

SUPPLEMENTAL MATERIAL

Table S1. Codes used to identify study variables.

	Algorithm
Heart failure	ICD-8: 427.0, 427.1 ICD-10: I50, I110, I130, I132
Cardiomyopathy	ICD-10: I42
Valvular heart disease	ICD-10: I00-I02, I05-I09, I34, I35, I36, I37, Q20-Q25, Q22, Q23
Myocardial infarction	ICD-10: I21;I22;I23
Atrial fibrillation or flutter	ICD-10: I48
Echocardiography	UXUC80
Diabetes	defined as a previous hospitalization with a hospital diagnosis of diabetes (ICD-8 259-250; ICD-10 E10-E14, H360), or at least one previous prescription for a glucose-lowering drug (ATC code A10), or presence of two occurrences of a HbA1c measurement > 6.5%
Chronic kidney disease	Defined as either a previous hospitalization with a hospital diagnosis of chronic nephritic syndrome (N03), glomerular disease (N08), chronic kidney disease / chronic renal failure (N18-N19), diabetic nephropathy (E102, E112, E122, E132, E142), or hypertension with renal failure (I120, I131, I132); or a previous dialysis procedure (BJFD2); or presence of two occurrences more than 90 days apart of a creatinine measurement corresponding to an eGFR <60 mL/min/1.73m ²
Hypertension	defined as a previous hospitalization with a hospital diagnosis of hypertension (I10-I15) or a previous prescription for at least two of the following classes of antihypertensive drugs: adrenergic blockers and others (C02), non-loop diuretics (C03A, C03B, C03D, C03E), β blockers (C07), calcium channel blockers (C08), RAAS inhibitors (C09)
Peripheral vascular disease	ICD-10: I70; I71; I72; I73; I74; I77
Cerebrovascular disease	ICD-10: I60-I69; G45; G46
Chronic pulmonary disease	ICD-10: J40-J47; J60-J67; J68.4; J70.1; J70.3; J84.1; J92.0; J96.1; J98.2; J98.3
Peptic ulcer disease	ICD-10: K22.1; K25-K28
Any malignant disease	ICD-10: C00-C96
Alcoholism-related or other substance-abuse related disorders	ICD-10: T36-T65; F10-F19; G312; G621; G721; I 426; K292; K860; K70; R780; T51; Z714; Z721
Medical obesity	ICD-10: E65-E66
ACEis	ATC: C09A, C09B
ARBs	ATC: C09C, C09D
Beta-blockers	ATC: C07
Potassium-sparing diuretics (spironolactone etc.)	ATC: C03D, C03E
Non-steroidal inflammatory drugs	ATC:M01A
Macrolides	J01FA
Trimethoprim	J01EA, J01EE

Potassium supplements	ATC: A12B
Hospitalization with any cardiac diagnoses	ICD-10: DI00-DI99
Hospitalization with ventricular arrhythmia	ICD-10: DI47, DI49
Hospitalization with cardiac arrest	ICD-10: DI46
Hospitalization with ICU admission	Codes: NABE, NABB
Hospitalization with dialysis procedure	Codes: BJFD2
Hospitalization with ventilator treatment	Codes: BGDA0
Hyperkalemia	Code NPU03230. Analysis numbers AAA00958, 110262, 111262 115230, 115231, 1511140, 1610147, 1613230, 1710304, 1713230, 1813230, 1817159, 1311140, 1411140

Abbreviations: ATC, anatomical therapeutic chemical classification; ICD, international classification of diseases

Table S2. Baseline characteristics of patients with incident heart failure in Northern Denmark, 2000-2012. Incidences of any (>5.0 mmol/L), moderate (>5.5 mmol/L), and severe (>6.0 mmol/L) hyperkalemia (HK) events are shown according to each characteristic.

Hyperkalemia event is defined as >5.0 mmol/L

	<i>Number</i>	<i>Median years to first HK event</i>	<i>Median number of measurements before the first HK event</i>	<i>Total person-years of follow-up (1,000)</i>	<i>Median person-years of follow-up</i>	<i>Incidence rate of HK per 1,000 person-years (95% CI)</i>	<i>1-year cumulative incidence proportion of HK (95% CI)</i>	<i>3-year cumulative incidence proportion of HK (95% CI)</i>
Total number	31,649 (100%)	0.34	8	69.32	0.86	178.02 (174.89-181.19)	25.2 (24.5-25.8)	32.1 (31.4-32.9)
Year of diagnosis								
2000-2006	19,286 (60.9%)	0.64	8	53.03	1.14	147.24 (144.00-150.55)	22.6 (21.8-23.4)	30.3 (29.4-31.2)
2007-2012	12,363 (39.1%)	0.14	7	16.28	0.59	278.25 (270.21-286.47)	29.1 (28.0-30.3)	35.0 (33.7-36.3)
Sex								
Women	14,809 (46.8%)	0.32	7	31.70	0.80	178.88 (174.26-183.60)	24.6 (23.7-25.5)	31.5 (30.4-32.6)
Men	16,840 (53.2%)	0.35	8	37.62	0.91	177.29 (173.06-181.60)	25.7 (24.8-26.5)	32.7 (31.6-33.7)
Age at diagnosis, years								
Median (quartiles)	78 (69.1-84.9)							
<18	80 (0.3%)	0.06	1	0.24	0.41	161.39 (114.21-221.52)	41.3 (22.9-59.6)	43.8 (24.4-63.1)
18-44	582 (1.8%)	0.31	9	2.11	2.36	99.69 (86.66-114.12)	23.2 (18.7-27.7)	28.0 (22.9-33.1)
45-59	2,851 (9.0%)	0.47	9	10.83	2.54	95.61 (89.87-101.61)	21.4 (19.5-23.3)	27.8 (25.6-30.1)
60-69	5,044 (15.9%)	0.47	9	14.91	1.63	146.97 (140.88-153.26)	26.1 (24.4-27.7)	33.8 (31.8-35.8)
70-79	9,376 (29.6%)	0.45	9	21.54	0.98	185.23 (179.52-191.06)	26.2 (25.0-27.4)	33.9 (32.5-35.4)
>=80	13,716 (43.3%)	0.21	6	19.70	0.44	247.51 (240.61-254.56)	24.9 (23.9-25.9)	31.3 (30.2-32.5)
Lowest level of eGFR measured before hyperkalemia/index date								

Hyperkalemia event is defined as >5.0 mmol/L

	<i>Number</i>	<i>Median years to first HK event</i>	<i>Median number of measurements before the first HK event</i>	<i>Total person-years of follow-up (1,000)</i>	<i>Median person-years of follow-up</i>	<i>Incidence rate of HK per 1,000 person-years (95% CI)</i>	<i>1-year cumulative incidence proportion of HK (95% CI)</i>	<i>3-year cumulative incidence proportion of HK (95% CI)</i>
No values below 60 mL/min/1.73m ²	7,679 (24.3%)	0.53	9	21.52	1.65	125.74 (121.05-130.57)	21.3 (20.1-22.4)	28.5 (27.1-29.9)
eGFR 45-59 mL/min/1.73m ²	6,931 (21.9%)	0.43	9	15.24	0.98	189.28 (182.44-196.32)	26.1 (24.7-27.5)	34.5 (32.8-36.2)
eGFR 30-44 mL/min/1.73m ²	5,800 (18.3%)	0.19	7	8.67	0.40	325.49 (313.60-337.73)	35.0 (33.1-36.9)	43.4 (41.2-45.7)
eGFR 15-29 mL/min/1.73m ²	3,707 (11.7%)	0.08	5	3.48	0.15	569.77 (544.97-595.40)	43.6 (40.8-46.5)	50.6 (47.4-53.9)
eGFR<15 mL/min/1.73m ²	1,166 (3.7%)	0.07	6	0.82	0.10	786.16 (726.47-849.45)	48.1 (42.6-53.6)	52.9 (46.8-59.0)
Dialysis	298 (0.9%)	0.17	8	0.20	0.20	827.42 (706.69-962.87)	47.7 (36.8-58.5)	55.0 (42.5-67.6)
No eGFR recorded	6,068 (19.2%)	3.91	7	19.39	1.92	58.49 (55.14-62.00)	2.8 (2.4-3.2)	6.9 (6.2-7.6)
Conditions underlying heart failure								
Cardiomyopathy	1,341 (4.2%)	0.38	8	3.61	1.41	153.73 (141.21-167.07)	26.8 (23.5-30.0)	34.1 (30.2-37.9)
Valvular heart disease	4,262 (13.5%)	0.25	8	7.67	0.59	236.90 (226.13-248.04)	29.8 (27.8-31.8)	36.7 (34.5-39.0)
Myocardial infarction	6,787 (21.4%)	0.36	8	14.43	0.82	192.57 (185.48-199.87)	26.43 (25.01-27.86)	34.18 (32.47-35.90)
Ischemic heart disease	12,734 (40.2%)	0.33	8	27.37	0.80	189.95 (184.82-195.18)	26.7 (25.6-27.7)	34.1 (32.9-35.4)
Atrial fibrillation	11,094 (35.1%)	0.38	8	23.60	0.88	183.59 (178.16-189.14)	25.1 (24.0-26.1)	32.0 (30.8-33.3)
Other comorbidities								
Diabetes	6,076 (19.2%)	0.25	7	10.12	0.53	292.43 (281.99-303.16)	33.7 (31.9-35.5)	42.0 (39.9-44.1)

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Chronic kidney disease	12,995 (41.1%)	0.16	7	17.89	0.34	352.13 (343.48-360.93)	36.0 (34.7-37.3)	44.1 (42.6-45.6)
Hypertension	19,581 (61.9%)	0.32	8	39.23	0.75	207.92 (203.43-212.48)	27.4 (26.5-28.3)	35.1 (34.0-36.1)
Peripheral vascular disease	3,673 (11.6%)	0.24	8	5.50	0.47	294.47 (280.31-309.16)	31.55 (29.36-33.75)	38.77 (36.20-41.34)
Cerebrovascular disease	5,489 (17.3%)	0.26	7	9.02	0.52	225.12 (215.44-235.13)	25.49 (23.94-27.03)	32.17 (30.35-34.00)
Chronic pulmonary disease	5,838 (18.4%)	0.30	8	9.96	0.63	238.30 (228.81-248.09)	27.18 (25.62-28.75)	34.58 (32.72-36.45)
Peptic ulcer disease	3,029 (9.6%)	0.24	8	4.96	0.48	249.32 (235.62-263.61)	28.62 (26.37-30.88)	35.42 (32.79-38.06)
Any malignant disease	4,778 (15.1%)	0.21	7	6.78	0.41	261.51 (249.48-273.97)	26.6 (24.9-28.3)	32.8 (30.8-34.8)
Alcoholism-related disorders	2,420 (7.6%)	0.27	8	4.56	0.71	225.82 (212.23-240.05)	29.3 (26.7-31.8)	36.7 (33.7-39.7)
Medical obesity	2,159 (6.8%)	0.40	9	5.13	1.12	190.21 (178.46-202.53)	28.3 (25.7-31.0)	36.7 (33.5-39.9)
Drug treatment before first admission								
ACEis overall	7,430 (23.5%)	0.29	7	14.20	0.75	224.90 (217.17-232.84)	29.0 (27.6-30.5)	36.8 (35.1-38.5)
Ramipril	2,714 (8.6%)	0.21	7	4.80	0.67	242.45 (228.72-256.80)	30.8 (28.3-33.3)	38.1 (35.1-41.0)
Enalapril	2,077 (6.6%)	0.30	8	3.62	0.65	259.35 (243.03-276.47)	31.7 (28.8-34.6)	40.0 (36.5-43.5)
Other ACEis	2,271 (7.2%)	0.56	8	5.24	1.01	180.43 (169.11-192.31)	24.0 (21.7-26.4)	32.4 (29.6-35.3)

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ACEis/diuretics combination	1,129 (3.6%)	0.23	8	2.13	0.77	212.13 (193.01-232.65)	27.4 (23.8-31.0)	34.4 (30.1-38.6)
ARBs overall	3,403 (10.8%)	0.27	8	6.35	0.75	230.84 (219.18-242.97)	29.8 (27.6-32.0)	37.3 (34.7-39.9)
Losartan	1,437 (4.5%)	0.25	8	2.65	0.73	209.33 (192.26-227.51)	27.1 (24.0-30.3)	32.8 (29.2-36.4)
Candesartan	579 (1.8%)	0.29	7	1.03	0.77	300.13 (267.65-335.47)	37.1 (30.9-43.4)	47.8 (40.0-55.6)
Other ARBs	512 (1.6%)	0.25	7	1.03	0.82	243.75 (214.52-275.84)	34.2 (27.9-40.4)	43.4 (35.8-50.9)
ARBs/diuretics combination	1,129 (3.6%)	0.23	8	2.13	0.77	212.13 (193.01-232.65)	27.4 (23.8-31.0)	34.4 (30.1-38.6)
Beta-blockers	9,742 (30.8%)	0.33	8	20.27	0.88	190.75 (184.78-196.86)	26.0 (24.8-27.2)	33.1 (31.7-34.5)
Spironolactone	3,451 (10.9%)	0.26	7	6.09	0.55	240.43 (228.27-253.07)	28.7 (26.6-30.8)	36.4 (33.8-38.9)
Potassium supplements	9,537 (30.1%)	0.28	8	16.54	0.60	219.95 (212.86-227.22)	25.4 (24.2-26.6)	32.1 (30.7-33.5)
Loop diuretics	12,484 (39.4%)	0.28	8	20.86	0.56	243.39 (236.74-250.18)	27.4 (26.3-28.5)	34.7 (33.4-36.0)
NSAIDs	7,076 (22.4%)	0.35	8	15.46	0.93	178.24 (171.64-185.02)	25.0 (23.7-26.4)	31.9 (30.3-33.5)
Trimetoprim	798 (2.5%)	0.16	6	1.07	0.38	242.70 (214.04-274.13)	24.4 (20.5-28.4)	29.2 (24.7-33.7)
Macrolides	3,774 (11.9%)	0.36	8	7.40	0.81	197.80 (187.80-208.20)	25.1 (23.3-27.0)	32.5 (30.3-34.8)

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Year of diagnosis	Total	31,649 (100%)	0.61	11	85.87	1.46	72.48 (70.69-74.30)	11.2 (10.8-11.6)	15.3 (14.9-15.8)
	2000-2006	19,286 (60.9%)	1.15	13	65.67	1.94	61.33 (59.45-63.26)	10.0 (9.5-10.4)	14.4 (13.8-15.0)
	2007-2012	12,363 (39.1%)	0.19	9	20.20	1.02	108.73 (104.23-113.38)	13.2 (12.5-13.8)	16.8 (16.0-17.6)
Sex	Women	14,809 (46.8%)	0.57	11	38.86	1.33	73.80 (71.12-76.55)	11.1 (10.6-11.7)	15.1 (14.5-15.8)
	Men	16,840 (53.2%)	0.64	12	47.01	1.58	71.39 (69.00-73.85)	11.3 (10.7-11.8)	15.5 (14.8-16.1)
Age at diagnosis, years	Median (quartiles)	78 (69.1-84.9)							
	<18	80 (0.3%)	0.08	3	0.30	2.32	83.16 (53.82-122.76)	26.3 (13.2-39.3)	31.3 (16.5-46.0)
	18-44	582 (1.8%)	0.22	12	2.61	3.64	37.96 (30.85-46.21)	11.7 (8.7-14.6)	14.4 (11.1-17.8)
	45-59	2,851 (9.0%)	0.81	14	13.04	3.65	39.42 (36.08-42.98)	9.3 (8.2-10.5)	13.0 (11.6-14.4)
	60-69	5,044 (15.9%)	1.06	15.5	19.02	2.75	58.26 (54.88-61.79)	10.8 (9.8-11.7)	15.3 (14.2-16.5)
	70-79	9,376 (29.6%)	0.84	13	27.15	1.74	75.37 (72.13-78.70)	11.7 (10.9-12.4)	16.2 (15.3-17.1)
	>=80	13,716 (43.3%)	0.34	8	23.76	0.73	102.37 (98.35-106.53)	11.3 (10.7-11.9)	15.1 (14.4-15.8)
Lowest level of eGFR measured before hyperkalemia/index date	No values below 60 mL/min/1.73m ²	7,679 (24.3%)	1.13	16	26.56	2.49	42.73 (40.28-45.29)	7.1 (6.5-7.7)	10.7 (9.9-11.5)
	eGFR 45-59 mL/min/1.73m ²	6,931 (21.9%)	0.87	13	19.93	1.74	68.49 (64.90-72.22)	10.3 (9.5-11.1)	14.6 (13.7-15.6)

