

# Heart failure in young adults: 20-year trends in hospitalization, aetiology, and case fatality in Sweden

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<b>Aims</b>	To describe trends in incidence and case fatality among younger (18–54 years) and older (55–84 years) Swedish patients with heart failure (HF).
<b>Methods and results</b>	Through linking the Swedish national hospital discharge and the cause-specific death registries, we identified patients aged 18–84 years that were discharged 1987–2006 with a diagnosis of HF. Age-specific mean incidence rates per 100 000 person-years were calculated in four 5-year periods. Kaplan–Meier survival curves were plotted up to 3 years. From 1987 to 2006, there were 443 995 HF hospitalizations among adults 18–84 years. Of these, 4660 (1.0%) and 13 507 (3.0%) occurred in people aged 18–44 and 45–54 years (31.6% women), respectively. From the first to the last 5-year period, HF incidence increased by 50 and 43%, among people aged 18–34 and 35–44 years, respectively. Among people $\geq 45$ years, incidence peaked in the mid-1990s and then decreased. Heart failure in the presence of cardiomyopathy increased more than two-fold among all age groups. Case fatality decreased for all age groups until 2001, after which no further significant decrease $< 55$ years was observed.
<b>Conclusion</b>	Increasing HF hospitalization in young adults in Sweden opposes the general trend seen in older patients, a finding which may reflect true epidemiological changes. Cardiomyopathy accounted for a substantial part of this increase. High case fatality and lack of further case fatality reduction after 2001 are causes for concern.
<b>Keywords</b>	Heart failure • Incidence • Prognosis • Comorbidity • Young adults

## Introduction

Heart failure (HF) among the young is rare, but may exert a greater impact on active and income-generating individuals.<sup>1</sup> Most HF-studies are based on older adults, and accordingly, little is known about the aetiology, incidence, and trends in HF among younger patients.<sup>2,3</sup>

While ischaemic heart disease (IHD) and hypertension are predominant causes of HF among older patients, the aetiological make-up of HF in young adults is more heterogeneous. Common causes of HF among the young include adult congenital heart

disease (ACHD), different types of cardiomyopathies, myocarditis, or alcohol- or drug-related myocardial lesions.<sup>4,5</sup>

Despite improved outcomes in the management of coronary heart disease and HF,<sup>6</sup> HF still carries a 50% 5-year mortality, parallel to that of many cancers.<sup>7,8</sup> Studies indicate that HF incidence and mortality in Sweden, Scotland, and Australia have been decreasing since the early 1990s.<sup>6,9–12</sup> Whether this change occurs in younger age groups has to our knowledge not been examined.

We used data from the Swedish national hospital discharge and cause-specific death registries to investigate age-specific trends in

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HF incidence, comorbidity and 1-year case fatality trends in ~440 000 hospital discharges over a period of 20 years.

## Methods

### The registries

Sweden has universal healthcare providing low-cost hospital care to all Swedish permanent residents, with all hospitals reporting discharge diagnoses to a nationwide hospital discharge registry. The data are person based and include primary and secondary discharge diagnoses of any given hospitalized patient.<sup>13</sup> Data from the national hospital discharge registry and cause-specific death registry were linked through a unique national personal identity number.

### Procedures

Because a large percentage of younger patients with HF had other primary aetiological diagnoses, we included all patients aged 18–84 years from 1987 to 2006 who had a first-ever HF diagnosis code in any position. First admission was defined as any hospital admission with no previous admission for HF in the past 7 years. This was done to ensure the probability of being admitted for the first time was similar for any given time period. From 1987 to 1996, the *International Classification of Diseases, Ninth Revision (ICD-9)* was in use, and thereafter ICD-10. We defined HF by 427.10, 427.00 (ICD-8), 428A, 428B, and 428X (ICD-9) and I50 (ICD-10). The following diagnoses for concomitant or pre-existing comorbidity were included up to the point of the HF yielding hospitalization: cardiomyopathy 425 (ICD-9), I42, I43 (ICD-10); IHD 410–414 (ICD-9), I20–I25 (ICD-10); valvulopathies 391, 394–398, 421, 424 (ICD-9), I05–I09, I33–I39 (ICD-10); and congenital heart disease 745–747 (ICD-9) and Q20–Q28, Q87, Q89 (ICD-10). Because of overlapping HF aetiologies, we assigned mutually exclusive causes of HF in the following hierarchical order: (i) congenital heart disease, (ii) valvulopathy, (iii) IHD and/or diabetes and/or hypertension, (iv) cardiomyopathy, and (v) other causes.

