

Supplementary Online Content

Le D, Grams M, Coresh J, Shin J-I. Combined sacubitril and valsartan in patients requiring hemodialysis. *JAMA Netw Open*. 2024;7(8):e2429237.
doi:10.1001/jamanetworkopen.2024.29237

eTable 1. Specification and Emulation of a Target Trial for Sacubitril-Valsartan vs ACEI/ARB in US Medicare Patients

eTable 2. Specific Medications Assessed Using Medicare Part D Dispense Records

eTable 3. ICD-9, ICD-10, and CPT Codes for Comorbidity and Outcome Assessment

eTable 4. ACEI/ARB Stratification by Total Daily Dose

eTable 5. Baseline Characteristics of Sacubitril-Valsartan Users by Quartile of Dialysis Vintage

eTable 6. Baseline Characteristics of Sacubitril-Valsartan Users by Initial Dispensed Dose

eTable 7. HR of All-Cause Mortality, CV Mortality, Any Hospitalization, HF Hospitalization, Hyperkalemia, and Hypotension Associated With Sacubitril-Valsartan Use (vs ACEI/ARB) in Medicare Recipients With HFrEF Receiving Hemodialysis

eFigure 1. Covariate Balance and Post 1:1 Propensity Score Matching Without Replacement

eFigure 2. Subgroup Analyses of the HR for All-Cause Mortality Comparing Sacubitril-Valsartan vs ACEI/ARB After 1:1 Match Across Demographics, Medical Comorbidities, and Medication Dispensed History

eFigure 3. Subgroup Analyses of the HR for All-Cause Hospitalization Comparing Sacubitril-Valsartan vs ACEI/ARB

eFigure 4. Dose-Response Relationship Comparing Both All-Cause Mortality and All-Cause Hospitalization With Sacubitril-Valsartan Initiation Dose

eFigure 5. Sacubitril/Valsartan Dosing Pattern During Follow-Up Defined Using the Starting Dispenses Dose, Maximum Dispensed Dose, and Most Recent Dispensed Dose

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Specification and Emulation of a Target Trial for Sacubitril-Valsartan vs ACEI/ARB in US Medicare Patients

	Target Trial	Emulated Trial Using Real-World Data
Eligibility	Individuals ≥18 years old starting sacubitril/valsartan or ACE/ARB on-center hemodialysis between 2015 – 2020 with HFrEF	Same + ≥90-day survival on hemodialysis (given recommendations by the USRDS for observational data) + ≥180 days of Medicare A, B, and D (primary payer) prior to study initiation + history of HFrEF defined by ICD9 428.2X or ICD10 I50.2X
Treatment Strategies	Sacubitril/valsartan versus ACE/ARB	Same. Date of sacubitril/valsartan or ACE/ARB dispense was defined as study start
Treatment Assignment	Patients are assigned at random stratified by history of ACE/ARB use	Individuals were defined by treatment strategy at baseline, and we emulated randomization with 1:1 matching
Primary Outcome	All-cause mortality + cardiovascular death, HF hospitalization, all hospitalization	Same as for target trial (via ICD-9/ICD-10 codes)
Follow-up	Follow-up starts day after medication dispense and ends at study outcome, death, transplant, renal recovery, or loss of Medicare	Same as for target trial
Causal Contrast	Intention-to-treat	Observational analog of intention-to-treat effect
Statistical Analysis	Cox proportional hazards	Propensity score match with Cox proportional hazards

Abbreviations: US, United States, USRDS, United States Renal Data System; ACE/ARB, Angiotensin Converting Enzyme inhibitor/Angiotensin Receptor Blocker; HFrEF, heart failure with reduced ejection fraction; ICD, International Classification of Disease; Cox PH, Cox proportional hazards; IPTW, inverse probability of treatment weighting.

eTable 2. Specific Medications Assessed Using Medicare Part D Dispense Records

Medication Class	Specific Medications
ACE/ARB	Azilsartan, Benazepril, Candesartan, Captopril, Enalapril, Fosinopril, Irbesartan, Lisinopril, Losartan, Olmesartan, Quinapril, Ramipril, Telmisartan, Valsartan
Aldosterone Antagonists	Eplerenone, Spironolactone
Antiplatelet	Aspirin, Cangrelor, Clopidogrel, Prasugrel, Ticagrelor, Ticlopidine
Beta Blockers	Atenolol, Bisoprolol, Carvedilol, Metoprolol, Nebivolol, Pindolol, Propranolol
CCB	Amlodipine, Diltiazem, Felodipine, Isradipine, Nicardipine, Nifedipine, Nimodipine, Nisoldipine, Verapamil
Diuretics	Chlorothiazide, Chlorthalidone, Hydrochlorothiazide, Indapamide, Metolazone, Bumetanide, Ethacrynic acid, Furosemide, Torsemide, Amiloride, Triamterene
DOAC	Apixaban, Dabigatran, Edoxaban, Rivaroxaban
GLP1 Agonists	Albiglutide, Dulaglutide, Exenatide, Liraglutide, Lixisenatide, Semaglutide, Tirzepatide
Insulin	Insulin
Phosphate Binders	Sevelamer Carbonate, Sevelamer Hydrochloride, Calcium Acetate, Ferric Citrate, Lanthanum Carbonate, Sucroferric Oxyhydroxide, Calcium Citrate
SGLT2i	Dapagliflozin, Canagliflozin, Empagliflozin, Ertugliflozin
Warfarin	Warfarin

