



## Individual income, mortality and healthcare resource use in patients with chronic heart failure living in a universal healthcare system: A population-based study in Catalonia, Spain

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### ABSTRACT

**Background:** To evaluate the associations between individual income, all-cause mortality and use of healthcare resources in a very large population of chronic heart failure (CHF) patients living in Catalonia (Spain), where access to public healthcare is granted by law.

**Methods and results:** We used 2016 data from the Catalan Health Surveillance System, a large, exhaustive, administrative healthcare database which includes information on medical diagnoses, healthcare resource use, and individual income for all Catalan residents ( $N = 7,638,524$ ). Individual annual income was categorized as high ( $>100,000€$ ), medium (18,000–100,000€), low ( $<18,000€$ ), and very low (welfare support). Among 155,883 CHF patients, lower individual income was associated with a shorter life expectancy at age 50 (life expectancy for high income patients 22.2 years, for very low income patients 12.8), and were independently associated with higher all-cause mortality adjusting for age, sex, comorbidities, and duration of the CHF diagnosis (odds ratio very low vs. medium income 1.21 [95% CI 1.11, 1.33]). Also, in patients with lower income levels the burden of public healthcare resource use was displaced towards urgent hospitalizations and frequent emergency department visits, as opposed to regular, specialized CHF ambulatory-based care.

**Conclusion:** In a very large population of CHF patients with access to universal healthcare, lower income was independently associated with higher mortality and with lower use of ambulatory-based healthcare resources. Our findings suggest that CHF patients may benefit from systematic assessment of their socioeconomic status, as this may aid the identification of vulnerable subgroups who may benefit from tailored health education and management.

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**Abbreviations:** ATC, Anatomical Therapeutic Chemical; CHF, chronic heart failure; CHSS, Catalan Health Surveillance System; ED, emergency department; GMA, adjusted morbidity groups (Spanish acronym for "Grupos de Morbilidad Ajustados"); ICD 9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; SES, socioeconomic status.

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## 1. Introduction

Chronic heart failure (CHF) is considered one of the pandemics of our time [1,2]. CHF results in increased mortality, morbidity, disability, need for recurrent hospitalizations, marked loss of quality of life, and increased healthcare costs [1–6]. With populations aging in most countries [7], CHF is expected to become one of the greatest threats to the public's health and to the sustainability of healthcare systems in the coming decades.

From a management standpoint, CHF is complex and resource-intensive, often requiring the combination of multiple structural, therapeutic and educational interventions [8–10]. In this context, the impact of the patient's socioeconomic status (SES), which is recognized as a powerful health determinant [11–13], on the health outcomes and healthcare resource use specifically of patients with CHF is not fully understood. A number of studies on the prognostic role of SES in patients with cardiovascular conditions have been conducted in the US [14–18], however, most of these studies focused on either acute cardiovascular conditions [14,15] or on selected subgroups of chronic patients [17,18]. In Europe, where access to care is greater than in the US [19,20], despite availability of a number of studies on the association between SES and health outcomes [21–34] the specific prognostic implications of SES in CHF patients from the general population have not been explored in detail. Very recently, a population-based study was conducted in the UK [35]; on the other hand, in Mediterranean Europe this type of analyses was not available as of now.

Understanding the importance of SES on the health outcomes of patients with CHF living in a universal healthcare system can help identify vulnerable patient subgroups for whom tailored, specialized interventions may be needed, beyond ensuring access to care. The objective of this study was thus to evaluate the associations between SES, measured using individual annual income, health outcomes and public healthcare resource use in CHF patients from the general population of Catalonia (Spain). Specifically, the main focus of our analysis was on the comparison between low/very low and medium income.

## 2. Methods

### 2.1. Study context

Catalonia is a region in the Northeast of Spain. As in most European regions, in Catalonia residents ( $N = 7,638,524$  as of 2016) are granted universal public healthcare coverage by law. Additionally, approximately 25% of the Catalan population has also access to private healthcare via professional private insurances. Decades ago some specific professionals were offered private healthcare coverage in substitution of the public coverage, but currently this group represents a very small proportion (approximately 1%) of the Catalan population.

Specifically for chronic conditions such as CHF, in the last two decades specialized units, disease management programs, improved transitional care, and enhanced long-term care, among other interventions, have been developed in Catalonia [36,39,40].

