ORIGINAL RESEARCH

Nurse-Led Heart Failure Clinics Are Associated With Reduced Mortality but Not Heart Failure Hospitalization

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***Background*—**Follow-up in a nurse-led heart failure (HF) clinic is recommended in HF guidelines, but its association with outcomes remains controversial, with previous studies including few and highly selected patients. Thus, large analyses of "real-world" samples are needed. Aims were to assess: (1) independent predictors of and (2) prognosis associated with planned referral to nurse-led HF clinics.

***Methods and Results*—**We analyzed data from the SwedeHF (Swedish HF Registry) using multivariable logistic regressions to identify independent predictors of planned referral to a nurse-led HF clinic and multivariable Cox regressions to test associations between planned referral and outcomes (all-cause death, HF hospitalization, and their composite). Of 40 992 patients, 39% were planned to be referred to a follow-up in a nurse-led HF clinic. Independent characteristics associated with planned referral were shorter duration of HF, clinical markers of more-severe HF, such as lower ejection fraction, higher New York Heart Association class and N-terminal pro-B-type natriuretic peptide, and lower blood pressure, as well as cohabitating versus living alone, male sex, fewer comorbidities, and more use of HF treatments. After adjustments, planned referral to a nurse-led HF clinic was associated with reduced mortality and mortality/HF hospitalization, but not HF hospitalization alone.

***Conclusions*—**In this nation-wide registry, 39% of our identified HF cohort was planned to be referred to a nurse-led HF clinic. Planned referral reflected more-severe HF, but also sex- and family-related factors, and it was independently associated with lower risk of death, but not of HF hospitalization. **(*J Am Heart Assoc*. 2019;8:e011737. DOI: 10.1161/JAHA.118.011737.)**

Key Words: follow-up • heart failure • hospitalization • nurse-led clinic • registry • survival

Heart failure (HF) is a common condition with 2% prevalence in the general population and >10% among people aged >70 years.[1,2] Because of aging of the population and life-prolonging cardiovascular treatments and care, prevalence of HF and HF-related hospital admissions and, consequently, overall costs are increasing.[1–4] Additionally, despite the improvements in treatments and organization of care, prognosis still remains poor, with postdischarge mortality rates up to 15% and 20% to 30% readmission rates within the first 30 days after discharge.[5] It is of greatest importance to improve the organization of care to provide evidence-based care of high quality in the most cost-effective way.

Sweden has a long tradition of providing follow-up in nurse-led HF clinics, which is relatively uniform across the country. Clinics can be both primary care[6] and hospital based,[7] but have similar structure and content. Nurses provide education on self-care and psychosocial support to patients and their family, and they independently perform physical examination and assess mental well-being. They can uptitrate medications to optimized doses and occasionally prescribe new treatments with co-signatures by the responsible physician. The number of follow-up visits is individualized for each patient based on symptoms, disease severity, and time needed to reach optimized treatment and sufficient self-care. Most patient come to the clinic for a series of visits, and more-unstable patients are followed over a longer period of time.[6,7] Nurses have a specialized education based on content of the curriculum for HF nurses developed by the European Society of Cardiology HF Association.[8] Although HF nurses do not make medical decisions or admit to the hospital, they work in close physical proximity to physicians who can assess patients and make decisions, if needed.

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An accompanying Table S1 is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011737

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Clinical Perspective

What Is New?

- Previous analyses assessing prognosis associated with referral to nurse-led heart failure (HF) clinics included few and highly selected patients, and large analyses of "real-world" populations are missing.
- In our analysis of the Swedish HF registry, 39% of this HF cohort was planned to be referred to a nurse-led HF clinic, and those patients who were planned for referral had more-severe HF, higher use of HF treatments, and less comorbidities at referral.
- Planned referral was independently associated with lower risk of death, but not of HF hospitalization.

What Are Clinical Implications?

- Referral to nurse-led HF clinics is associated with improved survival.
- Closer monitoring may foster earlier identification of patients with worsening status, who may be subsequently hospitalized preventing death.

Previous individual studies and meta-analyses showed improved outcomes in patients referred to nurse-led HF clinics.[9] According to the 2013 American College of Cardiology Foundation/American Heart Association and the 2016 European Society of Cardiology guidelines on HF, follow-up in a nurse-led HF clinic, as part of multidisciplinary management and monitoring of patients with HF, has recommendation and level of evidence of IB and IA, respectively.[2,4] However, previous analyses assessing prognosis associated with referral to nurse-led HF clinics included few and highly selected patients,[9–11] and large analyses of "real-world" populations are needed.

Aims of this analysis were to assess: (1) independent predictors of and (2) prognosis associated with planned referral to a nurse-led HF clinic in a large and unselected cohort of HF patients.

Methods

Study Protocol and Setting

The data that support the findings of this study are available from the corresponding author, provided that data sharing is permitted by European Union General Data Protection Regulation regulations and appropriate ethics committees.

The SwedeHF (Swedish Heart Failure Registry) (www.swedeHF.se) has been previously described.[12] The only inclusion criterion is clinician-diagnosed HF. Approximately 80 variables are recorded at discharge from hospital or after outpatient clinic visit on a web-based case report form and entered into a database managed by the Uppsala Clinical Research Center (www.ucr.uu.se).

The Swedish Board of Health and Welfare (www.socialstyrelsen.se) administers the Population Registry and the Patient Registry. The Population Registry provided date of death. From the Patient Registry, we obtained additional baseline comorbidities and HF hospitalization outcome, defined according to *International Classification of Diseases, Tenth Revision* (*ICD-10*) codes in the first position.

Statistics Sweden (www.scb.se) provided socioeconomic characteristics. All Swedish citizens have unique personal identification numbers that enable linking of disease-specific health registries and governmental health and statistical registries.

Establishment of the HF registry and this analysis with linking of the above registries were approved by a multisite ethics committee. Individual patient consent is not required, but patients in Sweden are informed of entry into national registries and allowed to opt out.

