Trends in death attributed to heart failure over the past two decades in Europe

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Aims
Little is known regarding temporal trends in mortality attributed to heart failure (HF) from a population perspective. The aim of this study was to assess the mortality related to HF as an underlying cause during the last 20 years in seven European countries.

Methods and results
The number of deaths with HF as the underlying cause was collected in seven European states: Germany, Greece, England and Wales, Spain, France, Finland, and Sweden from 1987 to 2008. Disease coding for HF was based on the International Classification of Diseases (ICD 9th and 10th versions). We computed age-standardized death rates (SDRs) per 100 000 inhabitants. Mean age at death from HF was also calculated for the same period. In the seven studied countries, the HF SDR decreased continuously from 54.2 (1987) to 32.6 (2008). Despite differences in the early 1990s, SDRs related to HF seemed to converge, in these seven European countries, to \( \approx 30 \) deaths per 100 000 population in the near future, for both men and women. During the study period, the mean age at death increased from 80.0 to 82.7 years. Half of the deaths from HF occurred in hospital, without change over time.

Conclusion
There has been a 40% reduction of the SDR due to HF in seven European countries during two decades and a concomitant increase in the mean age at death from HF. We hypothesize that these results may be related to a better management of chronic and acute HF patients over the past 20 years.

Keywords
Heart failure • Mortality • Death certificates • Epidemiology

Introduction
Cardiovascular disease mortality has a distinct spatial and temporal pattern. While there has been a strong decline in cardiovascular mortality in many western countries over the last few decades, in other parts of Europe the pattern is not so pronounced.1,2 Cardiovascular diseases are the main cause of mortality in the European Union, accounting for \(~40\%\) of deaths in the total population. Around 1–2% of the population in European countries suffers from heart failure (HF), with the prevalence rising to \(~10\%\) among the population aged \( \geq 70 \) years.3–7 The overall prevalence of HF is thought to increase because of the ageing of the population and of the success in prolonging survival in patients suffering coronary events.8,9

Data on mortality attributed to HF are scarce, and little is known regarding temporal trends in HF mortality among European countries.10

In the USA, a recent publication investigated the potential impact of optimal implementation of evidence-based HF therapies on mortality.11 This study suggests that a better use of evidence-based guidelines and recommended therapies could prevent a number of HF deaths. The European Society of Cardiology (ESC)/Heart Failure Association (HFA) has made extensive efforts in the last decades to increase the availability of evidence-based guidelines and
recommended therapies in HF.12,13 However, studies on trends in death attributed to HF over the past decades in Europe remain scarce. The objective of this study was to assess and compare mortality trends due to HF as an underlying cause of death between 1987 and 2008 in seven European countries. We also evaluated HF mortality trends according to gender and the age at death over time.

Methods

In most European countries, all causes of death have to be reported to the authorities. These data are based on information reported by medical doctors on each death certificate. This compulsory reporting and certification of deaths by medical professionals results in the ascertainment of causes of death with high accuracy.14 Collection and coding of causes of death are the subject of recommendations by the World Health Organization (WHO) since the sixth revision of the International Classification of Diseases (ICD) in 1946. All seven countries involved in this study (Germany, Greece, England and Wales, Spain, France, Finland, and Sweden) follow these recommendations for several decades. Using national mortality databases (see Appendix), we obtained in each of the seven studied countries exhaustive data on cause of death from 1987 to 2008. Of note, despite several attempts, we did not succeed in retrieving similar data from other European countries such as Romania, The Netherlands, Italy, Turkey, and the Czech Republic.

The death certificates are standardized between countries and contain two sections in which physicians enter the causes of death. Part I asks for the sequence of events leading directly to death from the ‘underlying’ cause of death (i.e. the disease that initiated the chain of events resulting in death) and the intermediate cause(s) affecting it directly. Part II allows the physician to enter other conditions (mostly co-morbidities) that indirectly contributed to death without being part of the direct causal sequence.

Data were retrieved from national mortality databases using the coding rules of the ICD. Over the period 1987–2008, two different versions of the ICD were used: ICD 9th and ICD 10th.15,16 Table S1 in the Supplementary material online indicates, for each country, the time periods corresponding to the use of the two ICD versions. Table S2 in the Supplementary material online further indicates the codes used for each ICD version to retrieve the number of annual deaths with HF as the underlying cause of death. Furthermore, in France, and England and Wales, ICD codes were used to retrieve HF as a ‘multiple’ cause of death that corresponds to HF mentioned in part I and/or II (HF as the underlying cause and/or as the associated cause).

In order to compute death rates, resident populations were obtained for each country and for each year from the same national mortality databases. Age-specific mortality rates were computed for each 5-year age group (0–4 to 80–84, and > 85 years) and calendar year. Age-standardized death rates (SDRs) per 100 000 population were calculated using the direct standardization method, on the basis of the 1976 European standard population (reference population recommended by Eurostat; Supplementary material online, Table S3). This standardization allows an accurate comparison of mortality rates among various populations with different age structures.14 These standardized death rates were per year, per country, and for the total population of the seven countries. No extrapolation was made if data were missing for any specific calendar year. Measures of mortality include the number of deaths (total and by gender) as well as the SDR by gender.

