Neurología. 2018;33(6):351—359

NEUROLOGÍA

www.elsevier.es/neurologia

ORIGINAL ARTICLE

Multiple sclerosis and alcohol use disorders: in-hospital mortality, extended hospital stays, and overexpenditures☆

M. Gili-Miner[a,b], J. López-Méndez[a,b,*], A. Vilches-Arenas[a,b], G. Ramírez-Ramírez[a,b], D. Franco-Fernández[c,d], J. Sala-Turrens[e], L. Béjar-Prado[a]

[a] *Departamento de Medicina Preventiva y Salud Pública, Universidad de Sevilla, Sevilla, Spain*
[b] *Servicio de Medicina Preventiva y Salud Pública, Hospital Universitario Virgen Macarena, Sevilla, Spain*
[c] *Departamento de Psiquiatría, Universidad de Sevilla, Sevilla, Spain*
[d] *Servicio de Salud Mental, Hospital Universitario Virgen Macarena, Sevilla, Spain*
[e] *Unidad de Documentación Clínica, Hospital Universitario Virgen Macarena, Sevilla, Spain*

Available online 2 June 2018

KEYWORDS
Multiple sclerosis;
Alcohol use disorders;
Mortality;
Hospital stay;
Costs

Abstract
Introduction: The objective of this study was to analyse the impact of alcohol use disorders (AUD) in patients with multiple sclerosis (MS) in terms of in-hospital mortality, extended hospital stays, and overexpenditures.
Methods: We conducted a retrospective observational study in a sample of MS patients obtained from minimal basic data sets from 87 Spanish hospitals recorded between 2008 and 2010. Mortality, length of hospital stays, and overexpenditures attributable to AUD were calculated. We used a multivariate analysis of covariance to control for such variables as age and sex, type of hospital, type of admission, other addictions, and comorbidities.
Results: The 10 249 patients admitted for MS and aged 18-74 years included 215 patients with AUD. Patients with both MS and AUD were predominantly male, with more emergency admissions, a higher prevalence of tobacco or substance use disorders, and higher scores on the Charlson comorbidity index. Patients with MS and AUD had a very high in-hospital mortality rate (94.1%) and unusually lengthy stays (2.4 days), and they generated overexpenditures (1116.9 euros per patient).

☆ Please cite this article as: Gili-Miner M, López-Méndez J, Vilches-Arenas A, Ramírez-Ramírez G, Franco-Fernández D, Sala-Turrens J, et al. Esclerosis múltiple y trastornos asociados al consumo de alcohol: mortalidad atribuible, prolongación de estancias y exceso de costes hospitalarios. Neurología. 2018;33:351—359.

* Corresponding author.
E-mail address: jlopezmendez@us.es (J. López-Méndez).

Conclusions: According to the results of this study, AUD in patients with MS results in significant increases in-hospital mortality and the length of the hospital stay and results in overexpenditures.

PALABRAS CLAVE
Esclerosis múltiple;
Trastornos asociados al consumo de alcohol;
Mortalidad;
Estancia hospitalaria;
Costes

Esclerosis múltiple y trastornos asociados al consumo de alcohol: mortalidad atribuible, prolongación de estancias y exceso de costes hospitalarios

Resumen
Introducción: El objetivo de este estudio es el análisis del impacto de los trastornos asociados al consumo de alcohol (TCA) en los pacientes con esclerosis múltiple (EM), en términos de exceso de mortalidad intrahospitalaria, prolongación de estancias y sobrecostes.
Métodos: Estudio observacional retrospectivo de una muestra de pacientes ingresados con EM recogidos en los conjuntos mínimos básicos de datos de 87 hospitales españoles durante el periodo 2008-2010. Se calculó la mortalidad, la prolongación de estancias y los sobrecostes atribuibles a los TCA controlando mediante análisis multivariado de la covarianza variables como la edad y el sexo, el tipo de hospital, el tipo de ingreso, otros trastornos adictivos y las comorbilidades.
Resultados: Se estudiaron 10.249 ingresos por EM de 18 a 74 años de edad, entre los cuales hubo 215 pacientes con TCA. Los ingresos con EM y TCA fueron predominantemente varones, mayor frecuencia de ingresos urgentes, con mayor prevalencia de trastornos por tabaco y drogas y con índices de comorbilidad de Charlson más elevados. Los pacientes con EM y TCA presentaron importantes excesos de mortalidad (94,1%), prolongación indebida de estancias (2,4 días) y sobrecostes por alta (1.116,9 euros).
Conclusiones: De acuerdo a los resultados de este estudio, los TCA en pacientes con EM aumentaron significativamente la mortalidad, la duración de la estancia hospitalaria y sus costes.

