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**Risk of readmission and death after hospitalization for worsening heart failure:
Role of post-discharge follow-up visits in a real-world study from the Grand Est Region of France**

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Abstract (249 words)

Background and Aims

Patients who experience hospitalizations due to heart failure (HF) face a significant risk of readmission and mortality. Our objective was to evaluate whether the risk of hospitalization and mortality following discharge from HF hospitalization differed based on adherence to the outpatient follow-up (FU) protocol comprising an appointment with a general practitioner (GP) within 15 days, a cardiologist within 2 months or both (termed combined FU).

Methods

We studied all adults admitted for a first HF hospitalization from 2016 to 2020 in France's Grand Est region. Association between adherence to outpatient FU and outcomes were assessed with time-dependent survival analysis model.

Results

Among 67476 admitted patients (mean age 80.3 ± 11.3 years, 53% women), 62156 patients (92.2%) were discharged alive and followed for 723 (317-1276) days. Combined FU within 2 months was used in 21.1% of patients, with lower rates among >85 years, women, and those with higher comorbidity levels ($p < 0.0001$ for all). Combined FU was associated with a lower one-year death or rehospitalization (adjusted HR=0.91, 0.88-0.94, $p < 0.0001$) mostly related to lower mortality (adjusted HR=0.65, 0.62-0.68, $p < 0.0001$) whereas HF readmission was higher (adjusted HR=1.19, 1.15-1.24, $p < 0.0001$). When analyzing components of combined FU separately, one-year mortality was more related to cardiologist FU (HR=0.65, 0.62 to 0.67, $p < 0.0001$), than GP FU (HR=0.87, 0.85 to 0.90, $p < 0.0001$).

Conclusion

Combined follow-up is carried out in a minority of patients following HF hospitalization, yet it is linked to a substantial reduction in one-year mortality, albeit at the expense of an increase in HF hospitalizations.

Keywords

Cardiovascular diseases, Heart failure, Epidemiology, Survival, Healthcare pathways.

Introduction

The burden of hospitalization for heart failure (HF) represents a major issue with in-hospital mortality ranging between 2.0% and 12.1% depending on the hemodynamic profile at presentation¹. In addition to in-hospital mortality, the readmission rate is approximately 20% at 30 days after discharge, with one-year mortality estimated at 24% in a recent meta-analysis². The rate of HF readmission or death is maximum in the few months following discharge and decreases progressively in the first year³⁻⁶.

Given that this post-discharge period is at very high-risk (often referred to as a “vulnerable period”³), the 2021 HFA/ESC guidelines⁷ state that “an early follow-up visit is recommended at weeks after discharge to assess signs of congestion, drug tolerance and initiate and/or up-titrate evidence-based therapy”, while further elaborating that this visit should occur 1 to 2 weeks after discharge. The STRONG-HF trial has demonstrated the safety and effectiveness of an intensive care approach for patients during their hospitalization for acute decompensated HF and for the six weeks following discharge. Considering this compelling new evidence, the 2023 Focused Update to the 2021 ESC Guidelines for HF strongly endorses the importance of frequent and careful follow-up visits within the six weeks following an HF-related hospitalization. This recommendation is classified as a Class I recommendation, supported by a Level B evidence rating.⁸ In France, the French “Haute Autorité de Santé” in 2014 recommended a general practitioner (GP) appointment within 15 days and a cardiologist appointment within 2 months⁹ after an HF hospitalization. The characteristics and prognosis of patients followed according to these modalities have never been reported.

The objective of this study was to describe outpatient healthcare utilization after HF hospitalization in an exhaustive geographic cohort and to assess the association of this post-discharge management with subsequent rehospitalization and mortality.

Materials and methods

Population and study design

Data were extracted from the French Health Insurance database (Système National des Données de Santé). Study participants included patients of the Grand Est region hospitalized for HF for the first time between 2016 to 2020 in any department (Cardiology, Internal Medicine, or other wards). The following selection criteria were applied: at least one night in hospital for patients aged 18 years or older; cases of HF were defined by a principal diagnosis code beginning with I50, I11, I13 or J81 (according to the International Classification of Diseases, 10th revision) with exclusion of a selected homogeneous group of patients (HGP) (05C14, 05C19 and 05K10) hospitalized for diagnostic tests (angiography, right heart catheterizations etc.) or surgical or interventional management of chronic cardiac pathologies that may present an acute cardiac decompensation (e.g. cardiac resynchronization therapy or cardioverter implantation, valve replacements, aorto-coronary bypasses, intra-thoracic interventions with or without extracorporeal circulation, etc.). The same method was used for associated diagnosis but with a homogeneous group of patients with chronic bronchopneumopathy (coded 04M08 and 04M20), indicative of pulmonary diseases associated with HF. The first hospital stay between 2016 and 2020 was referred as the index hospitalization. Only patients alive at discharge from the index hospitalization were considered in the survival analysis. Patients were followed until 12/31/2021, resulting in a follow-up of 1 to 6 years, depending on the inclusion date.

Outcomes

The considered outcomes were readmission for HF and all-cause mortality during the follow-up.

Groups based on post-discharge follow-up:

GP follow-up was defined as having a reimbursement for a GP, internist, or geriatrician consultation within 15 days following discharge from the HF index hospitalization. Similarly, cardiologist follow-up was defined as having a reimbursement for a consultation with a cardiologist or an echocardiogram within 2 months following discharge. Combined follow-up was defined as meeting both the GP and cardiologist follow-up criteria as described.

Definition of covariates

Severity of health status at the time of inclusion was assessed using the Charlson Comorbidity Index (CCI)¹⁰. To calculate this index, the 17 comorbid conditions included in the index were derived from the data of all hospital stay diagnoses for any causes at or before (up to 2014) the index hospitalization. A CCI score of 2 indicates low comorbidity (i.e., having only HF) and a score greater than 2 was considered as high comorbidity (HF and other comorbidities). Three chronic diseases included in the CCI were also considered as binary variables at inclusion: chronic pulmonary disease, diabetes, and renal disease.

Statistical analysis

Continuous variables are expressed as medians with interquartile 25-75% (IQ₂₅₋₇₅) range or as means (\pm standard deviation) and comparisons were carried out using Student's t-test. Categorical variables are expressed as frequencies (percentages) and compared using the chi-square test. Logistic regression was used to assess the parameters associated with combined follow-up according to French guidelines, i.e., GP within 15 days, cardiologist within 2 months. A sensitivity analysis was performed excluding patients who died before 15 days for GP follow-up and before 2 months for cardiologist or combined follow-up.

Survival probabilities are illustrated using Kaplan-Meier curves and compared with log-rank tests. Cox proportional hazard regression with time-dependent covariables was used to examine the association between follow-up and outcome in order to avoid immortal time bias¹¹. Within this time-dependent model, patients were considered in the no-combined FU group until they met the criteria to contribute to the combined FU group (appointment with GP within 15 days and appointment with a cardiologist within 2 months). Therefore, patients with GP FU after 15 days or cardiologist FU after 2 months or incomplete FU were considered in the no-combined FU group. Components of combined FU were also assessed individually (GP follow-up within 15 days and cardiologist within 2 months). Combined follow-up (or its components) and readmission for HF were considered as events of interest. Association between the events of interest and outcomes were considered only after the occurrence of the events (since no association between follow-up and outcome can be causal before the consultation). Cox regression model were adjusted for age, sex, and comorbidities (Charlson score at inclusion). The interaction between age and follow-up on outcome was evaluated, as was the interaction between combined follow-up and rehospitalization with one-year mortality.

We calculated the one-year risk of readmission for HF, considering the presence of competing risks, specifically mortality. We employed the cause-specific hazard function introduced by Fine and Gray. This approach allows for a more nuanced and comprehensive analysis, acknowledging that mortality and readmission are competing events and providing a more accurate assessment of the risk of HF-related readmission within a one-year timeframe.¹²

Three sensitivity analyses were performed: the first after excluding patients who died within 2 months of discharge, the second based on income level as assessed by access to complementary universal medical coverage (CMU-C) allocated to the lowest income patients living in the French territory. Finally, to mitigate baseline differences in characteristics among the follow-up groups at 2 months (no follow-up, general practitioner only, cardiologist only, and combined follow-up), a propensity score was generated, more specifically, inverse probability weighting (IPW) was used, considering age, gender, comorbidities based on the Charlson score, length of index stay, and access to CMU-C. We assessed the covariate balance between the 4 groups by computing the absolute standardized mean differences (ASMDs) both before and after applying weighting. Given the absence of a universally agreed-upon threshold for defining balanced covariates, we deemed a covariate to be balanced if its ASMD was below 0.10.

A two-sided p-value <0.05 was considered significant. Analyses were performed with SAS Enterprise Guide version 7.15 (SAS Institute Inc., Cary, N.C., USA) and R software version 4.1.2 (R Foundation for Statistical Computing).

Ethical statement

This is a retrospective observational study which did not modify the medical care of patients. Anonymity was preserved for both patients and health professionals. According to French law, ethical approval was therefore not required. Analyses were performed by the Statistical Department of the Direction Régionale du Service Médical de l'Assurance Maladie.