### Validity of the registers

From 1987 to 1996, a primary discharge diagnosis was lacking in <1% of all admissions. The diagnosis of HF in the Swedish discharge register has been validated showing 96% accuracy for primary diagnoses in internal medicine or cardiac wards, and 86 and 91% for secondary diagnoses in internal medicine and cardiac wards, respectively.<sup>14</sup>

### Statistical methods

Annual HF incidence rates per 100 000 person-years and 95% confidence intervals (CIs) were calculated using the method of direct standardization, using the median year 1996 as a standard. Descriptive statistics were applied to summarize the comorbidity prevalence within the identified HF population. In addition, we used joinpoint regression for the estimation of the annual percentage change and to find the specific years when significant changes in the trends occurred (Joinpoint Regression Program, version 3.3.1. April 2008; Statistical Research and Applications Branch, National Cancer Institute). We fitted the data in a log-linear model and set the number of possible joinpoints between 0 and 3. For each estimate of mean annual percentage change, 95% CIs were calculated. Further, 1-year, age- and sex-specific case fatality rates were calculated up to 1 year after admission in patients aged 18–34, 35–44, 45–54, and 55–84 years over the periods 1987–91, 1992–96, 1997–2001, and 2002–06. To estimate changes in 1-year case fatality, hazard ratios for each time period of hospitalization were calculated by means of Cox regression with the period of 1987–91 as reference, and adjusted for age, sex, diabetes, IHD, cardiomyopathy, and ACHD and/or valve disease.

Kaplan–Meier survival curves were applied to illustrate 3-year case fatality.

## Results

Between 1987 and 2006, 443 995 hospitalizations for HF were recorded among patients aged 18–84 years. Of these HFs, 4660 (1.0%) and 13 507 (3.0%) were in patients aged 18–44 and 45–54 years, respectively. About one-third of the patients were women (*Table 1*).

The overall burden of comorbidity in this young HF population was substantial. Of patients aged <45 years, 21% had IHD with 15% having acute myocardial infarction (MI). Fourteen per cent had diabetes, 4% a prior stroke, and 8% any cancer. For patients aged 45–54 years, IHD, MI and diabetes, stroke, and cancer was found in 39, 27, and 20, 5 and 9%, respectively. Concomitant cardiomyopathy was registered in 20% of those aged <45 years and in 13% of those aged 45–54 years. Cardiomyopathy increased from 15 to 25% and from 9 to 15% over the four periods in the <45 and 45–54 age groups, respectively. Concomitant valve disease and ACHD among patients younger than 45 years remained stable throughout the study (*Table 1*). About 5% had no other diagnosis than HF (data not shown).

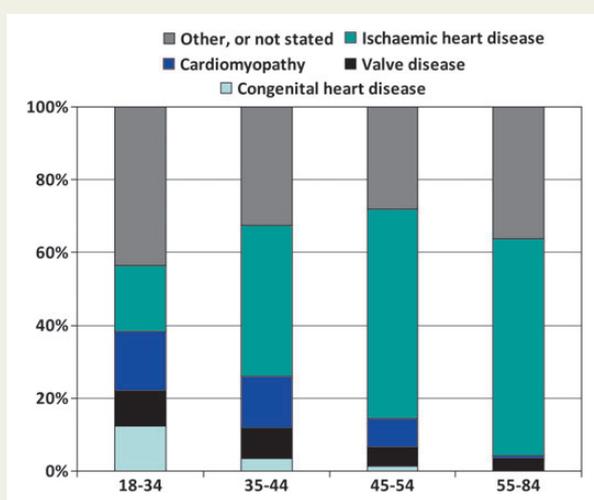
*Figure 1* and Supplementary material online, *Table S1* show the mutually exclusive categories of comorbidities by age over the entire study period. The proportion of IHD-related HF hospitalization increased substantially with age, whereas cardiomyopathies decreased. The proportion of patients diagnosed with ACHD was 12.0% among the youngest age group and 0.3% among the oldest. The proportion with valve disease and ACHD did not change materially over time in any age group. The prevalence of the combined common aetiologies of IHD, diabetes, and hypertension below the age of 55 years was stable throughout the study period in patients <55, but not in older patients (increase 54 to 66%), chiefly as a result of a decrease in other causes. Cardiomyopathy increased across all age groups. A closer look at the large and heterogeneous group of patients labelled ‘other’ revealed no qualitative differences between the first and the last periods, the most common diagnoses being malignancy, perimyocarditis, and infectious diseases.

