

Supplementary materials

Supplementary Table 1. *International Classification of Diseases (ICD) codes and Anatomical Therapeutic Classification (ATC) codes used in the study.*

	ICD-8	ICD-10	ATC code
Heart failure	42709, 42710, 42711, 42719, 42899, 78249	I110, I130, I132, I420, I426, I427, I428, I429, I500, I501, I502, I503, I508, I509	N/A
Coronary artery disease	410, 413, 411	I20-I21, I251, I259	N/A
Valvular heart disease	394-397	I05-I08, I098, I34-I37	
Hypertension	400-404	I10-I15	N/A
Atrial fibrillation or atrial flutter	42793, 42794	I48	N/A
Venous thromboembolism	450.99, 451.00	I26, I80.1-3	
Stroke	430-434	I60-I61, I63- I64	N/A
Intermittent claudication	44389-44399	I739	N/A
Diabetes mellitus	24900-24909 (excluding 24902), 25000-25009 (excluding 25002)	E10 (excluding E102), E11 (excluding E112), E14 (excluding E142)	A10A, A10B
Obesity	277	E65-E66	N/A
Cancer	140-209	C00-C96	N/A
Chronic pulmonary disease	490-493, 515-518	J40-J47, J60- J67, J684, J701, J703, J841, J920, J961, J982- J983	N/A
Chronic kidney disease	24902, 25002, 75310- 75319, 582- 584, 59009, 59320, 792	E102, E112, E142, N03, N05, N110, N14, N16, N18-N19, N269, Q611- Q614	N/A
Dementia	29009- 29019, 29309	F00-F03, G30	N/A
Depression	29609, 29629, 29809, 30049	F32-F33	N06A

Illicit drug abuse/alcohol abuse/smoking	303-304	F10-F19	N/A
Peptic ulcer disease	53091, 53098, 531-534	K221, K25-K28	N/A
Gastroesophageal reflux disease	535	K21	N/A
Anemia	280-281, 283-285	D50-55, D59, D61-D64	N/A
Liver disease	070, 570-571, 573, 456	B15-B19, K71-K77	N/A
Alcoholism-related disorders	980, 291.09-291.99, 303.09-303.99, 57109-57111, 57710	G31.2, G62.1, G72.1, K29.2, K70, K86.0, Z72.1, E244, E529A, K852, L278A, Z502, Z714	N/A
Musculoskeletal disorders	710-718	M00-M99	
Inflammatory bowel disease	56301, 56319	K50-K51	
Gastroscopy*		KUJD	
Coronary artery bypass graft surgery*		KFNA-KFNE, KFNH20	
Percutaneous coronary intervention*		KFNG, KFNF	
Exposure			
Histamine 2 receptor antagonists			MA02BA (cimetidin, ranitidin, famotidin, nizatidin, ranitidinbismuthcitrat)
Proton pump inhibitors			MA02BC (omeprazol, pantoprazol, lansoprazol, rabeprazol, esomeprazol)
Comedication in past 90 days			
Beta blockers	N/A	N/A	C07
Angiotensin converting enzyme inhibitors or angiotensin receptor II blockers	N/A	N/A	C09A, C09B, C09C, C09D
Diuretics	N/A	N/A	C03
Statins	N/A	N/A	C10AA, C10B
NSAIDs	N/A	N/A	M01A
Antithrombotics	N/A	N/A	MB01A
Benzodiazepines			MN05BA
Opioids			MN02A

Causes of death

Cardiovascular mortality N/A I00-I99 N/A

*Codes in accordance with the NOMESCO classification.

Supplementary Table 2. Characteristics of heart failure patients registered in the Danish Heart Failure Registry (1 January 2003–1 February 2014), by exposure group. Data are numbers (%).