Introduction

The mortality rate of patients with multiple sclerosis (MS) is higher than that of the general population; life expectancy of these patients is 7-14 years shorter.[1,2] In many cases, death is due to causes which are unrelated to the disease and frequent among the general population: cardiovascular disease, cancer, chronic respiratory diseases, infections, and injury (including self-harm).[3–6] Both chronic and acute alcohol use disorders (AUD) may worsen the progression of MS. In these patients, AUDs may promote or aggravate such conditions as obesity, arterial hypertension, diabetes mellitus, pancreatitis, cirrhosis, stroke, and tumours.[7] The prevalence of anxiety and depression disorders,[8–11] suicidal ideation, and self-harm is also higher among patients with MS and AUDs.[8,9,12,13] AUDs are usually associated with tobacco use, and many of the disorders cited may worsen when patients with MS are heavy smokers or have nicotine dependence.[14,15]

AUDs may worsen cognitive impairment in patients with MS[16,17] and are associated with poorer treatment compliance, which results in more severe disease progression.[18,19]

Despite the above, no studies have addressed the impact of AUDs on hospitalised patients with MS in Spain in terms of alcohol-attributable mortality, extended hospital stays, and overexpenditure.

In-hospital outcomes may also be influenced by such other variables as age, sex, hospital, type of admission (emergency vs scheduled), presence of other addictions, and comorbidities.[20–24] Therefore, any study aiming to evaluate the impact of AUDs on hospitalised patients with MS should consider the potential impact of confounding and the interaction effects of these predictive variables.

We gathered data from a sample of patients with MS, aged 18-74 years, from 87 Spanish centres, who were admitted to hospital between 2008 and 2010. We attempted to control for such confounding and interaction variables as age, sex, type of hospital, type of admission, concomitant addictions, and comorbidities.

The purpose of this study is to analyse the potential impact of AUDs on mortality, extended hospital stays, and overexpenditure for hospitalised patients with MS.

Patients and methods

Study design

We conducted a retrospective observational study using a sample of patients from Spanish hospitals.

Sample

To ensure that the sample was representative of Spain and of every autonomous community, and accounting for the stratification of hospitals into groups (according to size and complexity) proposed by the Spanish Ministry of Health, Social Services, and Equality,[25] we applied stratified sampling to select patients from 87 Spanish hospitals from every autonomous community.

Based on written and electronic data from the patients' clinical histories, diagnoses and procedures were coded according to the ninth revision of the International Classification of Diseases (ICD-9). Data were coded and recorded in the database by specialised staff. This type of database, called a minimum basic dataset (MBDS), contains demographic data, admission and discharge dates, type of admission and discharge, main and secondary diagnosis, external causes, and procedures; data are coded using the ICD-9. The database also uses the diagnosis-related group (DRG) system; hospitals are grouped by size and the type of care they provide.[25]

Variables

Presence of ICD-9 code 340 for any of the MBDS diagnostic codes was defined as MS.[26] Patients transferred to other centres were excluded.

The study only included patients aged 18-74 years. As an indicator of comorbidity, we calculated the Charlson Comorbidity Index (CCI)[27] for each comorbidity using the ICD-9 codes proposed by Quan et al.[28] AUDs were defined as problems associated with excessive alcohol consumption, either sporadic or chronic, identified with the following ICD-9 codes: alcohol dependence syndrome (303.00-303.93), non-dependent alcohol abuse (305.00-305.03), alcohol-induced mental disorders (291.0-291.9), alcoholic polyneuropathy (357.5), alcoholic cardiomyopathy (425.5), alcoholic gastritis (535.30-535.31), alcohol-induced liver damage (571.0-571.3), excessive blood level of alcohol (790.3), and toxic effect of alcohol and accidental poisoning by alcohol (980.0-980.9 and E860.0-E860.9).[29] We also used the ICD-9 codes for tobacco and other drug use.[29]

Hospitals were divided into 5 groups by size and type of care according to the classification of the Spanish Ministry of Health, Social Services, and Equality[25]; this step was essential to control for confounding and to calculate care costs.

Data analysis

The main purpose of the study was to determine the mortality rate, hospitalisation time, and hospital costs associated with AUDs in patients with MS. Costs were calculated using the hospital costs of each DRG, stratified by hospital group, based on the estimates published by the Spanish Ministry of Health, Social Services, and Equality for the years 2008-2010.

A bivariate analysis was performed to examine the association between MS and AUD, on the one hand, and sex, type of admission, and other addictions and comorbidities, on the other; we used the chi-square and *t* tests, or their non-parametric versions. To minimise confounding, we performed a multivariate analysis of covariance (MANCOVA) to determine the effect of AUDs on in-hospital mortality, duration of hospitalisation, and hospital costs in patients with MS. The requirements of continuous variables were verified and data were adjusted for age, sex, type of admission, addictions, hospital group, and health status (using the CCI) after selecting the model that best fitted the data. Statistical significance was set at $P < .0001$ due to the sample size and the fact that multiple comparisons were conducted. We calculated the adjusted mean of each dependent variable (mortality, hospitalisation time in days, costs at discharge) in patients with MS with and without AUDs, and evaluated the differences between both groups. Statistical analysis was performed with version 14.1 of the STATA/MP statistics software.