*Table 2* illustrates the divergent trends in HF hospitalization between younger and older patients. Whereas hospitalization in the 55–84 year age group peaked in 1992–96 at 854 per 100 000 decreasing to 603 per 100 000 in 2002–06, HF hospitalization among persons <45 years increased throughout the entire observation period. Trends among persons aged 45–54 years were similar to those aged 55–84 years with a less marked decrease after 1996. A joinpoint analysis confirmed the continuous increase throughout the period for the 18–34 year age group, and from 1999 to 2006 for the age group 35–44 years. Further in adults ≥45 years a rising then falling pattern was seen 1994 signifying the marked breaking point for a decline in HF rates (Supplementary material online, *Figure* and *Table S2*).

*Table 3* shows trends in the incidence of HF with concomitant cardiomyopathy, IHD, and all other causes. From 1987–1991 to 2002–2006, the mean incidence of HF with cardiomyopathy more than doubled in all age groups (HRs 2.0–3.0). In patients ≥55 years, this was not at the expense of other diagnoses as the incidence of HF

**Table 1** Characteristics of patients by age group (18–44 and 45–55 years) and period at first admission (1987–2006)

	1987–91	1992–96	1997–2001	2002–06	Total
<b>18–44</b>					
Number, n (%)	972 (100%)	1187 (100%)	1133 (100%)	1368 (100%)	4660 (100%)
Mean age, years (SD)	37.0 (6.9)	37.4 (6.4)	37.1 (6.4)	37.0 (6.6)	37.1 (6.6)
Women, n (%)	356 (36.6)	428 (36.1)	421 (37.2)	461 (33.7)	1666 (35.8)
Diabetes, n (%)	165 (17.0)	178 (15.0)	139 (12.3)	154 (11.3)	636 (13.6)
Hypertension, n (%)	109 (11.2)	147 (12.4)	153 (13.5)	232 (17.0)	641 (13.8)
Prior AMI, n (%)	144 (14.8)	226 (19.0)	150 (13.2)	157 (11.5)	677 (14.5)
Any IHD, n (%)	203 (20.9)	305 (25.7)	224 (19.8)	232 (17.0)	964 (20.7)
Valvular disease, n (%)	126 (13.0)	149 (12.6)	134 (11.8)	157 (11.5)	566 (12.1)
Congenital heart disease, n (%)	57 (5.9)	56 (4.7)	73 (6.4)	90 (6.6)	276 (5.9)
Cardiomyopathy, n (%)	141 (14.5)	198 (16.7)	243 (21.4)	335 (24.5)	917 (19.7)
Prior stroke, n (%)	40 (4.1)	50 (4.2)	36 (3.2)	42 (3.1)	168 (3.6)
Atrial fibrillation, n (%)	80 (8.2)	117 (9.9)	133 (11.7)	205 (15.0)	535 (11.5)
Malignancy, n (%)	102 (10.5)	94 (7.9)	71 (6.3)	81 (5.9)	348 (7.5)
<b>45–54</b>					
Number, n (%)	2456 (100%)	3830 (100%)	3806 (100%)	3415 (100%)	13 507 (100%)
Mean age, years (SD)	50.4 (2.8)	50.4 (2.7)	50.8 (2.7)	50.5 (2.8)	50.5 (2.7)
Women, n (%)	758 (30.9)	1220 (31.9)	1100 (28.9)	989 (29.0)	4067 (30.1)
Diabetes, n (%)	480 (19.5)	750 (19.6)	748 (19.7)	689 (20.2)	2667 (19.7)
Hypertension, n (%)	371 (15.1)	760 (19.8)	830 (21.8)	887 (26.0)	2848 (21.1)
Prior AMI, n (%)	690 (28.1)	1093 (28.5)	998 (26.2)	819 (24.0)	3600 (26.7)
Any IHD, n (%)	932 (37.9)	1601 (41.8)	1515 (39.8)	1243 (36.4)	5291 (39.2)
Valvular disease, n (%)	227 (9.2)	351 (9.2)	311 (8.2)	323 (9.5)	1212 (9.0)
Congenital heart disease, n (%)	35 (1.4)	46 (1.2)	46 (1.2)	40 (1.2)	167 (1.2)
Cardiomyopathy, n (%)	219 (8.9)	445 (11.6)	513 (13.5)	523 (15.3)	1700 (12.6)
Prior stroke, n (%)	138 (5.6)	209 (5.5)	202 (5.3)	172 (5.0)	721 (5.3)
Atrial fibrillation, n (%)	345 (14.0)	588 (15.4)	656 (17.2)	690 (20.2)	2279 (16.9)
Malignancy, n (%)	247 (10.1)	381 (9.9)	372 (9.8)	270 (7.9)	1270 (9.4)

