

Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Sacubitril/valsartan

Trial Indication(s)

Chronic Heart Failure

Protocol Number

CLCZ696BUS33

Protocol Title

A Pre-post Analysis of Healthcare Resource Utilization and Costs of Care in a New User Cohort of Sacubitril/valsartan Treated Adult Patients with Chronic Heart Failure

Clinical Trial Phase

IV

Phase of Drug Development

NA

Study Start/End Dates

Study start date: 02/08/2021

Study Completion date: 05/11/2021

Reason for Termination

NA

Study Design/Methodology

This was a non-interventional, retrospective cohort study using secondary data sources from the Optum Clinformatics® Data Mart (CDM) and 100% files of the CMS Medicare RIFs.

Two study cohorts were constructed to include adult Heart Failure with reduced ejection fraction (HFrEF) patients who newly initiated sacubitril/valsartan (Cohort 1) and adult Chronic Heart Failure (CHF) patients who newly initiated sacubitril/valsartan (Cohort 2).

The date of first prescription fill for sacubitril/valsartan during the cohort identification period was defined as index date. A 12-month washout period was employed to ascertain the “new user” status. The Healthcare Resource Utilization (HCRU) and costs of care outcomes was measured within both the 12 months post-index period and the 12 months pre-index period.

Centers

Novartis Investigative Site

Objectives:**Primary objective(s)**

- The primary objective was to compare the rate of HF-specific hospitalizations within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.

Secondary objective(s)

- To compare the mean number of HF-related hospitalizations within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean number of all-cause hospitalizations within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean number of urgent HF (UHF) visits within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean number of worsening HF (WHF) episodes within 12 months postvs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean costs of HF-specific hospitalizations within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean costs of HF-related hospitalizations within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean costs of all-cause hospitalizations within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean costs of UHF visits within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean costs of WHF episodes within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean HF-specific costs within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean HF-related costs within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean all-cause medical costs within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.
- To compare the mean all-cause pharmacy costs within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.

- To compare the mean all-cause total costs of care within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan in a new user cohort of adult HFrEF patients treated with sacubitril/valsartan.

Test Product (s), Dose(s), and Mode(s) of Administration

NA

Statistical Methods

Descriptive statistics of the cohort demographics and clinical variables will be reported as follows:

- Continuous variables will be summarized using number of patients (n), % non-missing, mean, median, minimum, maximum, standard deviation (SD), 25th and 75th percentiles and interquartile range.
- Categorical variables will be summarized using frequency counts and percentages.

For HCRU endpoints: patient counts, N missing, mean, standard deviation, range, median, 25th and 75th percentiles and interquartile range will be summarized. Negative binomial models will be conducted to estimate the differences in HCRU within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan.

For cost of care endpoints: patient counts, N missing, mean, standard deviation, range, median, 25th and 75th percentiles and interquartile range will be summarized. Generalized linear models (GLM) with a log link and gamma distribution will be conducted to estimate the differences in cost of care endpoints within 12 months post- vs. 12 months prior to initiation of sacubitril/valsartan.

Study Population: Key Inclusion/Exclusion Criteria**Inclusion criteria**Cohort 1 – Adult HFrEF patients

- Newly initiated sacubitril/valsartan during the cohort identification period;

- Presence of an International Classification of Diseases, Tenth revision (ICD-10) diagnosis code for systolic HF (I50.1x, I50.2x, I50.4x) on one inpatient hospital claim or two outpatient medical claims during the cohort identification period;
- That are ≥ 18 years old at index date;
- That are treated with sacubitril/valsartan continuously for a minimum of 90-days following treatment initiation;
- That are continuously enrolled in medical and prescription pharmacy benefits in both the pre-index and post-index period, with any gap in coverage of <45 days allowed.

Cohort 2 – Adult CHF patients

- Newly initiated sacubitril/valsartan during the cohort identification period;
- Presence of ICD-10 diagnosis code for systolic HF or diastolic HF (I50.1x, I50.2x, I50.3x, I50.4x) on one inpatient hospital claim or two outpatient medical claims during the cohort identification period;;
- That are ≥ 18 years old at index date;
- That are treated with sacubitril/valsartan continuously for a minimum of 90-days following treatment initiation;
- That are continuously enrolled in medical and prescription pharmacy benefits in both the pre-index and post-index period, with any gap in coverage of <45 days allowed.

Exclusion criteria

- Patients who died during the post-index period will be excluded.

Participant Flow

HFrEF Cohort (Cohort 1) Attrition Table

Criteria No.	Criteria	Number included	% retained	Number excluded	% excluded
1	Include patients that are initiated on sacubitril/Valsartan between 01-July-2015 and 30-June-2019	32,933	100.00%	0	0.00%
2	Include patients that are 18 or older at index date	32,923	99.97%	10	0.03%
3	Include patients that are treated with sacubitril/Valsartan for a minimum of 90 consecutive days from index date	14,209	43.15%	18,724	56.85%
4	Include patients that have a minimum of 12 months of pre-index data available	8,809	26.75%	24,124	73.25%
5	Include patients that have a minimum of 12 months of post-index data available	7,301	22.17%	25,632	77.83%

CHF Cohort (Cohort 2) Attrition Table

Criteria No.	Criteria	Number included	% retained	Number excluded	% excluded
1	Include patients that are initiated on sacubitril/Valsartan between 01-July-2015 and 30-June-2019	32,933	100.00%	0	0.00%
2	Include patients that are 18 or older at index date	32,923	99.97%	10	0.03%
3	Include patients that are treated with sacubitril/Valsartan for a minimum of 90 consecutive days from index date	14,209	43.15%	18,724	56.85%
4	Include patients that have a minimum of 12 months of pre-index data available	8,809	26.75%	24,124	73.25%
5	Include patients that have a minimum of 12 months of post-index data available	7,301	22.17%	25,632	77.83%

Baseline Characteristics

Baseline Patient Characteristics for HFrEF Cohort (Cohort 1)

			Overall cohort		Medicare Advantage		Commercial Insurance	
Characteristic	Variable	Statistic	N	%	N	%	N	%
Age (years) (continuous)		N (% non-missing)	9230, 100.00%		7503, 81.29%		1727, 18.71%	
		Mean	70.4		73.3		57.7	
		Std. Dev	11.25		8.9		11.55	
		Range	(20, 89)		(31, 89)		(20, 89)	
		Median	72		74		58	
		25th percentile	64		68		51	
		75th percentile	78		80		63	
		Interquartile range	14		12		12	
Sex	Male	n, %	6179	66.94%	4896	65.25%	1283	74.29%
	Female	n, %	3051	33.06%	2607	34.75%	444	25.71%
	Missing	n, %	0	0.00%	0	0.00%	0	0.00%
Census region	Northeast	n, %	1042	11.29%	870	11.60%	172	9.96%
	Midwest	n, %	1632	17.68%	1214	16.18%	418	24.20%
	South	n, %	4907	53.16%	4041	53.86%	866	50.14%

	West	n, %	1643	17.80%	1378	18.37%	265	15.34%
	Missing	n, %	6	0.07%			6	0.35%
Comorbidities	Hypertension	n, %	8543	92.56%	7086	94.44%	1457	84.37%
	Atrial fibrillation	n, %	4185	45.34%	3603	48.02%	582	33.70%
	Renal disease	n, %	3356	36.36%	2991	39.86%	365	21.13%
	Hyperlipidemia	n, %	7697	83.39%	6451	85.98%	1246	72.15%
	Diabetes mellitus	n, %	4668	50.57%	3964	52.83%	704	40.76%
	History of myocardial infarction	n, %	3447	37.35%	2876	38.33%	571	33.06%
	Chronic Kidney Disease	n, %	3238	35.08%	2895	38.58%	343	19.86%
	Ischemic heart disease	n, %	7286	78.94%	6086	81.11%	1200	69.48%
	COPD	n, %	2891	31.32%	2614	34.84%	277	16.04%
	Sleep apnea	n, %	2421	26.23%	1871	24.94%	550	31.85%
	Anemia	n, %	3052	33.07%	2638	35.16%	414	23.97%
	Depression	n, %	1821	19.73%	1566	20.87%	255	14.77%
	Peripheral vascular disease	n, %	2964	32.11%	2670	35.59%	294	17.02%
	Valvular disease	n, %	5246	56.84%	4273	56.95%	973	56.34%
	Dementia	n, %	439	4.76%	420	5.60%	19	1.10%
	Cerebrovascular disease	n, %	1844	19.98%	1626	21.67%	218	12.62%
	Obesity	n, %	2912	31.55%	2188	29.16%	724	41.92%
Medications	ACE inhibitors / ARBs	n, %	7601	82.35%	6200	82.63%	1401	81.12%
	Beta blockers	n, %	8548	92.61%	6924	92.28%	1624	94.04%
	Loop diuretic agents	n, %	6871	74.44%	5645	75.24%	1226	70.99%
	MRA	n, %	3502	37.94%	2696	35.93%	806	46.67%
	SGLT-2 inhibitors	n, %	224	2.43%	154	2.05%	70	4.05%

Days covered		N (% non-missing)	9230 (100.00%)		7503 (81.29%)		1727 (18.71%)	
		Mean	294.4		291.1		308.8	
		Std. Dev	80.99		82.78		70.95	
		Range	(90, 366)		(90, 366)		(90, 366)	
		Median	330		328		339	
		25th percentile	247		240		278	
		75th percentile	360		359		361	
		Interquartile range	113		119		83	
Proportion of days covered		N (% non-missing)	9230 (100%)		7503 (81.29%)		1727 (18.71%)	
		Mean	80.4		79.5		84.4	
		Std. Dev	22.13		22.62		19.38	
		Range	(25, 100)		(25, 100)		(25, 100)	
		Median	90		90		93	
		25th percentile	67		66		76	
		75th percentile	98		98		99	
		Interquartile range	31		32		23	

Baseline Patient Characteristics for CHF Cohort (Cohort 2)

			Overall cohort		Medicare Advantage		Commercial Insurance	
Characteristic	Variable	Statistic	N	%	N	%	N	%
Age (years) (continuous)		N (% non-missing)	9409 (100%)		7658 (81.39%)		1751 (18.61%)	
		Mean	70.5		73.4		57.7	
		Std. Dev	11.25		8.9		11.56	
		Range	(19, 89)		(31, 89)		(19, 89)	
		Median	72		74		58	
		25th percentile	64		68		51	
		75th percentile	78		80		63	
		Interquartile range	14		12		12	
Sex	Male	n, %	6271	66.65%	4971	64.91%	1300	74.24%
	Female	n, %	3138	33.35%	2687	35.09%	451	25.76%
	Missing	n, %						
Census region	Northeast	n, %	1070	11.37%	896	11.70%	174	9.94%
	Midwest	n, %	1656	17.60%	1230	16.06%	426	24.33%
	South	n, %	4999	53.13%	4124	53.85%	875	49.97%
	West	n, %	1678	17.83%	1408	18.39%	270	15.42%
	Missing	n, %	6	0.06%			6	0.34%
Comorbidities	Hypertension	n, %	8714	92.61%	7235	94.48%	1479	84.47%
	Atrial fibrillation	n, %	4258	45.25%	3667	47.88%	591	33.75%
	Renal disease	n, %	3421	36.36%	3053	39.87%	368	21.02%
	Hyperlipidemia	n, %	7844	83.37%	6579	85.91%	1265	72.24%
	Diabetes mellitus	n, %	4776	50.76%	4060	53.02%	716	40.89%
	History of myocardial infarction	n, %	3494	37.13%	2916	38.08%	578	33.01%
	Chronic Kidney Disease	n, %	3299	35.06%	2953	38.56%	346	19.76%
	Ischemic heart disease	n, %	7409	78.74%	6191	80.84%	1218	69.56%
	Chronic obstructive pulmonary disease (COPD)	n, %	2958	31.44%	2676	34.94%	282	16.11%
	Sleep apnea	n, %	2469	26.24%	1913	24.98%	556	31.75%

	Anemia	n, %	3113	33.09%	2696	35.21%	417	23.81%
	Depression	n, %	1858	19.75%	1598	20.87%	260	14.85%
	Peripheral vascular disease	n, %	3034	32.25%	2733	35.69%	301	17.19%
	Valvular disease	n, %	5341	56.76%	4354	56.86%	987	56.37%
	Dementia	n, %	447	4.75%	428	5.59%	19	1.09%
	Cerebrovascular disease	n, %	1892	20.11%	1670	21.81%	222	12.68%
	Obesity	n, %	2973	31.60%	2241	29.26%	732	41.80%
Medications	ACE inhibitors / ARBs	n, %	7745	82.31%	6327	82.62%	1418	80.98%
	Beta blockers	n, %	8699	92.45%	7051	92.07%	1648	94.12%
	Loop diuretic agents	n, %	6993	74.32%	5751	75.10%	1242	70.93%
	Mineralocorticoid Receptor Antagonist (MRA)	n, %	3535	37.57%	2722	35.54%	813	46.43%
	Sodium-glucose co-transporter-2 inhibitors	n, %	229	2.43%	159	2.08%	70	4.00%
Days covered		N (% non-missing)	9409 (100%)		7658 (81.39%)		1751 (18.61%)	
		Mean	294		291		309	
		Std. Dev	81.04		82.82		70.96	
		Range	(90, 366)		(90, 366)		(90, 366)	
		Median	330		328		339	
		25th percentile	247		240		278	
		75th percentile	360		359		361	
		Interquartile range	113		119		83	
Proportion of days covered		N (% non-missing)	9409 (100%)		7658 (81.39%)		1751 (18.61%)	
		Mean	80		80		84	
		Std. Dev	22.14		22.63		19.39	
		Range	(25, 100)		(25, 100)		(25, 100)	
		Median	90		90		93	
		25th percentile	67		66		76	
		75th percentile	98		98		99	
		Interquartile range	31		33		23	

Heart failure-specific hospitalizations	2301	1851	617	241
Heart failure-related hospitalizations	2737	2125	744	277
All-cause hospitalizations	3410	2505	846	336
Worsening Heart Failure Episodes	2766	2274	705	342
Heart Failure-specific hospitalization costs	2428	1321	627	236
Heart Failure-related hospitalization costs	2760	2124	728	266
All-cause hospitalizations costs	3360	2463	831	324
Worsening Heart Failure episodes costs	2723	2243	691	328
Heart Failure-specific costs	5992	6644	1455	1441
Heart Failure-related costs	6048	6694	1472	1462
All-cause medical costs	7310	7310	1668	1668
All-cause pharmacy cost	7337	7337	1669	1669
All-cause total cost of care	7340	7340	1675	1675

Primary Outcome Result(s)

Results for Heart Failure-Specific Hospitalizations - HFrEF Cohort

			Medicare Advantage								Commercially insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error
Heart failure-specific hospitalizations	Overall cohort		7503, 100%	N (% non-missing)	2301, 30.67%	1851, 24.67%					1727, 100%	N (% non-missing)	617, 35.73%	241, 13.95%				
				Mean	0.4	0.4						Mean	0.4	0.2				
				Std. Dev	0.84	0.86						Std. Dev	0.68	0.59				
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				
				Period (Post index vs pre index)			0.91	0.85	0.97	0.03		Period (Post index vs pre index)			0.47	0.41	0.55	0.07
				Concomitant beta blocker usage (Yes vs No)			0.88	0.72	1.08	0.10		Concomitant beta blocker usage (Yes vs No)			1.23	0.79	1.93	0.23
				Concomitant loop diuretic agent usage (Yes vs No)			0.96	0.80	1.14	0.09		Concomitant loop diuretic agent usage (Yes vs No)			0.71	0.44	1.15	0.25
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.74	1.04	0.09		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.53	1.26	0.22
Heart failure-specific hospitalizations	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	998, 13.17%	N (% non-missing)	300, 30.36%	298, 30.16%					151, 8.74%	N (% non-missing)	63, 41.72%	37, 24.5%				
				Mean	0.4	0.5						Mean	0.6	0.4				

			Medicare Advantage								Commercially Insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error
Heart failure-specific hospitalizations	Overall cohort		7503, 100%	N (% non-missing)	2301, 30.67%	1851, 24.67%					1727, 100%	N (% non-missing)	617, 35.73%	241, 13.95%				
				Mean	0.4	0.4						Mean	0.4	0.2				
				Std. Dev	0.84	0.86						Std. Dev	0.68	0.59				
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				
				Period (Post Index vs pre Index)			0.91	0.85	0.97	0.03		Period (Post Index vs pre Index)			0.47	0.41	0.55	0.07
				Concomitant beta blocker usage (Yes vs No)			0.88	0.72	1.08	0.10		Concomitant beta blocker usage (Yes vs No)			1.23	0.79	1.93	0.23
				Concomitant loop diuretic agent usage (Yes vs No)			0.96	0.80	1.14	0.09		Concomitant loop diuretic agent usage (Yes vs No)			0.71	0.44	1.15	0.25
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.74	1.04	0.09		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.53	1.26	0.22
Heart failure-specific hospitalizations	Proportion of days covered (POC)	POC ≥ 40% & < 60%	988, 13.17%	N (% non-missing)	300, 30.36%	298, 30.16%					151, 8.74%	N (% non-missing)	63, 41.72%	37, 24.5%				
				Mean	0.4	0.5						Mean	0.6	0.4				

				Std. Dev	0.85	1.11						Std. Dev	0.84	0.86																					
				Range	(0, 9)	(0, 9)						Range	(0, 5)	(0, 6)																					
				Median	0	0						Median	0	0																					
				25th percentile	0	0						25th percentile	0	0																					
				75th percentile	1	1						75th percentile	1	0																					
				Interquartile range	1	1						Interquartile range	1	0																					
				Period (Post-index vs pre-index)		1.22						1.02	1.46	0.09				Period (Post-index vs pre-index)		0.57	0.37	0.88	0.22												
				Concomitant beta blocker usage (Yes vs No)		0.96						0.56	1.62	0.27				Concomitant beta blocker usage (Yes vs No)		2.44	0.93	6.40	0.49												
				Concomitant loop diuretic agent usage (Yes vs No)		1.11						0.72	1.71	0.22				Concomitant loop diuretic agent usage (Yes vs No)		1.73	0.56	5.32	0.57												
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)		0.85						0.53	1.35	0.24				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)		0.44	0.14	1.35	0.57												
		PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non-missing)	374, 32.02%	321, 27.48%																N (% non-missing)	104, 41.77%	43, 17.27%											
				Mean	0.5	0.5																Mean	0.5	0.3											
				Std. Dev	0.86	0.95																Std. Dev	0.75	0.7											
				Range	(0, 6)	(0, 9)																Range	(0, 5)	(0, 5)											
				Median	0	0																Median	0	0											
				25th percentile	0	0																25th percentile	0	0											
				75th percentile	1	1																75th percentile	1	0											
				Interquartile range	1	1																Interquartile range	1	0											
				Period (Post-index vs pre-index)																		0.98	0.83	1.15				0.08	Period (Post-index vs pre-index)			0.51	0.36	0.71	0.17

				Concomitant beta blocker usage (Yes vs No)			1.13	0.69	1.86	0.25		Concomitant beta blocker usage (Yes vs No)			1.46	0.44	4.88	0.62
				Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.61	1.47	0.22		Concomitant loop diuretic agent usage (Yes vs No)			0.33	0.07	1.62	0.81
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.53	1.27	0.22		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.81	0.29	2.24	0.52
		POC ≈ 80%	4721, 62.92 %	N (% non-missing)	1422, 30.12%	1012, 21.44%					1249, 72.32 %	N (% non-missing)	425, 34.03%	134, 10.73%				
				Mean	0.4	0.3						Mean	0.4	0.1				
				Std. Dev	0.83	0.72						Std. Dev	0.62	0.45				
				Range	(0, 13)	(0, 8)						Range	(0, 5)	(0, 5)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.76	0.70	0.83	0.04		Period (Post-index vs pre-index)			0.37	0.31	0.45	0.10
				Concomitant beta blocker usage (Yes vs No)			0.77	0.59	1.02	0.14		Concomitant beta blocker usage (Yes vs No)			0.89	0.46	1.72	0.33
				Concomitant loop diuretic agent usage (Yes vs No)			0.84	0.66	1.07	0.12		Concomitant loop diuretic agent usage (Yes vs No)			0.72	0.37	1.40	0.34
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.97	0.78	1.21	0.11		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.92	0.52	1.64	0.29
Heart failure-specific hospitalizations	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5%	N (% non-missing)	1362, 34.58%	1078, 27.37%					702, 40.65 %	N (% non-missing)	274, 39.03%	120, 17.09%				
				Mean	0.5	0.4						Mean	0.5	0.3				

				Std. Dev	0.94	0.93						Std. Dev	0.74	0.66														
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 5)														
				Median	0	0						Median	0	0														
				25th percentile	0	0						25th percentile	0	0														
				75th percentile	1	1						75th percentile	1	0														
				Interquartile range	1	1						Interquartile range	1	0														
				Period (Post-index vs pre-index)								0.87	0.80	0.94					0.04	Period (Post-index vs pre-index)					0.54	0.44	0.67	0.11
				Concomitant beta blocker usage (Yes vs No)								1.02	0.77	1.35					0.14	Concomitant beta blocker usage (Yes vs No)					1.22	0.64	2.34	0.33
				Concomitant loop diuretic agent usage (Yes vs No)								0.88	0.69	1.11					0.12	Concomitant loop diuretic agent usage (Yes vs No)					0.87	0.45	1.69	0.34
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.93	0.75	1.16					0.11	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)					0.51	0.25	1.05	0.37
		No diagnosis of T2DM in pre-index period	3564, 47.5%	N (% non-missing)	939, 26.35%	773, 21.69%					1025, 59.35 %	N (% non-missing)	343, 33.46%	121, 11.8%														
				Mean	0.4	0.3						Mean	0.4	0.2														
				Std. Dev	0.69	0.78						Std. Dev	0.63	0.53														
				Range	(0, 6)	(0, 9)						Range	(0, 5)	(0, 6)														
				Median	0	0						Median	0	0														
				25th percentile	0	0						25th percentile	0	0														
				75th percentile	1	0						75th percentile	1	0														
				Interquartile range	1	0						Interquartile range	1	0														
				Period (Post-index vs pre-index)								0.98	0.88	1.08					0.05	Period (Post-index vs pre-index)					0.41	0.33	0.50	0.10

				Concomitant beta blocker usage (Yes vs No)			0.80	0.60	1.06	0.15		Concomitant beta blocker usage (Yes vs No)			1.32	0.71	2.44	0.31
				Concomitant loop diuretic agent usage (Yes vs No)			1.07	0.84	1.38	0.13		Concomitant loop diuretic agent usage (Yes vs No)			0.59	0.30	1.17	0.35
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.79	0.61	1.04	0.14		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.18	0.69	2.03	0.28
Heart failure-specific hospitalizations	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	1187, 41%	853, 29.46%					343, 19.86 %	N (% non-missing)	168, 48.98%	75, 21.87%				
				Mean	0.7	0.5						Mean	0.7	0.3				
				Std. Dev	1.07	1.01						Std. Dev	0.9	0.73				
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.78	0.71	0.85	0.05		Period (Post-index vs pre-index)			0.46	0.35	0.60	0.13
				Concomitant beta blocker usage (Yes vs No)			0.75	0.54	1.06	0.17		Concomitant beta blocker usage (Yes vs No)			1.77	0.80	3.95	0.41
				Concomitant loop diuretic agent usage (Yes vs No)			0.97	0.74	1.26	0.14		Concomitant loop diuretic agent usage (Yes vs No)			0.52	0.18	1.47	0.53
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.91	0.71	1.18	0.13		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.47	0.63	3.43	0.43
		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1114, 24.18%	998, 21.66%					1384, 80.14 %	N (% non-missing)	449, 32.44%	166, 11.99%				
				Mean	0.3	0.3						Mean	0.4	0.2				

				Std. Dev	0.62	0.75						Std. Dev	0.6	0.54				
				Range	(0, 10)	(0, 9)						Range	(0, 5)	(0, 5)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	0	0						75th percentile	1	0				
				Interquartile range	0	0						Interquartile range	1	0				
				Period (Post-index vs pre-index)			1.08	0.98	1.18	0.05		Period (Post-index vs pre-index)			0.47	0.40	0.56	0.09
				Concomitant beta blocker usage (Yes vs No)			1.02	0.80	1.30	0.12		Concomitant beta blocker usage (Yes vs No)			1.16	0.88	1.97	0.27
				Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.79	1.23	0.11		Concomitant loop diuretic agent usage (Yes vs No)			0.78	0.45	1.35	0.28
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.69	1.08	0.11		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.71	0.42	1.20	0.26
Heart failure-specific hospitalizations	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	328, 25.97%	264, 20.9%					505, 29.24 %	N (% non-missing)	184, 36.44%	48, 9.5%				
				Mean	0.3	0.3						Mean	0.4	0.1				
				Std. Dev	0.69	0.74						Std. Dev	0.63	0.43				
				Range	(0, 6)	(0, 8)						Range	(0, 4)	(0, 5)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.93	0.78	1.10	0.09		Period (Post-index vs pre-index)			0.30	0.22	0.41	0.16

