Spatial Patterns in Neurodegenerative Disease's Hospitalizations in Portugal (2000-2016)

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Abstract: Neurodegenerative diseases, usually arising from the death of nervous system cells, are a rising concern in the worlds' population increasing life expectancy. More precisely, the Portuguese population, along with that of other developed countries, is ageing at a fast rate. The understanding of such diseases' patterns is of utmost relevance to help manage the burden it represents in the health system. In this retrospective study, we analysed over 500 thousand hospitalizations with discharges between 2000 and 2016. We computed age-standardized hospitalization rates for each neurodegenerative disease. The most prevalent disease in our sample was Dementia with 43.4% of cases, and the least prevalent was Basal with only 0.2% of cases. The spatial analysis shows that Santarém and Portalegre (neighbour) districts in central Portugal, have the highest rates. The increase in hospitalization rates over the study period is also clear when looking at the spatio-temporal analysis. Although limited by the usage of secondary health data, this study represents a background for other studies on the field of neurodegenerative diseases, presenting with relevant insight into the spatio-temporal patterns of each and every neurodegenerative disease in Portugal at the moment.

1 INTRODUCTION

Global life expectancy has been increasing, from 66.8 in 2000 to 73.3 years in 2019 (WHO, 2022) , raising the concern on neurodegenerative diseases, since age is one of the main contributing factors to developing these pathologies. Neurodegeneration often occurs due to the pathological changes in the human brain arisen from aging (Spencer et al., 2016), which result in the death of cells either by necrosis or delayed apoptosis (Brown et al., 2005).

Among these diseases are Alzheimer's and other dementias, which contribute to 12% of the burden in disability-adjusted life years (DALYs), worsened by the fact that it is the most common form of late onset dementia globally (Rabinovici, 2019). Along with Parkinson's disease, they are the most common neurodegenerative diseases (de Lau & Breteler, 2006; Jankovic, 2008). Patients with these diseases are more susceptible to longer lengths of stay and represent a higher mortality rate, as well as a higher likeliness to be discharged to long-term care (Timmons et al., 2015). Other neurodegenerative diseases include Multiple Sclerosis, Huntington's, Basal Ganglia and Pick's.

Some risk factors to these diseases have been already discussed. For instance, atop from age as presented earlier, gender, hereditarianism and environmental exposure to pollution are all established risk factors for many of the neurodegenerative diseases. For instance, in

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literature, one third of Alzheimer's patients are female, while with Parkinson's the prevalence is greater in male patients (de Lau & Breteler, 2006). On the other hand, Huntington's disease is entirely acquired through hereditarianism, and some forms of Alzheimer's, mainly early-onset, are also transmitted through genetics (Price et al., 1998).

Furthermore, several studies have showed the significance of spatially analysing neurodegenerative disorders, displaying spatial patterns that uncover new correlations with variables such as latitude and environmental pollutants (Oliveira et al., 2020). Mapping such diseases and understanding the distribution and characteristics of the patients is of ultimate importance to plan and mitigate for such disorders.

To the authors' best knowledge, this is the first study developed in Portugal which describes the hospitalizations by neurodegenerative disorders, both statistically and spatially. With this retrospective study with data from 2000 to 2016, we hope to help provide insight on the distribution of these diseases.

2 MATERIALS AND METHODS

2.1 Study Area

This study was conducted with data from Portugal mainland, located in the southwest of Europe, with an area of approximately 89.000 km^2 and an aging population of around 10,000,000 inhabitants, 21% of which are 65 years old or older (INE, 2020). Figure 1 shows the distribution of age groups population for each district of Portugal, using 10 years-old categories. Population is also very heterogeneously distributed, as visible in Figure 2.

2.2 Data Acquisition

2.2.1 Health Data

Hospitalizations of patients with at least one neurodegenerative pathology coded as a diagnosis, both principal or secondary, were obtained from secondary hospitalization data, with discharges between 2000 to 2016. No further years were included since the provided data frame included only hospitalizations from 2000 to 2018, but both 2017 and 2018 were incomplete and would thus result in non-comparable results. Each record contains the year, patient's sex, age and residence (coded up to the parish), entry and leave dates, length of stay and coded diagnosis.

