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Economic burden of cirrhosis in Catalonia: a population-based analysis

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ABSTRACT

Background Cirrhosis is a chronic disease with high morbidity and mortality. Few studies have evaluated healthcare resource use in patients with cirrhosis.

Objective We aimed to describe the point prevalence of cirrhosis on 31 December 2012 and the population-level distribution of healthcare resource use and expenditures in a non-selected population of patients with cirrhosis, stratified by whether their disease was compensated or decompensated, and by comorbidity burden.

Methods This population study included all known patients aged >18 years with cirrhosis (according to International Classification of Diseases, ninth revision) in Catalonia, Spain, on 31 December 2012. We evaluated healthcare resource use and expenditure during 2013, taking into account the presence of decompensation before or during 2012.

Results We documented 34 740 patients diagnosed with cirrhosis (58.7% men; mean age 61.8±14 years), yielding a point prevalence of 460 per 100 000 inhabitants on 31 December 2012. Annual mortality was 9.1%. During 2013, healthcare expenditures on patients with cirrhosis totalled €142.1 million (€4234 per patient), representing 1.8% of the total 2013 healthcare budget of Catalonia. Hospitalisation costs accounted for 35.1% of the total expenditure and outpatient care accounted for 22.4%. MultivariateMultivariate logistic regression identified morbidity burden, HIV infection, hospitalisation and emergency room visits during 2012 as independent predictors of expenditure above the 85th centile (area under the receiver operating curve, 0.88 (95% CI 0.883 to 0.893, P<0.001)).

Conclusions Cirrhosis accounts for a high proportion of healthcare resource usage and expenditures; hospitalisation accounted for the highest expenditures.

INTRODUCTION

Cirrhosis is the late stage in progressive liver disease of varying aetiologies. Not much is known about the prevalence of cirrhosis among older adults but it is expected to increase, in part due to the rising incidence of non-alcoholic fatty liver disease and an ageing hepatitis C population.[1–3] In fact, there is an increasing trend of diagnosis of chronic liver disease and its decompensation and complications (including hepatocellular carcinoma).[4]

The time interval between the compensated phase of cirrhosis and the development

Strengths and limitations of this study

► We performed cost analysis using a population-based database including 34 740 patients diagnosed with cirrhosis in Catalonia, thus minimising selection bias.
► The study quantified the total economic impact of cirrhosis in relation to hepatic decompensation and determined the distribution of the costs involved in treating patients with this condition.
► We have not included important information such as the aetiology of cirrhosis and other important clinical data for characterising the study population and the evolution of the disease (ie, MELD, Child-Pugh or ACLF).
► The use of a validated risk assessment tool made it possible to calculate individuals' morbidity burden and to analyse the impact of multimorbidity on resource use and costs.
► Although the database is periodically monitored and has high quality data, using administrative data to identify patients with cirrhosis can lead to misclassification.

of complications (decompensated cirrhosis) is often long, with a reported median survival of 12 years.[5 6] Compared with age-matched patients without cirrhosis, patients with cirrhosis have worse health and more comorbid conditions, resulting in greater use of healthcare services, including more hospital visits, nursing home stays and physician visits.[2]

Chronic hepatitis C virus infection is one of the main causes of cirrhosis and it is the most common indication for liver transplantation in Spain and worldwide.[7 8] Hepatitis C infection affects the liver, and is associated with hypertension and other cardiovascular diseases, chronic renal impairment and diabetes mellitus. Some studies have estimated the costs of hepatitis C infection without, however, analysing the impact of complications of advanced liver disease.[4]

Knowing the impact of decompensated disease on outcomes and on the cost of treating advanced liver disease is important

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for planning resource allocation and preventive strategies, especially in a public health system.[8] Because of its importance in public health, a growing number of publications address chronic liver disease.[2 8–11]

This study aimed to describe overall healthcare resource use and expenditures in a non-selected population of patients with cirrhosis stratified into those with compensated disease and those with decompensated disease.

MATERIALS AND METHODS
Data source and study design
We analysed healthcare resource use and expenditures in 2013 in patients with cirrhosis residing in Catalonia, an autonomous region in North-East Spain with 7553 650 inhabitants (density, 232.8 inhabitants/km^2). The regional health department, named CatSalut, provides universal healthcare coverage to all residents and collects detailed information on healthcare usage, including information from the minimum basic data set registered by healthcare units (eg, hospitals, primary care centres, nursing facilities and mental health centres). CatSalut also collects information on drug prescription and billing for services (eg, outpatient visits to specialists, emergency department visits, non-urgent medical transportation, outpatient rehabilitation, home oxygen therapy and dialysis). Initially, the Catalan health administration deployed a series of registers to record healthcare units' activity. In 2011, the Catalan Health Surveillance System (CHSS) was created to integrate most of those activity registers, placing the patient (instead of the provider) in the centre of this information system, thus favouring longitudinal analysis and providing a more holistic and transversal view of health problems. CHSS includes all the diagnoses reported by the different providers, regardless of whether they were recorded as the primary or secondary diagnosis. This information system collects all information from the entire public health system, including all hospital admissions and healthcare visits. CHSS contains 529 million diagnoses, 440 million contacts with various public health services and 519 million prescriptions dispensed by pharmacies. Its automated data validation system checks the consistency of the data and identifies potential errors. Moreover, as this information is used for healthcare provider payment purposes, periodic external audits are carried out to ensure the quality and reliability of the data.

