ESC HEART FAILURE
ESC Heart Failure (2019)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12399

ORIGINAL RESEARCH ARTICLE

The current and future burden of heart failure in Portugal

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Abstract

Aims Heart failure (HF) is a clinical syndrome with significant social and economic burden. We aimed to estimate the burden of HF in mainland Portugal over a 22-year time horizon, between 2014 and 2036.

Methods and results Heart failure burden was measured in disability-adjusted life years (DALYs), resulting from the sum of years of life lost (YLL) due to premature death and years lost due to disability (YLD). YLL were estimated based on the Portuguese mortality rates reported by the European Detailed Mortality Database. For YLD, disease duration and the overall incidence were estimated using an epidemiological model developed by the World Health Organization (DISMOD II). Disability weights were retrieved from published literature. The impact of ageing was estimated with a shift-share analysis using official demographic projections. In 2014, 4688 deaths were attributed to HF, corresponding to 4.7% of the total deaths in mainland Portugal. DALYs totalled 21 162, 53.9% due to premature death (YLL: 11 398) and 46.1% due to disability (YLD: 9765). Considering only population ageing over a 22-year horizon, the deaths and burden of HF are expected to increase by 73.0% and 27.9%, respectively, reaching 8112 deaths and 27 059 DALYs lost due to HF in 2036. DALY's growth is mainly driven by the increase of YLL, whose contribution to overall burden will increase to 62.0%.

Conclusions Heart failure is an emerging and growing health problem where significant health gains may be obtained. The projected significant increase of HF burden highlights the need to set HF as a priority for healthcare system.

Keywords Heart failure; Global Burden of Disease; Morbidity; Mortality; Premature; Forecasting

Received: 18 July 2018; Accepted: 21 November 2018
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Introduction

Heart failure (HF) is a clinical syndrome characterized by typical symptoms that may be accompanied by signs caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress.[1] HF may have different aetiologies such as coronary artery disease, valvular heart disease, and hypertension.[2] Paradoxically, the development of therapeutic interventions that improved the prognosis of the above-mentioned aetiological conditions by reducing the associated mortality may have contributed to increase HF prevalence.[3] In addition, the currently available medicines and devices for the treatment of HF with reduced ejection fraction itself allowed the achievement of striking improvements in the management of HF, further contributing to the increased overall survival of these patients and, therefore, to the increased prevalence of HF.[3]

Heart failure is known to have an overall significant social and economic burden.[4] However, detailed characterization of the current and future magnitude of this health problem is scarce. This information is of paramount importance for all stakeholders in general, and for policymakers in particular, which have to prioritize health interventions at a regional or

country level. Furthermore, population ageing and the increasing prevalence of HF, particularly among the elderly, will pose additional challenges in the management of HF.

In this study, we estimated the current burden of HF in mainland Portugal as well as the projected HF burden for the following 22 years to estimate the future impact of ageing on the burden of the disease.

Methods

We performed a two-phase estimation. First, we estimated the burden of HF in mainland Portugal in 2014. Second, we estimated the burden of HF for the following 22 years (from 2015 to 2036).

Burden of heart failure in mainland Portugal in 2014

The burden of disease was estimated in disability-adjusted life years (DALYs), a measure, expressed in time, of the amount of health lost due to disability or premature death generated by the disease. DALYs include two components[5]: (i) years of life lost (YLL) due to premature death, with time lost estimated as the difference between age at death and standard life expectancy for that age and (ii) years lost due to disability (YLD), which considers time spent with disability. This methodology uses epidemiological data, including disease incidence by severity stages, duration of each stage, and patient mortality patterns.[6]

In particular, the number of DALYs lost by an individual was estimated using the following equation[7]:

$$DALY = \int_{a}^{a+L} DCxe^{-\beta x}e^{-r(x-a)}dx,$$

where

- a initial age;
- L length of disability or YLL due to premature death;
- D coefficient of disability, between 0 (without any disability, perfect health) and 1 (total disability or death);
- C constant—correction for age (0.04);
- x age, varies between a and $a + L$;
- β parameter from the rule for age correction (0.1658)[8]; and
- r rate of time discount (3%).