The study design and the analysis and presentation of results were based on the recommendations of the STROBE statement for observational studies.[30]

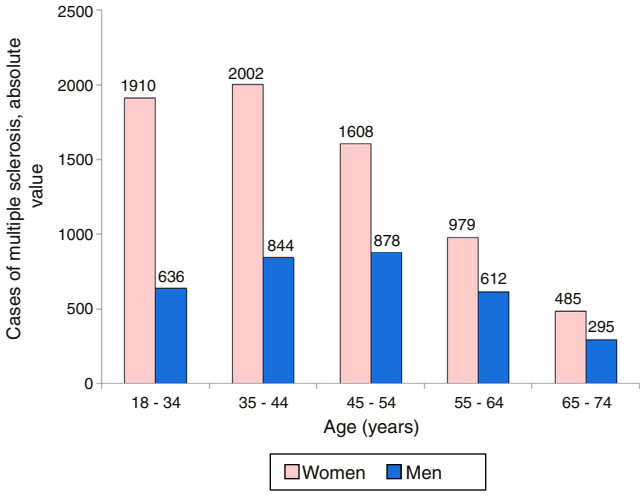

Figure 1 Distribution of patients with multiple sclerosis by age and sex.

Results

Patient characteristics

We identified 10 249 admissions due to MS: 6984 (68.1%) were women and 3265 (31.9%) were men. Fig. 1 shows the distribution of admissions by sex and age group. Most admissions of women with MS corresponded to the age group 35-44 years, followed by age groups 18-34 years and 45-54 years. Among men, admissions corresponded mainly to the

Table 1 Number of patients with multiple sclerosis admitted to different types of hospitals (classification of hospitals by the Spanish Ministry of Health, Social Services, and Equality).

Type of hospital	Characteristics	No. of admissions with MS (%)
Group 1	Small hospitals with a mean of fewer than 150 beds, little high-tech equipment, and low care complexity	55 (0.54)
Group 2	Basic general hospitals, with a mean of 200 beds and limited teaching activity, although some offer up to 8 residency specialties. Some high-tech equipment and a maximum of 2 complex departments	485 (4.73)
Group 3	Local hospitals with a mean of 500 beds (the number may vary considerably) and up to 160 residents, providing care to cases of intermediate complexity	3662 (35.73)
Group 4	Large hospitals, more heterogeneous in terms of equipment, size, and activity (500-1000 beds), with intense teaching activity (over 160 residents) and a mean of 4 complex departments	2391 (23.33)
Group 5	Very large hospitals of great importance to the healthcare system and providing a large volume of care, more than 900 beds, an approximate mean of 300 residents in 36 different specialties (minimum of 17), advanced technologies, and a wide variety of complex departments (at least 5)	3656 (35.67)
Total		10 249 (100.0)

MS: multiple sclerosis.

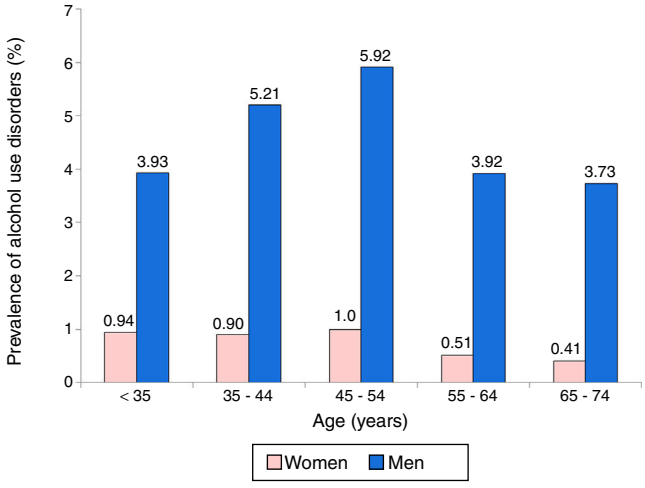

Figure 2 Prevalence of alcohol use disorders among patients with multiple sclerosis, by age and sex.