### 2.2. Data source

Since 2011, the Health Department of the Government of Catalonia uses an automated administrative healthcare database (the Catalan Health Surveillance System [CHSS]), which periodically collects detailed individual-level information on demographics and socioeconomic characteristics, as well as exhaustive health-related and medical resource use information generated by the interactions between Catalan residents and the public healthcare system. This longitudinal, quality-controlled, updated information system allows conducting epidemiological analyses, evaluations of healthcare interventions and programs, and public analysis and benchmarking of health indicators across healthcare areas, among other assessments.

Further details on the characteristics of the CHSS database have been reported elsewhere by our group [41]. Specifically for healthcare-related data, the database integrates information from a number of sources including the Minimum Basic Dataset for Healthcare Units registry (which includes hospitalizations, primary care visits, and skilled nursing facility visits), information on pharmacy prescription fillings, and billing records, which include outpatient hospital clinic visits to specialists and emergency department visits, among others. Medical conditions are coded using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) coding system. Vital status of each individual included in the database is updated using information from the National Statistics Institute, Spanish Statistical Office.

### 2.3. Study design and population

For the purposes of this study, we restricted the study period from January 1st, 2016 to December 31st, 2016. We screened all Catalan residents alive on January 1st, 2016; aged 50 years or older as of January 1st, 2016; and covered by the public healthcare system. Individuals had to have at least one ICD-9-CM code for CHF (see list of ICD-9-CM codes in Supplementary Appendix Table S1) recorded as of January 1st, 2016 (“prevalent cases of CHF”), or newly recorded between January 1st, 2016 and December 31st, 2016 (“incident cases”) to be considered for inclusion (Fig. 1, “CHF Study Population”). Additionally, to increase the specificity of the CHF case definition, for non-hospital CHF cases evidence of at least one dispensing of a loop diuretic (e.g. furosemide) during the study period was also required for individuals to be included in the study population (see list of Anatomical Therapeutic Chemical (ATC) Classification System medication codes in Supplementary Appendix Table S2).

To put these findings into context, we also evaluated the relevance of income on the life expectancy of the general population of Catalonia without CHF. For this, individuals alive on January 1st, 2016 who were 50 years of age or older, had access to the public healthcare system, and had no CHF codes recorded in the database, were included (Fig. 1, “Catalan adults 50 years of age or older without CHF”).

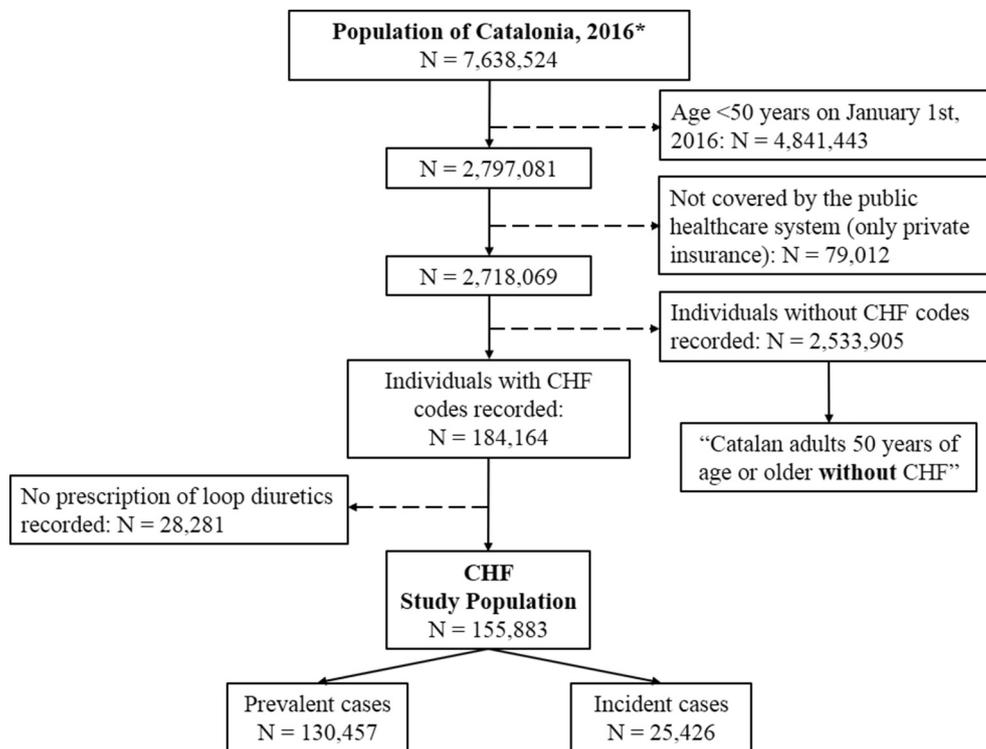
The present study was conducted in accordance with the Declaration of Helsinki, and was approved by the ethics committee of the Bellvitge Biomedical Research Institute (IDIBELL).

