



RESEARCH NOTE

Decrease in rate of multiple sclerosis-related hospitalizations in Portugal [version 1; referees: 2 approved]

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Abstract

We sought to investigate the rate of multiple sclerosis (MS)-related hospitalizations in Portugal and assess whether there have been temporal changes as described in other countries. Using data from the Portuguese National Discharge Registry, we observed that between 2008 and 2013 the rate of MS-related hospitalizations decreased by 44%, from 15.9/100 person-years (95% confidence interval (CI): 14.9-16.9) in 2008 to 8.9/100 person-years (95% CI: 8.2-9.6) in 2013. The change in hospitalization rates is in accordance with what has been observed in other countries, and coincides with the release of new therapies for MS in Portugal.

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Referee Status:

	Invited Referees	
	1	2
version 1 published 13 Jun 2016	 report	 report
1	João Correia de Sa , Santa Maria University Hospital - North Lisbon Hospital Center Portugal	
2	Bruce Taylor , University of Tasmania Australia	

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Introduction

Multiple sclerosis (MS) is a chronic, neurodegenerative autoimmune disorder of the central nervous system¹. With a prevalence of 1/800 in North America and Northern Europe, MS is the most common acquired neurological disorder in young adults¹, posing a substantial burden on healthcare systems. Recent studies have, however, suggested that MS-related hospitalization rates have been declining over the last decades^{2,3}.

Portugal is considered a region of medium MS prevalence⁴, but epidemiological data are limited. In the present study, we sought to investigate the difference in the rate of MS-related hospitalizations in Portugal between 2008 and 2013.

Methods

Data on the number of hospitalizations in 2008 and 2013 with an MS diagnosis [International Classification of Diseases, 9th revision (ICD 9): 340] were obtained from the National Hospital Discharge Registry, centrally held in the Portuguese Central Administration of the Health System. This database includes data about all hospitalizations in all public hospitals. In Portugal, the National Health Service provides universal access to healthcare and patients with MS are almost exclusively treated in public hospitals⁴. These years were chosen as MS prevalence data in 2008 and 2013 in Portugal were available from the Atlas of MS (<http://www.msif.org/wp-content/uploads/2014/09/Atlas-of-MS.pdf>)⁵. The total number of hospitalizations (1,177,048 in 2008 and 1,108,911 in 2013), as well as the estimates of the Portuguese population, were obtained from Portuguese official statistics⁶.

The incidence of hospitalizations (MS-related or all-cause hospitalizations) was calculated by dividing the number of hospitalizations in each year by the number of patients at risk in the same year. The Wald method was used to calculate 95% confidence intervals (CI). Two different definitions of MS-related hospitalizations were used: 1) where MS was the primary reason for admission — the MS ICD-9 diagnostic code was reported in the field of the primary diagnosis, and 2) where MS was reported as either a primary or a secondary reason for admission — the MS ICD 9 diagnostic code was in any position on the diagnoses fields (20 fields available). The proportion of MS-related hospitalizations in each year was obtained by dividing the number of MS-related hospitalizations in each year by the total number of hospitalizations in the same year. Demographic and clinical characteristics of patients with MS hospitalized in each year were described using number and percentage of patients for categorical variables, and mean and standard deviation (variables with a normal distribution) or median and interquartile range (variables with a skewed distribution) for continuous variables. Differences between characteristics in 2008 and 2013 were estimated using t-tests (variables with a normal distribution) or Mann–Whitney test (variables with a skewed distribution) for continuous variables, and Chi square test for other categorical variables. P values < 0.05 were considered to be statistically significant. Statistical analysis was performed using STATA software version 13.