	Histamine H₂ receptor antagonist initiators	Proton pump inhibitor initiators
Number of patients	200 (3)	7243 (97)
Left ventricular ejection fraction		
<25%	61 (31)	2022 (28)
25%-35%	61 (31)	2477 (34)
36%-40%	17 (9)	966 (13)
41%-49%	10 (5)	419 (6)
≥50%	14 (7)	553 (8)
Missing	37 (19)	806 (11)
New York Heart Association (NYHA) classification		
NYHA Class I	6 (3)	486 (7)
NYHA Class II	52 (26)	2557 (35)
NYHA Class III	49 (25)	1571 (22)
NYHA Class IV	6 (3)	170 (2)
Missing	87 (44)	2459 (34)
Alcohol intake		
Maximum 14 drinks for women and 21 for men per week	134 (67)	5208 (72)
More than 14 drinks for women and 21 for men per week	9 (5)	515 (7)
Missing	57 (29)	1520 (21)
Smoking habits		
Smoker	54 (27)	2147 (30)
Former smoker	64 (32)	2483 (34)
Never smoker	40 (20)	1511 (21)
Missing	42 (21)	1102 (15)

Supplementary Table 3. Total number of redeemed prescriptions and cumulative duration of treatment within 2 years for patients initiating histamine H₂ receptor antagonists.

No. of prescriptions	
1	1664 (50)
2	525 (16)
3	242 (7)
≥4	865 (26)
Cumulative duration of H2RA use*	
<30 days	964 (29)
30-49 days	640 (19)
50-149 days	837 (25)
≥150 days	855 (26)

*Sum of the duration of all prescriptions during 2 years after the first H2RA prescription. Duration of H2RA use was equal to the number of pills, assuming a daily dose of 300 mg.

Abbreviation: H2RA, histamine H₂ receptor antagonist

Supplementary Table 4. Overview of histamine H₂ receptor antagonist and proton pump inhibitor initiators and change of treatment during follow-up.

	No PPI initiation during follow-up (%)	PPI initiation during follow-up (%)	Median time, days (25th-75th percentile) from H2RA initiation until PPI initiation	Patients (%) initiating PPI < 1 year
H2RA initiators (n=3,296)	1694 (51)	1602 (49)	439 (84-1322)	746 (23)
	No H2RA initiation during follow-up	H2RA initiation during follow-up	Median time, days (25th-75th percentile) from PPI initiation until H2RA initiation	Patients (%) initiating H2RA < 1 year
PPI initiators (n=42,902)	41,955 (98)	947 (2)	302 (89-742)	525 (1)

Abbreviations: H2RA, histamine H₂ receptor antagonists; PPI, proton pump inhibitor

Supplementary Table 5. Baseline characteristics of the two study cohorts, by change of treatment during follow-up. Values are numbers (%) unless otherwise stated.

	Histamine H₂ receptor antagonist initiators		Proton pump inhibitor initiators	
	No PPI during follow-up	PPI during follow-up	No H2RA during follow-up	H2RA during follow-up
Total study population	1694 (51)	1602 (49)	41,955 (98)	947 (2)
Median age, years (25th-75th percentile)	78 (70-85)	74 (66-81)	78 (69-85)	75 (67-82)
Age groups				
<60 years	150 (9)	245 (15)	4299 (10)	124 (13)
60-69 years	252 (15)	307 (19)	7061 (17)	192 (20)
70-79 years	588 (35)	591 (37)	12,722 (30)	335 (35)
80+ years	704 (42)	459 (29)	17,873 (43)	296 (31)
Index-year groups				
1995–1999	868 (51)	690 (43)	3679 (9)	360 (38)
2000–2004	621 (37)	686 (43)	11,522 (27)	399 (42)
2005–2009	178 (11)	210 (13)	14,895 (36)	160 (17)
2010–2014	27 (2)	16 (1)	11,859 (28)	28 (3)
Female	816 (48)	777 (49)	19,246 (46)	475 (50)
Time from heart failure diagnosis to first prescription				
Median, days (25th-75th percentile)	266 (63-775)	337 (90-832)	452 (62-1361)	259 (44-782)
<3 months	536 (32)	397 (25)	12,010 (29)	309 (33)
≥3-<6 months	175 (10)	177 (11)	3162 (8)	93 (10)
≥6-<12 months	254 (15)	268 (17)	4217 (10)	138 (15)
≥12-<18 months	155 (9)	173 (11)	3064 (7)	82 (9)
≥18-<24 months	126 (7)	133 (8)	2545 (6)	75 (8)
≥24-<30 months	93 (5)	102 (6)	2255 (5)	54 (6)
≥30 months	355 (21)	352 (22)	14,702 (35)	196 (21)
Heart failure risk factors and comorbidity				
Coronary artery disease	814 (48)	845 (53)	22,574 (54)	516 (54)
Valvular heart disease	199 (12)	188 (12)	6367 (15)	132 (14)
Hypertension	396 (23)	458 (29)	17,201 (41)	288 (30)
Atrial fibrillation or atrial flutter	518 (31)	412 (26)	15,711 (37)	255 (27)
Venous thromboembolism	71 (4)	58 (4)	1744 (4)	39 (4)
Stroke	196 (12)	163 (10)	6368 (15)	93 (10)
Intermittent claudication	36 (2)	38 (2)	2064 (5)	25 (3)
Diabetes mellitus	288 (17)	293 (18)	9596 (23)	165 (17)
Obesity	106 (6)	122 (8)	3518 (8)	70 (7)
Cancer within 1 year	123 (7)	74 (5)	3543 (8)	49 (5)
Chronic pulmonary disease	422 (25)	400 (25)	10,819 (23)	221 (23)
Chronic kidney disease	83 (5)	65 (4)	4071 (10)	61 (6)
Dementia	52 (3)	30 (2)	1641 (4)	11 (1)
Depression	423 (25)	411 (26)	14,258 (34)	267 (28)
Illicit drug abuse/alcohol abuse/smoking	57 (3)	74 (5)	2557 (6)	54 (6)