Results

Patients' characteristics and post-discharge follow-up

A total of 67 476 patients (mean±SD age 80.3±11.3 years and 53% women) were included in the analysis (Table 1). The mean±SD length of hospital stay was 10.5±8.5 days. Patients had a high level of comorbidity as illustrated by a mean±SD Charlson Comorbidity index of 4.8±2.9; 79% of patients had at least one comorbidity on top of HF (30% COPD, 42% diabetes and 43% renal disease).

A total of 62 156 patients (92.2%) survived their hospital stay and were followed for 723 (317-1276) days.

The proportion of patients who had at least one GP appointment at 2 weeks was 52.6%, median delay 11 days, while the proportion of patients who had at least one cardiologist appointment at 2 months was 35.4%, median delay 57 days (Table 2). A minority of patients (21.1%) were followed according to the combined follow-up recommended by the French guidelines with a GP appointment within 15 days and cardiologist appointment within 2 months. The median delay for combined follow-up was 25 days. Appointment with a cardiologist and combined follow-up decreased gradually with age, while the time to appointment increased ($p<0.0001$ for all – Table 1).

Cardiologist appointments and combined follow-up were more frequent in younger patients (Table 3). In multivariable analysis, with patients over 85 as reference, patients <85 years were 2-3 times more likely to have a cardiologist appointment (OR ranging from 2.07 to 3.2) or combined follow-up (OR ranging from 1.95 to 2.32). Female sex (adjusted OR 0.82 [0.79 to 0.85]) and more comorbidities (OR ranging from 0.69 to 0.84) were associated with decreased access to combined follow-up ($p<0.0001$). In contrast, GP appointment within 15 days after HF decompensation was marginally different according to sex (adjusted OR 0.97 [0.94 to 0.99] for women), comorbidities (OR ranging from 0.98 to 1.05) or age (OR ranging from 1.14 to 1.30). In the sensitivity analysis carried out excluding patients who died before 15 days for GP follow-up and before 2 months for cardiologist or combined follow-up, the results were broadly similar (supplementary table 1).

Association of GP, cardiologist, or combined follow-up with hospital readmission and/or mortality

Results on the association of GP, cardiologist, or combined follow-up with outcome are presented in table 4. The mortality at 1 and 12 months after discharge was 5.9% and 27.1%, respectively. Combined follow-up was associated with a lower risk of composite endpoint of one-year death or rehospitalization (adjusted HR= 0.91, [0.88-0.94]; $p<0.0001$) related to a 35% reduction in one-year mortality (adjusted HR, 0.65 [0.62 to 0.68], $p<0.0001$) when adjusting for age, sex, comorbidity, and readmission for HF (which was an important predictor of mortality, HR, 3.33 [3.21 to 3.44]; $p<0.0001$) whereas one-year HF readmission risk was increased by 19% (adjusted HR 1.19, 1.15-1.24, $p<0.0001$).

The benefit of combined follow-up was maintained in the long-term, with a 28% lower mortality (HR, 0.72 [0.71 to 0.74], $p<0.0001$). Kaplan-Meier curves for one-year and long-term mortality and heart failure rehospitalization according to follow-up are represented in Figure 1A (log-rank test: $p<0.0001$) and in supplementary figure 1A, respectively.

When analyzing components of combined follow-up separately, follow-up by a cardiologist was associated with a similar 35% reduction in one-year mortality (adjusted HR, 0.65 [0.62 to 0.67], $p<0.0001$) whereas a GP follow-up was associated with an 13% lower risk of death (adjusted HR, 0.87 [0.85 to 0.90], $p<0.0001$). The overall risk of HF rehospitalization at 1 and 12 months after discharge was 9.3% and 28.2%, respectively. Figure 1B represents the

increased hospitalization risk associated with combined follow-up (log-rank test: $p < 0.0001$). GP and cardiologist were significantly associated with one-year readmission, (HR 1.10 and 1.24, respectively, $p < 0.0001$ for all).

Readmissions for heart failure were associated with a 3- to 4-fold increased risk of one-year mortality (HR, 2.69 [2.62 – 2.76, $p < 0.0001$] and 3.47 [3.29 - 3.66, $p < 0.0001$] in patients without and with combined follow-up respectively). Combined follow-up was associated with a significant 34 and 25% reduction in one-year mortality in patients without and with rehospitalization for HF (HR, 0.66 [0.63 to 0.68], $p < 0.0001$ and HR, 0.85 [0.81 to 0.88], $p < 0.0001$, interaction p -value < 0.0001).

Association between combined follow-up and outcomes according to age category

Results of the association between combined follow-up and outcomes according to age category are presented in Supplementary Table 2.

Regarding one-year outcome, combined follow-up was associated with increased HF readmission only in patients over 75 years (HR, 1.11, and 1.40 for 75-84 years, and over 85 years respectively, p for interaction < 0.0001). There was no significant interaction between age and combined follow-up on one-year mortality ($p = 0.24$). Similarly, association between combined follow-up and one-year HF rehospitalization or death was similar across age categories (HR, 0.86 to 0.93, p for interaction = 0.74).

Regarding long-term outcome, the association of combined follow-up with lower mortality was more pronounced in patients under the age of 55 (HR 0.49 [0.37-0.64], $p < 0.0001$, p for interaction = 0.006).

Sensitivity analysis after the exclusion of patients who died within 2 months.

Following the exclusion of patients who died within 2 months of index hospital discharge, GP follow-up within 15 days was associated with a 7% lower one-year mortality (adjusted HR, 0.93 [0.90 to 0.97], $p = 0.0003$). Conversely, cardiologist and combined follow-up within 2 months demonstrated an even more substantial lower mortality (adjusted HR, 0.70 [0.67 to 0.73], $p < 0.0001$ and adjusted HR, 0.70 [0.67 to 0.74], $p < 0.0001$, respectively).

Follow-up by a cardiologist and combined follow-up within two months were also associated with an approximately 20% lower long-term mortality (adjusted HR, 0.77 [0.75 to 0.79], $p < 0.0001$ and 0.79 [0.77 to 0.82], $p < 0.0001$) while GP follow-up was neutrally associated with outcome (adjusted HR, 1.01 [0.98 to 1.03], $p = 0.57$). Supplementary Table 3.

Sensitivity analysis by income level according to access to complementary universal medical coverage

Out of the total patient population, 1749 (2.6%) had access to complementary universal medical coverage. Adjusting for access to CMU-C did not significantly modify the results, with the exception of long-term mortality, which showed only a marginal and non-significant modification (Supplementary Table 4). Furthermore, we observed no significant interaction between CMU-C status and combined follow-up on outcomes (Supplementary Table 5).

Sensitivity analysis using propensity score to account for baseline differences

Supplementary Table 6 displays the key baseline characteristics of patients based on follow-up, both before and after inverse probability weighting. In summary, after IPW, baseline characteristics were comparable among the four groups (ASMD < 0.1 for all). Compared with patients without FU, GP, cardiologist or combined FU was associated with a 7%,

15% et 10% higher one-year readmission for HF respectively and a 20%, 46% and 44% lower one-year mortality (adjusted HR, 0.80 [0.78 to 0.83], $p < 0.0001$ for GP FU, adjusted HR, 0.54 [0.52 to 0.57], $p < 0.0001$ for cardiologist FU and adjusted HR, 0.56 [0.53 to 0.59], $p < 0.0001$ for combined FU). In addition, GP FU was associated with a 9% decrease of one-year readmission for HF or mortality and long-term mortality whereas cardiologist and combined FU were associated with a 21% reduction of one-year readmission for HF or mortality and 30% and 28% reduction of long term mortality (table 5).

Discussion

We report herein the current use of post-discharge healthcare provider follow-up after a HF hospitalization and the association with HF readmission and mortality in the greater northeast region of France, using exhaustive data from the healthcare system. The main findings were: 1) less than 20% of patients had a combined follow-up (GP within 15 days, cardiologist within 2 months), 2) female sex, age >85 and comorbidities were associated with less combined follow-up, 3) combined follow-up was associated with a 9% reduction in composite outcome of one-year mortality or rehospitalization for HF, a 35% lower one-year mortality but 20% increase in annual HF readmission rate, 4) association of the combined follow-up with one-year mortality or a composite of HF readmission or mortality at one year was not significantly different across age category.

Epidemiology and determinants associated with healthcare follow-up

Despite the recommendation of the French “Haute Autorité de Santé” issued in 2014 which should theoretically guide practice in France, access to healthcare providers remained limited following HF hospitalization: only one out of two patients had a consultation with a GP within 2 weeks, one out of three with the cardiologist within two months and one out of five for the combined follow-up. This rate is lower than previously published data on hospitals with disease management programs including early follow-up at discharge which reported that two thirds of patients were seen within 14 days^{13,14}. Specialized follow-up has previously been reported to range from 9% to 31%^{13,15}. These differences are likely explained by differences in healthcare settings: the present study encompassed the data of all patients admitted for HF in a region of France. Of note, our study suggests that female sex, age and comorbidity have a marked impact on access to optimal care following HF hospitalization, particularly when considering cardiologist follow-ups. In a Swedish cohort, these criteria were also associated with less follow-up in specialized (primary) care¹⁶ or in nurse-led heart failure clinics¹⁷. The disparity in accessing optimal follow-up for women, older patients, or those with comorbidities is a concerning issue that requires in-depth research. Several potential factors may contribute to this inequality, such as limited patient autonomy leading to difficulties in accessing consultations, restrictions imposed by healthcare providers, underestimation of the severity of the condition or the perceived benefits of follow-up consultations by both patients and caregivers. Gaining a better understanding of these underlying reasons is essential to design specific interventions and enhance equitable access to high-quality follow-up care for all patient demographics. In comparison, GP consultations were less dependent on patient characteristics. Of note, despite a decline in cardiovascular mortality after HF hospitalization across all age groups¹⁸, there was a smaller decrease in older age groups which could partly be explained by limited access to optimal follow-up (especially cardiologist appointments).

