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ORIGINAL RESEARCH ARTICLE

Incidence, prevalence, and mortality of heart failure: a nationwide registry study from 2013 to 2016

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Abstract

Aims Large-scaled population studies of incidence and prevalence of heart failure (HF) are needed for the development of healthcare policies and priorities. The aim of this study was to estimate the incidence, prevalence, and all-cause mortality of HF in Norway from 2013 to 2016 on the basis of a national registry.

Methods and results Using data from the nationwide Norwegian Prescription Database, we identified all patients ≥18 years of age in Norway with at least one drug prescription with HF during 2013–2016, defined by 10th revision of the International Classification of Diseases (ICD-10) codes I50, I11, I13, or I42. The individual index date was the date of the first prescription. Patients were followed up until death or end of follow-up (31 October 2017). Annual incidence and prevalence were estimated from 2013 to 2016, using a look-back period starting from 1 March 2008. We calculated standardized estimates by applying direct age and sex standardization to the 2013 European standard population. All-cause mortality from 2013 to 2016 was calculated among the prevalent HF patients. Standardized mortality ratio (SMR) was calculated by indirect standardization using general mortality in the Norwegian population as reference. We identified 54 542 unique patients (58% men) with a first-time diagnosis of HF. The median age was 72 ±14 years, and women were older than men (median age 76 vs. 70 years, respectively). The crude (standardized) incidence of HF was 3.44/1000 (4.23/1000) person-years in 2016 and did not increase over the 4 year period, while the prevalence increased from 2.0% (2.3%) to 2.4% (2.8%). Both incidence and prevalence were higher in men than in women and strongly associated with age. Crude mortality rates in the HF population declined from 94 to 82/1000 person-years from 2013 to 2016, and SMR declined from 2.01 to 1.84. Age-adjusted mortality rates were higher in men than in women.

Conclusions This nationwide registry study in Norway showed an increase in the prevalence of HF from 2013 to 2016, with stable incidence rates and improved survival.

Keywords Heart failure; NorPD; Epidemiology; Incidence; Prevalence; Mortality

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Introduction

Congestive heart failure (HF) is one of the leading causes of mortality, morbidity, and hospitalizations in the Western world and represents a major public health challenge.[1,2] Despite advances in the management of HF over the last decades, 5 year mortality remains high at approximately 50%, and the proportion of patients readmitted 30 days after hospitalization ranges between 20% and 25%.[3–5]

The prevalence of HF in developed countries is reported to be 1–2% of the adult population.[2,4] The prevalence of HF increases with age[3,6,7] and is estimated to be ≥10% among people > 70 years of age in South-western Europe.[3] The reported incidence has been relatively stable during the second half of the last century with an increasing prevalence.[8–10] Evidence from the last 20 years is scarce and conflicting, suggesting a stable or declining incidence and unchanged or increasing prevalence.[11–15] Data from randomized controlled

trials suggest that HF mortality has decreased by 10–40% during the last four decades.[2] However, randomized trials are performed on highly selected patient populations with poor generalizability[16] and do not fully reflect the demographics, co-morbidities, and prognosis seen in real-life patients.

The nationwide Norwegian Prescription Database (NorPD) contains complete data on all pharmacy prescriptions in Norway. Each prescription is linked to a diagnosis and a unique personal identification number. The aim of this study was to utilize the NorPD to characterize the adult HF population in Norway with respect to incidence, prevalence, and mortality in the period 2013 to 2016.

Methods

Data source

The data for this study were retrieved from NorPD, which is a nationwide registry containing a complete listing of all prescription drugs dispensed by pharmacies in Norway since 2004.[17] All pharmacies in Norway are obliged by law to forward prescription data electronically[18] to NorPD, ensuring complete registration. Drugs administered at institutions (hospitals and nursing homes) are not included, as these data are not registered at an individual level in NorPD. These account for approximately 3% of total dispensed prescriptions, measured in defined daily doses (DDDs).[19] Drugs are classified according to the Anatomical Therapeutic Chemical (ATC) classification.[20] From March 2009 (partly from March 2008), the diagnoses for drug reimbursement were also included in the NorPD. Diagnoses were registered according to the 10th revision of the International Classification of Diseases (ICD-10)[21] or version 2 of the International Classification of Primary Care (ICPC-2).[22] Each prescription is linked to a unique personal identification number that allows for tracking of each individual patient over time. Individual prescription data are captured until time of death or emigration. In our study, the following variables were included: unique personal identity number, sex, age, date of death, diagnostic codes, date of drug dispensing, and drug information including ATC code.