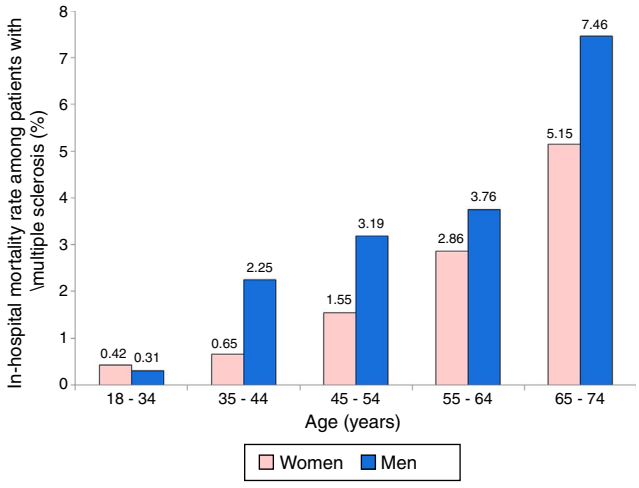

Figure 3 Raw in-hospital mortality rates in patients with multiple sclerosis, by age and sex.

age group 45-54 years, followed by groups 35-44 and 18-34 years.

Table 1 shows the distribution of cases of MS in each group of hospitals and the characteristics of each type of centre.

A total of 215 patients with MS had AUDs (2.1%); these were predominantly men (156 [4.8%] vs 59 women [0.8%]). Fig. 2 shows the distribution of patients with MS and AUDs by age and sex. AUDs were more frequent among men, especially in the age group 45-54 years, followed by the group of patients aged 35-44 years. Among women, prevalence of AUDs was higher in the 45-54 age group and the 18-34 year group.

Table 2 summarises patient characteristics by sex. Male patients were older than women, caused more emergency admissions, and had a higher prevalence of addictions (tobacco use disorders, 28.8%; AUDs 4.8%; other drug use disorders, 3.1%). Men also had higher prevalence of several of the comorbidities analysed at admission: arterial hypertension, arrhythmias, myocardial infarction, cerebrovascular diseases, chronic obstructive pulmonary disease, peptic ulcer, diabetes, and hemiparesis or paraplegia; they also displayed higher CCI scores.

Mortality

A total of 193 patients admitted due to MS died (99 women and 94 men). The raw mortality rate was 1.42% in women and 2.88% in men. Fig. 3 displays mortality rates by sex and age group; rates are higher among men and increase progressively with age.

Table 3 compares the characteristics of patients who died during hospitalisation to those of survivors. Deceased patients were older (mean age, 54.2) and were more frequently admitted on an emergency basis (90.2%). The

Table 2 Characteristics of patients admitted with MS, by sex.

Variables recorded	Women ($n = 6984$)		Men ($n = 3265$)		P[a]
	n	%	*n*	%	
Emergency admission	4550	65.1	2256	69.1	.0001
Age in years, mean (95% CI)	43.6 (43.3-43.9)		46.5 (46.0-46.9)		<.0001
Tobacco use disorders	1021	14.6	939	28.8	<.0001
Alcohol use disorders	59	0.8	156	4.8	<.0001
Other drug use disorders	78	1.1	101	3.1	<.0001
Comorbidities					
Obesity	176	2.5	60	1.8	.0319
Arterial hypertension without complications	526	7.5	336	10.3	<.0001
Arterial hypertension with complications	35	0.5	25	0.8	.1019
Cardiac arrhythmias	104	1.5	90	2.8	<.0001
Diseases of the pulmonary circulation	32	0.7	23	0.5	.1119
Valvular heart diseases	26	0.4	33	1.0	.0001
Anaemia due to nutritional deficiencies	185	2.6	26	0.8	<.0001
Posthaemorrhagic anaemia	121	1.7	4	0.1	<.0001
Electrolyte imbalances	101	1.4	61	1.9	.1104
Weight loss	64	0.9	45	1.4	.0037
Hypothyroidism	346	5.0	34	1.0	<.0001
Bleeding disorders	63	0.9	23	0.7	.3068
Depression	482	6.9	137	4.2	<.0001
History of myocardial infarction	27	0.4	82	2.5	<.0001
Congestive heart failure	51	0.7	46	1.4	.0009
Cerebrovascular diseases	82	1.2	81	2.5	<.0001
Dementia	16	0.2	7	0.2	.8835
Chronic obstructive pulmonary disease	146	2.1	124	3.8	<.0001
Autoimmune rheumatic diseases	28	0.4	9	0.3	.3245
Peptic ulcer	10	0.1	20	0.6	<.0001
Mild liver disease	53	0.8	22	0.7	.6378
Diabetes without chronic complications	218	3.1	201	6.1	<.0001
Diabetes with chronic complications	49	0.7	38	1.2	.0175
Hemiparesis or paraplegia	418	6.0	302	9.2	<.0001
Kidney disease	9	0.1	14	0.4	.0028
Moderate to severe liver disease	16	0.2	8	0.2	.8765
Cancer, leukaemia, or lymphoma	249	3.6	143	4.4	.0452
Metastatic cancer	84	1.2	39	1.2	.9715
AIDS	3	0.04	2	0.06	.6959
Mean CCI (95% CI)	0.37 (0.35-0.40)		0.56 (0.52-0.60)		<.0001

95% CI: 95% confidence interval; CCI: Charlson Comorbidity Index.
[a] Statistical significance was set at $P < .0001$.

prevalence of AUDs was considerably higher among these patients than among survivors (5.2% vs 2.0%). They also showed a considerably higher CCI and were more likely to display certain comorbidities at admission, including arrhythmias, diseases of the pulmonary circulation, electrolyte imbalances, weight loss, bleeding disorders, congestive heart failure, liver damage, hemiparesis or paraplegia, kidney disease, cancer, leukaemia, lymphoma, and metastatic cancer.

