



Original Article

National trends in diabetes mellitus hospitalization in Spain 1997–2010: Analysis of over 5.4 millions of admissions

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ABSTRACT

Aims: To analyze national trends in the rates of hospitalizations (all-cause and by principal discharge diagnosis) in total diabetic population of Spain.

Methods: We carried out a nation-wide population-based study of all diabetic patients hospitalized between 1997 and 2010. All-cause hospitalizations, hospitalizations by principal discharge diagnosis, mean age, Charlson Comorbidity Index, readmission rates and length of hospital stay were examined. Annual rates adjusted for age and sex were analyzed and trends were calculated.

Results: Over 14-years-period, all-cause hospitalizations of diabetic patients increased significantly, with an average annual percentage change of 2.5 (95%CI: 1.5–3.5; $P_{\text{trend}} < 0.01$). The greatest increase was observed in heart failure (5.4; 95%CI: 4.8–6.0; $P_{\text{trend}} < 0.001$), followed by neoplasms (4.9; 95%CI: 3.6–5.8; $P_{\text{trend}} < 0.001$), pneumonia (2.7; 95%CI: 2.0–4.0; $P_{\text{trend}} < 0.001$), stroke (2.4; 95%CI: 1.6–3.4; $P_{\text{trend}} < 0.001$), chronic obstructive pulmonary disease (2.0; 95%CI: 1.4–3.4; $P_{\text{trend}} < 0.001$) and coronary artery disease (1.6; 95%CI: 1.1–2.3; $P_{\text{trend}} < 0.01$). The adjusted number of all-cause hospitalizations of patients with diabetes per 100,000 inhabitants increased 2.6-fold. The increase in hospitalizations was significantly higher among patients ≥ 75 years old. Males experienced a greater increase in all-cause, neoplasm, heart failure, chronic obstructive pulmonary disease, and pneumonia hospitalizations ($p < 0.01$ for all). Hospitalized diabetic patients were progressively older and had more comorbidities, higher readmission rates and shorter hospital stays ($p < 0.05$ for all).

Conclusions: Hospitalizations of diabetic patients more than doubled in Spain during the study period. Heart failure and neoplasms experienced the greatest annual increases and remained the principal causes of hospitalization, probably associated with advanced age and comorbidities of hospitalized diabetics. Coronary and cerebrovascular diseases experienced a lower annual increase, suggesting an improvement in cardiovascular care in diabetes in Spain.

1. Introduction

The prevalence of diabetes mellitus (DM) has increased exponentially, becoming a major public health problem due to its associated morbidity and mortality [1]. Around the world, an estimated 415 million adults have diabetes, which represents 9% of the global population over age 18. An estimated 318 million people have impaired glucose tolerance. In Europe, the number of people with DM is estimated to be 59.8 million (9.1% of the adult population) and is expected to increase to 71.1 million (10.7%) by 2040 [2]. In Spain, the Di@bet

study reported a prevalence of DM of 13.8%, with the number of people diagnosed with DM more than doubling over the last decade due to an increasing obesity rate and an aging population [3].

The cost associated with the hospitalizations for DM and its complications are enormous; they are estimated to be 6–8% of total healthcare cost in developed countries. > 50% of all healthcare expenditures in this population are linked to the direct costs of DM-related complications, with high hospital admission rates and lengthy mean hospital stays [4–6].

Patients with DM are frequently admitted to the hospital. Admission

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rates for these patients are between 2 and 6 times higher and the lengths of hospital stays longer than those of patients without DM. These admissions are usually for treatment of conditions other than the diabetes [4,7]. Cardiovascular disease has been described as the main cause of hospitalization and death in these patients. Indeed, DM increases the risk of coronary disease and stroke, with a risk of death that is at least twice as high in diabetic patients than in non-diabetic patients [8]. Advanced age, insulin treatment, poor metabolic control, obesity, comorbidities, pre-existing nephropathy and macroangiopathic disease have been identified as predictors of hospitalization [4,8].

Although there is a considerable and growing interest in healthcare aspects related to DM in Spain, epidemiological data focused on main causes of hospitalizations for DM patients have not been sufficiently described. The aim of this study is to analyze national trends in hospitalizations rates (all-cause and by principal discharge diagnosis) for the total diabetic population in Spain between 1997 and 2010, broken down by age and sex. In addition, we described changes in mean age, Charlson Comorbidity Index (CCI), readmission rates, and length of hospital stay during the period of study.

