enteral feeding with gastrostomy [16]. A study from the USA on 1458 ALS patients found that NIV (15.6%) was used more than seven times as frequently as IMV (2.1%) [31], while in France 33% of patients included in the study had received NIV at time of death [16].

Future research should look in to the prevalence of these practices in different countries at a population-level, which would allow researchers and practitioners to understand possible factors that influence an inclination towards more or less use of healthcare at the end of life in patients with ALS, e.g. cultural preferences concerning the prolongation of life or economic incentives and disincentives. Comparative research is needed to further investigate whether cross-national variations in possibly appropriate or inappropriate end-of-life healthcare utilization, as well as differences in the place of death, can be explained by similar drivers as those described in other life-threatening illnesses such as

cancer [35,36] or COPD [37], and to discuss the impact that the local organization of palliative care resources in the healthcare system has in determining where and how people with ALS die. Including benchmarks in the EFNS guidelines for appropriate rates of medication and healthcare services use at the end of life in ALS at the population level could improve clinical assessment and allow for improved cross-national comparisons. As already observed, the nature of these observational data do not lend themselves to the assessment of the appropriateness of individual patient trajectories, and for this reason they should provoke further research into the clinical benefit and value of different clinical practices at the end of life and on the appropriateness of the clinical decision-making process itself [38], including its adherence to patients' preferences and values (e.g. how often the patient's preference about place of death is met).

5. Conclusion

About half the people who died from ALS in Belgium between 2010 and 2015 used specialized palliative care services, and four in ten died at home. Nevertheless, end-of-life hospital use was high, indicating potentially inappropriate end-of-life care in people who died from ALS. Drugs at the end of life were mainly administered to treat symptoms related to pain, fatigue and insomnia, and venous thrombosis. More evidence is needed on the advantages or disadvantages of initiating or terminating different treatments and medications at the end of life, including the use of riluzole. Routinely collected data (big data) can provide a valuable source of such evidence in relatively small populations such as those with ALS where classical RCTs face many practical challenges.

Authorship

The lead author affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained. AM, KB, JC and LD contributed to the conception and design of the article. AM collected and analyzed the data and wrote the main body of the manuscript. Interpretation of the data was done by all authors. All authors approved the final manuscript.

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Data sharing

In accordance with Belgian law, approvals for access to the various databases and the database integrating all databases were obtained from two separate national sectoral committees for privacy protection. Due to ethical concerns with regard to sensitive and potentially identifying data, the supporting data cannot be made publically available, as stated by the Sectoral Committee of Social Security and Health – Department Health and the Data Protection Authority. Both are subcommittees of the Belgian Commission for the Protection of Privacy. Further information about the data and access regulations are available on request.

Ethics and consent

No patient consent was required for the study. The study received approval from the ethics committee of Ghent University Hospital (B670201422382).

Declaration of Competing Interest

The author(s) declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Appendix A. Supplementary data

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