A total of 174 patients of the 6806 admitted on an emergency basis died (2.6%), compared to only 19 of the 3424 scheduled admissions (0.06%); the risk ratio was 4.6 (95% CI, 2.9-7.4; $P < .0001$).

The most common main diagnoses among the 193 patients with MS who died during hospitalisation were disorders directly associated with MS (28% of patients), respiratory diseases (18.1%), infections (17.1%), neoplasia (16.1%), cardiovascular diseases (9.3%), digestive disorders (4.7%), and other diagnoses (6.7%)

Associated mortality, extended hospital stays, and overexpenditure

Table 4 shows the results of the MANCOVA, which included age, sex, hospital group, type of admission, all addictions, and CCI.

The adjusted mortality rate in the multivariate model was significantly higher among patients with MS and AUDs (3.59% vs 1.85% in patients with no AUDs), with a difference between means of 1.74%; this represents a 94.1% increase in mortality attributable to AUDs.

Table 3 Characteristics of deceased patients with MS and survivors.

Variables recorded	Deceased patients ($n = 193$)		Survivors ($n = 10\,056$)		P[a]
	n	%	*n*	%	
Sex					
Women	99	51.3	6885	68.5	<.0001
Men	94	48.7	3171	31.5	<.0001
Emergency admission	174	90.2	6632	66.0	<.0001
Age in years, mean (95% CI)	54.2 (52.6-55.9)		44.4 (44.1-44.6)		<.0001
Tobacco use disorders	34	17.6	1926	19.1	.5909
Alcohol use disorders	10	5.2	205	2.0	.0025
Other drug use disorders	3	1.6	176	1.8	.8370
Comorbidities					
Obesity	5	2.6	231	2.3	.7877
Arterial hypertension without complications	26	13.5	836	8.3	.0105
Arterial hypertension with complications	3	1.6	57	0.6	.0748
Cardiac arrhythmias	18	9.3	176	1.8	<.0001
Diseases of the pulmonary circulation	7	3.6	48	0.5	<.0001
Valvular heart diseases	3	1.5	56	0.6	.0696
Anaemia due to nutritional deficiencies	7	3.6	204	2.0	.1214
Posthaemorrhagic anaemia	2	1.0	123	1.2	.8148
Electrolyte imbalances	24	12.4	138	1.4	<.0001
Weight loss	9	4.7	100	1.0	<.0001
Hypothyroidism	4	2.1	376	3.7	.2249
Bleeding disorders	10	5.2	76	0.8	<.0001
Depression	12	6.2	607	6.0	.9165
History of myocardial infarction	6	3.1	103	1.0	.0052
Congestive heart failure	10	5.2	87	0.9	<.0001
Cerebrovascular diseases	8	4.1	155	3.4	.0042
Dementia	0	0	23	0.2	.5060
Chronic obstructive pulmonary disease	12	6.2	258	2.6	.0017
Autoimmune rheumatic diseases	1	0.5	36	0.4	.7133
Peptic ulcer	1	0.5	29	0.3	.5584
Mild liver disease	5	2.6	70	0.7	.0022
Diabetes without chronic complications	16	8.3	403	4.0	.0029
Diabetes with chronic complications	2	1.0	85	0.8	.7745
Hemiparesis or paraplegia	33	17.1	687	6.8	<.0001
Kidney disease	4	2.1	19	0.2	<.0001
Moderate to severe liver disease	6	3.1	18	0.2	<.0001
Cancer, leukaemia, or lymphoma	36	18.7	356	3.5	<.0001
Metastatic cancer	23	11.9	100	1.0	<.0001
AIDS	0	0	5	0.05	.7567
Mean CCI (95% CI)	1.88 (1.49-2.27)		0.40 (0.38-0.42)		<.0001

95% CI: 95% confidence interval; CCI: Charlson Comorbidity Index.
[a] Statistical significance was set at $P < .0001$.

The mean hospital stay was also significantly longer in patients with AUDs (9.5 vs 7.1 days), with a mean increase in hospitalisation time of 2.4 days attributable to AUDs.

Mean hospitalisation costs were also significantly higher among patients with AUDs (€5488.70 vs €4371.80), with an overexpenditure of €1116.90 per case.