In the calculation of DALYs, a discount rate of 3% and an age-differentiated weighting were used, in which more weight was given to intermediate age groups (between 20 and 50, when people tend to take care of children) in comparison with younger and older groups.[6]

Years of life lost due to premature death

The YLL due to HF mortality refer to the 2014 mainland Portuguese population aged 25 years and over. In addition, the proportion of overall YLL due to HF mortality was also estimated. For this estimation, data on the number of deaths and standard life expectancy, by sex and age group, are needed. The overall mortality data were obtained from the National Statistics Institute, which has access to all death certificates in Portugal.[8] Mortality rates due to HF in Portugal were available in the European Detailed Mortality Database of the World Health Organization (WHO) Regional Office for Europe.[9] To increase robustness, we considered the average mortality rate due to HF for the last 3 years (2012–2014) (Supporting Information, *Table S1*). National rates were then applied to the population resident in mainland Portugal in 2014, according to the official estimations of Statistics Portugal.[10] The standard life expectancy was obtained from the mortality tables adopted by the WHO as a reference standard.[11]

Years lost due to disability

For the estimation of YLD, incidence, duration of disease, and HF disability weights by sex, age group, and disability class are needed. We assumed that patients with New York Heart Association (NYHA) Class I have no disability. Therefore, YLD were estimated for patients with HF NYHA Classes II–IV.

In the absence of robust and direct evidence on the incidence and duration of HF in Portugal, we used the DISMOD II model, a tool developed by the WHO,[12] to estimate these data, by sex and age group. This model ensures internal consistency between epidemiological parameters of the disease: incidence rates, prevalence, remission, lethality, mortality or relative risk of mortality, and disease duration.

The model baseline population was calibrated with the resident population of mainland Portugal in 2014[10] and with the 2013–2015 life table.[13] Afterwards, the model requires a minimum of three disease-specific inputs, which in this case were as follows: (i) prevalence; (ii) remission rate; and (iii) relative mortality risk due to HF.

Data on chronic HF NYHA Classes II–IV prevalence in mainland Portugal in 2014 (Supporting Information, *Table S2*) were derived from the distribution of individual patient data found in the Portuguese landmark study on HF prevalence (EPICA study),[2] a community-based epidemiological survey conducted in 1998–2000 and involving 5434 subjects older than 25 years attending primary care centres. The main baseline characteristics of HF patients identified in the EPICA study are shown in Supporting Information, *Table S3*.

In 2014, the estimated overall prevalence of chronic HF in Portuguese population aged 25 and above was 5.2% (95% CI: 4.5–5.8), 65.4% of which refer to patients with HF NYHA Classes II–IV. In our study, we assumed that HF prevalence at or below 25 years old was zero (as this population was not evaluated in the EPICA study).

The HF remission rate used in the model was also assumed to be null due to the rarity of chronic HF conditions that resolve completely without any *sequelae*.

The HF mortality risks used in the model were derived from the study by Muntwyler *et al.*,[14] which prospectively

included 411 consecutive patients with HF NYHA Classes II–IV enrolled in primary care offices throughout Switzerland. In this study, the standardized mortality ratios were 3.6 (95% CI: 2.6–5.1) and 2.2 (95% CI: 1.4–3.4) for men and women, respectively. These standardized ratios were used in the model as *proxies* of the HF relative mortality risks.

The outputs on the incidence and HF duration, by sex and age group, estimated by the DISMOD II model are shown in Supporting Information, *Table S4*.

The HF disability weights, also needed for the YLD estimation, were retrieved from the Global Burden of Disease 2015 study.[15] In the Global Burden of Disease study, HF was classified as mild, moderate, and severe. Because of the similarities in the disease severity definitions, these classes were considered as proxies for the II, III, and IV NYHA functional classes, respectively. Following these assumptions, the disability weights attributed to NYHA II, III, and IV were 0.041 (95% CI: 0.026–0.062), 0.072 (95% CI: 0.047–0.103), and 0.179 (95% CI: 0.122–0.251), respectively.

We assumed that the distribution of the incident cases by NYHA class was proportional to the prevalent cases, as reported in the EPICA study[2] (Supporting Information, *Table S5*). In the absence of robust data, we considered that disease duration was independent of the NYHA class. The disability weights were applied to the incident cases estimated by the DISMOD II model, by sex, age group, and NYHA class.