### 2.4. Assessment of individual SES

In the CHSS database, information on individual annual income (classified as <18,000€, 18,000–100,000€, >100,000€) is recorded and updated on a yearly basis, as well as information on receipt of economic support by the Government. For the purposes of our study, these variables were assessed on January 1st, 2016 for all patients, and we defined four individual income categories: an annual income >100,000€ was considered “high” income, 18,000–100,000€ was considered “medium” income, and <18,000€ was considered “low” income. These three categories included both active workers as well as retired individuals receiving a retirement pension. Finally, individuals who received welfare support by the Government were considered to have “very low income”. This categorization mirrors the one used in Catalonia for pharmaceutical copayment purposes. Information on education level was not available in the database.

### 2.5. Assessment of other covariates

Information on relevant covariates including age, sex, and comorbidities available as of January 1st, 2016 was used for all patients. Specifically for comorbidities, we used the “adjusted morbidity groups” (GMA [Spanish acronym for “Grupos de Morbilidad Ajustados”]) comorbidity classification system [42,43] (Supplementary Appendix Table S3). The GMA system has been developed specifically for



**Fig. 1.** Study population. This flowchart summarizes the source and population included in the present study. All analyses were conducted in the CHF Study Population. In addition, for reference purposes life expectancy analyses were also conducted in Catalan adults 50 years of age or older without CHF.

the Spanish healthcare system and includes 31 mutually exclusive categories of morbidity and complexity (social features not included [42,43]). Importantly, the GMA system has shown to outperform Charlson's comorbidity index in the Catalan population in terms of their ability to predict incident urgent hospitalizations. For the present study, based on the distribution of GMAs within the CHF study population, four GMA strata were defined: low, intermediate, high and very high.

## 2.6. Ascertainment of study endpoints

All-cause death was the primary endpoint of our study. As secondary endpoints, the following key CHF healthcare resource use endpoints were evaluated: urgent hospitalization (i.e., unplanned hospitalization, as opposed to planned hospitalizations, such as those for diagnostic or surgical procedures), urgent re-hospitalization (i.e., two or more urgent hospitalizations during the study period), emergency department (ED) visits, primary care visits, hospital daycare visits, and specialist clinic visits. Urgent hospitalization was defined as at least one urgent hospitalization during the study period, and re-hospitalization was defined as two or more urgent hospitalizations.

Because most CHF patients are frequent users of the healthcare system [3], for ED visits, primary care visits, hospital daycare visits, and specialist clinic visits, we specifically aimed at identifying heavy use of these healthcare resources. For this purpose, frequency distributions of use of each of these resources during the study period were created, and a frequency of use equal or greater than the 90th percentile of the respective distribution was considered "heavy use". Thus, frequent ED visits were defined a priori as 5 or more ED visits during the study period; frequent daycare visits were defined as patients seen in a hospital daycare clinic for 7 or more times during the study period; and frequent specialist clinic visits were also defined as 7 or more visits during the study period; regardless of their cause. Sensitivity analyses were

conducted using alternative definitions based on the 85th and 95th percentiles of the respective distributions.

## 2.7. Statistical analyses

The baseline characteristics of the CHF study population were described overall and by individual income strata. Categorical variables were reported using number and proportion, and continuous variables using median and interquartile range. Characteristics were compared across income strata using chi-squared and non-parametric tests, as appropriate.