Effect of combined follow-up on mortality

The effect of disease management programs on HF outcome is somewhat controversial. In a meta-analysis of 36 randomized clinical trials published between 1993 and 2005, the authors found a marginal reduction of 3% in mortality¹⁹. Although HF patients on optimal medical therapy with mild or moderate symptoms do not typically benefit from long-term follow-up in a specialized HF clinic and are safely managed by their GP²⁰, data are conversely difficult to interpret in unstable or severe patients and specialized follow-up is associated with a greater reduction in mortality^{21,22}. Indeed, worsening HF, defined by the deterioration of HF signs and symptoms requiring escalation of therapy, is a distinctive trajectory of patients with stage C HF^{23,24}, i.e., namely a very high risk of readmission even when receiving optimal HF therapy³⁻⁶. Despite the absence of definitive evidence in this setting, the ESC guidelines recommend (grade I level of evidence C) a follow-up at 1-2 weeks after discharge without specifying the professional responsible for this follow-up⁷. Our study is the first to assess individual and combined benefits of GP and cardiologist follow-ups in a modern era and performed using exhaustive data from health insurance. Cardiologist appointment was associated with a greater one-year mortality reduction compared with GP appointment (35% vs. 13% decrease in one-year mortality) even after adjusting for age, comorbidities, and HF readmission. The mortality reduction derived from this combined follow-up could be explained by several factors including 1) better congestion management, e.g. including ultrasound-guided strategies,^{25,26} which can reduce the detrimental burden of residual congestion^{1,27}, 2) early implementation of fast-acting drugs such as SGLT2i or sacubitril-valsartan^{4,28-30} whose effect may be more pronounced in the most severe patients^{4,31}. Importantly, the STRONG-HF trial recently highlighted that frequent outpatient visits, along with aggressive and rapid up-titration of current HF drugs is feasible and associated with a reduction in 180-day HF readmission or all-cause death³². Additionally, the results of this strategy demonstrated significant benefits across a wide range of ages and left ventricular ejection fraction (LVEF) spectrums in the study^{33,34}.

The differences in implementation of life-saving HF treatments by cardiologists comparatively to GPs have been described in other studies. Indeed, in the Swedish heart failure registry, non-cardiology care was associated with much lower use of beta-blockers and intracardiac devices, higher mortality, and lower risk of HF hospitalization³⁵. The significant p-value of the interaction between combined follow-up and heart failure rehospitalization on 1-year mortality strengthens this hypothesis. Rehospitalized patients predominantly receive specialized cardiac care during their hospital stay (including treatment implementation, risk factor correction, etc.). This cardiac management competes with outpatient follow-up and may explain the less pronounced effect of combined follow-up among rehospitalized patients. Conversely, for ambulatory patients, the entire implementation is facilitated through combined follow-up, explaining its more significant association. Similarly, ambulatory follow-up of HF patients by non-cardiology specialists was associated with lower use of mineralocorticoid receptor antagonists and cardiac resynchronization therapy^{36,37}.

Effect of combined follow-up on hospitalization

Combined follow-up was associated with a sizeable increase (19%) in one-year hospitalization. Follow-up by a cardiologist in our study was actually associated with a 24% higher HF readmission rate whereas GP appointment was associated with a 10% increase. Several hypotheses can be put forward to explain these results. First, the severity of symptoms could motivate a follow-up resulting in a higher risk for HF hospitalization due to an intrinsically higher risk profile. In a study assessing patients with acute HF hospitalization, most patients stated that the diagnosis was frequently (41.5%) made by their cardiologist³⁸, which suggests that cardiologists are sought in instances of ambulatory

decompensation in a number of cases. Second, cardiologists benefit from a network which can facilitate hospitalizations, particularly in the cardiology units³⁸.

Although the differential association of combined follow-up with hospitalization versus mortality may appear surprising, it has already been described¹⁷. Recently, the subpopulation of patients (5%) included in the ESC EORP Heart Failure Long-Term Registry participating to randomized clinical trial (RCT) experienced 19% all-cause mortality reduction and a non-significant 9% higher risk of HF rehospitalization³⁹. The hypothesis proposed by the authors to explain this apparent contradiction is the selection in RCT of a population with presumably modifiable HF events and above all, a better follow-up which is concordant with our findings. In the opposite direction, implementation of a hospital readmissions reduction program (HRRP) in the United States was associated with a 30-day readmission reduction while having a neutral to deleterious effect on mortality^{40,41}. Moreover, the increase in mortality for HF after implementation of the HRRP was mainly driven by patients who were not readmitted within 30 days of discharge⁴¹. While hospitalization was associated with a threefold increased risk of one-year mortality in our cohort, it also constitutes a key moment for treatment optimization and comorbidity management.

Impact in clinical practice

Only 20% of patients had a combined follow-up with limited access in the oldest, comorbid, and female patients. In light of the 35% lower risk of death in patients managed according to a combined GP/cardiologist follow-up after HF decompensation, this approach should be further promoted and implemented.

Of further importance, the effect of combined follow-up on one-year mortality and on the composite outcome of one-year rehospitalization or death was similar across all age groups. Patients over 85 years of age have three times less access to a combined follow-up even though they are a priority target for public health because of the large number of patients, the high event rate, and the identical effectiveness of follow-up.

On the other hand, given that the long-term benefits appeared even greater in patients < 55 years of age (association with a reduction of mortality by 2, particular attention to the implementation of early discharge follow-up should be paid in the youngest patients with HF, even if they are perceived as being less at risk of events. Accordingly, all young patients with HF may benefit from a follow-up with a cardiologist after discharge to target an improved long-term survival (possibly because of better/greater HF medication implementation).

Limitations

The main limitation of our study resides in its retrospective observational design, which prevents the establishment of causal relationships for all the described associations. Additionally, several important confounders, including clinical variables (e.g., creatinine, NTproBNP), echocardiographic parameters (such as left ventricular ejection fraction and filling pressure), and treatment associated with HF prognosis, were not assessed, which could have influenced the association with outcome. Similarly, HF nurse follow-up and telemedicine use were marginal in France and were not assessed. To validate our findings, demonstrating a decrease in cardiovascular mortality would have been intriguing. Nonetheless, it's crucial to recognize that mortality attributed to cardiovascular reasons, as documented in death certificates, is frequently accompanied by uncertainty and tends to be overstated^{42,43}. However, we can assume that one of the main benefits of the cardiologist consultation was the optimization of medication and cardiac devices.

The follow-up of heart failure, the organization of care and the reimbursement of specialists are specific to each country. However, the generalizability of our results remains possible in most Western countries that include GPs and cardiologists in their HF follow-up.

Conclusion

In this analysis performed on exhaustive data from the healthcare system, only 20% of patients had a combined follow-up after heart failure hospitalization soon after discharge from HF hospitalization. Combined follow-up was associated with a clinically significant reduction in mortality despite the increased risk of HF readmission. As the benefit of combined follow-up on one-year mortality and the composite outcome of one-year rehospitalization or mortality appeared similar across age categories, we should pay particular attention to elderly patients, who have limited access to combined follow-up.

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Conflict of interest

GB reports consulting fees from AstraZeneca, Boehringer-Ingelheim and Abbott, outside the submitted work. OP has nothing to disclose. PT has nothing to disclose. ZL has nothing to disclose. NA has nothing to disclose. NG reports personal fees from AstraZeneca, Bayer, Boehringer, Novartis and Vifor outside the submitted work. GS reports grants and personal fees from Vifor, grants and non-financial support from Boehringer Ingelheim, grants and personal fees from AstraZeneca, personal fees from Roche, personal fees from Servier, grants and personal fees from Novartis, grants and personal fees from Cytokinetics, personal fees from Medtronic, grants from Boston Scientific, grants and personal fees from Pharmacosmos, grants from Merck, grants from Bayer, funding through the Horizon 2022 programme, outside the submitted work. JPF has nothing to disclose.

Data availability statement

This study was performed using the PMSI (Programme de Médicalisation des Systèmes d'Information) French national database and restrictions apply to the availability of these data, which were used under license for this study.