**Figure 1** Comorbid prevalence (%) of mutually exclusive diagnoses among heart failure patients of different ages.

from other causes not related to IHD or cardiomyopathy also increased.

### Case fatality

One-year case fatality at the beginning of the study period was high in all age groups, with about one in four dead at ages 18–54 and 39%  $\geq 55$  years (Table 4). From 1987–1991 to 2002–06 a marked adjusted 1-year relative case fatality reduction of 60–62% at 18–44 years was observed, and correspondingly 56 and 38% at 45–54 and 55–84 years, respectively. Figure 2 demonstrates the survival benefit was sustained up to 3 years, but that no further significant improvement in case fatality occurred in the  $< 55$  year age group after 2001.

### Discussion

During the study period, we observed an increase in hospitalization for HF among people  $< 45$  years of age which was divergent from the continuing decrease after 1992–96 seen among persons  $\geq 45$  years of age. The incidence of concomitant cardiomyopathy more than doubled during this period in all age groups. Case fatality in

**Table 2** Incidence of first hospital admissions for heart failure per 100 000 person-years in Sweden 1987–2006 by age, sex, and period

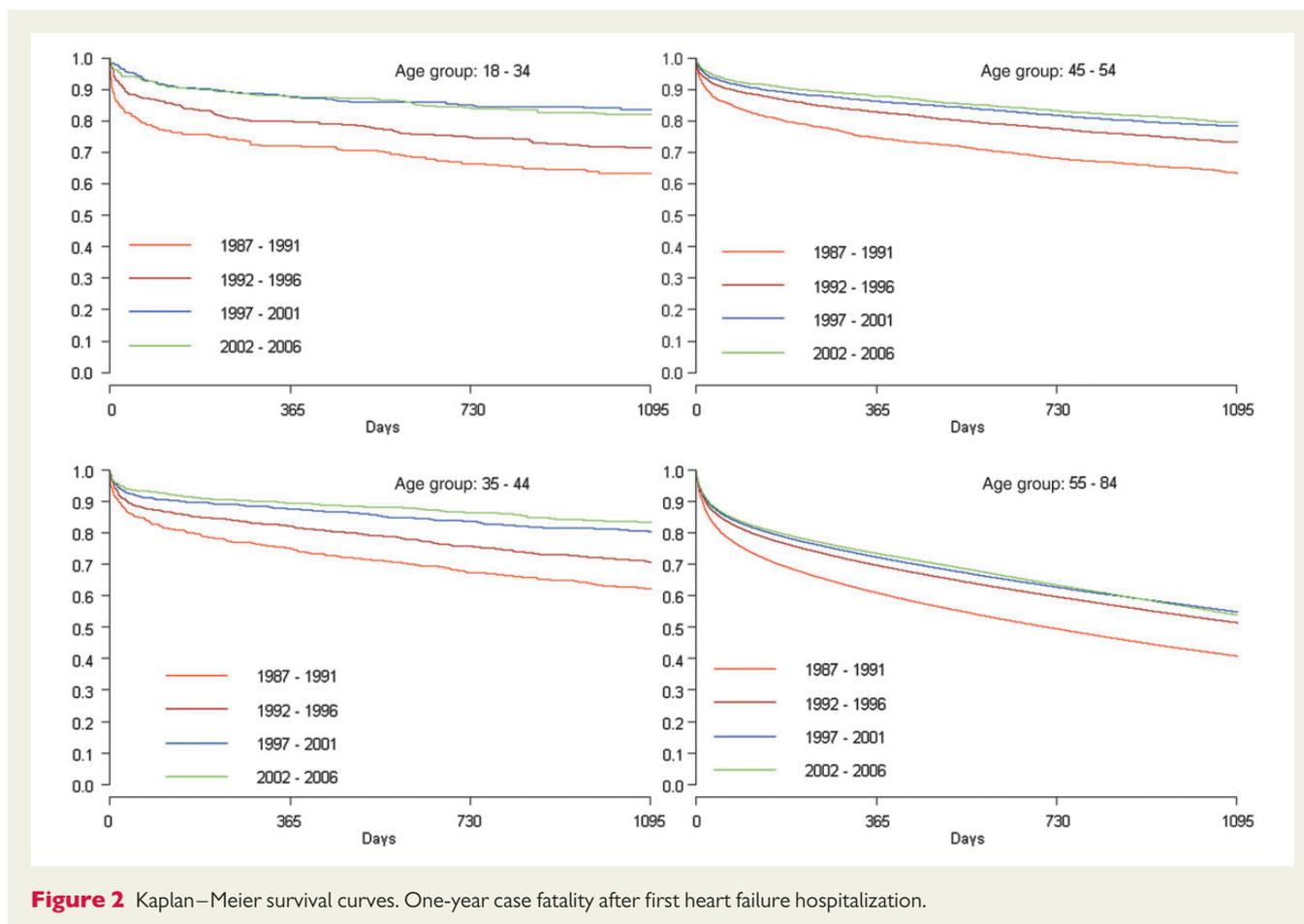
Age group	18–34	Per 100 000	Hazards ratio (95% CI)	35–44	Per 100 000	Hazards ratio (95% CI)	45–54	Per 100 000	Hazards ratio (95% CI)	55–84	Per 100 000	Hazards ratio (95% CI)
