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ORIGINAL RESEARCH ARTICLE

# Heart failure in Finland: clinical characteristics, mortality, and healthcare resource use

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## Abstract

**Aims** The aims of this study were to describe patient characteristics of the adult chronic heart failure (HF) population and to estimate the prevalence, incidence, healthcare resource utilization (HCRU), and mortality associated with HF in Southwest Finland.

**Methods and results** This was a retrospective biobank and clinical registry study. Adult patients with an HF diagnosis (International Statistical Classification of Diseases and Related Health Problems (ICD) code I50) during 2004–2013 in secondary care were included in the study and compared with age-matched and gender-matched control patients without an I50 diagnosis. HF patients were stratified in groups by left ventricular ejection fraction (LVEF) as follows: LVEF $<$ 40% [HF with reduced ejection fraction (HFrEF)]; LVEF $\geq$ 40% [HF with preserved ejection fraction (HFpEF)]; or unknown (LVEF unknown). HCRU was stratified by inpatient, outpatient, and emergency room visits. In 2013, the incidence of HF was 3.2/1000, and the prevalence was 13.9/1000 inhabitants ($n$ = 15 594). In the stratified analysis of HF patients ($n$ = 8833, average ± SD age 77.1 ± 11.2), 1115 (12.6%) patients had HFrEF (female 31.3%), 1449 (16.4%) had HFpEF (female 50.9%), and 6269 (71%) had unknown LVEF (female 52.1%). The most common co-morbidities were essential hypertension (58%), chronic elevated serum creatinine (57.3%), atrial fibrillation and flutter (55.1%), and chronic ischaemic heart disease (46.4%). Patients with HF diagnosis had higher HCRU compared with that of age-matched and gender-matched controls (3.7 more days per year at the hospital for HF patients compared with the controls). The total 5 year mortality was 62.6% for HF patients and 28.3% for controls, with higher age being the strongest predictor of mortality. Moreover, multivariable Cox regression analysis showed that patients with HFrEF had a 13% (95% confidence interval 2.7–25%) increased risk of mortality compared with HFpEF patients.

**Conclusions** The high mortality rate and HCRU among the studied HF patients highlight the severity of the disease and the economic and social burden on both patients and society. This calls for improved methods of care for this large patient population.

**Keywords** Heart failure; HCRU; HFrEF; HFpEF; Mortality

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## Introduction

Heart failure (HF) is defined as a complex syndrome in which patients have typical symptoms such as breathlessness, ankle swelling, and fatigue, as well as clinical signs related to an abnormality of cardiac structure or function.[1] The prevalence of HF is escalating rapidly worldwide, and the disease consumes significant healthcare resources, inflicts significant morbidity and mortality, and greatly impacts patient's quality of life.[2] HF is considered a public health problem due to the

significant prevalence and costs, mainly driven by high rates of hospitalization and mortality, despite available and recommended treatments.

The estimates of HF incidence and prevalence vary greatly across studies. Based on data from the Europe and the USA, the overall prevalence of HF ranges from 1 to 12%.[3] Depending on the applied definition, the prevalence of HF is estimated to be 1–2% in the adult population, rising to over 10% in people over 70 years of age.[4,5] One in six of people over 65 years of age coming to primary care with shortness of breath is estimated to have undiagnosed HF,[6] and the lifetime risk of HF at the age of 55 is 33% for men and 28% for women.[7] The total number of Americans living with HF is estimated to increase by 46% from 2012 to 2030.[8] The current prevalence of HF in Finland is not known.

The incidence of HF has gradually declined since the late 1990s as shown in multiple studies.[3] An older study of HF in Eastern Finland reported an age-adjusted incidence of 4.0 and 1.0 per 1000 patient years for men and women, respectively.[9] Schaufelberger *et al.*[10] estimated a peak incidence of HF in 1993, after which it has gradually declined until the end of their study period in 2000. On the other hand, a large population-based study found no changes in the incidence of HF between 1979 and 2000.[11] The differences historically seen in coronary heart disease-associated mortality between the Western and Eastern parts of Finland have disappeared in later years,[12] and thus, the incidence and prevalence of HF in Finland should be re-evaluated.

The ejection fraction (EF) of the heart can be used to classify HF into two groups: patients with preserved (HFpEF) or reduced (HFrEF) EF. Approximately half of the diagnosed HF patients have HFpEF.[13–16] HFpEF has been described to be more common in women, elderly patients, and patients with persistent hypertension.[4] Of importance, the distribution of HFpEF and HFrEF among chronic HF patients in Finland has not been described before. The first Finnish national guidelines for HF were published in 2017, and they use 40% as a cut-off for HFrEF vs. HFpEF.[17] Thus, we used that cut-off value in this study.