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Tables

Table 1: Baseline characteristics of the study population

	Global (N=67476)	No follow-up	Cardiologist follow-up within 2 months	GP follow-up within 15 days	Combined follow-up (Cardiologist and GP)	In-hospital death	p-value
Number of patients, n (%)		21014 (33.8 %)	7915 (12.7 %)	20096 (32.3 %)	13131 (21.1 %)	5320 (7.9%)	
Male, n (%)	31979 (47.4 %)	9071 (43.2 %)	4396 (55.5 %)	8954 (44.6 %)	7100 (54.1 %)	2458 (46.2%)	<0.0001
Age, mean ± sd	80.3 ± 11.3	81.4 ± 11.3	76.2 ± 12.0	81.6 ± 10.7	77.2 ± 11.3	84.8 ± 9.0	<0.0001
< 55 years	2063 (3.1 %)	573 (2.7 %)	425 (5.4 %)	451 (2.2 %)	573 (4.4 %)	41 (0.8 %)	<0.0001
55-64 years	4552 (6.7 %)	1284 (6.1 %)	840 (10.6 %)	1101 (5.5 %)	1172 (8.9 %)	155 (2.9 %)	
65-74 years	10815 (16.0 %)	2996 (14.3 %)	1814 (22.9 %)	2775 (13.8 %)	2747 (20.9 %)	483 (9.1 %)	
75-84 years	21105 (31.3 %)	5977 (28.4 %)	2633 (33.3 %)	6259 (31.1 %)	4838 (36.8 %)	1398 (26.3 %)	
≥ 85 years	28941 (42.9 %)	10184 (48.5 %)	2203 (27.8 %)	9510 (47.3 %)	3801 (28.9 %)	3243 (61.0 %)	
Length of hospital stay, days, mean ± sd	10.5 ± 8.5	11.8 ± 10.1	8.7 ± 6.8	10.8 ± 7.6	8.7 ± 5.8	10.9 ± 11.0	<0.0001
Charlson Score, mean ± sd	4.8 ± 2.9	4.9 ± 2.9	4.5 ± 2.8	4.9 ± 2.9	4.6 ± 2.9	4.8 ± 2.9	<0.0001
Charlson comorbidity score							
Score=2, n (%)	14089 (20.9 %)	4085 (19.4 %)	2067 (26.1 %)	3698 (18.4 %)	3171 (24.1 %)	1068 (20.1 %)	<0.0001
2<Score≤4, n (%)	25743 (38.2 %)	7907 (37.6 %)	2975 (37.6 %)	7773 (38.7 %)	5104 (38.9 %)	1984 (37.3 %)	
Score>4, n (%)	27644 (41.0 %)	9022 (42.9 %)	2873 (36.3 %)	8625 (42.9 %)	4856 (37.0 %)	2268 (42.6 %)	
Chronic obstructive pulmonary disease, n (%)	20626 (30.6 %)	6552 (31.2 %)	2154 (27.2 %)	6670 (33.2 %)	3756 (28.6 %)	1494 (28.1 %)	<0.0001
Diabetes mellitus, n (%)	28824 (42.7 %)	8589 (40.9 %)	3425 (43.3 %)	9017 (44.9 %)	5903 (45.0 %)	1890 (35.5 %)	<0.0001
Chronic renal disease, n (%)	29095 (43.1 %)	9151 (43.5 %)	3221 (40.7 %)	8906 (44.3 %)	5491 (41.8 %)	2326 (43.7 %)	<0.0001
Complementary universal medical coverage	1749 (2.6 %)	570 (2.7 %)	277 (3.5 %)	464 (2.3 %)	370 (2.8 %)	68 (1.3 %)	<0.0001

Table 2: Initial occurrence of events of interest after discharge

	Whole cohort	< 55	55-64	65-74	75-84	≥ 85	p-value
Appointment with a GP							<0.0001
median delay, days ^a	11	14	13	12	10	10	
proportion at 15 days	52.6%	49.4%	50.6%	52.2%	55.3%	51.3%	
proportion at 1 month	71.2%	68.9%	71.6%	72.6%	74.6%	68.1%	
proportion at 2 months	83.6%	81.6%	84.6%	85.4%	86.5%	80.6%	
proportion at 3 months	87.6%	86.5%	89.0%	89.7%	90.1%	84.5%	
Appointment with a cardiologist							<0.0001
median delay, days ^b	57	46	49	50	56	67	
proportion at 1 month	20.8%	31.3%	28.6%	27.9%	23.2%	13.7%	
proportion at 2 months	35.4%	49.2%	46.6%	45.1%	39.2%	25.1%	
proportion at 3 months	43.9%	59.4%	56.5%	54.9%	48.5%	31.8%	
median delay, days ^c	25	21	23	24	25	27	<0.0001
Combined follow-up within 2 months *	21.1 %	28.3 %	26.6 %	26.6 %	24.5 %	14.8 %	
Readmission for HF							<0.0001
median delay, days ^d	189	167.5	181.0	206.5	197.0	179.0	
proportion at 1 month	6.5%	4.9%	6.3%	6.1%	6.9%	6.5%	
proportion at 2 months	10.3%	7.2%	9.3%	9.7%	10.9%	10.6%	
proportion at 3 months	13.1%	8.7%	11.3%	12.2%	13.6%	13.6%	
proportion at 6 months	18.5%	11.2%	15.4%	16.8%	19.5%	19.6%	
proportion at 1 year	26.1%	15.1%	20.6%	23.4%	27.4%	28.4%	
Mortality							<0.0001
median delay, days, ^e	272.0	332.0	367.0	349.5	332.0	214.0	
proportion at 1 month	5.9%	1.3%	2.7%	3.5%	4.7%	8.6%	
proportion at 3 months	12.5%	3.5%	5.4%	7.9%	10.6%	17.7%	
proportion at 6 months	18.4%	6.0%	8.4%	12.4%	15.9%	25.5%	
proportion at 1 year	27.1%	8.9%	13.8%	18.4%	24.0%	36.6%	

^a Only considered in patients with GP follow-up

^b Only considered in patients with cardiologist follow-up

^c Only considered in patients with combined follow-up

^d Only considered in patients with HF readmission

^e Only considered in deceased patients

* GP within 15 days and cardiologist within 2 months

Table 3: Multivariate analysis of parameters associated with post-discharge follow-up

		Combined post-discharge FU analysis		Cardiologist within 2 months post-discharge FU analysis		GP within 15 days post-discharge FU analysis	
		OR (95% confidence interval)	p-value	OR (95% confidence interval)	p-value	OR (95% confidence interval)	p-value
Age	< 55	2.32 (2.09 - 2.57)	< 0.0001	3.20 (2.91 - 3.51)	< 0.0001	1.14 (1.05 - 1.25)	0.0033
	55 - 64	2.17 (2.01 - 2.34)	< 0.0001	2.83 (2.65 - 3.02)	< 0.0001	1.16 (1.09 - 1.24)	< 0.0001
	65 - 74	2.18 (2.06 - 2.31)	< 0.0001	2.69 (2.56 - 2.83)	< 0.0001	1.22 (1.16 - 1.27)	< 0.0001
	75 - 84	1.95 (1.86 - 2.04)	< 0.0001	2.07 (1.99 - 2.16)	< 0.0001	1.30 (1.25 - 1.34)	< 0.0001
	≥ 85	1 (reference)	-	1 (reference)	-	1 (reference)	-
Sex	Female	0.82 (0.79 - 0.85)	< 0.0001	0.77 (0.75 - 0.80)	< 0.0001	0.97 (0.94 - 0.99)	< 0.0001
	Male	1 (reference)	-	1 (reference)	-	1 (reference)	-
Comorbidities (Charlson score at inclusion)	Score=2 (HF only)	1 (reference)	-	1 (reference)	-	1 (reference)	-
	2<Score≤4	0.84 (0.80 - 0.88)	< 0.0001	0.76 (0.73 - 0.80)	< 0.0001	1.05 (1.00 - 1.09)	0.0322
	Score>4	0.69 (0.66 - 0.73)	< 0.0001	0.60 (0.58 - 0.63)	< 0.0001	0.98 (0.94 - 1.02)	0.3282

Combined post-discharge follow-up was defined as GP appointment within 15 days and cardiologist appointment within 2 months. FU: follow-up; GP: general practitioner; OR: odds ratio.

Adjustment for age, sex, comorbidities (Charlson score at inclusion).

Table 4: Association of GP, Cardiologist and combined follow-up with one-year and long-term outcome in Cox regression

		One-year HF readmission *		One-year mortality**		One-year HF readmission or mortality **		Long-term mortality **	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Adjusted model considering combined follow-up with no follow-up as reference	Combined follow-up (both GP and Cardiologist)	1.19 (1.15 - 1.24)	<0.0001	0.65 (0.62 - 0.68)	< 0.0001	0.91 (0.88 - 0.94)	< 0.0001	0.74 (0.72 - 0.77)	<0.0001
	Readmission for HF			3.33 (3.21 - 3.44)	< 0.0001			2.81 (2.75 - 2.88)	<0.0001
Adjusted model considering GP or cardiologist follow-up individually with no follow-up as reference	GP follow-up within 15 days	1.10 (1.06 - 1.13)	<0.0001	0.87 (0.85 - 0.90)	< 0.0001	0.99 (0.97 - 1.02)	0.45	0.95 (0.93 - 0.97)	<0.0001
	Cardiologist follow-up within 2 months	1.24 (1.19 - 1.28)	< 0.0001	0.65 (0.62 - 0.67)	< 0.0001	0.94 (0.91 - 0.97)	< 0.0001	0.72 (0.71 - 0.74)	<0.0001
	Readmission for HF			3.37 (3.26 - 3.49)	< 0.0001			2.84 (2.77 - 2.90)	<0.0001

GP: general practitioner; HF: heart failure; HR: hazard ratio.