2. Material and methods

We carried out a nation-wide, population-based study of all patients with DM who were hospitalized in Spain between 1997 and 2010. All-cause hospitalizations and principal discharge diagnosis (heart failure (HF), neoplasms, stroke, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD) and pneumonia), mean age, CCI, readmission rates, and length of hospital stay were analyzed. Annual rates were adjusted according to age and sex. Then, trends were calculated. Data from the Spanish National Hospital Discharge Database (CMBD, Conjunto Mínimo Básico de Datos) from the Spanish National Health System were used for the study.

The CMBD compiles validated patient data, including sex, birth date, admission and discharge dates, readmissions, up to 20 procedures performed during the hospital stay and up to 14 discharge diagnoses for all hospitals in Spain. It includes information on > 98% of hospitalizations. This national database is coordinated by the Spanish Ministry of Health, Social Services and Equality, which sets standards for record keeping and performs routine audits of the data [9].

The criteria for disease were established according to the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), which is used in the Spanish CMBD. We selected admissions of patients who had a diagnosis of DM (ICD-9-CM codes: 250.0–250.9). Clinical characteristics included information on overall comorbidity at the time of diagnosis, which was assessed by calculating the CCI [10].

2.1. Statistical analysis

Hospitalization rates for all causes and by principal discharge diagnosis were calculated per 100,000 people, adjusting for age and sex using the direct method. The total Spanish population as of 2010 was used as the standard population [11]. Data was stratified by age (≤ 18 , 19–44, 45–64, 65–74, and ≥ 75 years old) and sex (male and female) to quantify the trend in mean hospitalizations among DM patients during the study period. The average annual percent change (AAPC) and a 95% Confidence Interval (CI) was calculated for all causes and by principal discharge diagnosis and adjusted for age and sex. Change-point analysis was used when required. The trends were considered significant when the slope of the trend was not equal to zero and the p -value was < 0.05 .

Continuous data were shown as means \pm standard deviations and qualitative data as absolute value and percentage. A comparative analysis was conducted by carrying out repeated calculations of the analysis of variance (ANOVA).

Statistical analyses were performed using Epidat: programa para

análisis epidemiológico de datos, version 4.2 (Consellería de Sanidade, Xunta de Galicia. A Coruña., Galicia, España), Joinpoint Regression Program, version 4.2.0.2 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute. Bethesda., MD, USA) and SPSS Statistics for Windows, version 15.0 (SPSS Inc. Chicago., IL, USA).

2.2. Ethical considerations

Data confidentiality and patient anonymity were maintained at all times, in accordance with Spanish legislation on observational studies [12]. Patient identifying information was deleted before the database was analyzed. It is not possible to identify patients on an individual level either in this article or in the database. Due to the anonymous nature and mandatory collection of the information included in the dataset, informed consent from the patients was not necessary.

3. Results

During the 14-years study period, 48,060,888 admissions were recorded in Spain, 5,447,725 (12.8%) in patients with DM. The adjusted number of all-cause hospitalizations in patients with DM increased 2.6-fold, from 675 to 1743 admissions per 100,000 inhabitants (Fig. 1). Comparatively, the increase of hospitalizations in patients without DM was less marked than in patients with DM (1.2-fold, $p < 0.001$), from 8619 to 10,033 admissions per 100,000 inhabitants.

Over the study period, the adjusted rates of hospitalizations according to principal discharge diagnosis increased (Fig. 2). The increase was greater for HF and neoplasms, whereas discharges for CAD and COPD stabilized.

The AAPC for all-cause hospitalizations and according to principal discharge diagnosis for both the total population with DM and stratified by age and sex are shown in Table 1. All-cause hospitalizations showed a significant average annual increase. In regards to principal discharge diagnosis, the greatest average increase was observed in HF, followed by neoplasm, pneumonia, stroke, COPD and CAD. From 1997 to 2003, hospitalizations for CAD showed a significant increase (AAPC: 2.8; 95%CI: 1.8–4.0; $P_{\text{trend}} < 0.001$). However, from 2003 to 2010, a non-significant decrease was observed (AAPC: -0.8 ; 95%CI: -2.1 – (-0.2) ; $P_{\text{trend}} = 0.101$). In addition, the annual increase in hospitalization was higher among older patients, especially for those ≥ 75 years old, both for all-cause hospitalization and according to principal discharge diagnosis. There was a greater increase in all-cause, neoplasm, HF, COPD and pneumonia hospitalizations in males (all $p < 0.01$). All-cause hospitalizations in total population without DM showed a non-significant increase (AAPC: 1; 95%CI: 0.8–1.9; $P_{\text{trend}} = 0.09$).