The five strongest predictors of being hospitalized for HF are higher age, previous hospitalization for HF, oedema, lower systolic blood pressure, and lower estimated glomerular filtration rate.[18] HF hospitalization rates increased remarkably during the 1990s in several parts of the world[19,20] but have decreased since then.[20] However, the vast majority (80%) of costs attributed to HF are related to hospitalization, and as the population is ageing and the prevalence of HF is rising, these costs are projected to have a 2.5-fold increase by 2030.[8] HF is the most common reason for hospitalization of the elderly in Finland and thus a remarkable burden on the healthcare system.[21] Cook *et al.*[22] have estimated from World Bank data that in 2012, the economic burden of HF was $464m in Finland. Although the amount of avoidable hospitalizations has been slightly decreasing, Finland is still doing worse than the average Organization for Economic Cooperation and Development countries.[23]

In terms of 5 year survival from first HF hospitalization, HF is a more severe disease than most cancers, as described in a Scottish population-based study by Steward *et al.*[24] This study showed that of the four most common types of cancer, only lung cancer in men and lung and ovarian cancer in women had worse adjusted long-term survival than HF. Median survival time from the first hospitalization was 16 months, and only 25% of the patients with HF were alive after 5 years.[24] The Rotterdam study reported a 59% 5 year survival for HF, reflecting a threefold increase in the risk of death, compared with an age-matched and gender-matched population.[7] Even in the 21st century, the prognosis of HF patients remains poor; a Spanish population-based study reported the risk-adjusted 30 day, 1 year, and 4 year mortality in 2007 to be 12.1, 28.8, and 61.4%, respectively.[25]

The aims of this study were to describe the characteristics of the adult chronic HF population and to estimate the incidence and prevalence, mortality, survival, and healthcare resource utilization (HCRU) of patients with HF in Southwest Finland.

# Methods

## Data sources

This study was a non-interventional, retrospective registry study using data already available in electronic patient records. The study was conducted in the geographical area of the hospital district of Southwest Finland with an approximate population of 500 000 inhabitants.

For the analysis of HF incidence and prevalence, data were requested from Turku Clinical Research Center (CRC) for the whole hospital district of Southwest Finland. Prevalence and incidence of HF were estimated from hospital records of hospitalizations and outpatient visits, based on adult patients having an ICD-10 diagnosis for HF (I50) in their records between 2004 and 2013 ($n$ = 15 594). For these patients, only aggregate-level data (data pooled by age and gender) on ICD-10 code I50 stratified by age were obtained. Auria Biobank obtained an ethical approval for the data request (Approval AB16-1101).

For a subset of Turku CRC patients, who had given a consent to the Auria Biobank ($n$ = 8833), a more detailed analysis was performed with patient-level secondary care data (clinical data from hospital inpatient and outpatient visits were obtained and analysed for each patient individually). These data included inpatient care (HF hospitalizations), referrals from primary care (for diagnosis), medication started in the hospital after the diagnosis, and regular visits in outpatient care. The Finnish Biobank Act (Finlex 688/2012) enables

the use of biobank data in research and makes it possible to obtain data from other, for example, national registries, such as time of death (Statistics Finland) if justified for conducting the research. Auria Biobank is linked to the Turku University Hospital electronic health record systems, in which electronic clinical data are available from year 2004 and onwards. All patient-level variables, such as HCRU, N-terminal pro-BNP (NT-proBNP)/BNP, EF, and mortality used in this study, were acquired pseudonymized from the Auria Biobank registry. The ethical approval for the Auria Biobank data use was obtained by Novartis Finland (Approval AB16-1101). The investigation conforms with the principles outlined in the *Declaration of Helsinki* (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/).[26]

## Inclusion criteria

The study population included adult patients (>18 years) with HF diagnosis in their health records (identified by ICD-10 coding I50*), who had been treated in the hospitals of the hospital district from 1 January 2004 until 9 January 2013. A patient was enrolled to the study on the date when HF diagnosis was recorded for the first time anywhere in his or her electronic health record data (=index date) and followed until the time of death or until 9 January 2013. All patients enrolled in the study were evaluated regardless of follow-up time from index.