Patients

In the current study, patients were selected if they were registered in the SwedeHF as outpatients or discharged alive from the hospital between May 11, 2000 (the start of the registry) and December 31, 2012, they had no missing data for planned follow-up in nurse-led HF clinic and ejection fraction (EF), and had follow-up $\geq$0 days (ie, follow-up=0 days may be attributed to in-hospital death during the hospitalization that prompted the registration in the SwedeHF; follow-up $<$0 may be explained by the registration in the SwedeHF after death). When a patient reported more than 1 registration, the first 1 was selected. The index date was defined as the date of the outpatient clinic visit for HF or hospital discharge. End of follow-up was December 31, 2012.

Statistical Analysis

Baseline characteristics

Baseline characteristics were compared in patients planned to be versus not be referred to follow-up in a nurse-led HF clinic by *t* test or Wilcoxon–Mann–Whitney tests for continuous variables and by chi-squared for categorical variables. Missing data were handled by chained equations multiple imputation (10 data sets generated) in multivariable models. Variables included in the multiple imputation models are labeled with an asterisk ("*") in Table.

Determinants of planned follow-up in a nurse-led HF clinic

Multivariable logistic regressions, using planned follow-up in a nurse-led HF clinic as a dependent variable and 39 variables

Table. Baseline Characteristics

Variables	Planned Referral to Nurse-Led HF Clinic Fup 16 180 Pts (39%)	No Planned Referral to Nurse-Led HF Clinic Fup 24 812 Pts (61%)	*P* Value
Demographics			
Sex*			
Male	11 130 (69%)	14 762 (60%)	<0.001
Female	5050 (31%)	10 050 (40%)	
Age, mean (SD), y*	70 (12)	76 (12)	<0.001
Year of registration*			
2000–2006	2233 (14%)	5801 (23%)	<0.001
2007–2012	13 947 (86%)	19 011 (77%)	
Location when entered in the Swedish HF Registry at baseline*			
Inpatient	7379 (46%)	15 618 (63%)	<0.001
Outpatient	8801 (54%)	9194 (37%)	
Specialty when entered in the Swedish HF Registry at baseline*			
Cardiology	8335 (54%)	12 799 (55%)	0.07
Internal medicine or geriatrics	7126 (46%)	10 534 (45%)	
Follow-up referral specialty* (physician specialty; not same as the HF nurse Fup)			
Primary care or other care	1665 (10%)	13 841 (56%)	<0.001
Cardiology or internal medicine	14 246 (90%)	10 888 (44%)	
Clinical			
Duration of heart failure, mo*			
<6	9420 (59%)	10 793 (44%)	<0.001
≥6	6643 (41%)	13 870 (56%)	
NYHA*			
I to II	7768 (59%)	9879 (59%)	0.98
III to IV	5372 (41%)	6836 (41%)	
EF, %*			
≥50	2388 (15%)	6958 (28%)	<0.001
40 to 49	3207 (20%)	5619 (23%)	
<40%	10 585 (65%)	12 235 (49%)	
Body mass index, mean (SD), kg/m^2*	27.1 (5.4)	26.7 (5.5)	<0.001
Blood pressure, mean (SD), mm Hg			
Systolic	126 (21)	129 (21)	<0.001
Diastolic	74 (12)	73 (12)	0.005
Mean arterial blood pressure, mean (SD), mm Hg*	91 (13)	92 (13)	<0.001
Heart rate, mean (SD), bpm*	74 (15)	74 (15)	0.12
Laboratory values			
eGFR, median (IQR), mL/min per 1.73 m^{2*†}	65 (49–80)	58 (43–74)	<0.001
Hemoglobin, mean (SD), g/L	135 (17)	131 (17)	<0.001
NT-proBNP, median (IQR), pg/mL*	2500 (1112–5740)	2689 (1132–6161)	0.001

Continued

Table. Continued

Variables	Planned Referral to Nurse-Led HF Clinic Fup 16 180 Pts (39%)	No Planned Referral to Nurse-Led HF Clinic Fup 24 812 Pts (61%)	*P* Value
Concomitant medications			
ACE-I or ARB*	14 808 (92%)	19 907 (81%)	<0.001
Mineralocorticoid receptor blockers*	4908 (30%)	7083 (29%)	<0.001
Digoxin*	2632 (16%)	4433 (18%)	<0.001
Diuretic*	12 370 (77%)	20 193 (82%)	<0.001
Nitrate*	1976 (12%)	4795 (19%)	<0.001
Platelet inhibitor*	7906 (49%)	12 846 (52%)	<0.001
Oral anticoagulant*	6768 (42%)	9204 (37%)	<0.001
Statin*	8051 (50%)	10 767 (44%)	<0.001
Beta-blocker*	14 626 (91%)	20 842 (84%)	<0.001
Device therapy*			
No	15 301 (95%)	23 584 (96%)	<0.001
CRT-P	190 (1%)	320 (1%)	
CRT-D	238 (2%)	215 (1%)	
ICD	339 (2%)	413 (2%)	
History and comorbidity			
Smoking*			
Never	5526 (40%)	8472 (46%)	<0.001
Previous	6160 (45%)	7899 (42%)	
Current	2069 (15%)	2230 (12%)	
Hypertension*	9297 (57%)	15 270 (62%)	<0.001
Diabetes mellitus*	4126 (25%)	7016 (28%)	<0.001
Ischemic heart disease*	8198 (53%)	13 623 (57%)	<0.001
Coronary revascularization*	5163 (32%)	7192 (29%)	<0.001
Atrial fibrillation/flutter*	8307 (51%)	14 448 (58%)	<0.001
Peripheral artery disease*	1415 (9%)	2671 (11%)	<0.001
Stroke or transient ischemic attack including intracranial bleed*	2203 (14%)	4695 (19%)	<0.001
Severe bleeding*	2857 (18%)	5315 (21%)	<0.001
Valve disease*	3616 (23%)	6886 (29%)	<0.001
Anemia*	4813 (30%)	9204 (37%)	<0.001
Lung disease*	3718 (23%)	6635 (27%)	<0.001
Socioeconomic variables			
Family type*			
Living alone	7569 (47%)	13 356 (54%)	<0.001
Married/cohabitating	8556 (53%)	11 426 (46%)	
Education*			
Compulsory school	7248 (45%)	12 708 (52%)	<0.001
Secondary school	6287 (39%)	8544 (35%)	
University	2479 (16%)	3261 (13)	