Peptic ulcer disease	125 (7)	122 (8)	5133 (12)	141 (15)
Gastroesophageal reflux disease	38 (2)	57 (4)	1330 (3)	37 (4)
Anemia	186 (11)	125 (8)	7254 (17)	138 (15)
Liver disease	36 (2)	32 (2)	1065 (3)	26 (3)
Alcoholism-related disorders	37 (2)	54 (3)	1366 (3)	33 (3)
Musculoskeletal disorders	565 (33)	603 (38)	19,165 (45)	387 (41)
Inflammatory bowel disease	9 (1)	16 (1)	536 (1)	9 (1)
Cardiac surgery within past 90 days				
Coronary artery bypass grafting	88 (5)	89 (6)	917 (2)	30 (3)
Percutaneous coronary intervention	21 (1)	25 (2)	1351 (3)	26 (3)
Comedication within past 90 days				
Betablockers	394 (23)	444 (28)	15,412 (37)	272 (29)
ACEI/ARBs	644 (38)	697 (44)	18,827 (45)	386 (41)
Diuretics	1264 (75)	1115 (70)	26,893 (64)	618 (65)
Statins	167 (10)	261 (16)	10,173 (24)	151 (16)
NSAIDs	288 (17)	314 (20)	7323 (17)	181 (19)
Antithrombotics	775 (46)	789 (49)	23,415 (56)	474 (50)
Benzodiazepines	246 (15)	285 (18)	4377 (10)	145 (15)
Opioids	333 (20)	299 (19)	9747 (23)	204 (22)
Income				
Low	865 (51)	726 (45)	9555 (23)	391 (41)
Intermediate	326 (19)	361 (23)	10,615 (25)	236 (25)
High	250 (15)	254 (16)	10,880 (26)	151 (16)
Very high	250 (15)	258 (16)	10,864 (26)	168 (18)
Unknown	3 (0.2)	3 (0.2)	41 (0.1)	1 (0.1)
Employment				
Employed	163 (10)	180 (11)	4359 (10)	109 (12)
Early retirement, receiving sickness/incapacity/early retirement	13 (1)	28 (2)	540 (1)	14 (2)
Unemployed	173 (10)	267 (17)	4697 (11)	155 (16)
State pensioner	1343 (79)	1225 (70)	32,284 (77)	688 (71)
Unknown	2 (0.1)	2 (0.1)	75 (0.2)	1 (0.1)

Abbreviations: ACEI/ARBs, angiotensin-converting enzyme inhibitors/angiotensin receptor II blockers; H2RA, histamine H₂ receptor antagonists; NSAIDs, nonsteroidal anti-inflammatory drugs; PPI, proton pump inhibitor

Supplementary Table 6. One-year all-cause mortality in subgroups of heart failure patients, comparing new users of histamine H₂ receptor antagonists and new users of proton pump inhibitors.