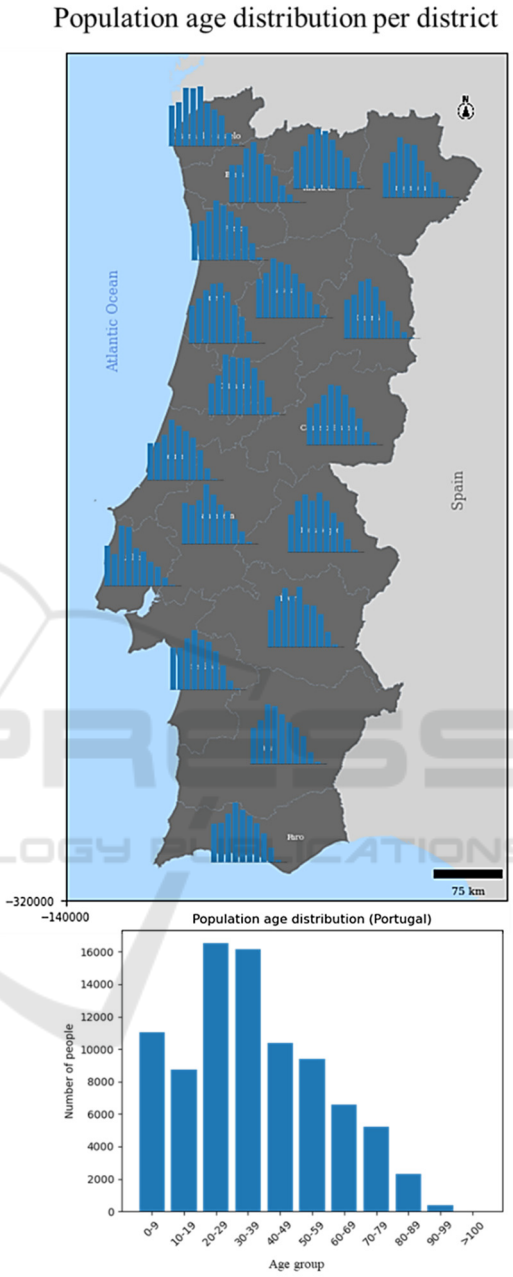

Figure 1: Population age distribution per groups of 10 years for each district (2000 to 2021 mean).

Neurodegenerative pathologies codes were retrieved from literature review (Kim et al., 2019; Lee et al., 2019; Min et al., 2020; Rochoy et al., 2019; St Germaine-Smith et al., 2012; Wetmore et al., 2019),along with counselling with coding experts. All resulting International Classification of Diseases (ICD) codes used are listed in Table 1.

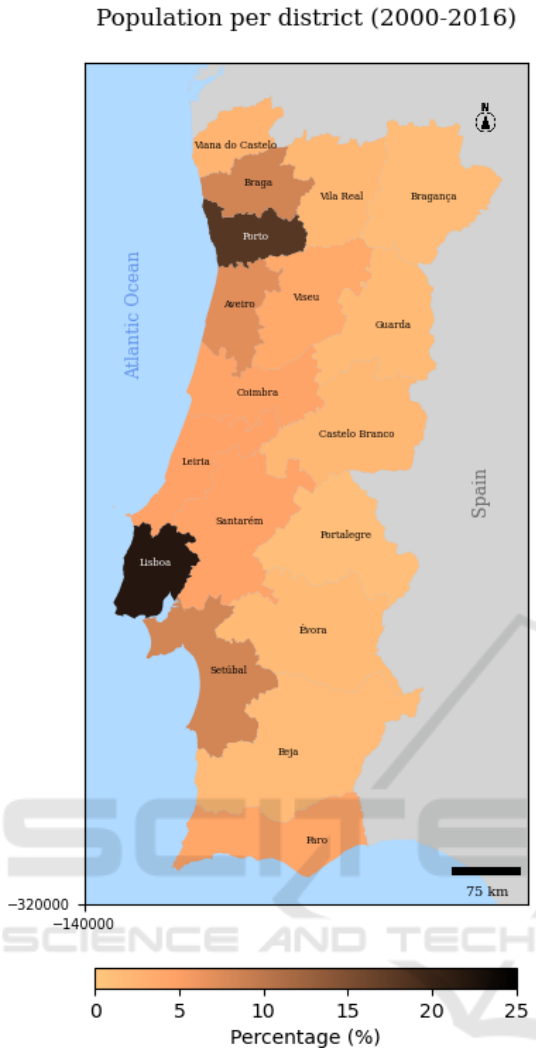

Figure 2: Population percentage per district.