				Concomitant beta blocker usage (Yes vs No)			0.60	0.31	1.13	0.33		Concomitant beta blocker usage (Yes vs No)			1.79	0.72	4.42	0.46
				Concomitant loop diuretic agent usage (Yes vs No)			0.77	0.45	1.32	0.28		Concomitant loop diuretic agent usage (Yes vs No)			0.57	0.19	1.71	0.56
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.50	1.32	0.25		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.49	0.17	1.43	0.55
		Other	6240, 83.17 %	N (% non-missing)	1973, 31.62%	1587, 25.43%					1222, 70.76 %	N (% non-missing)	433, 35.43%	193, 15.76%				
				Mean	0.5	0.4						Mean	0.4	0.2				
				Std. Dev	0.87	0.89						Std. Dev	0.7	0.64				
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.91	0.85	0.98	0.04		Period (Post-index vs pre-index)			0.54	0.45	0.64	0.09
				Concomitant beta blocker usage (Yes vs No)			0.92	0.74	1.13	0.11		Concomitant beta blocker usage (Yes vs No)			1.17	0.70	1.96	0.26
				Concomitant loop diuretic agent usage (Yes vs No)			0.97	0.80	1.16	0.09		Concomitant loop diuretic agent usage (Yes vs No)			0.73	0.42	1.25	0.28
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.89	0.74	1.07	0.09		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.94	0.58	1.52	0.25
Heart failure-specific hospitalizations	Concomitant use of spironolactone	Prescription fills for spironolactone with days of	3179, 42.37 %	N (% non-missing)	1092, 34.35%	870, 27.37%					880, 50.96 %	N (% non-missing)	341, 38.75%	124, 14.09%				
				Mean	0.5	0.5						Mean	0.5	0.2				

		supply overlapping with sacubitril/valsartan in the post-index period		Std. Dev	0.89	0.92						Std. Dev	0.71	0.61				
				Range	(0, 9)	(0, 9)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.91	0.82	1.00	0.05		Period (Post-index vs pre-index)			0.45	0.37	0.55	0.10
				Concomitant beta blocker usage (Yes vs No)			1.01	0.77	1.34	0.14		Concomitant beta blocker usage (Yes vs No)			0.65	0.33	1.28	0.35
				Concomitant loop diuretic agent usage (Yes vs No)			0.74	0.57	0.97	0.13		Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.55	1.80	0.30
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	1200, 27.06%	981, 22.60%					847, 49.04 %	N (% non-missing)	276, 32.50%	117, 13.81%				
				Mean	0.4	0.4						Mean	0.4	0.2				
				Std. Dev	0.8	0.82						Std. Dev	0.64	0.57				
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 5)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.90	0.82	0.99	0.05		Period (Post-index vs pre-index)			0.48	0.39	0.80	0.11

				Concomitant beta blocker usage (Yes vs No)			0.74	0.56	0.97	0.14		Concomitant beta blocker usage (Yes vs No)				1.95	1.12	3.42	0.29
				Concomitant loop diuretic agent usage (Yes vs No)			1.13	0.90	1.42	0.12		Concomitant loop diuretic agent usage (Yes vs No)				0.45	0.21	0.96	0.39
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							
Heart failure-specific hospitalizations	Concomitant use of Sodium-glucose co-transporter-2 (SGLT-2) inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237, 3.16%	N (% non-missing)	68, 28.69%	59, 24.89%						111, 6.43%	N (% non-missing)	37, 33.33%	15, 13.51%				
				Mean	0.4	0.4						Mean	0.4	0.2					
				Std. Dev	0.62	0.8						Std. Dev	0.61	0.66					
				Range	(0, 3)	(0, 5)						Range	(0, 2)	(0, 4)					
				Median	0	0						Median	0	0					
				25th percentile	0	0						25th percentile	0	0					
				75th percentile	1	0						75th percentile	1	0					
				Interquartile range	1	0						Interquartile range	1	0					
			Period (Post-index vs pre-index)			1.20	0.84	1.71	0.18			Period (Post-index vs pre-index)				NA	NA	NA	NA
			Concomitant beta blocker usage (Yes vs No)			0.77	0.20	2.93	0.68			Concomitant beta blocker usage (Yes vs No)				NA	NA	NA	NA
			Concomitant loop diuretic agent usage (Yes vs No)			0.26	0.06	1.16	0.76			Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA	NA
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.52	0.19	1.43	0.52			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				NA	NA	NA	NA
		No prescription fills for SGLT-2 inhibitors with days of supply	7266, 96.84 %	N (% non-missing)	2233, 30.73%	1792, 24.66%						1616, 93.57 %	N (% non-missing)	580, 35.89%	226, 13.99%				
				Mean	0.4	0.4						Mean	0.4	0.2					

		overlapping with sacubitril/valsartan in the post-index period		Std. Dev	0.85	0.87						Std. Dev	0.88	0.58				
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.90	0.84	0.97	0.03		Period (Post-index vs pre-index)			0.46	0.40	0.54	0.08
				Concomitant beta blocker usage (Yes vs No)			0.88	0.72	1.08	0.10		Concomitant beta blocker usage (Yes vs No)			1.37	0.87	2.14	0.23
				Concomitant loop diuretic agent usage (Yes vs No)			0.98	0.82	1.16	0.09		Concomitant loop diuretic agent usage (Yes vs No)			0.66	0.40	1.08	0.25
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.89	0.75	1.06	0.09		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.85	0.54	1.31	0.22
				Heart failure-specific hospitalizations	Age category	<65	1029, 13.71 %	N (% non-missing)	332, 32.26%	310, 30.13%						1352, 78.29 %	N (% non-missing)	499, 36.91%
Mean	0.5	0.5	Mean	0.4	0.2													
Std. Dev	0.94	0.96	Std. Dev	0.88	0.58													
Range	(0, 9)	(0, 8)	Range	(0, 5)	(0, 6)													
Median	0	0	Median	0	0													
25th percentile	0	0	25th percentile	0	0													
75th percentile	1	1	75th percentile	1	0													
Interquartile range	1	1	Interquartile range	1	0													
						0.99	0.84	1.17	0.09				0.41	0.35	0.49	0.09		

				Concomitant beta blocker usage (Yes vs No)			0.96	0.54	1.68	0.29		Concomitant beta blocker usage (Yes vs No)			1.35	0.82	2.24	0.26
				Concomitant loop diuretic agent usage (Yes vs No)			0.95	0.56	1.60	0.27		Concomitant loop diuretic agent usage (Yes vs No)			0.74	0.43	1.28	0.28
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.81	0.50	1.29	0.24		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.50	1.34	0.25
		65-74	2970, 39.58 %	N (% non-missing)	922, 31.04%	685, 23.06%					226, 13.09 %	N (% non-missing)	67, 29.65%	39, 17.26%				
				Mean	0.5	0.4						Mean	0.4	0.2				
				Std. Dev	0.87	0.89						Std. Dev	0.73	0.67				
				Range	(0, 13)	(0, 9)						Range	(0, 5)	(0, 5)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.89	0.79	0.99	0.06		Period (Post-index vs pre-index)			0.63	0.42	0.96	0.21
				Concomitant beta blocker usage (Yes vs No)			0.80	0.57	1.12	0.17		Concomitant beta blocker usage (Yes vs No)			1.19	0.35	4.05	0.62
				Concomitant loop diuretic agent usage (Yes vs No)			0.78	0.58	1.06	0.15		Concomitant loop diuretic agent usage (Yes vs No)			0.52	0.10	2.60	0.82
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.93	0.70	1.22	0.14		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.69	0.18	2.64	0.68
		75-94	2705, 36.05 %	N (% non-missing)	805, 29.76%	657, 24.29%					120, 6.95%	N (% non-missing)	41, 34.17%	32, 26.67%				
				Mean	0.4	0.4						Mean	0.4	0.3				

				Std. Dev	0.78	0.82						Std. Dev	0.57	0.55							
				Range	(0, 6)	(0, 9)						Range	(0, 2)	(0, 2)							
				Median	0	0						Median	0	0							
				25th percentile	0	0						25th percentile	0	0							
				75th percentile	1	0						75th percentile	1	1							
				Interquartile range	1	0						Interquartile range	1	1							
				Period (Post-index vs pre-index)			0.90	0.81	1.01	0.06		Period (Post-index vs pre-index)			NA	NA	NA	NA			
				Concomitant beta blocker usage (Yes vs No)			0.93	0.67	1.28	0.16		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA			
				Concomitant loop diuretic agent usage (Yes vs No)			1.11	0.84	1.45	0.14		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA			
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.89	0.68	1.18	0.14		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA			
				≥85	799, 10.65 %	N (% non-missing)	242, 30.29%	199, 24.91%						29, 1.68%	N (% non-missing)	10, 34.48%	8, 27.59%				
				Mean	0.4	0.4	Mean	0.4							0.3						
				Std. Dev	0.79	0.77	Std. Dev	0.56							0.45						
				Range	(0, 9)	(0, 5)	Range	(0, 2)							(0, 1)						
				Median	0	0	Median	0							0						
				25th percentile	0	0	25th percentile	0							0						
				75th percentile	1	0	75th percentile	1							1						
				Interquartile range	1	0	Interquartile range	1	1												
						Period (Post-index vs pre-index)			0.88	0.72	1.08	0.10	Period (Post-index vs pre-index)				NA	NA	NA	NA	

				Concomitant beta blocker usage (Yes vs No)			0.99	0.59	1.66	0.27		Concomitant beta blocker usage (Yes vs No)				NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.22	0.80	1.87	0.22		Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA	NA
				Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			0.73	0.42	1.27	0.28		Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)				NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Secondary Outcome Result(s)

Results for HF-Related Hospitalizations - HFReEF Cohort

			Medicare Advantage								Commercially insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error
Heart failure-related hospitalizations	Overall cohort		7503, 100%	N (% non-missing)	2737, 36.48%	2125, 28.32%					1727, 100%	N (% non-missing)	733, 42.44%	277, 16.04%				
				Mean	0.6	0.5						Mean	0.5	0.2				
				Std. Dev	0.98	1.01						Std. Dev	0.76	0.7				
				Range	(0, 14)	(0, 11)						Range	(0, 7)	(0, 7)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post index vs pre index)			0.88	0.82	0.93	0.03		Period (Post index vs pre index)			0.47	0.41	0.54	0.07
				Concomitant beta blocker usage (Yes vs No)			0.88	0.73	1.05	0.09		Concomitant beta blocker usage (Yes vs No)			1.04	0.68	1.59	0.22
				Concomitant loop diuretic agent usage (Yes vs No)			0.98	0.84	1.15	0.08		Concomitant loop diuretic agent usage (Yes vs No)			0.67	0.43	1.05	0.23
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.88	0.76	1.04	0.08		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.00	0.69	1.46	0.19
Heart failure-related	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17%	N (% non-missing)	355, 35.93%	336, 34.01%					151, 8.74%	N (% non-missing)	72, 47.68%	42, 27.81%				
				Mean	0.6	0.7						Mean	0.7	0.5				

hospitalizations				Std. Dev	1.01	1.3						Std. Dev	0.93	0.96															
				Range	(0, 10)	(0, 11)						Range	(0, 5)	(0, 6)															
				Median	0	0						Median	0	0															
				25th percentile	0	0						25th percentile	0	0															
				75th percentile	1	1						75th percentile	1	1															
				Interquartile range	1	1						Interquartile range	1	1															
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)							0.59	0.40	0.87	0.20							
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)							2.15	0.86	5.41	0.47							
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)							1.78	0.61	5.18	0.55							
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.38	0.13	1.15	0.56							
		PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non-missing)	451, 38.61%	369, 31.59%					249, 14.42 %	N (% non-missing)	119, 47.79%	56, 22.49%															
				Mean	0.6	0.6						Mean	0.7	0.4															
				Std. Dev	1.03	1.12						Std. Dev	0.82	0.88															
				Range	(0, 8)	(0, 10)						Range	(0, 5)	(0, 6)															
				Median	0	0						Median	0	0															
				25th percentile	0	0						25th percentile	0	0															
				75th percentile	1	1						75th percentile	1	0															
				Interquartile range	1	1						Interquartile range	1	0															
				Period (Post-index vs pre-index)								0.95	0.82	1.11							0.08	Period (Post-index vs pre-index)			0.59	0.44	0.80	0.16	

				Concomitant beta blocker usage (Yes vs No)			1.12	0.70	1.77	0.24		Concomitant beta blocker usage (Yes vs No)			0.98	0.30	3.19	0.60	
		Concomitant loop diuretic agent usage (Yes vs No)	0.91	0.60			1.37	0.21	Concomitant loop diuretic agent usage (Yes vs No)	0.26		0.05			1.21	0.79			
		Concomitant Mineralocorti cold Receptor Antagonist usage (Yes vs No)	0.80	0.53			1.21	0.21	Concomitant Mineralocorti cold Receptor Antagonist usage (Yes vs No)	1.19		0.53			2.66	0.41			
		PDC ≥ 80%	4721, 62.92 %	N (% non-missing)	1692, 35.84%	1162, 24.61%					1249, 72.32 %	N (% non-missing)	513, 41.07%	150, 12.01%					
		Mean	0.5	0.4	Mean	0.5					0.2								
		Std. Dev	0.97	0.84	Std. Dev	0.7					0.51								
		Range	(0, 14)	(0, 9)	Range	(0, 5)					(0, 6)								
		Median	0	0	Median	0					0								
		25th percentile	0	0	25th percentile	0					0								
		75th percentile	1	0	75th percentile	1					0								
		Interquartile range	1	0	Interquartile range	1					0								
		Period (Post-index vs pre-index)			0.72	0.66	0.78	0.04	Period (Post-index vs pre-index)			0.34	0.29	0.41	0.09				
		Concomitant beta blocker usage (Yes vs No)		0.84	0.66	1.08	0.13	Concomitant beta blocker usage (Yes vs No)	0.74		0.39	1.38	0.32						
		Concomitant loop diuretic agent usage (Yes vs No)		0.89	0.71	1.10	0.11	Concomitant loop diuretic agent usage (Yes vs No)	0.77		0.43	1.41	0.31						
		Concomitant Mineralocorti cold Receptor Antagonist usage (Yes vs No)		0.97	0.79	1.19	0.10	Concomitant Mineralocorti cold Receptor Antagonist usage (Yes vs No)	1.09		0.65	1.81	0.26						
		Heart failure-	Presence of Type 2 Diabetes Mellitus (T2DM)			N (% non-missing)	1606, 40.77%	1230, 31.23%					N (% non-missing)	328, 46.72%	137, 19.52%				

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		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1357, 29.45%	1153, 25.02%					1384, 80.14 %	N (% non-missing)	541, 39.09%	197, 14.23%				
				Mean	0.4	0.4						Mean	0.5	0.2				
				Std. Dev	0.74	0.89						Std. Dev	0.66	0.66				
				Range	(0, 12)	(0, 10)						Range	(0, 5)	(0, 7)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			1.03	0.95	1.12	0.04		Period (Post-index vs pre-index)			0.49	0.42	0.57	0.08
				Concomitant beta blocker usage (Yes vs No)			0.98	0.78	1.23	0.12		Concomitant beta blocker usage (Yes vs No)			0.92	0.56	1.52	0.26
				Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.81	1.22	0.10		Concomitant loop diuretic agent usage (Yes vs No)			0.72	0.43	1.20	0.26
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.71	1.07	0.11		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.95	0.62	1.47	0.22
Heart failure-related hospitalizations	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	404, 31.99%	304, 24.07%					505, 29.24 %	N (% non-missing)	212, 41.98%	55, 10.89%				
				Mean	0.5	0.4						Mean	0.5	0.2				
				Std. Dev	0.81	0.86						Std. Dev	0.7	0.55				
				Range	(0, 7)	(0, 8)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	0						75th percentile	1	0				
				Interquartile range	1	0						Interquartile range	1	0				

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Heart failure-related hospitalizations	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	1265, 39.79%	971, 30.54%					880, 50.96 %	N (% non-missing)	400, 45.45%	147, 16.7%				
				Mean	0.6	0.6						Mean	0.6	0.3				
				Std. Dev	1.04	1.09						Std. Dev	0.78	0.74				
				Range	(0, 10)	(0, 10)						Range	(0, 5)	(0, 7)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.88	0.81	0.97	0.05		Period (Post-index vs pre-index)			0.48	0.40	0.58	0.09
				Concomitant beta blocker usage (Yes vs No)			0.97	0.75	1.27	0.14		Concomitant beta blocker usage (Yes vs No)			0.55	0.29	1.04	0.33
				Concomitant loop diuretic agent usage (Yes vs No)			0.79	0.62	1.01	0.12		Concomitant loop diuretic agent usage (Yes vs No)			0.96	0.55	1.65	0.28
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	1472, 34.04%	1154, 26.69%					847, 49.04 %	N (% non-missing)	333, 39.32%	130, 15.35%				
				Mean	0.5	0.4						Mean	0.5	0.2				
				Std. Dev	0.94	0.94						Std. Dev	0.75	0.65				
				Range	(0, 14)	(0, 11)						Range	(0, 7)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				

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		No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	N (% non-missing)	2654, 36.53%	2057, 28.31%					1616, 93.57 %	N (% non-missing)	692, 42.82%	260, 16.09%				
				Mean	0.6	0.5						Mean	0.5	0.2				
				Std. Dev	0.99	1.01						Std. Dev	0.77	0.7				
				Range	(0, 14)	(0, 11)						Range	(0, 7)	(0, 7)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
Heart failure-related hospitalizations	Age category	<65	1029, 13.71 %	N (% non-missing)	390, 37.9%	340, 33.04%					1352, 78.29 %	N (% non-missing)	588, 43.49%	184, 13.61%				
				Mean	0.6	0.6						Mean	0.6	0.2				
				Std. Dev	1.1	1.15						Std. Dev	0.78	0.7				
				Range	(0, 10)	(0, 9)						Range	(0, 7)	(0, 7)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				

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		75-84	2705, 36.05 %	N (% non-missing)	959, 35.45%	745, 27.54%					120, 6.95 %	N (% non-missing)	49, 40.83%	36, 30%												
				Mean	0.5	0.5						Mean	0.5	0.4												
				Std. Dev	0.93	0.95						Std. Dev	0.61	0.57												
				Range	(0, 8)	(0, 11)						Range	(0, 2)	(0, 2)												
				Median	0	0						Median	0	0												
				25th percentile	0	0						25th percentile	0	0												
				75th percentile	1	1						75th percentile	1	1												
				Interquartile range	1	1						Interquartile range	1	1												
				Period (Post-index vs pre-index)		0.86						0.78	0.96	0.05					Period (Post-index vs pre-index)		NA	NA	NA	NA		
				Concomitant beta blocker usage (Yes vs No)		0.96						0.71	1.30	0.15					Concomitant beta blocker usage (Yes vs No)		NA	NA	NA	NA		
				Concomitant loop diuretic agent usage (Yes vs No)		1.01						0.78	1.31	0.13					Concomitant loop diuretic agent usage (Yes vs No)		NA	NA	NA	NA		
				Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)		0.86						0.66	1.12	0.14					Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)		NA	NA	NA	NA		
		≥85	799, 10.65 %	N (% non-missing)	298, 37.3%	242, 30.29%					29, 1.68 %	N (% non-missing)	12, 41.38%	10, 34.48%												
				Mean	0.5	0.5						Mean	0.6	0.3												
				Std. Dev	0.92	0.87						Std. Dev	0.74	0.48												
				Range	(0, 9)	(0, 6)						Range	(0, 2)	(0, 1)												
				Median	0	0						Median	0	0												
				25th percentile	0	0						25th percentile	0	0												
				75th percentile	1	1						75th percentile	1	1												
				Interquartile range	1	1						Interquartile range	1	1												

				Period (Post-index vs pre-index)			0.83	0.69	0.99	0.09		Period (Post-index vs pre-index)				NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.09	0.69	1.71	0.23		Concomitant beta blocker usage (Yes vs No)				NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.31	0.90	1.90	0.19		Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.74	0.45	1.20	0.25		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for All-Cause Hospitalizations – HFrEF Cohort

			Medicare Advantage								Commercially insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error
All-cause hospitalizations	Overall cohort		7503, 100%	N (% non-missing)	3410, 45.45%	2505, 33.39%					1727, 100%	N (% non-missing)	846, 48.99%	336, 19.46%				
				Mean	0.8	0.6						Mean	0.7	0.3				
				Std. Dev	1.2	1.13						Std. Dev	0.91	0.83				
				Range	(0, 14)	(0, 12)						Range	(0, 9)	(0, 9)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
			Period (Post index vs pre index)			0.77	0.73	0.82	0.03	Period (Post index vs pre index)			0.48	0.43	0.55	0.06		
			Concomitant beta blocker			0.93	0.79	1.10	0.08	Concomitant beta blocker			0.88	0.59	1.32	0.21		

				usage (Yes vs No)								usage (Yes vs No)													
				Concomitant loop diuretic agent usage (Yes vs No)			1.00	0.87	1.16	0.07		Concomitant loop diuretic agent usage (Yes vs No)							0.67	0.44	1.01	0.21			
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.88	0.76	1.02	0.07		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.99	0.70	1.41	0.18			
All-cause hospitalizations	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non-missing)	432, 43.72%	389, 39.37%					151, 8.74%	N (% non-missing)	81, 53.64%	48, 31.79%											
				Mean	0.8	0.8						Mean	0.8	0.5											
				Std. Dev	1.21	1.39						Std. Dev	1.04	1.19											
				Range	(0, 10)	(0, 11)						Range	(0, 5)	(0, 9)											
				Median	0	0						Median	1	0											
				25th percentile	0	0						25th percentile	0	0											
				75th percentile	1	1						75th percentile	1	1											
				Interquartile range	1	1						Interquartile range	1	1											
				Period (Post-index vs pre-index)		1.07						0.92	1.24	0.08					Period (Post-index vs pre-index)			0.62	0.43	0.89	0.19
				Concomitant beta blocker usage (Yes vs No)		0.82						0.51	1.30	0.24					Concomitant beta blocker usage (Yes vs No)			1.61	0.65	4.00	0.46
				Concomitant loop diuretic agent usage (Yes vs No)		1.17						0.81	1.69	0.19					Concomitant loop diuretic agent usage (Yes vs No)			1.41	0.49	4.07	0.54
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)		0.91						0.62	1.35	0.20					Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.58	0.21	1.56	0.51
		PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non-missing)	552, 47.26%	439, 37.59%					249, 14.42 %	N (% non-missing)	134, 53.82%	69, 27.71%											
				Mean	0.8	0.7						Mean	0.8	0.5											
				Std. Dev	1.26	1.24						Std. Dev	1.01	1.1											

				Range	(0, 14)	(0, 10)					Range	(0, 7)	(0, 7)																									
				Median	0	0					Median	1	0																									
				25th percentile	0	0					25th percentile	0	0																									
				75th percentile	1	1					75th percentile	1	1																									
				Interquartile range	1	1					Interquartile range	1	1																									
				Period (Post-index vs pre-index)							0.86	0.75	0.98					0.07	Period (Post-index vs pre-index)																			
				Concomitant beta blocker usage (Yes vs No)							1.11	0.74	1.69					0.21	Concomitant beta blocker usage (Yes vs No)																			
				Concomitant loop diuretic agent usage (Yes vs No)							0.91	0.63	1.32					0.19	Concomitant loop diuretic agent usage (Yes vs No)																			
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.87	0.60	1.24					0.18	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																			
				PDC ≥ 80%	4721, 62.92 %	N (% non-missing)					2132, 45.16%	1388, 29.4%									1249, 72.32 %	N (% non-missing)	597, 47.8%	187, 14.97%														
						Mean					0.8	0.5										Mean	0.6	0.2														
						Std. Dev					1.17	0.96										Std. Dev	0.82	0.58														
						Range					(0, 14)	(0, 10)										Range	(0, 5)	(0, 6)														
						Median					0	0										Median	0	0														
						25th percentile					0	0										25th percentile	0	0														
						75th percentile					1	1										75th percentile	1	0														
						Interquartile range					1	1										Interquartile range	1	0														
						Period (Post-index vs pre-index)																0.64	0.59	0.68					0.04	Period (Post-index vs pre-index)								
						Concomitant beta blocker usage (Yes vs No)																0.94	0.76	1.16					0.11	Concomitant beta blocker usage (Yes vs No)								