	No. Events	Mortality risk in the H2RA group, % (95% CI)	Adjusted HR (95% CI)*
Comorbidity			
Valvular heart disease	2250	25 (21-29)	0.79 (0.63-0.98)
No valvular heart disease	11,783	26 (24-27)	0.80 (0.74-0.87)
Hypertension	5320	23 (20-26)	0.76 (0.65-0.88)
No hypertension	8713	27 (25-28)	0.81 (0.75-0.88)
Atrial fibrillation or atrial flutter	5596	27 (24-30)	0.80 (0.70-0.91)
No atrial fibrillation or atrial flutter	8437	25 (23-27)	0.80 (0.73-0.87)
Venous thromboembolism	654	26 (20-35)	0.74 (0.51-1.06)
No venous thromboembolism	13,379	26 (24-27)	0.80 (0.74-0.87)
Stroke	2506	33 (28-38)	0.87 (0.72-1.06)
No stroke	11,527	25 (23-26)	0.79 (0.73-0.85)
Intermittent claudication	734	22 (14-33)	0.64 (0.38-1.08)
No intermittent claudication	13,299	26 (24-27)	0.80 (0.75-0.87)
Diabetes mellitus	3207	24 (21-28)	0.71 (0.60-0.85)
No diabetes mellitus	10,826	26 (24-28)	0.82 (0.75-0.89)
Obesity	924	17 (12-22)	0.62 (0.44-0.88)
No obesity	13,109	26 (25-28)	0.81 (0.75-0.87)
Cancer within 1 year	3847	41 (36-45)	0.80 (0.65-0.98)
No cancer within 1 year	10,186	23 (22-25)	0.81 (0.75-0.87)
Chronic pulmonary disease	4116	27 (24-31)	0.71 (0.61-0.81)
No chronic pulmonary disease	9917	25 (23-27)	0.84 (0.77-0.92)
Chronic kidney disease	1764	39 (31-47)	0.89 (0.68-1.18)
No chronic kidney disease	12,269	25 (24-27)	0.79 (0.74-0.86)
Dementia	817	38 (28-49)	0.71 (0.48-1.05)
No dementia	13,216	25 (24-27)	0.80 (0.74-0.86)
Depression	5081	27 (24-30)	0.76 (0.66-0.87)
No depression	8952	25 (24-27)	0.82 (0.75-0.89)
Illicit drug abuse/alcohol abuse/smoking	735	26 (19-34)	0.96 (0.66-1.39)
No illicit drug abuse/alcohol abuse/smoking	13,298	26 (24-27)	0.79 (0.74-0.86)
Peptic ulcer disease	1762	28 (22-34)	0.72 (0.55-0.92)
No peptic ulcer disease	12,271	25 (24-27)	0.81 (0.75-0.87)
Gastroesophageal reflux disease	355	23 (16-33)	0.91 (0.58-1.44)
No gastroesophageal reflux disease	13,678	26 (24-27)	0.80 (0.74-0.86)
Anemia	3044	40 (34-45)	0.94 (0.77-1.14)
No anemia	10,989	24 (23-26)	0.79 (0.73-0.85)
Liver disease	369	29 (20-42)	0.95 (0.58-1.54)
No liver disease	13,644	26 (24-27)	0.80 (0.74-0.86)
Alcoholism-related disorders	440	30 (21-40)	1.07 (0.70-1.63)
No alcoholism-related disorders	13,593	25 (24-27)	0.79 (0.74-0.85)
Musculoskeletal disorders	6095	27 (24-30)	0.87 (0.77-0.98)
No musculoskeletal disorders	7938	25 (23-27)	0.76 (0.69-0.83)