During the study period, the mean age of hospitalized patients rose progressively from 67.8 to 71.7 years old. Overall, approximately 98% of patients admitted to hospital were ≥ 45 years old and 93% ≥ 65 years old. The CCI and readmission rates significantly increased whereas the length of hospital stay decreased during the study period. These data are shown in Table 2. Similarly to patients with DM, significant increases were shown in hospitalized patients without DM for the mean age (from 69.8 to 73.9 years old, $p < 0.05$), the CCI (from 1.6 to 2.2, $p < 0.05$) and the readmission rates (from 6.1 to 8.2%, $p < 0.05$); and a significant decrease was shown for the length of hospital stay (from 9.2 to 7.1 days, $p < 0.05$) during the period of study. Patients without DM were significantly older ($p < 0.01$), had lower CCI ($p < 0.01$) and readmission rates ($p < 0.01$), and shorter hospital stay ($p < 0.01$) than those patients with DM.

4. Discussion

Our study found that age- and sex-adjusted all-cause hospitalizations in patients with DM increased from 1997 to 2010. HF and neoplasms remained the most frequent causes of hospitalization during the

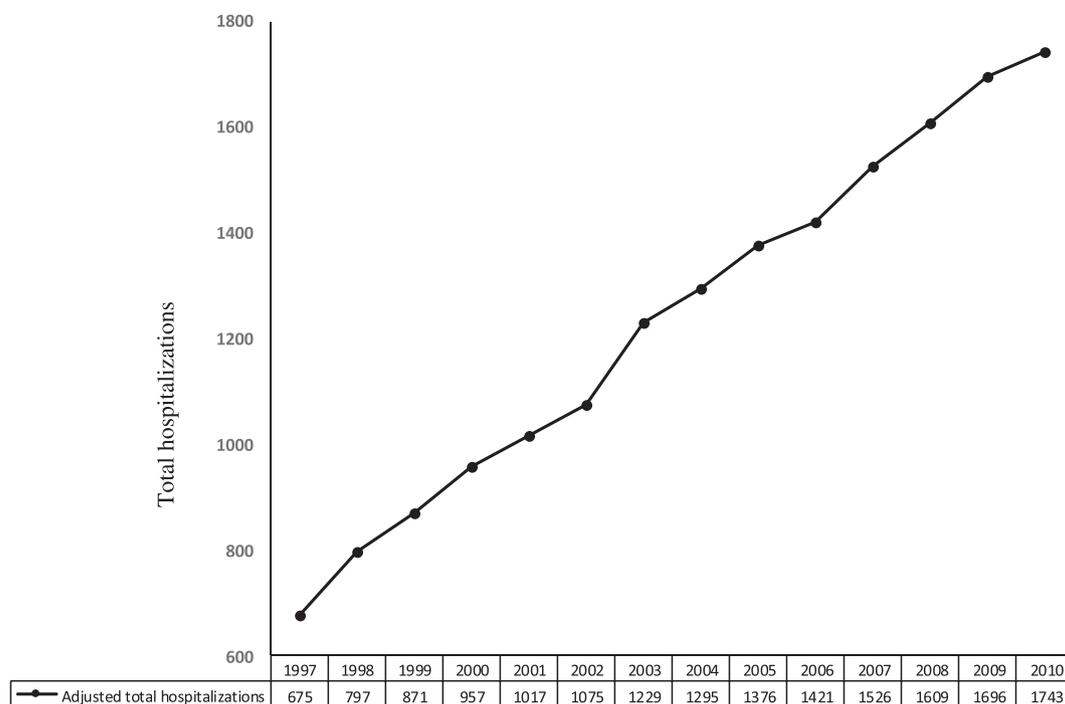


Fig. 1. Adjusted number of all-cause hospitalizations in patients with diabetes mellitus from 1997 to 2010. Data were calculated per 100,000 inhabitants per year.

period of study. Cerebrovascular and coronary diseases were the third and fourth causes of hospitalization, respectively, and admission for pulmonary diseases were less frequent. The greatest average annual increase was observed in HF, followed by neoplasm, pneumonia, stroke, COPD and CAD, though CAD showed a non-significant negative trend starting in 2003. Hospitalizations were higher among older patients, especially for those ≥ 75 years old, and there was a greater increase in all-cause, neoplasm, HF, COPD and pneumonia hospitalizations among males. Patients with DM who were hospitalized were progressively older, had more comorbidities, higher readmission rates, and shorter hospital stays.