Statistics Norway provided information on inhabitants by each age category and gender in Norway each calendar year.[23]

Population

We included all individuals ≥18 years of age having received one or more drug prescriptions with an HF diagnosis in the period on 1 January 2013 to 31 December 2016. HF was defined by ICD-10 codes I50 (HF), I11 (hypertensive heart disease), I13 (hypertensive heart and chronic kidney disease) and I42 (cardiomyopathy). The individual index date was the date of the first drug prescription with an HF diagnosis. A look-back period to 1 March 2008 was used to reduce the risk of underestimating prevalent HF cases and overestimating incident HF cases. Patients were followed up until 31 October 2017 or death, whichever came first.

Case definition of heart failure

Incident HF cases were defined as cases having the first drug prescription with an HF diagnosis in the period 1 January 2013 to 31 December 2016, excluding patients with an HF diagnosis before 1 January 2013. Prevalent HF cases were defined as cases having at least one drug prescription with an HF diagnosis, including patients with an HF diagnosis back to 1 March 2008.

Co-morbidities and treatment

For individuals with incident HF, we identified the following co-morbidities by ICD-10 codes before the index date: diabetes, atrial fibrillation, hypertension, ischaemic heart disease, myocardial infarction, peripheral vascular disease, cerebral vascular disease, and chronic obstructive pulmonary disease (COPD). Identification of drug treatment before and after the index date was regardless of the diagnosis with the prescription and included prescriptions from both primary (ICPC-2 codes) and secondary care (ICD-10 codes). ICD-10 codes used for identification of co-morbidities and ATC-codes used to identify drug treatment before and after index are outlined in the Supporting Information (*Table* S1).

Statistical analysis

Baseline characteristics are presented as numbers (*n*), frequencies (%), medians (inter-quartile range), or means (standard deviation) as appropriate. Incidence rates and prevalence of HF were calculated for each calendar year from 2013 to 2016 using the total Norwegian population ≥ 18 years, stratified by gender and 5 year age groups, as reference. Mid-year population numbers were used in the denominator for both incidence and prevalence calculations (mean population numbers 1 January in the calendar year of interest and 1 January the following year). Yearly incidence rates were calculated by dividing the number of new cases with HF each year by the estimated mid-year population, subtracted prevalent patients by 1 January each year. Yearly prevalence was calculated by dividing total number of prevalent cases with HF at any time in each year by the estimated mid-year population. Incidence rates and prevalence were calculated as crude, age specific, and age standardized. Standardized incidence rates and prevalence were

calculated by applying direct age and sex standardization to the 2013 European standard population,[24] using 5 year age bands up to 90 years of age. Mortality was calculated as crude and age-specific rates. Mortality is presented as all-cause mortality rates for patients with HF, calculated by dividing the number of HF patients who died each year by the HF population at risk each year (person-years). Standardized mortality ratios (SMRs) were calculated by indirect standardization and derived from the ratio of the number of observed deaths to the number of expected deaths using the general mortality in the Norwegian background population as reference.[25] Univariable and multivariable analyses of time to event data were performed using Cox proportional hazards regression to account for age, gender, HF diagnoses I50 and I11, and the following co-morbidities: diabetes mellitus, atrial fibrillation, ischaemic heart disease, hypertension (excluding ICD-10 codes I11 and I13), renal failure, cerebrovascular disease, and COPD. Survival probabilities at 1, 3 and 4 years were calculated as Kaplan–Meier estimates. For sensitivity analysis, we estimated incidence rates and prevalence for ICD-10 codes I50 and I11 separately. Python version 3.X was used for the statistical analysis and data management.

Ethics

The investigation conforms with the principles outlined in the Declaration of Helsinki. The protocol was approved by the Norwegian Data Protection Authority and Regional Committee for Medical and Health Research Ethics (2017/1243).