Statistical analysis

We performed a linear regression model to compare SDR by year, country, and the type of ICD. We similarly performed on the data a linear regression model including year, gender, and their interaction to explore SDRs. Associations between mortality rates and covariates were assessed using a partial Wald test. We performed an analysis of variance (ANOVA) to assess the impact of the country on the mortality rates.

Results

During the study period (1987–2008), the SDR with HF as an underlying cause decreased from 54.2 to 32.6 per 100 000 population in the whole cohort of the seven studied countries (Figure 1A).

Figure 1B shows a slight decrease in the total number of deaths with HF as an underlying cause from 150 158 in 1987 to 137 004 in 2008 for all the seven countries; data by country are shown in Supplementary material online, Figure S1. During the same period, the mean age at death due to HF increased from 80.0 to 82.7 years (Figure 1C); data by country are shown in Supplementary material online, Table S4. The trends in number of deaths, SDRs, and age at death in male and female populations are described in Figure 1. The SDR is consistently lower for females. A significant association was found with gender ($P < 0.0001$) as well as an interaction between gender and year ($P < 0.0001$). Figure 1B shows that the absolute number of deaths is greater in the female population during the study period. Furthermore, the mean age at death is 5 years older in the female population (Figure 1C).

Figure 2A describes the SDR with HF as an underlying cause in each of the seven studied countries. Figure 2A shows two trends of SDR over time among the studied countries. In a first group of countries, comprising France, Germany, Greece, and Spain, SDR due to HF was > 40 per 100 000 population in 1987 and continuously decreased until 2008. Despite the switch over between ICD-9 and ICD-10 in Europe during the study period, there was no discontinuity in the observed mortality trends. Furthermore, in Greece and France, a reduction in HF SDR was still observed in very recent years.

In a second group of countries, comprising England and Wales, Finland, and Sweden, the SDR from HF was < 25 per 100 000 population in 1987 and remained roughly stable up to 2008.

The results of the regression linear model show a decrease in SDR according to country ($P < 0.001$). It confirmed that the slope of the SDR over time is statistically different among countries ($P < 0.001$). More importantly, these analyses showed that the slope of the SDR over time was negative whether ICD-9 or ICD-10 was used.

The SDR with HF as a ‘multiple’ cause of death (HF either as the underlying and/or the associated cause) was calculated. In 15 years a 50% decrease was found in England and Wales, while a 36% decrease was observed in France over a 20 year period (Figure 2B).

Data on the place at death related to HF as an underlying cause (Finland and France) or with HF mentioned anywhere on the death certificate (England and Wales) were analysed. We observed that > 50% of deaths due to HF occurred in hospital, regardless of the year or country studied. Death occurred at home in
Figure 1  Heart failure as an underlying cause of death in Europe. (A) Age-standardized death rates; (B) number of deaths; and (C) mean age at death from heart failure. Data represent the total population of the seven studied European countries.

Figure 2  Death rates by European country. (A) Heart failure (HF) as the underlying cause of death; continuous lines correspond to the International Classification of Diseases (ICD) 9th revision and dashed lines correspond to the ICD 10th revision. The age-standardized death rate (SDR) with HF as the underlying cause remained stable from 1987 to 2008 in three countries (England and Wales, Finland, and Sweden) and decreased in the other four countries (France, Germany, Greece, and Spain). Of note, a sudden increase can be seen in 1993 for England and Wales, in 1996 for Finland, and in 1997 for Sweden. For Finland and Sweden, this corresponds to a change from ICD-9 to ICD-10; for England and Wales, it is related to the change in coding methods after 1993 described elsewhere. However the overall SDR trend remained similar for those three countries before and after the increase. (B) HF as multiple cause of death (i.e. mentioned anywhere on the death certificate).
Discussion

In the seven countries during the study period we demonstrated a 40% mean reduction in the SDR with HF as an underlying cause for a total population studied of 267 million inhabitants in 2008. Additionally a corresponding increase in the mean age at death from HF regardless of gender was found. Half of these deaths occurred in hospital without significant change over the 20-year study period. These patterns in mortality have important implications in understanding the burden of HF in European countries and the potential impact of improved care.

In our study, the marked reduction in HF mortality was specifically observed in four of the studied countries (France, Germany, Greece, and Spain). These four countries had the highest SDR in 1987 (≥ 40 per 100 000) and the greatest decrease in mortality (≥ 40% during the study period). The reduction in SDR was continuous, observed almost every year since 1987 in each country. In a few countries where data are available, including Spain and Scotland, a decrease in SDR was already present in the early 1980s.17,18 Interestingly, our study shows that the continuous reduction in SDR with HF as an underlying cause was still found in very recent years (e.g. 2005–2008). Mortality trends seem to be unaffected in any of these four countries by the two versions of the ICD implemented during the study period. Consequently, our study underscores the validity of the marked reduction of SDR with HF as an underlying cause in France, Germany, Greece, and Spain over the last two decades.