To our knowledge, this is the first epidemiological research study to analyze national trends in hospitalizations rates (all-cause and by principal discharge diagnosis) in the total diabetic population in Spain. These findings are important because they show increasing hospitalization rates in a large sample over an extended period of time. Furthermore, it provides valuable information such as the adjusted AAPC.

Patients with DM are at greater risk of being hospitalized than patients without DM, and a large percentage of these hospitalizations are due to DM-related complications, with an enormous direct medical costs associated with [13,14].

DM is a major risk factor for developing HF [15]. Patients with DM have a 2.5 times higher risk of HF; this risk is even greater when CAD is excluded. Several studies have explored the development of clinical HF in patients with DM, which is associated with an estimated 30% higher risk of requiring hospitalization than those without DM and a significantly poorer cardiovascular outcome [16–18]. This association between HF and DM is even stronger among elderly adults [19]. Our data regarding hospitalizations (all-cause and by principal discharge diagnosis) of patients with DM are consistent with these findings. Furthermore, our findings are in line with our previously-published study, which showed a significant increase in the absolute number of hospitalizations for HF in patients with DM in Spain from 1997 to 2010 [20].

Regarding neoplasms, other works have shown that patients with DM have higher cancer rates compared to those without DM [21]. DM

and cancer are closely linked and share pathogenic mechanisms that could induce structural and biomechanical remodeling in many tissues [22]. Patients with DM and cancer are more likely to be admitted to hospital and, furthermore, factors such as lower socioeconomic status, presence of comorbidities, and aggressive neoplasms have been associated with [22,23]. In this study, we found a steady increase in the number of hospitalizations for neoplasms in patients with DM, with a significant average annual percentage change in a population that was older and had more comorbidities. Although previous epidemiologic studies have described the association between DM and cancer, we are unaware of studies that analyze trends in hospitalization rates for neoplasms.

Stroke was the third cause of hospitalizations among patients with DM in our study. Though a positive AAPC was observed, it was less marked than the rate for HF and neoplasms. In contrast to our stroke finding, prior national health survey and registry-based studies have observed a decline in stroke trends worldwide [24–27]. In Spain, stroke mortality has been gradually declining in recent years [28] while time trends in hospitalization have increased significantly, especially among patients with DM [29]. Lower mortality rates with consequent higher survival rates would justify the increase in stroke hospitalization rates. On the other hand, a recent report warned that less than a third of Spanish diabetic patients had proper control of hypertension, the main risk factor for stroke [30].

Prior studies, principally from the beginning of 21st century, have shown decreased hospitalization rates for CAD. This has mainly been due to a reduction in acute myocardial infarction [24–26,31]. In Spain, an analysis of hospitalizations for acute myocardial infarction and use of percutaneous coronary interventions in patients with and without DM from 2001 to 2010 showed an initial increase in hospitalization rates for acute events followed by a gradual decline after 2004 [32]. Although our findings are consistent with these studies, these studies differ from ours in the fact that they have specifically analyzed not only trends in major cardiovascular events requiring hospital admission but also in cardiovascular interventions. These data reflect the positive effect of acute clinical care measures, improvements in the performance of the healthcare system, and preventive health strategies implemented