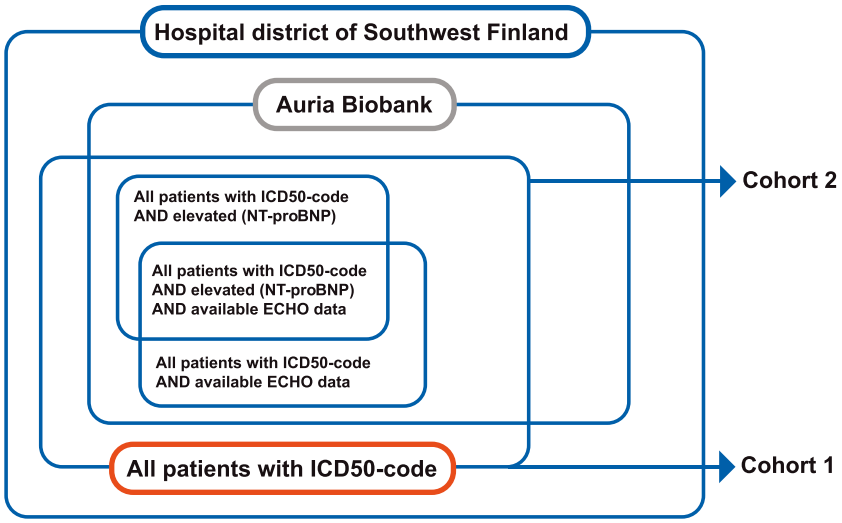
The data were analysed in different cohorts (*Figure 1*). The first cohort included all adult patients with I50 diagnosis in their hospital health records in the hospital district of Southwest Finland during the previously mentioned time period. These data were acquired at aggregate level (pooled by age and gender) from Turku CRC and used for prevalence and incidence estimates. The second cohort was a subset from Cohort 1 and included HF patients who had given the Auria Biobank consent and from whom pseudonymized patient-level (clinical data from each individual patient) data, for example, laboratory values, procedures, and HCRU, were obtained. This cohort was further divided into sub-cohorts based on EF.

The control group included individually 1:1 age-matched and gender-matched patients ($n$ = 8833) in the Auria Biobank patient population. Patients in the control group were not allowed to have I50 ICD-10 code anywhere in their electronic health records. The control group was used to compare HCRU, co-morbidities, and mortality between patients with and without an HF diagnosis.

## Prevalence and incidence

The prevalence and incidence of HF in Southwest Finland were estimated from all adult patients that had an I50 diagnosis in their hospital health records during 1 January 2004–9 January 2013 (Cohort 1). The annual incidence (newly diagnosed patients per year) and prevalence (existing diagnoses per year) were evaluated by calendar year in the hospital district of Southwest Finland and stratified by age group (5 year segments). These were extrapolated to the total population in each age segment, using data on the Finnish population structure from Statistics Finland.

**Figure 1** Different patient cohorts used in the study. The first cohort consisted of all adult patients in the Hospital District of Southwest Finland with I50* ICD-10 code. The second cohort consisted of a subset of the previous cohort, patients who had given the Auria Biobank consent. This cohort was further divided with specific characteristics [echocardiographic data/N-terminal pro-BNP (NT-proBNP) value].



### Clinical characteristics

A more specific clinical characterization was performed for patients that had given the Auria Biobank consent (Cohort 2). Summary statistics of variables of interest were calculated. Values were taken from the patient index date or closest available value to the index date up to 6 months from HF diagnosis. NT-proBNP/BNP values were retrieved from laboratory results. The patients were stratified by age, gender, and EF. The EF value was retrieved from the health records by using text mining algorithms, and the first available EF value was used for further stratifications. For EF, the patients were divided into HFpEF (EF $\geq$ 40% and NT-proBNP $\geq$ 125 ng/L), HFrEF (EF $<$ 40%), or with unknown EF status (not fulfilling the criteria for either HFpEF or HFrEF due to missing data). The patients within these EF groups were further stratified by age and gender.

For co-morbidities, the most common ICD-10 codes during follow-up were listed for both HF patients (also stratified by EF status) and control group. Renal failure was defined as having a serum creatinine value over the reference limit in three repeated measurements within 3 months.

### Mortality

Mortality was assessed as all-cause mortality. Time of death was obtained from Statistics Finland.

### Healthcare resource use

To determine the overall HCRU of HF patients, the number of outpatient visits, inpatient visits, the length of hospital stay, and emergency room (ER) visits were retrieved. The results included all HCRU for HF patients and for patients in the control group irrespective of the reason. HCRU of the HF patients was further stratified by EF.

### Statistical analyses

Results are shown in general as mean ± standard deviation. Survival was analysed using univariable and multivariable Cox proportional hazards models with time to event defined as time from HF diagnosis to death (all-cause mortality) or end of follow-up (9 January 2013, censoring event). In the univariable model, three risk factors were analysed: age (divided into five age group categories), gender, and EF group. In the multivariable model, all of the aforementioned risk factors were assessed simultaneously. Kaplan–Meier survival curves were used to visualize survival of the patients.

## Results

### Prevalence and incidence

The prevalence and incidence ($n$ = 15 594) of HF in secondary care did not show large fluctuation during the follow-up period (*Figure 2A*). The prevalence increased during the follow-up, partly due to the ageing of the population and partly due to the incident cohort formation where the number of diagnosed patients accumulates during the follow-up (*Figure 2A*). In 2013, the HF prevalence was 13.9/1000 persons and incidence 3.2/1000 persons. Prevalence and incidence stayed low among patients under 50 years of age but increased rapidly among the elderly being 153.4/1000 and 36.5/1000 for patients over 85 years and under 50 years of age, respectively (*Figure 2B*).