Results

Baseline characteristics

We identified 54 542 unique patients (58% men) with a first-time diagnosis of HF during the period of 2013–2016. The median age at index was 72 years and higher in women

Table 1 Baseline characteristics of the study population

		By gender		By ICD-10 code	
	All	Women	Men	I50	I11
Number, *n*	54 542	22 698	31 844	34 856	18 198
Age, median (IQR)	72 (19)	76 (18)	70 (18)	75 (18)	69 (17)
Age, mean (SD)	71.2 (13.8)	73.9 (13.9)	69.2 (13.4)	73.2 (13.7)	67.7 (12.9)
Male gender (%)	58	—	—	59	58
ICD-10 code, *n* (%)					
I50	34 856 (64%)	14 453 (64%)	20 403 (64%)	—	—
I11	18 198 (33%)	7698 (34%)	10 500 (33%)	—	—
I13	1406 (3%)	523 (2%)	883 (3%)	—	—
I42	82 (0%)	24 (0%)	58 (0%)	—	—
Co-morbidities[a]					
Hypertension	53%	54%	52%	27%	100%
Ischaemic heart disease	27%	23%	31%	30%	24%
Myocardial infarction	16%	12%	19%	19%	11%
Atrial fibrillation	26%	26%	26%	31%	18%
COPD	11%	11%	10%	12%	8%
Diabetes mellitus	8%	7%	9%	7%	9%
Cerebral vascular disease	4%	4%	4%	3%	4%
Renal failure	2%	2%	2%	2%	1%
Peripheral vascular disease	0%	0%	0%	0%	0%
Treatment before index (%)[b]					
ACEI/ARB	46%	46%	46%	43%	52%
BB	47%	47%	46%	49%	42%
MRA	2%	3%	2%	3%	2%
High-ceiling diuretics	20%	24%	18%	25%	11%
HF treatment after index[c]					
ACEI/ARB	73%	68%	76%	73%	72%
BB	79%	78%	80%	83%	74%
MRA	17%	15%	18%	22%	6%
High-ceiling diuretics	56%	60%	53%	74%	23%

Data are presented as frequencies (%), median [inter-quartile range (IQR)], or mean [standard deviation (SD)].
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta-blocker; HF, heart failure; MRA, mineralocorticoid receptor antagonist.
[a]Co-morbidities before index date.
[b]6 months prior to index.
[c]0–12 months from index.

compared with men (76 vs. 70 years, respectively). I50 was the most common first HF diagnosis (64%) followed by I11 (33%). During follow-up, 9% of patients received both an I11 and I50 diagnosis. Patients with the diagnosis I50 were older than patients with the I11 diagnosis (median 75 vs. 69 years, respectively). Sex distribution was similar in both groups. *Table* 1 shows the baseline characteristics for the incident patients, stratified by gender and ICD-10 codes.

Co-morbidities and co-medications at baseline

Hypertension was the most common co-morbidity, followed by ischaemic heart disease, atrial fibrillation, COPD, and diabetes mellitus (*Table* 1). Before the index date, 46% had a prior prescription of an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), and 47% of patients had a prior prescription of beta-blocker (BB).

Treatment

Following HF diagnosis, 73% of patients received an ACEI or ARB within 1 year, and 79% of patients received a BB (*Table* 2). Combination therapy was common, with 58% of patients receiving both an ACEI/ARB and a BB. Twelve of the incident population received combination of ACEI/ARB, BB, and mineralocorticoid receptor antagonist (MRA).

Incidence

The annual crude incidence rate of HF was 3.59/1000 person-years in 2013 and 3.44/1000 person-years in 2016 (*Table* 3). The incidence rate was higher in men than in women in all age groups (*Figure* 1). As expected, incidence rates increased with age, being 39.98/1000 person-years for men and 22.81/1000 person-years for women in 2016 in the age group ≥90 years of age (*Figure* S1). Age-standardized incidence rates were 4.43/1000 person-years in 2013 and 4.23/1000 person-years in 2016 (*Table* 3). *Figure* 1 shows crude and standardized age-specific incidence of HF in 2016 (absolute number of incident HF cases and standardized incidence per 1000 persons in the European Standard population), stratified by gender. The crude and standardized age-specific incidence of HF in 2013 and 2016 is shown in *Figure* 2.

Prevalence

In 2013, the crude prevalence of HF was 2.0% (77 673 individuals) compared with 2.4% (98 738 individuals) in 2016 (*Table* 3). The prevalence increased with age and was higher in men than in women (*Figure* 3). In the age group 75–79 years, prevalence was 9.5% (7.1% women and 12.3% men) in 2016 compared with 19.4% in the population ≥ 90 years of age (17.3% women and 24.8% men) (*Figure* 2). The increase in