We calculated the average life expectancy at age 50 for each income strata within the CHF study population, using the "LifeTables" package developed for R software. For reference purposes, the life expectancy analysis was also performed in the general population without CHF (i.e., Catalan adults 50 years of age or older without CHF).

Multivariable logistic regression models were used to assess the multivariable-adjusted associations between individual income level and each of the endpoints (see Section 2.6. Ascertainment of study endpoints) during the study period. In all analyses, medium income was set as the reference category. Analyses were adjusted for age, sex, comorbidities (using GMA strata) and duration of the CHF diagnosis.

We performed two sensitivity analyses to assess the robustness of the results. The mortality analyses were repeated restricted to incident (i.e., new) cases of CHF recorded during the study period. This analysis allowed assessing the relevance of the patient's income specifically at the time of CHF diagnosis and removing any potential influence of pre-existing, diagnosed CHF on the income level at study inclusion. Also, healthcare resource use analyses were repeated using alternative definitions of heavy use of each of those resources.

The focus of the analysis was on point estimates and 95% confidence intervals (CIs). Statistical analyses were performed using R (version 3.2) software.

### 3. Results

#### 3.1. Prevalence and incidence of CHF

During the study period, the net population of Catalonia was 7,638,524 inhabitants (Fig. 1). Of them, 2,718,069 were 50 years of age or older on January 1st, 2016 and were covered by the public healthcare system. Of these, 184,164 had at least one ICD-9-CM code for CHF. Of them, 155,883 (84.6%) either had a hospital diagnosis of CHF, or had a primary care diagnosis of CHF and at least one recorded dispensing of loop diuretics (“CHF study population”): 130,457 (83.7%) prevalent cases and 25,426 (16.3%) incident cases of CHF.

#### 3.2. Baseline characteristics and frequency of the study endpoints

Low income was the most frequent individual income stratum in the CHF study population (79% of the total), followed by medium income (16.6%) (Table 1). On the other hand, high income was very infrequent (0.3%). Median age ranged from 74 to 82 years, individuals in the low income stratum being the oldest, and individuals in the very low income groups being the youngest. The lower the individual income level the higher the proportion of women. The low and very low income groups had the highest burden of comorbidities, and the duration of the CHF diagnosis was also longer in these groups. 96.3% of participants got a retirement/welfare pension from the Government, 2.8% were active workers, and 0.8% were unemployed.

#### 3.3. Individual income and life expectancy

At any income level, individuals with CHF (CHF study population) had a shorter life expectancy at age 50 than individuals without CHF (Fig. 2, Catalan adults 50 years of age or older without CHF). In both groups, lower income was associated with shorter life expectancy, although this reduction was greater among CHF patients. Specifically, CHF patients with very low income had 9.4 years of life expectancy less than those in the high income group (42.3% reduction of life expectancy at age 50), while this difference was only 4.4 years among individuals without CHF (12.3% reduction). Supplementary Fig. 1 displays these results further stratified by sex.

#### 3.4. Individual income and all-cause mortality

Within the CHF study population, compared to the medium income level, lower income was associated with increased multivariable-adjusted odds of death. Specifically, when both prevalent and incident CHF cases were included in the analysis, patients with very low income had 1.21 higher odds of dying compared to CHF patients in the medium income group (Fig. 3a). The association was even stronger when the analysis was restricted to incident CHF cases during the study period (Fig. 3b; OR 1.44; 95% CI 1.18, 1.75). The number of CHF patients in the high income group was very small, leading to wide confidence intervals.

#### 3.5. Individual income and healthcare resource use

Within the CHF study population, lower income was associated with higher odds of urgent hospitalization (adjusted OR for very low income versus medium income 1.19; 95% CI 1.10, 1.28), as well as with higher odds of re-hospitalization during the study period (Fig. 3c). Lower income was also associated with higher odds of frequent ED visits (OR for very low income versus medium income 1.54; 95% CI 1.38, 1.71).

With regards to ambulatory healthcare resource use, lower income was associated with higher odds of frequent primary care visits, although for the latter a graded association was not observed. Conversely, having a lower income was associated with a lower odds of frequent hospital daycare visits (OR for very low income versus medium income 0.73; 95% CI 0.64, 0.85), as well as of frequent specialist clinic visits (OR for very low income versus medium income 0.67; 95% CI 0.63, 0.72) (Fig. 3d).