Information from private health centres was not available for analysis, because although private hospitals notify CatSalut of their activity, they do not associate the reported data with each patient's identification number. Therefore, CatSalut has information about the activity performed, but not for individual patients. CatSalut administrative data showed that in 2013, of 2878 unplanned hospitalisations of patients with cirrhosis, 2727 (94.8%) took place in public hospitals and only 151 (5.2%) in private hospitals.

Selection of patients
This retrospective fixed cohort study included all residents of Catalonia aged 18 years or older diagnosed with cirrhosis on or before 31 December 2012 who were alive on that date. The International Classification of Diseases, ninth revision, Clinical Modification codes were used to identify cases with cirrhosis (codes 571.2 and 571.5) (see online supplementary appendix 1) as well as complications of cirrhosis.

We defined hepatic decompensation as an unscheduled hospital admission for hepatic encephalopathy, ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, or hepatic complications such as hepatocellular carcinoma, oesophageal varices or portal hypertension. We divided patients into three groups:

▶ Compensated group: patients with cirrhosis who had not had any episode of hepatic decompensation before 2013.
▶ Previous decompensation group: patients who had had at least one episode of hepatic decompensation before 2012 but none during 2012.
▶ Recent decompensation group: patients who had at least one episode of hepatic decompensation during 2012.

Calculation of expenditure
The primary outcome variable of the study was expenditures related to healthcare resource use in 2013. In Catalonia, expenditures for healthcare and pharmacy services are normally directly attributed to each patient through their personal health identification number. Expenditures for primary care are calculated indirectly from a standard price per visit weighted by the attending professional (physician or nurse) and site of assistance. Expenditures for hospital care are weighted by diagnosis-related groups. Expenditures for inpatient care at hospitals, skilled nursing facilities and mental health centres are calculated according to length of stay (online supplementary table 1s shows the average price by activity in Catalonia). The costs are attributed to each person through their personal identification codes assigned by the public health system.

The prices used in the calculations are the rates that CatSalut pays healthcare providers, which are published annually in the Official Gazette of the Government of Catalonia.

CatSalut's budget for 2013 was €8085 million, of which €7885 million (97.5%) was devoted to healthcare services. Emergency medical transport and screening for breast and colon cancers accounted for the largest proportion of expenditures that were not individually allocated. The healthcare services in CatSalut's morbidity database accounted for €7502 million (€968 per capita), which represents 95.1% of CatSalut's expenditure on health services.

In this population-based study, the methods used allowed us to analyse the expenditures on patients with cirrhosis, but not the costs attributable only to the

Table 1 Demographic characteristics according to liver disease group

| | Total | Compensated group No hepatic decompensation | Hepatic decompensation | |
			Previous decompensation group Decompensation before 2012, but not during 2012	Recent decompensation group Decompensation during 2012
Cases	34 740	25 299	5393	4048
Patients/year	33 567	24 737	5195	3635
Age mean±SD (years)*	61.2±13.9	60.6±14.4	62.2±12.6	63.7±12.7
Women (%)	41.7	44.8	33.8	33.4
Morbidity				
Number of chronic comorbidities (mean)*	5.1	4.7	6.0	6.5
Stratification group (AMG)*				
Very high-risk stratum (%)	11.6	7.8	17.0	27.8
High-risk stratum (%)	30.6	26.0	41.0	45.4
Moderate-risk stratum (%)	35.2	38.4	32.3	22.3
Low-risk stratum (%)	22.2	27.8	9.7	4.5
Ischaemic heart disease (%)*	12.1	10.6	15.3	17.4
Stroke (%)*	6.1	5.4	7.7	8.5
Heart failure (%)*	7.4	6.0	9.8	12.7
Diabetes (%)*	28.7	25.0	37.9	39.7
Renal failure (%)*	7.3	4.9	13.3	14.6
COPD (%)*	15.8	12.7	20.1	21.3
Dementia (%)	3.1	3.0	3.2	3.7
Depression (%)	22.3	22.2	22.3	23.2
Malignancy (%)*	19.0	13.5	27.9	41.3
Malnutrition (%)*	0.5	0.2	1.0	1.3
Anaemia (%)*	21.3	12.1	42.5	50.7
HIV+ (%)*	2.6	1.7	5.1	5.0
Hepatitis C virus + (%)*	14.7	7.0	31.8	39.6
Alcohol (%)*	28.1	17.5	57.6	55.8
Drugs (%)*	4.2	3.0	7.5	7.5
Mortality and hepatic decompensation during 2013				
Mortality 2013 (%)*	6.7	4.3	8.5	19.4
Hepatic decompensation 2013 (%)*	11.7	2.7	21.3	54.8