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eGFR 30-44 mL/min/1.73m ²	5,800 (18.3%)	0.47	11	11.89	0.94	123.85 (117.60-130.34)	15.7 (14.6-16.8)	21.0 (19.6-22.3)
eGFR 15-29 mL/min/1.73m ²	3,707 (11.7%)	0.16	8	5.02	0.38	234.43 (221.22-248.21)	23.3 (21.5-25.1)	29.4 (27.3-31.5)
eGFR<15 mL/min/1.73m ²	1,166 (3.7%)	0.08	8	1.18	0.20	367.93 (334.09-404.28)	30.4 (26.6-34.2)	35.1 (30.9-39.3)
Dialysis	298 (0.9%)	0.25	11	0.28	0.33	465.87 (388.95-553.55)	32.6 (24.7-40.4)	41.3 (31.8-50.8)
No eGFR measurement recorded	6,068 (19.2%)	4.29	12	21.02	2.12	24.41 (22.34-26.62)	1.0 (0.8-1.3)	2.9 (2.5-3.3)
Conditions underlying heart failure								
Cardiomyopathy	1,341 (4.2%)	0.79	13	4.64	2.40	60.34 (53.48-67.83)	11.3 (9.4-13.2)	16.0 (13.6-18.3)
Valvular heart disease	4,262 (13.5%)	0.41	11	9.76	1.07	98.35 (92.23-104.78)	14.1 (12.9-15.4)	18.5 (17.0-19.9)
Myocardial infarction	6,787 (21.4%)	0.65	12	18.14	1.42	79.53 (75.48-83.75)	12.05 (11.17-12.93)	16.71 (15.64-17.77)
Ischemic heart disease	12,734 (40.2%)	0.58	12	34.65	1.43	76.05 (73.17-79.01)	11.9 (11.3-12.6)	16.3 (15.5-17.0)
Atrial fibrillation	11,094 (35.1%)	0.61	12	28.86	1.46	74.54 (71.42-77.76)	11.1 (10.4-11.8)	15.2 (14.4-16.0)
Other comorbidities								
Diabetes	6,076 (19.2%)	0.55	11	13.28	1.06	127.39 (121.39-133.61)	16.5 (15.4-17.6)	22.5 (21.2-23.9)
Chronic kidney disease	12,995 (41.1%)	0.31	10	24.61	0.77	141.92 (137.25-146.70)	17.7 (16.9-18.5)	23.3 (22.4-24.3)
Hypertension	19,581 (61.9%)	0.56	11	49.27	1.33	86.38 (83.80-89.01)	12.7 (12.1-13.2)	17.4 (16.7-18.0)

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Peripheral vascular disease	3,673 (11.6%)	0.41	11	7.14	0.84	123.20 (115.19-131.61)	15.38 (14.00-16.76)	20.09 (18.47-21.71)
Cerebrovascular disease	5,489 (17.3%)	0.47	11	11.14	0.90	93.39 (87.80-99.24)	11.55 (10.59-12.51)	15.56 (14.42-16.69)
Chronic pulmonary disease	5,838 (18.4%)	0.64	12	12.61	1.06	99.52 (94.09-105.18)	12.35 (11.39-13.31)	17.37 (16.19-18.55)
Peptic ulcer disease	3,029 (9.6%)	0.48	11	6.27	0.90	103.61 (95.80-111.89)	13.04 (11.66-14.42)	17.63 (15.98-19.28)
Any malignant disease	4,778 (15.1%)	0.38	10	8.49	0.69	108.75 (101.84-115.99)	12.4 (11.3-13.4)	16.4 (15.2-17.7)
Alcoholism-related disorders	2,420 (7.6%)	0.41	11	5.79	1.20	95.07 (87.29-103.36)	14.0 (12.4-15.7)	18.9 (17.0-20.9)
Medical obesity	2,159 (6.8%)	0.92	15	6.44	1.85	89.88 (82.71-97.51)	13.8 (12.1-15.5)	20.2 (18.1-22.3)
Drug treatment before first admission								
ACEis overall	7,430 (23.5%)	0.50	11	17.94	1.36	92.24 (87.85-96.80)	13.4 (12.5-14.2)	18.1 (17.0-19.2)
Ramipril	2,714 (8.6%)	0.35	10	6.12	1.30	97.15 (89.50-105.28)	14.0 (12.5-15.5)	18.6 (16.8-20.4)
Enalapril	2,077 (6.6%)	0.47	11	4.66	1.24	107.41 (98.21-117.24)	14.8 (13.0-16.6)	20.2 (18.0-22.3)
Other ACEis	2,271 (7.2%)	0.95	13	6.50	1.70	73.73 (67.27-80.63)	10.7 (9.3-12.2)	15.4 (13.7-17.2)
ACEis/diuretics combination	731 (2.3%)	0.23	10	1.56	1.35	109.06 (93.28-126.74)	16.0 (12.8-19.2)	20.5 (16.8-24.2)
ARBs	3,403 (10.8%)	0.44	11	8.02	1.30	98.72 (91.96-105.84)	14.4 (13.0-15.8)	19.5 (17.9-21.2)
Losartan	1,437 (4.5%)	0.42	12	3.24	1.12	90.94 (80.86-101.93)	13.1 (11.1-15.1)	16.8 (14.5-19.1)
Candesartan	579 (1.8%)	0.68	12	1.45	1.78	120.62 (103.41-139.88)	17.1 (13.4-20.8)	25.6 (20.8-30.3)
Other ARBs	512 (1.6%)	0.40	8.5	1.33	1.73	102.10 (85.66-120.78)	16.6 (12.7-20.5)	23.0 (18.3-27.8)
ARBs/diuretics combination	1,129 (3.6%)	0.44	12	2.59	1.25	95.59 (84.06-108.25)	13.8 (11.5-16.2)	18.4 (15.7-21.2)

Hyperkalemia event is defined as >5.5 mmol/L

	<i>Number</i>	<i>Median years to first HK event</i>	<i>Median number of measurements before the first HK event</i>	<i>Total person-years of follow-up (1,000)</i>	<i>Median person-years of follow-up</i>	<i>Incidence rate of HK per 1,000 person-years (95% CI)</i>	<i>1-year cumulative incidence proportion of HK (95% CI)</i>	<i>3-year cumulative incidence proportion of HK (95% CI)</i>
Beta-blockers	9,742 (30.8%)	0.51	11	24.83	1.45	78.95 (75.49-82.52)	12.0 (11.3-12.8)	16.4 (15.5-17.3)
Spironolactone	3,451 (10.9%)	0.43	10	7.66	1.01	104.48 (97.36-111.97)	14.3 (12.9-15.6)	19.0 (17.4-20.6)
Potassium supplements	9,537 (30.1%)	0.48	11	20.23	0.96	93.74 (89.57-98.06)	12.1 (11.4-12.9)	16.2 (15.3-17.1)
Loop diuretics	12,484 (39.4%)	0.48	11	25.93	0.94	106.00 (102.07-110.04)	13.4 (12.7-14.1)	18.0 (17.2-18.9)
NSAIDs	7,076 (22.4%)	0.62	11	19.11	1.56	73.10 (69.32-77.04)	11.5 (10.7-12.3)	15.3 (14.3-16.3)
Trimetoprim	798 (2.5%)	0.16	8	1.27	0.65	107.33 (90.05-126.96)	12.2 (9.6-14.7)	14.8 (11.9-17.7)
Macrolides	3,774 (11.9%)	0.60	12	9.17	1.28	82.74 (76.96-88.85)	11.8 (10.6-12.9)	16.1 (14.7-17.5)

Hyperkalemia event is defined as >6.0 mmol/L

	<i>Number</i>	<i>Median years to first HK event</i>	<i>Median number of measurements before the first HK event</i>	<i>Total person-years of follow-up (1,000)</i>	<i>Median person-years of follow-up</i>	<i>Incidence rate of HK per 1,000 person-years (95% CI)</i>	<i>1-year cumulative incidence proportion of HK (95% CI)</i>	<i>3-year cumulative incidence proportion of HK (95% CI)</i>
Total	31,649 (100%)	0.84	14	92.43	1.73	31.74 (30.61-32.91)	4.9 (4.7-5.2)	7.0 (6.7-7.3)
Year of diagnosis								
2000-2006	19,286 (60.9%)	1.45	16	70.65	2.30	26.93 (25.74-28.17)	4.3 (4.0-4.6)	6.4 (6.1-6.8)
2007-2012	12,363 (39.1%)	0.27	11	21.77	1.21	47.35 (44.51-50.33)	5.9 (5.5-6.3)	7.8 (7.3-8.3)
Sex								
Women	14,809 (46.8%)	0.86	14	41.80	1.59	32.80 (31.09-34.59)	4.9 (4.5-5.3)	6.9 (6.5-7.4)
Men	16,840 (53.2%)	0.83	14	50.63	1.85	30.87 (29.36-32.44)	4.9 (4.6-5.3)	7.0 (6.6-7.4)
Age at diagnosis, years								
Median (quartiles)	78 (69.1-84.9)							
<18	80 (0.3%)	0.05	1	0.34	3.88	40.65 (22.22-68.20)	15.0 (5.8-24.2)	17.5 (7.4-27.6)
18-44	582 (1.8%)	0.28	12.5	2.77	4.07	18.79 (14.03-24.64)	6.0 (4.0-8.1)	7.6 (5.2-9.9)
45-59	2,851 (9.0%)	1.22	20	13.85	4.15	18.41 (16.22-20.81)	4.1 (3.4-4.9)	6.0 (5.1-6.9)
60-69	5,044 (15.9%)	1.48	22	20.55	3.16	26.66 (24.48-28.99)	4.8 (4.1-5.4)	7.2 (6.4-7.9)
70-79	9,376 (29.6%)	1.03	16	29.50	2.07	32.14 (30.12-34.25)	5.0 (4.5-5.4)	7.3 (6.7-7.8)
>=80	13,716 (43.3%)	0.42	10	25.41	0.86	43.96 (41.42-46.62)	5.0 (4.6-5.4)	6.8 (6.4-7.3)
Lowest level of eGFR measured before hyperkalemia/index date								
No values below 60 mL/min/1.73m ²	7,679 (24.3%)	1.50	20	28.07	2.75	17.49 (15.98-19.11)	2.7 (2.3-3.1)	4.3 (3.9-4.8)
eGFR 45-59 mL/min/1.73m ²	6,931 (21.9%)	1.30	16	21.71	2.05	27.32 (25.16-29.61)	3.8 (3.4-4.3)	5.9 (5.3-6.5)

Hyperkalemia event is defined as >6.0 mmol/L

	<i>Number</i>	<i>Median years to first HK event</i>	<i>Median number of measurements before the first HK event</i>	<i>Total person-years of follow-up (1,000)</i>	<i>Median person-years of follow-up</i>	<i>Incidence rate of HK per 1,000 person-years (95% CI)</i>	<i>1-year cumulative incidence proportion of HK (95% CI)</i>	<i>3-year cumulative incidence proportion of HK (95% CI)</i>
eGFR 30-44 mL/min/1.73m ²	5,800 (18.3%)	0.70	13	13.38	1.23	51.43 (47.66-55.42)	6.7 (6.0-7.4)	9.3 (8.5-10.2)
eGFR 15-29 mL/min/1.73m ²	3,707 (11.7%)	0.22	9	5.91	0.54	102.08 (94.09-110.56)	11.7 (10.5-12.9)	15.1 (13.7-16.4)
eGFR<15 mL/min/1.73m ²	1,166 (3.7%)	0.09	8	1.45	0.31	161.19 (141.16-183.27)	15.7 (13.2-18.2)	18.6 (15.9-21.4)
Dialysis	298 (0.9%)	0.38	14	0.38	0.57	213.80 (169.79-265.73)	18.5 (13.1-23.9)	24.2 (17.8-30.6)
No eGFR recorded	6,068 (19.2%)	4.48	17	21.54	2.16	11.38 (10.00-12.89)	0.4 (0.2-0.6)	1.3 (1.0-1.5)
Conditions underlying heart failure								
Cardiomyopathy	1,341 (4.2%)	1.23	15	4.96	2.69	25.99 (21.70-30.88)	4.4 (3.3-5.5)	7.3 (5.8-8.8)
Valvular heart disease	4,262 (13.5%)	0.59	13	10.64	1.30	42.57 (38.74-46.68)	6.4 (5.6-7.2)	8.7 (7.8-9.7)
Myocardial infarction	6,787 (21.4%)	0.75	13	19.63	1.72	34.74 (32.18-37.45)	5.55 (4.98-6.13)	7.59 (6.91-8.27)
Ischemic heart disease	12,734 (40.2%)	0.77	14	37.55	1.74	32.39 (30.59-34.26)	5.2 (4.8-5.6)	7.2 (6.7-7.7)
Atrial fibrillation	11,094 (35.1%)	0.86	17	31.08	1.72	31.79 (29.84-33.84)	4.7 (4.3-5.1)	6.7 (6.2-7.2)
Comorbidities								
Diabetes	6,076 (19.2%)	0.75	15	14.85	1.34	59.25 (55.40-63.29)	8.0 (7.3-8.8)	11.4 (10.5-12.3)
Chronic kidney disease	12,995 (41.1%)	0.47	13	27.68	1.02	61.56 (58.67-64.55)	8.1 (7.6-8.6)	11.0 (10.4-11.6)
Hypertension	19,581 (61.9%)	0.75	14	53.42	1.61	38.41 (36.77-40.11)	5.7 (5.3-6.0)	8.1 (7.7-8.5)