### Clinical characteristics

The clinical characteristics of HF patients and patients in the control group are presented in *Table 1* ($n$ = 8833). Remarkably, 71% of the patients with HF diagnosis did not fulfil the criteria for HFpEF or HFrEF due to missing data. This might indicate that no echocardiogram was performed in the diagnostic phase or no record of it was available in the health records. The 12.6% of the HF patients were categorized as HFrEF patients with a mean age of 70.5 and 31.3% of the patients being of female gender. Correspondingly, 16.4% of the HF patients were categorized as HFpEF patients with a mean age of 74 and 50.6% having female gender. Patients without EF data were older and had a mean age of 79.1, and 56.1% of them were female. The average age of patients in the control group was 74.3, and 52.1% were females.

The most common co-morbidities among the HF patients were renal failure (defined by the serum creatinine value being over the reference limit in three repeated measurements within 3 months), essential hypertension, chronic ischaemic heart disease, pneumonia, type 2 diabetes, atrial fibrillation, myocardial infarction, and age-related cataract. No significant differences were seen in the prevalence of these co-morbidities between different HF types (HFrEF/HFpEF/unknown EF). The eight most common co-morbidities, except age-related cataract, were more prevalent among HF patients compared with patients in the control group (*Table 1*). The most common co-morbidities in the HF population and the corresponding percentage of these in the control population, as well as the most common co-morbidities within the control population and the corresponding percentage of these within the HF population, are illustrated in Supporting Information, *Figure S1*. There were no differences in the prevalence of diseases common in the elderly (age-related cataract, conductive hearing loss, and benign prostatic hyperplasia)

**Figure 2** Prevalence and incidence of heart failure in Southwest Finland between 2004 and 2013 per 1000 persons (A) and in 2013 among different age groups per 1000 persons (B). In 2013, the prevalence was 13.9/1000 persons and the incidence was 2.3/1000 persons (A). Both prevalence and incidence stayed low within patients under 50 years of age and increased rapidly within the elderly being 153.4/1000 and 36.5/1000 within patients over 85 years of age, respectively (B).