				Concomitant loop diuretic agent usage (Yes vs No)			0.95	0.78	1.15	0.10		Concomitant loop diuretic agent usage (Yes vs No)			0.84	0.49	1.42	0.27
				Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			0.89	0.74	1.07	0.10		Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			1.01	0.63	1.61	0.24
All-cause hospitalizati ons	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre- index period	3939, 52.5%	N (% non- missing)	1963, 49.83%	1435, 36.43%					702, 40.65 %	N (% non- missing)	376, 53.56%	162, 23.08%				
				Mean	0.9	0.7						Mean	0.8	0.4				
				Std. Dev	1.31	1.21						Std. Dev	1.01	0.97				
				Range	(0, 14)	(0, 11)						Range	(0, 9)	(0, 9)				
				Median	0	0						Median	1	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post- index vs pre- index)			0.74	0.69	0.80	0.04		Period (Post- index vs pre- index)			0.54	0.45	0.65	0.09
				Concomitant beta blocker usage (Yes vs No)			1.14	0.91	1.44	0.12		Concomitant beta blocker usage (Yes vs No)			0.93	0.52	1.67	0.30
				Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.77	1.14	0.10		Concomitant loop diuretic agent usage (Yes vs No)			0.83	0.47	1.46	0.29
				Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			0.90	0.74	1.08	0.10		Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			0.64	0.37	1.14	0.29
		No diagnosis of T2DM in pre- index period	3564, 47.5%	N (% non- missing)	1447, 40.6%	1070, 30.02%					1025, 59.35 %	N (% non- missing)	470, 45.85%	174, 16.98%				
				Mean	0.7	0.5						Mean	0.6	0.3				
				Std. Dev	1.04	1.03						Std. Dev	0.83	0.72				
				Range	(0, 9)	(0, 12)						Range	(0, 7)	(0, 7)				

				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.81	0.75	0.89	0.04		Period (Post-index vs pre-index)			0.43	0.36	0.51	0.09
				Concomitant beta blocker usage (Yes vs No)			0.77	0.60	0.98	0.12		Concomitant beta blocker usage (Yes vs No)			0.89	0.51	1.56	0.28
				Concomitant loop diuretic agent usage (Yes vs No)			1.09	0.89	1.35	0.11		Concomitant loop diuretic agent usage (Yes vs No)			0.55	0.30	1.00	0.31
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.86	0.69	1.07	0.11		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.40	0.90	2.18	0.22
All-cause hospitalizations	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	1654, 57.13%	1144, 39.52%					343, 19.86 %	N (% non-missing)	212, 61.81%	93, 27.11%				
				Mean	1.1	0.8						Mean	1	0.4				
				Std. Dev	1.45	1.27						Std. Dev	1.15	0.92				
				Range	(0, 14)	(0, 11)						Range	(0, 7)	(0, 6)				
				Median	1	0						Median	1	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	2	1						75th percentile	1	1				
				Interquartile range	2	1						Interquartile range	1	1				
				Period (Post-index vs pre-index)			0.68	0.63	0.73	0.04		Period (Post-index vs pre-index)			0.43	0.34	0.54	0.12
				Concomitant beta blocker usage (Yes vs No)			0.89	0.68	1.16	0.14		Concomitant beta blocker usage (Yes vs No)			1.28	0.60	2.76	0.39

				Concomitant loop diuretic agent usage (Yes vs No)			1.05	0.85	1.31	0.11		Concomitant loop diuretic agent usage (Yes vs No)			0.66	0.27	1.60	0.45	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.94	0.76	1.16	0.11		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.37	0.64	2.94	0.39	
		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1756, 38.11%	1361, 29.54%						1384, 80.14 %	N (% non-missing)	634, 45.81%	243, 17.56%				
				Mean	0.6	0.5							Mean	0.6	0.3				
				Std. Dev	0.94	1.02							Std. Dev	0.82	0.81				
				Range	(0, 12)	(0, 12)							Range	(0, 9)	(0, 9)				
				Median	0	0							Median	0	0				
				25th percentile	0	0							25th percentile	0	0				
				75th percentile	1	1							75th percentile	1	0				
				Interquartile range	1	1							Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.88	0.82	0.95	0.04		Period (Post-index vs pre-index)				0.50	0.44	0.58	0.07
				Concomitant beta blocker usage (Yes vs No)			1.01	0.82	1.24	0.11		Concomitant beta blocker usage (Yes vs No)				0.83	0.52	1.33	0.24
				Concomitant loop diuretic agent usage (Yes vs No)			1.00	0.83	1.20	0.10		Concomitant loop diuretic agent usage (Yes vs No)				0.67	0.41	1.07	0.24
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.86	0.71	1.03	0.10		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.93	0.62	1.39	0.20

				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.73	0.63	0.84	0.07		Period (Post-index vs pre-index)			0.33	0.26	0.43	0.13
				Concomitant beta blocker usage (Yes vs No)			0.70	0.43	1.15	0.25		Concomitant beta blocker usage (Yes vs No)			0.99	0.41	2.38	0.45
				Concomitant loop diuretic agent usage (Yes vs No)			1.05	0.70	1.58	0.21		Concomitant loop diuretic agent usage (Yes vs No)			0.56	0.21	1.49	0.50
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.71	0.47	1.06	0.21		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.67	0.29	1.55	0.43
		Other	6240, 83.17 %	N (% non-missing)	2877, 46.11%	2152, 34.49%					1222, 70.76 %	N (% non-missing)	607, 49.67%	269, 22.01%				
				Mean	0.8	0.6						Mean	0.7	0.4				
				Std. Dev	1.23	1.16						Std. Dev	0.95	0.91				
				Range	(0, 14)	(0, 12)						Range	(0, 9)	(0, 9)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.78	0.74	0.83	0.03		Period (Post-index vs pre-index)			0.54	0.47	0.62	0.07
				Concomitant beta blocker usage (Yes vs No)			0.96	0.81	1.15	0.09		Concomitant beta blocker usage (Yes vs No)			0.90	0.57	1.42	0.23

				Concomitant loop diuretic agent usage (Yes vs No)			0.98	0.84	1.14	0.08		Concomitant loop diuretic agent usage (Yes vs No)			0.68	0.42	1.08	0.24
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.91	0.78	1.06	0.08		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.11	0.75	1.64	0.20
All-cause hospitalizations	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	1482, 46.62%	1092, 34.35%					880, 50.96 %	N (% non-missing)	458, 52.05%	167, 18.98%				
				Mean	0.8	0.6						Mean	0.7	0.3				
				Std. Dev	1.22	1.19						Std. Dev	0.88	0.89				
				Range	(0, 10)	(0, 10)						Range	(0, 6)	(0, 9)				
				Median	0	0						Median	1	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
		Period (Post-index vs pre-index)																
				Period (Post-index vs pre-index)			0.79	0.73	0.86	0.04		Period (Post-index vs pre-index)			0.49	0.42	0.58	0.08
				Concomitant beta blocker usage (Yes vs No)			0.98	0.77	1.25	0.13		Concomitant beta blocker usage (Yes vs No)			0.47	0.26	0.88	0.32
				Concomitant loop diuretic agent usage (Yes vs No)			0.83	0.66	1.03	0.11		Concomitant loop diuretic agent usage (Yes vs No)			0.92	0.55	1.54	0.26
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsar	4324, 57.63 %	N (% non-missing)	1928, 44.59%	1413, 32.68%					847, 49.04 %	N (% non-missing)	388, 45.81%	169, 19.95%				
				Mean	0.8	0.6						Mean	0.7	0.3				
				Std. Dev	1.18	1.08						Std. Dev	0.94	0.78				
				Range	(0, 14)	(0, 12)						Range	(0, 9)	(0, 7)				

		tan in the post-index period		Median	0	0					Median	0	0										
				25th percentile	0	0					25th percentile	0	0										
				75th percentile	1	1					75th percentile	1	0										
				Interquartile range	1	1					Interquartile range	1	0										
				Period (Post-index vs pre-index)		0.75					0.70	0.81	0.04					Period (Post-index vs pre-index)		0.47	0.40	0.56	0.09
				Concomitant beta blocker usage (Yes vs No)		0.86					0.69	1.07	0.11					Concomitant beta blocker usage (Yes vs No)		1.48	0.89	2.47	0.26
				Concomitant loop diuretic agent usage (Yes vs No)		1.12					0.93	1.35	0.09					Concomitant loop diuretic agent usage (Yes vs No)		0.47	0.24	0.90	0.33
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)														Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)					
All-cause hospitalizations	Concomitant use of Sodium-glucose co-transporter-2 (SGLT-2) inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237, 3.16%	N (% non-missing)	110, 46.41%	77, 32.49%					111, 6.43%	N (% non-missing)	49, 44.14%	19, 17.12%									
				Mean	0.8	0.6					Mean	0.6	0.3										
				Std. Dev	1.1	1.04					Std. Dev	0.82	0.7										
				Range	(0, 7)	(0, 7)					Range	(0, 4)	(0, 4)										
				Median	0	0					Median	0	0										
				25th percentile	0	0					25th percentile	0	0										
				75th percentile	1	1					75th percentile	1	0										
				Interquartile range	1	1					Interquartile range	1	0										
				Period (Post-index vs pre-index)		0.77					0.57	1.04	0.15	Period (Post-index vs pre-index)						NA	NA	NA	NA
Concomitant beta blocker usage (Yes vs No)	1.46	0.57	3.70	0.48		Concomitant beta blocker usage (Yes vs No)	NA	NA	NA	NA													

				Concomitant loop diuretic agent usage (Yes vs No)			0.46	0.18	1.21	0.49		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.55	0.24	1.24	0.42		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
		No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	N (% non-missing)	3300, 45.42%	2428, 33.42%					1616, 93.57 %	N (% non-missing)	797, 49.32%	317, 19.62%				
				Mean	0.8	0.6						Mean	0.7	0.3				
				Std. Dev	1.2	1.13						Std. Dev	0.92	0.84				
				Range	(0, 14)	(0, 12)						Range	(0, 9)	(0, 9)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.77	0.73	0.82	0.03		Period (Post-index vs pre-index)			0.48	0.43	0.55	0.06
				Concomitant beta blocker usage (Yes vs No)			0.92	0.78	1.09	0.09		Concomitant beta blocker usage (Yes vs No)			0.99	0.66	1.48	0.21
				Concomitant loop diuretic agent usage (Yes vs No)			1.02	0.88	1.18	0.07		Concomitant loop diuretic agent usage (Yes vs No)			0.59	0.38	0.91	0.22
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.89	0.77	1.03	0.07		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.01	0.71	1.44	0.18

				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.89	0.77	1.03	0.07		Period (Post-index vs pre-index)			0.45	0.39	0.52	0.07
				Concomitant beta blocker usage (Yes vs No)			0.98	0.60	1.61	0.25		Concomitant beta blocker usage (Yes vs No)			1.02	0.65	1.60	0.23
				Concomitant loop diuretic agent usage (Yes vs No)			0.90	0.56	1.43	0.24		Concomitant loop diuretic agent usage (Yes vs No)			0.66	0.41	1.06	0.24
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.78	0.52	1.18	0.21		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.58	1.33	0.21
		65-74	2970, 39.58 %	N (% non-missing)	1323, 44.55%	911, 30.67%					226, 13.09 %	N (% non-missing)	98, 43.36%	52, 23.01%				
				Mean	0.8	0.6						Mean	0.6	0.3				
				Std. Dev	1.2	1.16						Std. Dev	0.87	0.78				
				Range	(0, 14)	(0, 12)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.77	0.70	0.84	0.05		Period (Post-index vs pre-index)			0.54	0.38	0.75	0.17
				Concomitant beta blocker usage (Yes vs No)			0.82	0.62	1.08	0.14		Concomitant beta blocker usage (Yes vs No)			0.80	0.26	2.49	0.58

				Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.73	1.19	0.12		Concomitant loop diuretic agent usage (Yes vs No)			0.52	0.14	1.92	0.67
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.98	0.78	1.24	0.12		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.29	0.52	3.21	0.47
		75-84	2705, 36.05 %	N (% non-missing)	1229, 45.43%	906, 33.49%					120, 6.95%	N (% non-missing)	58, 48.33%	45, 37.5%				
				Mean	0.8	0.6						Mean	0.6	0.5				
				Std. Dev	1.17	1.04						Std. Dev	0.81	0.66				
				Range	(0, 9)	(0, 11)						Range	(0, 5)	(0, 3)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	1				
				Interquartile range	1	1						Interquartile range	1	1				
				Period (Post-index vs pre-index)			0.73	0.67	0.80	0.05		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.03	0.79	1.34	0.14		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.02	0.81	1.29	0.12		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.69	1.10	0.12		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
		≥85	799, 10.65 %	N (% non-missing)	397, 49.69%	292, 36.55%					29, 1.68%	N (% non-missing)	18, 62.07%	12, 41.38%				
				Mean	0.8	0.6						Mean	0.8	0.5				
				Std. Dev	1.1	1.02						Std. Dev	0.73	0.63				
				Range	(0, 10)	(0, 6)						Range	(0, 2)	(0, 2)				

				Median	0	0						Median	1	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	1				
				Interquartile range	1	1						Interquartile range	1	1				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for Worsening HF Episodes – HFrEF Cohort

			Medicare Advantage								Commercially insured							
Characteristic	Variable	Subgroup	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Incident rate ratio	95% CI Lower	95% CI Upper	Standard Error
					N	N							N	N				
Worsening Heart Failure episodes	Overall cohort		7503, 100%	N (% non-missing)	2766, 36.87%	2274, 30.31%					1727, 100%	N (% non-missing)	705, 40.82%	342, 19.8%				
				Mean	0.6	0.6						Mean	0.6	0.3				
				Std. Dev	1.17	1.2						Std. Dev	0.85	0.79				
				Range	(0, 26)	(0, 15)						Range	(0, 12)	(0, 14)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				

				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post index vs pre index)			0.91	0.86	0.97	0.03		Period (Post index vs pre index)			0.56	0.49	0.64	0.07
				Concomitant beta blocker usage (Yes vs No)			0.83	0.68	0.99	0.10		Concomitant beta blocker usage (Yes vs No)			0.92	0.61	1.39	0.21
				Concomitant loop diuretic agent usage (Yes vs No)			1.01	0.86	1.19	0.08		Concomitant loop diuretic agent usage (Yes vs No)			0.73	0.48	1.12	0.21
				Concomitant Mineralocorti cold Receptor Antagonist usage (Yes vs No)			0.97	0.83	1.13	0.08		Concomitant Mineralocorti cold Receptor Antagonist usage (Yes vs No)			0.97	0.67	1.39	0.18
Worsening Heart Failure episodes	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non-missing)	355, 35.93%	353, 35.73%					151, 8.74 %	N (% non-missing)	71, 47.02%	45, 29.8%				
				Mean	0.7	0.8						Mean	0.8	0.6				
				Std. Dev	1.23	1.5						Std. Dev	1.43	1.52				
				Range	(0, 11)	(0, 15)						Range	(0, 12)	(0, 14)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	1				
				Interquartile range	1	1						Interquartile range	1	1				
				Period (Post-index vs pre-index)			1.17	0.98	1.38	0.09		Period (Post-index vs pre-index)			0.70	0.46	1.06	0.21
				Concomitant beta blocker usage (Yes vs No)			0.90	0.53	1.51	0.27		Concomitant beta blocker usage (Yes vs No)			1.60	0.55	4.67	0.55
				Concomitant loop diuretic agent usage (Yes vs No)			1.03	0.68	1.58	0.22		Concomitant loop diuretic agent usage (Yes vs No)			1.86	0.54	6.45	0.63

				Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			0.86	0.55	1.35	0.23		Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			0.32	0.09	1.11	0.63
	PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non- missing)	440, 37.67%	387, 33.13%					249, 14.42 %	N (% non- missing)	117, 46.99%	62, 24.9%					
			Mean	0.7	0.6						Mean	0.7	0.4					
			Std. Dev	1.41	1.26						Std. Dev	0.97	0.78					
			Range	(0, 26)	(0, 12)						Range	(0, 5)	(0, 5)					
			Median	0	0						Median	0	0					
			25th percentile	0	0						25th percentile	0	0					
			75th percentile	1	1						75th percentile	1	0					
			Interquartile range	1	1						Interquartile range	1	0					
			Period (Post- index vs pre- index)			0.94	0.80	1.09	0.08	Period (Post- index vs pre- index)				0.53	0.39	0.71	0.16	
			Concomitant beta blocker usage (Yes vs No)			0.97	0.60	1.59	0.25	Concomitant beta blocker usage (Yes vs No)				0.76	0.23	2.51	0.61	
			Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.61	1.43	0.22	Concomitant loop diuretic agent usage (Yes vs No)				0.38	0.10	1.43	0.67	
			Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			0.82	0.54	1.25	0.22	Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)				1.62	0.77	3.40	0.38	
	PDC ≥ 80%	4721, 62.92 %	N (% non- missing)	1723, 36.5%	1275, 27.01%					1249, 72.32 %	N (% non- missing)	486, 38.91%	206, 16.49%					
			Mean	0.6	0.5						Mean	0.5	0.2					
			Std. Dev	1.1	1.04						Std. Dev	0.71	0.56					
			Range	(0, 13)	(0, 15)						Range	(0, 6)	(0, 7)					
			Median	0	0						Median	0	0					
			25th percentile	0	0						25th percentile	0	0					

				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.78	0.72	0.84	0.04		Period (Post-index vs pre-index)			0.46	0.39	0.54	0.08
				Concomitant beta blocker usage (Yes vs No)			0.75	0.59	0.96	0.12		Concomitant beta blocker usage (Yes vs No)			0.83	0.49	1.43	0.28
				Concomitant loop diuretic agent usage (Yes vs No)			0.97	0.78	1.19	0.11		Concomitant loop diuretic agent usage (Yes vs No)			0.74	0.43	1.27	0.27
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.13	0.93	1.38	0.10		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.02	0.64	1.62	0.23
Worsening Heart Failure episodes	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5 %	N (% non-missing)	1622, 41.18%	1302, 33.05%					702, 40.65 %	N (% non-missing)	310, 44.16%	157, 22.36%				
				Mean	0.7	0.6						Mean	0.6	0.4				
				Std. Dev	1.33	1.3						Std. Dev	0.94	0.98				
				Range	(0, 26)	(0, 14)						Range	(0, 12)	(0, 14)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.87	0.80	0.94	0.04		Period (Post-index vs pre-index)			0.65	0.54	0.79	0.10
				Concomitant beta blocker usage (Yes vs No)			0.94	0.72	1.22	0.13		Concomitant beta blocker usage (Yes vs No)			0.87	0.46	1.62	0.32
				Concomitant loop diuretic agent usage (Yes vs No)			0.97	0.78	1.21	0.11		Concomitant loop diuretic agent usage (Yes vs No)			0.87	0.48	1.58	0.30

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.98	0.80	1.20	0.10		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.66	0.36	1.19	0.30
		No diagnosis of T2DM in pre-index period	3564, 47.5 %	N (% non-missing) Mean Std. Dev Range Median 25th percentile 75th percentile Interquartile range	1144, 32.1% 0.5 0.95 (0, 10) 0 0 1 1	972, 27.27% 0.5 1.07 (0, 15) 0 0 1 1					1025, 59.35 %	N (% non-missing) Mean Std. Dev Range Median 25th percentile 75th percentile Interquartile range	395, 38.54% 0.5 0.79 (0, 5) 0 0 1 1	185, 18.05% 0.2 0.61 (0, 6) 0 0 0 0				
				Period (Post-index vs pre-index)			0.98	0.89	1.08	0.05		Period (Post-index vs pre-index)			0.48	0.40	0.57	0.09
				Concomitant beta blocker usage (Yes vs No)			0.75	0.58	0.98	0.14		Concomitant beta blocker usage (Yes vs No)			1.01	0.58	1.76	0.28
				Concomitant loop diuretic agent usage (Yes vs No)			1.07	0.85	1.35	0.12		Concomitant loop diuretic agent usage (Yes vs No)			0.62	0.35	1.13	0.30
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.95	0.75	1.21	0.12		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.30	0.83	2.05	0.23
Worsening Heart Failure episodes	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing) Mean Std. Dev Range Median 25th percentile	1399, 48.32% 0.9 1.48 (0, 26) 0 0	1039, 35.89% 0.7 1.38 (0, 14) 0 0					343, 19.86 %	N (% non-missing) Mean Std. Dev Range Median 25th percentile	185, 53.94% 0.9 1.24 (0, 12) 1 0	97, 28.28% 0.5 1.12 (0, 14) 0 0				

				75th percentile	1	1						75th percentile	1	1														
				Interquartile range	1	1						Interquartile range	1	1														
				Period (Post-index vs pre-index)			0.79	0.72	0.86	0.04	Period (Post-index vs pre-index)			0.53	0.42	0.68	0.13											
				Concomitant beta blocker usage (Yes vs No)			0.77	0.57	1.05	0.16	Concomitant beta blocker usage (Yes vs No)			1.43	0.64	3.21	0.41											
				Concomitant loop diuretic agent usage (Yes vs No)			1.02	0.80	1.30	0.13	Concomitant loop diuretic agent usage (Yes vs No)			0.43	0.16	1.18	0.52											
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.91	0.72	1.15	0.12	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.53	0.68	3.43	0.41											
				No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1367, 29.67%	1235, 26.8%					1384, 80.14 %	N (% non-missing)	520, 37.57%	245, 17.7%												
						Mean	0.4	0.5						Mean	0.5	0.3												
		Std. Dev	0.87			1.05	Std. Dev	0.71						0.67														
		Range	(0, 12)			(0, 15)	Range	(0, 5)						(0, 7)														
		Median	0			0	Median	0						0														
		25th percentile	0			0	25th percentile	0						0														
		75th percentile	1			1	75th percentile	1						0														
		Interquartile range	1			1	Interquartile range	1						0														
		Period (Post-index vs pre-index)					1.07	0.98						1.16	0.04	Period (Post-index vs pre-index)									0.56	0.48	0.65	0.08
		Concomitant beta blocker usage (Yes vs No)					0.91	0.72						1.15	0.12	Concomitant beta blocker usage (Yes vs No)									0.84	0.52	1.35	0.24
		Concomitant loop diuretic agent usage (Yes vs No)					1.04	0.85						1.28	0.10	Concomitant loop diuretic agent usage (Yes vs No)									0.85	0.53	1.35	0.24

				Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			1.04	0.85	1.28	0.10		Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			0.91	0.60	1.37	0.21
Worsening Heart Failure episodes	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non- missing)	425, 33.65%	342, 27.08%					505, 29.24 %	N (% non- missing)	213, 42.18%	84, 16.63%				
				Mean	0.5	0.4						Mean	0.6	0.2				
				Std. Dev	0.95	0.95						Std. Dev	0.89	0.84				
				Range	(0, 8)	(0, 9)						Range	(0, 12)	(0, 14)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post- index vs pre- index)								0.89	0.76	1.04				
		Concomitant beta blocker usage (Yes vs No)	0.55	0.32			0.96	0.28	Concomitant beta blocker usage (Yes vs No)	1.07	0.47	2.41	0.42					
		Concomitant loop diuretic agent usage (Yes vs No)	0.96	0.61			1.51	0.23	Concomitant loop diuretic agent usage (Yes vs No)	0.50	0.20	1.27	0.47					
		Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)	0.91	0.60			1.37	0.21	Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)	0.60	0.27	1.34	0.41					
		Other	6240, 83.17 %	N (% non- missing)	2341, 37.52%	1932, 30.96%					1222, 70.76 %	N (% non- missing)	492, 40.26%	258, 21.11%				
				Mean	0.7	0.6						Mean	0.5	0.3				
				Std. Dev	1.21	1.24						Std. Dev	0.84	0.76				
				Range	(0, 26)	(0, 15)						Range	(0, 8)	(0, 7)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				

				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.92	0.86	0.98	0.03		Period (Post-index vs pre-index)			0.59	0.51	0.69	0.08
				Concomitant beta blocker usage (Yes vs No)			0.87	0.71	1.06	0.10		Concomitant beta blocker usage (Yes vs No)			0.91	0.56	1.47	0.24
				Concomitant loop diuretic agent usage (Yes vs No)			1.00	0.84	1.19	0.09		Concomitant loop diuretic agent usage (Yes vs No)			0.79	0.49	1.27	0.24
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.99	0.83	1.17	0.09		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.12	0.74	1.69	0.21
Worsening Heart Failure episodes	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	1285, 40.42%	1062, 33.41%					880, 50.96 %	N (% non-missing)	396, 45%	188, 21.36%				
				Mean	0.7	0.7						Mean	0.6	0.3				
				Std. Dev	1.28	1.3						Std. Dev	0.94	0.89				
				Range	(0, 26)	(0, 15)						Range	(0, 12)	(0, 14)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.94	0.85	1.02	0.05		Period (Post-index vs pre-index)			0.58	0.48	0.68	0.09
				Concomitant beta blocker usage (Yes vs No)			0.92	0.70	1.20	0.14		Concomitant beta blocker usage (Yes vs No)			0.52	0.28	0.95	0.31
				Concomitant loop diuretic agent usage (Yes vs No)			0.73	0.57	0.93	0.12		Concomitant loop diuretic agent usage (Yes vs No)			0.96	0.58	1.61	0.26

