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SUPPLEMENTAL APPENDIX

Association between a hospitalization for heart failure and the initiation/discontinuation of guideline-recommended treatments - An analysis from the Swedish heart failure registry

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8 *SwedeHF Study cohort*

9 SwedeHF is an ongoing nationwide registry prospectively enrolling in- and out-patients since
10 May 11th 2000. Until April 2017, clinician-judged HF was the only enrollment criterion. Thereafter,
11 patients were enrolled when a HF diagnosis according to the International Statistical Classification of
12 Diseases, Tenth Revision (ICD-10) codes I50.0, I50.1, I50.9, I42.0, I42.6, I42.7, I25.5, I11.0, I13.0,
13 I13.2 was recorded. Beyond the ~80 variables which are recorded at index date (day of hospital
14 discharge for in-patients and of an out-patient visit for out-patients) in SwedeHF, further data were
15 obtained by linkage with other nationwide registries through the Swedish Personal Identification
16 Number, i.e., to the National Patient Register which provided additional comorbidities and data on
17 hospitalizations, to Statistics Sweden which collects socioeconomic data, to the National Prescribed
18 Drug Register which provided data on the dispensed treatments, and to the Cause of Death Register
19 which reports date and cause of death. Further information on this study, e.g., the definition of
20 comorbidities via ICD-10 codes, is provided at <https://kiheartfailure.github.io/shfdb3/>.

21 This study, including the linkage of SwedeHF to other nationwide registries, was approved by
22 the Swedish Ethical Review Authority and was designed and conducted in agreement with the
23 Declaration of Helsinki. Individual patient consent is not requested, but patients are informed about
24 enrollment and can opt out.

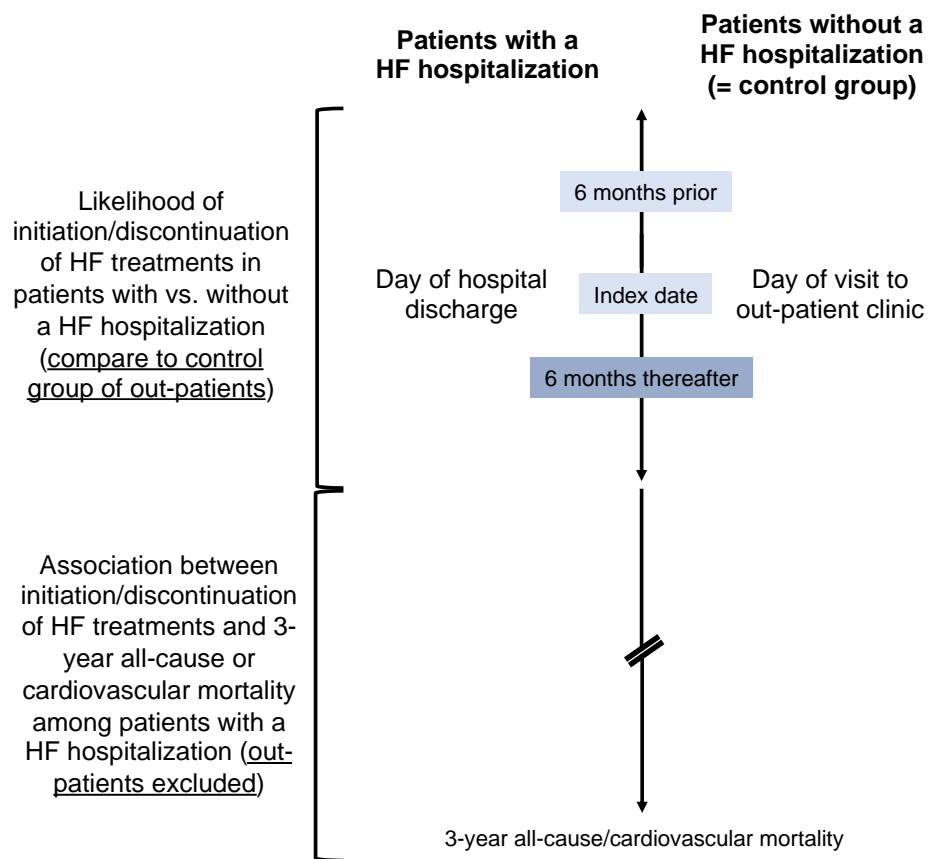
25 *Supplement Table 1. Association between a heart failure hospitalization and initiation/discontinuation*
 26 *of heart failure treatments stratified by renal function in three strata.*