Continued

Table. Continued

Variables	Planned Referral to Nurse-Led HF Clinic Fup 16 180 Pts (39%)	No Planned Referral to Nurse-Led HF Clinic Fup 24 812 Pts (61%)	*P* Value
Income*			
≤Median	6970 (43%)	13 445 (54%)	<0.001
>Median	9093 (57%)	11 291 (46%)	
No. of children, mean (SD)*	2 (1)	2 (1)	0.41

Variables labeled with an asterisk ("*") were included in multiple imputation models together with "Planned nurse-led HF clinic follow-up" and the outcome all-cause mortality/HF hospitalization, and in all the multivariable models. Variables were included in the models as reported in Figures 1 and 2 (except for year of registration included as continuous variable). ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; EF, ejection fraction; eGFR, estimated glomerular filtration rate; Fup, follow-up; HF heart failure; ICD, implantable cardioverter defibrillator; IQR, interquartile range; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.
†Calculated by the Modification of Diet in Renal Disease (MDRD) formula.

labeled with an asterisk ("*") in Table as covariates, were run to detect independent predictors of planned referral to a nurse-led HF clinic.

Prognosis in planned versus non-planned follow-up in a nurse-led HF clinic

Outcomes of our analysis were time to all-cause death, time to first HF hospitalization (with censoring at death), and time to all-cause death or first HF hospitalization (composite outcome). Unadjusted survivor functions were estimated using the Kaplan–Meier method. Multivariable Cox regression models were fitted in order to calculate the adjusted proportional hazard ratios (HRs) with 95% CIs. They included the same variables as in the logistic regression models as covariates. In order to assess the association between planned follow-up in a nurse-led HF clinic and prognosis in prespecified subgroups of patients, Cox regression models were performed including an interaction term between planned follow-up in a nurse-led HF clinic and relevant variables.

Sensitivity Analysis

Given that the time frame considered for this analysis (2000–2012) spanned different periods of HF care (ie, post–renin-angiotensin-system inhibitors and beta-blocker introduction, but before mineralocorticoid receptor antagonists and cardiac resynchronization therapy introduction, and post–mineralocorticoid receptor antagonist and –cardiac resynchronization therapy introduction) and we enrolled also patients with very short follow-up given that both the enrollment and the follow-up ended in 2012, we performed a sensitivity analysis including only patients registered between January 1, 2006 and December 31, 2011.

A value of $P<0.05$ was considered as statistically significant for all the analyses. Statistical analyses were performed by Stata software (version 14.2; StataCorp LLC, College Station, TX).

Results

Between May 11, 2000 and December 31, 2012, 80 772 registrations were recorded from 51 060 unique patients. Of cases, 40 992 patients had no missing data for planned follow-up in a nurse-led HF clinic or EF, or follow-up ≤0 days, and 16 180 (39%) were planned to be followed up in a nurse-led HF clinic.

Baseline Characteristics

Baseline characteristics are reported in Table. There were several differences between groups. Patients with planned follow-up in nurse-led HF clinics were more likely male, younger, registered as outpatients in the SwedeHF, followed up in specialty physician care, married or cohabitating, and with higher education and income. They were also more likely to have a shorter HF duration, HF with reduced EF, lower blood pressure and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels, and higher body mass index, estimated glomerular filtration rate, and hemoglobin levels. Finally, they were less likely to suffer from comorbidities and more likely to receive evidence-based HF therapy.

Predictors of Planned Referral to a Nurse-Led HF Clinic

We assessed independent associations of numerous characteristics with planned follow-up in a nurse-led HF clinic. We displayed the adjusted odds ratios in descending order of magnitude in forest plots (Figures 1 and 2).

Among the demographic/organizational variables, follow-up referral in specialist care, being registered in the SwedeHF