2.2.2 Population Data

Population data was retrieved from National Institute of Statistics (INE) Population Census for the years of 2001, 2011 and 2021, for each Portuguese mainland parish. These data were then linearly interpolated to obtain an approximate value of population by year, further used to normalize health data. District and municipality population was also computed from the sum of the contained parishes. Only integer values were used, due to the nature of the population variable.

2.3 Data Processing

All data pre-processing, descriptive analysis and mapping was done using *Python* programming language.

Table 1: ICD codes used to retrieve hospitalization data.

Diagnosis		ICD 9	ICD 10
Alzheimer		331.0	G30
Pick's		331.1	G31
Lewy		331.8	
Creutzfeldt		046	A81.0
Huntington		333.4	G10
Parkinson		332	G20
Motor neuron disease		335	G12.2
Multiple sclerosis		340	G35
Basal ganglia		333.0	G23
Dementia	Vascular	290.4	
	Unspecified	294	
	Senile	331.2	
	Cerebral degeneration	331.7	F01
	Presenile	290.1	F02
	Senile with delusion	290.2	F03
	Senile with delirium	290.3	
	Alcohol induced	291.2	
	Drug induced	292.82	
Other		331.9	G32

Health data was loaded and diagnosis codes were extracted and recoded as the disease they referred to. For example, ICD-9 code 331.0 and ICD-10 code G30 were both recoded as 'Alzheimer'. The category "Other", as stated in the ICD, represents the other neurodegenerative diseases not described elsewhere by the alternative codes. Age was grouped into three categories: under 20 years old, 20 to 70 years old, and over 70 years old. These categories were chosen to adapt to the available population categories, as well as to accommodate the distinction between paediatric, early onset and late onset neurodegenerative diseases (Fatima et al., 2022).

Afterwards, general descriptive statistics was computed. Then, data was grouped by either district, municipality or parish to proceed to mapping, and population in each administrative area, as well as the percentage of each age group, were used to compute age-standardized hospitalization rates (ASHR), using equation 1 (Curado et al., 2007). This rate allows data to be normalized and therefore enables comparison of the rates, both across space and time, with a lower degree of error.

$$ASHR = \frac{N_{AgeGroup}}{Population_{AgeGroup}} \times \%_{AgeGroup} \quad (1)$$

In equation 1, $N_{AgeGroup}$ represents the number of hospitalizations in each age group, *Population* represents the total population in the area corresponding to each age group (for example, each district) and %AgeGroup the percentage of the age group in the population. The resulting data was therefore mapped to establish spatio-temporal patterns.

3 RESULTS

3.1 Descriptive Statistics

A total of 502 245 hospitalizations were included in this study. As represented in the graphic in Figure 3, the most prevalent disease was Dementia (43.4%), followed by Other (22.7%) and Alzheimer (20.2%). Basal was the least prevalent disease (0.2%).

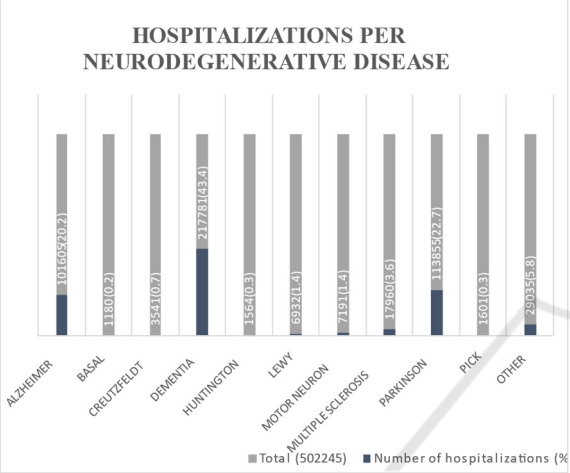

Figure 3: Number of hospitalizations and respective percentage per neurodegenerative disease, relative to the total number of hospitalizations.