	eGFR ≥60 ml/min/1.73m ²		eGFR 30-59 ml/min/1.73m ²		eGFR <30 ml/min/1.73m ²	
Initiation						
<i>MRA initiation</i>						
Event rate in out- vs. inpatients	634 (18.1%)	1082 (52.2%)	208 (13.6%)	794 (36.6%)	12 (7.5%)	80 (16.9%)
Crude OR (95% CI), p-value	4.9 (4.4-5.6), <0.001		3.7 (3.1-4.3), <0.001		2.5 (1.3-4.8), 0.004	
<i>RASi/ARNi initiation</i>						
Event rate in out- vs. inpatients	243 (61.7%)	524 (80.5%)	117 (45.0%)	375 (58.9%)	10 (21.3%)	64 (32.2%)
Crude OR (95% CI), p-value	2.6 (1.9-3.4), <0.001		1.7 (1.3-2.3), <0.001		1.8 (0.8-3.7), 0.147	
<i>Betablocker initiation</i>						
Event rate in out- vs. inpatients	287 (47.2%)	539 (75.5%)	92 (36.1%)	361 (68.0%)	6 (46.2%)	59 (66.3%)
Crude OR (95% CI), p-value	3.4 (2.7-4.4), <0.001		3.8 (2.7-5.1), <0.001		2.3 (0.7-7.4), 0.166	
<i>Loop diuretic initiation</i>						
Event rate in out- vs. inpatients	467 (16.0%)	814 (76.1%)	194 (27.4%)	562 (88.5%)	13 (43.3%)	65 (85.5%)
Crude OR (95% CI), p-value	16.7 (14.1-19.8), <0.001		20.4 (15.2-27.3), <0.001		7.7 (2.9-20.3), <0.001	
Discontinuation						
<i>MRA discontinuation</i>						
Event rate in out- vs. inpatients	176 (11.3%)	139 (14.0%)	156 (19.4%)	252 (24.8%)	18 (38.3%)	49 (36.0%)
Crude OR (95% CI), p-value	1.3 (1.0-1.6), 0.045		1.4 (1.1-1.7), 0.006		0.9 (0.5-1.8), 0.781	
<i>RASi/ARNi discontinuation</i>						
Event rate in out- vs. inpatients	125 (2.7%)	117 (4.8%)	91 (4.4%)	204 (8.0%)	31 (19.3%)	73 (17.8%)
Crude OR (95% CI), p-value	1.8 (1.4-2.4), <0.001		1.9 (1.5-2.4), <0.001		0.9 (0.6-1.5), 0.696	
<i>Betablocker discontinuation</i>						
Event rate in out- vs. inpatients	147 (3.3%)	120 (5.1%)	71 (3.4%)	118 (4.4%)	8 (4.1%)	34 (6.6%)
Crude OR (95% CI), p-value	1.6 (1.2-2.0), <0.001		1.3 (1.0-1.8), 0.076		1.6 (0.7-3.6), 0.219	
<i>Loop diuretic discontinuation</i>						
Event rate in out- vs. inpatients	492 (23.0%)	113 (5.7%)	221 (13.6%)	86 (3.4%)	13 (7.3%)	20 (3.8%)
Crude OR (95% CI), p-value	0.2 (0.2-0.2), <0.001		0.2 (0.2-0.3), <0.001		0.5 (0.2-1.0), 0.056	