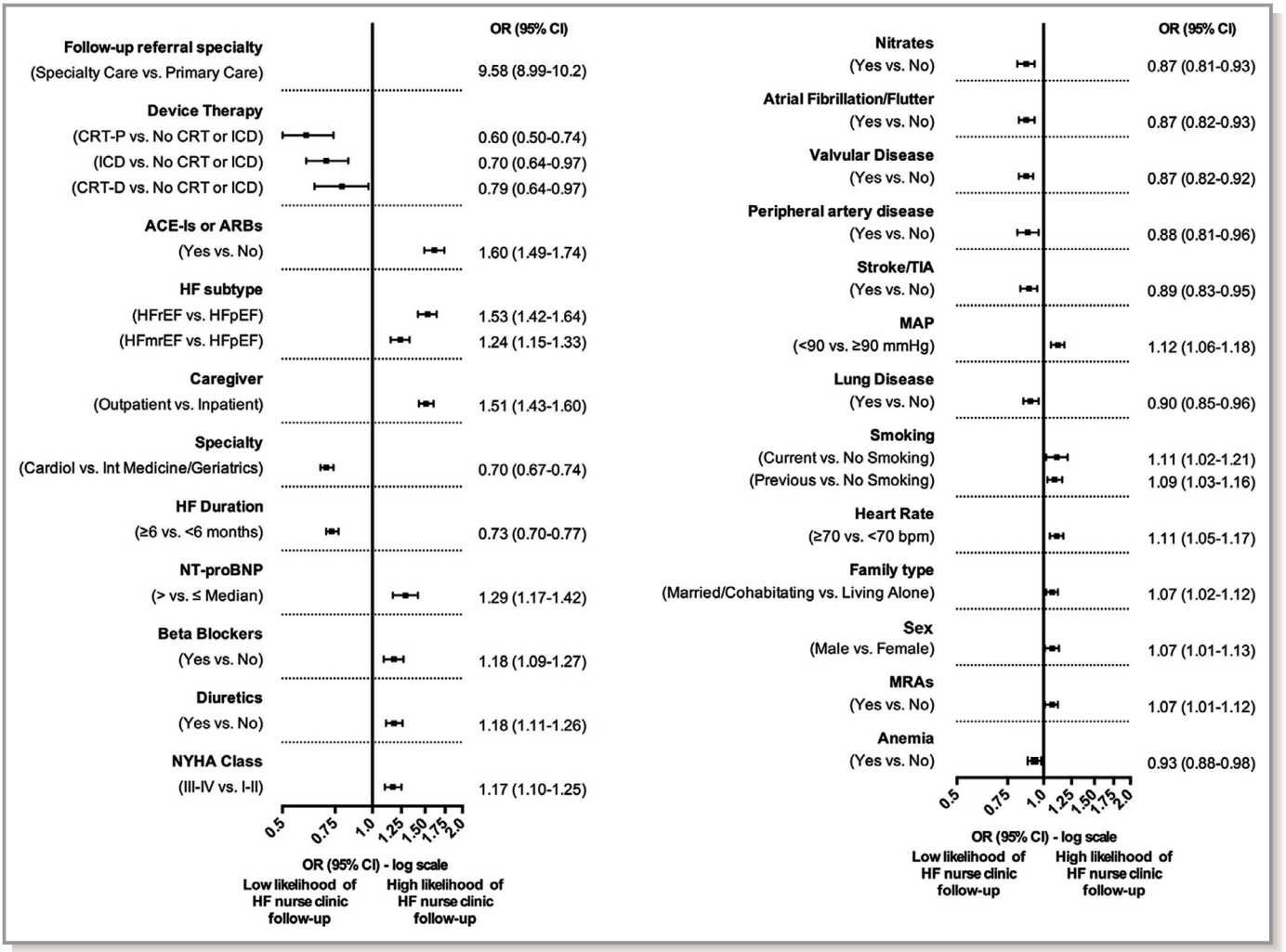

Figure 1. Variables independently associated with planned follow-up in nurse-led heart failure clinic. ACE-I indicates angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CRT-D, cardiac resynchronization therapy defibrillator; CRT-P, cardiac resynchronization therapy pacemaker; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter defibrillator; MAP, mean arterial pressure; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York heart association; OR, odds ratio; TIA, transient ischemic attack.

as an outpatient, male sex, and being married or cohabitating were associated with planned referral to a nurse-led HF clinic in unadjusted and adjusted analyses, whereas education, age, and income were no longer significant after adjustments. Conversely, in both study arms, patients were more likely to be registered in the SwedeHF in cardiology departments, but after adjustments, those registered in internal medicine/geriatric departments were more likely planned to be referred to nurse-led HF clinics.

Among the clinical/comorbidity variables, HF with reduced EF and HF with mid-range EF subtypes, shorter HF duration, higher NT-proBNP levels, and absence of comorbidities, such as anemia, atrial fibrillation, valvular disease, peripheral artery disease, history of stroke, lung disease, lower blood pressure, and current or previous smoking, were confirmed as independent predictors of planned follow-up in a nurse-led HF clinic after adjustments. In adjusted analyses, higher New York Heart Association (NYHA) class and higher heart rate were also independently associated with likelihood of receiving follow-up in a nurse-led HF clinic. Conversely, other comorbidities, such as body mass index, hypertension, diabetes mellitus, history of severe bleeding, renal function, history of ischemic heart disease, and coronary revascularization, were not independently associated with planned referral to a nurse-led HF clinic after adjustments.

We also investigated the different use of treatments in patients planned to be versus not to be referred to a nurse-led HF clinic. Being prescribed angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, beta-blockers, mineralocorticoid receptor antagonists, and diuretics was

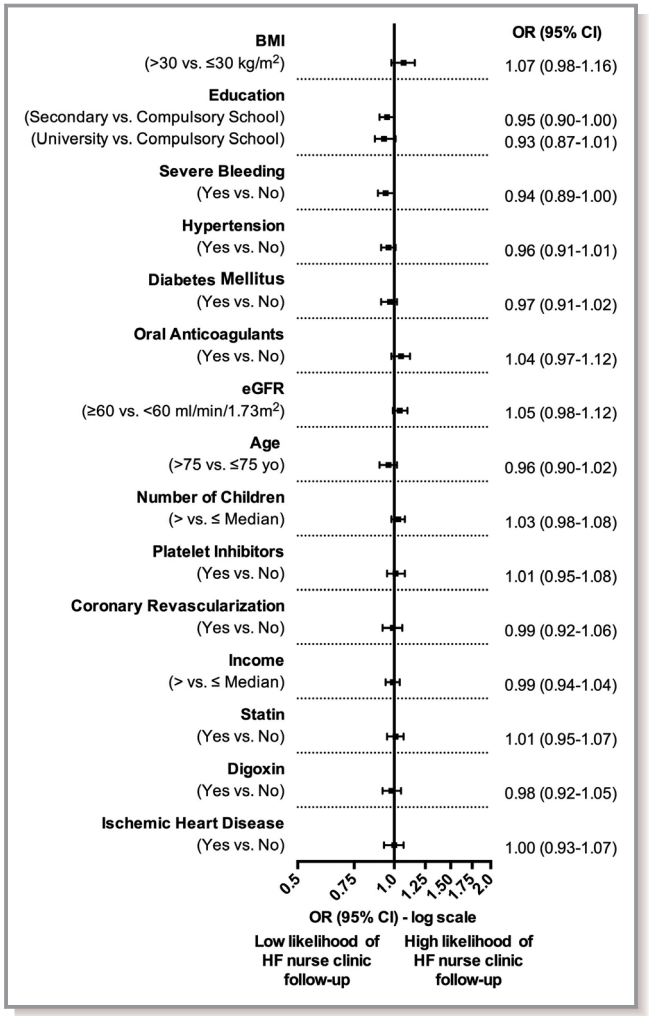

Figure 2. Variables not independently associated with planned follow-up in nurse-led heart failure clinic. BMI indicates body mass index; eGFR, estimated glomerular filtration rate; HF, heart failure; OR, odds ratio.

associated with higher likelihood of planned referral, whereas receiving cardiac resynchronization therapy or an implantable cardioverter defibrillator or nitrates was associated with less likelihood of planned referral to a nurse-led HF clinic.