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin receptor blockers; CCB, calcium channel blockers; DOAC, Direct Oral Anticoagulation; GLP-1, Glucagon Like Peptide – 1 Agonists; SGLT2i, Sodium-glucose cotransporter-2 inhibitor.

eTable 3. ICD-9, ICD-10, and CPT Codes for Comorbidity and Outcome Assessment

Comorbidities	ICD9-CM Codes	ICD10-CM Codes
Heart Failure with Reduced Ejection Fraction	428.2X	I50.2X
Atherosclerotic Heart Disease	410 – 414; V45.81, V45.82	I21, I22, I25; Z95, Z9861
Cerebrovascular Disease	430 – 438	G45, G46, H340, H341, H341, I60 – I69
Peripheral Vascular Disease	440 – 444, 447, 451, 453, 557;	I70 – I74, I77, I791, I80, I731, I738, I739, I771, I790, K551, K558, K559
Gastrointestinal Bleeding	456.20, 530.21, 530.7, 530.82, 531.x-534.x (x=0,2,4,6), 535.x1 (x=1-7), 537.83, 537.84, 578.0, 562.02, 562.03, 562.12, 562.13, 569.3, 569.85, 568.81, 569.86, 578.1, 578.9, 79.21	I85.01, I85.11, K22.11, K22.6, K25, K26 K27, K28, K29.x1 (x=0-9), K31.81, K31.82, K57.13, K92.0, K92.1, K50.x11 (x=0,1,8,9), K51.x11 (x=0,2,3,4,5,8,9), K55.2, K57.x1 (x=0,1,2,3,8), K62.5, K57.33, K56.60, K92.2, K57.91, K57.93
Other Cardiac Disease	420 – 424, 429, 785 – 785.3; V42.2, V43.3	9309, I31 – I38, I47, I51, I52, R002, R011, R012; Z95.4, Z95.3, Z95.5
Respiratory Disease	491 – 494, 496, 510	J01, J41, J43, J449, J45 – J47
Liver Disease	570, 571, 572.1, 572.4, 573.1 – 573.3; V42.7	B18, K700 – K703, K709, K713 – K715, K72, K75.1, K67.7, K73, K74.60; Z94.4
Dysrhythmia	426, 427; V45.0, V53.3	I44, I45, I47 – I49; Z95.0, Z95.810
Cancer	140 – 172, 174 – 208, 230 – 231, 233 – 234	C0X – C34, C37 – C43, C45 – C58, C60 – C86, C88, C90 – C96
Diabetes Mellitus	250, 357.2, 362.0X, 366.1	E08 – E11, E13
Outcomes		
Heart Failure	398.91, 422, 425, 428, 402.X1,	I11, I13, I3.2, I2.55, I42.0, I42.5 – I42.9.
Hospitalization	403.X1, 404.X1; V42.1	I43.X, I40.9, I50, I09.81; Z94.1
Hyperkalemia	276.7	E87.5
Hypotension	458.9	I95.9
Fracture	733.1, 802, 804 – 808, 810 – 817, 820 – 829, E2887	M484, M80, M84, Sx2 (x = 0 – 9)

Abbreviations: ICD, International Classification of Disease; CM, Clinical Modification; GIB, gastrointestinal bleed; NOS, Not Otherwise Specified (Location of GIB); HCPCS, Healthcare Common Procedures Coding System; EGD, esophagogastroduodenoscopy.

eTable 4. ACEI/ARB Stratification by Total Daily Dose

ACE/ARB Stratification by Total Daily Dose (mg)			
Medication	Low	Intermediate	High
Azilsartan	-	40	>80
Benazepril	≤5	>5 - ≤15	>15
Candesartan	≤4	>4 - ≤16	>16
Captopril	≤37.5	>37.5 - ≤75	>75
Enalapril	≤5	>5 - ≤20	>20
Fosinopril	≤5	>5 - ≤20	>20
Irbesartan	≤75	>75 - ≤150	>150
Lisinopril	≤5	>5 - ≤20	>20
Losartan	≤25	>25 - ≤75	>75
Olmesartan	≤10	>10 - ≤20	>20
Quinapril	5	10	>10
Ramipril	≤2.5	>2.5 - ≤7.5	>7.5
Telmisartan	≤20	>20 - ≤40	>40
Valsartan	≤40	>40 - ≤160	>160

Medication doses determined via National Drug Code (NDC) linkage with billed Medicare Part D dispense

eTable 5. Baseline Characteristics of Sacubitril-Valsartan Users by Quartile of Dialysis Vintage