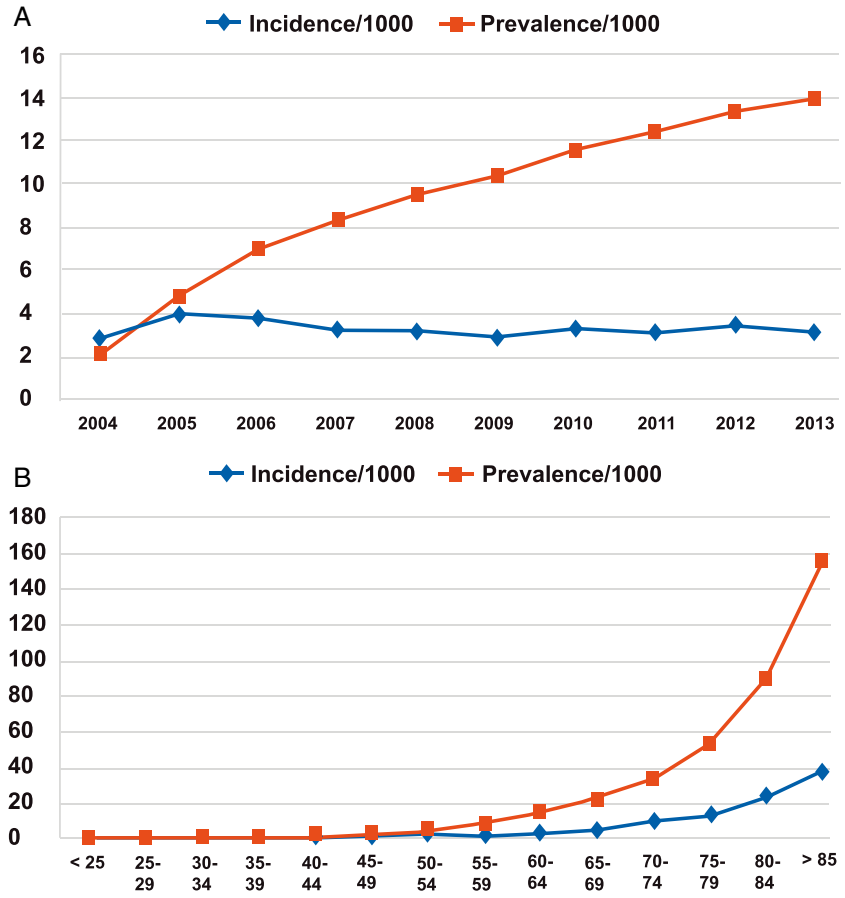



**Table 1** Basic characteristics of HF and control population

| | HFrEF | HFpEF | Unknown EF | HF total | Control group |
|---|---|---|---|---|---|
| *n* (%) | 1115 (12.6) | 1449 (16.4) | 6269 (71) | 8833 | 8833 |
| Age ± SD | 70.5 ± 12.4 | 74.0 ± 10.9 | 79.1 ± 10.4 | 77.1 ± 11.3 | 74.3 ± 11.3 |
| Female (%) | 349 (31.3) | 738 (50.9) | 3519 (56.1) | 4606 (52.1) | 4606 (52.1) |
| NT-proBNP ± SD (pg/mL) | 8061 ± 15620 | 6616 ± 15169 | 6805 ± 11474 | 6933 ± 12604 | |
| Co-morbidities | | | | | |
| Kidney failure[a] | 659 (59.1) | 906 (62.5) | 3500 (55.8) | 5065 (57.3) | 2626 (29.7) |
| Essential hypertension (I10) | 564 (50.6) | 983 (67.8) | 3579 (57.1) | 5126 (58.0) | 2761 (31.3) |
| Chronic ischaemic heart disease (I25) | 656 (58.8) | 682 (47.1) | 2759 (44.0) | 4097 (46.4) | 1283 (14.5) |
| Pneumonia unspecified organism (J18) | 294 (26.4) | 457 (31.5) | 2008 (32.0) | 2759 (31.2) | 890 (10.1) |
| Type 2 diabetes (E11) | 348 (31.2) | 478 (33.0) | 1734 (27.7) | 2560 (29.0) | 923 (10.4) |
| Atrial fibrillation (I48) | 568 (50.9) | 832 (57.4) | 3471 (55.4) | 4871 (55.1) | 1313 (14.9) |
| Myocardial infarction (I21) | 399 (35.8) | 396 (27.3) | 1495 (23.8) | 2290 (25.9) | 519 (5.9) |
| Age-related cataract (H25) | 218 (19.6) | 396 (27.3) | 1675 (26.7) | 2290 (25.9) | 2003 (22.7) |
| Conductive hearing loss (H90) | 140 (12.6) | 170 (11.7) | 956 (15.2) | 1266 (14.3) | 1212 (13.7) |
| Benign prostatic hyperplasia (N40) | 163 (14.6) | 188 (13.0) | 740 (11.8) | 1091 (12.4) | 1022 (11.6) |

EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; NT-proBNP, N-terminal pro-BNP; SD, standard deviation.
[a]Creatinine measurement over reference values in three repeated measurements within 3 months during the follow-up.

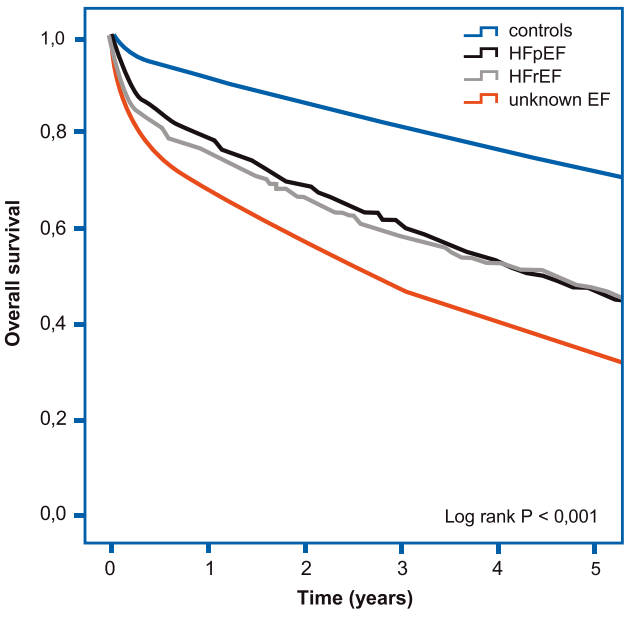
between the HF and control group populations (Supporting Information, *Figure S1*).

## Mortality

The all-cause mortality for the HF population and control group is illustrated with Kaplan–Meier survival curves (*Figure 3*). Twenty-five per cent of the HF patients died during the first year after the index date (*Figure 3*). For HF patients, the 5 year all-cause mortality was 62.6% compared with 28.3% for the control group (*Figure 3*). There were no differences between HFrEF and HFpEF patients in 5 year absolute all-cause mortality (55% for both). Patients with unknown EF had the worse 5 year prognosis (68% 5 year mortality). HF patients in all age groups had a worse 5 year survival compared with the same aged population without HF diagnosis (*Figure 4*).

