

SUPPLEMENTAL MATERIAL

Supplemental Table 1: Coding algorithms for outcomes and comorbidities

	Operationalized definitions				
	ICD-9 diagnosis	ICD-10 diagnosis	ICD-9 procedure	ICD-10 procedure	Medication class
Heart failure (any)	428.x 402.01 402.11 402.91 404.01 404.03 404.11 404.13 404.91 404.93 398.91	I50.x I11.0 I13.0 I13.2 I09.81	N/A	N/A	N/A
Cardiovascular disease (CEVD/Stroke, CAD, MI)	362.34 430.x-438.x, 414.0 410.x 412 414.8 414.9, 410.x 412.x	G45.x G46.x H34.0 I60.x- I69.x, I25.x I70.0 I24.x, I21.x I22.x I25.2x	36.1	N/A	N/A
Hyperkalemia	276.7	E87.5	N/A	N/A	N/A
Peripheral Artery Disease	443.9 440.2x-440.4x 707.1x 785.4	I70.2x I73.x	38.18 39.50 39.25 39.29	I73.9	N/A
Diabetes	250.x 357.2 362.0x 366.41	E08.x-E11.x E13.x	N/A	N/A	Diabetes drug
Cancer	140.x-172.x 174.x-208.x 238.6	C00.x-C26.x C30.x-C34.x C37.x-C41.x C43.x C45.x- C58.x C60.x- C85.x C88.x C90.x-C97.x	N/A	N/A	N/A
Cirrhosis	571.2 571.5 571.6	K74.3 - K74.6x	N/A	N/A	N/A
Ascites	789.5x	R18.x	N/A	N/A	N/A
Acute kidney injury	584.9	N17.9	N/A	N/A	N/A
Atrial fibrillation	427.3x	I48.x	N/A	N/A	N/A
Proteinuria	791.0	R80.x	N/A	N/A	N/A

Supplemental Table 1 Key: International Classification of Diseases (ICD); cerebrovascular disease (CEVD); coronary artery disease (CAD); myocardial infarction (MI)

Supplemental Table 2: Study population used for intention-to-treat analysis, pooled and stratified by cohort “trial” years