Results

Demographic and clinical characteristics of patients with MS hospitalized in 2008 and 2013 are summarized in [Table 1](#). Between 2008 and 2013, the incidence rate of MS-related hospitalizations decreased from 15.9/100 person-years (95% CI: 14.9–16.9) to 8.9/100 person-years (95% CI: 8.2–9.6), defined using only information recorded in the main diagnosis field, and from 25.5/100 person-years (95% CI: 24.4–26.8) to 19.4/100 person-years (95% CI: 18.5–20.4) using the main or secondary diagnoses respectively ([Figure 1](#)). In the same years, the incidence rate of all hospitalizations in Portugal decreased from 11.7/100 person-years (95% CI: 11.7–11.7) to 11.2/100 person-years (95% CI: 11.1–11.2) ([Figure 1](#)). The proportion of MS-related hospitalizations among all hospitalizations in Portugal decreased slightly from 0.07% to 0.05% between 2008 and 2013.

The age of the patients with MS hospitalized and the length of stay in the hospital increased significantly ([Table 1](#)) between 2008 and 2013, where MS was either only a primary diagnosis or a diagnosis anywhere on the patient record. There was an increase in the proportions of females admitted to hospital but this was only significant when MS was recorded in any of the diagnosis fields ([Table 1](#); p value = 0.062 for MS as main diagnosis and p value = 0.006 for MS as main or secondary diagnosis).

No differences were observed in the proportion of patients that died during hospitalization ([Table 1](#)). Where MS diagnosis was anywhere on the patient record, the proportion of MS patients with other diagnoses during hospitalization increased significantly between 2008 and 2013 for all groups of diseases considered, except for infectious and parasitic diseases, neoplasms, diseases of the nervous system and sense organs (excluding MS), and congenital anomalies ([Table 1](#)).

Dataset 1. Data of multiple sclerosis related hospitalizations in Portugal

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The raw data of incidence rate of multiple sclerosis related hospitalization between 2008 and 2013 are reported.

Discussion

Here we show a decrease in MS-related hospitalizations in Portugal from 2008 to 2013. Where MS was the primary diagnosis the decrease was substantial — approximately 44%. The rates of hospitalization observed in Portugal appear to be similar to that documented in Canada^{2,3}, suggesting perhaps that the thresholds for admission are similar between the two countries. The change in hospitalization rates cannot be explained entirely by a general change in admissions in Portugal, although this did decline by 4%. The change in hospitalization coincides with the release of new therapies for MS, the first of which, natalizumab (Tysabri®), became available in June 2007 in Portugal⁷. It is plausible that these newer therapies prevented some hospital admissions for patients with

Table 1. Demographic and clinical characteristics of patients with MS hospitalized in 2008 and 2013.

	MS as main diagnosis			MS as main or secondary diagnosis		
	2008 (N=795)	2013 (N=576)	P value	2008 (N=1277)	2013 (N=1264)	P value
Age of patients hospitalized, years						
Mean	39.1	40.5	0.033	42.8	46.5	<0.001
SD	11.9	12.3		13.4	14.6	
Gender, n (%)						
Male	264 (33.2)	164 (28.5)	0.062	457 (35.8)	387 (30.6)	0.006
Female	531 (66.8)	412 (71.5)		820 (64.2)	877 (69.4)	
Length of stay (days)						
Median	3	4	0.006	4	4	<0.001
IQR	1–6	1–6		1–7	2–8	
Deaths during hospitalization, n (%)	7 (0.9)	2 (0.4)	0.227	39 (3.0)	35 (2.8)	0.669
Other diagnosis during hospitalization, n (%)*						
Infectious and parasitic diseases	3 (0.4)	3 (0.5)	0.691	25 (2.0)	22 (1.7)	0.685
Neoplasms	7 (0.9)	9 (1.6)	0.246	62 (4.9)	74 (5.8)	0.263
Endocrine, nutritional and metabolic diseases and immunity disorders	93 (11.7)	112 (19.4)	<0.001	188 (14.7)	325 (25.7)	<0.001
Diseases of the blood and blood-forming organs	21 (2.6)	24 (4.2)	0.118	63 (4.9)	122 (9.6)	<0.001
Mental disorders	68 (8.6)	130 (22.6)	<0.001	136 (10.6)	277 (21.9)	<0.001
Diseases of the nervous system and sense organs (excluding MS)	347 (27.5)	154 (26.7)	<0.001	202 (15.8)	117 (14.7)	<0.001
Diseases of the circulatory system	60 (7.6)	106 (18.4)	<0.001	201 (15.7)	370 (29.3)	<0.001
Diseases of the respiratory system	24 (3.0)	23 (4.0)	0.328	126 (9.9)	180 (14.2)	0.001
Diseases of the digestive system	11 (1.4)	18 (3.1)	0.027	68 (5.3)	139 (11.0)	<0.001
Diseases of the genitourinary system	49 (6.2)	48 (8.3)	0.112	179 (14.0)	297 (23.5)	<0.001
Diseases of the skin and subcutaneous tissue	10 (1.3)	9 (1.6)	0.634	35 (2.7)	72 (5.7)	<0.001
Diseases of the musculoskeletal system and connective tissue	20 (2.5)	29 (5.0)	0.013	47 (3.7)	90 (7.1)	<0.001
Congenital anomalies	2 (0.2)	0 (0.0)	0.228	4 (0.3)	6 (0.5)	0.516
Symptoms, signs, and ill-defined conditions	43 (5.4)	118 (20.5)	<0.001	92 (7.2)	233 (18.4)	<0.001
Injury and poisoning	6 (0.8)	7 (1.2)	0.385	58 (4.5)	112 (8.9)	<0.001