	Dialysis Vintage in Months				p
	<22 Months N = 743	22 – 44 Months N = 703	45 – 74 Months N = 721	>75 Months N = 701	
Age (Years)	66.2 (13.6)	64.4 (14.4)	63.7 (13.3)	61.9 (12.6)	<0.01
Sex (Male)	488 (65.7)	466 (66.3)	468 (64.9)	450 (64.2)	0.86
Race					<0.01
White	501 (67.4)	462 (65.7)	398 (55.2)	316 (45.1)	
Black or AA	189 (25.4)	191 (27.2)	277 (38.4)	330 (47.1)	
Other	53 (7.1)	50 (7.1)	46 (6.4)	55 (7.8)	
Baseline Calendar Year					0.12
2015	<10*	<10*	<10*	<10*	
2016	34 (4.6)	40s*	50s*	30s*	
2017	98 (13.2)	79 (11.2)	105 (14.6)	85 (12.1)	
2018	137 (18.4)	129 (18.3)	135 (18.7)	145 (20.7)	
2019	240 (32.3)	231 (32.9)	237 (32.9)	219 (31.2)	
2020	234 (31.5)	217 (30.9)	193 (26.8)	222 (31.7)	
KT/V	1.5 [1.4, 1.7]	1.5 [1.4, 1.7]	1.6 [1.4, 1.7]	1.6 [1.4, 1.7]	0.11
Smoker at Dialysis Initiation	64 (8.6)	55 (7.8)	46 (6.4)	53 (7.6)	0.45
Medicare Part D Subsidy	440 (59.2)	475 (67.6)	517 (71.7)	566 (80.7)	<0.01
History of ESA use	514 (69.2)	577 (82.1)	658 (91.3)	650 (92.7)	<0.01
Kidney Failure Not from Diabetes	365 (49.1)	357 (50.8)	347 (48.1)	413 (58.9)	<0.01
Geographic Region					<0.01
Midwest	180 (24.2)	156 (22.2)	144 (20.0)	120 (17.1)	
Northeast	187 (25.2)	173 (24.6)	201 (27.9)	159 (22.7)	
South	247 (33.2)	243 (34.6)	255 (35.4)	302 (43.1)	
West	129 (17.4)	131 (18.6)	121 (16.8)	120 (17.1)	
Started Dialysis Via Catheter	639 (86.0)	576 (81.9)	552 (76.6)	476 (67.9)	<0.01
BMI (kg/m ²)	26.0 [22.4, 30.3]	26.7 [22.8, 31.6]	26.7 [23.0, 31.2]	26.0 [22.4, 30.2]	0.07
Atherosclerotic Heart Disease	452 (60.8)	395 (56.2)	424 (58.8)	356 (50.8)	<0.01
Cancer	95 (12.8)	89 (12.7)	73 (10.1)	72 (10.3)	0.21
Dysrhythmia	403 (54.2)	321 (45.7)	341 (47.3)	320 (45.6)	<0.01
Cerebrovascular Disease	158 (21.3)	145 (20.6)	173 (24.0)	135 (19.3)	0.17
Other Cardiac Disease	411 (55.3)	387 (55.0)	411 (57.0)	347 (49.5)	0.03
Diabetes	565 (76.0)	519 (73.8)	525 (72.8)	435 (62.1)	<0.01
History of GI Bleed	86 (11.6)	71 (10.1)	75 (10.4)	86 (12.3)	0.53
Hypertension	647 (87.1)	633 (90.0)	651 (90.3)	605 (86.3)	0.03
Inability to Ambulate	32 (4.3)	29 (4.1)	20 (2.8)	<10*	<0.01
Liver Disease	86 (11.6)	75 (10.7)	81 (11.2)	80 (11.4)	0.95
Peripheral Vascular Disease	393 (52.9)	348 (49.5)	344 (47.7)	350 (49.9)	0.25
Respiratory Disease	215 (28.9)	187 (26.6)	191 (26.5)	153 (21.8)	0.02
# of Hospitalizations [≤ 6 mo]	2.0 (2.0)	1.8 (1.9)	1.8 (1.8)	1.6 (1.8)	<0.01

# of PCP Visits [≤ 6 mo]	2.4 (3.5)	2.3 (3.3)	2.1 (3.2)	2.4 (3.5)	0.32
# of Medications [<90 days]	10.0 [7.0, 14.0]	10.0 [7.0, 14.0]	10.0 [7.0, 14.0]	10.0 [7.0, 13.0]	0.13
Aldosterone Antagonist	59 (7.9)	30 (4.3)	44 (6.1)	31 (4.4)	0.01
Antiplatelets	218 (29.3)	234 (33.3)	215 (29.8)	180 (25.7)	0.02
Beta-Blockers	584 (78.6)	549 (78.1)	554 (76.8)	541 (77.2)	0.84
Calcium Channel Blockers	194 (26.1)	209 (29.7)	214 (29.7)	206 (29.4)	0.35
Diuretics	310 (41.7)	218 (31.0)	177 (24.5)	93 (13.3)	<0.01
DOAC	103 (13.9)	95 (13.5)	74 (10.3)	110 (15.7)	0.02
GLP-1RA	11 (1.5)	<10*	<10*	<10*	0.3
Insulin	208 (28.0)	187 (26.6)	194 (26.9)	114 (16.3)	<0.01
Phosphate Binder	371 (49.9)	414 (58.9)	427 (59.2)	430 (61.3)	<0.01
SGLT2i	<10*	<10*	<10*	<10*	0.58
Warfarin	82 (11.0)	62 (8.8)	60 (8.3)	65 (9.3)	0.31
Baseline ACE/ARB use					<0.01
Low Dose	129 (17.4)	120 (17.1)	107 (14.8)	111 (15.8)	
Moderate Dose	122 (16.4)	133 (18.9)	145 (20.1)	141 (20.1)	
High Dose	71 (9.6)	94 (13.4)	118 (16.4)	101 (14.4)	
No use	421 (56.7)	356 (50.6)	351 (48.7)	348 (49.6)	
# of ACE/ARB Dispenses [≤ 6 mo]	1.1 (1.8)	1.3 (1.8)	1.4 (2.1)	1.3 (1.9)	0.05

Data reported as number (percent), mean (standard deviation)

*Cells with <10 were censored per USRDS reporting policy or rounded down (if multiple categories).