Models adjusted for age, sex, and comorbidities (Charlson score at inclusion)

* Fine and Gray model with death as competing risk

**Cox regression model with readmission for heart failure and follow-up (combined or GP and cardiologist) as time variant covariables

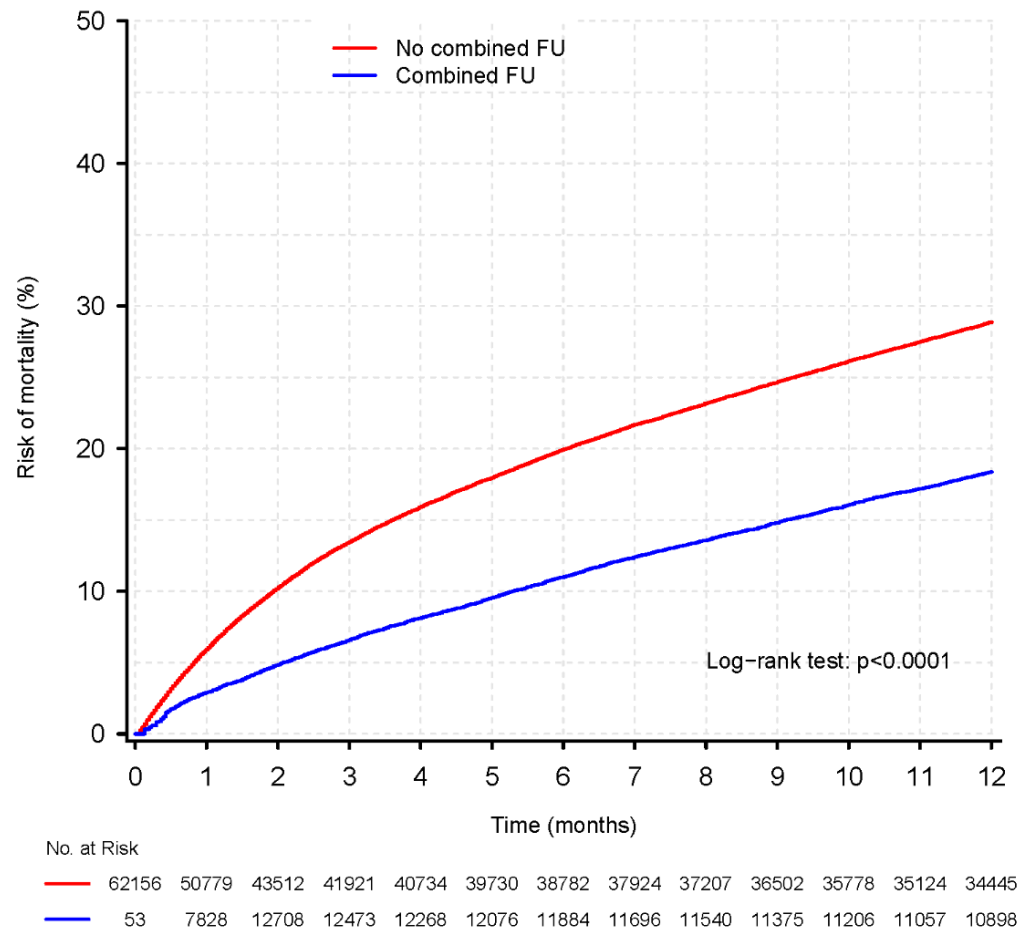
Table 5: Association of GP, Cardiologist and combined follow-up with one-year and long-term outcome in Cox regression after inverse probability weighting

	One-year readmission for HF		One-year mortality		One-year readmission for HF or mortality		Long-term mortality	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Combined follow-up (both GP and Cardiologist)	1.10 (1.06 - 1.15)	<0.0001	0.56 (0.53 - 0.59)	<0.0001	0.79 (0.76 - 0.81)	<0.0001	0.72 (0.70 - 0.74)	<0.0001
GP follow-up within 15 days	1.07 (1.03 - 1.11)	0.0002	0.80 (0.78 - 0.83)	<0.0001	0.91 (0.88 - 0.93)	<0.0001	0.91 (0.89 - 0.93)	<0.0001
Cardiologist follow-up within 2 months	1.15 (1.11 - 1.19)	<0.0001	0.54 (0.52 - 0.57)	<0.0001	0.79 (0.76 - 0.81)	<0.0001	0.70 (0.68 - 0.72)	<0.0001

Figures

Figure 1: Event curves for one-year mortality (A) and one-year heart failure rehospitalization (B) according to follow-up (FU)