Inflammatory bowel disease	173	20 (9-42)	0.53 (0.19-1.48)
No inflammatory bowel disease	13,860	26 (24-27)	0.80 (0.74-0.86)
Cardiac surgery			
Coronary artery bypass grafting	90	6 (3-11)	0.63 (0.31-1.30)
No coronary artery bypass grafting	13,943	27 (25-28)	0.80 (0.74-0.86)
Percutaneous coronary intervention	217	13 (6-27)	1.17 (0.48-2.82)
No percutaneous coronary intervention	13,816	26 (24-27)	0.80 (0.74-0.86)
Comedication			
Diuretics	10,003	29 (27-30)	0.82 (0.75-0.89)
No diuretics	4030	18 (16-21)	0.73 (0.62-0.86)
Statins	2251	11 (8-14)	0.69 (0.51-0.94)
No statins	11,782	28 (26-29)	0.81 (0.75-0.87)
NSAIDs	2442	28 (25-32)	0.82 (0.69-0.96)
No NSAIDs	11,591	25 (23-27)	0.79 (0.73-0.86)
Antithrombotics	7474	24 (22-26)	0.80 (0.72-0.90)
No antithrombotics	6559	27 (25-29)	0.79 (0.72-0.88)
Benzodiazepines	1706	25 (33-36)	0.72 (0.60-0.87)
No benzodiazepines	12,327	26 (24-27)	0.82 (0.76-0.89)
Opioids	4170	34 (31-38)	0.82 (0.71-0.95)
No opioids	9863	24 (22-25)	0.79 (0.73-0.86)
Income			
Low	3720	27 (25-30)	0.78 (0.70-0.86)
Intermediate	3881	28 (25-31)	0.84 (0.72-0.98)
High	3572	23 (20-27)	0.75 (0.62-0.92)
Very high	2854	20 (17-24)	0.83 (0.67-1.02)
Employment			
Employed	702	15 (12-19)	0.66 (0.49-0.90)
Early retirement, receiving sickness/incapacity/early retirement	74	10 (4-24)	0.71 (0.23-2.22)
Unemployed	941	13 (10-17)	0.73 (0.55-0.97)
State pensioner	12,304	30 (28-31)	0.81 (0.75-0.88)

*Adjusted by age group, sex, index-year categories, time from heart failure diagnosis until first prescription for PPI or H2RA, coronary artery disease, valvular heart disease, hypertension, atrial fibrillation or atrial flutter, venous thromboembolism, stroke, intermittent claudication, diabetes mellitus, obesity, cancer within 1 year, chronic pulmonary disease, chronic kidney disease, dementia, depression, illicit drug abuse/alcohol abuse/smoking, peptic ulcer disease, gastroesophageal reflux disease, anemia, chronic liver disease, alcoholism-related disorders, musculoskeletal disorders, inflammatory bowel disease, cardiac surgery within past 90 days (coronary artery bypass graft surgery and percutaneous coronary intervention), comedication within past 90 days (beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor II blockers, diuretics, statins, NSAIDs, antithrombotics, benzodiazepines, and opioids), income, and employment (except the stratifying variable).
Abbreviations: CI, confidence interval; HR, hazard ratio

Supplementary Table 7. Sensitivity analyses. Association between histamine H₂ receptor antagonist initiation and 1-year mortality.

	No. events	Mortality risk, % (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*
Danish Heart Failure Registry Cohort				
PPI	1584	22 (21-23)	Reference	Reference
H2RA	21	11 (7-16)	0.45 (0.29-0.69)	0.84 (0.55-1.31) [†]
Additional adjustment for gastroscopy within past 6 months				
PPI	12,996	31 (30-31)	Reference	Reference
H2RA	699	25 (23-26)	0.76 (0.71-0.82)	0.79 (0.73-0.85)
Patients assigned to exposure groups after the first year following hospitalization for heart failure[‡]				
PPI	1027	19 (18-20)	Reference	Reference
H2RA	85	17 (15-19)	0.87 (0.75-1.01)	0.81 (0.69-0.94)
PPI+H2RA	38	23 (19-27)	1.25 (1.02-1.54)	1.16 (0.94-1.43)
Patients assigned to exposure groups after the first year following hospitalization for heart failure and those with only one prescription of H2RA or PPI were excluded[‡]				
PPI	647	21 (20-21)	Reference	Reference
H2RA	44	18 (15-22)	0.89 (0.72-1.09)	0.79 (0.63-0.98)
Analyses restricted to second prescriptions				
PPI	7071	32 (31-32)	Reference	Reference
H2RA	334	26 (24-29)	0.80 (0.72-0.89)	0.82 (0.73-0.92)

*Adjusted by age group, sex, index-year categories, time from heart failure diagnosis until first prescription for PPI or H2RA, coronary artery disease, valvular heart disease, hypertension, atrial fibrillation or atrial flutter, venous thromboembolism, stroke, intermittent claudication, diabetes mellitus, obesity, cancer within 1 year, chronic pulmonary disease, chronic kidney disease, dementia, depression, illicit drug abuse/alcohol abuse/smoking, peptic ulcer disease, gastroesophageal reflux disease, anemia, chronic liver disease, alcoholism-related disorders, musculoskeletal disorders, inflammatory bowel disease, cardiac surgery within past 90 days (coronary artery bypass graft surgery and percutaneous coronary intervention), comedication within past 90 days (beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor II blockers, diuretics, statins, NSAIDs, antithrombotics, benzodiazepines, and opioids), income, and employment.