Abbreviations: SMD, absolute standardized mean difference; AA, African American, ESA, erythropoietin stimulating agent; BMI, body mass index; ACEARB, angiotensin converting enzyme/angiotensin receptor blocker; CCB, calcium-channel blocker; DOAC; KT/V, measure of dialysis adequacy; Direct oral anticoagulation; GLP, Glucagon-Like-Peptide 1; SGLT2, sodium-glucose cotransporter 2 inhibitor

eTable 6. Baseline Characteristics of Sacubitril-Valsartan Users by Initial Dispensed Dose

	Starting Dispense of Sacubitril/Valsartan			P-value
	24/26 mg N = 1115	49/51 mg N = 249	97/101 mg N = 70	
Age	65.3 (12.7)	61.3 (14.0)	61.0 (15.1)	<0.01
Sex (Male)	734 (65.8)	157 (63.1)	53 (75.7)	0.14
Race				0.32
White	669 (60.0)	133 (53.4)	38 (54.3)	
Black or AA	373 (33.5)	100 (40.2)	20s*	
Other	73 (6.5)	16 (6.4)	<10*	
Year				0.61
2015	<10*	<10*	<10*	
2016	60s*	10s*	<10*	
2017	129 (11.6)	37 (14.9)	13 (18.6)	
2018	209 (18.7)	48 (19.3)	13 (18.6)	
2019	374 (33.5)	70 (28.1)	20 (28.6)	
2020	337 (30.2)	77 (30.9)	19 (27.1)	
Dialysis Vintage	3.8 (1.8 – 6.3)	3.9 (2.1 – 6.1)	4.3 (1.8 – 6.0)	0.90
KT/V	1.5 [1.4, 1.7]	1.5 [1.4, 1.7]	1.5 [1.4, 1.7]	0.66
Current Smoker	78 (7.0)	25 (10.0)	7 (10.0)	0.20
Part D Subsidy	755 (67.7)	177 (71.1)	45 (64.3)	0.46
History of ESA Use	926 (83.0)	213 (85.5)	62 (88.6)	0.34
Non-Diabetic Kidney Failure	569 (51.0)	143 (57.4)	39 (55.7)	0.16
US Geographic Region				0.74
Midwest	232 (20.8)	51 (20.5)	19 (27.1)	
Northeast	291 (26.1)	59 (23.7)	14 (20.0)	
South	400 (35.9)	98 (39.4)	24 (34.3)	
West	192 (17.2)	41 (16.5)	13 (18.6)	
Started Dialysis Via Catheter	975 (80%)	209 (77%)	57 (77%)	0.69
BMI	26.2 [22.5, 30.4]	25.0 [22.6, 29.7]	27.3 [24.0, 30.9]	0.13
Atherosclerotic Heart Disease	668 (59.9)	117 (47.0)	40 (57.1)	<0.01
Cancer	127 (11.4)	25 (10.0)	<10*	0.48
Dysrhythmia	580 (52.0)	92 (36.9)	28 (40.0)	<0.01
Cerebrovascular Disease	245 (22.0)	49 (19.7)	14 (20.0)	0.69
Other Cardiac Disease	612 (54.9)	131 (52.6)	43 (61.4)	0.42
Diabetes	809 (72.6)	166 (66.7)	48 (68.6)	0.16
Hx of Gastrointestinal Bleed	142 (12.7)	23 (9.2)	<10*	0.21
Hypertension	974 (87.4)	225 (90.4)	64 (91.4)	0.28
Inability to Ambulate	35 (3.1)	<10*	<10*	0.22
Liver Disease	123 (11.0)	30 (12.0)	8 (11.4)	0.90
Peripheral Vascular Disease	589 (52.8)	105 (42.2)	23 (32.9)	<0.01

Respiratory Disease	295 (26.5)	61 (24.5)	14 (20.0)	0.43
# of Hospitalizations [$\leq$ 6 mo]	1.8 (1.9)	1.6 (1.9)	1.7 (2.7)	0.08
# of PCP Visits [$\leq$ 6 mo]	2.2 (3.0)	2.1 (2.9)	2.9 (5.2)	0.14
# of Medications [$<$ 90 days]	10.0 [7.0, 14.0]	10.0 [7.0, 14.0]	9.0 [6.0, 13.0]	0.14
Aldosterone Antagonist	54 (4.8)	20 (8.0)	$<10^*$	0.02
Antiplatelets	358 (32.1)	54 (21.7)	18 (25.7)	<0.01
Beta-Blockers	880 (78.9)	192 (77.1)	52 (74.3)	0.57
CCB	297 (26.6)	85 (34.1)	19 (27.1)	0.06
Diuretics	304 (27.3)	71 (28.5)	21 (30.0)	0.83
DOAC	154 (13.8)	24 (9.6)	$<10^*$	0.11
GLP-1RA	12 (1.1)	$<10^*$	$<10^*$	0.64
Insulin	287 (25.7)	54 (21.7)	$<10^*$	0.05
Phosphate Binder	629 (56.4)	136 (54.6)	31 (44.3)	0.13
SGLT2	$<10^*$	$<10^*$	$<10^*$	0.87
Warfarin	106 (9.5)	21 (8.4)	$<10^*$	0.72
Baseline ACE/ARB use				<0.01
Low Dose	194 (17.4)	31 (12.4)	$<10^*$	
Moderate Dose	186 (16.7)	68 (27.3)	10s*	
High Dose	114 (10.2)	56 (22.5)	19 (27.1)	
No use	621 (55.7)	94 (37.8)	34 (48.6)	
# of ACE/ARB Refills [$\leq$ 6 mo]	1.2 (1.8)	1.7 (2.0)	1.5 (1.8)	<0.01