A



B

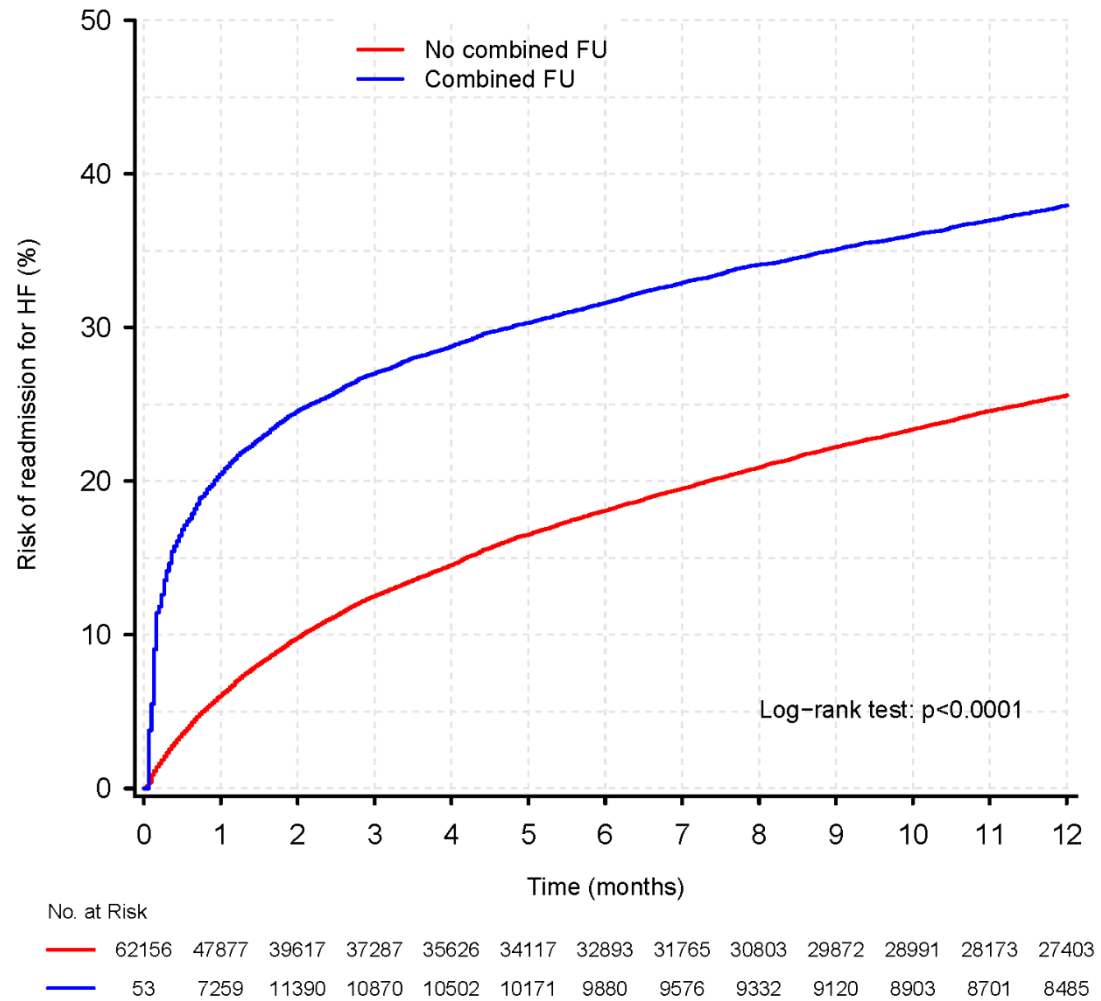
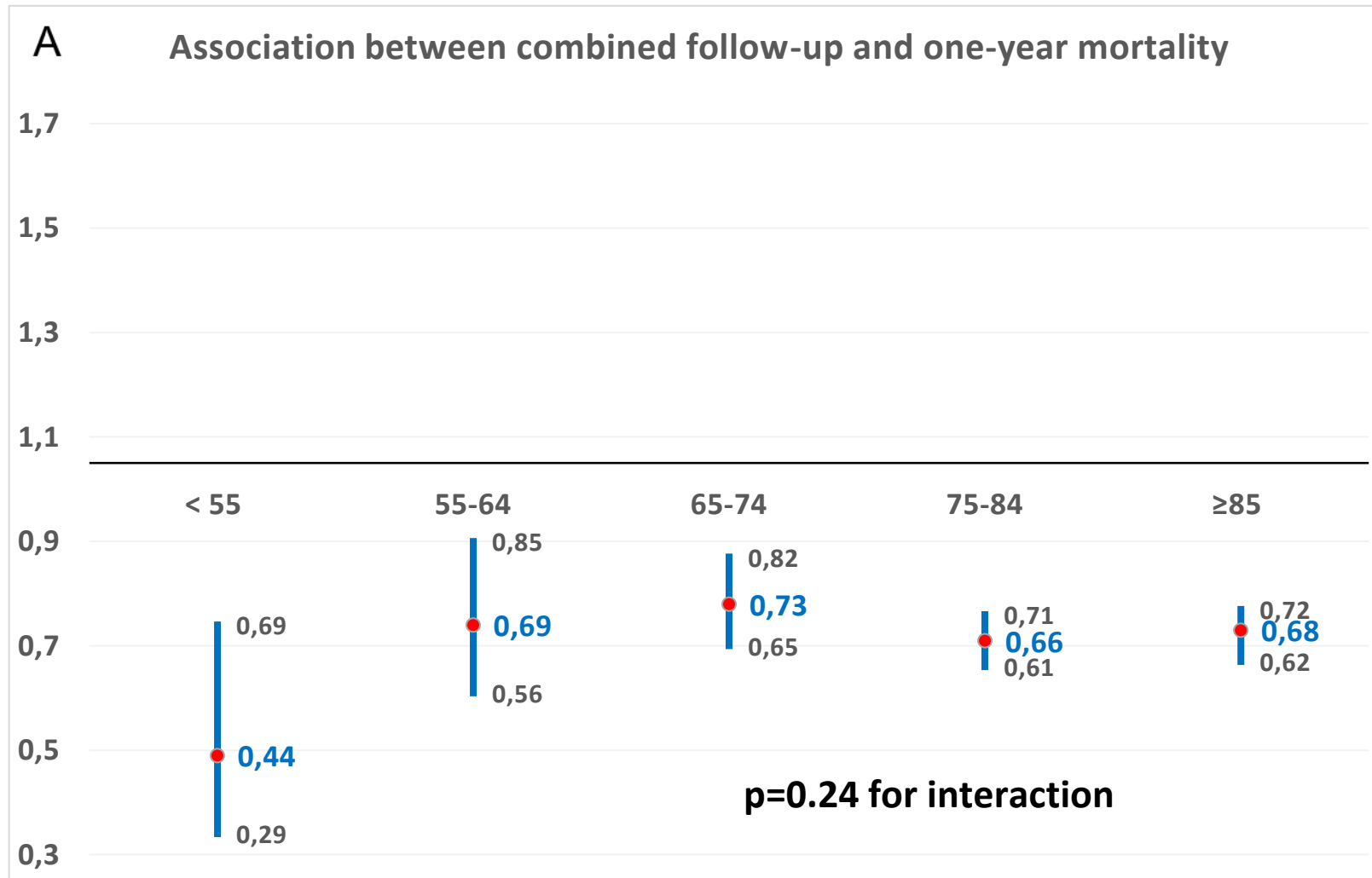
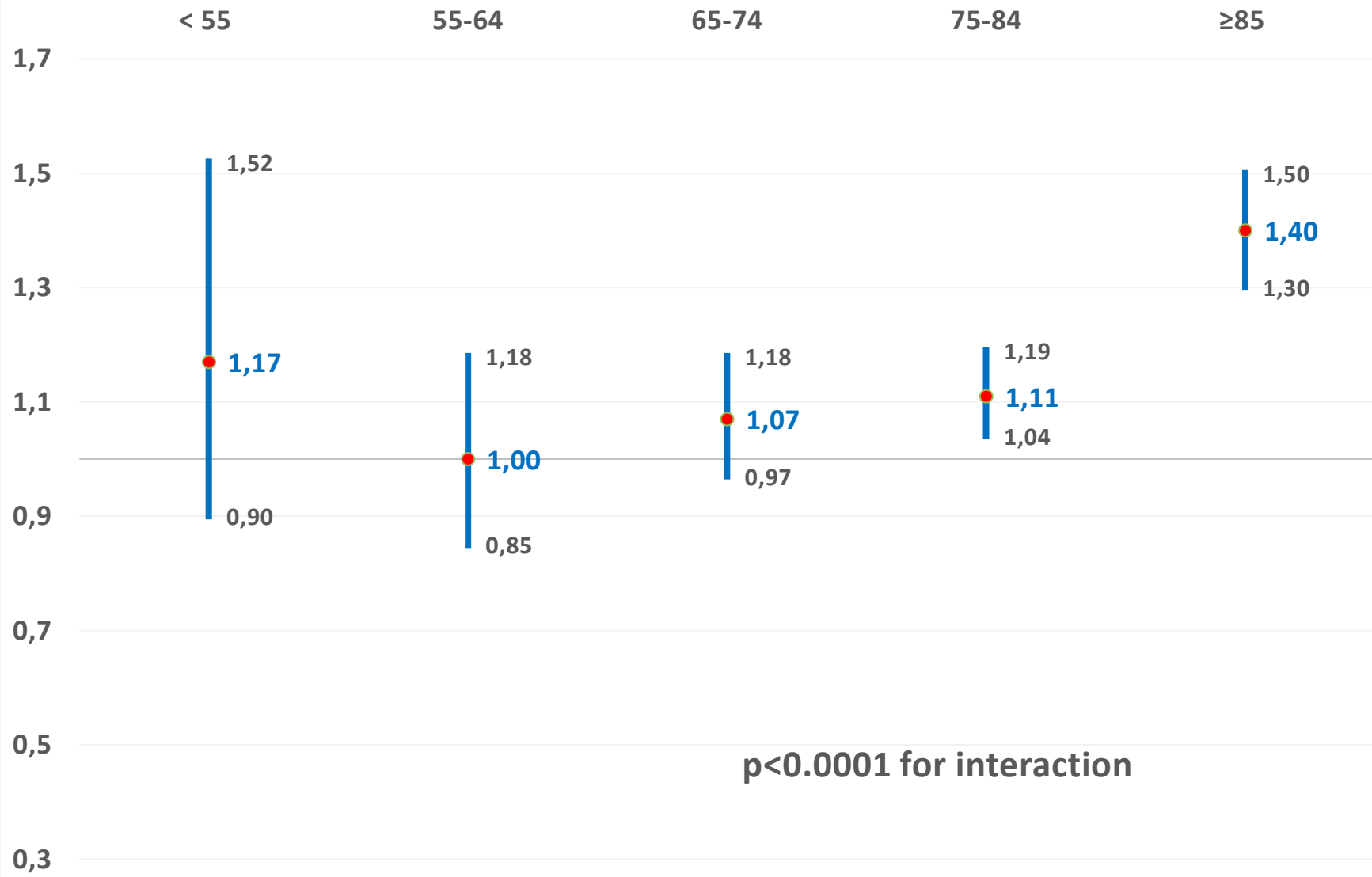


Figure 2: Association between combined follow-up and mortality (A) and rehospitalization (B) at one-year according to age categories



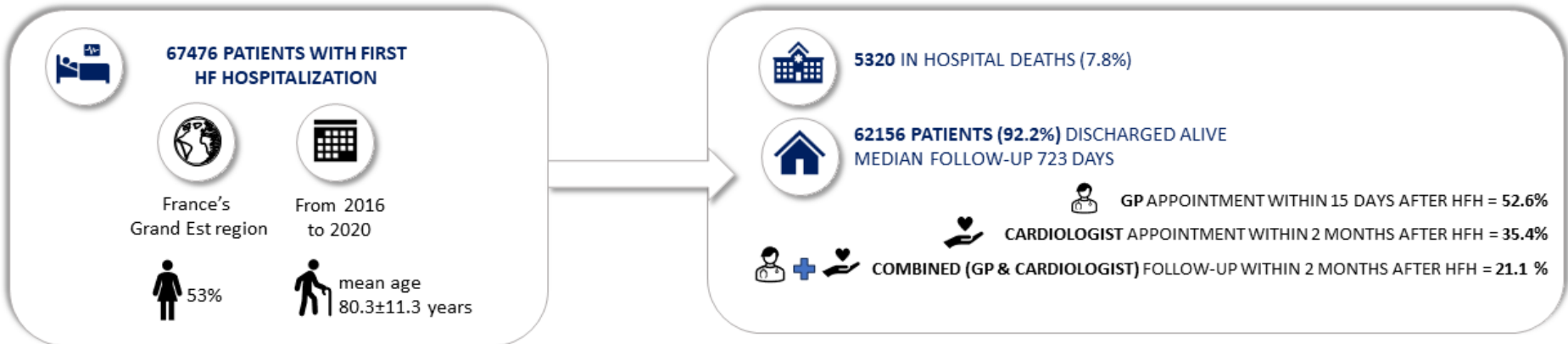
B

Association between combined follow-up and one-year rehospitalization



Graphical Abstract

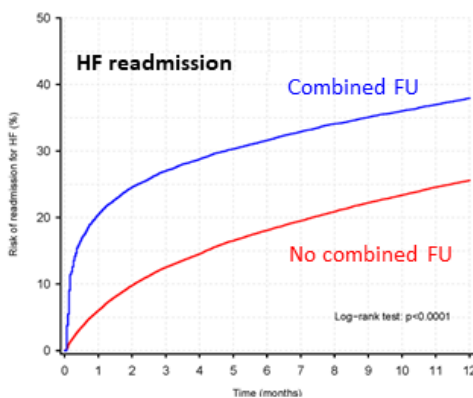
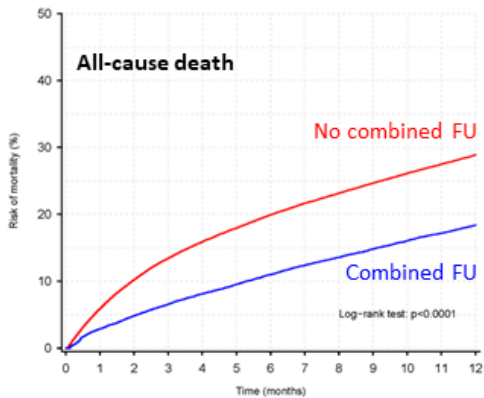
Risk of readmission and death after hospitalization for worsening heart failure: Role of post-discharge follow-up visits in a real-world study from the Grand Est Region of France