Table 2 Medication before and after heart failure diagnosis

	0–6 months before index date	0–12 months after index date	13–24 months after index date
	n = 54 542	*n* = 54 542	*n* = 46 441
Treatment by drug class (%)			
ARBs	29	34	32
ACEI	18	43	34
BB	47	79	69
MRAs	2	17	11
ACEI/ARB	46	73	64
High-ceiling diuretics	20	56	38
Drug combinations (%)			
ACEI/ARB and BB	25	46	41
ACEI/ARB and BB and MRA	1	12	8
BB and MRA	1	2	2
ACEI/ARB and MRA	0	2	1
ACEI/ARB only	20	13	14
BB only	20	19	18
MRA only	0	1	1
High-ceiling diuretics only	3	4	3
Other CV treatment (%)			
Statins	42	57	52
Amiodarone	2	6	3
Nitrates	12	17	12
Anticoagulants	26	42	37
Calcium channel blockers	23	25	21
Antiplatelets	41	52	46

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta-blocker; CV, cardiovascular; MRA, mineralocorticoid receptor antagonist.

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Table 3 Incidence, prevalence, mortality, and population at risk

	2013	2014	2015	2016
Norwegian adult mid-year population, *n*	3 923 233	3 978 629	4 030 393	4 074 380
Women, *n*	1 964 697	1 989 438	2 012 806	2 033 303
Men, *n*	1 958 536	1 989 191	2 017 587	2 041 077
Heart failure population, *n*	77 673	84 542	91 900	98 738
Women, *n*	32 141	34 749	37 484	40 004
Men, *n*	45 532	49 793	54 416	58 734
Heart failure prevalence, % (95% CI)	1.98% (1.97, 1.99)	2.12% (2.11, 2.14)	2.28% (2.27, 2.29)	2.42% (2.41, 2.44)
Women, %	1.64% (1.62, 1.65)	1.75% (1.73, 1.76)	1.86% (1.84, 1.88)	1.97% (1.95, 1.99)
Men, %	2.32% (2.30, 2.35)	2.50% (2.48, 2.52)	2.70% (2.67, 2.72)	2.88% (2.85, 2.90)
Standardized prevalence, %	2.34% (2.32, 2.35)	2.50% (2.48, 2.52)	2.67% (2.65, 2.68)	2.81% (2.79, 2.83)
Women, %	1.72% (1.70, 1.74)	1.84% (1.82, 1.86)	1.96% (1.94, 1.98)	2.06% (2.04, 2.08)
Men, %	3.07% (3.04, 3.10)	3.28% (3.25, 3.31)	3.51% (3.48, 3.54)	3.69% (3.66, 3.72)
Incident HF population, *n*	13 815	13 214	13 796	13 717
Women, *n*	5855	5494	5688	5661
Men, *n*	7960	7720	8108	8056
Incidence per 1000 PY, *n*	3.59 (3.53, 3.64)	3.39 (3.33, 3.45)	3.50 (3.44, 3.55)	3.44 (3.39, 3.50)
Women, *n*	3.02 (2.95, 3.10)	2.81 (2.73, 2.88)	2.88 (2.80, 2.95)	2.84 (2.76, 2.91)
Men, *n*	4.15 (4.06, 4.24)	3.97 (3.88, 4.06)	4.12 (4.03, 4.21)	4.06 (3.97, 4.14)
Standardized incidence/1000 PY, *n*	4.43 (4.36, 4.51)	4.19 (4.12, 4.27)	4.32 (4.25, 4.40)	4.23 (4.16, 4.30)
Women, *n*	3.35 (3.26, 3.43)	3.12 (3.03, 3.20)	3.19 (3.11, 3.28)	3.14 (3.06, 3.23)
Men, *n*	5.83 (5.70, 5.97)	5.56 (5.43, 5.69)	5.76 (5.63, 5.89)	5.60 (5.47, 5.73)
Deaths in HF population,[a] *n*	6345	6438	6879	7250
Women, *n*	2886	2953	3141	3282
Men, *n*	3459	3485	3738	3968
Mortality rates/1000 PY,[b] *n*	93.80 (86.70, 104.01)	86.06 (78.82, 96.54)	84.50 (77.22, 95.19)	82.09 (75.26, 92.22)
Women, *n*	104.01 (100.22, 107.81)	96.54 (93.06, 100.02)	95.19 (91.86, 98.51)	92.22 (89.06, 95.37)
Men, *n*	86.70 (83.81, 89.59)	78.82 (76.20, 81.43)	77.22 (74.75, 79.70)	75.26 (72.91, 77.60)

95% CI in brackets.
CI, confidence intervals; HF, heart failure; PY, person-years.
[a]All-cause deaths.
[b]HF person-years at risk in the denominator.

prevalence over the 4 year period was apparent in all age groups, being higher in the oldest age groups. Age-standardized prevalence was 2.3% in 2013 and 2.8% in 2016 (*Table* 3).