Outcome Analysis

Figure 3A shows the Kaplan–Meier curves for time to all-cause mortality, time to HF hospitalization, and time to all-cause mortality/HF hospitalization in patients planned to be versus not to be referred to a nurse-led HF clinic. In unadjusted analyses, planned follow-up in a nurse-led HF clinic was associated with a significant reduction of risk of all-cause death (HR, 0.61; 95% CI, 0.59–0.63), HF hospitalization (HR, 0.92; 95% CI, 0.89–0.95), and composite of all-cause death and HF hospitalization (HR, 0.77; 95% CI, 0.75–0.79). Median time (interquartile range) to event was 2.2 (0.9–4.1) years for all-cause death and 1.4 (0.4–3.3) years for HF hospitalization/all-cause death. After adjustments, risk of mortality (HR, 0.90; 95% CI, 0.86–0.93) and of the composite outcome (HR, 0.96; 95% CI, 0.93–0.99) remained significantly reduced, whereas risk of HF hospitalization was not significantly associated with planned referral to a nurse-led HF clinic (HR, 1.03; 95% CI, 0.99–1.07).

The association between planned follow-up in a nurse-led HF clinic and outcomes was consistent in most subgroups explored (Figure 4). However, in some of them, such as NYHA class I to II, HF duration <6 months, higher estimated glomerular filtration rate, and absence of concomitant diabetes mellitus and ischemic heart disease, planned referral to a nurse-led HF clinic was associated with even greater benefit in terms of mortality reduction. Planned follow-up in a nurse-led HF clinic was associated with higher risk of HF hospitalization in age ≤75 years, HF with reduced EF and HF with preserved EF, HF duration ≥6 months, and lower NT-proBNP. Risk of the composite outcome was lower in patients planned to be referred to a nurse-led HF clinic with age >75 years, NYHA class I to II, and HF duration <6 months and in patients who did not have diabetes mellitus.

Sensitivity Analysis

Between January 1, 2006 and December 31, 2011, 31 938 patients fulfilled the inclusion/exclusion criteria of our study. Consistently with the main analysis, 38% (12 273 patients) of our population was planned for referral to a nurse-led HF clinic. Distribution of the baseline characteristics of the population considered at the sensitivity analysis was similar to the main analysis (Table S1). After adjustments, planned follow-up in a nurse-led HF clinic was associated with a statistically significant reduction of the risk of all-cause mortality (HR, 0.90; 95% CI, 0.86–0.95) and of the composite outcome (HR, 0.96; 95% CI, 0.93–0.99), but not of HF hospitalization (HR, 1.02; 95% CI, 0.98–1.07; Figure 3B).

Discussion

In this large and comprehensive analysis from the SwedeHF, we observed that patients with more-severe HF were more likely to be planned for referral to nurse-led HF clinics. Indeed, sicker patients may have more need for this type of intervention because of expected poorer prognosis. On the contrary, patients with comorbidities were less likely to be planned for referral to a nurse-led HF clinic, although they had an even larger need for a structured and comprehensive follow-up. We also reported lower likelihood of being referred to a nurse-led HF clinic in patients living alone and women. Our results are concerning given that they show that there is