	Cohort "trial" years using ITT design					P-value
	Cohort 2004-2006	Cohort 2007-2009	Cohort 2010-2012	Cohort 2013-2016	Pooled	
N (total)	2,104 (8.7%)	4,876 (20.2%)	6,854 (28.4%)	10,293 (42.7%)	24,127	
Female	1,068 (50.8%)	2,529 (51.9%)	3,531 (51.5%)	5,371 (52.2%)	12,499 (51.8%)	.30
Non-white	34 (1.6%)	98 (2.0%)	150 (2.2%)	269 (2.6%)	551 (2.3%)	<.001
Age (mean), years	73.7 (12.3)	73.6 (12.4)	73.8 (12.5)	73.9 (13.0)	73.8 (12.7)	.15
CCI (mean)	6.7 (2.5)	7.2 (2.7)	7.5 (2.8)	7.8 (3.0)	7.5 (2.8)	<.001
Baseline labs						
K (mean), mg/dL	4.3 (0.4)	4.2 (0.4)	4.2 (0.4)	4.2 (0.4)	4.2 (0.4)	<.001
SCr (mean), mEq/L	1.2 (0.5)	1.2 (0.6)	1.2 (0.6)	1.2 (0.6)	1.2 (0.6)	<.001
Kidney function						
eGFR (mean)	61.8 (22.9)	61.4 (23.6)	60.4 (23.8)	59.6 (23.7)	60.4 (23.6)	<.001
≥90 mL/min/1.73m ²	275 (13.1%)	646 (13.3%)	907 (13.2%)	1,277 (12.4%)	3,105 (12.9%)	<.001
60-89 mL/min/1.73m ²	819 (38.9%)	1,830 (37.5%)	2,472 (36.1%)	3,635 (35.3%)	8,756 (36.3%)	.15
30-59 mL/min/1.73m ²	839 (39.9%)	1,971 (40.4%)	2,823 (41.2%)	4,368 (42.4%)	10,001 (41.5%)	<.001
<30 mL/min/1.73m ²	171 (8.1%)	429 (8.8%)	652 (9.5%)	1,013 (9.8%)	2,265 (9.4%)	<.001
Comorbidities						
CVD	1,412 (67.1%)	3,388 (69.5%)	4,877 (71.2%)	7,236 (70.3%)	16,913 (70.1%)	.01
Hyperkalemia	78 (3.7%)	284 (5.8%)	446 (6.5%)	869 (8.4%)	1,677 (7.0%)	<.001
PAD	410 (19.5%)	1,141 (23.4%)	1,665 (24.3%)	2,634 (25.6%)	5,850 (24.2%)	<.001
Diabetes	923 (43.9%)	2,322 (47.6%)	3,423 (49.9%)	4,996 (48.5%)	11,664 (48.3%)	<.001
Cancer	401 (19.1%)	928 (19.0%)	1,318 (19.2%)	2,078 (20.2%)	4,725 (19.6%)	.07
Cirrhosis	27 (1.3%)	60 (1.2%)	114 (1.7%)	209 (2.0%)	410 (1.7%)	<.001
Ascites	42 (2.0%)	110 (2.3%)	148 (2.2%)	214 (2.1%)	514 (2.1%)	.79
AKI	170 (8.1%)	694 (14.2%)	1,426 (20.8%)	2,814 (27.3%)	51,04 (21.2%)	<.001
Atrial fibrillation	762 (36.2%)	1,926 (39.5%)	2,947 (43.0%)	4,709 (45.7%)	10,344 (42.9%)	<.001
Proteinuria	109 (5.2%)	292 (6.0%)	479 (7.0%)	772 (7.5%)	1,652 (6.8%)	<.001
Medications						
ACEi or ARB	1,684 (80.0%)	3,984 (80.7%)	5,520 (80.5%)	7,517 (73.0%)	18,705 (77.6%)	<.001
Other antihypertensive	1,815 (86.3%)	4,354 (89.3%)	6,230 (90.9%)	9,150 (88.9%)	21,549 (89.3%)	.07
Anticoagulants	1,124 (53.4%)	2,888 (59.2%)	4,244 (61.9%)	6,143 (59.7%)	14,399 (59.7%)	<.001
Arrhythmic	399 (19.0%)	1,087 (22.3%)	1,590 (23.2%)	2,083 (20.2%)	5,159 (21.4%)	.34
Cardiac glycoside	533 (25.3%)	1,130 (23.2%)	1,405 (20.5%)	1,576 (15.3%)	4,644 (19.2%)	<.001
Statin	1,308 (62.2%)	3,286 (67.4%)	4,770 (69.6%)	6,703 (65.1%)	16,067 (66.6%)	.95
Thiazide diuretic	777 (36.9%)	1,654 (33.9%)	2,142 (31.3%)	2,546 (24.7%)	7,119 (29.5%)	<.001
Other k-sparing diuretic	69 (3.3%)	151 (3.1%)	205 (3.0%)	227 (2.2%)	652 (2.7%)	<.001

Supplemental Table 2 Key: Index date (T_0); Charlson Comorbidity Index (CCI); serum potassium (K); serum creatinine (SCr); estimated glomerular filtration rate (eGFR); heart failure (HF); cardiovascular disease (CVD); peripheral artery disease (PAD); acute kidney injury (AKI); angiotensin-converting-enzyme inhibitor (ACEi); angiotensin II receptor blockers (ARB); potassium-sparing (k-sparing); for mean values, parentheses designate standard deviation; time with HF is the mean time between initial HF diagnosis and first loop prescription after the initial HF diagnosis; proteinuria was defined using diagnosis codes; CVD is a composite category including cerebrovascular disease/stroke, coronary artery disease, and myocardial infarction.