The results of the sensitivity analyses using alternative definitions of each of the heavy healthcare resource use endpoints were consistent with those from the main analyses (Supplementary Figs. S2 and S3).

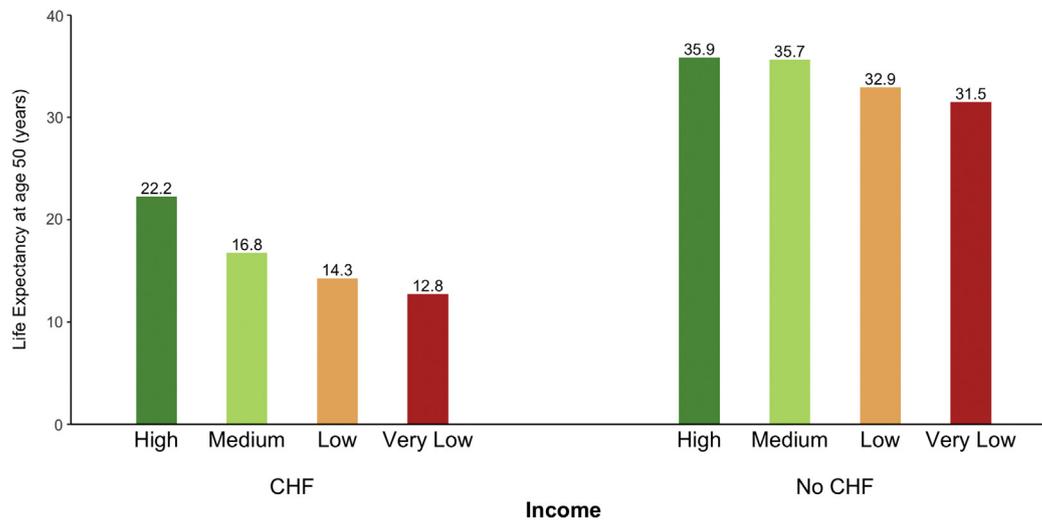
### 4. Discussion

In a very large population of patients with CHF living in a universal healthcare system, lower individual income levels were associated with worse survival; and in patients with CHF and lower income levels, the burden of public healthcare resource use was displaced towards

**Table 1**  
Baseline characteristics of the CHF study population, by individual income level.

	Overall (N = 155,883)	Individual Income				P value
		High (N = 437)	Medium (N = 25,810)	Low (N = 123,279)	Very Low (N = 6357)	
Age, years	81 (73, 86)	75 (65, 84)	78 (70, 85)	82 (74, 87)	74 (65, 82)	<0.001
Age categories						
50–64 years	15,938 (10.2%)	106 (24.3%)	3303 (12.8%)	10,964 (8.89%)	1565 (24.6%)	<0.001
64–74 years	28,887 (18.5%)	102 (23.3%)	6539 (25.3%)	20,624 (16.7%)	1622 (25.5%)	
75–84 years	58,417 (37.5%)	121 (27.7%)	9414 (36.5%)	46,847 (38.0%)	2035 (32.0%)	
≥85 years	52,641 (33.8%)	108 (24.7%)	6554 (25.4%)	44,844 (36.4%)	1135 (17.9%)	
Women	86,049 (55.2)	141 (32.3)	9888 (38.3)	71,615 (58.1)	4405 (69.3)	<0.001
GMA strata						
Low	89,532 (57.4)	329 (75.3)	16,169 (62.6)	69,531 (56.4)	3503 (55.1)	<0.001
Intermediate	41,000 (26.3)	74 (16.9)	6016 (23.3)	33,208 (26.9)	1702 (26.8)	
High	19,042 (12.2)	26 (6.0)	2745 (10.6)	15,438 (12.5)	833 (13.1)	
Very high	6309 (4.05)	8 (1.8)	880 (3.41)	5102 (4.14)	319 (5.02)	
Years since CHF diagnosis						<0.001
0	25,426 (16.3)	83 (19.0)	4530 (17.6)	19,871 (16.1)	942 (14.8)	
1	21,792 (14.0)	73 (16.7)	3810 (14.8)	17,071 (13.8)	838 (13.2)	
2–4	40,440 (25.9)	128 (29.3)	6927 (26.8)	31,701 (25.7)	1684 (26.5)	
≥ 5	68,224 (43.8)	153 (35.0)	10,543 (40.8)	54,635 (44.3)	2893 (45.5)	

Analyses conducted in the CHF Study Population. Data presented as n (%) for categorical variables and median (interquartile range) for continuous variables. CHF = chronic heart failure; GMA = adjusted morbidity groups (Spanish acronym).