Projection of the future burden of heart failure in a 22-year time horizon

For the YLL and YLD projections, we used the shift-share methodology.[16] This method allows to analyse the isolated demographic effect on the disease prevalence and burden, keeping everything else constant. In order to apply the methodology, we first computed the YLL and YLD rates in 2014 by sex and age group. We then applied these rates to the resident population projections, by sex and age group, from 2015 to 2036.[9,17] This methodology implies that the rates of incidence and mortality, by age and sex, as well as disease duration are constant over time. In other words, the evolution of HF burden depends only on the changes occurring in the demographic composition of the population over time.

Results

Current burden of heart failure in mainland Portugal

Years of life lost due to premature death

The distribution of deaths from all causes and from HF, by sex and age group, is shown in Supporting Information, *Figure S1* and *S2*, respectively. The total number of deaths attributable to HF in 2014 was 4688 (66.8% in women), which corresponds to 4.7% of overall mortality in Portugal (*Table 1*). Based on these results and the standard life expectancy, we estimated that in mainland Portugal in 2014, there were 11 398 YLL lost due to HF (60.9% in women), which corresponds to 2.4% of total YLL due to overall mortality (*Table 1*). *Figure 1* shows the distribution of YLL due to HF, by sex and age group.

Years lost due to disability

In mainland Portugal in 2014, the YLD due to HF totalled 9765 YLD (52.4% in women). *Figure 2* shows the distribution of YLD due to HF, by sex and age group.

Disability-adjusted life years

The overall burden of HF in mainland Portugal in 2014 was 21 162 DALYs (57.0% in women), corresponding to the sum of YLL and YLD. The relative contribution of the YLL and YLD to the overall burden of HF is different according to gender. The YLL account for 48.9% and 57.6% of the DALY in men and women, respectively.

Future burden of heart failure in mainland Portugal

Mortality due to HF is expected to increase by 73.0% in the next 20 years (with 8112 deaths for HF in 2036) as a consequence of both HF mortality rate being higher in the older population and population ageing. The YLL are expected to increase by 47.3% (reaching 16 788 YLL in 2036; *Figures 3* and *4*) due to the increased mortality, albeit this increment is lower than the mortality increment.

By 2036, The YLD are expected to increase by 5.2% (reaching 10 271 YLD in 2036; *Figures 3* and *4*). Here, the mean YLD per incident HF case will decrease due to population ageing. This result is a consequence of lower disease duration in older population.

Overall, the burden of HF in mainland Portugal will increase by 27.9% in a 22-year time horizon, going from 21 162 DALYs in 2014 to 27 059 DALYs in 2036. The relative contribution of YLL to the overall burden of HF will increase from 53.9% in 2014 to 62.0% in 2036 (*Figure 4*).

Table 1 Mortality and YLL prematurely due to HF, comparing with mortality and YLL of all causes. Portugal mainland, 2014

	Deaths due to HF		YLL due to HF	
	Number	% of all-cause deaths	Number	% of all-cause YLL
Male	1557	3.1	4454	1.6
Female	3130	6.4	6944	3.6
Overall	4688	4.7	11 398	2.4

HF, heart failure; YLL, years of life lost.

Figure 1 Years of life lost due to heart failure, by sex and age group, in mainland Portugal in 2014.

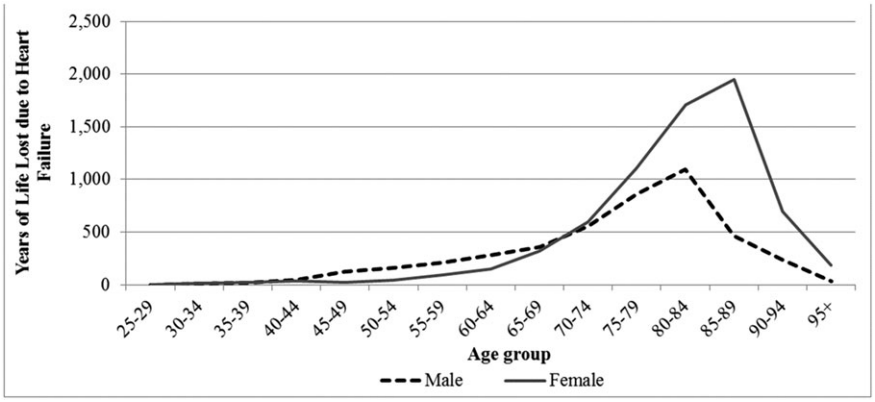


Figure 2 Years lost due to disability of heart failure in mainland Portugal in 2014, by sex and age group.