Period	<i>n</i>			<i>n</i>			<i>n</i>			<i>n</i>		
1987–91	266	2.5	1.00	706	10.2	1.00	2456	46.2	1.00	105 741	719	1.00
1992–96	312	2.8	1.15 (1.00–1.33)	875	13.6	1.33 (1.22–1.45)	3830	59.6	1.29 (1.22–1.36)	125 138	854	1.19 (1.15–1.23)
1997–2001	319	2.9	1.19 (1.03–1.37)	814	12.7	1.25 (1.14–1.36)	3806	55.6	1.20 (1.14–1.27)	102 067	688	0.96 (0.92–0.99)
2002–06	387	3.7	1.50 (1.31–1.71)	981	14.6	1.43 (1.31–1.55)	3415	53.6	1.16 (1.10–1.22)	92 882	603	0.84 (0.81–0.87)
Men												
1987–91	150	2.7	1.00	466	13.0	1.00	1698	63.1	1.00	57 399	947	1.00
1992–96	183	3.2	1.18 (0.94–1.47)	576	17.3	1.33 (1.19–1.49)	2610	79.9	1.27 (1.20–1.34)	66 766	1098	1.16 (1.12–1.20)
1997–2001	178	3.2	1.16 (0.93–1.46)	534	16.1	1.24 (1.10–1.39)	2706	77.8	1.23 (1.17;1.30)	55 847	896	0.95 (0.91–0.98)
2002–06	233	4.4	1.61 (1.30–1.99)	674	19.2	1.48 (1.33–1.65)	2426	74.4	1.18 (1.11–1.25)	51 244	777	0.82 (0.79–0.85)
Women												
1987–91	116	2.2	1.00	240	7.4	1.00	758	29	1.00	48 342	522	1.00
1992–96	129	2.4	1.09 (0.88–1.36)	299	9.8	1.33 (1.11–1.59)	1220	38.9	1.34 (1.22–1.48)	58 372	631	1.22 (1.17–1.27)
1997–01	141	2.6	1.19 (0.96–1.46)	280	9.2	1.25 (1.04–1.50)	1100	32.6	1.12 (1.02–1.24)	46 220	499	0.96 (0.92–1.00)
2002–06	154	3.1	1.38 (1.13–1.70)	307	9.5	1.30 (1.08–1.55)	989	31.4	1.08 (0.98–1.20)	41 638	436	0.84 (0.80–0.87)