The univariable Cox proportional hazards model showed that age was the strongest predictor of increased mortality (*Table 2*). In the univariable model, gender was a non-significant predictor of survival, and HFpEF and HFrEF had no significant survival differences, whereas patients with unknown EF had a poorer prognosis [41% increase in the risk of death, 95% confidence interval (CI) 31–51%]. In the multivariable model, all the assessed predictors of mortality were significant. The risk estimates for age groups were almost unchanged, whereas in the multivariable model, male gender was associated with significant 30% increase in the risk of death (95% CI 23.8–36.8%). Correspondingly, when assessed in the multivariable model, HFrEF patients were associated with 13% increased risk (95% CI 2.7–25%) and patients with unknown EF with 16% increased risk (95% CI 8.1–24.8%) of all-cause mortality compared with HFpEF patients.

**Figure 3** Absolute 5 year survival of patients in the control group and heart failure patients stratified by left ventricular ejection fraction. Heart failure with reduced ejection fraction (HFrEF) and heart failure with preserved ejection fraction (HFpEF) patients had 55% 5 year mortality; patients with unknown ejection fraction (EF) had 68% 5 year mortality, whereas the patients in the control group had 28.3% 5 year mortality.




## Healthcare resource use

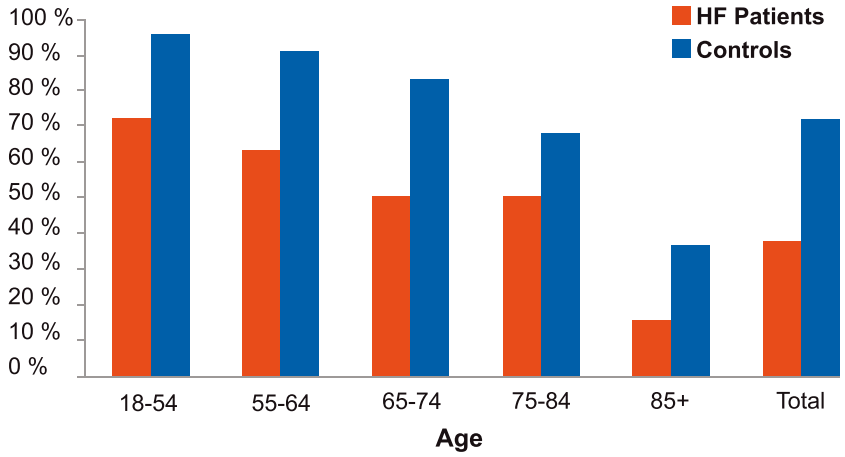
Heart failure patients had on average 7.3 visits to any hospital outpatient clinic for any reason during the index year and on average 7.8 visits per year during the following 4 years (*Figure 5A*). For patients in the control group, these figures were 4.7 and 4.5, respectively (*Figure 5A*). HF patients had on average 1.5 ER visits during the index year and 0.9 ER visits per year during the following 4 years, while for patients in the control group, these figures did not change during the follow-up (0.6 ER visits during the first year and 0.5 ER visits per year during the following 4 years) (*Figure 5B*). HF patients had on average 2.5 hospital admissions requiring at least one overnight stay, corresponding to 16.5 days spent in the hospital within the index year. Patients in the control group had on average one hospital admission lasting for 6.4 days during the index year (*Figure 5C* and *D*). In the following 4 years from the index, HF patients had 1.3 hospital admissions per year, lasting for 7.9 days, and patients in the control group had 0.7 hospital admissions, lasting for 4.2 days (*Figure 5C* and *D*). There were no clinically relevant differences in the HCRU between HFrEF and HFpEF patients or patients with unknown EF (Supporting Information, *Table S1*).

# Discussion

## Prevalence and incidence

The prevalence and incidence of HF showed no remarkable fluctuation in Southwest Finland during the follow-up of the study. The increase in prevalence can be partly explained by the overall ageing of the population and is also affected by the incident cohort creation. Overall, the incidence rates found in this study were comparable with those listed in the international literature and previously in Finland.[3,9,10] However, during the follow-up of this study, we did not saw a decrease in incidence, as previously reported.[10] Consistently with the previous studies, we also saw a strong increase in the prevalence and incidence according to age.[4,5] The overall prevalence reported here is in line with previous reports.[3–5,7] As no previous registry-based studies exist on the HF prevalence in Finland, it would be of interest to also investigate whether the prevalence of HF is higher in Eastern Finland where the cardiovascular mortality traditionally has been higher compared with Western Finland.[12]

**Figure 4** Five year survival for heart failure (HF) patients and patients in the control group in different age groups. The survival of HF patients was decreased within patients of all ages compared with that of patients in the control group.




## Clinical characteristics

We present descriptive data on the clinical characteristics of HF patients. Only 29% of the patients could be categorized as HFpEF or HFrEF patients due to missing EF data. As echocardiography is one of the cornerstones in the diagnosis of HF in the Finnish national guidelines,[17] this can be considered a low percentage. Only a small fragment of the patients had a structured procedure code for echocardiography recorded, and the EF results were mainly derived from the free text of the electronic health records, utilizing multiple search patterns. However, we still cannot overrule that some of the patients might have had echocardiography performed and that we could not find the data.