Hyperkalemia event is defined as >6.0 mmol/L

	<i>Number</i>	<i>Median years to first HK event</i>	<i>Median number of measurements before the first HK event</i>	<i>Total person-years of follow-up (1,000)</i>	<i>Median person-years of follow-up</i>	<i>Incidence rate of HK per 1,000 person-years (95% CI)</i>	<i>1-year cumulative incidence proportion of HK (95% CI)</i>	<i>3-year cumulative incidence proportion of HK (95% CI)</i>
Peripheral vascular disease	3,673 (11.6%)	0.54	15	7.89	1.05	52.22 (47.30-57.51)	6.70 (5.83-7.56)	9.34 (8.30-10.38)
Cerebrovascular disease	5,489 (17.3%)	0.59	13	12.01	1.08	39.89 (36.40-43.63)	5.03 (4.42-5.64)	6.83 (6.12-7.55)
Chronic pulmonary disease	5,838 (18.4%)	0.81	14	13.71	1.25	43.26 (39.84-46.88)	5.55 (4.93-6.17)	7.85 (7.10-8.59)
Peptic ulcer disease	3,029 (9.6%)	0.59	14	6.88	1.12	46.94 (41.96-52.34)	6.14 (5.23-7.05)	8.75 (7.65-9.85)
Any malignant disease	4,778 (15.1%)	0.49	12.5	9.17	0.82	49.96 (45.49-54.75)	5.7 (5.0-6.4)	7.9 (7.1-8.7)
Alcoholism-related disorders	2,420 (7.6%)	0.55	14	6.33	1.51	46.11 (40.97-51.71)	7.2 (6.1-8.3)	9.7 (8.4-11.0)
Medical obesity	2,159 (6.8%)	1.08	21	7.13	2.23	41.78 (37.17-46.81)	6.7 (5.5-7.8)	10.2 (8.8-11.7)
Drug treatment before first admission								
ACEis overall	7,430 (23.5%)	0.54	13	19.51	1.65	41.72 (38.90-44.69)	6.4 (5.8-7.0)	8.7 (8.0-9.4)
Ramipril	2,714 (8.6%)	0.44	12	6.63	1.52	42.25 (37.44-47.49)	6.6 (5.6-7.6)	8.7 (7.5-9.8)
Enalapril	2,077 (6.6%)	0.57	15	5.13	1.52	49.74 (43.82-56.24)	7.0 (5.8-8.2)	9.9 (8.5-11.3)
Other ACEis	2,271 (7.2%)	1.00	15	7.04	2.03	33.25 (29.12-37.79)	5.2 (4.2-6.1)	7.2 (6.1-8.4)
ACEis/diuretics combination	731 (2.3%)	0.28	12	1.72	1.62	50.45 (40.41-62.24)	7.8 (5.7-9.9)	10.3 (7.8-12.7)
ARBs overall	3,403 (10.8%)	0.63	14	8.87	1.68	41.03 (36.92-45.47)	6.3 (5.4-7.1)	8.6 (7.6-9.7)
Losartan	1,437 (4.5%)	0.42	14	3.53	1.33	37.69 (31.56-44.67)	6.1 (4.7-7.4)	7.3 (5.9-8.8)
Candesartan	579 (1.8%)	0.70	14	1.67	2.19	47.87 (37.96-59.57)	7.6 (5.3-9.9)	11.4 (8.5-14.3)

Hyperkalemia event is defined as >6.0 mmol/L

	<i>Number</i>	<i>Median years to first HK event</i>	<i>Median number of measurements before the first HK event</i>	<i>Total person-years of follow-up (1,000)</i>	<i>Median person-years of follow-up</i>	<i>Incidence rate of HK per 1,000 person-years (95% CI)</i>	<i>1-year cumulative incidence proportion of HK (95% CI)</i>	<i>3-year cumulative incidence proportion of HK (95% CI)</i>
Other ARBs	512 (1.6%)	0.96	15	1.50	2.25	44.77 (34.70-56.86)	7.0 (4.6-9.4)	10.5 (7.6-13.5)
ARBs/diuretics combination	1,129 (3.6%)	0.70	14	2.87	1.66	38.71 (31.85-46.62)	5.3 (3.9-6.7)	7.9 (6.2-9.6)
Beta-blockers	9,742 (30.8%)	0.71	14	26.71	1.74	34.86 (32.66-37.17)	5.3 (4.8-5.8)	7.5 (7.0-8.1)
Spironolactone	3,451 (10.9%)	0.50	12	8.38	1.30	46.45 (41.94-51.30)	6.6 (5.7-7.5)	9.4 (8.3-10.4)
Potassium supplements	9,537 (30.1%)	0.56	13	21.73	1.12	42.88 (40.17-45.72)	5.7 (5.2-6.2)	7.8 (7.2-8.4)
Loop diuretics	12,484 (39.4%)	0.56	13	28.16	1.14	48.48 (45.94-51.12)	6.4 (5.9-6.9)	8.8 (8.2-9.3)
NSAIDs	7,076 (22.4%)	0.75	13	20.51	1.81	32.03 (29.63-34.58)	5.1 (4.6-5.7)	7.1 (6.5-7.8)
Trimetoprim	798 (2.5%)	0.17	10	1.35	0.79	59.28 (47.00-73.77)	6.6 (4.8-8.5)	8.8 (6.6-10.9)
Macrolides	3,774 (11.9%)	0.72	15	9.85	1.51	37.65 (33.91-41.68)	5.5 (4.7-6.3)	7.8 (6.9-8.7)

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; HK, hyperkalemia; NSAIDs, non-steroidal anti-inflammatory drugs.

Table S3. Prevalence and prevalence ratios (PR) for risk factors prior to the hyperkalemia/index date among heart failure patients with hyperkalemia versus matched comparison patients divided in moderate (>5.5 mmol/L) and severe (>6.0 mmol/L) hyperkalemia.

	<i>Patients with heart failure and hyperkalemia >5.5 mmol/L</i>	<i>Matched comparisons without hyperkalemia*</i>	<i>PR (95% CI)</i>
No. of patients	6,224 (100%)	6,130 (100%)	
Females	2,868 (46.1%)	2,829 (46.2%)	
Age, median (quartiles), y	79 (70.9-85.2)	79 (71.2-85.2)	
K+ tests 6 mo. before HK/index date, median (quartiles)	7.0 (2.0-13.0)	2.0 (0.0-6.0)	
Acute heart failure hospitalizations 6 mo. before HK/index date median (quartiles)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	
Conditions underlying heart failure †			
Cardiomyopathy	487 (7.8%)	440 (7.2%)	1.09 (0.96-1.23)
Valvular heart disease	1,205 (19.4%)	903 (14.7%)	1.31 (1.21-1.42)
Myocardial infarction	1,881 (30.2%)	1,678 (27.4%)	1.10 (1.0-1.17)
Any ischemic heart disease	3,055 (49.1%)	2,779 (45.3%)	1.08 (1.04-1.12)
Atrial fibrillation	2,536 (40.7%)	2,359 (38.5%)	1.06 (1.01-1.11)
Lowest level of eGFR measured before hyperkalemia/index date			
No values below 60 mL/min/1.73m ²	507 (8.1%)	1,195 (19.5%)	0.42 (0.38-0.46)
eGFR 45-59 mL/min/1.73m ²	855 (13.7%)	1,449 (23.6%)	0.58 (0.54-0.63)
eGFR 30-44 mL/min/1.73m ²	1,708 (27.4%)	1,428 (23.3%)	1.18 (1.11-1.25)
eGFR 15-29 mL/min/1.73m ²	2,127 (34.2%)	922 (15.0%)	2.27 (2.12-2.43)
eGFR<15 mL/min/1.73m ²	742 (11.9%)	212 (3.5%)	3.45 (2.97-4.00)
Dialysis	204 (3.3%)	38 (0.6%)	5.29 (3.75-7.46)
No eGFR recorded	81 (1.3%)	886 (14.5%)	0.09 (0.07-0.11)
Selected risk factors for hyperkalemia			
Diabetes	2,002 (32.2%)	1,261 (20.6%)	1.56 (1.47-1.66)
Chronic kidney disease ‡	4,650 (74.7%)	3,052 (49.8%)	1.50 (1.46-1.55)
Hypertension	5,310 (85.3%)	4,855 (79.2%)	1.08 (1.06-1.10)
Other comorbidities			
Peripheral vascular disease	1,167 (18.8%)	764 (12.5%)	1.50 (1.4-1.64)

	<i>Patients with heart failure and hyperkalemia >5.5 mmol/L</i>	<i>Matched comparisons without hyperkalemia*</i>	<i>PR (95% CI)</i>
Cerebrovascular disease	1,335 (21.4%)	1,187 (19.4%)	1.11 (1.0-1.19)
Chronic pulmonary disease	1,856 (29.8%)	1,463 (23.9%)	1.25 (1.2-1.33)
Peptic ulcer disease	826 (13.3%)	667 (10.9%)	1.22 (1.1-1.34)
Any malignant disease	1,159 (18.6%)	928 (15.1%)	1.23 (1.14-1.33)
Alcoholism-related disorders	673 (10.8%)	496 (8.1%)	1.34 (1.20-1.49)
Medical obesity	678 (10.9%)	445 (7.3%)	1.50 (1.34-1.68)
Use of specific hyperkalemia-associated medications			
ACEis	2,882 (46.3%)	2,637 (43.0%)	1.08 (1.03-1.12)
Ramipril	1,416 (22.8%)	1,223 (20.0%)	1.14 (1.07-1.22)
Enalapril	691 (11.1%)	550 (9.0%)	1.24 (1.11-1.38)
Other ACEis	783 (12.6%)	846 (13.8%)	0.91 (0.83-1.00)
ACEis/diuretics combination	165 (2.7%)	132 (2.2%)	1.23 (0.98-1.54)
ARBs overall	972 (15.6%)	908 (14.8%)	1.06 (0.98-1.15)
Losartan	430 (6.9%)	433 (7.1%)	0.98 (0.86-1.11)
Candesartan	230 (3.7%)	189 (3.1%)	1.20 (0.99-1.45)
Other ARBs	165 (2.7%)	137 (2.2%)	1.19 (0.95-1.48)
ARBs/diuretics combination	229 (3.7%)	242 (3.9%)	0.93 (0.78-1.11)
Spironolactone	2,394 (38.5%)	1,523 (24.8%)	1.55 (1.47-1.63)
Potassium supplements	3,235 (52.0%)	3,113 (50.8%)	1.02 (0.99-1.06)
Loop diuretics	4,401 (70.7%)	3,974 (64.8%)	1.09 (1.06-1.12)
NSAIDs	1,416 (22.8%)	1,336 (21.8%)	1.04 (0.98-1.11)
Trimetoprim	249 (4.0%)	204 (3.3%)	1.20 (1.00-1.44)
Macrolides	883 (14.2%)	709 (11.6%)	1.23 (1.12-1.35)

	<i>Patients with heart failure and hyperkalemia >6.0 mmol/L</i>	<i>Matched comparisons without hyperkalemia*</i>	<i>PR (95% CI)</i>
No. of patients	2,934 (100%)	2,891 (100%)	
Females	1,371 (46.7%)	1,353 (46.8%)	
Age, median (quartiles), y	79 (70.5-85.2)	79 (70.9-85.2)	
K+ tests 6 mo. before HK/index date, median (quartiles)	7.0 (3.0-15.0)	2.0 (0.0-5.0)	
Acute heart failure hospitalizations 6 mo. before HK/index date median (quartiles)	0.0 (0.0-1.0)	0.0 (0.0-0.0)	
Conditions underlying heart failure †			
Cardiomyopathy	236 (8.0%)	218 (7.5%)	1.07 (0.89-1.27)
Valvular heart disease	591 (20.1%)	441 (15.3%)	1.32 (1.18-1.48)
Myocardial infarction	896 (30.5%)	842 (29.1%)	1.05 (1.00-1.13)
Any ischemic heart disease	1,455 (49.6%)	1,355 (46.9%)	1.06 (1.00-1.12)
Atrial fibrillation	1,227 (41.8%)	1,125 (38.9%)	1.07 (1.01-1.14)
Lowest level of eGFR measured before hyperkalemia/index date			
No values below 60 mL/min/1.73m ²	179 (6.1%)	526 (18.2%)	0.34 (0.29-0.39)
eGFR 45-59 mL/min/1.73m ²	291 (9.9%)	632 (21.9%)	0.45 (0.40-0.52)
eGFR 30-44 mL/min/1.73m ²	707 (24.1%)	725 (25.1%)	0.96 (0.88-1.05)
eGFR 15-29 mL/min/1.73m ²	1,102 (37.6%)	455 (15.7%)	2.39 (2.17-2.63)
eGFR<15 mL/min/1.73m ²	482 (16.4%)	115 (4.0%)	4.13 (3.39-5.03)
Dialysis	144 (4.9%)	22 (0.8%)	6.45 (4.13-10.07)
No eGFR measurements recorded	29 (1.0%)	416 (14.4%)	0.07 (0.05-0.10)
Selected risk factors for hyperkalemia			
Diabetes	1,039 (35.4%)	652 (22.6%)	1.57 (1.44-1.71)
Chronic kidney disease ‡	2,297 (78.3%)	1,480 (51.2%)	1.53 (1.47-1.59)
Hypertension	2,562 (87.3%)	2,367 (81.9%)	1.07 (1.04-1.09)
Other comorbidities			
Peripheral vascular disease	561 (19.1%)	391 (13.5%)	1.41 (1.3-1.59)
Cerebrovascular disease	629 (21.4%)	531 (18.4%)	1.17 (1.1-1.29)
Chronic pulmonary disease	901 (30.7%)	702 (24.3%)	1.26 (1.2-1.38)
Peptic ulcer disease	424 (14.5%)	307 (10.6%)	1.36 (1.2-1.56)

	<i>Patients with heart failure and hyperkalemia >6.0 mmol/L</i>	<i>Matched comparisons without hyperkalemia*</i>	<i>PR (95% CI)</i>	
Use of specific hyperkalemia-associated medications	Any malignant disease	591 (20.1%)	427 (14.8%)	1.36 (1.22-1.53)
	Alcoholism-related disorders	372 (12.7%)	245 (8.5%)	1.50 (1.28-1.74)
	Medical obesity	371 (12.6%)	222 (7.7%)	1.65 (1.41-1.93)
	ACEis overall	1,426 (48.6%)	1,246 (43.1%)	1.13 (1.07-1.19)
	Ramipril	693 (23.6%)	614 (21.2%)	1.11 (1.01-1.22)
	Enalapril	369 (12.6%)	243 (8.4%)	1.50 (1.28-1.74)
	Other ACEis	363 (12.4%)	382 (13.2%)	0.94 (0.82-1.07)
	ACEis/diuretics combination	83 (2.8%)	58 (2.0%)	1.41 (1.01-1.96)
	ARBs overall	459 (15.6%)	450 (15.6%)	1.01 (0.89-1.13)
	Losartan	206 (7.0%)	220 (7.6%)	0.92 (0.77-1.11)
	Candesartan	108 (3.7%)	83 (2.9%)	1.28 (0.97-1.70)
	Other ARBs	81 (2.8%)	71 (2.5%)	1.12 (0.82-1.54)
	ARBs/diuretics combination	97 (3.3%)	124 (4.3%)	0.77 (0.59-1.00)
	Spironolactone	1,200 (40.9%)	712 (24.6%)	1.66 (1.54-1.79)
	Potassium supplements	1,586 (54.1%)	1,420 (49.1%)	1.10 (1.05-1.16)
	Loop diuretics	2,170 (74.0%)	1,837 (63.5%)	1.16 (1.12-1.21)
	NSAIDs	672 (22.9%)	646 (22.3%)	1.03 (0.93-1.13)
	Trimetoprim	134 (4.6%)	95 (3.3%)	1.39 (1.07-1.80)
	Macrolides	456 (15.5%)	332 (11.5%)	1.35 (1.19-1.54)

* Heart failure comparison patients without hyperkalemia matched on age, sex, and duration of heart failure on the hyperkalemia/index date

† As present at the time of heart failure diagnosis.