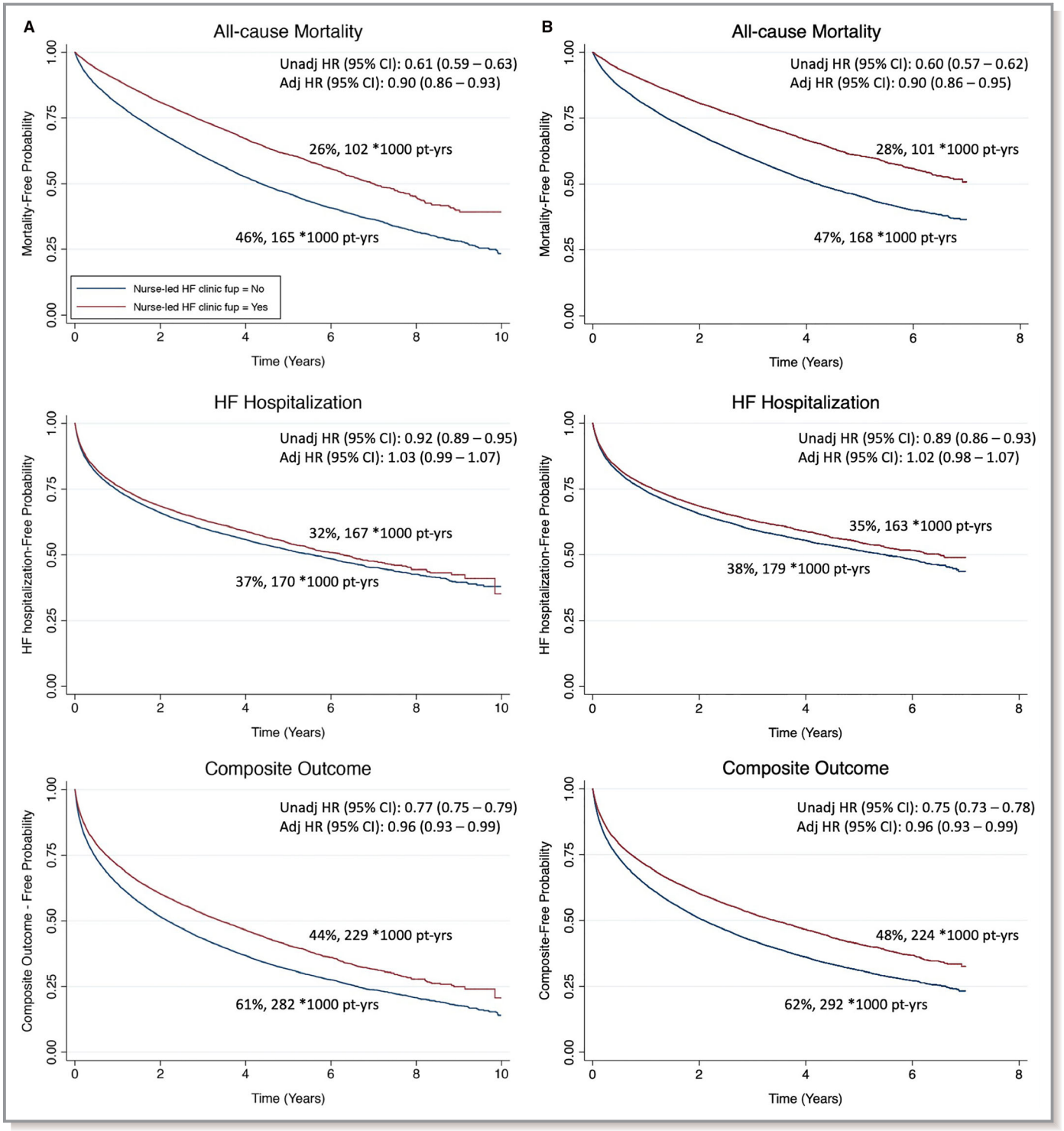

Figure 3. Outcome analysis (**A**) in the overall population and (**B**) in patients enrolled between 2006 and 2011 (sensitivity analysis). In each graph, the number of events, as % of the number of patients, and the event rates, as patient-years, are reported for each study arm. adj indicates adjusted; HF, heart failure; HR, hazard ratio; pt-yrs, patient-years; unadj, unadjusted.

an unjustified limited referral to this type of follow-up. Indeed, as observed for many other treatments in HF,[13,14] referral to a nurse-led clinic was limited, although it was associated with reduced mortality.

Utilization of Nurse-Led HF Clinics

In HF, a well-structured follow-up should be provided during the disease trajectory. Indeed, early follow-up during the

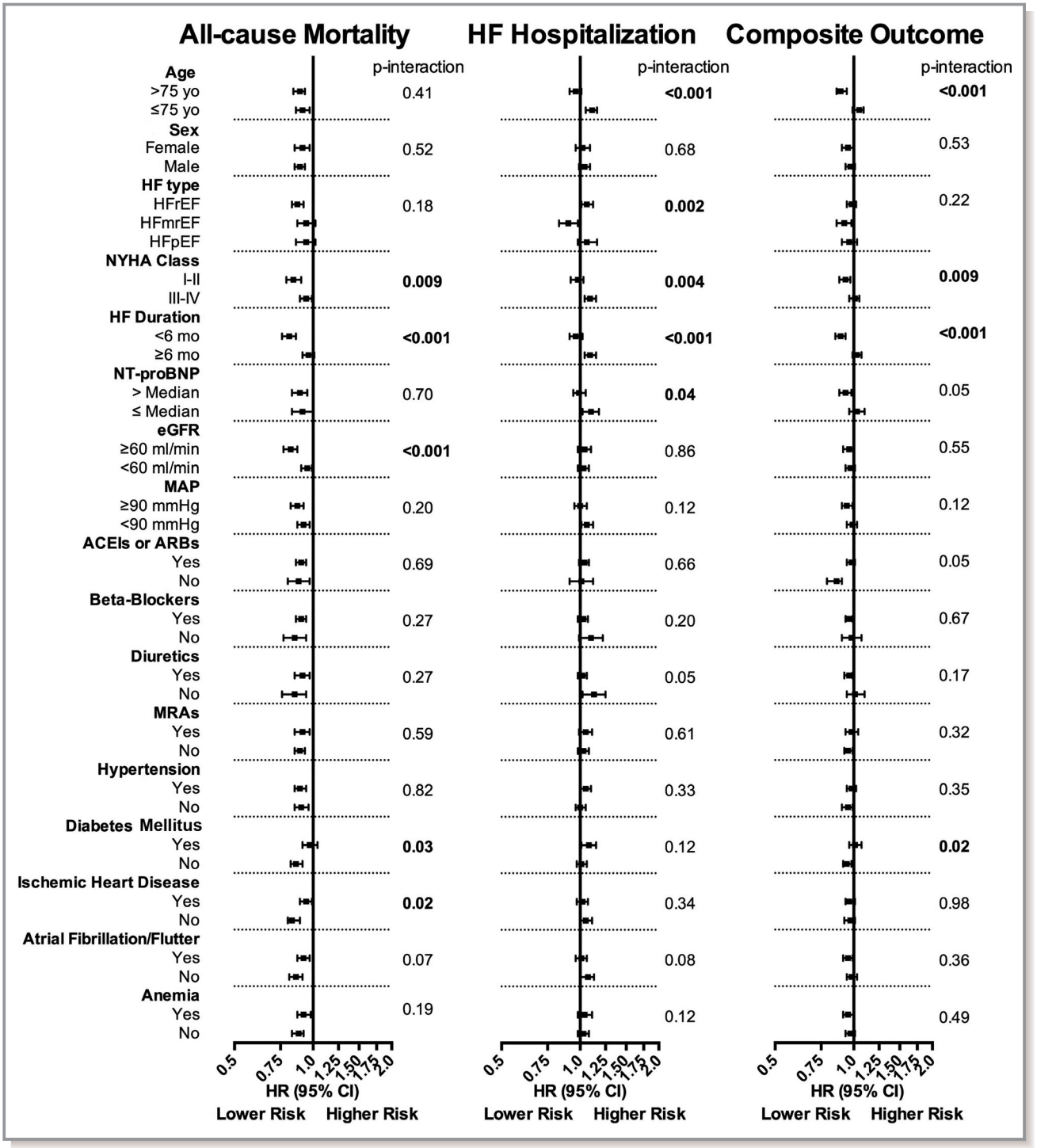

Figure 4. Forest plot reporting hazard ratios for planned follow-up in nurse-led heart failure clinic in prespecified subgroups. ACE-I indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; HF, heart failure; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR, hazard ratio; MAP, mean arterial pressure; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association.