Most patients were female (56.3%) and 81.3% of all patients were over 70 years old, with only 0.4% of the cases representing paediatric disorders (under 20 years old). Of these, Motor Neuron was by far the most prevalent neurodegenerative disease with 748 cases (Table 2).

3.2 Spatial Analysis

As expected, mapping the available data provided frther insight on the spatio-temporal distribution, otherwise difficult to grasp from algebraic statistical methods.

Although the descriptive statistics pointed the Centre as the area with the most prevalence of overall neurodegenerative diseases, mostly coded as "Dementia", the map of the hospitalization rates (Figure 4) shows that the most incidence is found in the district of Bragança, located in the north of Portugal. Furthermore, Porto district, where a main metropolis of Portugal is located, has lower hospitalization rates, contrarily to Lisbon, the other major metropolis of Portugal. Each individual disease is also mapped in Figure 5.

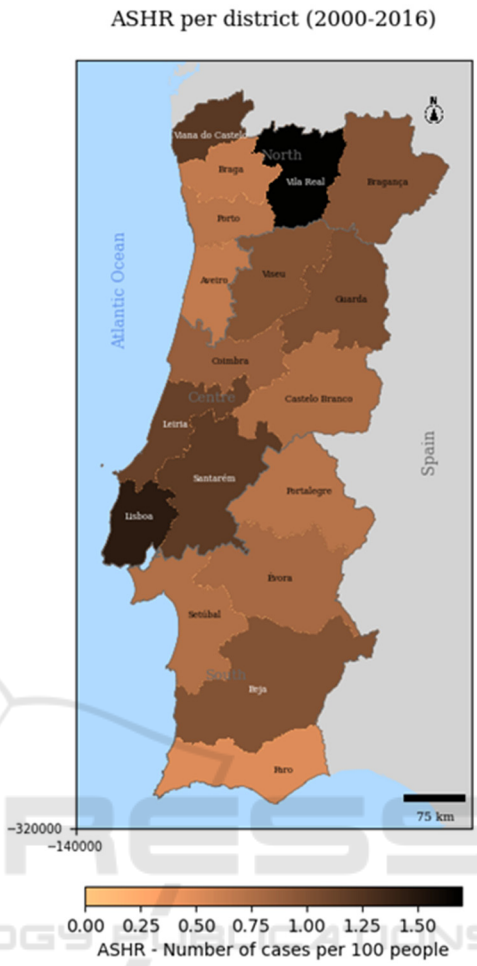

Figure 4: Age-standardized hospitalization rates by neurodegenerative diseases per district for the years 2000 to 2016.

Another relevant aspect to be mapped is the temporal series. In this, the results clearly show that most districts exhibited a consistent increase throughout the years, particularly Portalegre in the southeast (Figure 6).

4 DISCUSSION

To the best of the authors' knowledge, this is the first population based spatio-temporal descriptive study of neurodegenerative pathologies in Portugal. This work relies on the availability of nationwide hospitalization data from public hospital for 17 years, thus representing a significant sample of patients with neurodegenerative diseases in Portugal. Furthermore, the availability of each patient's residence allows for a spatial analysis not available as standard practice.

Table 2: Descriptive statistics of each neurodegenerative disease included in this study, as well as their total. Categorical data (sex, age group and residence) is described by its absolute frequency and percentage, while continuous data (age and length of stay, which are both asymmetrically distributed), is described by its median and interquartile range. The total row describes the total frequency of each disease and their respective percentage. yo: years old.