‡ Manifest chronic kidney disease was defined on the date of the second of two measurements more than 90 days apart of a creatinine value corresponding to an eGFR below 60 mL/min/1.73m², or on the first date of a hospital diagnosis of chronic kidney disease, see text and Supplementary material with codes

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; NSAIDs, non-steroidal anti-inflammatory drugs. PR, prevalence ratio

Table S4. Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK separate for moderate and (>5.5 mmol/L) and severe (>6.0 mmol/L) HK

	Heart failure patients with first HK >5.5 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted‡ Hazard Ratio (95% CI)
Any hospital outpatient contact	3,975 (4,051.21)	3,170 (1,645.62)	2.03 (1.92-2.14)	1.57 (1.48-1.67)
Any acute hospitalization	5,117 (7,257.35)	2,484 (1,183.59)	3.92 (3.71-4.14)	2.83 (2.67-3.01)
Any non-acute hospitalization	1,331 (856.24)	887 (344.90)	2.35 (2.14-2.59)	1.74 (1.55-1.93)
Any cardiac diagnosis	4,128 (4,219.94)	2,006 (900.10)	3.40 (3.20-3.61)	2.65 (2.49-2.81)
Ventricular arrhythmia	218 (116.89)	118 (42.12)	2.84 (2.21-3.65)	2.34 (1.77-3.24)
Cardiac arrest	104 (54.41)	15 (5.30)	11.53 (6.44-20.63)	13.70 (4.02-49.62)
Dialysis procedure	201 (107.35)	28 (9.90)	2.83 (1.86-4.29)	1.28 (0.78-2.06)
Ventilator treatment	657 (363.37)	94 (33.35)	11.82 (9.38-14.90)	6.16 (4.28-9.10)
ICU admission	1,146 (679.53)	247 (88.79)	7.55 (6.50-8.77)	4.74 (3.80-5.99)
Heart failure re-admission	2,840 (2,176.16)	1,467 (623.56)	2.84 (2.64-3.05)	2.37 (2.20-2.53)
ACEi prescription	1,867 (1,460.69)	2,461 (1,298.93)	0.98 (0.91-1.05)	0.90 (0.86-0.95)
ARB prescription	547 (312.83)	780 (305.61)	0.79 (0.70-0.89)	0.93 (0.85-1.01)
Spironolactone prescription	1,332 (885.95)	1,494 (641.90)	0.87 (0.80-0.94)	0.70 (0.66-0.75)
Potassium supplement prescription	1,674 (1,170.86)	2,909 (1,625.12)	0.77 (0.72-0.82)	0.66 (0.63-0.70)
Death	2,887 (1,500.55)	747 (263.52)	4.93 (4.51-5.38)	-

	Heart failure patients with first HK >6.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted Hazard Ratio
Any hospital outpatient contact	1,932 (5,256.27)	1,437 (1,559.45)	2.61 (2.40-2.83)	1.96 (1.78-2.14)
Any acute hospitalization	2,603 (12,392.70)	1,108 (1,085.77)	5.95 (5.47-6.47)	3.68 (3.35-4.02)
Any non-acute hospitalization	579 (920.35)	390 (317.48)	2.75 (2.36-3.20)	1.86 (1.53-2.15)
Any cardiac diagnosis	2,078 (5,994.61)	887 (821.60)	4.76 (4.34-5.22)	3.12 (2.85-3.44)
Ventricular arrhythmia	122 (163.11)	44 (33.14)	5.06 (3.41-7.49)	3.29 (2.04-5.32)
Cardiac arrest	58 (75.05)	8 (5.98)	13.45 (5.99-30.19)	10.00 (1.36-57.21)
Dialysis procedure	136 (183.48)	12 (8.97)	4.59 (2.40-8.78)	2.13 (1.05-4.72)
Ventilator treatment	323 (440.36)	36 (27.01)	18.51 (12.74-26.88)	5.64 (3.19-9.89)
ICU admission	613 (925.15)	99 (75.17)	12.79 (10.10-16.19)	4.44 (3.12-6.11)
Heart failure re-admission	1,402 (2,750.84)	624 (546.13)	3.86 (3.46-4.31)	2.88 (2.59-3.21)
ACEi prescription	723 (1,342.91)	1,162 (1,302.98)	0.78 (0.70-0.87)	0.78 (0.72-0.85)
ARB prescription	209 (292.88)	395 (329.42)	0.63 (0.52-0.77)	0.87 (0.76-0.99)
Spironolactone prescription	508 (808.87)	679 (611.97)	0.70 (0.61-0.80)	0.63 (0.57-0.70)
Potassium supplement prescription	691 (1,162.62)	1,327 (1,536.74)	0.75 (0.67-0.83)	0.64 (0.58-0.69)
Death	1,608 (2,064.20)	344 (256.73)	6.87 (6.03-7.84)	-

* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

† Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡ The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Table S5. Chronic heart failure: Baseline characteristics among patients with first hospital diagnosed heart failure, stratified by eGFR category and subsequent incidence of hyperkalemia.

	eGFR category (mL/min/1.73m2)*						Dialysis	No eGFR recorded	Total
	eGFR≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR<15				
Number of HF patients (row %)	2,194 (23.5%)	2,232 (23.9%)	2,043 (21.9%)	1,466 (15.7%)	436 (4.7%)	160 (1.7%)	796 (8.5%)	9,327 (100%)	
Female	529 (24.1%)	766 (34.3%)	885 (43.3%)	711 (48.5%)	225 (51.6%)	56 (35.0%)	340 (42.7%)	3,512 (37.7%)	
Median age (quartiles)	64 (55.9-72.8)	71 (63.1-78.6)	77 (69.3-82.7)	79 (71.8-84.9)	78 (69.3-83.6)	69 (58.9-77.2)	76 (66.5-82.1)	73 (63.6-80.8)	
Echocardiography performed before / at first HF admission	2,194 (100%)	2,232 (100%)	2,043 (100%)	1,466 (100%)	436 (100%)	160 (100%)	796 (100%)	9,327 (100%)	
Heart failure as primary diagnosis	920 (41.9%)	992 (44.4%)	874 (42.8%)	596 (40.7%)	179 (41.1%)	68 (42.5%)	386 (48.5%)	4,015 (43.0%)	
Conditions underlying heart failure †									
Cardiomyopathy	455 (20.7%)	373 (16.7%)	260 (12.7%)	152 (10.4%)	38 (8.7%)	11 (6.9%)	98 (12.3%)	1,387 (14.9%)	
Valvular heart disease	289 (13.2%)	376 (16.8%)	443 (21.7%)	366 (25.0%)	93 (21.3%)	27 (16.9%)	122 (15.3%)	1,716 (18.4%)	
Myocardial infarction	829 (37.8%)	889 (39.8%)	871 (42.6%)	625 (42.6%)	183 (42.0%)	70 (43.8%)	238 (29.9%)	3,705 (39.7%)	
Any ischemic heart disease	1,246 (56.8%)	1,289 (57.8%)	1,267 (62.0%)	935 (63.8%)	270 (61.9%)	110 (68.8%)	386 (48.5%)	5,503 (59.0%)	
Atrial fibrillation	807 (36.8%)	991 (44.4%)	985 (48.2%)	701 (47.8%)	204 (46.8%)	52 (32.5%)	370 (46.5%)	4,110 (44.1%)	
Other comorbidities									
Diabetes	441 (20.1%)	450 (20.2%)	504 (24.7%)	460 (31.4%)	184 (42.2%)	72 (45.0%)	161 (20.2%)	2,272 (24.4%)	
Chronic kidney disease [‡]	20 (0.9%)	957 (42.9%)	1,390 (68.0%)	1,179 (80.4%)	377 (86.5%)	160 (100%)	46 (5.8%)	4,129 (44.3%)	
Hypertension	2,194 (100%)	2,232 (100%)	2,043 (100%)	1,466 (100%)	436 (100%)	160 (100%)	796 (8.5%)	9,327 (100%)	
Peripheral vascular disease	191 (8.7%)	258 (11.6%)	329 (16.1%)	294 (20.1%)	110 (25.2%)	62 (38.8%)	85 (10.7%)	1,329 (14.2%)	

eGFR category (mL/min/1.73m2)*

	eGFR≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR<15	Dialysis	No eGFR recorded	Total
Cerebrovascular disease	255 (11.6%)	346 (15.5%)	416 (20.4%)	347 (23.7%)	132 (30.3%)	40 (25.0%)	125 (15.7%)	1,661 (17.8%)
Chronic pulmonary disease	340 (15.5%)	405 (18.1%)	392 (19.2%)	358 (24.4%)	113 (25.9%)	26 (16.3%)	115 (14.4%)	1,749 (18.8%)
Peptic ulcer disease	143 (6.5%)	177 (7.9%)	184 (9.0%)	216 (14.7%)	60 (13.8%)	31 (19.4%)	64 (8.0%)	875 (9.4%)
Any malignant disease	168 (7.7%)	279 (12.5%)	328 (16.1%)	257 (17.5%)	73 (16.7%)	30 (18.8%)	80 (10.1%)	1,215 (13.0%)
Alcoholism-related disorders	241 (11.0%)	189 (8.5%)	176 (8.6%)	157 (10.7%)	56 (12.8%)	23 (14.4%)	66 (8.3%)	908 (9.7%)
Medical obesity	229 (10.4%)	192 (8.6%)	179 (8.8%)	142 (9.7%)	61 (14.0%)	20 (12.5%)	49 (6.2%)	872 (9.3%)
Drug treatment, before first admission								
ACEis overall	1,948 (88.8%)	1,925 (86.2%)	1,633 (79.9%)	1,102 (75.2%)	288 (66.1%)	104 (65.0%)	668 (83.9%)	7,668 (82.2%)
Ramipril	1,094 (49.9%)	1,134 (50.8%)	900 (44.1%)	579 (39.5%)	156 (35.8%)	60 (37.5%)	126 (15.8%)	4,049 (43.4%)
Enalapril	293 (13.4%)	306 (13.7%)	301 (14.7%)	245 (16.7%)	75 (17.2%)	20 (12.5%)	118 (14.8%)	1,358 (14.6%)
Other ACEis	621 (28.3%)	530 (23.7%)	481 (23.5%)	305 (20.8%)	75 (17.2%)	28 (17.5%)	451 (56.7%)	2,491 (26.7%)
ACEis/diuretics combination	71 (3.2%)	90 (4.0%)	103 (5.0%)	90 (6.1%)	26 (6.0%)	1 (0.6%)	16 (2.0%)	397 (4.3%)
ARBs overall	438 (20.0%)	476 (21.3%)	529 (25.9%)	376 (25.6%)	142 (32.6%)	53 (33.1%)	161 (20.2%)	2,175 (23.3%)
Losartan	243 (11.1%)	246 (11.0%)	262 (12.8%)	169 (11.5%)	73 (16.7%)	27 (16.9%)	81 (10.2%)	1,101 (11.8%)
Candesartan	88 (4.0%)	110 (4.9%)	111 (5.4%)	56 (3.8%)	36 (8.3%)	24 (15.0%)	25 (3.1%)	450 (4.8%)
Other ARBs	54 (2.5%)	57 (2.6%)	82 (4.0%)	61 (4.2%)	18 (4.1%)	5 (3.1%)	30 (3.8%)	307 (3.3%)
ARBs/diuretics combination	102 (4.6%)	112 (5.0%)	139 (6.8%)	139 (9.5%)	32 (7.3%)	3 (1.9%)	44 (5.5%)	571 (6.1%)
Beta-blockers	2,116 (96.4%)	2,136 (95.7%)	1,927 (94.3%)	1,376 (93.9%)	408 (93.6%)	151 (94.4%)	754 (94.7%)	8,868 (95.1%)
Spirolactone	871 (39.7%)	1,000 (44.8%)	920 (45.0%)	655 (44.7%)	182 (41.7%)	19 (11.9%)	389 (48.9%)	4,036 (43.3%)
Potassium supplements	1,154 (52.6%)	1,402 (62.8%)	1,458 (71.4%)	1,096 (74.8%)	314 (72.0%)	58 (36.3%)	541 (68.0%)	6,023 (64.6%)

		eGFR category (mL/min/1.73m2)*							
		eGFR ≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR <15	Dialysis	No eGFR recorded	Total
	Loop diuretics	1,463 (66.7%)	1,744 (78.1%)	1,796 (87.9%)	1,384 (94.4%)	419 (96.1%)	135 (84.4%)	686 (86.2%)	7,627 (81.8%)
	NSAIDs	520 (23.7%)	503 (22.5%)	482 (23.6%)	374 (25.5%)	114 (26.1%)	24 (15.0%)	209 (26.3%)	2,226 (23.9%)
	Trimetroprim	23 (1.0%)	50 (2.2%)	66 (3.2%)	71 (4.8%)	23 (5.3%)	2 (1.3%)	28 (3.5%)	263 (2.8%)
	Macrolides	254 (11.6%)	337 (15.1%)	304 (14.9%)	227 (15.5%)	68 (15.6%)	27 (16.9%)	106 (13.3%)	1,323 (14.2%)
Hyperkalemia event >5.0 mmol/L									
	Total number of events	495 (22.6%)	719 (32.2%)	842 (41.2%)	659 (45.0%)	203 (46.6%)	101 (63.1%)	257 (32.3%)	3,276 (35.1%)
	Median years to event in pts with event	1.59	1.10	0.96	0.65	0.52	0.39	3.48	1.02
	Median no. K+ tests before the event	7	5	5	6	8	5	7	6
	1-year cumulative incidence, % (95% CI)	8.7 (7.4-9.9)	15.2 (13.5-17.0)	21.3 (19.1-23.6)	27.9 (24.7-31.1)	32.1 (25.7-38.6)	48.1 (33.2-63.0)	3.8 (2.4-5.1)	17.4 (16.5-18.3)
	Incidence rate of HK / 1,000 person-years (95% CI)	67.98 (62.12-74.24)	111.96 (103.93-120.46)	175.34 (163.69-187.59)	252.03 (233.15-272.03)	320.99 (278.35-368.31)	615.89 (501.66-748.37)	74.97 (66.09-84.72)	129.26 (124.87-133.76)
Hyperkalemia event >5.5 mmol/L									
	Total number of events	169 (7.7%)	293 (13.1%)	395 (19.3%)	366 (25.0%)	112 (25.7%)	78 (48.8%)	119 (14.9%)	1,532 (16.4%)
	Median years to event in pts with event	2.39	1.86	1.53	1.01	0.84	0.54	3.48	1.48
	Median no. K+ tests before the event	15	11	11	10	13	9	10	11
	1-year cumulative incidence, % (95% CI)	2.0 (1.4-2.6)	4.4 (3.5-5.3)	7.5 (6.3-8.8)	12.4 (10.5-14.3)	14.0 (10.2-17.8)	33.1 (22.2-44.0)	1.4 (0.6-2.2)	6.5 (5.9-7.0)
	Incidence rate of HK / 1,000 person-years (95% CI)	20.74 (17.74-24.12)	37.49 (33.32-42.04)	65.03 (58.77-71.77)	110.77 (99.71-122.72)	137.80 (113.46-165.81)	356.04 (281.43-444.35)	31.65 (26.22-37.87)	50.84 (48.33-53.45)
Hyperkalemia event >6.0 mmol/L									
	Total number of events	76 (3.5%)	119 (5.3%)	167 (8.2%)	156 (10.6%)	60 (13.8%)	50 (31.3%)	57 (7.2%)	685 (7.3%)

	eGFR category (mL/min/1.73m2)*							No eGFR recorded	Total
	eGFR ≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR <15	Dialysis			
Median years to event in pts with event	2.57	2.14	1.53	1.26	1.02	0.74	3.79	1.67	
Median no. K+ tests before the event	18	18	13	13	18	13	13	14	
1-year cumulative incidence, % (95% CI)	0.5 (0.2-0.9)	1.7 (1.2-2.2)	3.1 (2.4-3.9)	4.6 (3.5-5.8)	6.9 (4.3-9.4)	18.8 (11.3-26.2)	0.8 (0.1-1.4)	2.7 (2.3-3.0)	
Incidence rate of HK / 1,000 person-years (95% CI)	9.07 (7.15-11.35)	14.39 (11.92-17.22)	25.43 (21.72-29.59)	43.03 (36.54-50.34)	65.02 (49.62-83.70)	174.49 (129.51-230.04)	14.74 (11.17-19.10)	21.46 (19.88-23.13)	

* Patients categorized according to lowest measured eGFR before or on admission date with heart failure; presence of dialysis overrules any eGFR measurement result.

† Conditions possibly underlying heart failure; hierarchical categorization: presence before/at first heart failure diagnosis of 1) cardiomyopathy (with or without any of the following diagnoses); 2) valvular heart disease (with or without any of the other diagnoses except cardiomyopathy); 3) myocardial infarction (with or without atrial fibrillation); 4) atrial fibrillation only; and 5) none of these diagnoses.