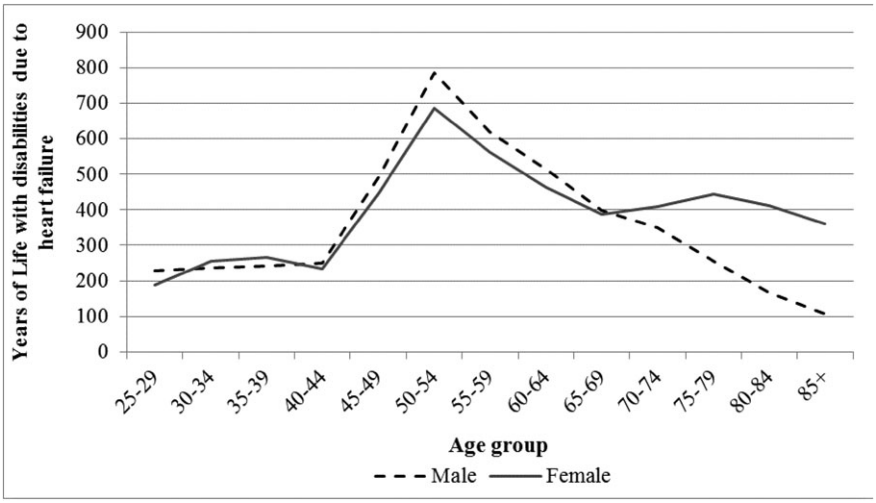
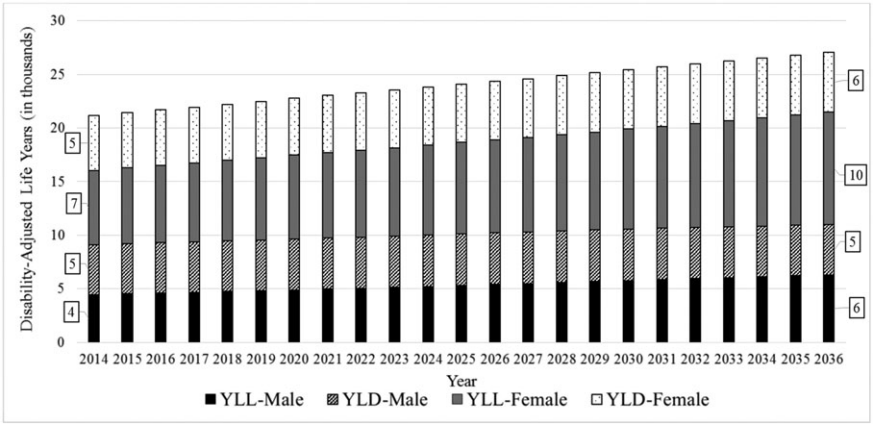
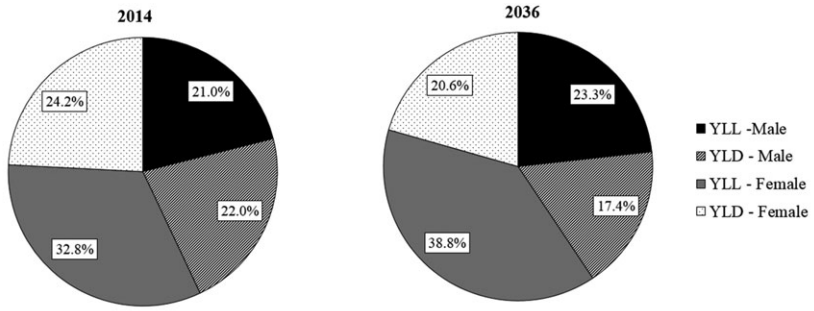


Figure 3 Increase of heart failure burden in Portugal mainland, from 2014 to 2036, according to sex and type of disability-adjusted life years. YLD, years lost due to disability; YLL, years of life lost.