		Alzheimer	Basal	Creutzfeldt	Dementia	Huntington	Lewy	Motor Neuron	Multiple Sclerosis	Parkinson	Pick	Other	Total
Sex	Female	62349 (61.4)	659 (55.8)	1209 (34.1)	127694 (58.6)	736 (47.1)	3458 (49.9)	3272 (45.5)	12062 (67.2)	56977 (50.0)	722 (45.1)	13775 (47.4)	282913 (56.3)
	Male	39256 (38.6)	521 (44.2)	2332 (65.9)	90087 (41.4)	828 (52.9)	3474 (50.1)	3919 (54.5)	5898 (32.8)	56877 (50.0)	879 (54.9)	15260 (52.6)	219331 (43.7)
Age (yo)		81 [76, 85]	72 [61, 79]	48 [38, 68]	82 [76, 87]	58 [47, 70]	78 [70, 84]	65 [53, 73]	43 [33, 54]	79 [73, 84]	68 [60, 77]	76 [66, 83]	80 [74, 86]
Age Group	< 20 yo	16 (0.0)	39 (3.3)	116 (3.3)	157 (0.1)	29 (1.9)	130 (1.9)	748 (10.4)	403 (2.2)	59 (0.1)	2 (0.1)	187 (0.6)	1886 (0.4)
	20-70 yo	9018 (8.9)	511 (43.3)	2649 (74.8)	25241 (11.6)	1169 (74.7)	1656 (23.9)	4087 (56.8)	16775 (93.4)	20052 (17.6)	956 (59.7)	9740 (33.5)	91854 (18.3)
	> 70 yo	92571 (91.1)	630 (53.4)	776 (21.9)	192383 (88.3)	366 (23.4)	5146 (74.2)	2356 (32.8)	782 (4.4)	93744 (82.3)	643 (40.2)	19108 (35.8)	408505 (81.3)
Length of stay (days)		8 [4, 13]	8 [4, 15]	15 [7, 34]	8 [5, 14]	9 [4, 16]	9 [5, 16]	7 [3, 13]	5 [2, 9]	8 [4, 14]	12 [6, 24]	9 [5, 17]	8 [4, 14]
Residence	North	37116 (36.5)	513 (43.5)	973 (27.5)	79156 (36.3)	437 (27.9)	2687 (38.8)	2396 (33.3)	5411 (30.1)	35190 (30.9)	554 (34.6)	22274 (76.7)	186707 (37.2)
	Centre	49750 (49.0)	518 (43.9)	1897 (53.6)	114337 (52.5)	882 (56.4)	3642 (52.5)	3621 (50.4)	9487 (52.8)	61947 (54.4)	901 (56.3)	5225 (18.0)	252207 (50.2)
	South	14739 (14.5)	149 (12.6)	671 (18.9)	24288 (11.2)	245 (15.7)	603 (8.7)	1174 (16.3)	3062 (17.0)	16718 (14.7)	146 (9.1)	1536 (5.3)	63331 (12.6)
Total		101605 (20.2)	1180 (0.2)	3541 (0.7)	217781 (43.4)	1564 (0.3)	6932 (1.4)	7191 (1.4)	17960 (3.6)	113855 (22.7)	1601 (0.3)	29035 (5.8)	502245 (100)

As expected, elders were the most prevalent age group, representing over 81% of the overall patients. Only for Creutzfeldt, Huntington, Motor Neuron, Multiple Sclerosis and Pick was the age mean lower than 65 years old. Most patients were women (56%) and patients were hospitalized for a median of 8 days. As for the spatial patterns found, the centre showed a slightly higher incidence of neurodegenerative diseases although the rates are similar throughout the country.

Porto didn't show especially high rates of hospitalizations, even though it is one of the most populated cities of Portugal. This may be due to easier access to health, which may allow for the better management of the diseases, avoiding hospitalization. On the opposite side, the higher rate of hospitalizations in the interior of the country where isolation and aging population are combined to hinder health access may be thus explained. Other reason may involve lower literacy, which is a known risk factor for developing neurodegenerative diseases, and highly inequal between the interior and the coast of the country (Ávila, 2006).

Furthermore, the aging of the population is well represented in the higher rates of hospitalizations along the time period of the study.

4.1 Limitations

One of the major limitations in our work is the fact that the hospitalizations dataset does not include a unique patient identifier, to allow us to attempt to identify patients unequivocally. As such, if a patient with a neurodegenerative disease has been hospitalized more than once, it will appear repeated in our database, without us being able to realize it and filter it out. For this reason, data here represented may be oversampling some disease that would naturally require more hospitalizations than other. Ideally, datasets should include a unique patient identifier to advert this issue.