**Fig. 2.** Life expectancy at age 50 by individual income level, Catalan adults with (left panel) and without (right panel) CHF. The x axis represents categories of individual income, and the y axis represents life expectancy at age 50, in years. Abbreviations: CHF = chronic heart failure.

urgent hospitalizations and frequent ED visits, as opposed to ambulatory-based care. These observations were robust, and were independent of age, sex, GMAs, and duration of the CHF diagnosis. To the best of our knowledge, this is the first study to assess patterns of all-cause mortality and of healthcare resource use in a very large population of CHF patients from the general population living in a universal healthcare environment, and may have important implications for the assessment and management of CHF.

The independent association between lower (as compared to medium) individual income and higher all-cause mortality is consistent with previous studies, in which worse health outcomes were observed in individuals with low SES from the general population, as well as among low SES patients with acute or chronic cardiovascular conditions. In the general population, lower SES has been found to be associated with increased mortality [13,21,27,28], as well as with a higher incidence of coronary heart disease [12] and CHF [22], among other conditions. Specifically, in a recent analysis in the UK, individuals with low SES had a 60% increased risk of developing incident HF compared to affluent individuals, and their burden of comorbidities was greater [35]. Lower SES has also been associated with a worse prognosis in small subgroups of patients with CHF including subgroups of patients with reduced [17,18] and preserved ejection fraction [29], as well as in elderly Medicare beneficiaries [30].

A number of mechanisms may explain these associations. Prior studies conducted in the US and Europe suggest that low SES individuals have limited access to care [19,20], clustering of unhealthy behaviors and CVD risk factors [28,31], limited recovery after acute health conditions [32], limited social support [33], and accumulation of adverse psychosocial features [44,45]. Also, people of lower SES tend to live in more deprived areas [46], which tend to have limited access to healthy foods, lower walkability and lower access to physical activity resources, and increased exposure to air pollution, among other detrimental features [34]. These mechanisms may also be relevant in our study population; nevertheless, the relevance of lack of access to healthcare, which is considered a key factor in SES studies conducted in the US [19,20], is likely attenuated in a universal healthcare coverage system such as Catalonia's.