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 28 Initiation/discontinuation of heart failure treatments is compared between patients with a heart failure hospitalization vs. out-
 29 patients (i.e., patients without a heart failure hospitalization), stratified by eGFR. For initiation of heart failure treatments, no prior
 30 treatment was defined as no dispensed prescription within 8 months to 1 day before the index date, and post treatment was
 31 defined as 2 dispensed prescriptions from the index date until 8 months thereafter, and vice versa for discontinuation of heart
 32 failure treatments. Crude event rates and crude odds ratios are shown. eGFR: Estimated glomerular filtration rate; OR: Odds
 33 ratio; CI: Confidence interval; MRA: Mineralocorticoid receptor antagonist; HF_rEF: Heart failure with reduced ejection fraction;
 34 HF_{mr}EF: Heart failure with mildly reduced ejection fraction; RASi: Renin-aldosteron-system inhibitors; ARNi: Angiotensin-
 35 receptor neprilysin-inhibitors.

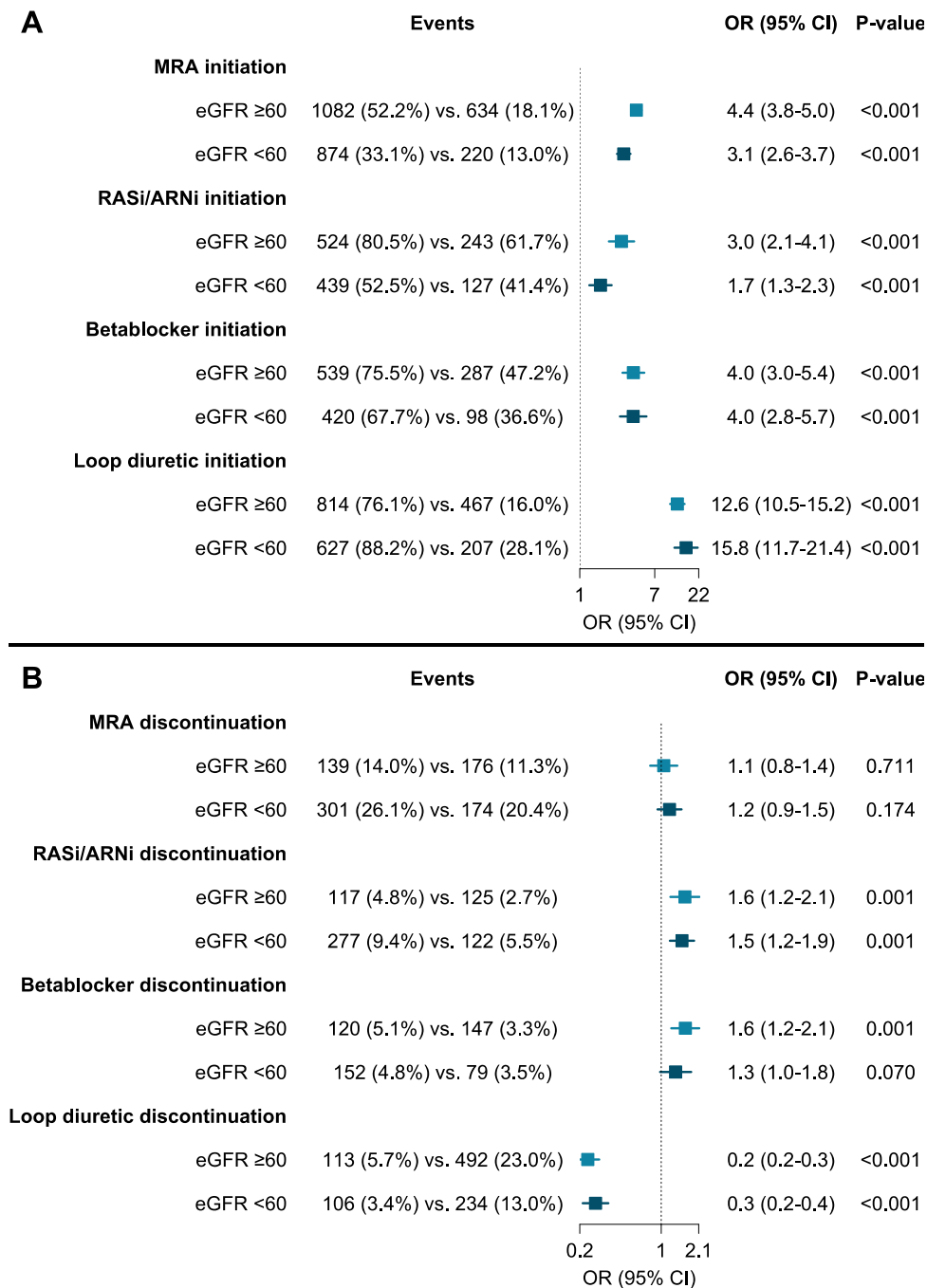
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Supplement Figure 1. Outline of the study design.