‡ Manifest chronic kidney disease was defined on the date of the second of two measurements more than 90 days apart of a creatinine value corresponding to an eGFR below 60 mL/min/1.73m2, or on the first date of a hospital diagnosis of chronic kidney disease.

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; HK, hyperkalemia; NSAIDs, non-steroidal anti-inflammatory drugs.

Table S6. Chronic heart failure: Prevalence of risk factors at time of hyperkalemia/index date among heart failure patients and matched comparisons without hyperkalemia

	<i>Heart failure patients with first hyperkalemia >5.0 mmol/L</i>	<i>Matched heart failure comparisons without hyperkalemia*</i>	<i>Matched prevalence ratio (95% CI)</i>
No. of patients	3,276 (100%)	3,094 (100%)	1.00 (1.00-1.00)
Females	1,247 (38.1%)	1,154 (37.3%)	1.02 (0.96-1.09)
Age, median (quartiles), y	76 (68.1-82.9)	76 (68.6-82.6)	
K+ tests 6 mo. before HK/index date, median (quartiles)	4.0 (1.0-9.0)	1.0 (0.0-3.0)	
Acute heart failure hospitalizations 6 mo. before HK/index date median (quartiles)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	
Conditions underlying heart failure †			
Cardiomyopathy	507 (15.5%)	439 (14.2%)	1.09 (0.97-1.23)
Valvular heart disease	713 (21.8%)	639 (20.7%)	1.05 (0.96-1.16)
Myocardial infarction	1,407 (42.9%)	1,257 (40.6%)	1.06 (1.0-1.12)
Any ischemic heart disease	2,138 (65.3%)	1,919 (62.0%)	1.05 (1.01-1.09)
Atrial fibrillation	1,578 (48.2%)	1,466 (47.4%)	1.02 (0.97-1.07)
Lowest level of eGFR measured before hyperkalemia/index date			
No value below 60 mL/min/1.73m ²	319 (9.7%)	617 (19.9%)	0.49 (0.43-0.55)
eGFR 45-59 mL/min/1.73m ²	613 (18.7%)	798 (25.8%)	0.73 (0.66-0.80)
eGFR 30-44 mL/min/1.73m ²	987 (30.1%)	801 (25.9%)	1.16 (1.08-1.26)
eGFR 15-29 mL/min/1.73m ²	941 (28.7%)	546 (17.6%)	1.63 (1.48-1.79)
eGFR<15 mL/min/1.73m ²	265 (8.1%)	123 (4.0%)	2.03 (1.65-2.51)
Dialysis	122 (3.7%)	25 (0.8%)	4.61 (3.01-7.07)
No eGFR measurement recorded	29 (0.9%)	184 (5.9%)	0.15 (0.10-0.22)
Selected risk factors for hyperkalemia			
Diabetes	1,146 (35.0%)	704 (22.8%)	1.54 (1.42-1.67)
Chronic kidney disease ‡	2,414 (73.7%)	1,716 (55.5%)	1.33 (1.28-1.38)
Hypertension	3,276 (100%)	3,094 (100%)	1.00 (1.00-1.00)
Other comorbidities			

	<i>Heart failure patients with first hyperkalemia >5.0 mmol/L</i>	<i>Matched heart failure comparisons without hyperkalemia*</i>	<i>Matched prevalence ratio (95% CI)</i>
Peripheral vascular disease	718 (21.9%)	467 (15.1%)	1.45 (1.30-1.61)
Cerebrovascular disease	706 (21.6%)	587 (19.0%)	1.14 (1.0-1.25)
Chronic pulmonary disease	835 (25.5%)	580 (18.7%)	1.36 (1.2-1.49)
Peptic ulcer disease	426 (13.0%)	296 (9.6%)	1.36 (1.2-1.56)
Any malignant disease	538 (16.4%)	435 (14.1%)	1.17 (1.04-1.31)
Alcoholism-related disorders	364 (11.1%)	230 (7.4%)	1.49 (1.28-1.75)
Medical obesity	341 (10.4%)	242 (7.8%)	1.33 (1.14-1.56)
Use of specific hyperkalemia-associated medications			
ACEis	2,384 (72.8%)	2,152 (69.6%)	1.05 (1.01-1.08)
Ramipril	1,240 (37.9%)	1,064 (34.4%)	1.10 (1.03-1.18)
Enalapril	487 (14.9%)	377 (12.2%)	1.22 (1.08-1.38)
Other ACEis	729 (22.3%)	728 (23.5%)	0.95 (0.86-1.03)
ACEis/diuretics combination	84 (2.6%)	91 (2.9%)	0.87 (0.65-1.17)
ARBs	702 (21.4%)	678 (21.9%)	0.98 (0.89-1.07)
Losartan	317 (9.7%)	341 (11.0%)	0.88 (0.76-1.01)
Candesartan	194 (5.9%)	138 (4.5%)	1.33 (1.07-1.64)
Other ARBs	117 (3.6%)	111 (3.6%)	1.00 (0.77-1.28)
ARBs/diuretics combination	125 (3.8%)	149 (4.8%)	0.79 (0.63-1.00)
Spironolactone	1,728 (52.7%)	1,168 (37.8%)	1.40 (1.32-1.48)
Potassium supplements	1,875 (57.2%)	1,618 (52.3%)	1.09 (1.05-1.14)
Loop diuretics	2,738 (83.6%)	2,270 (73.4%)	1.14 (1.11-1.17)
NSAIDs	709 (21.6%)	610 (19.7%)	1.10 (1.00-1.21)
Trimetoprim	131 (4.0%)	84 (2.7%)	1.47 (1.12-1.93)
Macrolides	473 (14.4%)	320 (10.3%)	1.40 (1.22-1.59)

* Heart failure comparison patients without hyperkalemia matched on age, sex, and duration of heart failure on the hyperkalemia/index date

† As present at the time of heart failure diagnosis.

‡ Manifest CKD was defined on the date of the second of two measurements more than 90 days apart of a creatinine value corresponding to an eGFR below 60 mL/min/1.73m², or on the first date of a hospital diagnosis of chronic kidney disease, see text and Supplementary material with codes

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; NSAIDs, non-steroidal anti-inflammatory drugs; PR, prevalence ratio

Table S7. Chronic heart failure. Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK.

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted Hazard Ratio (95% CI)
Any hospital outpatient contact	2,246 (3,091.43)	1,448 (1,312.78)	1.98 (1.85-2.13)	1.50 (1.37-1.64)
Any acute hospitalization	1,967 (2,499.73)	678 (506.10)	3.72 (3.39-4.08)	2.10 (1.87-2.37)
Any non-acute hospitalization	745 (659.76)	298 (208.70)	2.74 (2.38-3.16)	1.98 (1.67-2.35)
Any cardiac diagnosis	1,498 (1,604.57)	449 (320.60)	3.85 (3.45-4.31)	2.21 (1.92-2.55)
Ventricular arrhythmia	110 (83.26)	25 (16.67)	4.06 (2.58-6.41)	2.07 (1.18-3.80)
Cardiac arrest	32 (23.68)	5 (3.32)	7.29 (2.70-19.70)	7.23 (0.00-378E6)
Dialysis procedure	94 (70.86)	11 (7.32)	3.44 (1.53-7.78)	2.29 (1.24-4.27)
Ventilator treatment	174 (131.55)	26 (17.29)	7.26 (4.73-11.16)	2.62 (0.94-6.28)
ICU admission	413 (326.52)	58 (38.72)	8.01 (6.02-10.66)	4.85 (3.25-7.57)
Heart failure re-admission	761 (661.07)	170 (115.99)	4.27 (3.58-5.08)	2.10 (1.72-2.56)
ACEi prescription	1,781 (2,582.50)	1,819 (2,289.60)	1.02 (0.95-1.09)	0.96 (0.92-1.00)
ARB prescription	506 (430.54)	599 (465.76)	0.93 (0.82-1.06)	0.96 (0.90-1.03)
Spironolactone prescription	1,122 (1,155.93)	896 (751.44)	1.01 (0.92-1.10)	0.86 (0.81-0.92)
Potassium supplement prescription	1,128 (1,137.80)	1,287 (1,238.69)	0.84 (0.77-0.91)	0.80 (0.75-0.85)
Death	773 (570.99)	162 (107.61)	4.76 (3.98-5.69)	-

* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

† Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡ The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Table S8. Restricted analysis to patients with 5 K+ tests: Baseline characteristics among patients with first hospital diagnosed heart failure, stratified by eGFR category and subsequent incidence of hyperkalemia.

	eGFR category (mL/min/1.73m2)*						Dialysis	No eGFR recorded	Total
	eGFR>= 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR<15				
Number of HF patients (row %)	5,824 (28.5%)	5,401 (26.4%)	4,568 (22.3%)	3,008 (14.7%)	961 (4.7%)	215 (1.1%)	479 (2.3%)	20,456 (100%)	
Female	1,931 (33.2%)	2,513 (46.5%)	2,513 (55.0%)	1,628 (54.1%)	505 (52.5%)	67 (31.2%)	202 (42.2%)	9,359 (45.8%)	
Median age (quartiles)	70 (60.4-78.7)	78 (69.5-83.9)	81 (74.2-86.6)	82 (75.6-87.2)	81 (72.6-85.8)	69 (60.2-78.7)	72 (62.0-79.1)	77 (68.1-84.3)	
Echocardiography performed before / at first HF admission	4,030 (69.2%)	3,509 (65.0%)	2,835 (62.1%)	1,936 (64.4%)	636 (66.2%)	176 (81.9%)	285 (59.5%)	13,407 (65.5%)	
Heart failure as primary diagnosis	2,345 (40.3%)	2,083 (38.6%)	1,687 (36.9%)	1,022 (34.0%)	321 (33.4%)	93 (43.3%)	188 (39.2%)	7,739 (37.8%)	
Conditions underlying heart failure †									
Cardiomyopathy	393 (6.7%)	250 (4.6%)	161 (3.5%)	110 (3.7%)	21 (2.2%)	9 (4.2%)	20 (4.2%)	964 (4.7%)	
Valvular heart disease	676 (11.6%)	766 (14.2%)	766 (16.8%)	523 (17.4%)	167 (17.4%)	40 (18.6%)	94 (19.6%)	3,032 (14.8%)	
Myocardial infarction	1,083 (18.6%)	1,141 (21.1%)	1,106 (24.2%)	817 (27.2%)	260 (27.1%)	76 (35.3%)	92 (19.2%)	4,575 (22.4%)	
Any ischemic heart disease	2,062 (35.4%)	2,209 (40.9%)	2,010 (44.0%)	1,445 (48.0%)	437 (45.5%)	119 (55.3%)	202 (42.2%)	8,484 (41.5%)	
Atrial fibrillation	1,902 (32.7%)	2,103 (38.9%)	1,817 (39.8%)	1,171 (38.9%)	349 (36.3%)	57 (26.5%)	124 (25.9%)	7,523 (36.8%)	
Other comorbidities									
Diabetes	962 (16.5%)	943 (17.5%)	1,005 (22.0%)	857 (28.5%)	319 (33.2%)	82 (38.1%)	83 (17.3%)	4,251 (20.8%)	
Chronic kidney disease‡	33 (0.6%)	2,803 (51.9%)	3,659 (80.1%)	2,653 (88.2%)	890 (92.6%)	215 (100%)	18 (3.8%)	10,271 (50.2%)	
Hypertension	2,916 (50.1%)	3,432 (63.5%)	3,367 (73.7%)	2,439 (81.1%)	800 (83.2%)	200 (93.0%)	214 (44.7%)	13,368 (65.4%)	
Peripheral vascular disease	436 (7.5%)	586 (10.8%)	590 (12.9%)	547 (18.2%)	222 (23.1%)	70 (32.6%)	46 (9.6%)	2,497 (12.2%)	

eGFR category (mL/min/1.73m2)*

	eGFR≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR<15	Dialysis	No eGFR recorded	Total
Cerebrovascular disease	691 (11.9%)	870 (16.1%)	946 (20.7%)	707 (23.5%)	243 (25.3%)	45 (20.9%)	41 (8.6%)	3,543 (17.3%)
Chronic pulmonary disease	999 (17.2%)	1,005 (18.6%)	915 (20.0%)	615 (20.4%)	178 (18.5%)	42 (19.5%)	59 (12.3%)	3,813 (18.6%)
Peptic ulcer disease	385 (6.6%)	452 (8.4%)	498 (10.9%)	402 (13.4%)	151 (15.7%)	41 (19.1%)	33 (6.9%)	1,962 (9.6%)
Any malignant disease	667 (11.5%)	811 (15.0%)	804 (17.6%)	596 (19.8%)	190 (19.8%)	44 (20.5%)	37 (7.7%)	3,149 (15.4%)
Alcoholism-related disorders	623 (10.7%)	343 (6.4%)	300 (6.6%)	267 (8.9%)	109 (11.3%)	34 (15.8%)	28 (5.8%)	1,704 (8.3%)
Medical obesity	457 (7.8%)	351 (6.5%)	313 (6.9%)	267 (8.9%)	109 (11.3%)	16 (7.4%)	26 (5.4%)	1,539 (7.5%)
Drug treatment, before first admission								
ACEis overall	1,125 (19.3%)	1,260 (23.3%)	1,235 (27.0%)	933 (31.0%)	304 (31.6%)	71 (33.0%)	102 (21.3%)	5,030 (24.6%)
Ramipril	434 (7.5%)	498 (9.2%)	457 (10.0%)	361 (12.0%)	109 (11.3%)	34 (15.8%)	21 (4.4%)	1,914 (9.4%)
Enalapril	332 (5.7%)	373 (6.9%)	373 (8.2%)	277 (9.2%)	95 (9.9%)	24 (11.2%)	24 (5.0%)	1,498 (7.3%)
Other ACEis	284 (4.9%)	306 (5.7%)	329 (7.2%)	247 (8.2%)	73 (7.6%)	12 (5.6%)	53 (11.1%)	1,304 (6.4%)
ACEis/diuretics combination	132 (2.3%)	146 (2.7%)	141 (3.1%)	105 (3.5%)	45 (4.7%)	4 (1.9%)	8 (1.7%)	581 (2.8%)
ARBs overall	485 (8.3%)	579 (10.7%)	614 (13.4%)	509 (16.9%)	195 (20.3%)	48 (22.3%)	35 (7.3%)	2,465 (12.1%)
Losartan	204 (3.5%)	235 (4.4%)	251 (5.5%)	205 (6.8%)	86 (8.9%)	17 (7.9%)	15 (3.1%)	1,013 (5.0%)
Candesartan	85 (1.5%)	104 (1.9%)	99 (2.2%)	79 (2.6%)	37 (3.9%)	22 (10.2%)	5 (1.0%)	431 (2.1%)
Other ARBs	72 (1.2%)	91 (1.7%)	96 (2.1%)	73 (2.4%)	26 (2.7%)	9 (4.2%)	10 (2.1%)	377 (1.8%)
ARBs/diuretics combination	173 (3.0%)	192 (3.6%)	205 (4.5%)	193 (6.4%)	59 (6.1%)	5 (2.3%)	6 (1.3%)	833 (4.1%)
Beta-blockers	1,429 (24.5%)	1,626 (30.1%)	1,570 (34.4%)	1,241 (41.3%)	418 (43.5%)	132 (61.4%)	122 (25.5%)	6,538 (32.0%)
Spironolactone	361 (6.2%)	455 (8.4%)	599 (13.1%)	510 (17.0%)	167 (17.4%)	4 (1.9%)	49 (10.2%)	2,145 (10.5%)
Potassium supplements	1,064 (18.3%)	1,452 (26.9%)	1,583 (34.7%)	1,259 (41.9%)	378 (39.3%)	49 (22.8%)	143 (29.9%)	5,928 (29.0%)
Loop diuretics	1,380 (23.7%)	1,815 (33.6%)	2,002 (43.8%)	1,794 (59.6%)	622 (64.7%)	142 (66.0%)	190 (39.7%)	7,945 (38.8%)