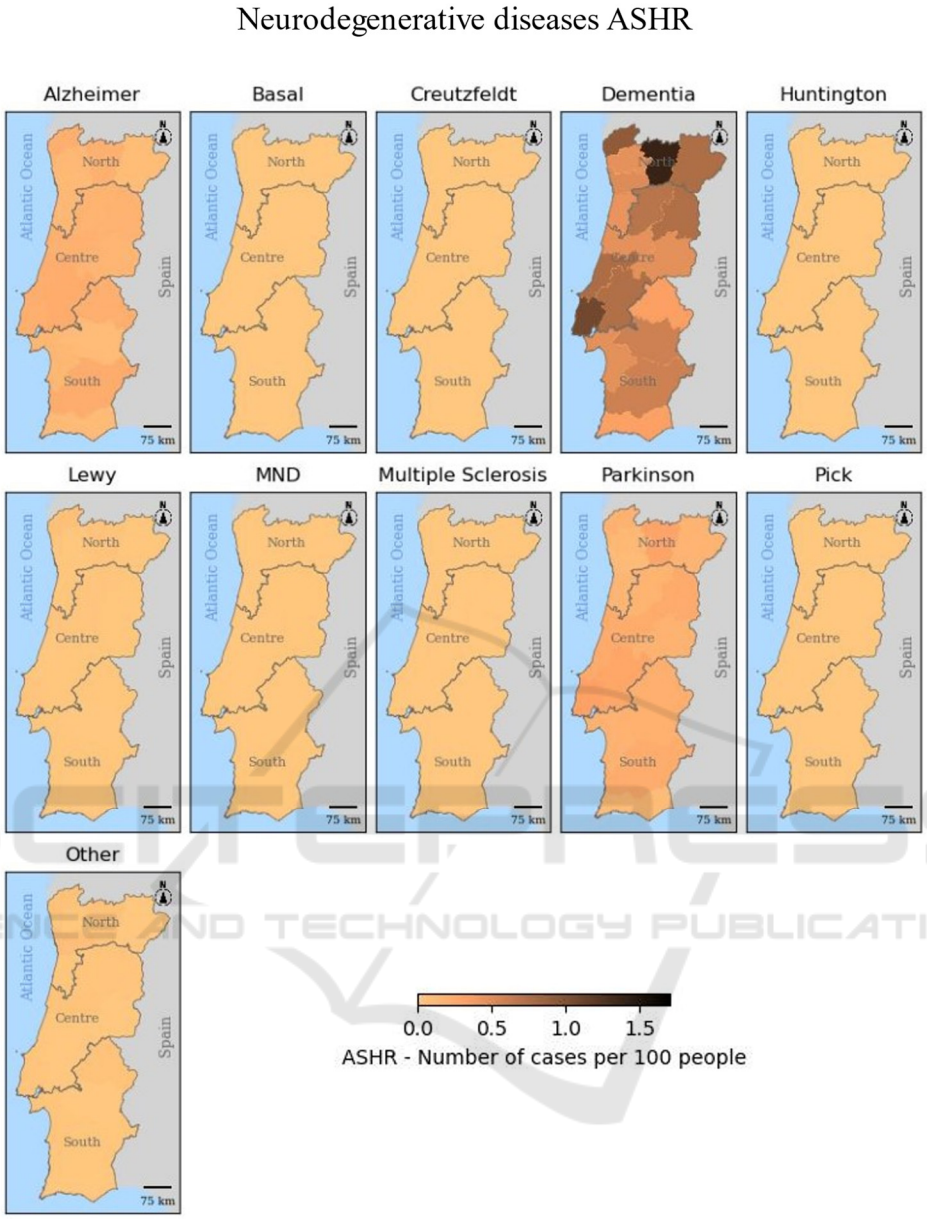

Figure 5: Neurodegenerative diseases' spatial distribution per district.

Reusing data is not always as accurate as desirable. Nevertheless, it is the best available option when studying a large population throughout a large time frame, without the implications of collecting data prospectively.