* Described according to the groups of diseases defined in the International Classification of Diseases 9th revision MS, multiple sclerosis; SD, standard deviation; IQR, interquartile range

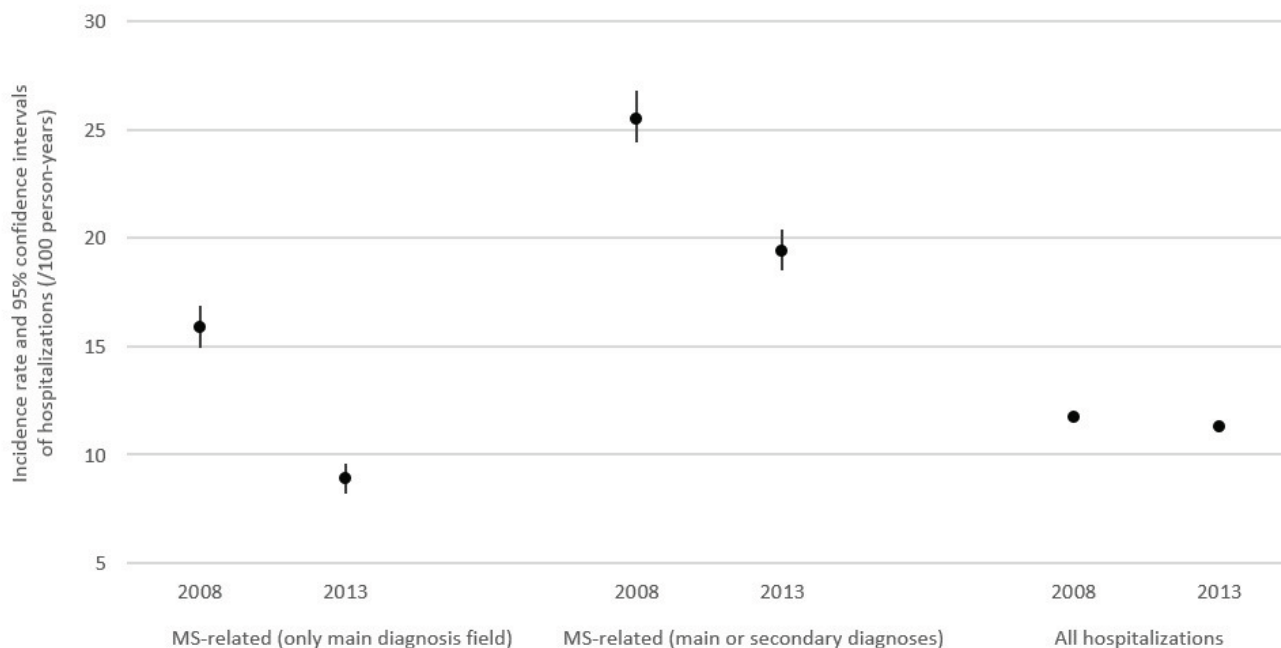


Figure 1. Incidence rate of MS-related and all hospitalizations in Portugal in 2008 and 2013.