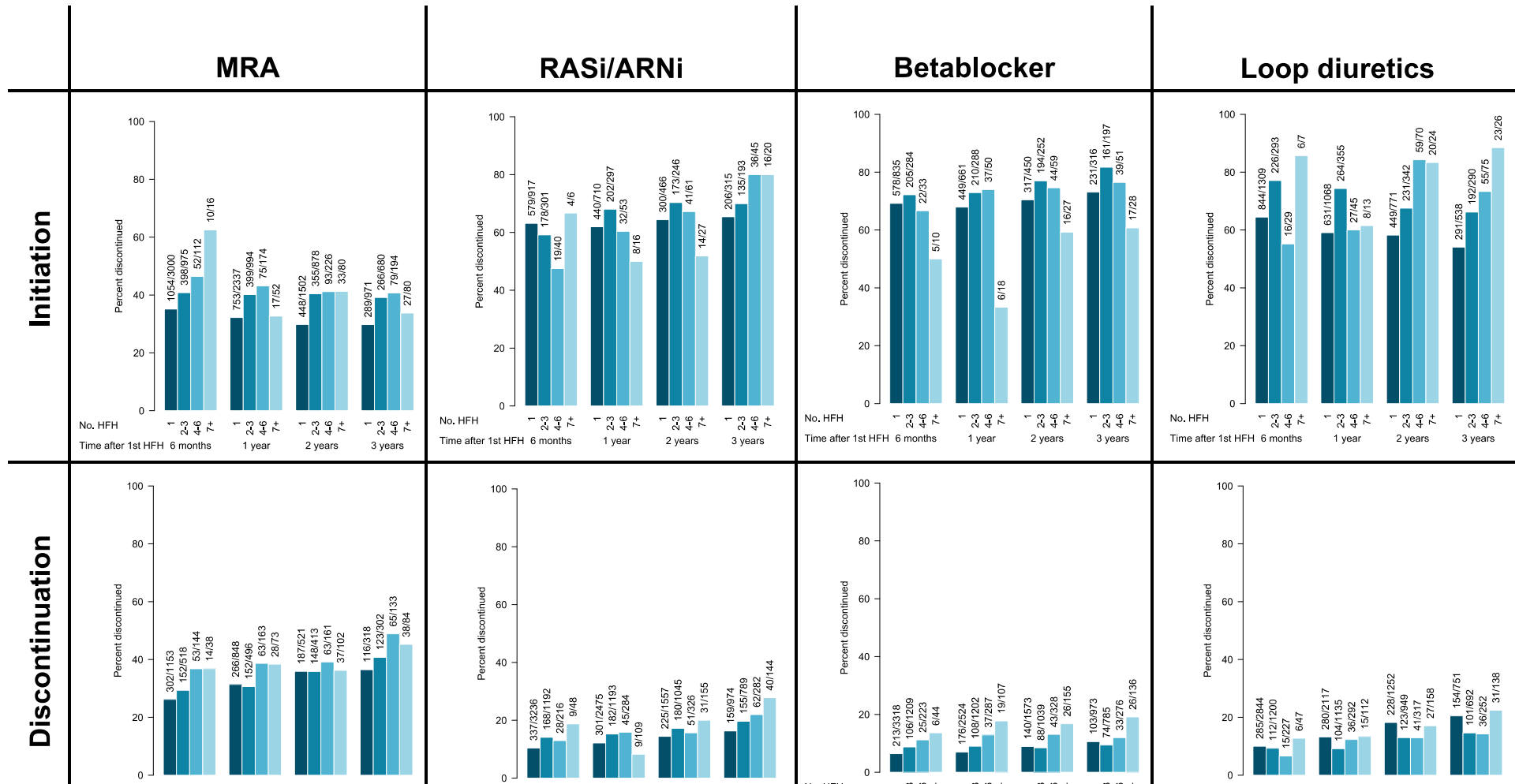
HF: Heart failure.