*P <0.001.
AMG, Adjusted Morbidity Grouper; COPD, chronic obstructive pulmonary disease.

disease itself. Thus, we calculated the total healthcare expenditure per person per year (in euros) for patients with cirrhosis (including cirrhosis-related care and care related to comorbidities), rather than the expenditure specifically associated with cirrhosis care. This approach enabled a comprehensive analysis of healthcare expenditures in this group of complex patients. To account for shorter follow-up periods due to deaths, time at risk was calculated in days from 31 December 2012 to the date of death (or 365 days otherwise) and transformed to years. Thus, the unit of analysis is not the patient but rather the patient/year.

Assessment of predictors of increased expenditure
We also sought to identify independent predictors associated with yearly expenditures greater than or equal to the 85th centile of the distribution in the study population. This analysis included only patients who survived

Table 2 Health services utilisation in 2013 in function of liver disease group

| | Compensated group No hepatic decompensation | Hepatic decompensation | |
		Previous decompensation group Decompensation before 2012, but not during 2012	Recent decompensation group Decompensation during 2012
Cases	25 299	5393	4048
Admission rate (×100)*	29.2	60.8	117.9
Mean length of hospitalisation (days)*	1.8	4.5	9.6
Unplanned admission rate (×100)*	16.5	37.8	78.3
Patients with unplanned admission (%)*	10.8	22.9	40.3
Patients >1 unplanned admission (%)*	3.4	8.4	18.5
Emergency visit rates (×100)*	71.2	111.1	186.8
Patients with emergency visit (%)*	33.8	45.5	61.4
Patients with >1 emergency visits (%)*	15.7	25.7	38.8
Gastroenterology/hepatology specialist outpatient visits (average)*	0.6	1.8	2.6
Other hospital outpatient visits (average)	3.1	4.3	4.8
Primary care visits (average)*	11.8	13.4	16.5
Users of a skilled nursing facility (%)*	4.0	7.3	15.7
Mental health outpatient visits rate (×100)	16.6	13.5	15.1
Psychiatric hospital admission rate (×100)	0.6	0.7	1.6

*P< 0.001
Likewise, the mean length of hospitalisation increased from 1.8 days in compensated patients to 4.5 days in previously decompensated patients to 9.6 days in recently decompensated patients.

the whole study period (n=32 414). Predictors assessed were age, sex, comorbidities included in the Charlson Index,[12 13] previous healthcare utilisation and a novel population-based health risk assessment tool deployed in Catalonia, the Adjusted Morbidity Grouper (AMG), which is used to calculate an individual's morbidity burden.[14] AMG categorises each patient in a risk-stratification pyramid with five strata:

► Basal-risk stratum: comprising individuals with minimum morbidity burden; 50% of individuals in the overall population of Catalonia (but 0% of patients with cirrhosis) fall into this stratum.
► Low-risk stratum: comprising individuals with low level complexity; 30% of individuals in the overall population of Catalonia (but 22.2% of patients with cirrhosis) fall into this stratum.
► Moderate-risk stratum: comprising individuals with higher complexity than the previous risk stratum; 15% of individuals in the overall population of Catalonia (but 35.6% of patients with cirrhosis) fall into this stratum.
► High-risk stratum: comprising individuals with a greater morbidity burden than the previous stratum; 4% of individuals in the overall population of Catalonia (but 30.6% of patients with cirrhosis) fall into this stratum.
► Very high-risk stratum: comprising individuals with the highest morbidity burden; 1% of individuals in

the overall population of Catalonia (but 11.6% of patients with cirrhosis) fall into this stratum.

Statistical analysis

Continuous variables are reported as means±SDs. For the univariate analysis, we used χ^2 tests to compare categorical variables and analysis of variance to compare continuous variables. To identify independent predictors of increased healthcare expenditure, we used Multivariate logistic regression. Variables were entered in the model one by one and retained when their significance was <0.10. To evaluate the discriminatory ability of the resulting predictive model for identifying patients with cirrhosis with healthcare expenditures ≥85th centile, we calculated the area under the receiver operating characteristic (ROC) curve.[15] Goodness of fit of the model was evaluated using the Hosmer-Lemeshow method. Statistical analyses were performed using SPSS software, V.18.0. All statistical tests and CIs were constructed with a type I error level of 5% and P values <0.05 were considered statistically significant.