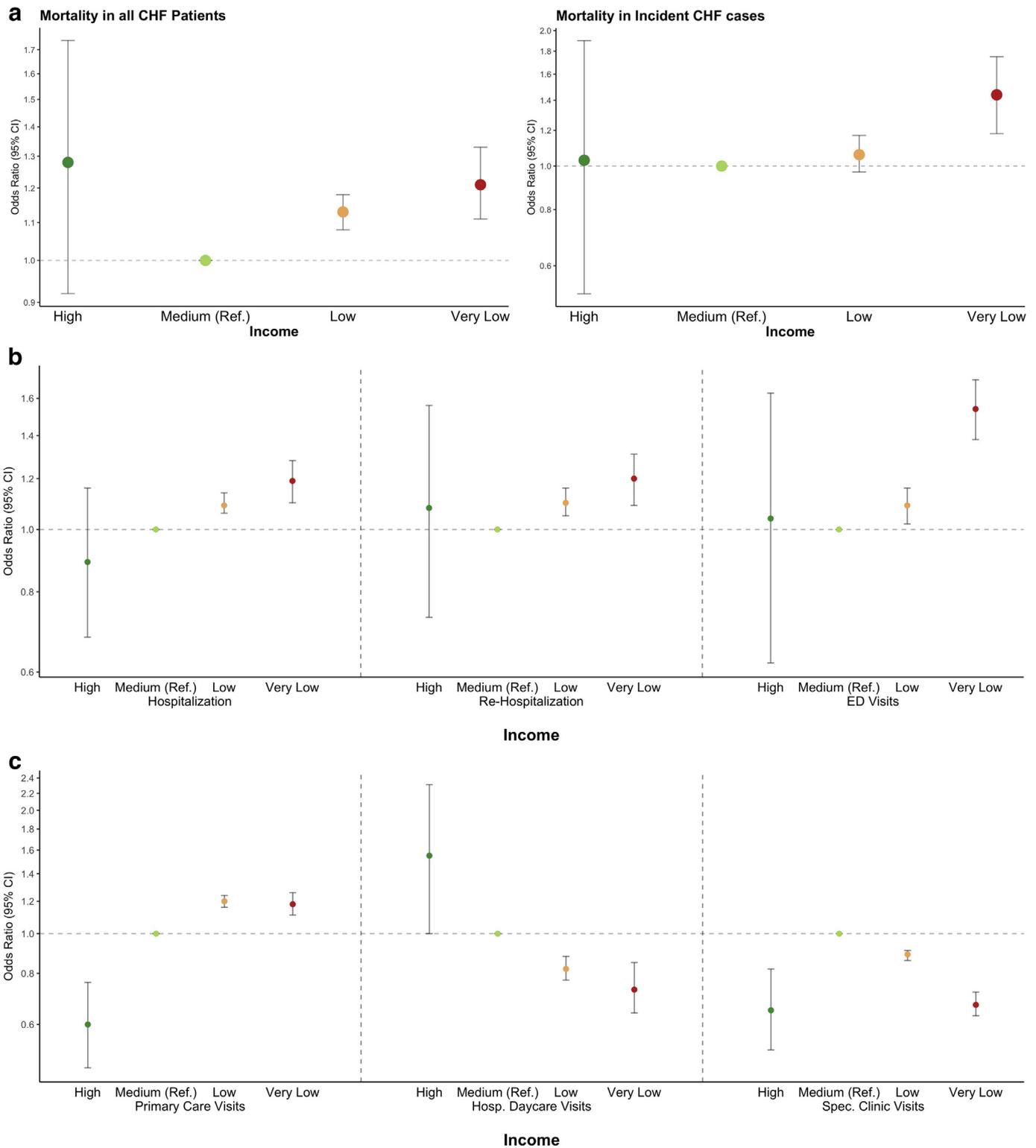
In addition, specific features relevant to the management of CHF may also play a role. Educational and self-care interventions are crucial in the setting of CHF [47]; in this sense, among Italian CHF patients lower SES is associated with worse self-care [48]. Social support is also key to ensure adherence to pharmacotherapies and other interventions,

particularly among patients with cognitive decline or mental health conditions, and lack of this support may be an issue particularly in patients in the lower income stratum [49]. In Denmark, lower SES has been associated with reduced access to key therapies such as implantable cardiac defibrillators [26], stressing the relevance of lack of access to specific therapies as a potential causal factor even in universal healthcare systems.

The second key finding of our study is the shifting in the use of healthcare resources in lower SES patients towards urgent hospitalizations and frequent ED visits, as opposed to regular hospital clinic-based ambulatory care (which was more frequent among medium income CHF patients). The mechanisms discussed above, all of which can lead to worsened health outcomes, could also explain the greater use of urgent healthcare resources among lower SES CHF patients. Competing risks with ED visits and urgent hospitalizations could also explain—at least partially—these observations.

In our study, we used individual annual income (and receipt of government welfare support) as a measure of SES. Nevertheless, “SES” is a complex construct which also includes education, employment status, social support, or marital status, among other components, most of which were not available in the CHSS database. In this context, further studies are needed to better understand whether income is per se the causal factor underpinning the observed associations, or whether it is as a marker of other SES features which could have a more direct impact on the outcomes and healthcare resource use of CHF patients, such as education level [47,48] or social support [49].