MS. The average age of MS patients admitted in 2013 was older as compared to 2008. As MS prevalence has increased over the period, the decrease in hospitalization rate may reflect a diluting by more newly diagnosed patients with lower disease severity. There may also be a change in the way healthcare is delivered, with a possible shift to more outpatient services as seen in other countries. This may explain why the average length of stay for MS-related admissions has increased while the rate of admissions has decreased, although this change in disease management has generally preceded the time period we have investigated in other countries.

Limitations of this study include the lack of clinical data and information on potential confounders. There are also the uncertainties associated with the prevalence data we had available to us. Despite these limitations, our results are in accordance with previous results on hospital admissions in patients with MS. Our findings provide further epidemiological data on MS in Portugal, healthcare resource use in these patients, and impetus to investigate other efforts to reduce hospitalizations in this population.

Data availability

The Portuguese Central Administration of the Health System provided the database and gave permission to use the data to describe

in the article. The data are not available online, but are available upon request after approval of the study objectives.

F1000Research: Dataset 1. Data of multiple sclerosis related hospitalizations in Portugal, <http://dx.doi.org/10.5256/f1000research.8787.d125589>⁸

Author contributions

MP performed the analysis. SVR contributed to the analysis and interpretation of the data. MP wrote the first draft and all authors contributed to subsequent drafts and the final paper.

Competing interests

MP, DL and SVR are employees of Evidera.

Grant information

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[Data Source](#)

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Current Referee Status:



Version 1

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Bruce Taylor

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This is an interesting short report that documents a significant fall in the number of hospitalisations for MS in Portugal following the release of higher potency disease modifying drugs. The observation is interesting and adds some support to the presumed greater efficacy of these therapies. Although causality cannot be determined from such an observational study.

The finding that the age of admissions increased is also interesting as it may indicate that those with longer duration of disease (directly correlated with age) may have acquired more complications of MS for example urosepsis and have required greater admission rates.

To directly answer the question significantly more detail and prospective acquisition of data is required. however this report does provide a strong background rationale to undertake these studies and to acquire this type of data which is invaluable in assessing the benefits or otherwise of expensive and potentially higher risk therapies in MS.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.

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The paper by Pereira and co-workers addresses an relevant issue: to bring to public some data about the hospitalization rates of MS patients in Portugal.

There are no methodological errors but, in my opinion, some changes should be introduced:

1. About Introduction when the authors say that the epidemiological data in Portugal are limited I can't agree. Portugal is a small country of about 10 million people and 3 prevalence studies and 1

incidence study published bring data enough for a knowledge of the basic epidemiological picture of MS in the country. There is of course other missing data (for instance mortality data/ burden of the disease for the society) but these are often missing in other countries. I considered changing saying for instance that though prevalence and incidence in MS in Portugal are now known, other epidemiological data about the disease are still lacking.

2. The author stay that they have found a "decrease in MS related hospitalizations..... from 2008 to 2013". In fact they have only these two dates for comparison. They have no data among these two years so that some variability can not be excluded.
3. In Portugal there are a great diversity of neurological care. Central Hospitals in Lisbon, Oporto and Coimbra treat MS in ambulatory but in other Towns: Évora, Beja, Leiria, Covilhã, Santarem, for example patients are admitted for treating relapses with Methyl, and for Natalizumab infusion because Day-Hospital units are not available. This should be taken in consideration in discussion and could certainly explain why there are so many short-time admissions

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Competing Interests: No competing interests were disclosed.