	eGFR category (mL/min/1.73m2)*							No eGFR recorded	Total
	eGFR ≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR <15	Dialysis			
NSAIDs	1,276 (21.9%)	1,169 (21.6%)	996 (21.8%)	734 (24.4%)	237 (24.7%)	19 (8.8%)	122 (25.5%)	4,553 (22.3%)	
Trimetoprim	62 (1.1%)	114 (2.1%)	136 (3.0%)	129 (4.3%)	49 (5.1%)	3 (1.4%)	5 (1.0%)	498 (2.4%)	
Macrolides	723 (12.4%)	641 (11.9%)	507 (11.1%)	382 (12.7%)	119 (12.4%)	30 (14.0%)	57 (11.9%)	2,459 (12.0%)	
Hyperkalemia event >5.0 mmol/L									
Total number of events	785 (13.5%)	956 (17.7%)	1,080 (23.6%)	950 (31.6%)	338 (35.2%)	91 (42.3%)	84 (17.5%)	4,284 (20.9%)	
Median years to event in pts with event	0.11	0.10	0.09	0.04	0.03	0.12	0.29	0.08	
Median no. K+ tests before the event	2	2	2	1	1	1	1	2	
1-year cumulative incidence, % (95% CI)	13.5 (12.5-14.5)	17.7 (16.5-18.9)	23.6 (22.0-25.3)	31.6 (29.2-34.0)	35.2 (30.5-39.8)	42.3 (30.9-53.8)	17.5 (13.4-21.7)	20.9 (20.2-21.6)	
Incidence rate of HK / 1,000 person-years (95% CI)	40.48 (37.70-43.41)	61.94 (58.07-65.99)	110.99 (104.47-117.81)	213.88 (200.50-227.93)	295.93 (265.22-329.22)	414.30 (333.57-508.67)	38.92 (31.05-48.19)	81.57 (79.14-84.05)	
Hyperkalemia event >5.5 mmol/L									
Total number of events	192 (3.3%)	272 (5.0%)	396 (8.7%)	400 (13.3%)	151 (15.7%)	52 (24.2%)	33 (6.9%)	1,496 (7.3%)	
Median years to event in pts with event	0.11	0.10	0.10	0.04	0.02	0.22	0.30	0.08	
Median no. K+ tests before the event	2	2	2	1	1	2	1	2	
1-year cumulative incidence, % (95% CI)	3.3 (2.8-3.8)	5.0 (4.4-5.7)	8.7 (7.8-9.6)	13.3 (11.9-14.7)	15.7 (13.0-18.4)	24.2 (16.6-31.7)	6.9 (4.5-9.3)	7.3 (6.9-7.7)	
Incidence rate of HK / 1,000 person-years (95% CI)	9.01 (7.78-10.37)	15.62 (13.82-17.59)	35.33 (31.94-38.99)	73.89 (66.83-81.50)	105.90 (89.68-124.20)	179.54 (134.09-235.44)	13.96 (9.61-19.60)	25.17 (23.91-26.48)	
Hyperkalemia event >6.0 mmol/L									
Total number of events	58 (1.0%)	99 (1.8%)	142 (3.1%)	167 (5.6%)	72 (7.5%)	20 (9.3%)	9 (1.9%)	567 (2.8%)	
Median years to event in pts with event	0.12	0.12	0.10	0.06	0.01	0.25	0.17	0.09	

	eGFR category (mL/min/1.73m2)*							No eGFR recorded	Total
	eGFR ≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR <15	Dialysis			
Median no. K+ tests before the event	2	3	2	2	1	2	1	2	
1-year cumulative incidence, % (95% CI)	1.0 (0.7-1.3)	1.8 (1.5-2.2)	3.1 (2.6-3.6)	5.6 (4.7-6.4)	7.5 (5.7-9.3)	9.3 (5.0-13.6)	1.9 (0.6-3.1)	2.8 (2.5-3.0)	
Incidence rate of HK / 1,000 person-years (95% CI)	2.69 (2.04-3.47)	5.55 (4.51-6.76)	12.15 (10.23-14.32)	29.01 (24.77-33.75)	47.67 (37.30-60.04)	56.53 (34.53-87.31)	3.72 (1.70-7.07)	9.27 (8.52-10.06)	

* Patients categorized according to lowest measured eGFR before or on admission date with heart failure; presence of dialysis overrules any eGFR measurement result.

† Conditions possibly underlying heart failure; hierarchical categorization: presence before/at first heart failure diagnosis of 1) cardiomyopathy (with or without any of the following diagnoses); 2) valvular heart disease (with or without any of the other diagnoses except cardiomyopathy); 3) myocardial infarction (with or without atrial fibrillation); 4) atrial fibrillation only; and 5) none of these diagnoses.

‡ Manifest chronic kidney disease was defined on the date of the second of two measurements more than 90 days apart of a creatinine value corresponding to an eGFR below 60 mL/min/1.73m2, or on the first date of a hospital diagnosis of chronic kidney disease.

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; HK, hyperkalemia; NSAIDs, non-steroidal anti-inflammatory drugs.

Table S9. Restricted analysis to patients with 5 K+ tests: Prevalence of risk factors at time of hyperkalemia/index date among heart failure patients and matched comparisons without hyperkalemia

	<i>Heart failure patients with first hyperkalemia >5.0 mmol/L</i>	<i>Matched heart failure comparisons without hyperkalemia*</i>	<i>Matched prevalence ratio (95% CI)</i>
No. of patients	4,284 (100%)	4,204 (100%)	1.00 (1.00-1.00)
Females	1,995 (46.6%)	1,964 (46.7%)	1.00 (0.95-1.04)
Age, median (quartiles), y	78.7 (70.2-85.2)	78.9 (70.8-85.2)	
K+ tests 6 mo. before HK/index date, median (quartiles)	1.0 (0.0-3.0)	1.0 (0.0-3.0)	
Acute heart failure hospitalizations 6 mo. before HK/index date median (quartiles)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	
Conditions underlying heart failure †			
Cardiomyopathy	261 (6.1%)	247 (5.9%)	1.04 (0.88-1.23)
Valvular heart disease	720 (16.8%)	628 (14.9%)	1.13 (1.02-1.24)
Myocardial infarction	1,159 (27.1%)	1,141 (27.1%)	1.00 (0.9-1.07)
Any ischemic heart disease	1,877 (43.8%)	1,798 (42.8%)	1.02 (0.98-1.08)
Atrial fibrillation	1,534 (35.8%)	1,623 (38.6%)	0.93 (0.88-0.98)
Lowest level of eGFR measured before hyperkalemia/index date			
No value below 60 mL/min/1.73m ²	502 (11.7%)	854 (20.3%)	0.58 (0.52-0.64)
eGFR 45-59 mL/min/1.73m ²	762 (17.8%)	1,124 (26.7%)	0.67 (0.61-0.72)
eGFR 30-44 mL/min/1.73m ²	1,154 (26.9%)	1,112 (26.5%)	1.02 (0.95-1.09)
eGFR 15-29 mL/min/1.73m ²	1,232 (28.8%)	766 (18.2%)	1.58 (1.46-1.71)
eGFR<15 mL/min/1.73m ²	463 (10.8%)	198 (4.7%)	2.29 (1.95-2.70)
Dialysis	117 (2.7%)	43 (1.0%)	2.67 (1.89-3.78)
No eGFR measurement recorded	54 (1.3%)	107 (2.5%)	0.50 (0.36-0.69)
Selected risk factors for hyperkalemia			
Diabetes	1,194 (27.9%)	850 (20.2%)	1.38 (1.28-1.49)
Chronic kidney disease ‡	2,815 (65.7%)	2,247 (53.4%)	1.23 (1.19-1.27)

	<i>Heart failure patients with first hyperkalemia >5.0 mmol/L</i>	<i>Matched heart failure comparisons without hyperkalemia*</i>	<i>Matched prevalence ratio (95% CI)</i>
Other comorbidities			
Hypertension	3,436 (80.2%)	3,264 (77.6%)	1.03 (1.01-1.06)
Peripheral vascular disease	680 (15.9%)	579 (13.8%)	1.15 (1.0-1.28)
Cerebrovascular disease	803 (18.7%)	814 (19.4%)	0.97 (0.9-1.06)
Chronic pulmonary disease	1,051 (24.5%)	906 (21.6%)	1.14 (1.1-1.23)
Peptic ulcer disease	509 (11.9%)	448 (10.7%)	1.11 (1.0-1.26)
Any malignant disease	704 (16.4%)	681 (16.2%)	1.01 (0.92-1.12)
Alcoholism-related disorders	398 (9.3%)	330 (7.8%)	1.18 (1.03-1.36)
Medical obesity	330 (7.7%)	260 (6.2%)	1.25 (1.06-1.46)
Use of specific hyperkalemia-associated medications			
ACEis overall	1,829 (42.7%)	1,641 (39.0%)	1.09 (1.04-1.15)
Ramipril	1,240 (37.9%)	1,064 (34.4%)	1.11 (1.02-1.21)
Enalapril	433 (10.1%)	358 (8.5%)	1.19 (1.04-1.36)
Other ACEis	469 (10.9%)	477 (11.3%)	0.96 (0.86-1.09)
ACEis/diuretics combination	137 (3.2%)	104 (2.5%)	1.29 (1.01-1.66)
ARBs overall	637 (14.9%)	549 (13.1%)	1.14 (1.02-1.27)
Losartan	246 (5.7%)	235 (5.6%)	1.03 (0.86-1.22)
Candesartan	170 (4.0%)	107 (2.5%)	1.56 (1.23-1.98)
Other ARBs	94 (2.2%)	92 (2.2%)	1.00 (0.75-1.33)
ARBs/diuretics combination	173 (4.0%)	174 (4.1%)	0.98 (0.79-1.20)
Spironolactone	1,289 (30.1%)	856 (20.4%)	1.48 (1.37-1.59)
Potassium supplements	1,969 (46.0%)	2,021 (48.1%)	0.96 (0.91-1.00)
Loop diuretics	2,628 (61.3%)	2,464 (58.6%)	1.05 (1.01-1.08)
NSAIDs	904 (21.1%)	929 (22.1%)	0.95 (0.88-1.04)
Trimetoprim	130 (3.0%)	129 (3.1%)	0.99 (0.78-1.26)
Macrolides	539 (12.6%)	456 (10.8%)	1.16 (1.03-1.30)

* Heart failure comparison patients without hyperkalemia matched on age, sex, and duration of heart failure on the hyperkalemia/index date

† As present at the time of heart failure diagnosis.

‡ Manifest CKD was defined on the date of the second of two measurements more than 90 days apart of a creatinine value corresponding to an eGFR below 60 mL/min/1.73m², or on the first date of a hospital diagnosis of chronic kidney disease, see text and Supplementary material with codes

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; NSAIDs, non-steroidal anti-inflammatory drugs; PR, prevalence ratio

Table S10. Restricted analysis to patients with 5 K+ tests: Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK.

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted Hazard Ratio (95% CI)
Any hospital outpatient contact	2,604 (3,326.63)	2,571 (2,293.14)	1.35 (1.27-1.42)	1.35 (1.26-1.45)
Any acute hospitalization	3,270 (5,344.31)	2,386 (2,123.88)	1.99 (1.89-2.11)	2.10 (1.97-2.24)
Any non-acute hospitalization	914 (787.09)	930 (582.76)	1.33 (1.20-1.46)	1.29 (1.17-1.46)
Any cardiac diagnosis	2,823 (3,861.86)	2,025 (1,668.35)	1.88 (1.77-1.99)	2.07 (1.92-2.21)
Ventricular arrhythmia	148 (106.70)	95 (51.39)	1.99 (1.52-2.59)	2.11 (1.55-3.00)
Cardiac arrest	59 (41.51)	27 (14.40)	2.95 (1.84-4.74)	3.43 (1.32-10.18)
Dialysis procedure	105 (75.05)	28 (14.94)	2.76 (1.78-4.26)	1.67 (1.11-2.39)
Ventilator treatment	367 (269.33)	105 (56.57)	4.53 (3.63-5.66)	3.93 (2.81-5.81)
ICU admission	620 (478.84)	265 (146.38)	3.08 (2.65-3.57)	3.18 (2.58-3.97)
Heart failure re-admission	2,270 (2,567.94)	1,612 (1,219.48)	1.77 (1.65-1.89)	2.01 (1.87-2.15)
ACEi prescription	1,351 (1,434.42)	1,682 (1,371.36)	0.94 (0.87-1.01)	0.86 (0.81-0.92)
ARB prescription	397 (307.06)	453 (262.90)	1.06 (0.92-1.22)	0.99 (0.88-1.10)
Spirinolactone prescription	920 (817.07)	999 (654.70)	0.93 (0.85-1.02)	0.72 (0.66-0.78)
Potassium supplement prescription	1,080 (997.58)	1,956 (1,655.61)	0.65 (0.60-0.70)	0.63 (0.58-0.67)
Death	1,764 (1,235.55)	717 (381.14)	2.95 (2.70-3.23)	-

* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

†Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Table S11. Primary heart failure diagnosis: Baseline characteristics among patients with a first primary hospital diagnosis of heart failure, stratified by eGFR category and subsequent incidence of hyperkalemia

	eGFR category (mL/min/1.73m2)*						No eGFR recorded	Total
	eGFR >= 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR<15	Dialysis		
Number of HF patients (row %)	2,977 (25.0%)	2,586 (21.7%)	2,109 (17.7%)	1,277 (10.7%)	412 (3.5%)	124 (1.0%)	2,423 (20.3%)	11,908 (100%)
Females	995 (33.4%)	1,160 (44.9%)	1,141 (54.1%)	683 (53.5%)	211 (51.2%)	39 (31.5%)	1,154 (47.6%)	5,383 (45.2%)
Median age in years (quartiles)	70 (59.6-78.7)	78 (69.3-83.9)	82 (74.7-87.3)	83 (76.2-87.9)	81 (72.7-86.4)	68 (60.5-78.4)	79 (70.9-85.5)	78 (68.3-84.9)
Echocardiography performed before / at first HF admission	2,107 (70.8%)	1,712 (66.2%)	1,313 (62.3%)	784 (61.4%)	267 (64.8%)	86 (69.4%)	1,008 (41.6%)	7,277 (61.1%)
Heart failure as primary diagnosis	2,977 (100%)	2,586 (100%)	2,109 (100%)	1,277 (100%)	412 (100%)	124 (100%)	2,423 (100%)	11,908 (100%)
Conditions underlying HF								
Cardiomyopathy	258 (8.7%)	172 (6.7%)	94 (4.5%)	53 (4.2%)	8 (1.9%)	5 (4.0%)	82 (3.4%)	672 (5.6%)
Valvular heart disease	333 (11.2%)	355 (13.7%)	345 (16.4%)	233 (18.2%)	70 (17.0%)	21 (16.9%)	247 (10.2%)	1,604 (13.5%)
Myocardial infarction	466 (15.7%)	525 (20.3%)	474 (22.5%)	351 (27.5%)	116 (28.2%)	41 (33.1%)	362 (14.9%)	2,335 (19.6%)
Ischemic heart disease	858 (28.8%)	897 (34.7%)	809 (38.4%)	566 (44.3%)	181 (43.9%)	60 (48.4%)	692 (28.6%)	4,063 (34.1%)
Atrial fibrillation	864 (29.0%)	933 (36.1%)	822 (39.0%)	493 (38.6%)	132 (32.0%)	25 (20.2%)	738 (30.5%)	4,007 (33.6%)
Other comorbidities								
Diabetes	498 (16.7%)	442 (17.1%)	439 (20.8%)	351 (27.5%)	125 (30.3%)	48 (38.7%)	407 (16.8%)	2,310 (19.4%)
Chronic kidney disease ‡	21 (0.7%)	1,339 (51.8%)	1,663 (78.9%)	1,130 (88.5%)	379 (92.0%)	124 (100%)	92 (3.8%)	4,748 (39.9%)
Hypertension	1,490 (50.1%)	1,671 (64.6%)	1,539 (73.0%)	1,017 (79.6%)	337 (81.8%)	113 (91.1%)	1,132 (46.7%)	7,299 (61.3%)
Peripheral vascular disease	186 (6.2%)	263 (10.2%)	261 (12.4%)	220 (17.2%)	96 (23.3%)	46 (37.1%)	258 (10.6%)	1,330 (11.2%)
Cerebrovascular disease	354 (11.9%)	409 (15.8%)	395 (18.7%)	278 (21.8%)	105 (25.5%)	31 (25.0%)	370 (15.3%)	1,942 (16.3%)
Chronic pulmonary disease	387 (13.0%)	416 (16.1%)	327 (15.5%)	215 (16.8%)	54 (13.1%)	19 (15.3%)	345 (14.2%)	1,763 (14.8%)
Peptic ulcer disease	183 (6.1%)	214 (8.3%)	227 (10.8%)	175 (13.7%)	50 (12.1%)	23 (18.5%)	207 (8.5%)	1,079 (9.1%)
Any malignant disease	366 (12.3%)	375 (14.5%)	370 (17.5%)	261 (20.4%)	83 (20.1%)	25 (20.2%)	260 (10.7%)	1,740 (14.6%)
Alcoholism-related disorders	283 (9.5%)	158 (6.1%)	137 (6.5%)	102 (8.0%)	37 (9.0%)	10 (8.1%)	138 (5.7%)	865 (7.3%)