Discussion

Our results suggest that AUDs have a considerable impact on in-hospital mortality in patients with MS and result in significantly longer hospital stays and higher expenses. Both isolated episodes of excessive alcohol consumption and chronic alcohol use disorders have an impact on the course of the disease and result in severe complications.

Some of the most frequent causes of death in these patients were diseases frequently associated with AUDs, such as pneumonia and other respiratory tract infections,[31] sepsis,[32] urinary tract infections, and other types of infections, which are closely linked to immunosuppression associated with AUDs.[33] According to the literature, patients with MS are 3.7 times more likely to experience pneumococcal pneumonia than the general population[34]; the incidence of urinary and respiratory tract infections, gastrointestinal

Table 4 In-hospital mortality, extended hospital stays, and overexpenditure attributable to alcohol use disorders in patients with multiple sclerosis.[a]

	Adjusted mean in patients without AUDs	Adjusted mean in patients with AUDs	Difference between adjusted means attributable to AUDs	95% CI of the increase in means attributable to AUDs	*P*
Adjusted mortality rate (%)	1.85	3.59	1.74	1.1-3.3	<.0001
Adjusted hospitalisation time (days)	7.1	9.5	2.4	1.2-3.6	<.0001
Adjusted costs (€)	4371.8	5488.7	1116.9	832.3-2101.5	<.0001

95% CI: 95% confidence interval; AUD: alcohol use disorder.
[a] Multivariate analysis of covariance adjusted for age, sex, hospital group, type of admission, tobacco use disorders, drug use disorders, and Charlson Comorbidity Index.

infections, and other types of infections increases the risk of MS relapses.[35,36]

Given the large sample size and the wide range of hospitals represented in our study, our results may be extrapolated to other populations. To our knowledge, this is the first Spanish study analysing increased mortality, extended hospital stays, and overexpenditure attributable to AUDs in patients with MS.

Adequately controlling for confounding is the main challenge of studies analysing the impact of AUDs on prognosis and other outcome measures in hospitalised patients. Hospital stays, costs, and in-hospital mortality vary depending on a number of causes, including reason for admission, disease severity, comorbidities, type of hospital, and other patient social and demographic characteristics.[37] Inclusion of the hospital group in the multivariate model to control for the confounding effect is extremely important: previous research suggests that centre type, available equipment, and care standards have an impact on quality of care.[31]

Our study has a number of limitations. We used only data from the MBDS and did not include complementary patient data. We also used the definitions of addictions, MS, and comorbidities used by physicians at each centre; these were subsequently coded and recorded into the database by specialised staff who were not aware of inter-centre variability. The ICD-9 code for MS is used internationally in studies using databases of hospital discharges, but does not enable comparison of these diagnoses with clinical, imaging, and laboratory findings from patients' clinical histories. Previous studies have reported a high sensitivity and specificity of ICD-9 code 340 in hospitalised patients with MS[26] when all diagnostic codes (not only the main diagnosis) are included; on many occasions, patients with MS are admitted with complications or other diagnoses that are recorded as the main diagnosis, leaving MS as a secondary diagnosis. To avoid this information bias, we considered all diagnostic codes and not only the main diagnosis. Another limitation of our study is that the MBDS does not include data on patient disability (for example, Expanded Disability Status Scale scores), which prevents us from assessing the impact of the level of disability on mortality, hospital stays, and hospitalisation costs.

Using these databases also has considerable advantages. The data included are usually entered after discharge; as all cases are registered, they provide fairly accurate information on the incidence, prevalence, comorbidities, complications, and mortality of the diseases attended in hospitals.[37,38] These data may be analysed retrospectively, unlike in studies with other designs requiring prospective data collection. The collection of data from large samples and for long periods, as in the present study, can be relatively fast and easy; as data are gathered systematically, costs are considerably lower. The risk of selection bias in these studies is lower since patients (or their legal representatives) cannot refuse to participate in the study. The availability of data about costs for each DRG, stratified by hospital group and year, is another significant advantage, as this makes it easier to calculate overexpenditure due to MS and AUDs.

A consensus document drafted by several Spanish scientific societies recommends pneumococcal vaccination of adults with underlying diseases, including AUDs[39]; this recommendation should be followed at all healthcare levels, including hospital services identifying patients with AUDs. The impact of AUDs on mortality, hospital stay duration, and overexpenditure associated with pneumococcal pneumonia in Spain supports this recommendation.[40] Recent review articles recommend vaccination not only against pneumococcal infection but also against meningococcal and *Haemophilus influenzae* infection in patients with MS, mainly among those receiving immunosuppressive or immunomodulatory therapy.[34,41]

Diagnosing and beginning to treat alcohol, tobacco, and other drug use disorders should be one of the main therapeutic goals before discharging a patient with MS. Enquiring into alcohol, tobacco, and other drug use is essential from an ethical and from a professional viewpoint. Several studies have shown the effectiveness of a brief intervention on alcohol, tobacco, and other drug use, and informing the primary care physician about the problem in the discharge report[42–44]; this approach may prevent complications and hospital readmissions. Reducing the number of admissions and readmissions attributable to these disorders would help reduce the costs associated with patients' absence from

work and hospital stays, increasing hospital bed availability and considerably decreasing the risk of mortality.