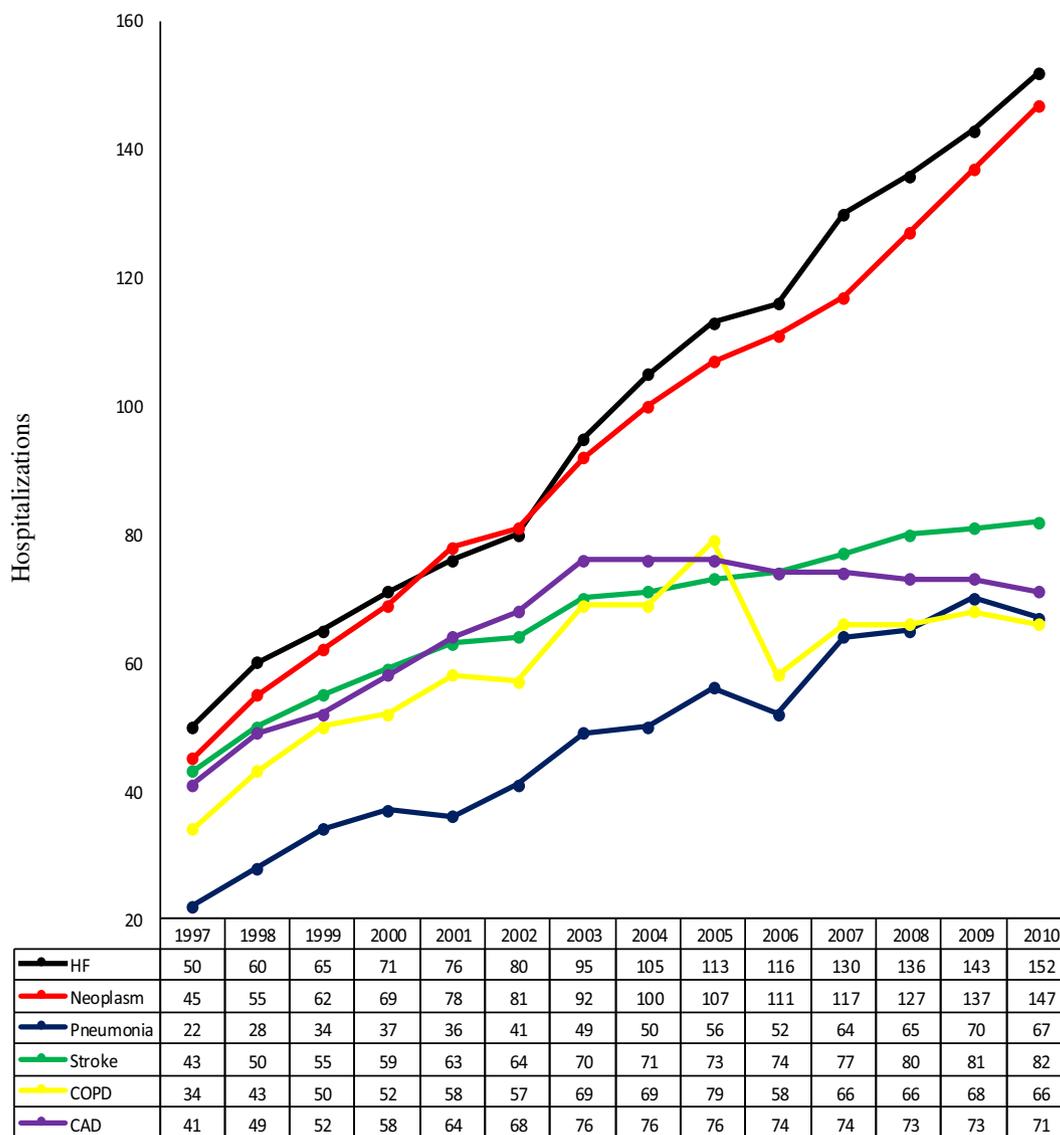


Fig. 2. Adjusted number of hospitalizations according to principal discharge diagnosis in patients with diabetes mellitus from 1997 to 2010. Data were calculated per 100,000 inhabitants per year.

CAD: coronary artery disease; COPD: chronic obstructive pulmonary disease; HF: heart failure.

to prevent CAD in patients with DM [24].

In our study, pulmonary diseases such as pneumonia and COPD contributed considerably to the causes of hospitalization in patients with DM though in a smaller proportion than cardiovascular diseases and neoplasms. However, there was a higher average annual increase in pneumonia hospitalizations than in cardiovascular diseases and COPD hospitalizations during the period of study. These results are consistent with several reports around the world [33–35], which noted increased rates of hospitalizations for pulmonary diseases among patients with DM. In Spain, a recent report published by López-de-Andrés et al. [36], concluded that pneumonia rates were higher, increasing from 2004 to 2013 among patients with DM, and that mortality decreased over this period. On the other hand, hospitalization trends for COPD, analyzed in various studies, have shown a decrease or stabilization for COPD hospital admissions in the total population [37,38]. This phenomenon was also shown in the only study carried out on the general population of Spain from 2006 to 2010 [38]. These findings are partially in line with our results, as we have shown an overall increase during the studied period; however, the slope was not steady. Furthermore, we have specifically focused on patients with DM, which could explain the

differences.