DOI: 10.1002/ehf2.12399

Figure 4 Relative proportions of disability-adjusted life years in 2014 and 2036, according to the gender and component of disability-adjusted life years. YLD, years lost due to disability; YLL, years of life lost.



	2014			2036		
	Male	Female	Total	Male	Female	Total
YLL	4,454	6,944	11,398	6,292	10,496	16,788
YLD	4,647	5,118	9,765	4,703	5,569	10,271
Total	9,101	12,062	21,162	10,995	16,065	27,059

Discussion

Heart failure is a clinical syndrome with many different aetiologies, usually representing a late stage in heart diseases. It is possible that healthcare improvements in the management of HF aetiologic factors and HF with reduced ejection fraction treatment, as well as population ageing, may have contributed to the increase prevalence of HF. Currently, in mainland Portugal, HF is responsible for 4.7% of all deaths and 2.4% of all YLL (almost 11 400 years lost in 2014 due to premature death). The relative weight of HF in overall YLL (2.4%) is about half the weight in overall mortality (4.7%), which can be explained by the fact that, on average, deaths from HF occur at older ages in comparison with deaths from other causes. In terms of disability, it was estimated that about 9800 years of life have been lost in 2014 due to disability attributable to HF. Overall, the burden of HF was estimated at 21 162 DALYs.

We found that the overall burden in women is overall higher than in men (57% vs. 43%). The main driver of this difference is the higher contribution of YLL for the overall burden in women than in men (61% vs. 39%). Sex differences in YLL estimation are a consequence of the higher mortality rate of HF in the very old population (80+ years; Supporting Information, *Table S1*), two-thirds of which are women. In contrast, the distribution of YLD by sex is more balanced (52% vs. 48% in women and men, respectively) due to net result of two mechanisms with opposite effects. From one side, HF incidence is higher in men in relatively younger population (<74 years; Supporting Information, *Table S4*), leading to an overall higher disease duration among men. Furthermore, the age weighting in our study attributes a higher disability to younger individuals. On the other side, there is a higher incidence of HF in the very old population, most of which are women.

The projection for disease burden over a 20-year time horizon suggests a 27.9% increase in the overall burden of HF, mostly due to the increase in the years lost due to premature death. It should be highlighted that this increment of YLL due to HF is lower than the overall expected mortality increment, resulting in a decreasing YLL per death. This is because more deaths are occurring in the elder population to which we attributed lower social weight (i.e. society values less deaths occurring in elder population than deaths occurring in younger population).

Our results overlap with the literature in which HF is presented as an emergent public health problem, with increasing relevance.[18–20] The present results are also in line with a recent study by Conrad *et al.*[21] that retrospectively assessed temporal trends in incidence and prevalence of HF in a large general population cohort from the UK. The authors found that absolute incidence and prevalence of HF increased by 13% and 23%, respectively, in the last 13 years (from 2002 to 2014). In this study, ageing was one of the main reasons for the HF burden increase. In our study, we estimated for the coming years an annual average absolute increase of 1.6% in HF incidence due to ageing.

We have conducted other recent studies using similar methodologies to evaluate the burden of other cardiovascular diseases, risk factors, and oncological diseases in Portugal. Although we acknowledge the limitations of this type of indirect comparisons, the burden associated with HF reported in this study is roughly half and two-thirds the burden attributed to alcohol[22] consumption and lung cancer,[23] respectively; it is similar to the burden associated with atrial fibrillation[24] and female breast cancer[25] and twice the burden associated with hypercholesterolaemia.[26] All together, these results emphasize the need of urgent prioritization of HF in the health agenda, taking into account the increasing

prevalence of HF, the high morbidity and mortality, and the socio-economic burden for patients, families, and society.