Conclusions

Among hospitalised patients with MS, AUDs increase in-hospital mortality rate by 94.1%, extend hospital stays an additional 2.4 days, and result in an overexpenditure of €1116.90. Such preventive measures as controlling alcohol use and administering specific vaccinations may contribute to reducing the magnitude of the problem in these patients.

Funding

This study was funded by the Spanish Ministry of Health, Social Services, and Equality as part of the national drugs plan (grant 2009I017, project G41825811), and by the Andalusian Regional Department of Health and Social Affairs funding for biomedical and health science research in 2013 (PI-0271-2013).

Conflicts of interest

The authors have no conflicts of interest to declare.

References

1. Ragonese P, Aridon P, Salemi G, d'Amelio M, Savettieri G. Mortality in multiple sclerosis: a review. Eur J Neurol. 2008;15:123—7.
2. Scalfari A, Knappertz V, Cutter G, Goodin DS, Ashton R, Ebers GC. Mortality in patients with multiple sclerosis. Neurology. 2013;81:184—92.
3. Bronnum-Hansen H, Koch-Henriksen N, Stenager E. Trends in survival and cause of death in Danish patients with multiple sclerosis. Brain. 2004;127:844—50.
4. Grytten Torkildsen N, Lie SA, Aarseth JH, Nyland H, Myhr KM. Survival and cause of death in multiple sclerosis: results from a 50-year follow-up in Western Norway. Mult Scler. 2008;14:1191—8.
5. Hirst C, Swingler R, Compston DA, Ben-Shlomo Y, Robertson NP. Survival and cause of death in multiple sclerosis: a prospective population-based study. J Neurol Neurosurg Psychiatry. 2008;79:1016—21.
6. Smestad C, Sandvik L, Celius EG. Excess mortality and cause of death in a cohort of Norwegian multiple sclerosis patients. Mult Scler. 2009;15:1263—70.
7. Turner AP, Hawkins EJ, Haselkorn JK, Kivlahan DR. Alcohol misuse and multiple sclerosis. Arch Phys Med Rehabil. 2009;90:842—8.
8. Bombardier CH, Blake KD, Ehde DM, Gibbons LE, Moore D, Kraft GH. Alcohol and drug abuse among persons with multiple sclerosis. Mult Scler. 2004;10:35—40.
9. Quesnel S, Feinstein A. Multiple sclerosis and alcohol: a study of problem drinking. Mult Scler. 2004;10:197—201.
10. Feinstein A. Multiple sclerosis and depression. Mult Scler. 2011;17:1276—8.
11. Beier M, d'Orio V, Spat J, Shuman M, Foley FW. Alcohol and substance use in multiple sclerosis. J Neurol Sci. 2014;338:122—7.
12. Feinstein A. An examination of suicidal intent in patients with multiple sclerosis. Neurology. 2002;59:674—8.
13. Pompili M, Forte A, Palermo M, Stefani H, Lamis DA, Serafini G, et al. Suicide in multiple sclerosis: a systematic review of current literature. J Psychosom Res. 2012;73:411—7.
14. Jafari N, Hintzen RQ. The association between cigarette smoking and multiple sclerosis. J Neurol Sci. 2011;311:78—85.
15. Arruti M, Castillo-Triviño T, Egüés N, Olascoaga J. Tabaco y esclerosis multiple. Rev Neurol. 2015;60:169—78.
16. Vik PW, Cellucci T, Jarchow A, Hedt J. Cognitive impairment in substance abuse. Psychiatr Clin North Am. 2004;27:97—109.
17. Chiaravalloti ND, DeLuca J. Cognitive impairment in multiple sclerosis. Lancet Neurol. 2008;7:1139—51.
18. Tremlett H, van der Mei I, Pittas F, Blizzard L, Paley G, Dwyer T, et al. Adherence to the immunomodulatory drugs for multiple sclerosis: contrasting factors affect stopping drug and missing doses. Pharmacoepidemiol Drug Saf. 2008;17:565—76.
19. Bryson CL, Au DH, Sun H, Williams EC, Kivlahan DR, Bradley KA. Alcohol screening scores and medication nonadherence. Ann Intern Med. 2008;149:795—803.
20. Scalfari A, Neuhaus A, Daumer M, Ebers GC, Muraro PA. Age and disability accumulation in multiple sclerosis. Neurology. 2011;77:1246—52.
21. Marrie RA, Horwitz R, Cutter G, Tyry T, Campagnolo D, Vollmer T. High frequency of adverse health behaviors in multiple sclerosis. Mult Scler. 2009;15:105—13.
22. Degenhardt A, Ramagopalan SV, Scalfari A, Ebers GC. Clinical prognostic factors in multiple sclerosis: a natural history review. Nat Rev Neurol. 2009;5:672—82.
23. Marrie RA, Horwitz RI, Cutter G, Tyry T, Vollmer T. Association between comorbidity and clinical characteristics of MS. Acta Neurol Scand. 2011;124:135—41.
24. Overs S, Hughes CM, Haselkorn JK, Turner AP. Modifiable comorbidities and disability in multiple sclerosis. Curr Neurol Neurosci Rep. 2012;12:610—7.
25. de Sanidad M, Sociales e Igualdad S. Registro de altas de los hospitales generales del Sistema Nacional de Salud. CMBD. Norma Estatal. 2012. Avaiable from: http://www.msssi.gob.es/estadEstudios/estadisticas/cmbd.htm [accessed 15.02.16].
26. St.Germaine-Smith C, Metcalfe A, Pringsheim T, Roberts JI, Beck CA, Hemmelgarn BR, et al. Recommendations for optimal ICD codes to study neurologic conditions. A systematic review. Neurology. 2012;79:1049—55.
27. Charlson ME, Pompei P, Ales KL, McKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373—83.
28. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43:1130—9.
29. Gili-Miner M, Bejar-Prado L, Gili-Ortiz E, Ramírez-Ramírez G, López-Méndez J, López-Millán JM, et al. Alcohol use disorders among surgical patients: unplanned 30-days readmissions, length of hospital stay, excessive costs and mortality. Drug Alcohol Depend. 2014;137:55—61.
30. Vandenbroucke JP, von Elm E, Altman DG, Gøtzsche PC, Mulrow CD, Pocock SJ, et al. STROBE initiative. Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration. Epidemiology. 2007;18:805—35.
31. Samokhvalov AV, Irving HM, Rehm J. Alcohol consumption as a risk factor for pneumonia: a systematic review and meta-analysis. Epidemiol Infect. 2010;138:1789—95.
32. Moss M. Epidemiology of sepsis: race, sex, and chronic alcohol abuse. Clin Infect Dis. 2005;41 Suppl. 7:S490—7.
33. Szabo G, Mandrekar P. A recent perspective on alcohol, immunity, and host defense. Alcohol Clin Exp Res. 2009;33:220—32.
34. Wotton CJ, Goldacre MJ. Risk of invasive pneumococcal disease in people admitted to hospital with selected immune-mediated