Sensitivity analyses of the time trends in incidence and prevalence by ICD codes I50 and I11 separately are shown in the Supporting Information (*Figure* S2 and S3).

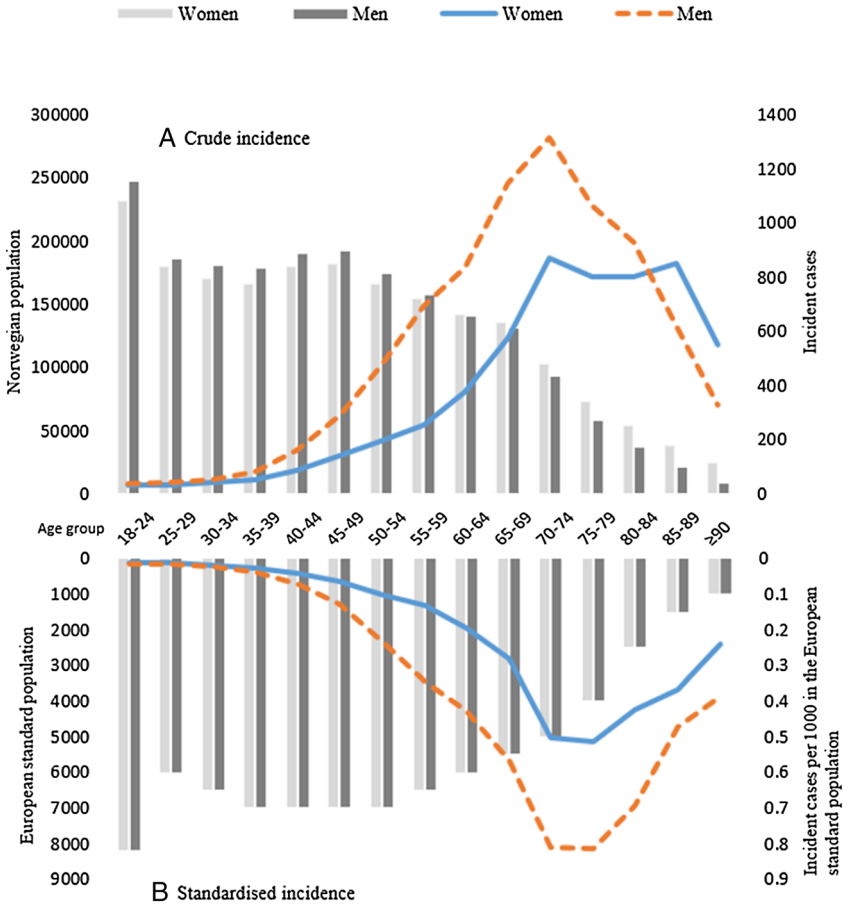
Mortality and survival

The crude all-cause mortality rates among patients with HF were 93.80/1000 person-years in 2013 and 82.09/1000 person-years in 2016 (*Table* 3). The crude mortality rate was higher in women than in men. SMR was 2.01 in 2013 and 1.84 in 2016 compared with the Norwegian population and higher in men than in women (*Table* 4 and Supporting Information, *Table* S2). The 1, 3, and 4 year survival probabilities from the first recorded diagnosis were 88.9% [95% confidence interval (CI) 88.6–89.2%], 76.3% (CI 75.9–76.7%), and 70.4% (CI 69.9–70.9%), respectively. The all-cause death rate for any reason after a recorded diagnosis of HF was lower in men than in women [hazard ratio (HR) 0.85, 95% CI 0.82–0.88]. However, when adjustment was made for age, the death rate was higher in men than in women (HR 1.20, CI 1.16–1.25). The higher death rate for men vs. women remained unchanged when co-morbidities were accounted for (HR 1.20, CI 1.15–1.24). A first recorded HF diagnosis of I50 constituted a higher death rate compared with a first recorded HF diagnosis of I11 (HR 2.92, CI 2.78–3.06). When adjustment was made for age and gender, the risk was attenuated but remained higher (HR 2.07, CI 1.98–2.18).