Ethics

The study used retrospective data from administrative databases and patients were anonymous to the researchers. Our ethics committee stated that under Spanish legislation informed consent and ethics committee approval were not required.
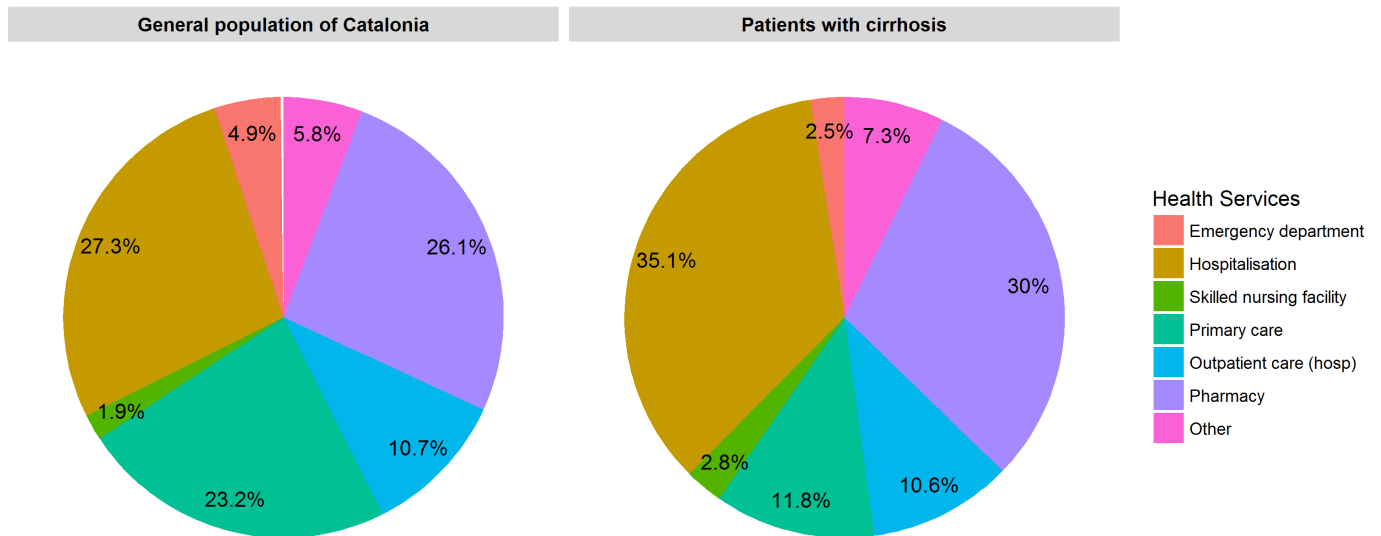
Figure 1 Health expenditure by type of resource in the general population and in patients with cirrhosis, in millions of euros. The category 'Other' includes mental health services, non-urgent medical transportation, outpatient rehabilitation and home oxygen therapy.

RESULTS
Demographics of included patients
We documented 34 740 patients in Catalonia with cirrhosis on 31 December 2012 (460 per 100 000 inhabitants); of these 25 299 (72.8%) had never had any episode of hepatic decompensation (compensated group), 5393 (15.5%) had had at least one episode of decompensation before 2012 (previous decompensation group) and 4048 (11.7%) had at least one episode of decompensation during 2012 (recent decompensation group). In the entire group, mean age was 61.2±14 years and 41.8% were women; however, the proportion of women decreased with worsening disease (44.8% in the compensated group, 33.8% in the previous

decompensation group and 33.4% in the recent decompensation group) (P<0.001).

Patients with advanced liver disease had more comorbidities and their comorbidities were more severe than those with less advanced disease. There were no significant differences in dementia or depression between groups (table 1; see also online supplementary table 2s).

Hepatitis C infection was more common in patients who had episodes of decompensation, as was the use of sedatives and alcohol and/or drug abuse.

Overall mortality during 2013 was 6.7%. Mortality was 4.3% in the compensated group, 8.5% in the previous decompensation group and 19.4% in the recent decompensation group.
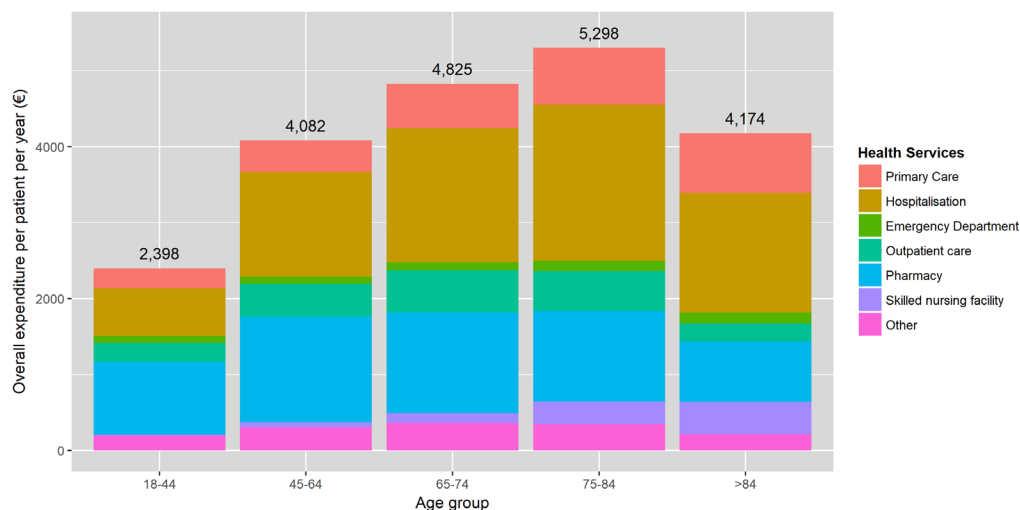