diseases: record linkage cohort analyses. J Epidemiol Community Health. 2012;66:1177—81.
35. Handel AE, Giovannoni G, Ebers GC, Ramagopalan SV. Environmental factors and their timing in adult-onset multiple sclerosis. Nat Rev Neurol. 2010;6:156—66.
36. Correale J, Fiol M, Gilmore W. The risk of relapses in multiple sclerosis during systemic infections. Neurology. 2006;67:652—9.
37. Powell AE, Davies HTO, Thomson RG. Using routine comparative data to assess the quality of healthcare: understanding and avoiding common pitfalls. Qual Saf Health Care. 2003;12:122—8.
38. Needham DM, Scales DC, Lapaucis A, Pronovost PJ. A systematic review of the Charlson comorbidity index using Canadian administrative databases: a perspective on risk adjustment in critical care research. J Crit Care. 2005;20:12—9.
39. Picazo JJ, González-Romo F, García A, Pérez-Trallero E, Gil P, de la Cámara R, et al. Consenso sobre la vacunación antineumocócica en el adulto con patología de base. Rev Esp Quimioter. 2013;26:232—52.
40. Gili-Miner M, López-Méndez J, Béjar-Prado L, Ramírez-Ramírez G, Vilches-Arenas A, Sala-Turrens J. Trastornos por consumo de alcohol y neumonía neumocócica adquirida en la comunidad: mortalidad atribuible, prolongación de estancias y sobrecostes. Arch Bronconeumol. 2015;51:564—70.
41. Loebermann M, Winkelmann A, Hartung HP, Hengel H, Reisinger EC, Zettl UK. Vaccination against infection in patients with multiple sclerosis. Nat Rev Neurol. 2012;8:143—51.
42. Rehm J, Roerecke M. Reduction of drinking in problem drinkers and all-cause mortality. Alcohol Alcohol. 2013;48:509—13.
43. Villalbí JR, Bosque M, Gili M, Espelt A, Brugal T. Políticas para prevenir los daños causados por el alcohol. Rev Esp Salud Pública. 2014;88:515—28.
44. Coleman T. ABC of smoking cessation. Use of simple advice and behavioural support. BMJ. 2004;328:397—9.