Consistent with previously reported data,[4,13] approximately half of the HF patients with EF data available had HFpEF, and this was associated with older age and female gender. Moreover, these patients also had more essential hypertension. HF patients with unknown EF were on average 9 years older than HF patients in general. This might indicate that due to higher age, echocardiography would not have changed their treatment and was thus not performed.

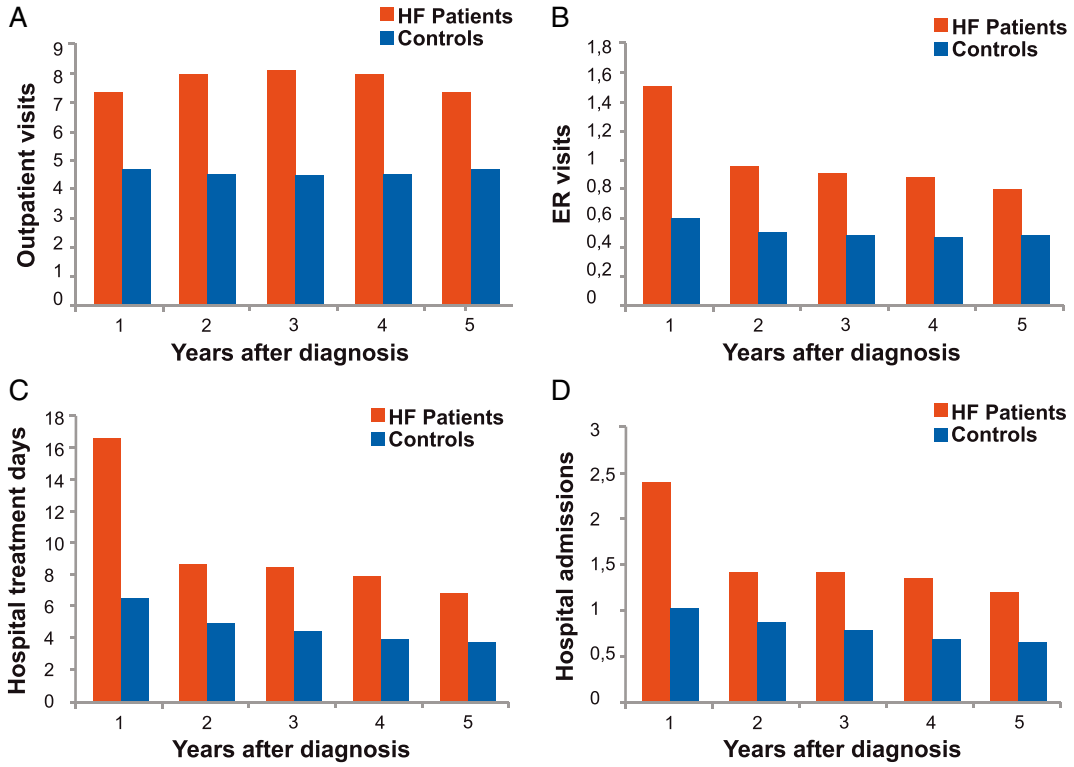
In this study, we did not assess the aetiology of HF but merely the co-morbidities of the patients included. HF should not be assessed in isolation as it is a common disease in the elderly. The most common co-morbidities listed in this study (such as hypertension, ischaemic heart disease, type 2 diabetes, myocardial infarction, and atrial fibrillation) were well

**Table 2** Mortality of HF patients assessed by univariable and multivariable Cox proportional hazard models

| | Univariable | | | | Multivariable | | | |
|---|---|---|---|---|---|---|---|---|
| Variable | HR | Lower 95% CI | Upper 95% CI | *P* value | HR | Lower 95% CI | Upper 95% CI | *P* value |
| Age group | | | | | | | | |
| 18–54 | Ref. cat. | | | | Ref. cat. | | | |
| 55–64 | 1.534 | 1.264 | 1.863 | <0.001 | 1.532 | 1.261 | 1.861 | <0.001 |
| 65–74 | 2.340 | 1.953 | 2.803 | <0.001 | 2.370 | 1.977 | 2.841 | <0.001 |
| 75–84 | 3.696 | 3.102 | 4.403 | <0.001 | 3.884 | 3.255 | 4.636 | <0.001 |
| 85+ | 6.129 | 5.132 | 7.319 | <0.001 | 6.555 | 5.472 | 7.853 | <0.001 |
| Gender | | | | | | | | |
| Female | Ref. cat. | | | | Ref. cat. | | | |
| Male | 1.031 | 0.983 | 1.083 | 0.210 | 1.301 | 1.238 | 1.368 | <0.001 |
| EF group | | | | | | | | |
| HFpEF | Ref. cat. | | | | Ref. cat. | | | |
| HFrEF | 1.018 | 0.924 | 1.122 | 0.719 | 1.133 | 1.027 | 1.250 | 0.013 |
| Unknown EF | 1.407 | 1.310 | 1.510 | <0.001 | 1.162 | 1.081 | 1.248 | <0.001 |

CI, confidence interval; EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, hazard ratio; Ref. cat., reference population.
In univariable model, age was the strongest predictor of poor prognosis. For HFrEF and HFpEF patients, the prognosis was similar, but patients with unknown EF status had a poorer prognosis. When analysed in multivariable model, all assessed predictors became significant.