Figure 2 Healthcare resource use in patients with cirrhosis by age.
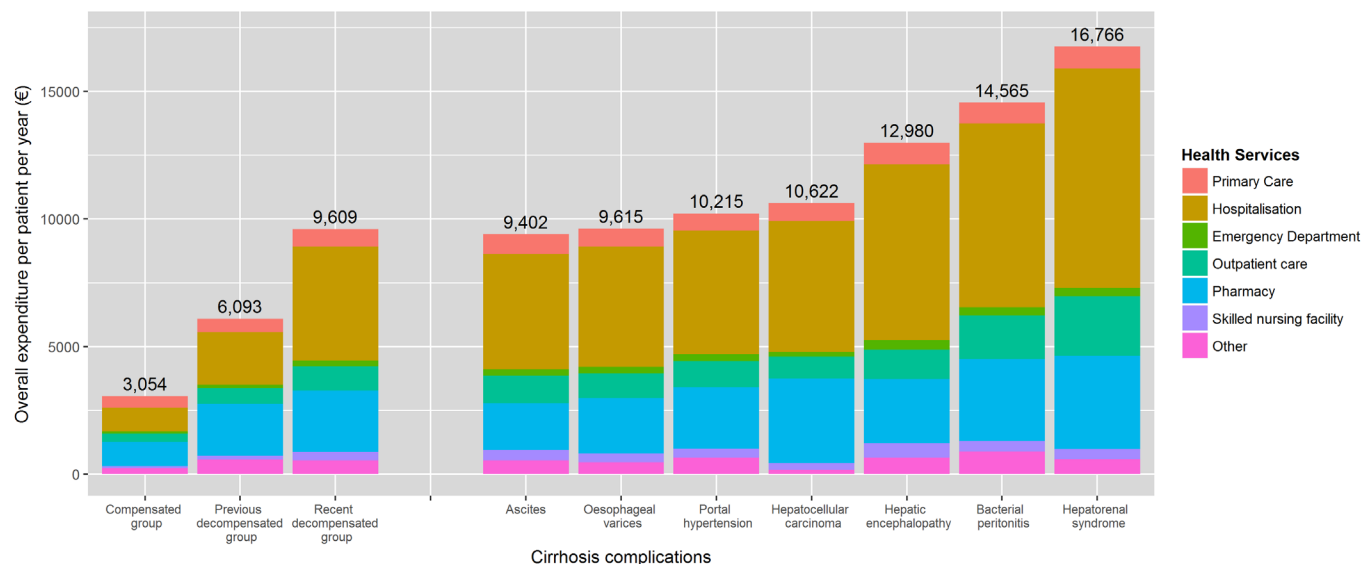
Figure 3 Healthcare resource use in patients with cirrhosis by hepatic decompensation.

Online supplementary table 3s shows these patients' probability of dying, adjusted for different factors.

Use of health resources

The overall rate of hospitalisations was 44.4 per 100 patients; the rate increased with severity (29.2 in the compensated group, 60.8 in the previous decompensation group and 117.9 in the recent decompensation group; P<0.0001) (table 2). Online supplementary table 4s shows the probability of having at least one urgent hospital admission, adjusted by different factors.

The rate of hospital admissions from the emergency room in the entire group was 27 per 100 patients, being 16.5 in the compensated group, 37.8 in the previous decompensation group and 78.3 in the recent decompensation group (P<0.0001). Whereas 33.8% of the patients in the compensated group presented at the emergency department at least once and 15.7% more than once, 45.5% of those in the previous decompensation group presented at least once and 25.7% more than once and 61.4% of those in the recent decompensation group presented at least once and 38.8% more than once (table 2 and online supplementary table 5s).