Abbreviations: SMD, absolute standardized mean difference; AA, African American, ESA, erythropoietin stimulating agent; BMI, body mass index; GI, gastrointestinal; mo, months; #, Number; DOAC, Direct Oral Anticoagulation; GLP-1RA, Glucagon Like Peptide – 1 Receptor Agonists; SGLT2, Sodium-glucose cotransporter-2 inhibitor; ACE/ARB, angiotensin converting enzyme/angiotensin receptor blocker

*Cells with <10 were censored per USRDS reporting policy or rounded down (if multiple categories).

eTable 7. HR of All-Cause Mortality, CV Mortality, Any Hospitalization, HF Hospitalization, Hyperkalemia, and Hypotension Associated With Sacubitril-Valsartan Use (vs ACEI/ARB) in Medicare Recipients With HFrEF Receiving Hemodialysis

No. of Events			IR (95% CI), per 1000 PYs			
<i>Intention To Treat</i>	Sacubitril/ valsartan	ACE/ ARB	Sacubitril/ valsartan	ACE/ARB	HR	CRR*
All-Cause Mortality	554	618	318 (293, 346)	391 (361, 423)	0.82 (0.73 - 0.92)	
CV Mortality	299	272	172 (153, 192)	172 (153, 194)	1.01 (0.86 - 1.19)	1.09 (0.92 – 1.28)
Any Hospitalization	1,057	1,083	1,379 (1,297, 1464)	1,694 (1,595, 1,797)	0.86 (0.79 - 0.93)	0.88 (0.81 – 0.96)
HF hospitalization	631	649	653 (604, 706)	748 (692, 807)	0.91 (0.82 - 1.02)	0.93 (0.84 – 1.04)
<i>As Treated</i>	Sacubitril/ valsartan	ACE/ ARB	Sacubitril/ valsartan	ACE/ARB	HR	CRR
All-Cause Mortality	232	286	242 (212, 274)	317 (281, 355)	0.80 (0.67 - 0.95)	
CV Mortality	132	135	138 (115, 162)	149 (126, 176)	0.97 (0.76 - 1.23)	1.01 (0.80 – 1.29)
Any Hospitalization	808	889	1,518 (1415, 1625)	1,927 (1803, 2056)	0.84 (0.77 - 0.93)	0.87 (0.79 – 0.95)
HF hospitalization	488	539	771 (705, 842)	939 (861, 1020)	0.89 (0.79 - 1.01)	0.96 (0.86 – 1.07)
<i>Intention To Treat</i>	Sacubitril/ valsartan	ACE/ ARB	Sacubitril/ valsartan	ACE/ ARB	HR	CRR
HyperK (Any)	367	456	276 (249, 305)	414 (377, 453)	0.71 (0.62 - 0.81)	0.75 (0.65 – 0.86)
HyperK (Hosp)	295	381	214 (190, 239)	331 (299, 365)	0.69 (0.59 - 0.80)	0.72 (0.62 – 0.84)
Hypotension (Any)	246	232	163 (143, 184)	169 (148, 191)	0.99 (0.83 - 1.19)	1.05 (0.88 – 1.26)
Hypotension (Hosp)	11	<10**	6 (3, 11)	5 (2, 9)	1.30 (0.52 - 3.23)	1.37 (0.55 – 3.41)
<i>As Treated</i>	Sacubitril/ valsartan	ACE/ ARB	Sacubitril/ valsartan	ACE/ ARB	HR	CRR
HyperK (Any)	241	338	299 (263, 339)	482 (433, 536)	0.67 (0.57 - 0.80)	0.71 (0.60 – 0.84)
HyperK (Hosp)	201	286	242 (210, 278)	396 (352, 444)	0.67 (0.56 - 0.80)	0.70 (0.59 – 0.84)
Hypotension (Any)	131	149	149 (125, 176)	177 (150, 207)	0.90 (0.71 - 1.13)	0.93 (0.73 – 1.18)
Hypotension (Hosp)	<10**	<10**	4 (1, 10)	7 (3, 13)	0.67 (0.19 - 2.38)	0.70 (0.20 – 2.52)

(Any) refers to both inpatient and outpatient claims while (Hosp) refers to hospitalization claims only.