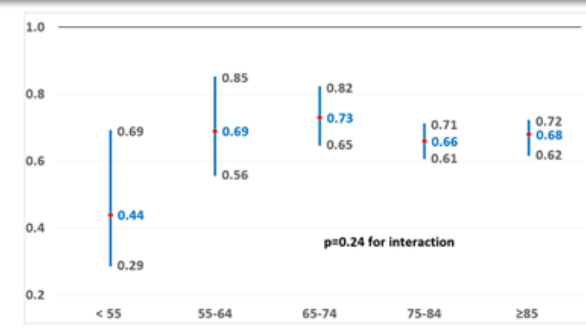
POST-DISCHARGE COMBINED (GP & CARDIOLOGIST) FOLLOW-UP

↓↓ MORTALITY
Adjusted HR=0.65, 0.62-0.68, p<0.0001

↑ HF READMISSION
Adjusted HR=1.19, 1.15-1.24, p<0.0001



ASSOCIATION BETWEEN COMBINED (GP & CARDIOLOGIST) FOLLOW-UP AND ONE-YEAR MORTALITY



- Combined GP & Cardiologist follow-up after HFH :**
- One patient out of 5
 - ↓ 35 % mortality
 - ↑ 19 % more HF rehospitalization

Supplementary material

Supplementary Table 1: Multivariate analysis of parameters associated with post-discharge follow-up excluding patients who died before 15 days for GP follow-up and before 2 months for cardiologist or combined follow-up

		Combined post-discharge FU analysis		Cardiologist within 2 months post-discharge FU analysis		GP within 15 days post-discharge FU analysis	
		OR (95% confidence interval)	p-value	OR (95% confidence interval)	p-value	OR (95% confidence interval)	p-value
Age	< 55	1.86 (1.67 – 2.06)	< 0.0001	2.52 (2.30 – 2.78)	< 0.0001	0.91 (0.83 – 1.00)	0.0528
	55 - 64	1.77 (1.64 – 1.91)	< 0.0001	2.32 (2.17 – 2.49)	< 0.0001	0.96 (0.90 - 1.02)	0.1944
	65 - 74	1.84 (1.73 – 1.95)	< 0.0001	2.29 (2.18 - 2.41)	< 0.0001	1.03 (0.98 - 1.08)	0.2335
	75 - 84	1.74 (1.66 – 1.83)	< 0.0001	1.87 (1.79 – 1.95)	< 0.0001	1.18 (1.13 - 1.22)	< 0.0001
	≥ 85	1 (reference)	-	1 (reference)	-	1 (reference)	-
Sex	Female	0.79 (0.76 - 0.83)	< 0.0001	0.74 (0.71 - 0.76)	< 0.0001	0.93 (0.90 - 0.96)	< 0.0001
	Male	1 (reference)	-	1 (reference)	-	1 (reference)	-
Comorbidities (Charlson score at inclusion)	Score=2 (HF only)	1 (reference)	-	1 (reference)	-	1 (reference)	-
	2<Score≤4	0.85 (0.81 - 0.90)	< 0.0001	0.76 (0.73 - 0.79)	< 0.0001	1.05 (1.00 - 1.10)	0.0313
	Score>4	0.71 (0.67 - 0.75)	< 0.0001	0.61 (0.59 - 0.64)	< 0.0001	0.99 (0.95 - 1.04)	0.9105

Supplementary Table 2: Association between combined follow-up and outcomes according to age category

	Readmission for HF at one year		One-year mortality		Readmission for HF or mortality at one year		Long-term mortality	
	HR (CI 95 %)	p-value	HR (CI 95 %)	p-value	HR (CI 95 %)	p-value	HR (CI 95 %)	p-value
<55 years	1.17 (0.90 - 1.52)	0.24	0.44 (0.29 - 0.69)	0.0003	0.88 (0.70 - 1.11)	0.061	0.49 (0.37 - 0.64)	<0.0001
55-64 years	1.00 (0.85 - 1.18)	0.95	0.69 (0.56 - 0.85)	0.0005	0.86 (0.75 - 0.99)	0.0002	0.71 (0.63 - 0.81)	<0.0001
65-74 years	1.07 (0.97 - 1.18)	0.19	0.73 (0.65 - 0.82)	<0.0001	0.89 (0.82 - 0.96)	0.036	0.73 (0.68 - 0.79)	<0.0001
75-84 years	1.11 (1.04 - 1.19)	0.003	0.66 (0.61 - 0.71)	<0.0001	0.89 (0.84 - 0.94)	0.0007	0.78 (0.75 - 0.82)	<0.0001
>=85 years	1.40 (1.30 - 1.50)	<0.0001	0.68 (0.63 - 0.72)	<0.0001	0.93 (0.88 - 0.98)	0.038	0.78 (0.75 - 0.82)	<0.0001
Interaction p-value:	<0.0001		0.24		0.74		0.006	

Supplementary Table 3: Association of GP, Cardiologist and combined follow-up with one-year and long-term outcome in Cox regression excluding patients deceased before 2 months

		One-year mortality analysis		Long-term mortality analysis	
		HR (95% CI)	p-value	HR (95% CI)	p-value
Adjusted model considering combined follow-up with no follow-up as reference	Combined follow-up within 2 months	0.70 (0.67 - 0.74)	<0.0001	0.79 (0.77 - 0.82)	<0.0001
	Readmission for HF within 2 months	2.01 (1.91 - 2.12)	<0.0001	1.55 (1.49 - 1.61)	<0.0001
Adjusted model considering GP or cardiologist follow-up individually with no follow-up as reference	GP follow-up within 15 days	0.93 (0.90 - 0.97)	0.0003	1.01 (0.98 - 1.03)	0.57
	Cardiologist follow-up within 2 months	0.70 (0.67 - 0.73)	<0.0001	0.77 (0.75 - 0.79)	<0.0001
	Readmission for HF within 2 months	2.04 (1.93 - 2.15)	<0.0001	1.56 (1.50 - 1.62)	<0.0001

GP: general practitioner; HF: heart failure; HR: hazard ratio.

Cox regression model with readmission for heart failure and follow-up (combined or GP and cardiologist) as time variant covariables. Models adjusted for age, sex, and comorbidities (Charlson score at inclusion)

Supplementary Table 4: Association of GP, cardiologist and combined follow-up with one-year and long-term outcome in Cox regression with adjustment for access to complementary universal medical coverage (on top of age, sex and comorbidities).

		One-year readmission for HF		One-year mortality		One-year readmission for HF or mortality		Long-term mortality	
		HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Adjusted model considering combined follow-up with no follow-up as reference	Combined follow-up	1.20 (1.15 - 1.25)	<0.0001	0.65 (0.62 - 0.68)	< 0.0001	0.91 (0.88 - 0.94)	< 0.0001	0.74 (0.72 - 0.77)	<0.0001
	Readmission for HF^a			3.33 (3.21 - 3.44)	< 0.0001			2.81 (2.75 - 2.88)	<0.0001
Adjusted model considering GP or cardiologist follow-up individually with no follow-up as reference	GP follow-up	1.13 (1.09 - 1.17)	<0.0001	0.87 (0.85 - 0.90)	< 0.0001	0.99 (0.97 - 1.02)	0.45	0.95 (0.93 - 0.97)	<0.0001
	Cardiologist follow-up	1.27 (1.22 - 1.32)	< 0.0001	0.65 (0.62 - 0.67)	< 0.0001	0.94 (0.91 - 0.97)	< 0.0001	0.72 (0.71 - 0.74)	<0.0001
	Readmission for HF			3.37 (3.26 - 3.49)	< 0.0001			2.84 (2.77 - 2.90)	<0.0001

GP: general practitioner; HF: heart failure; HR: hazard ratio.