Supplement Figure 2. Likelihood of initiation/discontinuation of heart failure treatments in patients with vs. without a heart failure hospitalization, stratified by renal function in two strata.



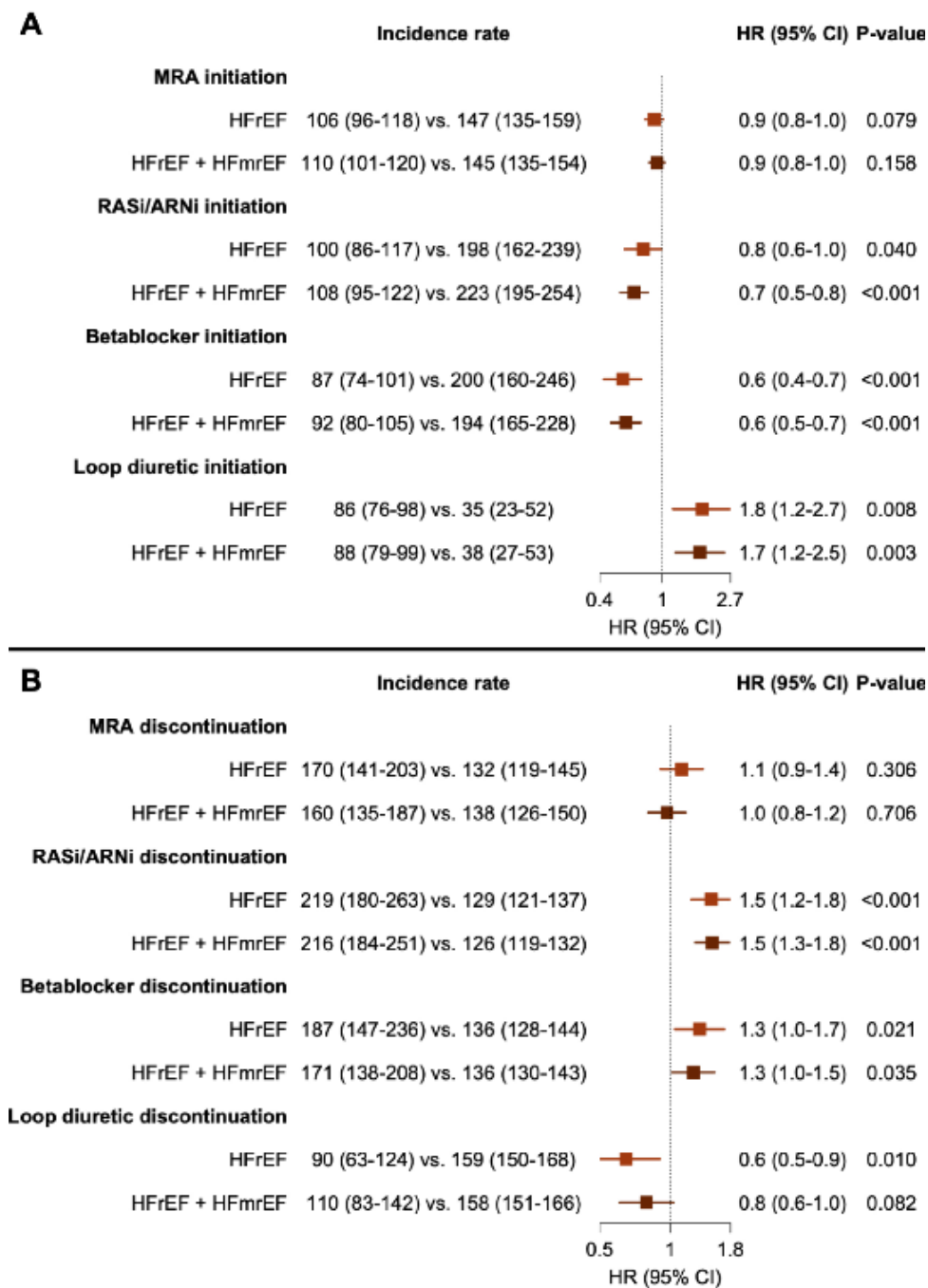
Initiation/discontinuation of heart failure treatments is compared between patients with a heart failure hospitalization vs. outpatients (i.e., patients without a heart failure hospitalization), stratified by eGFR in two strata. For initiation of heart failure treatments (A), no prior treatment was defined as no dispensed prescription within 6 months to 1 day before the index date, and post treatment is defined as 1 dispensed prescription from the index date until 6 months thereafter, and vice versa for discontinuation of heart failure treatments (B). Crude event rates and adjusted odds ratios are shown, and variables used for adjustment in the underlying logistic regression model are reported in *Table 1*. An OR >1 indicates a higher, and an OR <1 indicates a lower likelihood of initiation/discontinuation of heart failure treatments in hospitalized patients. eGFR: Estimated glomerular filtration rate; OR: Odds ratio; CI: Confidence interval; MRA: Mineralocorticoid receptor antagonist; HFrEF: Heart failure with reduced ejection fraction; HFmrEF: Heart failure with mildly reduced ejection fraction; RASi: Renin-aldosterone-system inhibitors; ARNi: Angiotensin-receptor neprilysin-inhibitors.