	eGFR category (mL/min/1.73m2)*							No eGFR recorded	Total
	eGFR >= 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR<15	Dialysis			
Medical obesity	249 (8.4%)	165 (6.4%)	145 (6.9%)	92 (7.2%)	37 (9.0%)	9 (7.3%)	129 (5.3%)	826 (6.9%)	
Drug treatment before first HF diagnosis									
ACEis overall	609 (20.5%)	671 (25.9%)	559 (26.5%)	380 (29.8%)	127 (30.8%)	42 (33.9%)	452 (18.7%)	2,840 (23.8%)	
Ramipril	263 (8.8%)	276 (10.7%)	220 (10.4%)	160 (12.5%)	51 (12.4%)	18 (14.5%)	84 (3.5%)	1,072 (9.0%)	
Enalapril	156 (5.2%)	179 (6.9%)	155 (7.3%)	112 (8.8%)	39 (9.5%)	16 (12.9%)	129 (5.3%)	786 (6.6%)	
Other ACEis	156 (5.2%)	171 (6.6%)	151 (7.2%)	95 (7.4%)	30 (7.3%)	8 (6.5%)	234 (9.7%)	845 (7.1%)	
ACEis/diuretics combination	61 (2.0%)	72 (2.8%)	61 (2.9%)	38 (3.0%)	16 (3.9%)	2 (1.6%)	26 (1.1%)	276 (2.3%)	
ARBs overall	228 (7.7%)	270 (10.4%)	289 (13.7%)	204 (16.0%)	72 (17.5%)	32 (25.8%)	152 (6.3%)	1,247 (10.5%)	
Losartan	93 (3.1%)	111 (4.3%)	120 (5.7%)	89 (7.0%)	33 (8.0%)	15 (12.1%)	75 (3.1%)	536 (4.5%)	
Candesartan	39 (1.3%)	52 (2.0%)	47 (2.2%)	32 (2.5%)	14 (3.4%)	11 (8.9%)	25 (1.0%)	220 (1.8%)	
Other ARBs	28 (0.9%)	46 (1.8%)	51 (2.4%)	24 (1.9%)	10 (2.4%)	6 (4.8%)	29 (1.2%)	194 (1.6%)	
ARBs/diuretics combination	86 (2.9%)	81 (3.1%)	93 (4.4%)	73 (5.7%)	18 (4.4%)	3 (2.4%)	40 (1.7%)	394 (3.3%)	
Beta blockers	763 (25.6%)	797 (30.8%)	731 (34.7%)	504 (39.5%)	166 (40.3%)	76 (61.3%)	565 (23.3%)	3,602 (30.2%)	
Spironolactone	193 (6.5%)	220 (8.5%)	269 (12.8%)	207 (16.2%)	70 (17.0%)	2 (1.6%)	326 (13.5%)	1,287 (10.8%)	
Potassium supplements	563 (18.9%)	691 (26.7%)	761 (36.1%)	528 (41.3%)	163 (39.6%)	24 (19.4%)	864 (35.7%)	3,594 (30.2%)	
Loop diuretics	757 (25.4%)	917 (35.5%)	966 (45.8%)	755 (59.1%)	260 (63.1%)	74 (59.7%)	1,066 (44.0%)	4,795 (40.3%)	
NSAIDs	644 (21.6%)	534 (20.6%)	447 (21.2%)	305 (23.9%)	100 (24.3%)	11 (8.9%)	569 (23.5%)	2,610 (21.9%)	
Trimetoprim	32 (1.1%)	51 (2.0%)	60 (2.8%)	67 (5.2%)	24 (5.8%)	2 (1.6%)	75 (3.1%)	311 (2.6%)	
Macrolides	369 (12.4%)	299 (11.6%)	208 (9.9%)	160 (12.5%)	48 (11.7%)	10 (8.1%)	309 (12.8%)	1,403 (11.8%)	
HK event >5.0 mmol/L									
Total N (%) with a first HK event	1,164 (39.1%)	1,168 (45.2%)	1,104 (52.3%)	715 (56.0%)	220 (53.4%)	78 (62.9%)	486 (20.1%)	4,935 (41.4%)	
Median years to event in pts with event	0.52	0.44	0.19	0.10	0.11	0.15	3.81	0.37	
Median no. K+ tests before first event	9	8	7	6	6	7	8	8	
1-year cumulative incidence, % (95% CI)	23.4 (21.4-25.4)	29.2 (26.7-31.6)	37.9 (34.6-41.3)	45.5 (40.5-50.5)	45.9 (37.0-54.8)	51.6 (33.4-69.8)	3.1 (2.4-3.8)	26.5 (25.5-27.6)	

	eGFR category (mL/min/1.73m2)*						No eGFR recorded	Total
	eGFR ≥ 60	eGFR 45-59	eGFR 30-44	eGFR 15-29	eGFR <15	Dialysis		
Incidence rate per 1,000 person-years	144.6	220.1	380.3	639.5	725.4	1,151.7	63.3	194.1
HK event >5.5 mmol/L								
Total N (%) with a first HK event	477 (16.0%)	587 (22.7%)	611 (29.0%)	441 (34.5%)	151 (36.7%)	61 (49.2%)	232 (9.6%)	2,560 (21.5%)
Median years to event in pts with event	1.10	0.82	0.47	0.19	0.09	0.22	4.28	0.64
Median no. K+ tests before first event	14	12	10	8	7	10	12	11
1-year cumulative incidence, % (95% CI)	7.8 (6.8-8.9)	12.0 (10.6-13.4)	17.8 (15.8-19.8)	25.2 (22.0-28.4)	28.6 (22.5-34.8)	34.7 (21.9-47.5)	1.2 (0.8-1.6)	12.0 (11.4-12.7)
Incidence rate per 1,000 person-years	46.4	80.0	150.0	269.7	338.8	635.5	27.7	79.4
HK event >6.0 mmol/L								
Total N (%) with a first HK event	204 (6.9%)	257 (9.9%)	302 (14.3%)	235 (18.4%)	77 (18.7%)	37 (29.8%)	109 (4.5%)	1,221 (10.3%)
Median years to event in pts with event	1.61	1.34	0.76	0.26	0.16	0.38	4.15	0.92
Median no. K+ tests before first event	18	17	13	9	8	10	14	13
1-year cumulative incidence, % (95% CI)	2.9 (2.2-3.5)	4.4 (3.5-5.2)	7.7 (6.5-8.9)	13.3 (11.2-15.5)	14.6 (10.6-18.5)	21.0 (11.9-30.0)	0.4 (0.2-0.7)	5.3 (4.8-5.7)
Incidence rate per 1,000 person-years	18.7	31.7	64.1	123.1	138.2	253.4	12.7	34.9

* Patients categorized according to lowest measured eGFR before or on admission date with heart failure; presence of dialysis overrules any eGFR measurement result.

† Conditions possibly underlying heart failure; hierarchical categorization: presence before/at first heart failure diagnosis of 1) cardiomyopathy (with or without any of the following diagnoses); 2) valvular heart disease (with or without any of the other diagnoses except cardiomyopathy); 3) myocardial infarction (with or without atrial fibrillation); 4) atrial fibrillation only; and 5) none of these diagnoses.

‡ Manifest chronic kidney disease was defined on the date of the second of two measurements more than 90 days apart of a creatinine value corresponding to an eGFR below 60 mL/min/1.73m², or on the first date of a hospital diagnosis.

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; HK,

Table S12. Primary heart failure diagnosis: Prevalence of risk factors at time of hyperkalemia/index date among heart failure patients and matched comparisons without hyperkalemia

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK	Matched Prevalence Ratio (95% CI)
No. of patients	4,935 (100%)	4,679 (100%)	
Females	2,164 (43.9%)	2,046 (43.7%)	
Age, median (quartiles), y	78.4 (69.7-85.1)	78.6 (70.5-84.9)	
K+ tests 6 mo. before HK/index date, median (quartiles)	5.0 (2.0-10.0)	2.0 (0.0-5.0)	
Acute heart failure hospitalizations 6 mo. before HK/index date median (quartiles)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	
Conditions underlying heart failure †			
Cardiomyopathy	500 (10.1%)	434 (9.3%)	1.09 (0.97-1.23)
Valvular heart disease	888 (18.0%)	702 (15.0%)	1.20 (1.10-1.31)
Myocardial infarction	1,184 (24.0%)	995 (21.3%)	1.13 (1.0-1.22)
Any ischemic heart disease	2,120 (43.0%)	1,836 (39.2%)	1.09 (1.04-1.15)
Atrial fibrillation	1,889 (38.3%)	1,712 (36.6%)	1.05 (0.99-1.10)
Lowest eGFR measured before HK/index date			
No values below 60 mL/min/1.73m ²	661 (13.4%)	1,020 (21.8%)	0.61 (0.56-0.67)
eGFR 45-59 mL/min/1.73m ²	1,011 (20.5%)	1,157 (24.7%)	0.83 (0.77-0.89)
eGFR 30-44 mL/min/1.73m ²	1,501 (30.4%)	943 (20.2%)	1.51 (1.41-1.62)
eGFR 15-29 mL/min/1.73m ²	1,242 (25.2%)	537 (11.5%)	2.19 (2.00-2.41)
eGFR <15 mL/min/1.73m ²	312 (6.3%)	110 (2.4%)	2.69 (2.17-3.33)
Dialysis	112 (2.3%)	36 (0.8%)	2.95 (2.03-4.28)
No eGFR measurement recorded	96 (1.9%)	876 (18.7%)	0.10 (0.08-0.13)
Selected pre-defined risk factors for HK			
Diabetes	1,360 (27.6%)	955 (20.4%)	1.35 (1.26-1.45)
Chronic kidney disease ‡	3,209 (65.0%)	2,023 (43.2%)	1.50 (1.45-1.56)
Hypertension	4,201 (85.1%)	3,738 (79.9%)	1.07 (1.05-1.09)
Other comorbidities			
Peripheral vascular disease	795 (16.1%)	577 (12.3%)	1.31 (1.2-1.44)
Cerebrovascular disease	932 (18.9%)	744 (15.9%)	1.19 (1.1-1.30)
Chronic pulmonary disease	1,116 (22.6%)	949 (20.3%)	1.11 (1.0-1.20)
Peptic ulcer disease	511 (10.4%)	437 (9.3%)	1.11 (1.0-1.25)
Any malignant disease	818 (16.6%)	651 (13.9%)	1.19 (1.08-1.31)
Alcoholism-related disorders	458 (9.3%)	325 (6.9%)	1.34 (1.17-1.53)
Medical obesity	435 (8.8%)	344 (7.4%)	1.20 (1.05-1.37)

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK	Matched Prevalence Ratio (95% CI)
Use of hyperkalemia-associated medications			
ACEis overall	2,471 (50.1%)	2,186 (46.7%)	1.07 (1.03-1.12)
Ramipril	1,231 (24.9%)	1,039 (22.2%)	1.12 (1.05-1.21)
Enalapril	524 (10.6%)	426 (9.1%)	1.17 (1.03-1.32)
Other ACEis	728 (14.8%)	722 (15.4%)	0.96 (0.87-1.05)
ACEis/diuretics combination	120 (2.4%)	106 (2.3%)	1.07 (0.83-1.39)
ARBs overall	734 (14.9%)	663 (14.2%)	1.05 (0.95-1.16)
Losartan	335 (6.8%)	331 (7.1%)	0.96 (0.83-1.11)
Candesartan	191 (3.9%)	119 (2.5%)	1.52 (1.21-1.91)
Other ARBs	119 (2.4%)	107 (2.3%)	1.05 (0.81-1.36)
ARBs/diuretics combination	146 (3.0%)	161 (3.4%)	0.86 (0.69-1.07)
Spironolactone	1,908 (38.7%)	1,247 (26.7%)	1.45 (1.37-1.54)
Potassium supplements	2,567 (52.0%)	2,539 (54.3%)	0.96 (0.92-1.00)
Loop diuretics	3,438 (69.7%)	3,246 (69.4%)	1.00 (0.98-1.03)
NSAIDs	1,039 (21.1%)	996 (21.3%)	0.99 (0.92-1.07)
Trimetoprim	153 (3.1%)	156 (3.3%)	0.93 (0.75-1.16)
Macrolides	607 (12.3%)	579 (12.4%)	0.99 (0.89-1.11)

* Heart failure comparison patients without hyperkalemia matched on age, sex, and duration of heart failure on the hyperkalemia/index date

As present at the time of heart failure diagnosis.