[†]Additional adjustment for alcohol abuse and smoking yielded an adjusted HR of 0.83 (95% CI, 0.48-1.45)

[‡]For this analysis, follow-up was started one year after the heart failure admission date. Therefore the analysis was not adjusted for time since heart failure diagnosis.

Abbreviations: CI, confidence interval; HR, hazard ratio; H2RA, histamine H₂ receptor antagonist; PPI, proton pump inhibitor

Supplementary Table 8. All-cause mortality in the second year after the heart failure admission date, by number of H2RA prescriptions during the first year.

No. of H2RA prescriptions	No. events	Mortality risk, % (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*
0	9185	19 (18-20)	Reference	Reference
1	531	15 (13-18)	0.79 (0.64-0.97)	0.82 (0.67-1.01)
2	161	14 (10-20)	0.74 (0.51-1.08)	0.71 (0.48-1.04)
3	88	21 (14-31)	1.13 (0.73-1.76)	0.95 (0.61-1.48)
≥4	222	20 (16-26)	1.09 (0.83-1.45)	0.85 (0.64-1.13)

*Adjusted by age group, sex, index-year categories, coronary artery disease, valvular heart disease, hypertension, atrial fibrillation or atrial flutter, venous thromboembolism, stroke, intermittent claudication, diabetes mellitus, obesity, cancer within 1 year, chronic pulmonary disease, chronic kidney disease, dementia, depression, illicit drug abuse/alcohol abuse/smoking, peptic ulcer disease, gastroesophageal reflux disease, anemia, chronic liver disease, alcoholism-related disorders, musculoskeletal disorders, inflammatory bowel disease, cardiac surgery within past 90 days (coronary artery bypass graft surgery and percutaneous coronary intervention), comedication within past 90 days (beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor II blockers, diuretics, statins, NSAIDs, antithrombotics, benzodiazepines, and opioids), income, and employment.

Abbreviations: CI, confidence interval; HR, hazard ratio; H2RA, histamine H₂ receptor antagonist

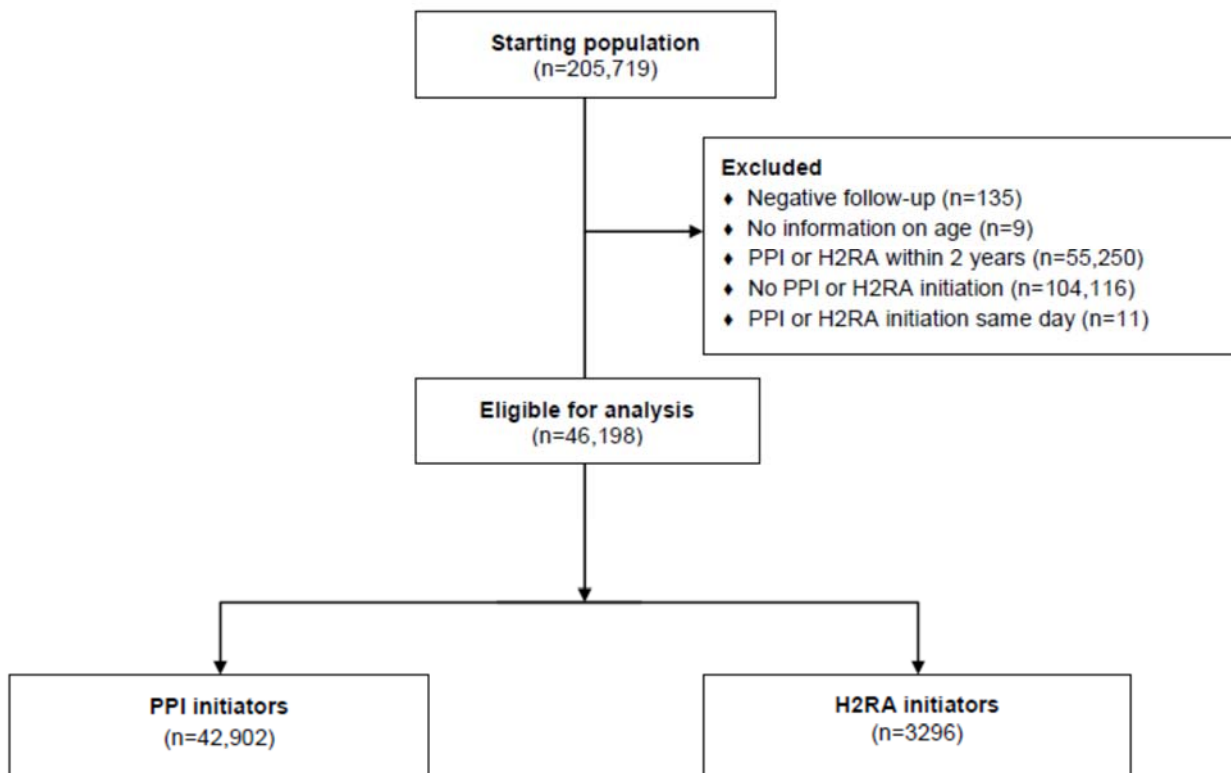
Supplementary Table 9. Association between histamine H₂ receptor antagonists and 1-year mortality, by time periods and time since heart failure admission date.