Discussion

Twenty years ago, HF was identified as an emerging epidemic.[26] This prediction has subsequently been borne out by numerous studies in multiple geographies that document an increasing prevalence.[14,15] In this study, we used the nationwide NorPD to estimate incidence, prevalence, and mortality of HF in Norway. The results provide a comprehensive picture of HF in Norway. We found that the prevalence of HF increased from 2.0% in 2013 to 2.4% in 2016, whereas incidence rates did not increase during this

Figure 1 Incidence of heart failure by gender and age group in 2016. (A) Crude incidence. Lines: absolute number of cases of incident heart failure in the Norwegian population in 2016 (red dashed line, women; blue line, men). Columns: Norwegian population ≥ 18 years of age in 2016. Light grey columns: female Norwegian population; dark grey columns: male Norwegian population. (B) Standardized incidence. Lines: Number of cases of incident heart failure per 1000 persons in the European standard population in 2016 (red dashed line, women; blue line, men). Columns: European standard population ≥ 18 years of age in 2016. Light grey columns: female standard population; dark grey columns: male standard population.



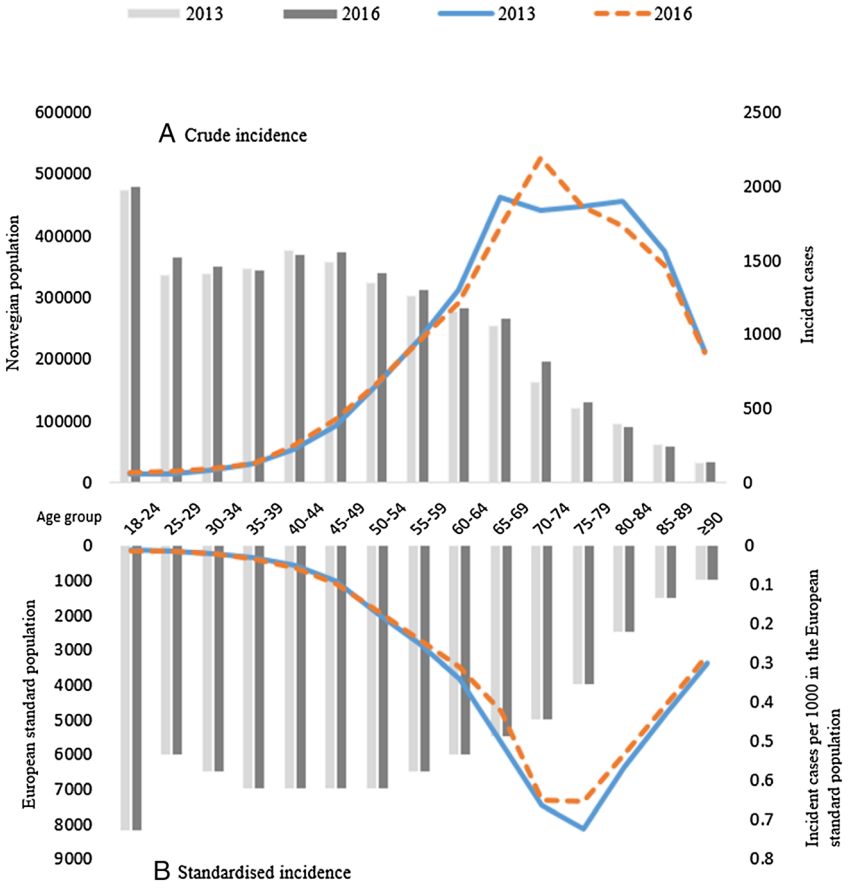
period. We found that mortality rates in the HF population were reduced during the period. There was a positive association with age with respect to prevalence, incidence, and mortality.

Epidemiologic studies on HF vary considerably with regard to study population, study setting, and case definition. As previous studies have employed different approaches to age standardization, comparison between countries is challenging. Differences between studies should therefore be interpreted with caution. In general, our findings are consistent with other reports showing a stable or declining HF incidence and improved survival in Europe and the US.[14,15]

The crude incidence rate of HF in Norway was 3.59 and 3.44 cases per 1000 person-years in 2013 and 2016, respectively. A Swedish study by Zarrinkoub *et al*. using data from an administrative database reported 380 new cases of HF per 100 000 person-years in 2010 with a decline from 2006.[11] A study based on Danish health registries found that HF incidence between 1995 and 2012 declined among older individuals (>50 years) but increased among patients ≤ 50 years of age.[27] Conrad *et al*. applied direct age and sex standardization utilizing the 2013 European standard population when estimating temporal trends in HF incidence in UK, reporting a decline in standardized incidence by 7%, being 332 per 100 000 in 2014.[15] In our study, age-standardized incidence rates declined by 5% over the 4 year period, reflecting a population growth that is higher in the older age groups.