It is well-known that older adults with DM are at higher risk of developing complications than younger adults. In addition, they have higher rates of poly medication, functional disabilities, morbidity and mortality compared to older individuals without DM [39]. However, the differences according to sex, though widely analyzed, have not been clearly established and results have been diverse and controversial [18,20,23,32]. In our study, hospitalization rates were higher among older patients, especially for those ≥75 years old, and males experienced a greater increase in all-cause, neoplasm, HF, COPD and pneumonia hospitalizations. In addition, hospitalized patients with DM were progressively older, had more comorbidities, higher readmissions rates, and shorter hospital stays.

We would like to acknowledge some limitations of this study. Firstly, we did not have accurate denominator data for diabetic patients. We were therefore unable to calculate diabetes-specific admissions rates in the population due to the diabetes prevalence over the time is not well documented. Changes in diabetes prevalence during this period of time could bias our results. To partially address these concerns, because other factors could be associated with the increasing

Table 1
Annual average percentage change for all-cause hospitalizations and according to principal discharge diagnosis: total population and stratified by age and sex (1997–2010).

	AAPC	95%CI	p-value (Trend)
All-cause hospitalizations			
≤ 18 years	0.1	0.1 to 0.3	0.141
19–44 years	1.7	1.2 to 3.0	0.012
45–64 years	2.1	1.4 to 3.6	< 0.01
65–74 years	2.2	1.4 to 3.7	< 0.01
≥ 75 years	4.9	3.2 to 6.1	< 0.001
Male	2.6	1.9 to 3.8	< 0.01
Female	2.1	1.4 to 3.3	< 0.01
Total population	2.5	1.5 to 3.5	< 0.01
Neoplasms			
≤ 18 years	1.3	1.1 to 2.9	0.031
19–44 years	2.8	2.5 to 3.5	< 0.01
45–64 years	5.9	5.4 to 6.4	< 0.001
65–74 years	5.9	5.5 to 6.5	< 0.001
≥ 75 years	9.2	8.5 to 10.6	< 0.001
Male	7.9	6.6 to 9.2	< 0.001
Female	2.9	2.2 to 3.5	< 0.01
Total population	4.9	3.6 to 5.8	< 0.001
Heart failure			
≤ 18 years	0.1	0.1 to 0.3	0.194
19–44 years	1.1	1.0 to 2.1	0.041
45–64 years	1.7	1.3 to 3.3	< 0.01
65–74 years	1.9	1.3 to 3.3	< 0.01
≥ 75 years	8.9	7.9 to 9.8	< 0.001
Male	5.5	5.1 to 5.8	< 0.001
Female	5.1	4.5 to 6.1	< 0.001
Total population	5.4	4.8 to 6.0	< 0.001
Coronary artery disease			
≤ 18 years	-0.2	-0.4 to -0.1	0.201
19–44 years	1.1	1.0 to 2.1	0.044
45–64 years	1.9	1.4 to 2.9	0.029
65–74 years	1.3	1.1 to 3.0	0.044
≥ 75 years	2.9	2.0 to 4.1	< 0.001
Male	1.3	1.1 to 2.5	0.024
Female	1.2	1.1 to 2.3	0.034
Total population	1.6	1.1 to 2.3	< 0.01
Stroke			
≤ 18 years	-0.2	-0.3 to -0.1	0.189
19–44 years	1.1	1.0 to 2.6	0.044
45–64 years	1.9	1.2 to 2.9	< 0.01
65–74 years	1.4	1.1 to 2.7	0.021
≥ 75 years	3.1	2.0 to 4.0	< 0.001
Male	2.2	1.5 to 3.7	< 0.001
Female	2.0	1.5 to 3.3	< 0.001
Total population	2.4	1.6 to 3.4	< 0.001
Chronic obstructive pulmonary disease			
≤ 18 years	0.2	0.1 to 0.4	0.202
19–44 years	2.0	1.4 to 3.1	< 0.01
45–64 years	1.9	1.3 to 3.0	< 0.01
65–74 years	1.6	1.1 to 3.1	0.024
≥ 75 years	3.0	1.9 to 4.0	< 0.001
Male	2.1	1.9 to 3.9	< 0.01
Female	1.6	1.2 to 2.9	0.021
Total population	2.0	1.4 to 3.4	< 0.001
Pneumonia			
≤ 18 years	-0.2	-0.4 to -0.1	0.241
19–44 years	1.3	1.1 to 2.2	0.037
45–64 years	2.1	1.4 to 3.2	< 0.01
65–74 years	2.8	1.9 to 3.9	< 0.001
≥ 75 years	4.8	3.7 to 5.9	< 0.001
Male	2.9	2.0 to 3.9	< 0.001
Female	2.3	1.9 to 3.8	< 0.001
Total population	2.7	2.0 to 4.0	< 0.001