vulnerable phase after hospitalization is vital to prevent readmissions and death.[10] Based on American and European HF guidelines, multidisciplinary care is recommended, and a nurse-led HF clinic is 1 established model of this type of care.[2,4] Despite guidelines recommendations and several meta-analyses that provided evidence of improved survival/

morbidity,[2,4,9–11,15] multidisciplinary approaches and referral to nurse-led HF clinics have not been fully implemented in HF care in many countries.[16]

In Sweden, follow-up in nurse-led HF clinics has been implemented in almost all hospitals[7,17] and, to some extent, also in primary care.[6] Nevertheless, we showed that less than half of the population enrolled in our study was planned for referral to a nurse-led HF clinic. Major gains could be made referring patients to this type of follow-up, especially in terms of improving event-free survival, as suggested by our and previous studies.[17,18]

In Sweden[19] as well as in many other countries worldwide,[20] healthcare legislation provides equal access to care to all citizens. In this report, we found less likelihood of being planned for a follow-up in an HF clinic based on female sex and living alone, which is consistent with previous studies.[13,21] However, in Sweden, there are no financial or organizational hurdles to implement hospital- and primary-care–based, nurse-led HF clinics, and most patients state that they prefer this type of follow-up.[6] One proposed reason for a lack of structured nurse-led HF referral is that many healthcare providers neglect the importance of monitoring symptoms, optimizing treatment and providing education and psychosocial support to patients with HF.[22] Furthermore, we showed that having comorbidities and suffering from HF with preserved EF/HF with mid-range EF and of less-severe HF (ie, lower NYHA class and NT-proBNP levels and high mean arterial blood pressure) were associated with less likelihood of being planned for referral to HF clinics. A potential explanation for this finding might be that physicians expect more benefit of referral to a nurse-led HF clinic in patients with more-severe HF and less comorbidities. However, this proposed hypothesis is not supported by our data. Indeed, we showed similar benefits in terms of mortality/morbidity in patients with different EF, high versus low NT-proBNP, and lower HR for mortality in those with NYHA I to II and overall reduced risk of outcomes regardless of comorbidities. Additionally, presence of comorbidities in HF is associated with poorer survival and quality of life.[23] As a consequence, a stricter and more-comprehensive follow-up in an HF nurse-led clinic might be even more effective in these patients. Interestingly, we showed that patients registered at baseline in medicine/geriatrics rather than cardiology departments were more likely to be planned for referral, suggesting that referral may have been considered more needed. Patients with planned referral to specialty versus primary-care follow-up care were also more likely to be planned for referral to a nurse-led clinic, suggesting that specialists and HF nurses work in synergy to determine initiation and titration of HF medications and devices during follow-up.[24] There are 2 potential explanations for the association between planned referral to a nurse-led HF clinic and optimized use of HF treatments shown in our analysis. First, patients reported as planned for referral at the index date had been previously referred to an HF nurse-led clinic, which may explain the optimized use of HF therapies. Second, patients who were better treated were also more likely to be planned for referral to nurse-led HF clinic as part of the treatment plan. We also found that patients with HF diagnosed within the past 6 months were more likely to be planned for referral, which may be interpreted by higher expected benefit of intensive HF therapy initiation and titration in the early stages of the condition, as confirmed by our subgroup analysis.

Prognosis Associated With Planned Referral to a Nurse-Led HF Clinic

In previous meta-analyses,[9–11,15] follow-up in a nurse-led clinic was associated with improved survival and reduced risk of hospital readmission. However, several individual studies have been inconclusive and have shown inconsistent results.[25,26] Most trials compared an intervention with "usual care," but whether usual care in trials published during the early 1990s is comparable to current practice is not clear.[9–11,15] Additional issues of published trials were low power, inclusion of highly selected cohort, and use of different control arms, which ranged from intensive follow-up by cardiologists[25] to almost no follow-up at all.[18] Therefore, it is not clear whether previous studies are comparable with current practice and whether their findings may be generalized to real-world setting.

The current analysis, including more than 40 000 patients from the large and unselected HF population of the SwedeHF, showed reduced mortality associated with planned referral to a nurse-led HF clinic, which is consistent with previous evidences.[9–11,15] However, similar risk of HF hospitalization was observed in patients who were versus those who were not planned for referral. As previously hypothesized,[27,28] referral to nurse-led HF clinics could impact on survival by several mechanisms. It could foster treatment optimization and improve patients' understanding of HF and self-care. It could also promote involvement of other people in patient's self-care, psychosocial support, and well-being. Finally, it could provide an easier access to health professionals and continuity of care with stricter and longer follow-up.

Referral to HF clinics has been associated with reduced risk of hospitalization in some studies,[18,29] but not in others[25,26] and in ours. Inconsistent findings may be explained by differences in content of the interventions, settings, and patient populations.[18,25,26,29] Some hospital admissions may be necessary and beneficial in terms of improving symptoms, health-related quality of life, and survival. Finally, closer monitoring may foster earlier identification of patients with worsening status, who were subsequently hospitalized.

Limitations

Our observational study is subject to confounding and selection bias. Indeed, although we performed extensive adjustments, we cannot rule out potential residual confounding. Exposure in the current analysis was *planned* referral to a nurse-led HF clinic, so similarly to what happens in trials where treatment is considered according to an intention-to-treat protocol, we cannot exclude that some patients may not have undergone or completed follow-up although suggested at the time of registration in the SwedeHF. Notably, each nurse-led HF clinic may vary, based on nurses' experience, knowledge base in HF, time spent communicating with patients, techniques used in communication (ie, motivational interviewing), teach-back and shared decision making, and, also, based on expectations of physician providers of each practice. Additionally, HF nurse-led clinics may have changed in scope of work over time, as HF therapies advanced. A propensity-matched study design based on temporal trends would consider changes in practice over time and increase comparability between study arms, but limit sample size and generalizability of findings. We do not know the value of nurse-led clinics based on contemporary management; they could be more or less valuable now compared with 2000. Another limitation is the time frame of this report (2000–2012) given that treatments have advanced over time. Our study population was enrolled over 12 years characterized by important changes in HF care (ie, introduction of mineralocorticoid receptor antagonists and cardiac resynchronization therapy). Although we adjusted our analysis for the year of enrollment and baseline therapy, we cannot exclude residual confounding effect of time of enrollment on our findings.