**Table 3** Incidence of heart failure and concomitant cardiomyopathy, ischaemic heart disease and all other causes per 100 000 person-years by age, sex, and period (1987–2006)

Age	18–34				35–44				45–54				55–84				
	Period	n	Inc*	HR	95% CI	n	Inc*	HR	95% CI	n	Inc*	HR	95% CI	n	Inc*	HR	95% CI
Cardiomyopathy																	
1987–91	37	0.3	1.00	—	104	1.5	1.00	—	219	4.3	1.00	—	925	8.3	1.00	—	
1992–96	58	0.5	1.51	(1.00–2.28)	140	2.2	1.46	(1.15–1.84)	445	7.2	1.69	(1.44–1.99)	1708	15.4	1.85	(1.70–2.02)	
1997–01	69	0.6	1.82	(1.21–2.71)	174	2.8	1.80	(1.45–2.24)	513	8.0	1.88	(1.60–2.20)	1974	17.1	2.06	(1.89–2.25)	
2002–06	108	1.0	2.98	(2.05–4.33)	227	3.4	2.23	(1.81–2.74)	523	8.7	2.04	(1.74–2.39)	2305	18.7	2.25	(2.07–2.45)	
Ischaemic heart disease, IHD																	
1987–91	16	0.2	1.00	—	177	2.3	1.00	—	901	16.6	1.00	—	42 928	300	1.00	—	
1992–96	34	0.3	1.98	(1.20–3.27)	262	3.6	1.58	(1.27–1.96)	1540	23.4	1.41	(1.30–1.53)	54 446	380	1.27	(1.20–1.34)	
1997–01	21	0.2	1.20	(0.72–2.00)	187	2.6	1.14	(0.91–1.43)	1443	20.4	1.23	(1.13–1.34)	44 817	303	1.01	(0.96–1.07)	
2002–06	25	0.2	1.45	(0.89–2.36)	188	2.5	1.09	(0.87–1.37)	1177	17.9	1.08	(0.98–1.18)	41 675	266	0.89	(0.84–0.94)	
All other diagnoses																	
1987–91	213	2.0	1.00	—	425	6.4	1.00	—	1336	25.3	1.00	—	61 888	406	1.00	—	
1992–96	220	2.0	1.02	(0.86–1.19)	473	7.5	1.17	(1.05–1.31)	1845	28.8	1.14	(1.07–1.22)	68 984	452	1.11	(1.08–1.15)	
1997–01	229	2.2	1.08	(0.92–1.27)	453	7.3	1.14	(1.02–1.27)	1850	27.1	1.07	(1.01–1.15)	55 276	361	0.89	(0.86–0.91)	
2002–06	254	2.5	1.25	(1.07–1.45)	566	8.6	1.35	(1.22–1.49)	1715	26.7	1.06	(0.99–1.13)	48 902	311	0.76	(0.74–0.79)	

HR, hazard ratio for HF hospitalization. Inc\*, incidence per 100 000 person-years.