The prevalence of HF in our dataset increased from 2.0% in 2013 to 2.4% in 2016. A study from Sweden found a crude prevalence of HF of 2.2% in 2010 that remained stable from 2006.[11] Previous studies in community-based cohorts have found an increase in HF prevalence that slows over time, possibly reflecting declining incidence and/or improved survival.[13] The increase in prevalence in our study was not explained by a correspondent increase in incidence.

Figure 2 Incidence of heart failure in 2013 and 2016 (A) Crude incidence. Lines: absolute number of cases of incident heart failure in the Norwegian population (blue line, 2013; red dashed line, 2016). Columns: Norwegian population ≥ 18 years of age in 2013 (light grey columns) and 2016 (dark grey columns). (B) Standardized incidence. Lines: number of cases of incident heart failure per 1000 persons in the European standard population (blue line, 2013; red dashed line, 2016). Columns: European standard population ≥ 18 years of age in 2013 (light grey columns) and 2016 (dark grey columns).



We found that the annual all-cause mortality rate in the prevalent HF population declined from 94 to 82 per 1000 person-years from 2013 to 2016, corresponding to a relative decrease in mortality of 13% during the period. SMRs also declined over the period, reflecting improved survival relative to the background Norwegian population. A decrease in mortality is consistent with most previous studies, possibly reflecting improved medical treatment in HF.[8,11] The 1, 3, and 4 year survival estimates from the first recorded HF diagnosis were 88.9%, 76.3%, and 70.4%, respectively, which are higher than what have been reported from other studies.[4,11,28,29] These differences may reflect the inclusion of both chronic and acute HF patients in our study, differences in case definition, or study population. The crude mortality risk was lower for men compared with women, consistent with the higher age of women among HF patients. The relationship was inverted when adjusting for age. We found that patients with a first diagnosis of I50 had two-fold higher risk of death than had patients with I11 as first diagnosis. Patients with an I11 diagnosis may be more likely to have HF with preserved ejection fraction, which in previous studies has been associated with a better prognosis than HF with reduced ejection fraction.[30,31]

We found that use of HF drugs linked to a different diagnosis (e.g. hypertension or atrial fibrillation) was common prior to the first HF diagnosis. Following HF diagnosis, the use of both ACEI/ARB, BBs, high-ceiling diuretics, and MRA increased. The data do not allow discrimination between HF with reduced vs. preserved ejection fraction, so it is not possible to assess the degree of guideline adherence with regard to drug treatment.

Our study was not designed to understand the specific contributors to the changes in incidence, prevalence, and mortality. However, we observed that increasing prevalence was not explained by increased incidence rates. Declining mortality rates within the HF population during the study period might be a partial contributor to increasing prevalence,

Figure 3 Prevalence of heart failure by age group and gender from 2013 to 2016. Crude prevalence in %. Women in blue lines and men in red lines.