The second group of studied countries, England and Wales, Finland, and Sweden, had an SDR with HF as an underlying cause < 25 per 100 000 in 1987 that remained roughly stable throughout the study period. Our data are in line with the data recorded since 1950 in England and Wales showing that SDR related to HF fell markedly from 1970 till the mid 1980s and remained stable thereafter.19

We further considered SDR with HF mentioned anywhere on the death certificate in France, and England and Wales, the only countries where those data were available. As expected, the reduction of SDR with HF paralleled the reduction observed for HF as the underlying cause in France. Interestingly, the SDR with HF markedly decreased (50% over the last 15 years) in England and Wales despite the SDR with HF as an underlying cause remaining stable.

Notably, Figure 2A shows that, in all studied countries, the SDR with HF as an underlying cause approaches ≏ 30 per 100 000 inhabitants. Hopefully the number of patients with HF as an underlying cause of death may decrease to < 100 000 deaths/year in the seven studied countries, corresponding to < 5000 per year for Greece and < 20 000 per year for France, within the next decade. Likewise, Figure 2B shows that, in France, and England and Wales, mortality with HF mentioned anywhere on the death certificate has already converged to a similar rate.

Mechanism(s) of the reduction of the SDR with HF as an underlying or multiple cause and the reason for differences in the SDR related to HF among the seven studied countries remain unclear.
Those beneficial results are unlikely to be related to a decreased number of patients with chronic HF, as several studies observed an increase in the number of HF patients in Europe.\textsuperscript{20–22} During the period studied there was an increase in availability of evidence-based guidelines\textsuperscript{12,13} and recommended therapies in HF [angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, aldosterone antagonists, and cardiac resynchronization therapy].\textsuperscript{23–26} Indeed, our data are in line with the observational study of the patients hospitalized with a first episode of HF in Scotland between 1986 and 2003.\textsuperscript{27} In that study, adjusted 30-day, 1-year, and 5-year survival rates improved over time and paralleled the prescribing rates of HF therapies.\textsuperscript{27} Accordingly, the beneficial results observed in the study period are probably related to the awareness and implementation of these guidelines resulting in a better management of chronic HF with reduced left ventricular ejection fraction (LVEF).\textsuperscript{28–32} A better management of acute decompensated HF in emergency rooms and intensive care units further contributes to improve the outcome of HF patients.\textsuperscript{33–35}

Our study further shows that in the past two decades the main place where death occurs from HF remains the hospital. This may reflect no change in the proportion of sudden deaths, although other factors may play a part.

**Limitations**

The use of mortality data in evaluating disease burden has limitations. First, the mortality rate is an incomplete indicator of disease burden. Such indicators have limitations as well, most notably that they depend on the quality of the medical certification and of the coding system. The main potential issue is the reliability of death certification and validity in various countries.\textsuperscript{36–39} Inaccuracies in death certificates and changes in classification of causes of death are potential limitations in the interpretation of mortality trends. However the use of death certificates to assess mortality is common in various area of medicine including cancer or human immunodeficiency virus (HIV).\textsuperscript{36–39} Death certificates are increasingly used in cardiovascular diseases.\textsuperscript{40–42} Furthermore, HF is a syndrome that may not be individualized as a disease by physicians, therefore it may have been underreported in the death certificates either as the underlying cause of death or being mentioned anywhere on the death certificate.\textsuperscript{43} The value of measuring temporal trends in death rates rather than in relative survival is that death rates are much less susceptible to artefactual changes from screening and lead time or length bias. Although the quality of certification of cause of death may have improved over the years, this is unlikely to account for the large drops in mortality for HF either as an underlying cause of death or when mentioned anywhere in the death certificate. No significant discontinuities in the mortality trends occurred with the implementation of ICD-10. Further, any effect of the introduction of revised ICD coding on mortality trends is transient, and should not affect long-term trends. Despite all these limitations of the death certification among physicians and among countries and the use of two ICD coding systems, the continuous reduction in the SDR with HF as the underlying cause of death or mentioned anywhere in the death certificate in many studied countries seems to represent the reality.\textsuperscript{44}

**Conclusion**

In summary, this study shows a substantial and continuous decrease in HF as the underlying cause of death in the past 20 years, similar to what was already described in other cardiovascular diseases. There has been an accompanying increase in age at death from HF in both men and women. We hypothesize that these results may be related to a better management of chronic and acute HF patients over the past 20 years. Improved availability of European guidelines on the management of HF may have had beneficial effects.

**Supplementary material**

Supplementary material is available at European Journal of Heart Failure online.

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