Similarly, the number of gastroenterology outpatient visits significantly increased with hepatic decompensation. The number of outpatient visits to other departments
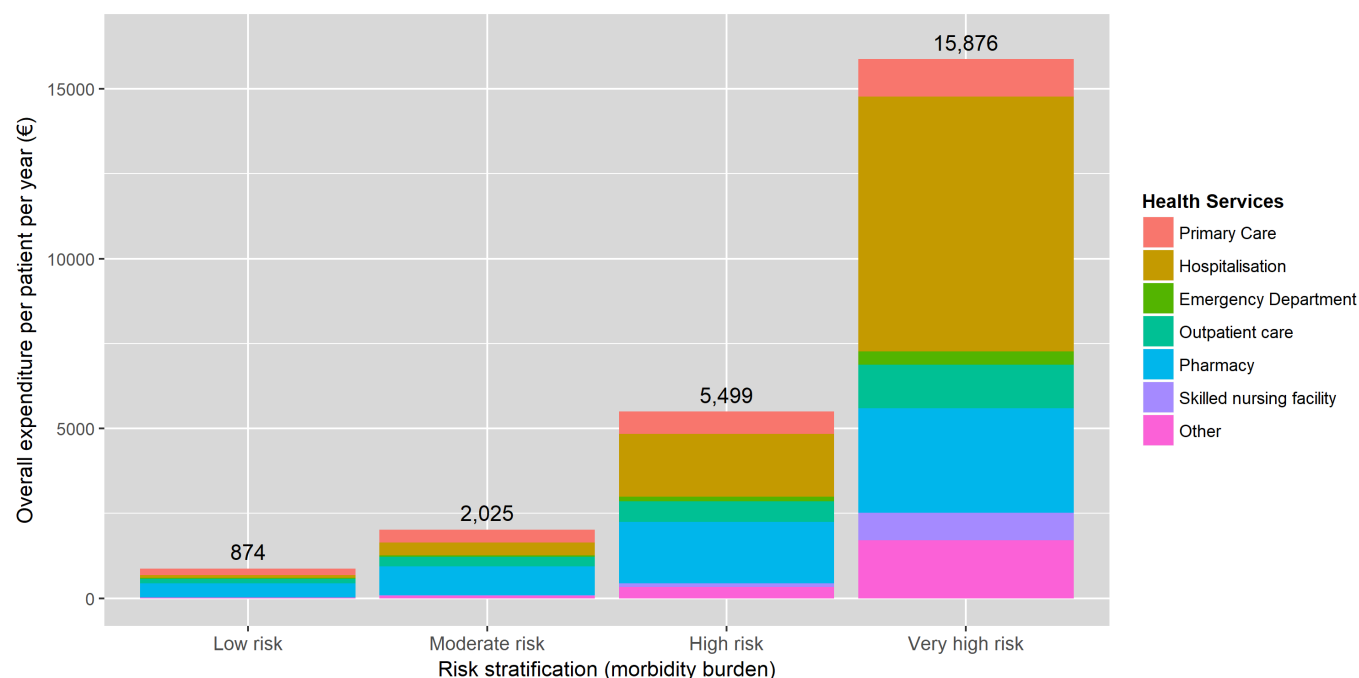

Figure 4 Healthcare resource use in patients with cirrhosis by risk stratification (morbidity burden).

Table 3 Multivariate logistic regression analysing factors associated with expenditure higher than the 85th percentile

	n	β coefficient	OR	95% CI	
Sex					
Male	18 783		1	–	–
Female	13 631	−0.034	0.967	0.890	1.050
Age group					
18–44 years old	4152		1	–	–
45–64 years old	15 027	0.037	1.037	0.881	1.222
65–74 years old	7540	−0.154	0.858	0.720	1.022
75–84 years old	4750	−0.515	0.597	0.496	0.720
>84 years old	945	−1.209	0.299	0.225	0.396
Hepatic decompensation					
Compensated group	24 219		1	–	–
Previous decompensation group	4934	0.311	1.364	1.230	1.514
Recent decompensation group	3261	0.687	1.988	1.770	2.234
Risk stratum (morbidity burden)					
Low-risk stratum	7694		1	–	–
Moderate-risk stratum	12 202	1.126	3.082	2.454	3.870
High-risk stratum	9758	2.769	15.944	12.780	19.891
Very high-risk stratum	2760	4.850	127.704	100.533	162.218
Chronic kidney disease	2075	0.113	1.120	0.988	1.269
Hepatitis C virus +	4377	0.429	1.536	1.389	1.699
HIV+	823	2.930	18.734	15.374	22.828
Unplanned hospitalisation during 2012					
0	27 687		1	–	–
1	3208	0.117	1.124	0.992	1.274
2	944	0.168	1.183	0.974	1.437
3	326	0.461	1.586	1.176	2.139
>3	249	0.507	1.660	1.166	2.363
Emergency department visits during 2012					
0	20 034		1	–	–
1–2	8919	0.190	1.209	1.095	1.334
3–5	2648	0.415	1.514	1.314	1.743
>5	813	0.580	1.785	1.431	2.226
Skilled nursing facility during 2012	820	−0.339	0.713	0.587	0.865
Constant		−4.593	0.010	–	–

also increased, but the difference did not reach statistical significance.