4.2 Implications and Future Work

This study may be used as a base for further studies concerning neurodegenerative pathologies, as it gives insight on the spatial patterns expected, as well as to anticipating the statistical distribution of Portuguese public hospitalization data.

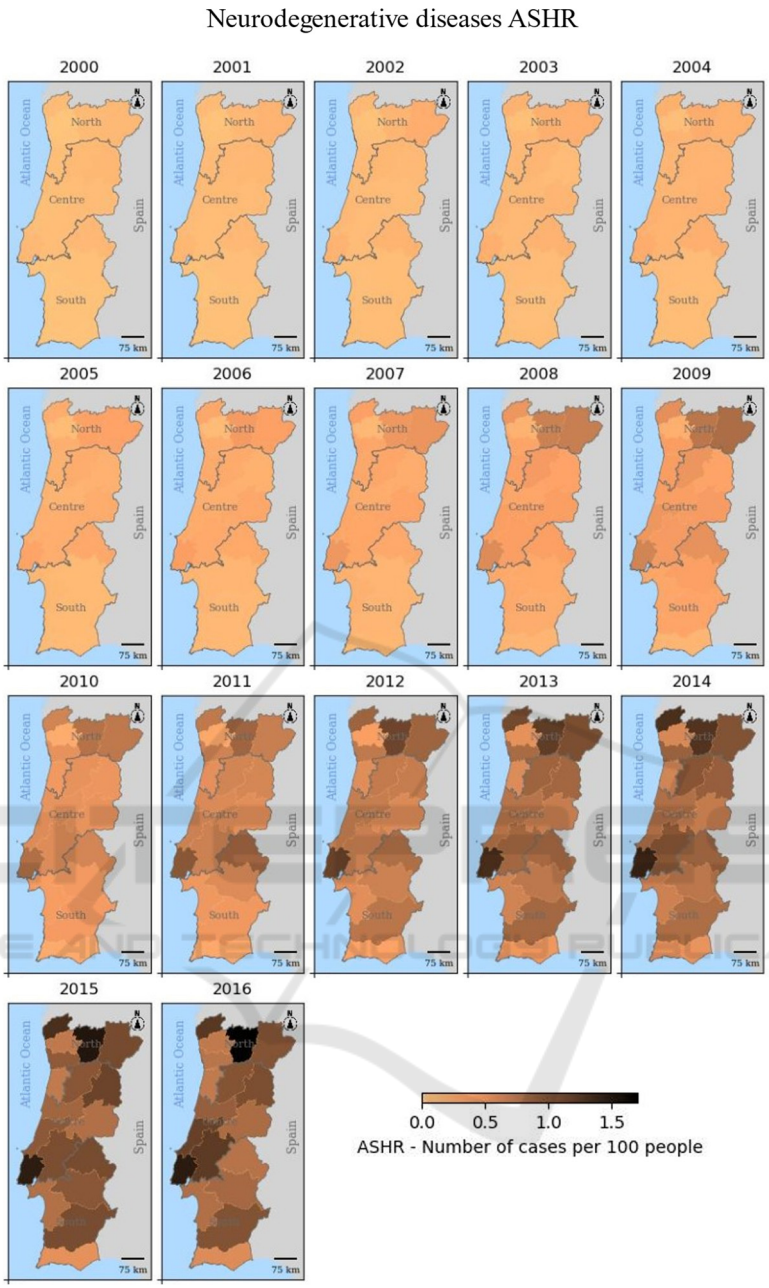

Figure 6: Spatio-temporal age-standardized hospitalization rates by neurodegenerative diseases per district for each year, from 2000 to 2016.

5 CONCLUSION

This work describes the spatio-temporal patterns of age-standardized hospitalization rates of neurodegenerative diseases, in Portugal mainland, from 2000 to 2016. The most prevalent disease was Dementia, and the least prevalent was Basal.

The aging Portuguese population is notorious on the temporal analysis, where it becomes clear that neurodegenerative diseases incidence is increasing. Also, disparities in health access become clear as interior districts have higher hospitalization rates than littoral ones and, mostly, than the larger metropolis.

With this work, we hope that the established patterns may be of use when working with similar data sources.

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