Cox regression model with readmission for heart failure and follow-up (combined or GP and cardiologist) as time variant covariables. Models adjusted for age, sex, and comorbidities (Charlson score at inclusion)

Supplementary Table 5: Interaction between complementary universal medical coverage status and combined FU (dependent-time variable) on outcomes

CMU-C status	One-year readmission for HF			One-year mortality			One-year readmission for HF or mortality			Long-term mortality		
	HR (CI 95 %)	p-value	Interaction p-value	HR (CI 95 %)	p-value	Interaction p-value	HR (CI 95 %)	p-value	Interaction p-value	HR (CI 95 %)	p-value	Interaction p-value
No CMU-C	1.16 (1.11 - 1.21)	<0.0001	0.69	0.61 (0.58 - 0.64)	<0.0001	0.77	0.84 (0.82 - 0.87)	<0.0001	0.78	0.70 (0.68 - 0.72)	<0.0001	0.28
CMU-C	1.09 (0.84 - 1.43)	0.51		0.64 (0.46 - 0.90)	0.011		0.87 (0.70 - 1.09)	0.23		0.61 (0.48 - 0.77)	<0.0001	1

CMU-C = complementary universal medical coverage

Supplementary Table 6: Baseline characteristics according to follow-up before and after inverse probability weighting

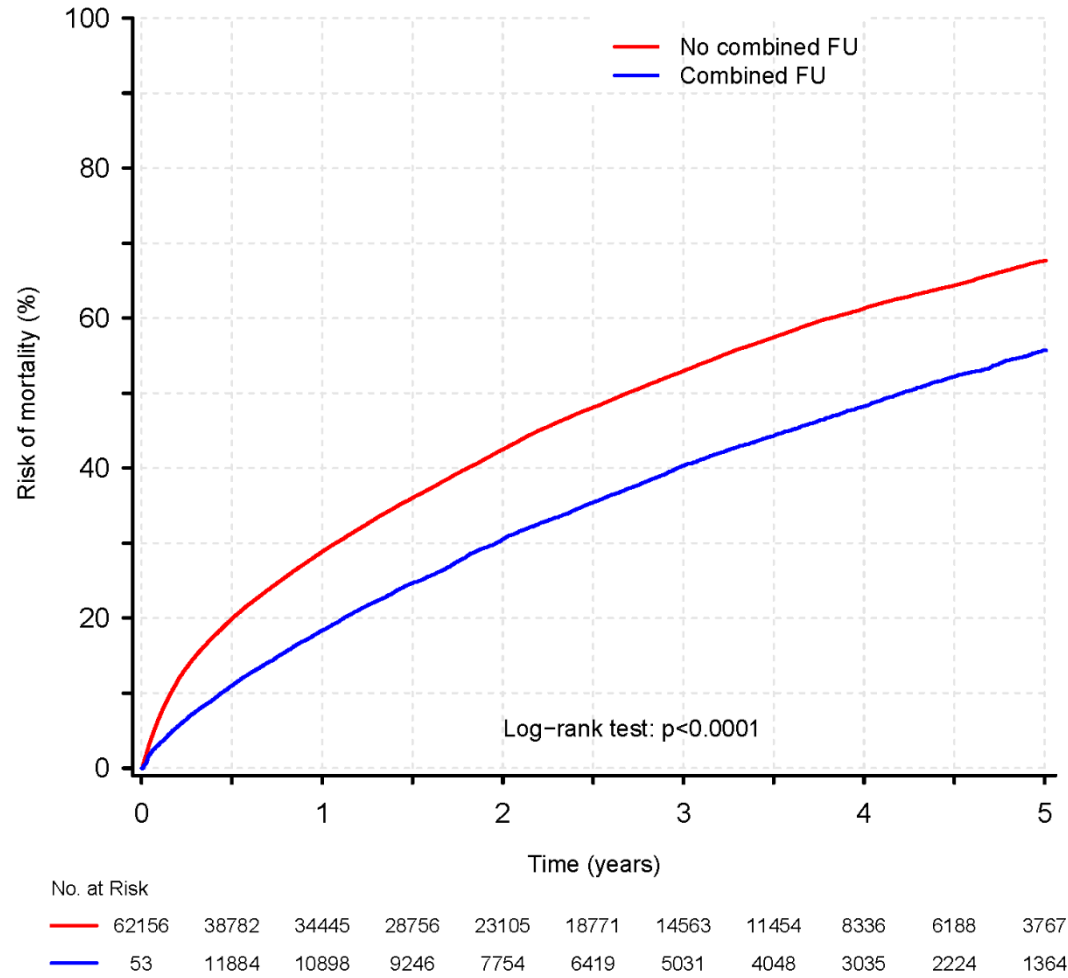
Before IPW					ASMD
	No Follow-up	Cardiologist Follow-up	GP Follow-up	Combined Follow-up	
Sum of weights	21014	7915	20096	13131	
Age, years	81.4 ± 11.3	76.2 ± 12.0	81.6 ± 10.7	77.2 ± 11.3	0.296
Female, n (%)	11943 (56.8%)	3519 (44.5%)	11142 (55.4%)	6031 (45.9%)	0.156
Length of stay, days	11.8 ± 10.1	8.7 ± 6.8	10.8 ± 7.6	8.7 ± 5.8	0.245
Score de Charlson	4.9 ± 2.9	4.5 ± 2.8	4.9 ± 2.9	4.6 ± 2.9	0.085
CMU-C status	570 (2.7%)	277 (3.5%)	464 (2.3%)	370 (2.8%)	0.037

After IPW					ASMD
	No Follow-up	Cardiologist Follow-up	GP Follow-up	Combined Follow-up	
Sum of weights	21083.9	7903.5	20096.5	12965.6	
Age, years	79.6 ± 12.4	79.4 ± 10.6	79.8 ± 11.7	79.2 ± 10.3	0.030
Female, n (%)	11008.2 (52.2 %)	4143.5 (52.4 %)	10569.4 (52.6 %)	6646.8 (51.3 %)	0.014
Length of stay, days	10.3 ± 8.5	10.8 ± 9.3	10.5 ± 7.4	10.1 ± 7.5	0.045
Score de Charlson	4.8 ± 2.9	4.8 ± 3.0	4.8 ± 2.9	4.8 ± 3.0	0.006
CMU-C status	584.7 (2.8 %)	222.4 (2.8 %)	556.2 (2.8 %)	375.5 (2.9 %)	0.004

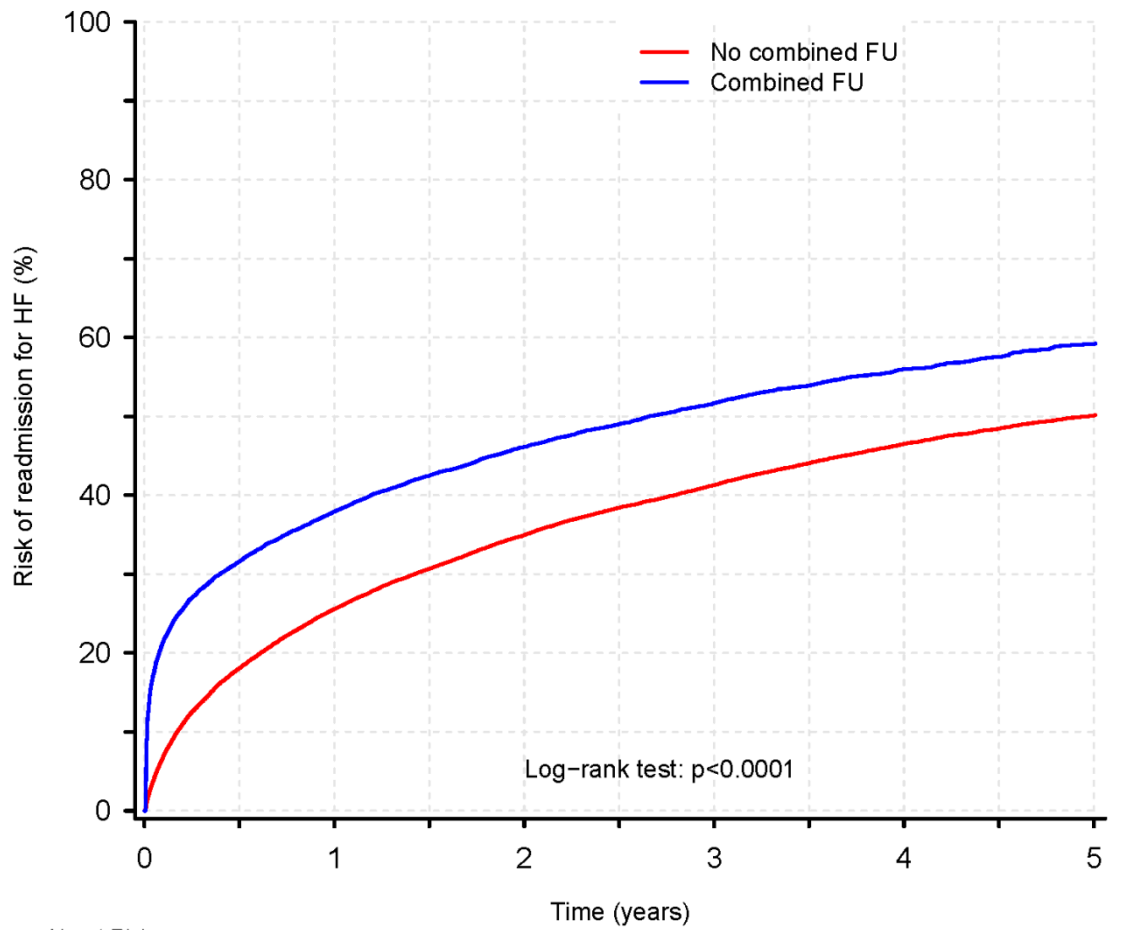
IPW= inverse probability weighting

Supplementary Figure 1: Event curves for mortality (A) and heart failure rehospitalization (B) according to follow-up (FU)

A



B



No. at Risk

—	62156	32893	27403	21840	16799	13244	9998	7681	5451	3990	2388
—	53	9880	8485	6859	5553	4451	3380	2634	1931	1402	839