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	1481, 34.25%	1212, 28.03%					847, 49.04 %	N (% non-missing)	309, 36.48%	154, 18.18%				
				Mean	0.6	0.5						Mean	0.5	0.3				
				Std. Dev	1.08	1.11						Std. Dev	0.75	0.65				
				Range	(0, 13)	(0, 15)						Range	(0, 5)	(0, 6)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.89	0.82	0.97	0.04		Period (Post-index vs pre-index)			0.53	0.44	0.65	0.10
				Concomitant beta blocker usage (Yes vs No)			0.74	0.57	0.95	0.13		Concomitant beta blocker usage (Yes vs No)			1.60	0.94	2.72	0.27
				Concomitant loop diuretic agent usage (Yes vs No)			1.30	1.06	1.60	0.11		Concomitant loop diuretic agent usage (Yes vs No)			0.50	0.25	0.98	0.35
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
Worsening Heart Failure episodes	Concomitant use of Sodium-glucose co-transporter-2 (SGLT-2) inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237, 31.6 %	N (% non-missing)	80, 33.76%	72, 30.38%					111, 6.43 %	N (% non-missing)	43, 38.74%	24, 21.62%				
				Mean	0.5	0.5						Mean	0.5	0.3				
				Std. Dev	0.94	1.06						Std. Dev	0.67	0.77				
				Range	(0, 6)	(0, 6)						Range	(0, 3)	(0, 4)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				

				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
				N (% non-missing)	2686, 36.97%	2202, 30.31%						N (% non-missing)	662, 40.97%	318, 19.68%				
				Mean	0.6	0.6						Mean	0.6	0.3				
				Std. Dev	1.18	1.2						Std. Dev	0.87	0.79				
				Range	(0, 26)	(0, 15)						Range	(0, 12)	(0, 14)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						

				Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			0.98	0.83	1.15	0.08		Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			1.01	0.70	1.46	0.19
Worsening Heart Failure episodes	Age category	<65	1029, 13.71 %	N (% non- missing)	400, 38.87%	375, 36.44%					1352, 78.29 %	N (% non- missing)	566, 41.86%	242, 17.9%				
				Mean	0.8	0.7						Mean	0.6	0.3				
				Std. Dev	1.36	1.43						Std. Dev	0.88	0.8				
				Range	(0, 11)	(0, 15)						Range	(0, 12)	(0, 14)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
			Period (Post- index vs pre- index)			1.00	0.85	1.17	0.08	Period (Post- index vs pre- index)				0.52	0.45	0.60	0.08	
			Concomitant beta blocker usage (Yes vs No)			0.88	0.52	1.52	0.28	Concomitant beta blocker usage (Yes vs No)				0.88	0.55	1.40	0.24	
			Concomitant loop diuretic agent usage (Yes vs No)			0.92	0.56	1.51	0.25	Concomitant loop diuretic agent usage (Yes vs No)				0.81	0.51	1.31	0.24	
			Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)			0.92	0.60	1.42	0.22	Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)				0.97	0.64	1.47	0.21	
		65-74	2970, 39.58 %	N (% non- missing)	1089, 36.67%	822, 27.68%					226, 13.09 %	N (% non- missing)	81, 35.84%	50, 22.12%				
				Mean	0.6	0.5						Mean	0.5	0.3				
				Std. Dev	1.22	1.21						Std. Dev	0.84	0.79				
				Range	(0, 26)	(0, 12)						Range	(0, 6)	(0, 7)				
				Median	0	0						Median	0	0				
25th percentile	0			0	25th percentile	0						0						

				75th percentile	1	1						75th percentile	1	0				
				Interquartile range	1	1						Interquartile range	1	0				
				Period (Post-index vs pre-index)			0.90	0.81	0.99	0.05		Period (Post-index vs pre-index)			0.66	0.46	0.95	0.19
				Concomitant beta blocker usage (Yes vs No)			0.75	0.55	1.03	0.16		Concomitant beta blocker usage (Yes vs No)			1.17	0.39	3.49	0.56
				Concomitant loop diuretic agent usage (Yes vs No)			0.86	0.65	1.13	0.14		Concomitant loop diuretic agent usage (Yes vs No)			0.39	0.08	1.87	0.80
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.98	0.76	1.27	0.13		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.74	0.23	2.37	0.59
		75-84	2705, 36.05 %	N (% non-missing)	969, 35.82%	826, 30.54%					120, 6.95 %	N (% non-missing)	46, 38.33%	41, 34.17%				
				Mean	0.6	0.5						Mean	0.5	0.4				
				Std. Dev	1.07	1.13						Std. Dev	0.66	0.61				
				Range	(0, 10)	(0, 15)						Range	(0, 2)	(0, 2)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	1				
				Interquartile range	1	1						Interquartile range	1	1				
				Period (Post-index vs pre-index)			0.89	0.80	0.98	0.05		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			0.83	0.62	1.12	0.15		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.22	0.95	1.56	0.13		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.08	0.84	1.38	0.13		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
		≥85	799, 10.65 %	N (% non-missing)	308, 38.55%	251, 31.41%					29, 1.68 %	N (% non-missing)	12, 41.38%	9, 31.03%				
				Mean	0.6	0.5						Mean	0.6	0.3				
				Std. Dev	1.05	1.01						Std. Dev	0.74	0.55				
				Range	(0, 12)	(0, 9)						Range	(0, 2)	(0, 2)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	1	1						75th percentile	1	1				
				Interquartile range	1	1						Interquartile range	1	1				
				Period (Post-index vs pre-index)			0.90	0.75	1.08	0.09		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.03	0.65	1.64	0.24		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.16	0.79	1.71	0.20		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.69	0.42	1.13	0.25		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA

Table 10-4-1e Results for Costs of HF-Specific Hospitalizations - HFrEF Cohort

			Medicare Advantage								Commercially insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error

Heart Failure-specific hospitalization costs	Overall cohort		7503, 100%	N (% non-missing)	2428, 32.36%	1921, 25.6%					1727, 100%	N (% non-missing)	627, 36.31%	236, 13.67%				
				Mean	11949.785	9436.608						Mean	15957.376	6457.293				
				Std. Dev	29413.3468	26507.9971						Std. Dev	35566.244	26301.4312				
				Range	(0, 235294)	(0, 285429)						Range	(0, 227973)	(0, 288386)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	11134.25	1224.5						75th percentile	18331.75	0				
				Interquartile range	11134.25	1224.5						Interquartile range	18331.75	0				
				Period (Post-index vs pre-index)			0.79	0.79	0.79	0.00		Period (Post-index vs pre-index)			0.41	0.40	0.41	0.01
				Concomitant beta blocker usage (Yes vs No)			0.68	0.67	0.69	0.00		Concomitant beta blocker usage (Yes vs No)			0.85	0.80	0.91	0.03
				Concomitant loop diuretic agent usage (Yes vs No)			0.86	0.86	0.87	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.45	0.43	0.48	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.86	0.85	0.87	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.66	0.61	0.70	0.03
Heart Failure-specific hospitalization costs	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non-missing)	310, 31.38%	306, 30.97%					151, 8.74 %	N (% non-missing)	63, 41.72%	34, 22.52%				
				Mean	11793.02	12911.429						Mean	17710.716	11281.054				
				Std. Dev	30134.4391	33074.2248						Std. Dev	32977.6438	36684.4803				
				Range	(0, 233861)	(0, 262486)						Range	(0, 189185)	(0, 288386)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	9312.25	9460.25						75th percentile	20868	0				
				Interquartile range	9312.25	9460.25						Interquartile range	20868	0				
				Period (Post-index vs pre-index)			1.10	1.09	1.11	0.00		Period (Post-index vs pre-index)			0.65	0.56	0.75	0.07

				Concomitant beta blocker usage (Yes vs No)			1.20	1.18	1.22	0.01		Concomitant beta blocker usage (Yes vs No)			1.86	1.55	2.23	0.09
				Concomitant loop diuretic agent usage (Yes vs No)			1.07	1.05	1.09	0.01		Concomitant loop diuretic agent usage (Yes vs No)			1.13	0.85	1.50	0.14
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.76	0.75	0.78	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.04	0.03	0.05	0.12
	PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non-missing)	395, 33.82%	333, 28.51%						249, 14.42 %	N (% non-missing)	107, 42.97%	43, 17.27%				
			Mean	11455.334	12039.537							Mean	16984.776	7988.577				
			Std. Dev	27837.0726	31712.8725							Std. Dev	32646.3002	27618.3076				
			Range	(0, 230519)	(0, 285429)							Range	(0, 196751)	(0, 260098)				
			Median	0	0							Median	0	0				
			25th percentile	0	0							25th percentile	0	0				
			75th percentile	11415	4859							75th percentile	21093.75	0				
			Interquartile range	11415	4859							Interquartile range	21093.75	0				
			Period (Post-index vs pre-index)				1.05	1.04	1.06	0.00		Period (Post-index vs pre-index)			0.48	0.45	0.51	0.03
			Concomitant beta blocker usage (Yes vs No)				0.98	0.96	1.00	0.01		Concomitant beta blocker usage (Yes vs No)			1.36	1.12	1.66	0.10
			Concomitant loop diuretic agent usage (Yes vs No)				0.95	0.93	0.97	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.27	0.23	0.33	0.09
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.61	0.60	0.61	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.71	0.60	0.85	0.09
	PDC ≥ 80%	4721, 62.92 %	N (% non-missing)	1511, 32.01%	1054, 22.33%						1249, 72.32 %	N (% non-missing)	435, 34.83%	137, 10.97%				
			Mean	11850.148	7389.915							Mean	15982.182	5041.767				
			Std. Dev	29178.5531	22315.6888							Std. Dev	37142.7872	23559.5898				

				Range	(0, 235294)	(0, 274442)						Range	(0, 227973)	(0, 264017)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	10558	0						75th percentile	17839	0				
				Interquartile range	10558	0						Interquartile range	17839	0				
				Period (Post-index vs pre-index)			0.6 2	0.62	0.63	0.00		Period (Post-index vs pre-index)			0.3 2	0.31	0.33	0.01
				Concomitant beta blocker usage (Yes vs No)			0.5 6	0.55	0.57	0.01		Concomitant beta blocker usage (Yes vs No)			0.7 0	0.64	0.77	0.05
				Concomitant loop diuretic agent usage (Yes vs No)			0.7 7	0.75	0.79	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.3 2	0.29	0.35	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.9 7	0.95	0.99	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.7 1	0.65	0.78	0.05
Heart Failure-specific hospitalization costs	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5 %	N (% non-missing)	1435, 36.43%	1116, 28.33%					702, 40.65 %	N (% non-missing)	279, 39.74%	114, 16.24%				
				Mean	13903.057	10643.854						Mean	17730.932	8176.445				
				Std. Dev	31225.6906	28088.3165						Std. Dev	37211.9844	28787.4618				
				Range	(0, 233861)	(0, 285429)						Range	(0, 220232)	(0, 260098)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	15760	4150						75th percentile	19776.25	0				
				Interquartile range	15760	4150						Interquartile range	19776.25	0				
				Period (Post-index vs pre-index)			0.7 7	0.76	0.77	0.00		Period (Post-index vs pre-index)			0.4 7	0.46	0.48	0.01
				Concomitant beta blocker usage (Yes vs No)			0.8 2	0.81	0.84	0.01		Concomitant beta blocker usage (Yes vs No)			1.3 2	1.19	1.46	0.05
				Concomitant loop diuretic			0.7 8	0.77	0.79	0.01		Concomitant loop diuretic			0.7 1	0.65	0.78	0.05

				agent usage (Yes vs No)							agent usage (Yes vs No)											
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)											
								0.94	0.92	0.95	0.01						0.77	0.70	0.84	0.05		
No diagnosis of T2DM in pre-index period		No diagnosis of T2DM in pre-index period	3564, 47.5 %	N (% non-missing)	993, 27.86%	805, 22.59%					1025, 59.35 %	N (% non-missing)	348, 33.95%	122, 11.9%								
				Mean	9798.603	8107.041						Mean	14754.139	5290.966								
				Std. Dev	27120.4619	24586.048						Std. Dev	34371.3994	24417.3229								
				Range	(0, 235294)	(0, 239297)						Range	(0, 227973)	(0, 288386)								
				Median	0	0						Median	0	0								
				25th percentile	0	0						25th percentile	0	0								
				75th percentile	2823	0						75th percentile	17238.75	0								
				Interquartile range	2823	0						Interquartile range	17238.75	0								
			Period (Post-index vs pre-index)			0.83	0.82	0.83	0.00	Period (Post-index vs pre-index)				0.36	0.35	0.37	0.01					
			Concomitant beta blocker usage (Yes vs No)			0.58	0.57	0.59	0.01	Concomitant beta blocker usage (Yes vs No)				0.69	0.63	0.75	0.05					
			Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.98	1.00	0.01	Concomitant loop diuretic agent usage (Yes vs No)				0.31	0.28	0.33	0.04					
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.76	0.75	0.77	0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.61	0.56	0.67	0.05					
			Heart Failure-specific hospitalization costs	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	1253, 43.28%	895, 30.92%					343, 19.86 %	N (% non-missing)	169, 49.27%	72, 20.99%					
							Mean	17182.084	11463.986						Mean	22249.777	7988.726					
Std. Dev	34567.972	28377.7475					Std. Dev	40633.5947	26640.1608													
Range	(0, 235294)	(0, 262486)					Range	(0, 216859)	(0, 251137)													
Median	0	0					Median	1449	0													
25th percentile	0	0					25th percentile	0	0													

				75th percentile	19104.5	8827						75th percentile	28137.75	0																									
				Interquartile range	19104.5	8827						Interquartile range	28137.75	0																									
				Period (Post-index vs pre-index)																	Period (Post-index vs pre-index)					0.36	0.35	0.37	0.02										
				Concomitant beta blocker usage (Yes vs No)																	0.67					0.54	0.83	0.11											
				Concomitant loop diuretic agent usage (Yes vs No)																	0.07					0.06	0.09	0.09											
				Concomitant Mineralocorti coid Receptor Antagonist usage (Yes vs No)																	0.28					0.23	0.34	0.10											
		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1175, 25.5%	1026, 22.27%														1384, 80.14 %	N (% non-missing)	458, 33.09%	164, 11.85%																
				Mean	8680.595	8169.883															Mean	14420.859	6083.338																
				Std. Dev	25129.6472	25190.1172															Std. Dev	34055.3086	26214.2372																
				Range	(0, 220631)	(0, 285429)															Range	(0, 227973)	(0, 288386)																
				Median	0	0															Median	0	0																
				25th percentile	0	0															25th percentile	0	0																
				75th percentile	894	0															75th percentile	16601.5	0																
				Interquartile range	894	0															Interquartile range	16601.5	0																
				Period (Post-index vs pre-index)																											Period (Post-index vs pre-index)					0.42	0.42	0.43	0.01
				Concomitant beta blocker usage (Yes vs No)																											0.94					0.88	1.01	0.03	
				Concomitant loop diuretic agent usage (Yes vs No)																											0.93					0.92	0.93	0.00	
				Concomitant Mineralocorti coid Receptor Antagonist																											0.91					0.90	0.91	0.00	

				usage (Yes vs No)							usage (Yes vs No)																	
Heart Failure-specific hospitalization costs	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	359, 28.42%	276, 21.85%					505, 29.24 %	N (% non-missing)	186, 36.83%	47, 9.31%														
				Mean	10092.258	6907.405						Mean	16264.293	3893.735														
				Std. Dev	28129.0289	20561.6095						Std. Dev	36079.3669	19277.6608														
				Range	(0, 219609)	(0, 200488)						Range	(0, 200648)	(0, 216493)														
				Median	0	0						Median	0	0														
				25th percentile	0	0						25th percentile	0	0														
				75th percentile	3263.5	0						75th percentile	18010	0														
				Interquartile range	3263.5	0						Interquartile range	18010	0														
				Period (Post-index vs pre-index)								0.69	0.68	0.69					0.01	Period (Post-index vs pre-index)					0.24	0.23	0.25	0.03
				Concomitant beta blocker usage (Yes vs No)								0.24	0.23	0.25					0.02	Concomitant beta blocker usage (Yes vs No)					0.62	0.53	0.73	0.08
				Concomitant loop diuretic agent usage (Yes vs No)								0.60	0.57	0.62					0.02	Concomitant loop diuretic agent usage (Yes vs No)					0.79	0.67	0.93	0.08
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.73	0.70	0.76					0.02	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)					0.18	0.16	0.21	0.08
		Other	6240, 83.17 %	N (% non-missing)	2069, 33.16%	1645, 26.36%					1222, 70.76 %	N (% non-missing)	441, 36.09%	189, 15.47%														
				Mean	12326.198	9949.13						Mean	15830.401	7517.856														
				Std. Dev	29654.8413	27530.1688						Std. Dev	35366.0384	28649.2277														
				Range	(0, 235294)	(0, 285429)						Range	(0, 227973)	(0, 288386)														
				Median	0	0						Median	0	0														
				25th percentile	0	0						25th percentile	0	0														
				75th percentile	12200.75	1755.25						75th percentile	18548	0														
				Interquartile range	12200.75	1755.25						Interquartile range	18548	0														

[illegible]

		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	1305, 30.18%	1035, 23.94%					847, 49.04 %	N (% non-missing)	284, 33.53%	118, 13.93%												
				Mean	10397.458	8520.392						Mean	15047.919	6488.367												
				Std. Dev	26727.9347	24689.3967						Std. Dev	34465.5197	27363.0992												
				Range	(0, 230519)	(0, 274442)						Range	(0, 227973)	(0, 288386)												
				Median	0	0						Median	0	0												
				25th percentile	0	0						25th percentile	0	0												
				75th percentile	7858.25	0						75th percentile	17078.75	0												
				Interquartile range	7858.25	0						Interquartile range	17078.75	0												
				Period (Post-index vs pre-index)								0.82	0.82	0.82					0.00	Period (Post-index vs pre-index)			0.43	0.42	0.45	0.02
				Concomitant beta blocker usage (Yes vs No)								0.57	0.57	0.58					0.01	Concomitant beta blocker usage (Yes vs No)			1.31	1.18	1.44	0.05
				Concomitant loop diuretic agent usage (Yes vs No)								0.92	0.91	0.94					0.01	Concomitant loop diuretic agent usage (Yes vs No)			0.45	0.41	0.50	0.05
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
Heart Failure-specific hospitalization costs	Concomitant use of Sodium-glucose transporter-2 inhibitor (SGLT-2)	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237, 3.16 %	N (% non-missing)	72, 30.38%	60, 25.32%					111, 6.43 %	N (% non-missing)	38, 34.23%	14, 12.61%												
				Mean	12473.722	9299.211						Mean	12613.809	8035.564												
				Std. Dev	31285.6951	25726.9128						Std. Dev	24578.2016	34638.1908												
				Range	(0, 193339)	(0, 184539)						Range	(0, 147389)	(0, 260098)												
				Median	0	0						Median	0	0												
				25th percentile	0	0						25th percentile	0	0												
				75th percentile	10005	479						75th percentile	19182.5	0												
				Interquartile range	10005	479						Interquartile range	19182.5	0												
				Period (Post-index vs pre-index)								0.81	0.77	0.85					0.03	Period (Post-index vs pre-index)			NA	NA	NA	NA

				Concomitant beta blocker usage (Yes vs No)			0.08	0.07	0.09	0.06		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.12	1.00	1.25	0.06		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.22	0.20	0.24	0.04		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
		No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	N (% non-missing)	2356, 32.42%	1861, 25.61%					1616, 93.57 %	N (% non-missing)	589, 36.45%	222, 13.74%				
				Mean	11932.608	9441.113						Mean	16186.959	6348.922				
				Std. Dev	29352.0802	26534.9324						Std. Dev	36192.8252	25640.3184				
				Range	(0, 235294)	(0, 285429)						Range	(0, 227973)	(0, 288386)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	11204	1227						75th percentile	18317.75	0				
				Interquartile range	11204	1227						Interquartile range	18317.75	0				
				Period (Post-index vs pre-index)			0.79	0.79	0.79	0.00		Period (Post-index vs pre-index)			0.39	0.39	0.40	0.01
				Concomitant beta blocker usage (Yes vs No)			0.70	0.70	0.71	0.00		Concomitant beta blocker usage (Yes vs No)			0.90	0.84	0.96	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			0.89	0.88	0.90	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.48	0.45	0.52	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.89	0.88	0.90	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.67	0.63	0.72	0.03
Heart Failure-specific hospitalization costs	Age category	<65	1029, 13.71 %	N (% non-missing)	337, 32.75%	317, 30.81%					1352, 78.29 %	N (% non-missing)	503, 37.2%	157, 11.61%				
				Mean	12444.764	12122.933						Mean	17028.729	6202.85				
				Std. Dev	30164.2819	31839.534						Std. Dev	36280.1849	25594.4311				

				Range	(0, 233861)	(0, 262486)						Range	(0, 227973)	(0, 288386)											
				Median	0	0						Median	0	0											
				25th percentile	0	0						25th percentile	0	0											
				75th percentile	12193.25	9845						75th percentile	19534.75	0											
				Interquartile range	12193.25	9845						Interquartile range	19534.75	0											
				Period (Post-index vs pre-index)			0.97	0.97	0.98	0.00		Period (Post-index vs pre-index)			0.36	0.36	0.37	0.01							
				Concomitant beta blocker usage (Yes vs No)			0.45	0.44	0.46	0.01		Concomitant beta blocker usage (Yes vs No)			0.68	0.64	0.74	0.04							
				Concomitant loop diuretic agent usage (Yes vs No)			0.98	0.96	1.01	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.43	0.40	0.47	0.04							
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.73	0.71	0.74	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.45	0.42	0.49	0.04							
65-74	2970, 39.58 %	N (% non-missing)	959, 32.29%	695, 23.4%						226, 13.09 %	N (% non-missing)	72, 31.86%	39, 17.26%												
		Mean	12500.391	8917.118							Mean	16480.204	7187.867												
		Std. Dev	30639.9978	25826.7629							Std. Dev	39893.7791	25998.6097												
		Range	(0, 230519)	(0, 285429)							Range	(0, 220232)	(0, 181028)												
		Median	0	0							Median	0	0												
		25th percentile	0	0							25th percentile	0	0												
		75th percentile	11887	0							75th percentile	17268	0												
		Interquartile range	11887	0							Interquartile range	17268	0												
		Period (Post-index vs pre-index)									0.71	0.71	0.72					0.00	Period (Post-index vs pre-index)			0.43	0.40	0.47	0.04
		Concomitant beta blocker usage (Yes vs No)									0.43	0.42	0.43					0.01	Concomitant beta blocker usage (Yes vs No)			1.49	1.18	1.88	0.12
		Concomitant loop diuretic									0.54	0.53	0.55					0.01	Concomitant loop diuretic			0.05	0.04	0.06	0.12

			agent usage (Yes vs No)								agent usage (Yes vs No)						
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.74	0.72	0.75	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.83	0.67	1.05	0.12
	75-84	2705, 36.05 %	N (% non-missing)	856, 31.65%	693, 25.62%						120, 6.95 %	N (% non-missing)	41, 34.17%	32, 26.67%			
			Mean	11957.222	9498.542							Mean	5758.475	7693.275			
			Std. Dev	29822.1095	26495.1225							Std. Dev	14769.0502	33373.7998			
			Range	(0, 235294)	(0, 256836)							Range	(0, 97664)	(0, 251556)			
			Median	0	0							Median	0	0			
			25th percentile	0	0							25th percentile	0	0			
			75th percentile	9813	1282							75th percentile	3402.75	2087.75			
			Interquartile range	9813	1282							Interquartile range	3402.75	2087.75			
			Period (Post-index vs pre-index)			0.79	0.79	0.80	0.00		Period (Post-index vs pre-index)				NA	NA	NA
			Concomitant beta blocker usage (Yes vs No)			0.99	0.97	1.00	0.01		Concomitant beta blocker usage (Yes vs No)				NA	NA	NA
			Concomitant loop diuretic agent usage (Yes vs No)			1.11	1.10	1.13	0.01		Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.98	0.96	1.00	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				NA	NA	NA
	≥85	799, 10.65 %	N (% non-missing)	276, 34.54%	216, 27.03%						29, 1.68 %	N (% non-missing)	11, 37.93%	8, 27.59%			
			Mean	9254.753	7700.102							Mean	4673.241	7414.103			
			Std. Dev	21164.7519	20661.6199							Std. Dev	12372.3064	28913.3021			
			Range	(0, 144287)	(0, 180129)							Range	(0, 61976)	(0, 154619)			
			Median	0	0							Median	0	0			
			25th percentile	0	0							25th percentile	0	0			

				75th percentile	10214.25	1459.5						75th percentile	3895	1841				
				Interquartile range	10214.25	1459.5						Interquartile range	3895	1841				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
							0.83	0.82	0.84	0.00					NA	NA	NA	NA
							1.08	1.05	1.11	0.02					NA	NA	NA	NA
							1.26	1.23	1.29	0.01					NA	NA	NA	NA
							1.05	1.02	1.08	0.02					NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for Costs of HF-Related Hospitalizations – HFrEF Cohort