	No. events	Mortality risk, % (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*
Time period				
1995–1999				
PPI	1419	35 (34-37)	Reference	Reference
H2RA	461	30 (27-32)	0.80 (0.72-0.89)	0.84 (0.76-0.94)
2000–2004				
PPI	3996	34 (33-34)	Reference	Reference
H2RA	294	23 (20-25)	0.62 (0.55-0.70)	0.74 (0.65-0.83)
2005–2009				
PPI	4507	30 (29-31)	Reference	Reference
H2RA	73	19 (15-23)	0.59 (0.47-0.74)	0.73 (0.58-0.92)
2010–2014				
PPI	3268	28 (27-29)	Reference	Reference
H2RA	15	35 (23-51)	1.30 (0.78-2.15)	1.46 (0.87-2.43)
Time since heart failure admission date				
<3 months				
PPI	3877	32 (31-32)	Reference	Reference
H2RA	274	29 (27-32)	0.91 (0.80-1.03)	0.89 (0.77-1.01)
≥3-<6 months				
PPI	1044	32 (31-34)	Reference	Reference
H2RA	90	26 (21-31)	0.76 (0.61-0.94)	0.76 (0.60-0.95)
≥6-<12 months				
PPI	1375	32 (30-33)	Reference	Reference
H2RA	128	25 (21-28)	0.73 (0.61-0.87)	0.73 (0.60-0.88)
≥12-<18 months				
PPI	943	30 (28-32)	Reference	Reference
H2RA	75	23 (19-28)	0.72 (0.57-0.91)	0.64 (0.50-0.82)
≥18-<24 months				
PPI	775	30 (28-31)	Reference	Reference
H2RA	62	24 (19-30)	0.77 (0.60-1.00)	0.79 (0.60-1.04)
≥24-<30 months				
PPI	653	28 (27-30)	Reference	Reference
H2RA	48	25 (19-31)	0.83 (0.62-1.12)	0.93 (0.68-1.27)
≥30 months				
PPI	4523	30 (30-31)	Reference	Reference
H2RA	166	23 (21-27)	0.73 (0.63-0.86)	0.79 (0.67-0.92)

*Adjusted by age group, sex, index-year categories, time from heart failure diagnosis until first prescription for PPI or H2RA, coronary artery disease, valvular heart disease, hypertension, atrial fibrillation or atrial flutter, venous thromboembolism, stroke, intermittent claudication, diabetes mellitus, obesity, cancer within 1 year, chronic pulmonary disease, chronic kidney disease, dementia, depression, illicit drug abuse/alcohol abuse/smoking, peptic ulcer disease, gastroesophageal reflux disease, anemia, chronic liver disease, alcoholism-related disorders, musculoskeletal disorders, inflammatory bowel disease, cardiac surgery within past 90 days (coronary artery bypass graft surgery and percutaneous coronary intervention), comedication within past 90 days (beta blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor II blockers, diuretics, statins, NSAIDs, antithrombotics, benzodiazepines, and opioids), income, and employment (except the stratifying variable).