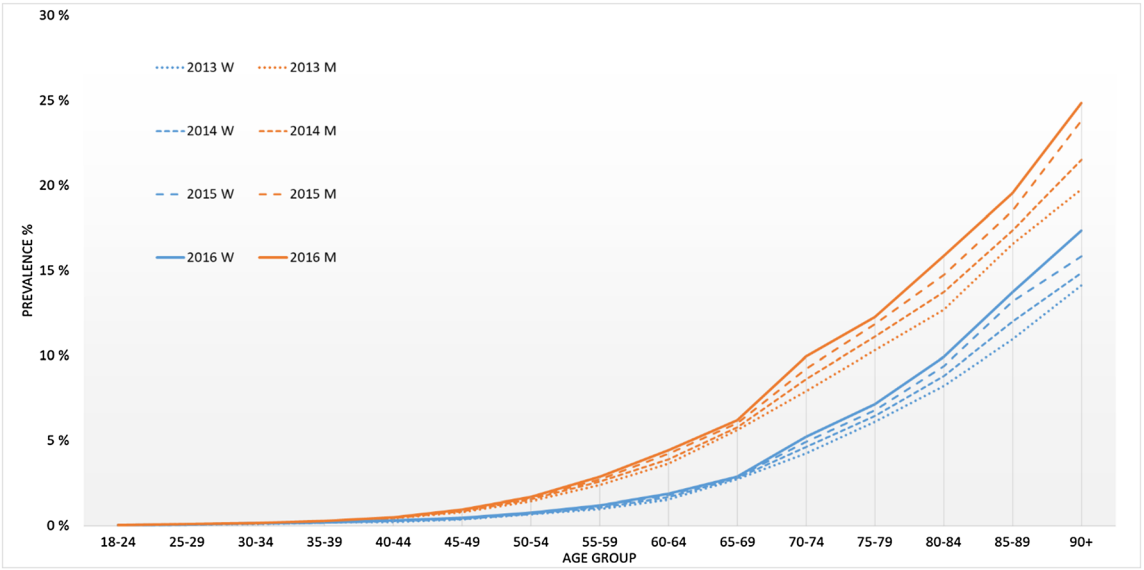


Table 4 Standardized all-cause mortality ratios by gender from 2013 to 2016

		Observed deaths	Expected deaths	SMR	95% CI
2013	Women	2886	1981.11	1.46	(1.40, 1.51)
	Men	3459	1181.42	2.93	(2.83, 3.03)
	Total	6345	3162.54	2.01	(1.96, 2.06)
2014	Women	2953	2155.21	1.37	(1.32, 1.42)
	Men	3485	1277.66	2.73	(2.64, 2.82)
	Total	6438	3432.88	1.88	(1.83, 1.92)
2015	Women	3141	2307.75	1.36	(1.31, 1.41)
	Men	3738	1421.47	2.63	(2.55, 2.72)
	Total	6879	3729.22	1.84	(1.80, 1.89)
2016	Women	3282	2433.34	1.35	(1.30, 1.40)
	Men	3968	1543.50	2.57	(2.49, 2.65)
	Total	7250	3976.84	1.82	(1.78, 1.87)

CI, confidence interval; SMR, standardized mortality ratio.

although population growth and shifts in age distribution most likely explain the majority of the increase. The average age of death for the incident population changed from 79 to 82 years of age in 2013 and 2016, respectively. Whether this increase in average death age reflects improved survival due to HF treatment or co-morbidities remains unknown. While the prevalence increased from 2.0% to 2.4%, the absolute number of people living with HF increased by 27% in 4 years, reflecting the increasing burden of the disease. These data are important for decision makers to plan for healthcare resource utilization and prioritization.

The strength of this study is the complete coverage of the Norwegian population, overcoming the challenges with biased participation, limited sample size, and domestic migration. NorPD should therefore provide valid estimates of the number of HF patients. The results reported here should however be considered in the context of important limitations. We defined HF by a prescription with an HF diagnosis**,** thus only including drug-treated HF patients. The use of a case definition that required an ICD-10 code of HF means that patients exclusively diagnosed in primary care will not be captured. Patients dying in-hospital at time of index hospitalization or before the first dispensed prescription drug are not captured in this database and will probably underestimate incidence, prevalence, and mortality. In 2016, approximately 30 000 individuals lived in nursing homes, constituting 13% of the population above 80 years of age.[23] The mean living time at nursing homes in Norway in 2016 was 2 years (median 1.3 years).[23] Data from NorPD show that deliveries to hospitals and nursing homes accounted for 3% of total prescriptions dispensed, measured by DDDs.[19] This small proportion will likely lead to a minor underestimation of incidence and prevalence in the oldest patient groups. A minimum of 4 years look-back may not have been sufficiently long to completely exclude patients with a previous HF diagnosis. This could potentially lead to an overestimation of incidence the first years following index date. The administrative database used in this study may also contain errors related to inaccurate information. Up to date, the ICD-10 codes for HF have not been validated in Norway. The use of ICD-10 codes from prescriptions to estimate co-morbidities will probably underestimate most of the co-morbidities and in particular diabetes, renal failure, and peripheral vascular disease. Finally,

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the database lacks clinical information including disease severity and HF phenotype.

Conclusion

The data presented here, which extends from a nationwide Norwegian registry, highlight the increasing burden of HF in Norway with an increasing prevalence of HF from 2013 to 2016, with stable incidence and improved survival.

Conflict of interest

KMO is an employee of Novartis Norway AS. JH was an employee of Novartis Norway AS at the time the study was conducted. SH reports speakers' honoraria from Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Pfizer, Sanofi and Merck, outside the submitted work. SSL and HOM report consultancy fees from Novartis during the conduct of the study; and personal fees from Novartis and Takeda, outside the submitted work.

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Supporting information

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

Table S1. Codes used for identification of patients with heart failure, comorbidities and drugs
Table S2 Standardised Mortality Ratio (SMR) by gender and 5-year age-groups
Figure S1 Incidence rates of heart failure by age-group and gender from 2013 to 2016.
Figure S2 Sensitivity analysis. Time trends in incidence stratified by ICD-10 code and gender.
Figure S3 Sensitivity analysis. Time trends in prevalence stratified by ICD-10 code and gender.

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