Conclusions

In this nation-wide registry, 39% of our identified HF cohort was planned to be referred to a nurse-led HF clinic. Patients who were planned for referral had more-severe HF, higher use of HF treatments, and less comorbidities at referral. Planned referral was independently associated with lower risk of death, but not of HF hospitalization.

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Disclosures

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SUPPLEMENTAL MATERIAL

Table S1. Baseline characteristics in patients enrolled between 2006 and 2011 (sensitivity analysis).

Variables	No planned referral to nurse-led HF clinic fup 19,665 pts (38%)	Planned referral to nurse-led HF clinic fup 12,273 pts (62%)	**p**
Sex			<0.001
Male	11708 (59.5%)	8452 (68.9%)	
Female	7957 (40.5%)	3821 (31.1%)	
Age, mean (SD), y	76 (12)	70 (12)	<0.001
Location when entered in the Swedish HF Registry at baseline			
Inpatient	12448 (63.3%)	5575 (45.4%)	<0.001
Outpatient	7217 (36.7%)	6698 (54.6%)	
Specialty when entered in the Swedish HF Registry at baseline			
Internal medicine/Geriatrics	7864 (43.3%)	5498 (47.0%)	<0.001
Cardiology	10315 (56.7%)	6189 (53.0%)	
Follow-up referral specialty (physician specialty; not same as the HF nurse FUP)			
Cardiology or Internal medicine	8500 (43.3%)	10751 (89.5%)	<0.001
Primary care or Other care	11108 (56.7%)	1258 (10.5%)	
Duration of heart failure, months			
<6	8417 (43.0%)	7010 (57.5%)	<0.001
≥6	11136 (57.0%)	5189 (42.5%)	
NYHA			
I-II	7817 (59.2%)	5983 (59.2%)	0.99
III-IV	5384 (40.8%)	4122 (40.8%)	
EF, %			
≥50	5574 (28.3%)	1797 (14.6%)	<0.001
40-49	4463 (22.7%)	2484 (20.2%)	
<30	9628 (49.0%)	7992 (65.2%)	
Body mass index, mean (SD), kg/m2	27 (6)	27 (5)	<0.001
Blood pressure, mean (SD), mmHg			
Systolic	129 (21)	126 (21)	<0.001
Diastolic	73 (12)	73 (12)	0.062
Mean arterial blood pressure, mean (SD), mmHg	92 (13)	91 (13)	<0.001
Heart Rate, mean (SD), beats/min	74 (15)	74 (15)	0.033
eGFR, median (IQR), ml/min/1.73m2	58 (43, 74)	64 (49, 80)	<0.001
Hemoglobin, mean (SD), g/L	131 (17)	135 (17)	<0.001

NT-proBNP, median (IQR), pg/mL	2640 (1110, 6140)	2513 (1131, 5468)	0.053
ACE-I or ARB	15848 (81.1%)	11248 (91.8%)	<0.001
Mineralocorticoid receptor blockers	5532 (28.3%)	3634 (29.7%)	0.007
Digoxin	3405 (17.4%)	2021 (16.5%)	0.038
Diuretic	15887 (81.1%)	9342 (76.4%)	<0.001
Nitrate	3785 (19.4%)	1504 (12.3%)	<0.001
Platelet inhibitor	10259 (52.5%)	6124 (50.1%)	<0.001
Oral anticoagulant	7226 (37.0%)	5063 (41.4%)	<0.001
Statin	8781 (44.9%)	6226 (50.9%)	<0.001
Beta-Blocker	16501 (84.3%)	11099 (90.6%)	<0.001
Device therapy			<0.001
CRT-P	296 (1.5%)	174 (1.4%)	
CRT-D	188 (1.0%)	172 (1.4%)	
ICD	339 (1.7%)	253 (2.1%)	
Smoking			
Never	6612 (45.1%)	4213 (40.4%)	<0.001
Previous	6276 (42.8%)	4689 (45.0%)	
Current	1769 (12.1%)	1529 (14.7%)	
Hypertension	12270 (62.4%)	7081 (57.7%)	<0.001
Diabetes	5600 (28.5%)	3121 (25.4%)	<0.001
Ischemic heart disease	10830 (56.6%)	6350 (53.8%)	<0.001
Coronary revascularization	5803 (29.5%)	4018 (32.7%)	<0.001
Atrial fibrillation/flutter	11511 (58.5%)	6318 (51.5%)	<0.001
Peripheral artery disease	2168 (11.0%)	1072 (8.7%)	<0.001
Stroke or transient ischemic attack incl intracranial bleed	3733 (19.0%)	1664 (13.6%)	<0.001
Severe bleeding	4384 (22.3%)	2180 (17.8%)	<0.001
Valve disease	5414 (28.1%)	2762 (22.8%)	<0.001
Anemia	7407 (37.7%)	3649 (29.7%)	<0.001
Lung disease	5378 (27.3%)	2820 (23.0%)	<0.001
Family type			
Living alone	10622 (54.1%)	5708 (46.7%)	<0.001
Married/cohabitating	9019 (45.9%)	6521 (53.3%)	
Education			
Compulsory school	9977 (51.4%)	5528 (45.6%)	<0.001
Secondary school	6847 (35.3%)	4753 (39.2%)	
University	2580 (13.3%)	1843 (15.2%)	
Income			
≤ median	9099 (46.4%)	6854 (56.3%)	<0.001
> median	10506 (53.6%)	5325 (43.7%)	
Number of children, mean (SD)*	2 (1)	2 (1)	0.50