**Figure 5** Healthcare resource utilization among heart failure (HF) patients and patients in the control group. HF patients had increased amount of outpatient visit (A), emergency room (ER) visits (B), hospital treatment days (C), and hospital admissions (D) during all five follow-up years when compared with the patients in the control group.




aligned with those listed in the recent large trials of HFrEF[27] and HFpEF.[28]

## Mortality

Our results showed a poor 5 year survival for HF patients when compared with the patients in the control group. High mortality among HF patients in secondary care (i.e. patients treated within hospital inpatient or outpatient clinics) highlights the severity of the disease as these patients can be expected to receive optimized HF care. For HFpEF and HFrEF patients, the 5 year mortality was 55%. This and the absolute overall mortality of HF patients are in line with the previous reports of 5 year mortality.[7,24,25] In a previous study from Finland assessing the mortality of patients with acute decompensated chronic HF and *de novo* acute HF, the overall 5 year mortality was 60.3%[29] and well in line with our results. In univariate analysis, EF status did not affect the survival of the HF patients as reported earlier.[15] As in this study, left ventricular dysfunction has also previously been described as an individual predictor of mortality when assessed in multivariable regression models.[30] In univariable model, gender was a non-significant predictor of HF mortality, but in multivariable model, male gender had a higher risk for death.

As previously reported,[15,24] this study also found age to be the strongest predictor of mortality. In all age groups of HF patients, the 5 year survival was worse compared with the age-matched and gender-matched controls. The difference was especially pronounced in patients over 65 years.

## Healthcare resource utilization

As expected, the overall HCRU of HF patients was high and higher in all HCRU subtypes than for patients in the control group. HF patients had almost 2.5 hospital admissions for any reason, contributing to over 16 days in hospital, during the first year. As this in most cases included the acute episode leading to HF diagnosis, the number of hospital admissions was down to approximately 1.5 and just under 8 days per year for the following years. When over seven visits in the outpatient clinics and one ER visit per year are added to these figures, it is clear that the disease represents a major cost for society and affects the quality of life of HF patients.

## Study limitations

Major study limitations include uncertainties in the use of diagnosis and procedure codes. In this study, only the I50

diagnosis code was used for inclusion, and this might exclude some HF patients diagnosed, for example, with cardiomyopathies or alcohol-induced HF.

There is no traditional disease registry for HF patients in Finland, and the available clinical and biobank data are restricted to only secondary care data with some linkage to national databases, for example, Statistics Finland. It is a clear limitation of the study that the resource use of HF patients in the primary care setting is not included. However, to be correctly diagnosed, the diagnosis of HF needs secondary care assessments, and thus, all diagnoses should be given in secondary care.

## Conclusions

This study shows that HF patients have a poor prognosis and use large amounts of healthcare resources when compared with age-matched and gender-matched controls. This is also the first time the HF patients are stratified and characterized according to their EF status in Finland. The study offers a great possibility to further study the medication and diagnostic patterns of HF patients, in order to improve the care and decrease healthcare-associated costs for this patient population in the future.

We conclude that according to this study, the prevalence and incidence of HF in Finland, as well as the clinical characteristics of the HF patients, are well in line with the previous reports. The high mortality and HCRU of HF patients in secondary HF care highlight the severity of the disease and call for further actions to improve HF care and optimize the treatment of these patients.

## Conflict of interest

J.H. and T.P. are employees of Novartis Finland Oy. At the time of the study, E.G. and S.B.W. were employees of Novartis Sweden AB.

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## Supporting information

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

**Figure S1**: The eight most common comorbidities within HF population and the corresponding percentage of these in the control group (A). The eight most common comorbidities within the control group and the corresponding percentage of these within the HF population (B). There were no differences in the prevalence of diseases common in the elderly (age-related cataract, conductive hearing loss and benign prostatic hyperplasia) between the HF and control group populations. I10: essential hypertension; Crea: creatinine over reference values in three repeated measurements within three months during the follow-up; H25: age-related cataract; I48: atrial fibrillation; I25: chronic ischemic heart disease; J18: pneumonia NAS; E11: type 2 diabetes; H90: conductive hearing loss; I21: myocardial infarction; N40: benign prostatic hyperplasia.

**Table S1**: HCRU of HFrEF, HFpEF, patients with unknown EF status and control patients.

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