Our findings have important implications. From a clinical standpoint, our results suggest that CHF patients may benefit from systematic assessment of their income as part of a holistic CHF evaluation. In these patients, the presence of low income could be considered a marker of vulnerability, helping identify individuals likely to have poor health outcomes, who may benefit from closer ambulatory follow-up, tailored educational programs adapted to their skills, knowledge and environment; and from more intensive interventions. In terms of health systems management, lower income may help identify subgroups of patients who may benefit from adapted structural interventions (e.g., improving their social support; reducing physical/economic barriers to hospital ambulatory resources), aimed at improving their adherence to the recommended management plans and their use of specialized ambulatory CHF care resources [50]. Finally, from a policy standpoint, our results provide some support to policies aimed at



**Fig. 3.** Multivariable-adjusted associations between individual income level and the study endpoints. a. Multivariable-adjusted associations between individual income level and all-cause mortality for prevalent and incident cases of CHF during the study period. b. Multivariable-adjusted associations between individual income level and all-cause mortality for incident cases of CHF, during the study period. c. Multivariable-adjusted associations between individual income level and urgent hospitalization, re-hospitalization, and frequent emergency department visits during the study period, among Catalan adults with CHF. d. Multivariable-adjusted associations between individual income level and frequent primary care visits, frequent hospital day care visits, and frequent specialist clinic visits, during the study period, among Catalan adults with CHF. Results are presented as odds ratios from the logistic regression models (y axis in the log scale). Analyses are adjusted for age, sex and comorbidities. Medium income was set as the reference category. Abbreviations: CHF = chronic heart failure; CI = confidence interval; ED = emergency department; Hosp. = hospital; Ref. = reference; Spec. = specialty.

improving the SES of vulnerable groups. Currently, European cities such as Barcelona, Utrecht and Helsinki are exploring interventions aimed at reducing inequalities by providing a basic universal income [51].

Further research will help better delineate the key components to be included in each of these interventions, as well as their potential benefits.

#### 4.1. Strengths

Our study has a number of strengths. Because the CHSS database covers the entire population of Catalonia, we were able to perform a population-based analysis including all Catalan residents with recorded evidence of CHF. In this context, the large study population allowed providing precise effect estimates for the low and very low income strata. Also, the setting (a region covered by universal, high quality public healthcare) allowed evaluating the importance of SES beyond lack of access to healthcare, which is a key health determinant in other countries. Finally, while most of previous research on SES used area-level deprivation data or household income information, we were able to use individual-level income data.

#### 4.2. Limitations

First, as in any study using administrative healthcare databases, under-recording of medical conditions such as CHF is a possibility. However, if purely at random, non-differential under-recording of CHF across income strata is unlikely to explain the observed associations; rather, it may have biased them towards the null.

Second, interactions between Catalan residents and private healthcare institutions were not captured in the CHSS database. Nevertheless, as a chronic, complex, resource-intensive disease, in Catalonia patients with CHF typically use the public healthcare system [41]. Therefore, this is unlikely to have had a great impact on our estimates. Moreover, differential access to private healthcare is unlikely to explain the differences observed between the low and very low income groups.

Third, in the database annual income was captured as a categorical variable rather than as a continuous measure. This limited our ability to define exposure categories; in particular, the medium income stratum was very broad, and likely heterogeneous. Also, because the high income category included very few individuals, confidence intervals for this group were very wide, limiting our ability to draw conclusions. However, the focus of this study was on the effect of low/very low income as compared to medium, and estimates for these comparisons were very precise.

Finally, the clinical reason leading to ED, primary care, hospital day care, specialist clinic visits and hospitalizations was not ascertained. Nonetheless, the focus of our analysis was on the overall survival and healthcare resource use implications of lower income in CHF patients, who are typically complex, usually have several comorbidities, and often have exacerbations affecting several systems. Therefore, a holistic analysis assessing overall healthcare resource use may be more informative in this patient population, than an analysis focused on the specific use of cardiology healthcare resources.

#### 5. Conclusions

In this study including 155,883 CHF patients from the general population of Catalonia, a region with high-quality, public universal healthcare coverage, lower individual income was independently and robustly associated with higher mortality. From a healthcare resource use standpoint, lower income was also associated with a greater burden of urgent visits and hospitalizations, as well as with a lower use of specialized ambulatory healthcare resources. Our findings suggest that CHF patients may benefit from systematic assessment of their SES, as this may aid the identification of vulnerable individuals who may benefit from tailored education and management. Moreover, in an era of increasing inequalities, our findings may inform structural interventions, as well as policies aimed at minimizing SES disparities.

#### Authorship statement

All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

#### Declaration of conflicts of interest

The authors declare that they have no conflicts of interest relevant to the content of this manuscript.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2018.10.099>.

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