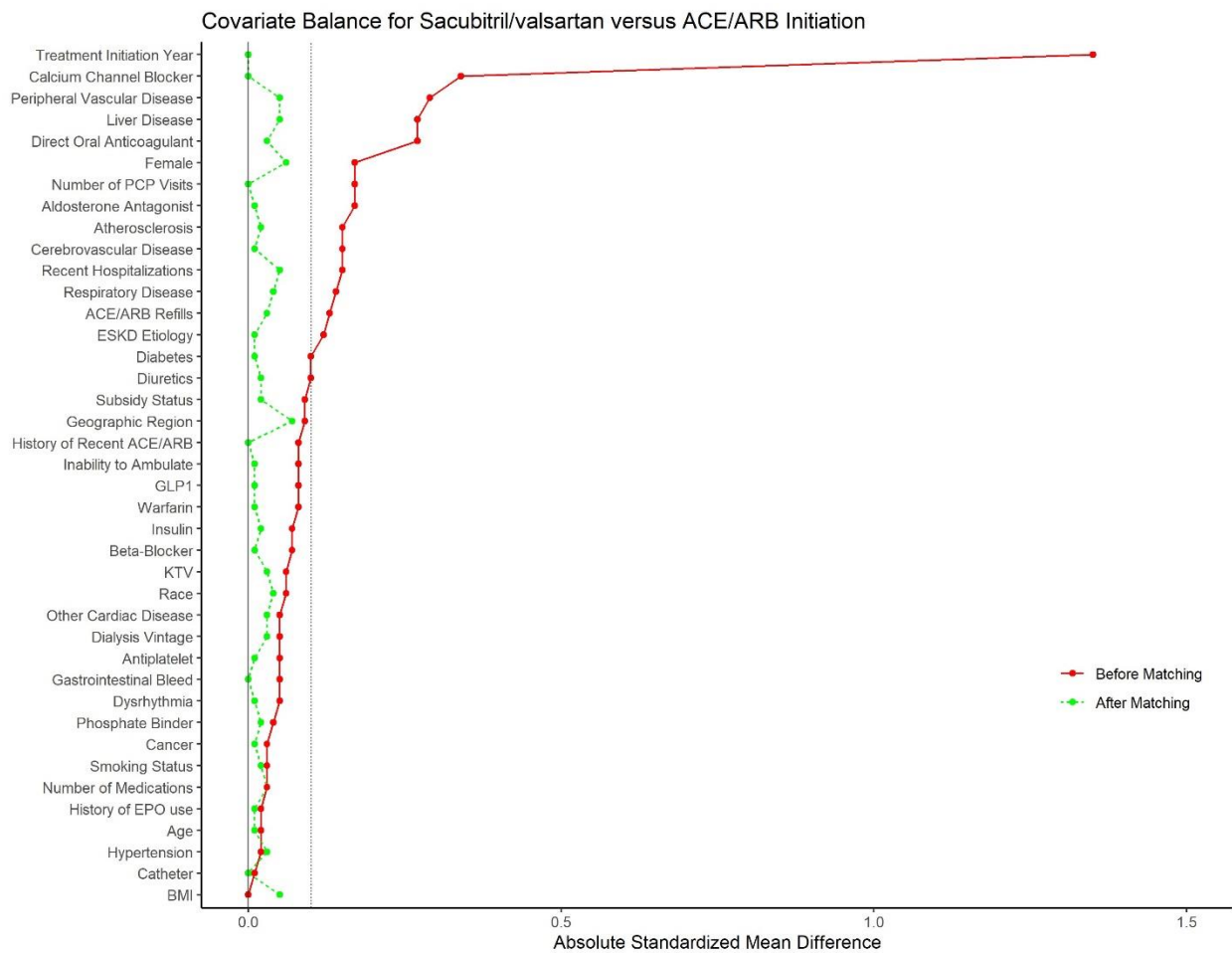
Hyperkalemia and Hypotension were defined by ICD9/ICD10 codes.

* Competing risk regression models

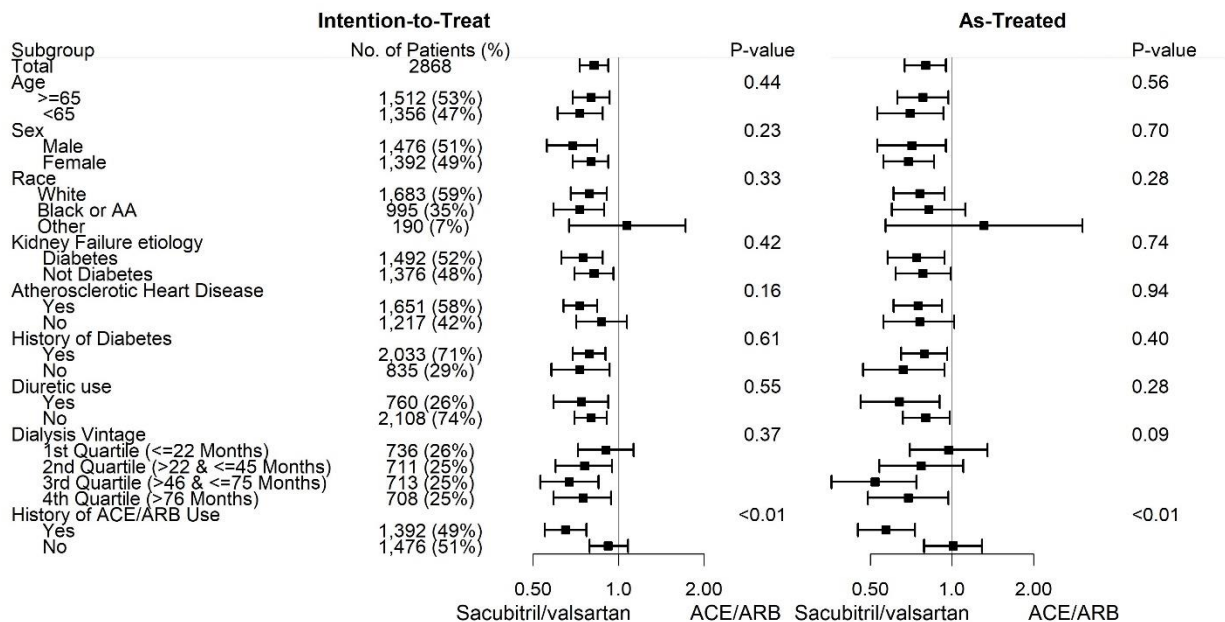
** Cells with <10 were censored per USRDS reporting policy.