All patients had frequent contact with primary care physicians and/or nurses; the number of primary care visits increased with decompensation (11.8 in the compensated group, 13.4 in the previous decompensation group and 16.5 in the recent decompensation group; P<0.0001). The rate of outpatient visits to mental health centres and the rate of psychiatric hospitalisation did not differ among groups. Moreover, the sicker the patients were, the more they required social services from convalescence centres, intermediate-stay or long-stay centres and palliative care centres.

Assessment of healthcare expenditure

During 2013, a total of €142.1 million was spent in the care of patients with cirrhosis in Catalonia (1.8% of the total 2013 healthcare budget), representing an average expenditure of €4234 per patient/year.

Figure 1 displays the distribution of healthcare-related expenditures in patients with cirrhosis and in the general population of Catalonia. In patients with cirrhosis, the main source of expenditure was hospitalisation (for all causes), which accounted for 35.1% of

the total; pharmacy costs accounted for 30%, primary care for 11.8% and hospital outpatient care for 10.6%. In contrast, in the general population the main sources of expenses were hospitalisation (27.3%), pharmacy (26.1%), primary care (23.2%) and hospital outpatient care (10.7%).

Figure 2 shows the distribution of healthcare-related expenditures inpatients with cirrhosis, stratified by age group. Despite some differences in resource use and expenditure among the different age groups, hospitalisation accounted for the greatest expenditure in all groups.

Total medical expenditure was significantly higher for patients in the recent decompensation group than for those in the previous decompensation and compensated groups. In the recent decompensation group, hospitalisation was the main expenditure, accounting for more than half of all costs (figure 3). By contrast, the total expenditure in the compensated group was divided nearly equally among pharmacy, hospitalisation and outpatient care (hospital and primary care). The distribution of expenditures in the previous decompensation group lay between those of the other two groups. Figure 3 also shows the distribution of expenditures in 2013 in patients in the recent decompensation group according to the type of hepatic decompensation occurring in 2012; hepatorenal syndrome, followed by spontaneous bacterial peritonitis and hepatic encephalopathy, generated much higher expenditures than other complications, mainly due to hospitalisation.

In patients with cirrhosis, the average healthcare expenditure increased with the number of chronic comorbidities, from €773/year in patients with one comorbidity to €14,853/year in those with more than nine comorbidities. The AMG stratum was higher in patients with more comorbidities and expenditures increased exponentially with increasing AMG strata, from <€900 for patients in the low-risk stratum to >€15 000 for those in the very high-risk stratum (figure 4).

In patients with lower healthcare resource use (with expenditures <85th centile), expenditures were nearly equally distributed among primary care, pharmacy and hospitalisation. In patients with the highest healthcare resource use (expenditures ≥85th percentile), hospitalisation accounted for nearly half of all expenditures; total healthcare expenditure in this group was 10 times higher (€17 822 per patient/year vs €1806 per patient/year) than in patients with lower resource use.

Table 3 reports the Multivariate logistic regression analysis to identify predictors of high expenditure. Morbidity burden (AMG stratum), HIV infection, hospitalisation and emergency room visits during 2012 were associated with expenditures ≥85th centile (ie, >€7275 per patient). The area under the ROC curve for identifying patients with expenditures ≥85th centile was 0.888 (95% CI 0.883 to 0.893, Hosmer-Lemeshow test: X^2=29.997 (P<0.001)). These results show that the model identifies which patients will have higher health expenditures.

DISCUSSION

In our study, liver cirrhosis had an important impact on healthcare expenditures, and hospitalisation and pharmacy accounted for the largest proportion of costs associated with treating patients with cirrhosis. To our knowledge, this is the first population-based study to quantify the total economic impact of cirrhosis in relation to hepatic decompensation and to determine the distribution of costs (including those related with primary, nursing, hospital and mental healthcare as well as physical therapy and pharmacy) in treating patients with this condition.

This population-based study conducted in Catalonia included around 7500 000 million people, which is comparable to the population of some European countries.

In recent years, many studies have estimated the economic burden of hepatitis and cirrhosis[16] because these conditions are associated with high morbidity, mortality and economic costs. Although one of these studies analysed the cost of care over the last year of life in patients with an end-stage liver disease,[17] it was not a population-based study like ours. Another study described the direct costs related to hospital admissions in patients with cirrhosis.[10] By contrast, our study included all healthcare-related expenses in patients with cirrhosis (during hospitalisation and afterwards). Another study analysed direct and indirect costs of chronic liver disease, but included all patients, not only those with cirrhosis.[18]

Liver cirrhosis leads to 800 000 deaths every year, representing 1.3% of all deaths worldwide. According to WHO, cirrhosis is among the 18 most common causes of death.[11] Five-year survival is 36% in alcoholic cirrhosis and 14% in non-alcoholic cirrhosis.[11] We found that mortality increased significantly in patients who had a recent hepatic decompensation and the risk of mortality increased nearly 20% in patients with a decompensation in the previous 12 months.