AAPC: Average annual percentage change; 95%CI: 95% Confidence Interval.

prevalence of diabetes, we calculated age- and sex-adjusted rates for all-cause hospitalizations each year, using a standard population as reliable standard of measurement. Secondly, our data source was an

Table 2
Change in mean age, Charlson Comorbidity Index, readmission rates, and length of hospital stay for patients with diabetes mellitus from 1997 to 2010.

	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	p-value
Age (years)	67.8 ± 18.3	68.3 ± 18.3	68.8 ± 18.3	69.0 ± 18.4	69.1 ± 18.4	69.4 ± 18.4	69.9 ± 18.4	70.1 ± 18.5	70.5 ± 18.5	70.6 ± 18.5	71.0 ± 18.5	71.3 ± 18.6	71.4 ± 18.6	71.7 ± 18.6	< 0.05
CCI	2.1 ± 1.3	2.2 ± 1.3	2.2 ± 1.3	2.3 ± 1.3	2.3 ± 1.3	2.3 ± 1.3	2.4 ± 1.6	2.4 ± 1.6	2.4 ± 1.6	2.5 ± 1.6	2.5 ± 1.6	2.5 ± 1.6	2.5 ± 1.6	2.6 ± 1.6	< 0.05
RA (%)	7.4	8.2	8.6	8.9	9.4	9.4	9.6	10.3	9.8	10.4	10.9	10.4	11.3	10.5	< 0.05
HS (days)	11.1 ± 8.6	10.9 ± 8.6	10.5 ± 8.6	10.5 ± 8.5	10.3 ± 8.5	10.2 ± 8.5	10.2 ± 8.5	9.9 ± 8.4	9.7 ± 8.4	9.3 ± 8.4	9.5 ± 8.4	9.3 ± 8.4	9.3 ± 8.5	8.9 ± 8.5	< 0.05

Continuous data are shown as means ± standard deviations and qualitative data as absolute value and percentage.
CCI: Charlson Comorbidity Index; HS: Hospital stay; RA: Readmission.

administrative database based on hospital discharge records, which led to significant underestimation of diabetes cases due to inadequate classification. Thirdly, using ICD-9-CM codes to describe disease trends may lead to bias and inaccuracy, depending on the validity of the coding. In this regard, we were unable to differentiate between type 1 diabetes, type 2 diabetes, and others with a degree of certainty, as diagnosis codes are not reliable in this regard. Fourthly, criteria for diagnosing principal discharge causes, such as HF or CAD, might have changed in clinical practice during the study period. Fifthly, we did not study geographical variations, social and individual disparities or the accessibility to DM care that could be suggested as possible reasons for increasing admissions. Sixthly, due to the limited information obtained from the Spanish National Discharge Database we could not perform further analysis in order to determine the impact of hospitalization for DM on the long-term outcomes as readmissions or mortality, or to establish associations between them. Finally, it is difficult to compare rates across countries and studies because definitions of disease and methodology may differ.

5. Conclusion

This study showed a significant increase in hospitalizations in patients with diabetes. Hospitalized diabetic patients were progressively older and had more comorbidities. Heart failure and neoplasm showed the greatest annual increases and remained the main causes of hospitalization, most likely associated with progressive aging and presence of comorbidities. In contrast, coronary and cerebrovascular diseases showed a lower annual increase than heart failure and neoplasms, suggesting an improvement in cardiovascular care and preventative measures for diabetes in Spain. Further specific research is needed to fully identify the reasons behind these trends in hospitalization rates that could be important in order to improve our daily clinical practice and implement the medical expenditure for diabetes in developed countries.

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The authors have no conflict of interests to disclose.

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