Our study has several limitations. During the execution of this study, we found a substantial lack of HF epidemiological data for the Portuguese population, in particular incidence and disease duration. To overcome this limitation, we used a model developed by the WHO[12] (DISMOD II model) to estimate these data. DISMOD model is a software tool initially developed for burden of disease analysis.[27] The model exploits the interdependency between disease incidence, prevalence, remission, case fatality, and mortality to estimate missing epidemiological information. Although the internal estimates of the model are mathematically consistent, in some occasions, the epidemiological results obtained may be inconsistent with the expected disease pattern. To overcome these inconsistencies, the model allows for several adjustment options (e.g. fitting mathematical curves, interpolation methods, moving average, and application of other disease age patterns). The more accurate epidemiological inputs used, the more accurate estimations are calculated by the model. As previously mentioned, the HF epidemiological data in Portugal are scarce, and therefore, we had to make some assumptions to calibrate DISMOD model (such as a null HF prevalence in the population younger than 25 years old, a null HF remission rate, lack of disability among patients with NYHA Class I, similar distribution by NYHA class for incident and prevalent cases, and disease duration independency from NYHA class). These assumptions may have led to less accurate estimates. However, we anticipate that the errors that may have been incorporated tend to go in opposite directions. For instance, assuming no disability for NYHA I leads to an underestimation of the burden while considering null remission rate leads to its overestimation.

Most epidemiological data used in our study were derive from the analysis of individual patient data from the Portuguese landmark study on HF prevalence (EPICA study).[2] However, this study has several limitations for the purpose of the present study. First, the EPICA study was conducted in 1998–2000, and significant prevalence changes may have occurred. Second, it only included individuals aged 25 years or older. We assumed that the prevalence rate in the age group between 0 and 25 years was zero. Third, the EPICA study estimated the prevalence of chronic HF among people attending primary care centres, excluding patients with acute HF and patients followed at tertiary referral hospitals. The epidemiological estimations from EPICA study included in the analysis should therefore be interpreted as conservative. Fourth, the potential impact of some externalities on HF burden was not considered for the purpose of epidemiological estimations. For example, it has been shown that economic and financial crisis affect cardiovascular morbidity and mortality through a complex interaction of several components (from prevention to detection and treatment).[28,29] The Great Recession in Portugal led to austerity measures between 2011 and 2014 and may have had an impact on cardiovascular burden in general and in HF in particular.

We believe that the mortality attributed to HF, based on the International Classification of Disease codes (10th version) present in the European Detailed Mortality Database,[8] may be underestimated. It is possible that the cause of death is linked to the cause (e.g. coronary artery disease and cardiomyopathy) and not the consequence (HF). The proportion of sudden deaths related to HF may also be underestimated. Therefore, the data presented for YLL due to premature death may also be underestimated.

A further limitation of this study is that time changes in the distribution of incidence among NYHA classes, mortality rate, and disease duration were not included in the projections. In other words, our estimation of future burden of HF only accounts for the demographic changes (i.e. population ageing) considering everything else constant.

In conclusion, the burden of HF is expected to increase by 28% between 2014 and 2036, reaching 27 059 DALYs in 2036. We estimate that in 2036, YLL will represent 62% of DALY due to HF (compared with 54% in 2014). These results indicate that HF is an emerging and growing health problem where significant health gains may be obtained. The projected significant increase of the burden of HF in the following years highlights the need to set HF as a priority for the healthcare system. In Portugal, the Ministry of Health acknowledged the current and future health impact of HF and has recently decided to create a dedicated working group to implement an integrated management of HF in Portugal.[30]

Acknowledgements

We thank the investigators of EPICA study for giving access to individual patient data.

Conflict of interest

C.F. has received consulting and speaker fees from Servier Portugal, Novartis, Vifor, Bayer, and Orion. M.G., R.A., F.F., J.C., D.C., P.B., and M.B. have no conflict of interest to declare.

Funding

This study was supported by Novartis Farma, Produtos Farmacêuticos SA through an unrestricted grant to the Research and Development Association of Lisbon University School of Medicine (AIDFM). Funding was independent of the study outcomes. The promoter did not participate in any phase of the study.

Ethical approval

Not required. No experiments involving animals or humans were conducted for the purpose of this study.

Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. mortality for all causes by sex and age group, in mainland portugal in 2014.

Figure S2. mortality for heart failure by sex and age group, in mainland portugal in 2014.

Table S1. heart failure mortality rate per 100,000 inhabitants in mainland portugal (average 2012-2014).

Table S2. heart failure (nyha class ii-iv) prevalence rates estimates by sex and age group, in mainland portugal in 2014.

Table S3. baseline characteristics of heart failure patients identified in the epica study.

Table S4. estimates of heart failure incidence and disease duration by sex and age group, in portugal mainland in 2014.

Table S5. distribution of heart failure incident cases by new york heart association functional classes and age group.

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