Abbreviations: CV, cardiovascular; HF, heart failure; ACE/ARB, angiotensin converting enzyme/angiotensin receptor blocker; IR, incidence rate; PY, person years; IRD, incidence rate difference; HR, hazard ratio; CRR, Competing Risk Regression

eFigure 1. Covariate Balance and Post 1:1 Propensity Score Matching Without Replacement



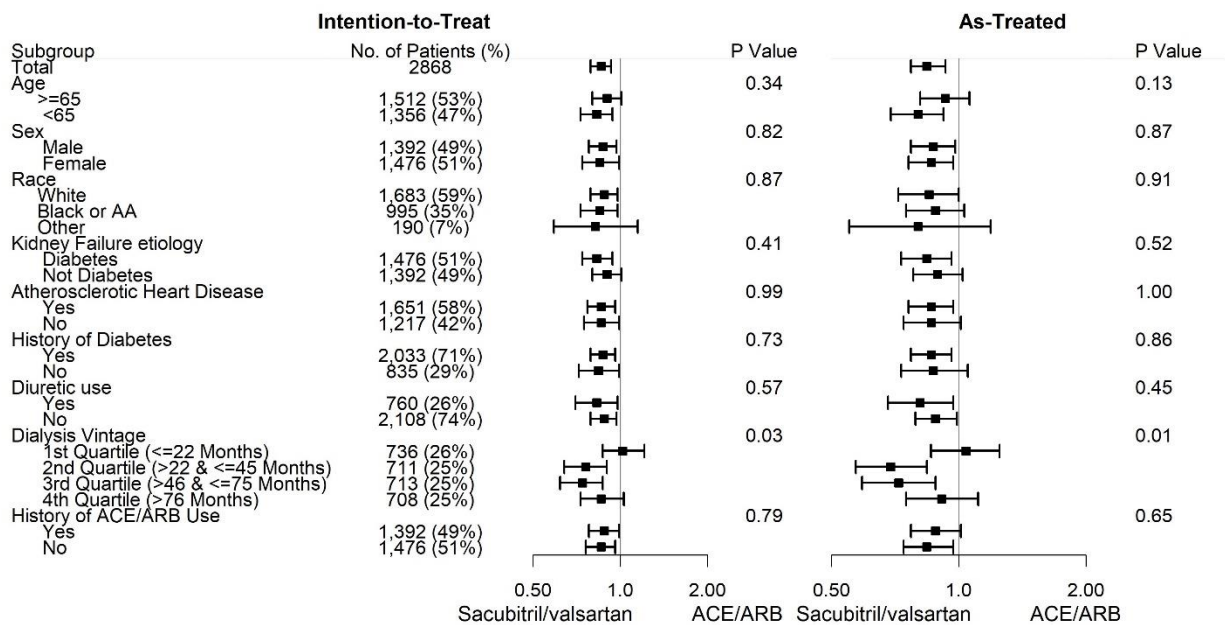
eFigure 2. Subgroup Analyses of the HR for All-Cause Mortality Comparing Sacubitril-Valsartan vs ACEI/ARB After 1:1 Match Across Demographics, Medical Comorbidities, and Medication Dispensed History



Covariates with poor balance (SMD > 0.10) were included as regression coefficients in the cox-proportional hazards model. P-value from test for interaction.

Abbreviations: AA, African American; ACE/ARB, Angiotensin Converting Enzyme inhibitor/Angiotensin Receptor Blocker