‡ Manifest chronic kidney disease was defined on the date of the second of two measurements more than 90 days apart of a creatinine value corresponding to an eGFR below 60 mL/min/1.73m², or on the first date of a hospital diagnosis of chronic kidney disease, see text and Supplementary material with codes

Abbreviations: ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin-receptor II blockers; CI, confidence interval; eGFR, estimated Glomerular Filtration Rate; HK, hyperkalemia; NSAIDs, non-steroidal anti-inflammatory drugs; PR, prevalence ratio

Table S13. Primary heart failure diagnosis: Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted‡ Hazard Ratio (95% CI)
Any hospital outpatient contact	3,029 (2,949.79)	2,449 (1,680.51)	1.56 (1.47-1.66)	1.36 (1.27-1.46)
Any acute hospitalization	3,465 (3,883.09)	1,872 (1,173.22)	2.66 (2.49-2.83)	2.16 (2.04-2.31)
Any non-acute hospitalization	1,130 (767.97)	716 (364.29)	2.08 (1.87-2.30)	1.68 (1.50-1.93)
Any cardiac diagnosis	2,874 (2,701.82)	1,546 (920.94)	2.43 (2.27-2.60)	2.15 (2.01-2.30)
Ventricular arrhythmia	165 (93.24)	67 (31.10)	3.01 (2.21-4.12)	1.85 (1.32-2.79)
Cardiac arrest	54 (29.75)	8 (3.69)	8.47 (3.91-18.33)	11.87 (3.12-70.70)
Dialysis procedure	107 (59.68)	20 (9.23)	2.36 (1.43-3.89)	1.72 (1.07-2.68)
Ventilator treatment	287 (162.76)	54 (25.01)	6.08 (4.48-8.24)	4.08 (2.39-7.15)
ICU admission	565 (336.49)	140 (65.48)	5.24 (4.30-6.39)	4.13 (3.02-5.56)
Heart failure re-admission	2,063 (1,606.34)	1,192 (671.69)	2.07 (1.91-2.24)	1.94 (1.81-2.10)
ACEi prescription	2,021 (1,874.45)	2,130 (1,585.87)	1.05 (0.98-1.12)	0.98 (0.93-1.03)
ARB prescription	525 (321.02)	607 (311.84)	0.95 (0.83-1.07)	0.98 (0.90-1.07)
Spirolactone prescription	1,508 (1,148.79)	1,369 (806.60)	1.03 (0.95-1.12)	0.82 (0.78-0.88)
Potassium supplement prescription	1,630 (1,271.59)	2,381 (1,833.14)	0.77 (0.72-0.82)	0.74 (0.69-0.78)
Death	1,645 (903.28)	549 (252.85)	3.36 (3.02-3.74)	-

* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

† Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡ The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor II blocker, CI, confidence interval; HK, hyperkalemia; ICU, intensive care unit

Table S14. Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK, restricted to potassium measured in-hospital.

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted‡ Hazard Ratio (95% CI)
Any hospital outpatient contact	5,087 (4,451.14)	4,206 (1,864.31)	1.96 (1.87-2.05)	1.55 (1.47-1.63)
Any acute hospitalization	7,366 (18,262.56)	3,838 (1,726.00)	4.35 (4.16-4.55)	3.81 (3.63-4.02)
Any non-acute hospitalization	2,092 (1,218.32)	1,368 (450.87)	2.35 (2.19-2.54)	1.93 (1.75-2.12)
Any cardiac diagnosis	6,273 (8,756.88)	3,342 (1,417.80)	3.27 (3.12-3.42)	3.20 (3.03-3.39)
Ventricular arrhythmia	389 (172.72)	184 (54.12)	2.69 (2.23-3.25)	2.91 (2.19-3.75)
Cardiac arrest	146 (62.14)	34 (9.87)	6.21 (4.17-9.25)	10.04 (4.81-25.59)
Dialysis procedure	147 (63.03)	48 (13.94)	2.25 (1.60-3.18)	1.74 (1.14-2.52)
Ventilator treatment	951 (436.06)	150 (43.91)	8.48 (7.08-10.14)	5.35 (3.84-7.30)
ICU admission	1,716 (875.82)	364 (108.40)	6.71 (5.96-7.56)	5.56 (4.63-6.95)
Heart failure re-admission	4,708 (4,031.60)	2,716 (1,080.47)	2.45 (2.33-2.58)	2.66 (2.51-2.83)
ACEi prescription	2,227 (1,398.51)	2,999 (1,312.24)	0.99 (0.93-1.05)	1.01 (0.96-1.07)
ARB prescription	570 (260.35)	898 (286.35)	0.82 (0.73-0.91)	0.97 (0.89-1.04)
Spirolactone prescription	1,597 (857.69)	1,852 (659.39)	1.06 (0.98-1.13)	0.88 (0.82-0.94)
Potassium supplement prescription	2,467 (1,539.61)	3,749 (1,796.90)	0.84 (0.80-0.89)	0.77 (0.73-0.81)
Death	3,727 (1,570.93)	1,152 (333.49)	3.92 (3.65-4.21)	-

* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

† Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡ The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor II blocker, CI, confidence interval; HK, hyperkalemia; ICU, intensive care unit

Table S15. Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK, restricted to potassium measured in the primary health care sector.

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted‡ Hazard Ratio (95% CI)
Any hospital outpatient contact	2,673 (2,090.32)	2,238 (1,495.87)	1.26 (1.19-1.34)	1.26 (1.18-1.35)
Any acute hospitalization	1,734 (1,070.90)	1,263 (693.57)	1.39 (1.28-1.50)	1.25 (1.16-1.35)
Any non-acute hospitalization	694 (372.72)	545 (275.03)	1.29 (1.15-1.46)	1.26 (1.09-1.43)
Any cardiac diagnosis	1,219 (689.96)	856 (444.82)	1.33 (1.20-1.46)	1.26 (1.15-1.40)
Ventricular arrhythmia	61 (29.90)	46 (21.70)	1.03 (0.68-1.56)	1.29 (0.87-2.07)
Cardiac arrest	10 (4.87)	7 (3.28)	1.72 (0.59-5.04)	2.05 (0.65-7.83)
Dialysis procedure	76 (37.35)	13 (6.11)	1.65 (0.89-3.06)	0.72 (0.33-1.30)
Ventilator treatment	39 (19.01)	35 (16.46)	1.07 (0.65-1.75)	0.98 (0.54-1.68)
ICU admission	121 (59.49)	95 (45.00)	1.12 (0.83-1.50)	1.32 (0.93-1.88)
Heart failure re-admission	601 (312.81)	431 (212.04)	1.26 (1.10-1.44)	1.20 (1.05-1.37)
ACEi prescription	2,203 (1,799.25)	1,864 (1,311.05)	1.09 (1.02-1.17)	0.93 (0.89-0.96)
ARB prescription	653 (358.75)	508 (260.31)	1.27 (1.12-1.45)	1.04 (0.97-1.12)
Spironolactone prescription	1,585 (1,048.59)	1,024 (573.22)	1.04 (0.96-1.14)	0.81 (0.76-0.85)
Potassium supplement prescription	1,642 (1,098.47)	2,170 (1,586.37)	0.76 (0.71-0.81)	0.73 (0.70-0.77)
Death	730 (355.17)	390 (182.92)	2.00 (1.74-2.30)	-

* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

† Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡ The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor II blocker, CI, confidence interval; HK, hyperkalemia; ICU, intensive care unit

Table S16. Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK, restricted to patients with less than 10 potassium tests.

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted‡ Hazard Ratio (95% CI)
Any hospital outpatient contact	4,278 (3,053.33)	3,954 (2,014.09)	1.39 (1.33-1.46)	1.36 (1.29-1.44)
Any acute hospitalization	5,359 (4,953.68)	3,752 (1,994.11)	1.96 (1.88-2.05)	2.07 (1.97-2.17)
Any non-acute hospitalization	1,564 (770.64)	1,391 (521.71)	1.41 (1.30-1.52)	1.61 (1.45-1.79)
Any cardiac diagnosis	4,660 (3,597.83)	3,326 (1,665.22)	1.78 (1.70-1.86)	1.94 (1.83-2.06)
Ventricular arrhythmia	266 (109.04)	181 (59.60)	1.73 (1.41-2.11)	2.30 (1.72-3.10)
Cardiac arrest	102 (40.73)	32 (10.37)	4.11 (2.71-6.24)	8.30 (3.48-25.71)
Dialysis procedure	105 (42.15)	48 (15.56)	1.41 (0.98-2.02)	0.97 (0.63-1.40)
Ventilator treatment	577 (241.00)	146 (47.76)	4.76 (3.94-5.74)	5.04 (3.71-7.59)
ICU admission	1,009 (444.64)	371 (123.88)	3.41 (3.01-3.86)	4.17 (3.40-5.17)
Heart failure re-admission	3,790 (2,445.76)	2,769 (1,292.29)	1.61 (1.53-1.70)	1.78 (1.68-1.88)
ACEi prescription	2,514 (1,576.24)	2,700 (1,318.74)	1.04 (0.98-1.10)	0.95 (0.91-1.00)
ARB prescription	680 (297.26)	750 (264.99)	1.05 (0.95-1.17)	1.06 (0.97-1.14)
Spironolactone prescription	1,738 (897.09)	1,701 (679.34)	1.04 (0.97-1.12)	0.81 (0.76-0.86)
Potassium supplement prescription	2,112 (1,157.71)	3,462 (1,877.08)	0.69 (0.66-0.74)	0.70 (0.66-0.74)
Death	2,568 (1,018.82)	1,172 (378.73)	2.65 (2.46-2.85)	-

* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

† Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡ The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor II blocker, CI, confidence interval; HK, hyperkalemia; ICU, intensive care unit

Table S17. Hazard ratios for clinical outcomes 6 months after hyperkalemia (HK) versus fully matched comparisons without HK, restricted to patients with 10 or more potassium tests.

	Heart failure patients with first HK >5.0 mmol/L	Matched* heart failure comparisons without HK		
Outcome	n (Rate per 1,000 person-y)	n (Rate per 1,000 person-y)	Fully adjusted† Hazard Ratio (95% CI)	Prior-event-rate-ratio adjusted‡ Hazard Ratio (95% CI)
Any hospital outpatient contact	3,482 (3,412.02)	2,490 (1,391.83)	1.98 (1.87-2.10)	1.46 (1.37-1.57)
Any acute hospitalization	3,741 (3,976.74)	1,349 (623.64)	4.59 (4.28-4.93)	2.93 (2.74-3.15)
Any non-acute hospitalization	1,222 (788.58)	522 (222.18)	3.30 (2.94-3.70)	1.97 (1.75-2.23)
Any cardiac diagnosis	2,832 (2,384.05)	872 (381.75)	4.53 (4.15-4.94)	3.40 (3.11-3.72)
Ventricular arrhythmia	184 (99.32)	49 (19.74)	3.96 (2.79-5.62)	3.14 (2.17-4.57)
Cardiac arrest	54 (28.41)	9 (3.61)	9.28 (3.88-22.16)	8.59 (3.14-34.09)
Dialysis procedure	118 (62.91)	13 (5.22)	3.05 (1.69-5.50)	1.84 (1.01-3.21)
Ventilator treatment	413 (224.65)	39 (15.69)	15.04 (10.40-21.74)	5.44 (3.43-9.06)
ICU admission	828 (480.27)	88 (35.57)	11.64 (9.21-14.71)	7.16 (5.39-9.62)
Heart failure re-admission	1,519 (986.73)	378 (157.26)	4.72 (4.15-5.38)	4.08 (3.61-4.65)
ACEi prescription	1,916 (1,568.09)	2,163 (1,303.21)	1.00 (0.93-1.07)	1.03 (0.99-1.08)
ARB prescription	543 (315.34)	656 (290.62)	0.93 (0.81-1.06)	1.00 (0.93-1.08)
Spirolactone prescription	1,444 (1,005.45)	1,175 (561.90)	1.04 (0.95-1.13)	0.92 (0.87-0.98)
Potassium supplement prescription	1,997 (1,568.89)	2,457 (1,526.17)	0.94 (0.88-1.01)	0.83 (0.79-0.87)
Death	1,889 (990.44)	370 (148.48)	5.60 (4.94-6.36)	-

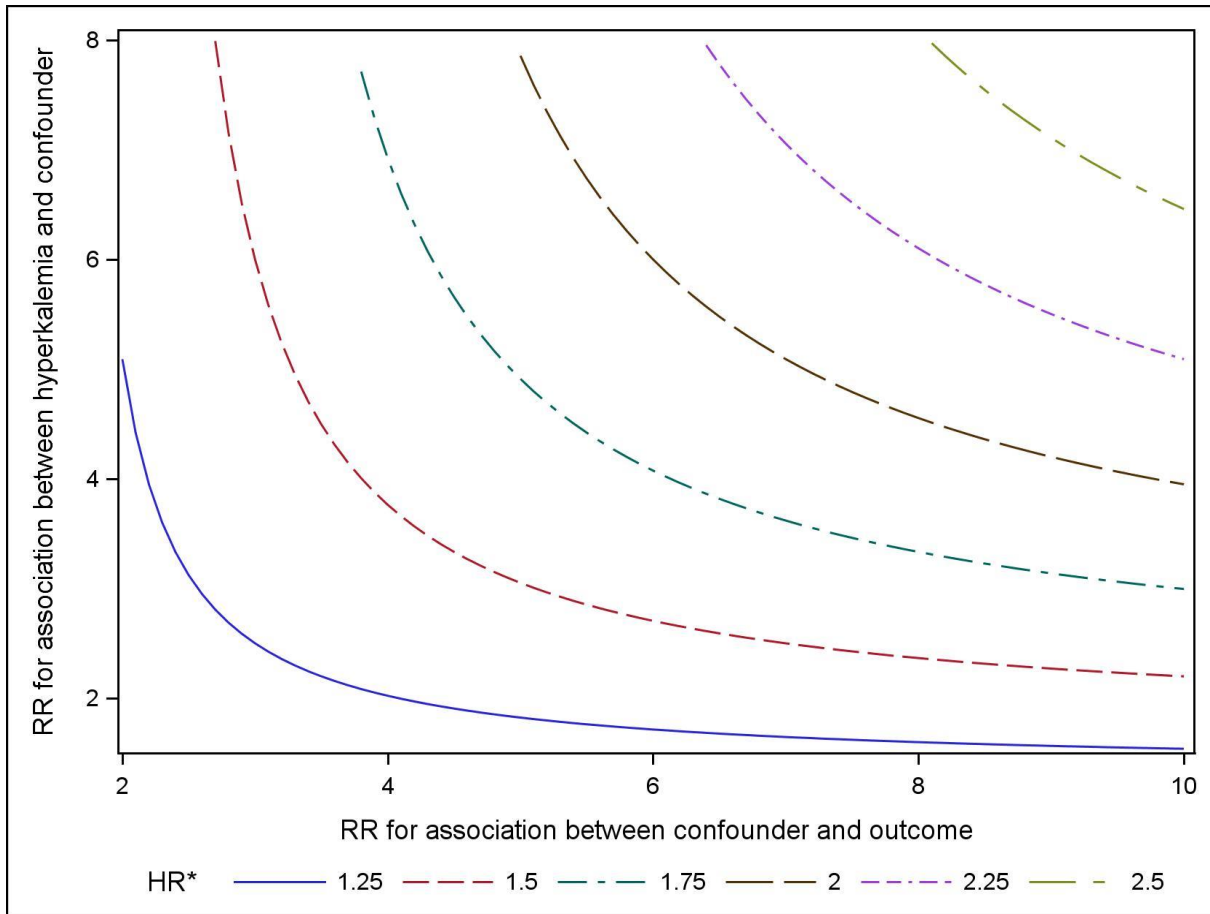
* Heart failure comparisons without HK individually matched to heart failure patients with HK on age, sex, and heart failure duration, see text.

† Adjusted for age, sex, and heart failure duration by matched design, and, by Cox regression analyses, for heart failure treatment regimen, number of acute heart failure hospitalizations 6 months before the HK/index date, eGFR category, Charlson Comorbidity Index score, presence of diabetes/chronic kidney disease/ hypertension, use of ACEis/ARBs, spironolactone, or potassium supplements

‡ The prior-event-rate-ratio adjusted hazard ratio is the ratio of the two age, sex, and heart failure duration matched rate ratios observed 6 months after vs. 6 months before the HK/index date, see text

Abbreviations: ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin-receptor II blocker, CI, confidence interval; HK, hyperkalemia; ICU, intensive care unit

Figure S1. Required strength of an unmeasured confounder to explain our associations assuming that 50% of the heart failure population had hyperkalemia and that the prevalence of the unmeasured confounder was 25%.



*HR indicates hazard ratio for the association between hyperkalemia and the different outcomes. For example, to explain an adjusted HR of ~ 2.0 (brown line) for acute hospitalization associated with hyperkalemia, a confounder that is four times more frequent among hyperkalemia than non-hyperkalemia patients would need to increase the hazard of acute hospitalization by a factor of 10 or more to explain our findings fully, if no increased hazard actually existed.