			Medicare Advantage								Commercially insured							
Characteristic	Variable	Subgroup	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
					N	N							N	N				
Heart Failure-related hospitalization costs	Overall cohort		7503, 100%	N (% non-missing)	2760, 36.79%	2124, 28.31%					1727, 100%	N (% non-missing)	728, 42.15%	266, 15.4%				
				Mean	15097.121	11927.504						Mean	20637.841	8114.4				
				Std. Dev	33876.5578	32128.4425						Std. Dev	41387.9301	31469.8204				
				Range	(0, 259020)	(0, 334113)						Range	(0, 258730)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	16502.5	4518						75th percentile	21120	0				
				Interquartile range	16502.5	4518						Interquartile range	21120	0				

				Period (Post-index vs pre-index)			0.79	0.79	0.79	0.00		Period (Post-index vs pre-index)				0.39	0.39	0.40	0.00							
				Concomitant beta blocker usage (Yes vs No)			0.66	0.65	0.67	0.00		Concomitant beta blocker usage (Yes vs No)				0.73	0.69	0.78	0.03							
				Concomitant loop diuretic agent usage (Yes vs No)			0.86	0.85	0.86	0.00		Concomitant loop diuretic agent usage (Yes vs No)				0.51	0.48	0.54	0.03							
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.85	0.84	0.86	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.58	0.55	0.62	0.03							
Heart Failure-related hospitalization costs	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non-missing)	353, 35.73%	327, 33.1%					151, 8.74 %	N (% non-missing)	70, 46.36%	39, 25.83%												
				Mean	14134.715	16603.491						Mean	20038.135	12889.703												
				Std. Dev	33090.1869	41031.815						Std. Dev	34872.3479	39206.9563												
				Range	(0, 240553)	(0, 326923)						Range	(0, 189185)	(0, 322392)												
				Median	0	0						Median	0	0												
				25th percentile	0	0						25th percentile	0	0												
				75th percentile	14950.5	13674.5						75th percentile	26211.75	2118												
				Interquartile range	14950.5	13674.5						Interquartile range	26211.75	2118												
				Period (Post-index vs pre-index)								1.18	1.17	1.18					0.00	Period (Post-index vs pre-index)			0.66	0.58	0.75	0.07
				Concomitant beta blocker usage (Yes vs No)								0.95	0.92	0.97					0.01	Concomitant beta blocker usage (Yes vs No)			1.67	1.40	1.98	0.09
				Concomitant loop diuretic agent usage (Yes vs No)								1.23	1.21	1.26					0.01	Concomitant loop diuretic agent usage (Yes vs No)			1.03	0.79	1.34	0.13
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.82	0.80	0.84					0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.03	0.03	0.04	0.11
		PDC ≥ 60% & < 80%		N (% non-missing)	450, 38.53%	367, 31.42%						N (% non-missing)	116, 46.59%	51, 20.48%												

			1168, 15.57 %	Mean	14740.951	15496.632					249, 14.42 %	Mean	20414.89	10244.343				
				Std. Dev	32397.4198	38151.4418						Std. Dev	36737.3247	30586.8174				
				Range	(0, 257613)	(0, 320115)						Range	(0, 196751)	(0, 260098)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	17144.5	11686.5						75th percentile	24628	0				
				Interquartile range	17144.5	11686.5						Interquartile range	24628	0				
				Period (Post-index vs pre-index)			1.0 5	1.05	1.06	0.00		Period (Post-index vs pre-index)			0.5 1	0.48	0.53	0.03
				Concomitant beta blocker usage (Yes vs No)			0.9 3	0.92	0.94	0.01		Concomitant beta blocker usage (Yes vs No)			1.0 9	0.91	1.31	0.09
				Concomitant loop diuretic agent usage (Yes vs No)			0.9 0	0.89	0.91	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.2 1	0.18	0.25	0.08
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.7 5	0.74	0.75	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.6 7	0.58	0.79	0.08
		PDC ≥ 80%	4721, 62.92 %	N (% non-missing)	1714, 36.31%	1172, 24.83%					1249, 72.32 %	N (% non-missing)	515, 41.23%	151, 12.09%				
				Mean	15123.914	9020.665						Mean	20946.074	6066.364				
				Std. Dev	34108.4607	25482.746						Std. Dev	43240.8117	27376.1187				
				Range	(0, 259020)	(0, 274442)						Range	(0, 258730)	(0, 301704)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	16394.5	0						75th percentile	20368	0				
				Interquartile range	16394.5	0						Interquartile range	20368	0				
				Period (Post-index vs pre-index)			0.6 0	0.59	0.60	0.00		Period (Post-index vs pre-index)			0.2 9	0.29	0.29	0.00
				Concomitant beta blocker			0.5 8	0.56	0.59	0.01		Concomitant beta blocker			0.4 5	0.41	0.49	0.05

				usage (Yes vs No)							usage (Yes vs No)															
				Concomitant loop diuretic agent usage (Yes vs No)							Concomitant loop diuretic agent usage (Yes vs No)							0.45	0.42	0.49	0.04					
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.59	0.53	0.64	0.05					
Heart Failure-related hospitalization costs	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5 %	N (% non-missing)	1614, 40.97%	1219, 30.95%					702, 40.65 %	N (% non-missing)	324, 46.15%	131, 18.66%												
				Mean	17415.844	13383.468						Mean	22507.275	11388.334												
				Std. Dev	36033.9024	33928.3904						Std. Dev	42612.768	38569.4597												
				Range	(0, 259020)	(0, 334113)						Range	(0, 250991)	(0, 322392)												
				Median	0	0						Median	0	0												
				25th percentile	0	0						25th percentile	0	0												
				75th percentile	18720	10933						75th percentile	23764	0												
				Interquartile range	18720	10933						Interquartile range	23764	0												
				Period (Post-index vs pre-index)								0.77	0.77	0.77					0.00	Period (Post-index vs pre-index)			0.51	0.50	0.52	0.01
				Concomitant beta blocker usage (Yes vs No)								0.82	0.81	0.84					0.01	Concomitant beta blocker usage (Yes vs No)			1.22	1.11	1.34	0.05
				Concomitant loop diuretic agent usage (Yes vs No)								0.78	0.77	0.79					0.01	Concomitant loop diuretic agent usage (Yes vs No)			0.51	0.47	0.55	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.87	0.86	0.89					0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.61	0.56	0.67	0.04
		No diagnosis of T2DM in pre-index period	3564, 47.5 %	N (% non-missing)	1146, 32.15%	905, 25.39%					1025, 59.35 %	N (% non-missing)	404, 39.41%	135, 13.17%												
				Mean	12545.937	10325.575						Mean	19368.314	5891.08												
				Std. Dev	31137.9412	29946.71						Std. Dev	40506.9936	25329.0645												
				Range	(0, 240553)	(0, 323876)						Range	(0, 258730)	(0, 301704)												

				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	11516	1104.5						75th percentile	20135	0				
				Interquartile range	11516	1104.5						Interquartile range	20135	0				
				Period (Post-index vs pre-index)			0.82	0.82	0.83	0.00		Period (Post-index vs pre-index)			0.30	0.30	0.31	0.00
				Concomitant beta blocker usage (Yes vs No)			0.54	0.54	0.55	0.01		Concomitant beta blocker usage (Yes vs No)			0.52	0.47	0.57	0.05
				Concomitant loop diuretic agent usage (Yes vs No)			0.97	0.96	0.99	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.50	0.45	0.54	0.05
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.80	0.79	0.81	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.56	0.50	0.61	0.05
Heart Failure-related hospitalizations on costs	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	1391, 48.05%	974, 33.64%					343, 19.86 %	N (% non-missing)	186, 54.23%	76, 22.16%				
				Mean	21323.729	14381.375					Mean	28733.806	10012.069					
				Std. Dev	39673.2474	34297.9128					Std. Dev	48472.7406	33504.6481					
				Range	(0, 259020)	(0, 326923)					Range	(0, 221242)	(0, 322392)					
				Median	0	0					Median	4148	0					
				25th percentile	0	0					25th percentile	0	0					
				75th percentile	24065	13830					75th percentile	32539.5	0					
				Interquartile range	24065	13830					Interquartile range	32539.5	0					
				Period (Post-index vs pre-index)			0.67	0.67	0.68	0.00	Period (Post-index vs pre-index)				0.35	0.34	0.36	0.02
				Concomitant beta blocker usage (Yes vs No)			0.63	0.61	0.65	0.02	Concomitant beta blocker usage (Yes vs No)				0.55	0.44	0.68	0.11
				Concomitant loop diuretic agent usage (Yes vs No)			0.87	0.85	0.90	0.01	Concomitant loop diuretic agent usage (Yes vs No)				0.06	0.05	0.07	0.10

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.84	0.82	0.87	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.22	0.18	0.26	0.10	
		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1369, 29.71%	1150, 24.96%						1384, 80.14 %	N (% non-missing)	542, 39.16%	190, 13.73%				
				Mean	11208.711	10395.104							Mean	18666.803	7652.395				
				Std. Dev	29022.7646	30600.1536							Std. Dev	39239.0445	30949.3686				
				Range	(0, 257613)	(0, 334113)							Range	(0, 258730)	(0, 319583)				
				Median	0	0							Median	0	0				
				25th percentile	0	0							25th percentile	0	0				
				75th percentile	8629	438							75th percentile	19948.75	0				
				Interquartile range	8629	438							Interquartile range	19948.75	0				
				Period (Post-index vs pre-index)			0.93	0.93	0.93	0.00			Period (Post-index vs pre-index)			0.41	0.41	0.42	0.00
				Concomitant beta blocker usage (Yes vs No)			0.74	0.73	0.74	0.00			Concomitant beta blocker usage (Yes vs No)			0.84	0.79	0.90	0.03
				Concomitant loop diuretic agent usage (Yes vs No)			0.90	0.90	0.91	0.00			Concomitant loop diuretic agent usage (Yes vs No)			0.64	0.60	0.69	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.88	0.87	0.88	0.00			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.70	0.65	0.75	0.03
Heart Failure-related hospitalization costs	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	419, 33.17%	307, 24.31%						505, 29.24 %	N (% non-missing)	207, 40.99%	56, 11.09%				
				Mean	12855.521	8711.61							Mean	19187.248	5263.822				
				Std. Dev	31223.8201	24532.4627							Std. Dev	38860.763	24815.6359				
				Range	(0, 219609)	(0, 203330)							Range	(0, 200648)	(0, 322392)				
				Median	0	0							Median	0	0				
				25th percentile	0	0							25th percentile	0	0				
				75th percentile	11810.25	0							75th percentile	19769	0				

				Interquartile range	11810.25	0					Interquartile range	19769	0																
				Period (Post-index vs pre-index)			0.68	0.67	0.68	0.00		Period (Post-index vs pre-index)				0.28	0.27	0.29	0.02										
				Concomitant beta blocker usage (Yes vs No)			0.40	0.38	0.41	0.02		Concomitant beta blocker usage (Yes vs No)				0.50	0.43	0.58	0.07										
				Concomitant loop diuretic agent usage (Yes vs No)			0.66	0.63	0.69	0.02		Concomitant loop diuretic agent usage (Yes vs No)				0.71	0.61	0.83	0.08										
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.65	0.63	0.68	0.02		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.23	0.20	0.26	0.07										
				Other	6240, 83.17 %	N (% non-missing)	2341, 37.52%	1817, 29.12%					1222, 70.76 %	N (% non-missing)	521, 42.64%	210, 17.18%													
						Mean	15551.079	12578.772						Mean	21238.459	9294.68													
						Std. Dev	34373.4402	33421.4087						Std. Dev	42391.2293	33783.1514													
						Range	(0, 259020)	(0, 334113)						Range	(0, 258730)	(0, 319583)													
						Median	0	0						Median	0	0													
						25th percentile	0	0						25th percentile	0	0													
						75th percentile	17192	6736.75						75th percentile	22042.75	0													
						Interquartile range	17192	6736.75						Interquartile range	22042.75	0													
						Period (Post-index vs pre-index)								0.81	0.81	0.81					0.00	Period (Post-index vs pre-index)				0.44	0.43	0.44	0.00
						Concomitant beta blocker usage (Yes vs No)								0.70	0.69	0.70					0.00	Concomitant beta blocker usage (Yes vs No)				0.73	0.68	0.79	0.04
						Concomitant loop diuretic agent usage (Yes vs No)								0.88	0.87	0.88					0.00	Concomitant loop diuretic agent usage (Yes vs No)				0.50	0.46	0.53	0.03
						Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.88	0.87	0.89					0.00	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.71	0.66	0.76	0.04

Heart Failure-related hospitalization costs	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	1257, 39.54%	966, 30.39%					880, 50.96 %	N (% non-missing)	395, 44.89%	138, 15.68%				
				Mean	17213.253	13835.047						Mean	21143.804	8942.31				
				Std. Dev	36391.1563	36272.7124						Std. Dev	41840.6288	34013.8195				
				Range	(0, 257613)	(0, 334113)						Range	(0, 258730)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	18520.5	10658						75th percentile	21635	0				
				Interquartile range	18520.5	10658						Interquartile range	21635	0				
				Period (Post-index vs pre-index)			0.80	0.80	0.81	0.00		Period (Post-index vs pre-index)			0.42	0.42	0.43	0.01
				Concomitant beta blocker usage (Yes vs No)			0.74	0.73	0.75	0.01		Concomitant beta blocker usage (Yes vs No)			0.33	0.31	0.36	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			0.78	0.77	0.79	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.47	0.44	0.50	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	1503, 34.76%	1158, 26.78%					847, 49.04 %	N (% non-missing)	333, 39.32%	128, 15.11%				
				Mean	13548.959	10531.947						Mean	20113.206	7255.936				
				Std. Dev	31826.9443	28644.2806						Std. Dev	40931.5465	28589.0705				
				Range	(0, 259020)	(0, 299610)						Range	(0, 227973)	(0, 264210)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	13601	2367						75th percentile	20602.5	0				
				Interquartile range	13601	2367						Interquartile range	20602.5	0				

				Period (Post-index vs pre-index)			0.78	0.77	0.78	0.00		Period (Post-index vs pre-index)			0.36	0.35	0.38	0.02	
				Concomitant beta blocker usage (Yes vs No)			0.58	0.57	0.59	0.01		Concomitant beta blocker usage (Yes vs No)			1.30	1.16	1.46	0.06	
				Concomitant loop diuretic agent usage (Yes vs No)			0.93	0.91	0.94	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.37	0.33	0.41	0.06	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							
Heart Failure-related hospitalization costs	Concomitant use of Sodium-glucose transporter-2 inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237,316 %	N (% non-missing)	87, 36.71%	66, 27.85%					111,643 %	N (% non-missing)	41, 36.94%	16, 14.41%					
				Mean	14675.602	10974.343						Mean	15312.364	9528.964					
				Std. Dev	32033.1709	27736.2116						Std. Dev	30865.755	37231.321					
				Range	(0, 193339)	(0, 184539)						Range	(0, 193014)	(0, 260098)					
				Median	0	0						Median	0	0					
				25th percentile	0	0						25th percentile	0	0					
				75th percentile	14679.25	2957						75th percentile	23273.5	0					
				Interquartile range	14679.25	2957						Interquartile range	23273.5	0					
				Period (Post-index vs pre-index)			0.75	0.71	0.78	0.02		Period (Post-index vs pre-index)				NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			0.16	0.14	0.18	0.06		Concomitant beta blocker usage (Yes vs No)				NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			0.14	0.12	0.15	0.04		Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.36	0.33	0.39	0.04		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				NA	NA	NA	NA
		No prescription fills for SGLT-2		N (% non-missing)	2673, 36.79%	2058, 28.32%							N (% non-missing)	687, 42.51%	250, 15.47%				

		inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	Mean	15110.895	11958.652					1616, 93.57 %	Mean	21003.739	8017.209				
				Std. Dev	33937.1198	32263.0779						Std. Dev	41996.9131	31046.0335				
				Range	(0, 259020)	(0, 334113)						Range	(0, 258730)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	16539.5	4552.25						75th percentile	21096	0				
				Interquartile range	16539.5	4552.25						Interquartile range	21096	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
Heart Failure-related hospitalization costs	Age category	<65	1029, 13.71 %	N (% non-missing)	385, 37.41%	340, 33.04%					1352, 78.29 %	N (% non-missing)	578, 42.75%	172, 12.72%				
				Mean	15516.311	15330.955						Mean	21892.951	7899.411				
				Std. Dev	34172.2267	41047.4583						Std. Dev	41956.5906	31552.3571				
				Range	(0, 238038)	(0, 329438)						Range	(0, 258730)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	15909	11614.25						75th percentile	23296.5	0				
				Interquartile range	15909	11614.25						Interquartile range	23296.5	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker								Concomitant beta blocker						

				usage (Yes vs No)							usage (Yes vs No)																		
				Concomitant loop diuretic agent usage (Yes vs No)																0.93	0.91	0.96	0.01	Concomitant loop diuretic agent usage (Yes vs No)		0.49	0.46	0.53	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																0.73	0.71	0.74	0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)		0.39	0.36	0.42	0.04
		65-74	2970, 39.58 %	N (% non-missing)	1089, 36.67%	785, 26.43%					226, 13.09 %	N (% non-missing)	86, 38.05%	47, 20.8%															
				Mean	15758.69	11832.439						Mean	21499.637	8703.633															
				Std. Dev	35196.7535	32457.5194						Std. Dev	46780.5685	28534.2835															
				Range	(0, 259020)	(0, 334113)						Range	(0, 250991)	(0, 221532)															
				Median	0	0						Median	0	0															
				25th percentile	0	0						25th percentile	0	0															
				75th percentile	17367.75	2156.5						75th percentile	20085.75	0															
				Interquartile range	17367.75	2156.5						Interquartile range	20085.75	0															
			Period (Post-index vs pre-index)			0.75	0.75	0.75	0.00	Period (Post-index vs pre-index)				0.40	0.37	0.43	0.04												
			Concomitant beta blocker usage (Yes vs No)							0.47								0.47	0.48	0.01	Concomitant beta blocker usage (Yes vs No)	1.18	0.93	1.50	0.12				
			Concomitant loop diuretic agent usage (Yes vs No)							0.62								0.61	0.63	0.01	Concomitant loop diuretic agent usage (Yes vs No)	0.04	0.03	0.05	0.12				
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.79								0.78	0.81	0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)	0.89	0.71	1.11	0.11				
		75-84	2705, 36.05 %	N (% non-missing)	973, 35.97%	754, 27.87%					120, 6.95 %	N (% non-missing)	51, 42.5%	37, 30.83%															
				Mean	15223.962	11480.854						Mean	8642.525	9505.292															
Std. Dev	34256.1473			29901.7366	Std. Dev	21721.5546						36384.5063																	
Range	(0, 240553)			(0, 320003)	Range	(0, 155839)						(0, 251556)																	

				Median	0	0					Median	0	0															
				25th percentile	0	0					25th percentile	0	0															
				75th percentile	16209.25	4255.5					75th percentile	7399.25	2899.5															
				Interquartile range	16209.25	4255.5					Interquartile range	7399.25	2899.5															
				Period (Post-index vs pre-index)							0.75	0.75	0.76					0.00	Period (Post-index vs pre-index)			NA	NA	NA	NA			
				Concomitant beta blocker usage (Yes vs No)							0.90	0.89	0.92					0.01	Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA			
				Concomitant loop diuretic agent usage (Yes vs No)							1.03	1.01	1.05					0.01	Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA			
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.93	0.91	0.94					0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA			
				≥85	799, 10.65 %	N (% non-missing)					313, 39.17%	245, 30.66%									29, 1.68 %	N (% non-missing)	13, 44.83%	10, 34.48%				
				Mean	11690.039	9426.397					Mean	5735.966									7671.345							
				Std. Dev	26236.7278	23791.4755					Std. Dev	12771.7629									28863.3543							
				Range	(0, 242462)	(0, 227257)					Range	(0, 61976)									(0, 154619)							
				Median	0	0					Median	0									0							
				25th percentile	0	0					25th percentile	0									0							
				75th percentile	12959.5	5363.75					75th percentile	5050									2332							
				Interquartile range	12959.5	5363.75					Interquartile range	5050									2332							
													0.81					0.80	0.81	0.00	Period (Post-index vs pre-index)				NA	NA	NA	NA
													0.99					0.95	1.02	0.02	Concomitant beta blocker usage (Yes vs No)				NA	NA	NA	NA
													1.20					1.17	1.23	0.01	Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA	NA

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.93	0.90	0.96	0.02		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
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*NA: Not applicable. Statistics not calculated due to small sample size.

Results for Costs of All-Cause Hospitalizations – HFrEF Cohort

			Medicare Advantage								Commercially insured							
Characteristic	Variable	Subgroup	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
					N	N							N	N				
All-cause hospitalizations costs	Overall cohort		7503, 100%	N (% non-missing)	3360, 44.78%	2463, 32.83%					1727, 100%	N (% non-missing)	831, 48.12%	324, 18.76%				
				Mean	19466.66	13661.729						Mean	24378.637	9860.004				
				Std. Dev	37951.0983	33708.122						Std. Dev	44539.5791	34243.977				
				Range	(0, 259119)	(0, 331898)						Range	(0, 258730)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	20909	11780						75th percentile	28897	0				
				Interquartile range	20909	11780						Interquartile range	28897	0				
				Period (Post-index vs pre-index)			0.70	0.70	0.70	0.00		Period (Post-index vs pre-index)			0.40	0.40	0.41	0.00
				Concomitant beta blocker usage (Yes vs No)			0.71	0.70	0.72	0.01		Concomitant beta blocker usage (Yes vs No)			0.64	0.60	0.68	0.03
				Concomitant loop diuretic agent usage (Yes vs No)			0.84	0.82	0.85	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.43	0.41	0.46	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.80	0.79	0.81	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.55	0.52	0.59	0.03
All-cause hospitalizations costs	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17%	N (% non-missing)	422, 42.71%	379, 38.36%					151, 8.74%	N (% non-missing)	79, 52.32%	45, 29.8%				
				Mean	17760.364	18644.484						Mean	25214.453	14908.831				
				Std. Dev	36836.4948	42226.3587						Std. Dev	42620.9631	41770.1989				
				Range	(0, 259119)	(0, 326923)						Range	(0, 249923)	(0, 322392)				

			Median	0	0						Median	5300	0				
			25th percentile	0	0						25th percentile	0	0				
			75th percentile	18493.5	18084.5						75th percentile	30580.25	8954.75				
			Interquartile range	18493.5	18084.5						Interquartile range	30580.25	8954.75				
			Period (Post-index vs pre-index)			1.05	1.05	1.05	0.00		Period (Post-index vs pre-index)			0.59	0.54	0.64	0.04
			Concomitant beta blocker usage (Yes vs No)			0.93	0.92	0.94	0.01		Concomitant beta blocker usage (Yes vs No)			1.11	0.93	1.32	0.09
			Concomitant loop diuretic agent usage (Yes vs No)			1.13	1.11	1.14	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.66	0.53	0.83	0.11
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.86	0.88	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.07	0.06	0.09	0.08
			N (% non-missing)	547, 46.83%	432, 36.99%						N (% non-missing)	130, 52.21%	66, 26.51%				
			Mean	18476.091	17287.139						Mean	24453.717	14110.27				
			Std. Dev	35709.2255	39955.7947						Std. Dev	40693.2133	36758.5318				
			Range	(0, 257613)	(0, 320115)						Range	(0, 252114)	(0, 260098)				
			Median	0	0						Median	3091.5	0				
			25th percentile	0	0						25th percentile	0	0				
			75th percentile	22154	15686						75th percentile	33037.25	2146.75				
			Interquartile range	22154	15686						Interquartile range	33037.25	2146.75				
			Period (Post-index vs pre-index)			0.94	0.93	0.94	0.00		Period (Post-index vs pre-index)			0.60	0.56	0.65	0.04
			Concomitant beta blocker usage (Yes vs No)			0.95	0.93	0.96	0.01		Concomitant beta blocker usage (Yes vs No)			1.60	1.36	1.89	0.08
			Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.93	0.95	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.19	0.16	0.23	0.09
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.74	0.74	0.75	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.99	0.84	1.16	0.08
			N (% non-missing)	2104, 44.57%	1373, 29.08%						N (% non-missing)	591, 47.32%	185, 14.81%				
			Mean	19794.85	10718.732						Mean	24313.42	7334.754				

				Std. Dev	38292.908	27593.5026						Std. Dev	45478.1004	29669.9702				
				Range	(0, 259020)	(0, 278737)						Range	(0, 258730)	(0, 301704)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	21155	5488						75th percentile	25969	0				
				Interquartile range	21155	5488						Interquartile range	25969	0				
				Period (Post-index vs pre-index)			0.54	0.54	0.54	0.00		Period (Post-index vs pre-index)			0.30	0.30	0.30	0.00
				Concomitant beta blocker usage (Yes vs No)			0.65	0.63	0.67	0.02		Concomitant beta blocker usage (Yes vs No)			0.39	0.36	0.43	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			0.74	0.72	0.76	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.39	0.36	0.43	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.80	0.85	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.51	0.47	0.56	0.05
				N (% non-missing)	1924, 48.84%	1407, 35.72%						N (% non-missing)	369, 52.56%	156, 22.22%				
				Mean	21932.265	15338.392						Mean	26703.457	12875.564				
				Std. Dev	39708.0854	35635.5744						Std. Dev	46928.4596	40615.8894				
				Range	(0, 259020)	(0, 331898)						Range	(0, 252114)	(0, 322392)				
				Median	0	0						Median	3567.5	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	26867	15199.25						75th percentile	30570.5	0				
				Interquartile range	26867	15199.25						Interquartile range	30570.5	0				
				Period (Post-index vs pre-index)			0.70	0.70	0.70	0.00		Period (Post-index vs pre-index)			0.48	0.47	0.50	0.01
				Concomitant beta blocker usage (Yes vs No)			0.93	0.91	0.95	0.01		Concomitant beta blocker usage (Yes vs No)			1.00	0.91	1.10	0.05
				Concomitant loop diuretic agent usage (Yes vs No)			0.80	0.79	0.82	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.39	0.36	0.43	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.86	0.85	0.88	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.51	0.47	0.56	0.04
All-cause hospitalizations costs	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5%								702, 40.65%							