The total cost of treating patients with cirrhosis in Catalonia in 2013 was almost €150 million (€4234 per patient). Hospitalisation remains the main source of healthcare-related expenditure, followed by medication, although hospital mortality has decreased in recent years.[16] Patients with more advanced liver disease required more healthcare (more days hospitalised, emergency visits and primary care visits) and more medication, generating greater expenditures. In patients with cirrhosis, the probability of dying within a year of a hepatic decompensation is 34%.[19] In our study, mortality was nearly 2.3 times higher in patients with a recent decompensation than in patients who had gone at least a year since a prior decompensation and 4.5 times higher than those who had never had a decompensation. Our model's ability to differentiate patients who will require high expenditures suggests that our study can be useful in health planning, resource allocation and evaluation of results.

Our large database allowed us to calculate the morbidity burden using AMG[20] and to stratify the risk of morbimortality. In our population, morbidities were common and

greater severity of liver disease was associated with higher morbidity burden (>75% of all patients were in the moderate-risk or higher-risk strata: 72.2% in the compensated group, 90.3% in the previous decompensation group and 95.5% in the recent decompensation group). Moreover, expenditures increased with increasing AMG strata, so controlling comorbidities is one way to reduce costs.

Another way to reduce costs is to modify the natural history of the liver disease. Studies that have analysed the direct and indirect costs of treating hepatitis C infection point out that costs rise with the natural history of the disease.[17 21 22] New antiviral agents against hepatitis C have modified the natural history of the disease, but the impact of these agents on the overall cost of treating patients with hepatitis C infection will not become clear until a few years have passed.[23] Nevertheless, our results suggest that this impact is likely to be significant because expenditures in patients with recent hepatic decompensation totalled more than twice those in patients who had not had a decompensation for at least 1 year and more than three times those in patients with compensated cirrhosis.

Although some studies have analysed the costs of caring for other diseases such as diabetes mellitus[24] or heart failure,[20] to our knowledge, this is the first population-based study to analyse morbidity and costs in patients with liver disease taking into account hepatic decompensation. Although several studies have evaluated some aspects involved in caring for patients with cirrhosis (hospitalisation, caregiving hours),[2] our study analysed overall costs, including expenditures on nursing, primary care and mental health.

This study has some limitations. The use of a general population database minimised selection bias and allowed us to analyse a real-world population. However, using administrative data to identify patients with cirrhosis can lead to misclassification, especially in patients diagnosed in private centres who have not used public resources.

Moreover, this administrative database did not include important information such as the aetiology of cirrhosis (although alcohol consumption and/or hepatitis C infection are recorded in the database) or other important clinical data for characterising and understanding the study population and the evolution of the disease. For these reasons, we cannot calculate classical scores such as Model For End-Stage Liver Disease (MELD), Child-Pugh or Acute-on-chronic Liver Failure (ACLF).

Patients' need for social services increases when liver disease becomes decompensated. The costs associated with this increase are, however, difficult to quantify and vary widely among health systems. Although these data are provided in the supplementary data, caution is warranted in interpreting these results.

Finally, we excluded patients who died during 2013 from the analysis of risk factors, although they were included in the analysis of healthcare expenditures. The reason for this exclusion is that patients who died during the study period were excluded from the assessment of predictors of increased expenditure. Although this exclusion could lead to bias, the cost of these patients after their death was zero. Therefore, the inclusion of dead patients in the analysis could lead to a possible bias in the calculation of the ORs of risk factors and consequently to errors in interpretation when diseases with high mortality are analysed. Among the possible solutions for this bias, we opted for the simplest solution and we analysed only patients who remained alive throughout the year. This strategy has two main advantages: simplicity and robustness. In contrast to similar strategies, each of which introduces some sort of bias, we believe it is better to use the simplest and easiest strategy to explain and understand the data. Moreover, one of the strengths of our study is that as it is a population-based study with real data, there is no need for methodological sophistication when a simpler strategy can be used.

CONCLUSIONS

Cirrhosis results in high healthcare resource utilisation, leading to high expenditures. On 31 December 2012, the point prevalence in Catalonia was 459.9 per 100 000 inhabitants. The cost of treating patients with cirrhosis was high because more than 75% had moderate to very high risk according to their AMG morbidity burden. The main expenditure was hospitalisation; its weight in the total expenditure increased with decompensation.

Avoiding excessive alcohol consumption and eradicating hepatitis C infection with the new antiviral agents will probably modify the natural history of cirrhosis, reducing morbidity and mortality and consequently expenditures in these patients.

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