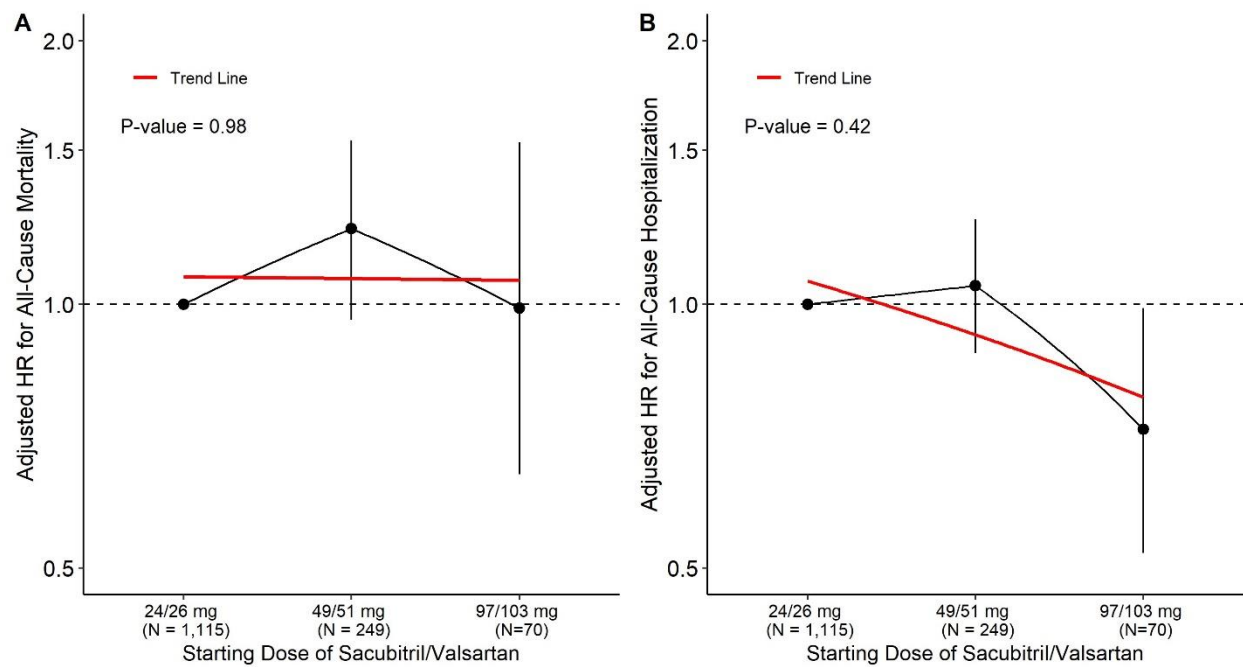
eFigure 3. Subgroup Analyses of the HR for All-Cause Hospitalization Comparing Sacubitril-Valsartan vs ACEI/ARB



Post 1:1 propensity score match across demographics, medical comorbidities, and medication dispense history. Covariates with poor balance (SMD > 0.10) were included as regression coefficients in the cox-proportional hazards model. P-value from test for interaction.

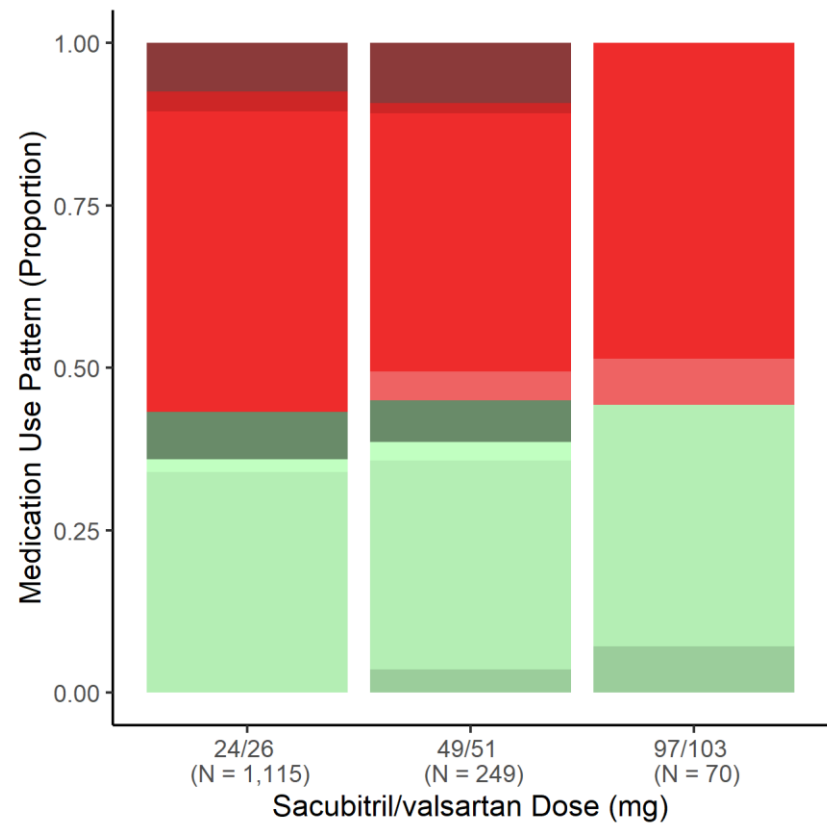
Abbreviations: AA, African American; ACE/ARB, Angiotensin Converting Enzyme inhibitor/Angiotensin Receptor Blocker

eFigure 4. Dose-Response Relationship Comparing Both All-Cause Mortality and All-Cause Hospitalization With Sacubitril-Valsartan Initiation Dose



“24/26 mg” is reference. All-cause mortality (A) and all-cause hospitalization (B). We plot the adjusted cox regression HR with a linear test for trend across the dose range.

eFigure 5. Sacubitril/Valsartan Dosing Pattern During Follow-Up Defined Using the Starting Dispenses Dose, Maximum Dispensed Dose, and Most Recent Dispensed Dose



Medication Use Pattern		Discontinued	Dose Pattern
	Discontinued After Increase	Yes	Start < max & max = final
	Discontinued After Failed Titration	Yes	Start < max & max > final
	Discontinued Starting Dose	Yes	Start = max & max = final
	Discontinued After Decrease	Yes	Start = max & max > final
	Increased	No	Start < max & max = final
	Failed Titration	No	Start < max & max > final
	Stayed on Starting Dose	No	Start = max & max = final
	Decreased	No	Start = max & max > final

X-axis values represent the initial dispense dose. Discontinuation was defined as 30 days after end of last dispense without another dispense. Percentages not shown due to some groups having <10 individuals per USRDS reporting policy.