		No diagnosis of T2DM in pre-index period	3564, 47.5%	N (% non-missing)	1436, 40.29%	1056, 29.63%					1025, 59.35%	N (% non-missing)	462, 45.07%	168, 16.39%				
				Mean	16754.285	11817.257						Mean	22796.753	7808.118				
				Std. Dev	35728.6615	31353.214						Std. Dev	42789.3746	28965.1413				
				Range	(0, 259119)	(0, 323876)						Range	(0, 258730)	(0, 301704)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	17554.5	6712						75th percentile	27145	0				
				Interquartile range	17554.5	6712						Interquartile range	27145	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
All-cause hospitalizations costs	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2995, 38.58%	N (% non-missing)	1626, 56.17%	1122, 38.76%					343, 19.86%	N (% non-missing)	205, 59.77%	89, 25.95%				
				Mean	26414.516	16488.265						Mean	33418.493	12917.448				
				Std. Dev	43558.9443	36104.1637						Std. Dev	52540.6256	38891.8375				
				Range	(0, 259020)	(0, 326923)						Range	(0, 249923)	(0, 322392)				
				Median	6067.5	0						Median	12645	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	32760.75	17792.75						75th percentile	34868	1817.5				
				Interquartile range	32760.75	17792.75						Interquartile range	34868	1817.5				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist								Concomitant Mineralocorticoid Receptor Antagonist						

				usage (Yes vs No)								usage (Yes vs No)						
All-cause hospitalizations costs	Sacubitril/valsartan dosing regimen at last prescription	No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1734, 37.63%	1341, 29.1%					1384, 80.14 %	N (% non-missing)	626, 45.23%	235, 16.98%				
				Mean	15126.711	11896.146						Mean	22174.596	9114.557				
				Std. Dev	33258.3142	31998.4857						Std. Dev	42088.7879	32984.4806				
				Range	(0, 259119)	(0, 331898)						Range	(0, 258730)	(0, 319583)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	15653	5478						75th percentile	24575.25	0				
				Interquartile range	15653	5478						Interquartile range	24575.25	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
All-cause hospitalizations costs	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	525, 41.57%	349, 27.63%					505, 29.24 %	N (% non-missing)	235, 46.53%	66, 13.07%				
				Mean	17243.837	9635.997						Mean	23448.004	6357.928				
				Std. Dev	34856.6476	25300.5904						Std. Dev	43145.699	26947.4636				
				Range	(0, 231711)	(0, 203330)						Range	(0, 238478)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	18776.5	2643.25						75th percentile	27180	0				
				Interquartile range	18776.5	2643.25						Interquartile range	27180	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						

				Concomitant loop diuretic agent usage (Yes vs No)		0.6 3	0.60	0.67	0.03		Concomitant loop diuretic agent usage (Yes vs No)			0.4 8	0.41	0.55	0.08		
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)		0.5 8	0.55	0.61	0.03		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.1 9	0.16	0.21	0.07		
	Other	6240, 83.17 %	N (% non-missing)	2835, 45.43%	2114, 33.88%					1222, 70.76 %	N (% non-missing)	596, 48.77%	258, 21.11%						
			Mean	19916.606	14476.623						Mean	24764.603	11312.437						
			Std. Dev	38534.2977	35111.7728						Std. Dev	45116.9579	36761.061						
			Range	(0, 259119)	(0, 331898)						Range	(0, 258730)	(0, 319583)						
			Median	0	0						Median	0	0						
			25th percentile	0	0						25th percentile	0	0						
			75th percentile	21902.5	12644						75th percentile	29511.25	0						
			Interquartile range	21902.5	12644						Interquartile range	29511.25	0						
			Period (Post-index vs pre-index)			0.7 3	0.73	0.73	0.00		Period (Post-index vs pre-index)			0.4 6	0.45	0.46	0.00		
			Concomitant beta blocker usage (Yes vs No)			0.7 6	0.75	0.77	0.01		Concomitant beta blocker usage (Yes vs No)			0.6 5	0.60	0.69	0.03		
			Concomitant loop diuretic agent usage (Yes vs No)			0.8 6	0.84	0.87	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.4 3	0.40	0.45	0.03		
			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.8 4	0.83	0.85	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.6 9	0.64	0.73	0.03		
All-cause hospitalizations costs	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	1450, 45.61%	1070, 33.66%					880, 50.96 %	N (% non-missing)	450, 51.14%	159, 18.07%					
				Mean	21235.595	15283.271						Mean	25261.898	10488.224					
				Std. Dev	40183.4313	37561.8036						Std. Dev	45048.3374	36657.2261					
				Range	(0, 257613)	(0, 331898)						Range	(0, 258730)	(0, 322392)					
				Median	0	0						Median	2478	0					
				25th percentile	0	0						25th percentile	0	0					
				75th percentile	23878.5	13389						75th percentile	28710.5	0					
				Interquartile range	23878.5	13389						Interquartile range	28710.5	0					
				Period (Post-index vs pre-index)			0.7 2	0.72	0.72	0.00		Period (Post-index vs pre-index)			0.4 2	0.41	0.42	0.01	

				Concomitant beta blocker usage (Yes vs No)		0.69	0.68	0.71	0.01		Concomitant beta blocker usage (Yes vs No)			0.29	0.27	0.32	0.04
				Concomitant loop diuretic agent usage (Yes vs No)		0.73	0.72	0.75	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.41	0.38	0.44	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	1910, 44.17%	1393, 32.22%					N (% non-missing)	381, 44.98%	165, 19.48%				
				Mean	18172.647	12475.538					Mean	23460.593	9207.044				
				Std. Dev	36181.1245	30533.1677					Std. Dev	44012.6454	31549.4088				
				Range	(0, 259119)	(0, 313315)					Range	(0, 252114)	(0, 264210)				
				Median	0	0					Median	0	0				
				25th percentile	0	0					25th percentile	0	0				
				75th percentile	19463.25	10292.25					75th percentile	29032	0				
				Interquartile range	19463.25	10292.25					Interquartile range	29032	0				
				Period (Post-index vs pre-index)			0.69	0.69	0.00		Period (Post-index vs pre-index)			0.40	0.38	0.41	0.02
				Concomitant beta blocker usage (Yes vs No)			0.72	0.70	0.73	0.01	Concomitant beta blocker usage (Yes vs No)			1.19	1.07	1.33	0.06
				Concomitant loop diuretic agent usage (Yes vs No)			0.93	0.91	0.94	0.01	Concomitant loop diuretic agent usage (Yes vs No)			0.31	0.28	0.35	0.05
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
All-cause hospitalizations costs	Concomitant use of Sodium-glucose co-transporter-2 (SGLT-2) inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237, 3.16%	N (% non-missing)	109, 45.99%	76, 32.07%					N (% non-missing)	49, 44.14%	18, 16.22%				
				Mean	19562.373	12723.466					Mean	21237.991	10021.636				
				Std. Dev	35766.1591	30256.6667					Std. Dev	40733.8446	39633.8513				
				Range	(0, 202327)	(0, 184539)					Range	(0, 252114)	(0, 260098)				
				Median	0	0					Median	0	0				
				25th percentile	0	0					25th percentile	0	0				
				75th percentile	24163.5	10424.75					75th percentile	30407	0				
				Interquartile range	24163.5	10424.75					Interquartile range	30407	0				

				Period (Post-index vs pre-index)			0.65	0.62	0.68	0.02		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			0.69	0.60	0.79	0.07		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			0.29	0.26	0.32	0.05		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.25	0.23	0.28	0.04		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
				N (% non-missing)	3251, 44.74%	2387, 32.85%						N (% non-missing)	782, 48.39%	306, 18.94%				
				Mean	19463.528	13692.428						Mean	24594.691	9848.884				
				Std. Dev	38022.8035	33816.5497						Std. Dev	44793.1465	33855.8868				
				Range	(0, 259119)	(0, 331898)						Range	(0, 258730)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	20807	11803						75th percentile	28664	0				
				Interquartile range	20807	11803						Interquartile range	28664	0				
				Period (Post-index vs pre-index)			0.70	0.70	0.70	0.00		Period (Post-index vs pre-index)			0.40	0.40	0.40	0.00
				Concomitant beta blocker usage (Yes vs No)			0.71	0.70	0.72	0.01		Concomitant beta blocker usage (Yes vs No)			0.69	0.65	0.74	0.03
				Concomitant loop diuretic agent usage (Yes vs No)			0.85	0.84	0.87	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.46	0.43	0.49	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.81	0.83	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.58	0.54	0.62	0.03
				N (% non-missing)	454, 44.12%	389, 37.8%						N (% non-missing)	657, 48.59%	215, 15.9%				
				Mean	18831.638	17620.529						Mean	25985.037	9764.761				
				Std. Dev	37364.2381	43394.2231						Std. Dev	45427.3383	34348.1341				
				Range	(0, 259119)	(0, 331898)						Range	(0, 258730)	(0, 322392)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				

				75th percentile	20735.75	14892.75						75th percentile	30692.75	0				
				Interquartile range	20735.75	14892.75						Interquartile range	30692.75	0				
				Period (Post-index vs pre-index)			0.93	0.93	0.94	0.00		Period (Post-index vs pre-index)			0.38	0.37	0.38	0.00
				Concomitant beta blocker usage (Yes vs No)			0.60	0.58	0.61	0.01		Concomitant beta blocker usage (Yes vs No)			0.57	0.53	0.61	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			1.11	1.08	1.13	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.44	0.41	0.47	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.65	0.63	0.66	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.41	0.38	0.44	0.04
				N (% non-missing)	1296, 43.64%	885, 29.8%						N (% non-missing)	98, 43.36%	52, 23.01%				
				Mean	20097.456	13371.915						Mean	23694.712	9608.022				
				Std. Dev	39336.7063	33820.4375						Std. Dev	47558.4406	29743.6733				
				Range	(0, 259020)	(0, 326923)						Range	(0, 250991)	(0, 221532)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	22158.25	8802.75						75th percentile	25743.25	0				
				Interquartile range	22158.25	8802.75						Interquartile range	25743.25	0				
				Period (Post-index vs pre-index)			0.67	0.66	0.67	0.00		Period (Post-index vs pre-index)			0.40	0.38	0.43	0.03
				Concomitant beta blocker usage (Yes vs No)			0.55	0.53	0.56	0.01		Concomitant beta blocker usage (Yes vs No)			0.95	0.75	1.20	0.12
				Concomitant loop diuretic agent usage (Yes vs No)			0.63	0.62	0.65	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.04	0.03	0.05	0.11
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.80	0.78	0.82	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.81	0.65	1.01	0.11
				N (% non-missing)	1214, 44.88%	899, 33.23%						N (% non-missing)	58, 48.33%	45, 37.5%				
				Mean	20187.411	13195.884						Mean	12192.75	11840.333				
				Std. Dev	38716.744	31284.3061						Std. Dev	27983.8351	41739.2276				
				Range	(0, 256590)	(0, 320003)						Range	(0, 180578)	(0, 251556)				

				Median	0	0					Median	0	0				
				25th percentile	0	0					25th percentile	0	0				
				75th percentile	22013	12325.5					75th percentile	12445.5	3883.25				
				Interquartile range	22013	12325.5					Interquartile range	12445.5	3883.25				
				Period (Post-index vs pre-index)							Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)							Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)							Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
				N (% non-missing)	396, 49.56%	290, 36.3%					N (% non-missing)	18, 62.07%	12, 41.38%				
				Mean	15523.847	11240.258					Mean	6238.483	8010.414				
				Std. Dev	29830.9767	25737.4962					Std. Dev	12599.5547	28817.3244				
				Range	(0, 242462)	(0, 227257)					Range	(0, 61976)	(0, 154619)				
				Median	0	0					Median	2788	0				
				25th percentile	0	0					25th percentile	0	0				
				75th percentile	18469.5	12322.75					75th percentile	5099	3171				
				Interquartile range	18469.5	12322.75					Interquartile range	5099	3171				
				Period (Post-index vs pre-index)							Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)							Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)							Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for Costs of Worsening HF Episodes - HFrEF Cohort

			Medicare Advantage								Commercially insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
Worsening Heart Failure episodes costs	Overall cohort		7503, 100%	N (% non-missing)	2723, 36.29%	2243, 29.89%					1727, 100%	N (% non-missing)	691, 40.01%	328, 18.99%				
				Mean	12052.806	9523.816						Mean	16048.402	6330.033				
				Std. Dev	29129.1669	26073.7053						Std. Dev	35253.6592	24739.5041				
				Range	(0, 224629)	(0, 256836)						Range	(0, 221199)	(0, 260098)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	11508	2344.75						75th percentile	18503	0				
				Interquartile range	11508	2344.75						Interquartile range	18503	0				
				Period (Post-index vs pre-index)			0.79	0.79	0.79	0.00		Period (Post-index vs pre-index)			0.40	0.39	0.40	0.01
				Concomitant beta blocker usage (Yes vs No)			0.69	0.68	0.69	0.00		Concomitant beta blocker usage (Yes vs No)			0.85	0.80	0.91	0.03
				Concomitant loop diuretic agent usage (Yes vs No)			0.87	0.87	0.88	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.49	0.46	0.53	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.88	0.87	0.88	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.73	0.68	0.78	0.03
Worsening Heart Failure episodes costs	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17%	N (% non-missing)	345, 34.92%	344, 34.82%					151, 8.74%	N (% non-missing)	69, 45.7%	41, 27.15%				
				Mean	11685.912	12790.235						Mean	18193.789	9568.701				
				Std. Dev	29225.5171	32032.7448						Std. Dev	33210.161	28739.7885				
				Range	(0, 214662)	(0, 248234)						Range	(0, 190287)	(0, 164633)				
				Median	0	0						Median	0	0				

				25th percentile	0	0						25th percentile	0	0																						
				75th percentile	9346.75	9641.75						75th percentile	23457	1275.5																						
				Interquartile range	9346.75	9641.75						Interquartile range	23457	1275.5																						
				Period (Post-index vs pre-index)								1.1 0	1.09	1.10					0.00	Period (Post-index vs pre-index)			0.5 5	0.46	0.67	0.10										
				Concomitant beta blocker usage (Yes vs No)								1.1 6	1.14	1.18					0.01	Concomitant beta blocker usage (Yes vs No)			2.0 9	1.68	2.62	0.11										
				Concomitant loop diuretic agent usage (Yes vs No)								1.1 2	1.10	1.14					0.01	Concomitant loop diuretic agent usage (Yes vs No)			1.6 6	1.23	2.24	0.15										
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.7 7	0.76	0.78					0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.0 4	0.03	0.05	0.16										
				PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non-missing)						435, 37.24%	384, 32.88%									249, 14.42 %	N (% non-missing)	115, 46.18%	59, 23.69%											
				Mean		11432.984						12007.069	Mean										17416.037	8339.992												
				Std. Dev		27008.9637						30792.6992	Std. Dev										32665.8364	27757.7564												
				Range		(0, 215014)						(0, 256836)	Range										(0, 196751)	(0, 260098)												
				Median		0						0	Median										0	0												
				25th percentile		0						0	25th percentile										0	0												
				75th percentile		12261.5						5782.5	75th percentile										21872.25	0												
				Interquartile range		12261.5						5782.5	Interquartile range										21872.25	0												
				Period (Post-index vs pre-index)									1.0 5										1.04	1.06	0.00					Period (Post-index vs pre-index)			0.5 3	0.47	0.59	0.06
				Concomitant beta blocker usage (Yes vs No)									0.9 8										0.96	1.00	0.01					Concomitant beta blocker usage (Yes vs No)			2.1 7	1.78	2.66	0.10
				Concomitant loop diuretic agent usage (Yes vs No)									0.9 6										0.95	0.98	0.01					Concomitant loop diuretic agent usage (Yes vs No)			0.2 0	0.16	0.25	0.12

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.62	0.61	0.62	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.01	0.82	1.26	0.11	
		PDC ≥ 80%	4721, 62.92 %	N (% non-missing)	1700, 36.01%	1262, 26.73%						1249, 72.32 %	N (% non-missing)	480, 38.43%	204, 16.33%				
				Mean	12009.037	7516.331							Mean	15963.995	4990.439				
				Std. Dev	29095.9215	22111.6745							Std. Dev	36698.3642	22500.6137				
				Range	(0, 224629)	(0, 243325)							Range	(0, 221199)	(0, 251556)				
				Median	0	0							Median	0	0				
				25th percentile	0	0							25th percentile	0	0				
				75th percentile	11013.5	753.75							75th percentile	17842.5	0				
				Interquartile range	11013.5	753.75							Interquartile range	17842.5	0				
				Period (Post-index vs pre-index)			0.63	0.62	0.63	0.00		Period (Post-index vs pre-index)				0.32	0.31	0.32	0.01
				Concomitant beta blocker usage (Yes vs No)			0.56	0.55	0.58	0.01		Concomitant beta blocker usage (Yes vs No)				0.67	0.61	0.73	0.05
				Concomitant loop diuretic agent usage (Yes vs No)			0.78	0.76	0.80	0.01		Concomitant loop diuretic agent usage (Yes vs No)				0.37	0.34	0.40	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.99	0.97	1.01	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.79	0.72	0.87	0.05
Worsening Heart Failure episodes costs	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5 %	N (% non-missing)	1590, 40.37%	1279, 32.47%						702, 40.65 %	N (% non-missing)	303, 43.16%	150, 21.37%				
				Mean	13990.423	10646.652							Mean	17958.403	8413.675				
				Std. Dev	30864.7919	27211.0301							Std. Dev	37223.4479	28924.4428				
				Range	(0, 220631)	(0, 256836)							Range	(0, 220232)	(0, 260098)				
				Median	0	0							Median	0	0				
				25th percentile	0	0							25th percentile	0	0				
				75th percentile	16001	5099.25							75th percentile	19874.25	0				

				Interquartile range	16001	5099.25						Interquartile range	19874.25	0					
				Period (Post-index vs pre-index)			0.76	0.76	0.76	0.00			Period (Post-index vs pre-index)			0.47	0.46	0.49	0.01
				Concomitant beta blocker usage (Yes vs No)			0.83	0.82	0.84	0.01			Concomitant beta blocker usage (Yes vs No)			1.24	1.12	1.37	0.05
				Concomitant loop diuretic agent usage (Yes vs No)			0.79	0.78	0.80	0.01			Concomitant loop diuretic agent usage (Yes vs No)			0.73	0.67	0.80	0.05
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.95	0.94	0.97	0.01			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.86	0.78	0.94	0.05
			No diagnosis of T2DM in pre-index period	3564, 47.5 %	N (% non-missing)	1133, 31.79%	964, 27.05%					1025, 59.35 %	N (% non-missing)	388, 37.85%	178, 17.37%				
					Mean	9920.992	8288.443						Mean	14748.775	4912.256				
					Std. Dev	26935.1721	24707.0407						Std. Dev	33804.9039	21329.21				
					Range	(0, 224629)	(0, 248234)						Range	(0, 221199)	(0, 251137)				
					Median	0	0						Median	0	0				
		25th percentile			0	0	25th percentile						0	0					
		75th percentile			3887.75	933.25	75th percentile						17268	0					
		Interquartile range			3887.75	933.25	Interquartile range						17268	0					
		Period (Post-index vs pre-index)				0.84	0.83	0.84	0.00		Period (Post-index vs pre-index)			0.34	0.33	0.35	0.01		
		Concomitant beta blocker usage (Yes vs No)				0.58	0.58	0.59	0.01		Concomitant beta blocker usage (Yes vs No)			0.75	0.68	0.83	0.05		
		Concomitant loop diuretic agent usage (Yes vs No)				0.99	0.98	1.01	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.32	0.29	0.35	0.05		
		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				0.78	0.77	0.79	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.66	0.60	0.73	0.05		

Worsening Heart Failure episodes costs	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	1371, 47.36%	1019, 35.2%					343, 19.86 %	N (% non-missing)	181, 52.77%	91, 26.53%				
				Mean	17235.523	11568.575						Mean	22448.25	8085.943				
				Std. Dev	33971.4749	28038.4538						Std. Dev	40726.2066	26647.9982				
				Range	(0, 224629)	(0, 228312)						Range	(0, 216859)	(0, 251137)				
				Median	0	0						Median	2123.5	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	19389	9283						75th percentile	28364.5	283				
				Interquartile range	19389	9283						Interquartile range	28364.5	283				
				Period (Post-index vs pre-index)			0.67	0.67	0.67	0.00		Period (Post-index vs pre-index)			0.36	0.35	0.37	0.02
				Concomitant beta blocker usage (Yes vs No)			0.64	0.62	0.66	0.02		Concomitant beta blocker usage (Yes vs No)			0.67	0.54	0.83	0.11
				Concomitant loop diuretic agent usage (Yes vs No)			0.88	0.86	0.90	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.07	0.06	0.08	0.09
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.86	0.83	0.88	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.28	0.23	0.34	0.10
		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	1352, 29.34%	1224, 26.56%					1384, 80.14 %	N (% non-missing)	510, 36.85%	237, 17.12%				
				Mean	8817.699	8247.455						Mean	14482.234	5900.328				
				Std. Dev	25114.7436	24685.8443						Std. Dev	33611.2299	24240.5233				
				Range	(0, 220631)	(0, 256836)						Range	(0, 221199)	(0, 260098)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	2412	703						75th percentile	17022	0				
				Interquartile range	2412	703						Interquartile range	17022	0				

				Period (Post-index vs pre-index)			0.94	0.93	0.94	0.00		Period (Post-index vs pre-index)			0.41	0.41	0.42	0.01
				Concomitant beta blocker usage (Yes vs No)			0.77	0.77	0.78	0.00		Concomitant beta blocker usage (Yes vs No)			0.97	0.90	1.04	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			0.93	0.93	0.94	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.64	0.60	0.68	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.93	0.92	0.93	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.81	0.94	0.04
Worsening Heart Failure episodes costs	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	420, 33.25%	340, 26.92%					505, 29.24 %	N (% non-missing)	211, 41.78%	82, 16.24%				
				Mean	10301.001	7082.248						Mean	16457.084	4017.617				
				Std. Dev	28228.8191	20607.5855						Std. Dev	36119.1234	19280.9783				
				Range	(0, 224629)	(0, 200488)						Range	(0, 200648)	(0, 216493)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	4347	934.25						75th percentile	18010	0				
				Interquartile range	4347	934.25						Interquartile range	18010	0				
				Period (Post-index vs pre-index)			0.69	0.68	0.70	0.01		Period (Post-index vs pre-index)			0.24	0.23	0.25	0.02
				Concomitant beta blocker usage (Yes vs No)			0.26	0.25	0.27	0.02		Concomitant beta blocker usage (Yes vs No)			0.59	0.51	0.70	0.08
				Concomitant loop diuretic agent usage (Yes vs No)			0.62	0.60	0.65	0.02		Concomitant loop diuretic agent usage (Yes vs No)			0.64	0.54	0.75	0.08
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.73	0.70	0.76	0.02		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.21	0.18	0.25	0.08
				Other								N (% non-missing)	480, 39.28%	246, 20.13%				