Supplement Figure 3. Initiation/discontinuation of heart failure treatments in relation to recurrent heart failure hospitalizations over time.



Initiation/discontinuation of heart failure treatments in patients after an heart failure hospitalization (x-axis) is displayed in relation to the number of heart failure hospitalizations within a given time period (y-axis). MRA: Mineralocorticoid receptor antagonist; RASi: Renin-aldosteron-system inhibitors; ARNi: Angiotensin-receptor neprilysin-inhibitors; HFH: Heart failure hospitalization

Supplement Figure 4. Association between initiation/discontinuation of heart failure treatments and 3-year cardiovascular mortality following a heart failure hospitalization.



Cox regression models were fitted to evaluate the association between initiation/discontinuation vs. no initiation/no discontinuation (reference) in heart failure treatments and 3-year cardiovascular mortality among patients with a heart failure hospitalization. For initiation of heart failure treatments (A), no prior treatment was defined as no dispensed prescription within 6 months to 1 day before the index date, and post treatment was defined as 1 dispensed prescription from the index date until 6 months thereafter, and vice versa for discontinuation of heart failure treatments (B). Crude event rates and adjusted hazard ratios are shown; and variables used for adjustment in the underlying Cox regression model are reported in *Table 1*. HR: Hazard ratio; CI: Confidence interval; MRA: Mineralocorticoid receptor antagonist; HFrEF: Heart failure with reduced ejection fraction; HFmrEF: Heart failure with mildly reduced ejection fraction; RASi: Renin-aldosterone-system inhibitors; ARNi: Angiotensin-receptor neprilysin-inhibitors.