**Figure 2** Kaplan–Meier survival curves. One-year case fatality after first heart failure hospitalization.

these patients are highly likely to have been admitted for investigation regardless the time period. Accordingly, our findings may suggest a change in phenotype, with an increasing proportion of HF due to cardiomyopathy, most notably in the youngest patients in whom IHD is rare.

Obesity, which has more than tripled in Sweden among the young 1985–2002,<sup>22</sup> changes in drug abuse patterns and excessive alcohol consumption are all potentially contributing factors, but their impact could not be assessed in our population.

### Decreasing case fatality among young adults

One-year case fatality was substantially reduced in all age groups. Mortality data among persons <55 years of age with HF are exiguous. Rochester population-based data show stable 1-year mortality ranging from 23 to 28% (mean age 74 years).<sup>23</sup> In contrast, another survey from the same population (1979–2000) reported a 52% survival improvement among men in their 60 s, but only 28% among men in their 80 s, a finding congruent to the more pronounced case fatality reduction observed among younger subjects in our population.<sup>24</sup>

Our data did not show any further improvement in fatality after 2001. Neurohormonal blockade has improved survival in patients with systolic HF.<sup>25–27</sup> The largest relative reduction in case fatality occurred from 1987–1991 to 1997–2001, i.e. prior to the publication of the landmark trials validating beta-blocking agents in HF treatment,

suggesting either that beta-blocker treatment had not been fully implemented,<sup>26,27</sup> or did not impact fatality in this population. Beta-blockers and ACE-inhibitors were, however, at the time widely employed in the treatment of hypertension and IHD and may have curtailed the emergence or at least a further increase in HF during this time period.

### Limitations

The study has several advantages, such as an unselected and large population and near-complete follow-up. However, there are also some limitations. First, using discharge diagnosis codes poses a risk of underestimation.<sup>28</sup> Secondly, hospital admission rates and not true incidence were employed. It is reasonable to believe that young patients with new onset HF undergo comprehensive assessment, including echocardiography in a cardiac ward where the validity of the HF diagnosis is higher than stated by Ingelsson *et al.*<sup>14</sup> in their study of elderly men. Additionally the lack of further mortality reduction over the last period would not indicate a spurious inflation in incidence because of inclusion of milder cases. Coding practices may certainly have influenced the data, but if so most likely at all ages.

A further limitation is the lack of important biological variables, increasingly used over the period, such as the measurement of natriuretic peptides, or ejection fraction. The absence of such objective measurements obviously detracts from the comparability of HF rates over time.

HF is, however, largely a clinical diagnosis, and though we contend that the lack of biological variables is unlikely to explain the diverging

changes in HF incidence over time in the different age groups, we acknowledge that their addition would have added value to the study.

Diagnosing practices for cardiomyopathy changed in the mid-1990s.<sup>18</sup> Accordingly, the group classified as other, could have harboured undiagnosed cases of cardiomyopathy from earlier periods. Recent unpublished data from an on-going validation study by our group showed that a diagnosis of DCM could be confirmed in 92% (202 out of 219 cases, using data from medical records from five calendar years over the period 1989–2009) with a further 4% classified as suspected DCM, and, importantly, no change in diagnostic accuracy over time. A systematic and variable underreporting of hypertension, a major cause of HF, was probably present, but this is unlikely to have influenced hospitalization rates differentially in different age groups. The stagnating mortality reduction observed does not support a falsely inflated incidence rate in the young. Thus, potential drifts in diagnoses and classifications are unlikely to explain the opposing trends in HF incidence in younger and older patients.

## Conclusion

Increasing HF admission in young adults opposes the general trend noted in older patients. Although the cause for this is not known, it may reflect true epidemiological changes and may serve as an ominous sign of stagnating morbidity reduction among young adults. Declining case fatality reduction with lack of further improvement after 2001 is a cause for concern.

## Supplementary material

Supplementary material is available at *European Heart Journal* online.

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**Conflict of interest:** none declared.

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