			6240, 83.17 %	Mean	12408.139	10019.058					1222, 70.76 %	Mean	15878.907	7289.074				
				Std. Dev	29297.8614	27022.5367						Std. Dev	34902.2006	26626.0962				
				Range	(0, 220631)	(0, 256836)						Range	(0, 221199)	(0, 260098)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	12465.5	2669.25						75th percentile	18764.75	0				
				Interquartile range	12465.5	2669.25						Interquartile range	18764.75	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
Worsening Heart Failure episodes costs	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	1259, 39.6%	1044, 32.84%					880, 50.96 %	N (% non-missing)	386, 43.86%	177, 20.11%				
				Mean	14167.887	10854.688						Mean	17069.471	6419.542				
				Std. Dev	32196.1687	28422.8762						Std. Dev	36648.0765	23859.6534				
				Range	(0, 220631)	(0, 250280)						Range	(0, 221199)	(0, 251556)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	15414	4885						75th percentile	19293.5	0				
				Interquartile range	15414	4885						Interquartile range	19293.5	0				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker								Concomitant beta blocker						

				usage (Yes vs No)							usage (Yes vs No)																	
				Concomitant loop diuretic agent usage (Yes vs No)							0.80							0.79	0.81	0.01	Concomitant loop diuretic agent usage (Yes vs No)	0.41	0.38	0.45	0.04			
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	1464, 33.86%	1199, 27.73%						847, 49.04 %	N (% non-missing)	305, 36.01%	151, 17.83%													
				Mean	10504.432	8549.532							Mean	14997.017	6237.867													
				Std. Dev	26558.4863	24166.866							Std. Dev	33747.2266	25627.8201													
				Range	(0, 224629)	(0, 256836)							Range	(0, 216859)	(0, 260098)													
				Median	0	0							Median	0	0													
				25th percentile	0	0							25th percentile	0	0													
75th percentile	8258			1322.5	75th percentile	17122.25							0															
Interquartile range	8258			1322.5	Interquartile range	17122.25							0															
Period (Post-index vs pre-index)					0.81	0.81							0.82	0.00	Period (Post-index vs pre-index)							0.42	0.40	0.44	0.02			
Concomitant beta blocker usage (Yes vs No)			0.58	0.58	0.59	0.01	Concomitant beta blocker usage (Yes vs No)			1.37	1.24	1.52	0.05															
Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.93	0.95	0.01	Concomitant loop diuretic agent usage (Yes vs No)			0.45	0.41	0.50	0.05															
Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																					
Worsening Heart Failure episodes costs	Concomitant use of Sodium-glucose transporter-2 inhibitor (SGLT-2)	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan	237, 3.16 %	N (% non-missing)	80, 33.76%	72, 30.38%					111, 6.43 %	N (% non-missing)	42, 37.84%	23, 20.72%														
				Mean	12660.477	9557.958						Mean	12947.518	8369.973														
				Std. Dev	31266.5869	25784.2724						Std. Dev	24573.2243	34641.1813														
				Range	(0, 193339)	(0, 184539)						Range	(0, 147389)	(0, 260098)														

		rtan in the post-index period		Median	0	0					Median	0	0				
				25th percentile	0	0					25th percentile	0	0				
				75th percentile	10032	2005					75th percentile	19645.5	0				
				Interquartile range	10032	2005					Interquartile range	19645.5	0				
				Period (Post-index vs pre-index)			0.77	0.74	0.80	0.02	Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			0.12	0.11	0.13	0.04	Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			0.70	0.63	0.77	0.05	Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.28	0.26	0.30	0.04	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
		No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	N (% non-missing)	2643, 36.37%	2171, 29.88%					1616, 93.57 %	N (% non-missing)	649, 40.16%	305, 18.87%			
				Mean	12032.868	9522.696					Mean	16261.721	6189.7				
				Std. Dev	29058.474	26084.9129					Std. Dev	35867.4726	23916.8233				
				Range	(0, 224629)	(0, 256836)					Range	(0, 221199)	(0, 251556)				
				Median	0	0					Median	0	0				
				25th percentile	0	0					25th percentile	0	0				
				75th percentile	11609.5	2356					75th percentile	18435	0				
				Interquartile range	11609.5	2356					Interquartile range	18435	0				
				Period (Post-index vs pre-index)			0.79	0.79	0.79	0.00	Period (Post-index vs pre-index)			0.38	0.38	0.39	0.01
				Concomitant beta blocker usage (Yes vs No)			0.71	0.70	0.72	0.00	Concomitant beta blocker usage (Yes vs No)			0.90	0.84	0.96	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			0.90	0.89	0.91	0.00	Concomitant loop diuretic agent usage (Yes vs No)			0.53	0.49	0.56	0.03

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.91	0.90	0.91	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.75	0.70	0.81	0.04
Worsening Heart Failure episodes costs	Age category	<65	1029, 13.71 %	N (% non-missing)	394, 38.29%	370, 35.96%					1352, 78.29 %	N (% non-missing)	553, 40.9%	228, 16.86%				
				Mean	12428.172	12044.738						Mean	17113.116	6024.475				
				Std. Dev	29393.1746	30728.6648						Std. Dev	35878.4596	23510.1883				
				Range	(0, 224629)	(0, 228312)						Range	(0, 221199)	(0, 260098)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	12304.25	9885						75th percentile	19709	0				
				Interquartile range	12304.25	9885						Interquartile range	19709	0				
				Period (Post-index vs pre-index)			0.97	0.96	0.98	0.00		Period (Post-index vs pre-index)			0.35	0.35	0.36	0.00
				Concomitant beta blocker usage (Yes vs No)			0.46	0.45	0.47	0.01		Concomitant beta blocker usage (Yes vs No)			0.70	0.65	0.75	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			1.01	0.99	1.04	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.49	0.46	0.53	0.04
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.76	0.74	0.78	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.54	0.50	0.59	0.04
		65-74	2970, 39.58 %	N (% non-missing)	1066, 35.89%	805, 27.1%					226, 13.09 %	N (% non-missing)	80, 35.4%	50, 22.12%				
				Mean	12578.575	8888.223						Mean	16592.333	7249.262				
				Std. Dev	30381.6006	24951.3365						Std. Dev	39957.5173	26012.5983				
				Range	(0, 220631)	(0, 250280)						Range	(0, 220232)	(0, 181028)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	12498.5	1005						75th percentile	17270	0				

				Interquartile range	12498.5	1005						Interquartile range	17270	0				
				Period (Post-index vs pre-index)			0.71	0.70	0.71	0.00		Period (Post-index vs pre-index)			0.43	0.40	0.47	0.04
				Concomitant beta blocker usage (Yes vs No)			0.44	0.43	0.45	0.01		Concomitant beta blocker usage (Yes vs No)			1.52	1.20	1.91	0.12
				Concomitant loop diuretic agent usage (Yes vs No)			0.55	0.54	0.56	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.05	0.04	0.06	0.12
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.76	0.74	0.78	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.69	1.09	0.12
		75-84	2705, 36.05 %	N (% non-missing)	957, 35.38%	819, 30.28%					120, 6.95 %	N (% non-missing)	46, 38.33%	41, 34.17%				
				Mean	12085.213	9747.573						Mean	5915.425	7743.558				
				Std. Dev	29614.0758	26698.711						Std. Dev	14784.159	33363.6364				
				Range	(0, 215793)	(0, 256836)						Range	(0, 97664)	(0, 251556)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	10232	2529						75th percentile	3554	2120.25				
				Interquartile range	10232	2529						Interquartile range	3554	2120.25				
				Period (Post-index vs pre-index)			0.81	0.80	0.81	0.00		Period (Post-index vs pre-index)			1.36	1.12	1.66	0.10
				Concomitant beta blocker usage (Yes vs No)			0.99	0.97	1.00	0.01		Concomitant beta blocker usage (Yes vs No)			0.00	0.00	0.00	0.53
				Concomitant loop diuretic agent usage (Yes vs No)			1.12	1.10	1.13	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.69	0.38	1.25	0.31
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.99	0.98	1.01	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			6.44	5.94	6.99	0.04

		≥85	799, 10.65 %	N (% non-missing)	306, 38.3%	249, 31.16%					29, 1.68 %	N (% non-missing)	12, 41.38%	9, 31.03%				
				Mean	9521.678	7886.312						Mean	4744.241	7415.241				
				Std. Dev	21275.1364	20768.7583						Std. Dev	12351.0272	28913.0005				
				Range	(0, 149305)	(0, 180129)						Range	(0, 61976)	(0, 154619)				
				Median	0	0						Median	0	0				
				25th percentile	0	0						25th percentile	0	0				
				75th percentile	10920	2562.25						75th percentile	3976	1841				
				Interquartile range	10920	2562.25						Interquartile range	3976	1841				
				Period (Post-index vs pre-index)			0.83	0.82	0.84	0.00		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.08	1.05	1.11	0.02		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.25	1.23	1.28	0.01		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.04	1.01	1.08	0.02		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for HF-Specific Costs – HFrEF Cohort

			Medicare Advantage								Commercially insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
Heart Failure-specific costs	Overall cohort		7503, 100%	N (% non-missing)	5992, 79.86%	6644, 88.55%					1727, 100%	N (% non-missing)	1455, 84.25%	1441, 83.44%				
				Mean	15708.571	14858.796						Mean	21978.655	14237.623				
				Std. Dev	31150.9473	29824.0388						Std. Dev	38091.1876	33216.9226				

				Range	(0, 199012.08)	(0, 197372.42)						Range	(0, 198971.78)	(0, 198622.06)				
				Median	1322.4	1486.94						Median	3390.46	1135.64				
				25th percentile	185.6	388.6						25th percentile	352.93	271.73				
				75th percentile	17818.69	13683.77						75th percentile	24249.32	5971.05				
				Interquartile range	17633.09	13295.17						Interquartile range	23896.39	5699.32				
				Period (Post-index vs pre-index)			0.95	0.94	0.95	0.00		Period (Post-index vs pre-index)			0.65	0.64	0.65	0.00
				Concomitant beta blocker usage (Yes vs No)			0.99	0.99	1.00	0.00		Concomitant beta blocker usage (Yes vs No)			1.00	0.96	1.03	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.15	1.15	1.16	0.00		Concomitant loop diuretic agent usage (Yes vs No)			1.05	1.01	1.08	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.20	1.20	1.21	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.06	1.03	1.10	0.02
Heart Failure-specific costs	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non-missing)	792, 80.16%	858, 86.84%					151, 8.74 %	N (% non-missing)	126, 83.44%	123, 81.46%				
				Mean	15138.158	17250.996						Mean	23203.83	17000.534				
				Std. Dev	30880.7552	33344.7572						Std. Dev	37131.5489	35596.6376				
				Range	(0, 195804.06)	(0, 187603.7)						Range	(0, 184696.49)	(0, 153476)				
				Median	1214.76	1770.71						Median	4951.49	1067.78				
				25th percentile	224.46	379.32						25th percentile	303.92	265.93				
				75th percentile	16153.75	17017.8						75th percentile	29345.89	10822.68				
				Interquartile range	15929.29	16638.48						Interquartile range	29041.97	10556.75				
				Period (Post-index vs pre-index)			1.14	1.13	1.14	0.00		Period (Post-index vs pre-index)			0.73	0.70	0.76	0.02
				Concomitant beta blocker usage (Yes vs No)			0.90	0.88	0.92	0.01		Concomitant beta blocker usage (Yes vs No)			1.45	1.32	1.58	0.05
				Concomitant loop diuretic			1.17	1.16	1.19	0.01		Concomitant loop diuretic			1.33	1.19	1.49	0.06

				agent usage (Yes vs No)							agent usage (Yes vs No)											
				Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)											
				0.9 4							0.92								0.96	0.01	1.0 5	0.94
PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non- missing)	904, 77.4%	1047, 89.64%					249, 14.42 %	N (% non- missing)	211, 84.74%	203, 81.53%										
		Mean	14130.143	16948.901						Mean	23413.206	12123.821										
		Std. Dev	28140.6407	32950.425						Std. Dev	36212.5202	27829.6102										
		Range	(0, 199012.08)	(0, 197372.42)						Range	(0, 187436)	(0, 160799.34)										
		Median	1133.32	1409.98						Median	8778.05	999.02										
		25th percentile	126.44	382.51						25th percentile	468.23	299.86										
		75th percentile	16592.12	17349.47						75th percentile	30525.41	6090.99										
		Interquartile range	16465.68	16966.96						Interquartile range	30057.18	5791.13										
		Period (Post- index vs pre- index)								Period (Post- index vs pre- index)									NA	NA	NA	NA
		Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)									NA	NA	NA	NA
		Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)									NA	NA	NA	NA
		Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)									NA	NA	NA	NA
PDC ≥ 80%	4721, 62.92 %	N (% non- missing)	3799, 80.47%	4180, 88.54%					1249, 72.32 %	N (% non- missing)	1059, 84.79%	1059, 84.79%										
		Mean	15911.616	13219.034						Mean	22062.577	13980.002										
		Std. Dev	31540.5461	27246.2551						Std. Dev	39128.5053	33192.1876										
		Range	(0, 198862.52)	(0, 197072.17)						Range	(0, 198971.78)	(0, 198622.06)										
		Median	1401.86	1443.04						Median	2855.18	1210.78										
		25th percentile	191.11	384.64						25th percentile	368.3	275.36										

				75th percentile	18188.37	10675.76						75th percentile	23260.29	5226.01				
				Interquartile range	17997.26	10291.12						Interquartile range	22891.99	4950.65				
				Period (Post-index vs pre-index)			0.8 3	0.83	0.84	0.00		Period (Post-index vs pre-index)			0.6 4	0.63	0.64	0.01
				Concomitant beta blocker usage (Yes vs No)			1.0 6	1.04	1.07	0.01		Concomitant beta blocker usage (Yes vs No)			1.0 1	0.96	1.05	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.1 3	1.11	1.14	0.01		Concomitant loop diuretic agent usage (Yes vs No)			1.1 1	1.06	1.16	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.3 3	1.31	1.34	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.1 9	1.14	1.25	0.02
Heart Failure-specific costs	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5 %	N (% non-missing)	3204, 81.34%	3495, 88.73%					702, 40.65 %	N (% non-missing)	603, 85.9%	589, 83.9%				
				Mean	17837.702	16147.074					Mean	22952.508	15965.508					
				Std. Dev	32773.8514	31110.1402					Std. Dev	38130.1926	34361.7484					
				Range	(0, 199012.08)	(0, 197072.17)					Range	(0, 198971.78)	(0, 185214.84)					
				Median	1701.92	1632.12					Median	4127.9	1216.26					
				25th percentile	221.56	425.72					25th percentile	457.04	301.6					
				75th percentile	20726.61	16884.82					75th percentile	26460	8957.83					
				Interquartile range	20505.05	16459.1					Interquartile range	26002.96	8656.23					
				Period (Post-index vs pre-index)			0.9 1	0.90	0.91	0.00		Period (Post-index vs pre-index)			0.7 0	0.69	0.70	0.00
				Concomitant beta blocker usage (Yes vs No)			1.1 6	1.15	1.17	0.00		Concomitant beta blocker usage (Yes vs No)			0.9 5	0.90	0.99	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.0 7	1.06	1.08	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.8 9	0.85	0.93	0.02
				Concomitant Mineralocorticoid Receptor Antagonist			1.1 6	1.16	1.17	0.00		Concomitant Mineralocorticoid Receptor Antagonist			0.9 5	0.91	0.99	0.02

				usage (Yes vs No)							usage (Yes vs No)																	
		No diagnosis of T2DM in pre-index period	3564, 47.5 %	N (% non-missing)	2788, 78.23%	3149, 88.36%					1025, 59.35 %	N (% non-missing)	852, 83.12%	852, 83.12%														
				Mean	13365.922	13441.324						Mean	21320.672	13070.18														
				Std. Dev	29086.5579	28278.2753						Std. Dev	38069.7455	32385.7325														
				Range	(0, 196548.16)	(0, 197372.42)						Range	(0, 198046.97)	(0, 198622.06)														
				Median	1053.12	1343.55						Median	3015.47	1108.47														
				25th percentile	134.27	366.68						25th percentile	314.9	252.88														
				75th percentile	11857.15	10176.76						75th percentile	22133.1	5051.22														
				Interquartile range	11722.88	9810.08						Interquartile range	21818.2	4798.34														
				Period (Post-index vs pre-index)		1.0 1						1.00	1.01	0.00					Period (Post-index vs pre-index)		0.6 1	0.61	0.62	0.01				
		Concomitant beta blocker usage (Yes vs No)	0.8 9	0.88		0.90	0.01	Concomitant beta blocker usage (Yes vs No)	1.0 5	1.00	1.11	0.03																
		Concomitant loop diuretic agent usage (Yes vs No)	1.2 7	1.26		1.28	0.00	Concomitant loop diuretic agent usage (Yes vs No)	1.1 7	1.11	1.23	0.03																
		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)	1.2 6	1.25		1.27	0.00	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)	1.1 6	1.10	1.23	0.03																
		Heart Failure-specific costs	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	2436, 84.15%	2586, 89.33%					343, 19.86 %	N (% non-missing)	309, 90.09%	283, 82.51%												
Mean	21262.272					16559.212	Mean	26662.864						13825.558														
Std. Dev	35159.7123					31644.8484	Std. Dev	40766.3242						30341.9015														
Range	(0, 198862.52)					(0, 194925.4)	Range	(0, 186125.28)						(0, 184656.34)														
Median	3112.05					1776.63	Median	9739.45						1524.03														
25th percentile	381.38					468.31	25th percentile	1089.91						315.66														
75th percentile	26592.58					17743.27	75th percentile	31412.81						9116.12														
Interquartile range	26211.2					17274.96	Interquartile range	30322.9						8800.46														

				Period (Post-index vs pre-index)			0.78	0.78	0.78	0.00		Period (Post-index vs pre-index)			0.52	0.51	0.53	0.01
				Concomitant beta blocker usage (Yes vs No)			0.80	0.78	0.82	0.01		Concomitant beta blocker usage (Yes vs No)			0.26	0.23	0.30	0.07
				Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.97	1.00	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.79	0.69	0.91	0.07
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.10	1.08	1.12	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.72	0.62	0.82	0.07
		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	3556, 77.17%	4058, 88.06%					1384, 80.14 %	N (% non-missing)	1146, 82.8%	1158, 83.67%				
				Mean	12248.329	13799.35						Mean	20841.408	14337.666				
				Std. Dev	27817.2134	28583.5515						Std. Dev	37340.1943	33887.9325				
				Range	(0, 199012.08)	(0, 197372.42)						Range	(0, 198971.78)	(0, 198622.06)				
				Median	857.82	1312.86						Median	2545.51	1049.8				
				25th percentile	126.44	350.03						25th percentile	276.66	264.86				
				75th percentile	9820.99	11361.16						75th percentile	22125.44	5451.26				
				Interquartile range	9694.55	11011.13						Interquartile range	21848.78	5186.4				
				Period (Post-index vs pre-index)			1.13	1.12	1.13	0.00		Period (Post-index vs pre-index)			0.69	0.68	0.70	0.00
				Concomitant beta blocker usage (Yes vs No)			1.18	1.17	1.19	0.00		Concomitant beta blocker usage (Yes vs No)			1.12	1.08	1.16	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.33	1.32	1.34	0.00		Concomitant loop diuretic agent usage (Yes vs No)			1.10	1.06	1.14	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.32	1.32	1.33	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.14	1.11	1.18	0.02
Heart Failure-	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)		N (% non-missing)	1028, 81.39%	1147, 90.82%						N (% non-missing)	432, 85.54%	432, 85.54%				

specific costs			1263, 16.83 %	Mean	13420.456	13321.14					505, 29.24 %	Mean	23310.754	11145.458				
				Std. Dev	28585.6442	26867.7251						Std. Dev	40113.5436	27715.8625				
				Range	(0, 188618.55)	(0, 197372.42)						Range	(0, 198046.97)	(0, 182705.67)				
				Median	1235.69	1631.05						Median	4117.98	1122.68				
				25th percentile	184.47	467.33						25th percentile	469.31	303.62				
				75th percentile	13027.31	12927.42						75th percentile	24039.57	4520.53				
				Interquartile range	12842.84	12460.09						Interquartile range	23570.26	4216.91				
				Period (Post-index vs pre-index)			0.99	0.99	0.99	0.00		Period (Post-index vs pre-index)			0.48	0.47	0.49	0.01
				Concomitant beta blocker usage (Yes vs No)			0.90	0.90	0.90	0.00		Concomitant beta blocker usage (Yes vs No)			0.69	0.63	0.76	0.05
				Concomitant loop diuretic agent usage (Yes vs No)			1.01	1.01	1.02	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.91	0.83	1.00	0.05
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.02	1.02	1.03	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.82	0.75	0.90	0.05
		Other	6240, 83.17 %	N (% non-missing)	4964, 79.55%	5497, 88.09%					1222, 70.76 %	N (% non-missing)	1023, 83.72%	1009, 82.57%				
				Mean	16175.062	15172.287						Mean	21421.738	15530.378				
				Std. Dev	31630.3158	30383.9643						Std. Dev	37216.5048	35193.6744				
				Range	(0, 199012.08)	(0, 197072.17)						Range	(0, 198971.78)	(0, 198622.06)				
				Median	1347.92	1445.56						Median	3058.52	1152.93				
				25th percentile	185.6	379.32						25th percentile	324.8	252.88				
				75th percentile	18650.91	13783.11						75th percentile	24323.35	6433.61				
				Interquartile range	18465.31	13403.79						Interquartile range	23998.55	6180.73				
				Period (Post-index vs pre-index)			0.94	0.94	0.94	0.00		Period (Post-index vs pre-index)			0.73	0.72	0.73	0.00
				Concomitant beta blocker			1.01	1.00	1.01	0.00		Concomitant beta blocker			1.12	1.08	1.15	0.02

				usage (Yes vs No)							usage (Yes vs No)															
				Concomitant loop diuretic agent usage (Yes vs No)							Concomitant loop diuretic agent usage (Yes vs No)								1.1 5	1.12	1.19	0.02				
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								1.1 8	1.14	1.22	0.02				
Heart Failure-specific costs	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	2588, 81.41%	2878, 90.53%					880, 50.96 %	N (% non-missing)	750, 85.23%	750, 85.23%												
				Mean	17944.245	16944.573						Mean	21979.534	15521.058												
				Std. Dev	33096.6534	31082.7311						Std. Dev	37022.6354	33862.0418												
				Range	(0, 198734.68)	(0, 194925.4)						Range	(0, 198971.78)	(0, 198622.06)												
				Median	2025.2	2205.74						Median	5458.91	1536.93												
				25th percentile	257.08	513.23						25th percentile	494.02	410.15												
				75th percentile	20373.75	18686.58						75th percentile	24264.58	7553.75												
				Interquartile range	20116.67	18173.35						Interquartile range	23770.56	7143.6												
				Period (Post-index vs pre-index)								0.9 4	0.94	0.95					0.00	Period (Post-index vs pre-index)			0.7 1	0.70	0.71	0.00
				Concomitant beta blocker usage (Yes vs No)								1.0 7	1.07	1.08					0.00	Concomitant beta blocker usage (Yes vs No)			0.7 3	0.70	0.75	0.02
				Concomitant loop diuretic agent usage (Yes vs No)								1.0 2	1.01	1.02					0.00	Concomitant loop diuretic agent usage (Yes vs No)			0.8 4	0.82	0.87	0.02
		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																	
				No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsarta	4324, 57.63 %	N (% non-missing)	3404, 78.72%	3766, 87.1%					847, 49.04 %	N (% non-missing)	705, 83.23%	691, 81.58%										
Mean	14088.79	13347.617	Mean	21977.762		12934.159																				
Std. Dev	29560.1079	28787.2429	Std. Dev	39168.8606		32517.1346																				
Range	(0, 199012.08)	(0, 197372.42)	Range	(0, 197588.45)		(0, 190116.96)																				

		rtan in the post-index period		Median	1015	1136.22						Median	2184.47	835.78				
				25th percentile	139.27	310.59						25th percentile	252.88	150.22				
				75th percentile	14357.22	9356.65						75th percentile	24177.61	4379.78				
				Interquartile range	14217.95	9046.06						Interquartile range	23924.73	4229.56				
				Period (Post-index vs pre-index)			0.95	0.94	0.95	0.00	Period (Post-index vs pre-index)			0.59	0.58	0.60	0.01	
				Concomitant beta blocker usage (Yes vs No)			0.90	0.89	0.91	0.00	Concomitant beta blocker usage (Yes vs No)			1.24	1.17	1.33	0.03	
				Concomitant loop diuretic agent usage (Yes vs No)			1.25	1.24	1.25	0.00	Concomitant loop diuretic agent usage (Yes vs No)			1.21	1.13	1.30	0.03	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							

Heart Failure-specific costs	Concomitant use of Sodium-glucose co-transporter-2 (SGLT-2) inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237,316%	N (% non-missing)	185, 78.06%	216, 91.14%					111.643%	N (% non-missing)	88, 79.28%	92, 82.88%												
				Mean	19138.257	13964.284						Mean	21700.267	18684.235												
				Std. Dev	36343.1014	25305.2763						Std. Dev	32898.1372	36662.7437												
				Range	(0, 191383.6)	(0, 128908.32)						Range	(0, 146091.04)	(0, 182705.67)												
				Median	1198.28	1690.7						Median	5349.73	1611.82												
				25th percentile	144.42	446.02						25th percentile	200.39	385.12												
				75th percentile	20091.63	16753.56						75th percentile	30530.62	9332.03												
				Interquartile range	19947.21	16307.54						Interquartile range	30330.23	8946.91												
				Period (Post-index vs pre-index)								0.73	0.71	0.75					0.01	Period (Post-index vs pre-index)			0.85	0.80	0.90	0.03
				Concomitant beta blocker usage (Yes vs No)								0.36	0.33	0.38					0.03	Concomitant beta blocker usage (Yes vs No)			0.17	0.14	0.19	0.07
				Concomitant loop diuretic agent usage (Yes vs No)								0.58	0.54	0.63					0.04	Concomitant loop diuretic agent usage (Yes vs No)			0.13	0.12	0.15	0.05