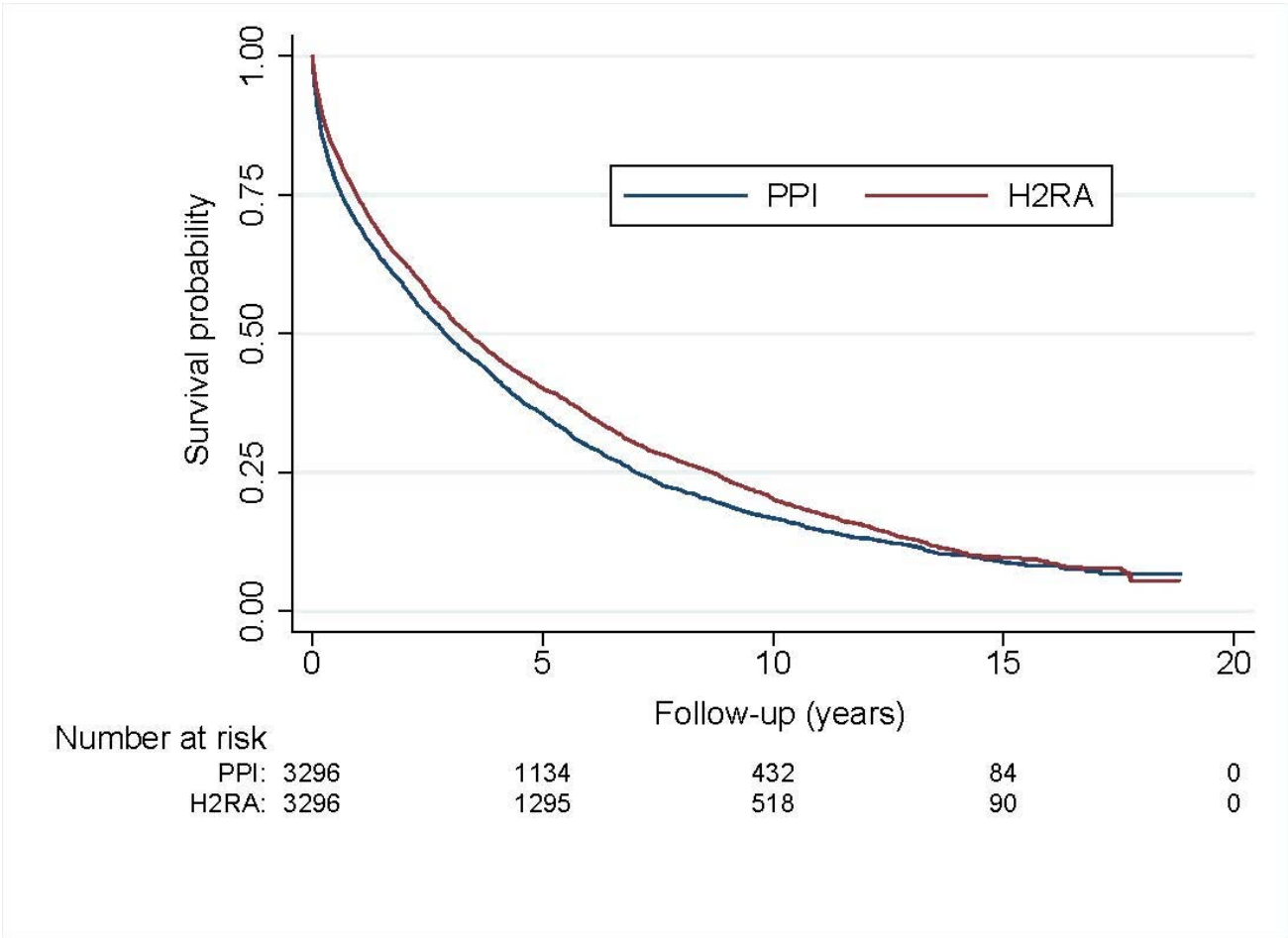
Abbreviations: CI, confidence interval; HR, hazard ratio; H2RA, histamine H₂ receptor antagonist; PPI: proton pump inhibitor

Supplementary Figure 1. Flowchart of inclusion of study participants.



Abbreviations: H2RA, histamine H₂ receptor antagonist; PPI, proton pump inhibitor

Supplementary Figure 2. Kaplan-Meier survival curve for initiators of proton pump inhibitors and histamine H₂ receptor antagonists after propensity score matching.



Abbreviations: H2RA, histamine H₂ receptor antagonist; PPI, proton pump inhibitor