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.6 6	0.61	0.70	0.03		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.3 7	0.32	0.43	0.08
		No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	N (% non-missing)	5807, 79.92%	6428, 88.47%					1616, 93.57 %	N (% non-missing)	1367, 84.59%	1349, 83.48%				
				Mean	15596.963	14887.905						Mean	21997.604	13934.959				
				Std. Dev	30963.9332	29960.7026						Std. Dev	38428.2512	32960.2932				
				Range	(0, 199012.08)	(0, 197372.42)						Range	(0, 198971.78)	(0, 198622.06)				
				Median	1326.17	1475.72						Median	3270.21	1113.73				
				25th percentile	186.8	386.71						25th percentile	360.03	264.96				
				75th percentile	17678.16	13548.42						75th percentile	23786.54	5946.5				
				Interquartile range	17491.36	13161.71						Interquartile range	23426.51	5681.54				
				Period (Post-index vs pre-index)			0.9 5	0.95	0.96	0.00		Period (Post-index vs pre-index)			0.6 4	0.63	0.64	0.00
				Concomitant beta blocker usage (Yes vs No)			1.0 2	1.01	1.02	0.00		Concomitant beta blocker usage (Yes vs No)			1.0 8	1.04	1.12	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.1 7	1.17	1.18	0.00		Concomitant loop diuretic agent usage (Yes vs No)			1.1 4	1.10	1.18	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.2 3	1.22	1.23	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.1 4	1.10	1.19	0.02
Heart Failure-specific costs	Age category	<65	1029, 13.71 %	N (% non-missing)	844, 82.02%	924, 89.8%					1352, 78.29 %	N (% non-missing)	1140, 84.32%	1122, 82.99%				
				Mean	16188.494	17448.986						Mean	23495.121	14993.724				
				Std. Dev	31477.4763	32047.1879						Std. Dev	39132.8709	34411.6649				
				Range	(0, 199012.08)	(0, 189268.66)						Range	(0, 198046.97)	(0, 198622.06)				
				Median	1461.94	1919.16						Median	5255.38	1152.46				
				25th percentile	245.13	468.78						25th percentile	391.79	264.86				
				75th percentile	18030.5	18897.94						75th percentile	26954	6086.82				

				Interquartile range	17785.37	18429.16						Interquartile range	26562.21	5821.96				
				Period (Post-index vs pre-index)			1.08	1.07	1.08	0.00		Period (Post-index vs pre-index)			0.64	0.63	0.64	0.00
				Concomitant beta blocker usage (Yes vs No)			1.02	1.00	1.03	0.01		Concomitant beta blocker usage (Yes vs No)			0.90	0.86	0.93	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.30	1.29	1.31	0.00		Concomitant loop diuretic agent usage (Yes vs No)			1.06	1.03	1.11	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.05	1.03	1.06	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.99	0.95	1.03	0.02
		65-74	2970, 39.58 %	N (% non-missing)	2362, 79.53%	2611, 87.91%					226, 13.09 %	N (% non-missing)	190, 84.07%	196, 86.73%				
				Mean	16199.131	14886.957						Mean	21501.786	14299.79				
				Std. Dev	31359.557	30112.5472						Std. Dev	39044.2801	33198.359				
				Range	(0, 198734.68)	(0, 194925.4)						Range	(0, 198971.78)	(0, 185214.84)				
				Median	1524.82	1398						Median	1731.64	1047.77				
				25th percentile	185.6	364.82						25th percentile	266.22	358.44				
				75th percentile	18650.91	12400.14						75th percentile	25959	5871.94				
				Interquartile range	18465.31	12035.32						Interquartile range	25692.78	5513.5				
				Period (Post-index vs pre-index)			0.92	0.92	0.92	0.00		Period (Post-index vs pre-index)			0.66	0.64	0.69	0.02
				Concomitant beta blocker usage (Yes vs No)			0.87	0.86	0.88	0.01		Concomitant beta blocker usage (Yes vs No)			1.33	1.17	1.51	0.06
				Concomitant loop diuretic agent usage (Yes vs No)			1.09	1.08	1.11	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.80	0.70	0.91	0.07
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.28	1.26	1.29	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.28	1.15	1.44	0.06

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				Period (Post-index vs pre-index)			0.90	0.89	0.91	0.01		Period (Post-index vs pre-index)				NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.23	1.19	1.26	0.01		Concomitant beta blocker usage (Yes vs No)				NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.33	1.30	1.35	0.01		Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.12	1.09	1.15	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for HF-Related Costs – HFrEF Cohort

			Medicare Advantage								Commercially insured							
					12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation							12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
Heart Failure-related costs	Overall cohort		7503, 100%	N (% non-missing)	6048, 80.61%	6694, 89.22%					1727, 100%	N (% non-missing)	1472, 85.23%	1462, 84.66%				
				Mean	18653.995	17876.601						Mean	26000.065	17105.62				
				Std. Dev	34910.4101	34613.8663						Std. Dev	42697.8068	38264.0774				
				Range	(0, 219366.34)	(0, 227463.86)						Range	(0, 209645.24)	(0, 226904.73)				
				Median	1788.14	1768.32						Median	6349.13	1338.76				
				25th percentile	211.12	438.77						25th percentile	428.62	308.56				
				75th percentile	20751.57	18122.55						75th percentile	29217.07	8663.39				
				Interquartile range	20540.45	17683.78						Interquartile range	28788.45	8354.83				
				Period (Post-index vs pre-index)			0.96	0.96	0.96	0.00		Period (Post-index vs pre-index)			0.66	0.65	0.66	0.00
				Concomitant beta blocker usage (Yes vs No)			1.00	1.00	1.01	0.00		Concomitant beta blocker usage (Yes vs No)			1.09	1.06	1.13	0.02

				Concomitant loop diuretic agent usage (Yes vs No)			1.1 5	1.14	1.15	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.9 7	0.94	1.00	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.2 2	1.21	1.22	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.0 6	1.02	1.09	0.02
Heart Failure-related costs	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non-missing)	799, 80.87%	873, 88.36%					151, 8.74%	N (% non-missing)	124, 82.12%	123, 81.46%				
				Mean	17783.02	21164.513					Mean	24187.87	18720.89					
				Std. Dev	34056.6072	39420.7909					Std. Dev	38667.8144	37109.2146					
				Range	(0, 216897.27)	(0, 227463.86)					Range	(0, 184696.49)	(0, 153476)					
				Median	1589.01	2160.33					Median	5887.28	1067.78					
				25th percentile	252.88	448.49					25th percentile	418.76	317.26					
				75th percentile	20650.91	22794.17					75th percentile	28864.19	13628.63					
				Interquartile range	20398.03	22345.68					Interquartile range	28445.43	13311.37					
				Period (Post-index vs pre-index)			1.1 9	1.19	1.20	0.00	Period (Post-index vs pre-index)			0.7 7	0.74	0.81	0.03	
				Concomitant beta blocker usage (Yes vs No)			0.9 4	0.91	0.96	0.01	Concomitant beta blocker usage (Yes vs No)			1.5 9	1.46	1.73	0.04	
				Concomitant loop diuretic agent usage (Yes vs No)			1.2 6	1.24	1.28	0.01	Concomitant loop diuretic agent usage (Yes vs No)			1.5 2	1.37	1.69	0.05	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.0 5	1.03	1.08	0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.1 1	1.00	1.24	0.06	
		PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non-missing)	918, 78.6%	1056, 90.41%					249, 14.42 %	N (% non-missing)	214, 85.94%	208, 83.53%				
				Mean	17673.774	20658.26					Mean	25218.84	16598.149					
				Std. Dev	33113.0327	38575.0981					Std. Dev	37063.0025	36982.7278					
				Range	(0, 219366.34)	(0, 225834.9)					Range	(0, 187436)	(0, 216735.2)					
				Median	1623.94	1693.6					Median	11764.37	1151.88					

				25th percentile	157.18	449.5					25th percentile	513.3	326.88						
				75th percentile	20499.22	21112.73					75th percentile	33848.48	10245.63						
				Interquartile range	20342.04	20663.23					Interquartile range	33335.18	9918.75						
				Period (Post-index vs pre-index)			1.17	1.17	1.17	0.00	Period (Post-index vs pre-index)			0.66	0.64	0.67	0.01		
				Concomitant beta blocker usage (Yes vs No)			1.10	1.08	1.12	0.01	Concomitant beta blocker usage (Yes vs No)			0.84	0.75	0.94	0.06		
				Concomitant loop diuretic agent usage (Yes vs No)			1.21	1.20	1.23	0.01	Concomitant loop diuretic agent usage (Yes vs No)			0.41	0.37	0.45	0.05		
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.21	1.19	1.23	0.01	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.58	0.53	0.63	0.04		
				PDC ≥ 80%	4721, 62.92 %	N (% non-missing)	3836, 81.25%	4210, 89.18%					1249, 72.32 %	N (% non-missing)	1075, 86.07%	1075, 86.07%			
		Mean	18766.823			15766.408	Mean	26826.587						16426.151					
		Std. Dev	35185.057			31386.67	Std. Dev	44511.4516						37423.652					
		Range	(0, 218460.03)			(0, 225756.47)	Range	(0, 209645.24)						(0, 226904.73)					
		Median	1886.04			1689.02	Median	5821.69						1398					
		25th percentile	217.35			427.6	25th percentile	438.19						317.4					
		75th percentile	20432.5			14522.75	75th percentile	28959.59						6881.1					
		Interquartile range	20215.15			14095.15	Interquartile range	28521.4						6563.7					
		Period (Post-index vs pre-index)					0.84	0.84	0.84	0.00	Period (Post-index vs pre-index)			0.61	0.61	0.62	0.00		
		Concomitant beta blocker usage (Yes vs No)					1.04	1.03	1.06	0.01	Concomitant beta blocker usage (Yes vs No)			0.97	0.92	1.01	0.02		
		Concomitant loop diuretic agent usage (Yes vs No)					1.12	1.10	1.13	0.01	Concomitant loop diuretic agent usage (Yes vs No)			0.96	0.92	1.00	0.02		

				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.3 2	1.30	1.33	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.1 3	1.08	1.18	0.02
Heart Failure-related costs	Presence of Type 2 Diabetes (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5%	N (% non-missing)	3223, 81.82%	3517, 89.29%					702, 40.65 %	N (% non-missing)	612, 87.18%	602, 85.75%				
				Mean	21069.738	19449.772						Mean	27445.733	20786.179				
				Std. Dev	36337.662	35962.9264						Std. Dev	42881.0651	42923.1167				
				Range	(0, 218460.03)	(0, 225756.47)						Range	(0, 208973.59)	(0, 226904.73)				
				Median	2501.13	1962.06						Median	8129.94	1428.2				
				25th percentile	254.04	474.15						25th percentile	530.7	351.48				
				75th percentile	25341.99	20670.89						75th percentile	30546.2	15456.97				
				Interquartile range	25087.95	20196.74						Interquartile range	30015.5	15105.49				
				Period (Post-index vs pre-index)			0.9 2	0.92	0.93	0.00		Period (Post-index vs pre-index)			0.7 6	0.75	0.77	0.01
				Concomitant beta blocker usage (Yes vs No)			1.1 4	1.13	1.15	0.00		Concomitant beta blocker usage (Yes vs No)			1.3 0	1.25	1.36	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.1 3	1.12	1.14	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.8 9	0.85	0.93	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.1 9	1.18	1.20	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.9 4	0.90	0.98	0.02
		No diagnosis of T2DM in pre-index period	3564, 47.5%	N (% non-missing)	2825, 79.26%	3177, 89.14%					1025, 59.35 %	N (% non-missing)	860, 83.9%	860, 83.9%				
				Mean	16005.864	16152.095						Mean	25019.487	14609.144				
				Std. Dev	33078.6201	32990.8659						Std. Dev	42566.4926	34550.2471				
				Range	(0, 219366.34)	(0, 227463.86)						Range	(0, 209645.24)	(0, 214463.53)				
				Median	1365.42	1563.49						Median	4591.97	1234.94				
				25th percentile	161.75	403.1						25th percentile	350.9	279.99				
				75th percentile	17319.29	14125.04						75th percentile	27929	6177.52				

				Interquartile range	17157.54	13721.94						Interquartile range	27578.1	5897.53				
				Period (Post-index vs pre-index)			1.01	1.01	1.01	0.00		Period (Post-index vs pre-index)			0.59	0.58	0.59	0.01
				Concomitant beta blocker usage (Yes vs No)			0.92	0.91	0.93	0.00		Concomitant beta blocker usage (Yes vs No)			0.98	0.93	1.03	0.03
				Concomitant loop diuretic agent usage (Yes vs No)			1.19	1.18	1.20	0.00		Concomitant loop diuretic agent usage (Yes vs No)			1.05	1.00	1.11	0.03
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.26	1.25	1.27	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.18	1.12	1.25	0.03
Heart Failure-related costs	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	2451, 84.66%	2607, 90.05%					343, 19.86 %	N (% non-missing)	312, 90.96%	287, 83.67%				
				Mean	25125.023	20035.715						Mean	32876.795	17160.786				
				Std. Dev	39450.1279	36738.8895						Std. Dev	46937.7131	35974.741				
				Range	(0, 219366.34)	(0, 225756.47)						Range	(0, 207670.52)	(0, 216735.2)				
				Median	4704.71	2189.76						Median	13876.07	1692.73				
				25th percentile	477	524.96						25th percentile	1361.03	376.27				
				75th percentile	32620.35	21206.53						75th percentile	40620.41	15290.51				
				Interquartile range	32143.35	20681.57						Interquartile range	39259.38	14914.24				
				Period (Post-index vs pre-index)			0.80	0.79	0.80	0.00		Period (Post-index vs pre-index)			0.52	0.52	0.52	0.00
				Concomitant beta blocker usage (Yes vs No)			0.93	0.91	0.95	0.01		Concomitant beta blocker usage (Yes vs No)			0.66	0.57	0.75	0.07
				Concomitant loop diuretic agent usage (Yes vs No)			1.03	1.01	1.04	0.01		Concomitant loop diuretic agent usage (Yes vs No)			0.75	0.66	0.85	0.07
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.20	1.18	1.22	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.63	0.56	0.72	0.06

		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	3597, 78.06%	4087, 88.69%					1384, 80.14 %	N (% non-missing)	1160, 83.82%	1175, 84.9%				
				Mean	14628.431	16533.437						Mean	24337.893	17092.285				
				Std. Dev	31092.8563	33156.6745						Std. Dev	41455.9438	38809.8417				
				Range	(0, 218249.92)	(0, 227463.86)						Range	(0, 209645.24)	(0, 226904.73)				
				Median	1028.63	1549.83						Median	4566.58	1203.2				
				25th percentile	126.44	388.09						25th percentile	343.36	301.6				
				75th percentile	14363.84	14782.04						75th percentile	27566.89	7238.75				
				Interquartile range	14237.4	14393.95						Interquartile range	27223.53	6937.15				
				Period (Post-index vs pre-index)			1.13	1.13	1.13	0.00		Period (Post-index vs pre-index)			0.70	0.70	0.71	0.00
				Concomitant beta blocker usage (Yes vs No)			1.11	1.10	1.12	0.00		Concomitant beta blocker usage (Yes vs No)			1.20	1.16	1.24	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.28	1.27	1.29	0.00		Concomitant loop diuretic agent usage (Yes vs No)			1.03	1.00	1.06	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.27	1.26	1.28	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.16	1.12	1.20	0.02
Heart Failure-related costs	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	1041, 82.42%	1154, 91.37%					505, 29.24 %	N (% non-missing)	440, 87.13%	438, 86.73%				
				Mean	16395.322	16090.895						Mean	26853.425	13289.214				
				Std. Dev	32615.1163	31251.8962						Std. Dev	43834.5484	31944.9255				
				Range	(0, 208602.76)	(0, 211191.33)						Range	(0, 209645.24)	(0, 226904.73)				
				Median	1581.38	2010.28						Median	6966.92	1218.99				
				25th percentile	207.06	517.94						25th percentile	529.94	353.8				
				75th percentile	17874.11	16695.66						75th percentile	28418.07	5733.67				
				Interquartile range	17667.05	16177.72						Interquartile range	27888.13	5379.87				

				Period (Post-index vs pre-index)			0.98	0.98	0.98	0.00		Period (Post-index vs pre-index)			0.50	0.49	0.50	0.01
				Concomitant beta blocker usage (Yes vs No)			0.98	0.98	0.99	0.00		Concomitant beta blocker usage (Yes vs No)			0.68	0.63	0.74	0.04
				Concomitant loop diuretic agent usage (Yes vs No)			1.07	1.07	1.07	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.81	0.74	0.89	0.05
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.06	1.05	1.06	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.87	0.80	0.95	0.05
		Other	6240, 83.17 %	N (% non-missing)	5007, 80.24%	5540, 88.78%					1222, 70.76 %	N (% non-missing)	1032, 84.45%	1024, 83.8%				
				Mean	19115.377	18241.37						Mean	25642.042	18706.774				
				Std. Dev	35345.726	35252.4522						Std. Dev	42225.4123	40529.141				
				Range	(0, 219366.34)	(0, 227463.86)						Range	(0, 208973.59)	(0, 221475.69)				
				Median	1838.81	1728.65						Median	5887.28	1393.88				
				25th percentile	213.58	424.85						25th percentile	386.57	300.44				
				75th percentile	21620.29	18439.87						75th percentile	29418.88	10419.33				
				Interquartile range	21406.71	18015.02						Interquartile range	29032.31	10118.89				
				Period (Post-index vs pre-index)			0.95	0.95	0.96	0.00		Period (Post-index vs pre-index)			0.73	0.72	0.74	0.00
				Concomitant beta blocker usage (Yes vs No)			1.00	1.00	1.01	0.00		Concomitant beta blocker usage (Yes vs No)			1.26	1.22	1.30	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.15	1.15	1.16	0.00		Concomitant loop diuretic agent usage (Yes vs No)			1.09	1.06	1.13	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.25	1.24	1.25	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.14	1.10	1.18	0.02
Heart Failure-	Concomitant use of spironolactone	Prescription fills for		N (% non-missing)	2613, 82.2%	2895, 91.07%						N (% non-missing)	763, 86.7%	763, 86.7%				

related costs		spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	Mean	21369.159	21110.687					880, 50.96 %	Mean	26372.877	18274.26				
				Std. Dev	37249.1605	37631.9066						Std. Dev	42376.0572	38303.4033				
				Range	(0, 219366.34)	(0, 226206.74)						Range	(0, 209645.24)	(0, 226904.73)				
				Median	2976.11	2713.33						Median	9053.64	1686.64				
				25th percentile	300.44	587.72						25th percentile	599.44	477.92				
				75th percentile	24641.76	23871.41						75th percentile	29487.56	11277.49				
				Interquartile range	24341.32	23283.69						Interquartile range	28888.12	10799.57				
				Period (Post-index vs pre-index)			0.99	0.99	0.99	0.00		Period (Post-index vs pre-index)			0.69	0.69	0.70	0.00
				Concomitant beta blocker usage (Yes vs No)			1.09	1.09	1.09	0.00		Concomitant beta blocker usage (Yes vs No)			0.69	0.67	0.72	0.02
				Concomitant loop diuretic agent usage (Yes vs No)			1.07	1.07	1.07	0.00		Concomitant loop diuretic agent usage (Yes vs No)			0.76	0.74	0.79	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	3435, 79.44%	3799, 87.86%					847, 49.04 %	N (% non-missing)	709, 83.71%	699, 82.53%				
				Mean	16681.869	15527.562						Mean	25618.749	15910.324				
				Std. Dev	32972.825	32045.6629						Std. Dev	43046.5283	38209.8227				
				Range	(0, 218460.03)	(0, 227463.86)						Range	(0, 207670.52)	(0, 221475.69)				
				Median	1278.9	1316.6						Median	3635.08	954.1				
				25th percentile	164.43	367.43						25th percentile	288.84	200.1				
				75th percentile	18797.66	13465.73						75th percentile	28864.19	6357.8				
				Interquartile range	18633.23	13098.3						Interquartile range	28575.35	6157.7				
				Period (Post-index vs pre-index)			0.93	0.93	0.93	0.00		Period (Post-index vs pre-index)			0.62	0.61	0.63	0.01
				Concomitant beta blocker			0.90	0.90	0.91	0.00		Concomitant beta blocker			1.53	1.44	1.63	0.03

				usage (Yes vs No)								usage (Yes vs No)														
				Concomitant loop diuretic agent usage (Yes vs No)			1.18	1.17	1.19	0.00		Concomitant loop diuretic agent usage (Yes vs No)				1.20	1.12	1.28	0.03							
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)														
Heart Failure-related costs	Concomitant use of Sodium-glucose co-transporter-2 (SGLT-2) inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237, 3.16%	N (% non-missing)	192, 81.01%	217, 91.56%					111, 6.43%	N (% non-missing)	92, 82.88%	94, 84.68%												
				Mean	20728.568	17353.158						Mean	23388.77	25007.53												
				Std. Dev	36285.1173	32671.3177						Std. Dev	34719.5182	47046.5255												
				Range	(0, 191383.6)	(0, 214861.75)						Range	(0, 146091.04)	(0, 218462.05)												
				Median	2564.15	2099.39						Median	6224.65	2519.96												
				25th percentile	214.02	524.96						25th percentile	269.7	430.68												
				75th percentile	24175.62	19805.74						75th percentile	31417.96	17672.05												
				Interquartile range	23961.6	19280.78						Interquartile range	31148.26	17241.37												
				Period (Post-index vs pre-index)								0.84	0.82	0.86					0.01	Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)								0.34	0.33	0.36					0.02	Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)								0.50	0.47	0.53					0.03	Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.76	0.71	0.80					0.03	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
		No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsar	7266, 96.84 %	N (% non-missing)	5856, 80.59%	6477, 89.14%					1616, 93.57 %	N (% non-missing)	1380, 85.4%	1368, 84.65%												
				Mean	18586.428	17893.649						Mean	26180.668	16559.104												
				Std. Dev	34865.2828	34677.3312						Std. Dev	43198.4879	37537.6202												
				Range	(0, 219366.34)	(0, 227463.86)						Range	(0, 209645.24)	(0, 226904.73)												

		tan in the post-index period		Median	1769.54	1758.54						Median	6350.26	1291.59												
				25th percentile	210.83	436.16						25th percentile	435.73	302.02												
				75th percentile	20680.91	18053.64						75th percentile	29058.51	7922.47												
				Interquartile range	20470.08	17617.48						Interquartile range	28622.78	7620.45												
				Period (Post-index vs pre-index)								0.96	0.96	0.97					0.00	Period (Post-index vs pre-index)			0.63	0.63	0.64	0.01
				Concomitant beta blocker usage (Yes vs No)								1.02	1.02	1.03					0.00	Concomitant beta blocker usage (Yes vs No)			1.18	1.13	1.22	0.02
				Concomitant loop diuretic agent usage (Yes vs No)								1.17	1.16	1.17					0.00	Concomitant loop diuretic agent usage (Yes vs No)			1.05	1.02	1.10	0.02
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								1.24	1.23	1.24					0.00	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.13	1.08	1.17	0.02
Heart Failure-related costs	Age category	<65	1029, 13.71 %	N (% non-missing)	848, 82.41%	926, 89.99%					1352, 78.29 %	N (% non-missing)	1149, 84.99%	1135, 83.95%												
				Mean	19183.207	20276.659						Mean	27731.415	17390.614												
				Std. Dev	34754.753	36947.5556						Std. Dev	43843.7661	38357.5654												
				Range	(0, 211457.71)	(0, 226206.74)						Range	(0, 209645.24)	(0, 221226.55)												
				Median	2153.53	2432.59						Median	8509.48	1325.3												
				25th percentile	273.03	501.36						25th percentile	444.13	302.02												
				75th percentile	20842.82	20271.61						75th percentile	31088.59	8207.89												
				Interquartile range	20569.79	19770.25						Interquartile range	30644.46	7905.87												
				Period (Post-index vs pre-index)								1.06	1.05	1.06					0.00	Period (Post-index vs pre-index)			0.63	0.62	0.63	0.00
				Concomitant beta blocker usage (Yes vs No)								1.06	1.04	1.08					0.01	Concomitant beta blocker usage (Yes vs No)			0.99	0.95	1.02	0.02
				Concomitant loop diuretic agent usage (Yes vs No)								1.41	1.41	1.42					0.00	Concomitant loop diuretic agent usage (Yes vs No)			1.00	0.96	1.04	0.02

			Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.1 2	1.11	1.14	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.9 6	0.92	1.00	0.02
65-74	2970, 39.58 %	N (% non-missing)	2393, 80.57%	2632, 88.62%					226, 13.09 %	N (% non-missing)	194, 85.84%	201, 88.94%					
		Mean	19088.257	18060.633						Mean	25612.472	20360.968					
		Std. Dev	35391.2388	35024.2478						Std. Dev	43678.6263	45034.7787					
		Range	(0, 219366.34)	(0, 227463.86)						Range	(0, 207670.52)	(0, 226904.73)					
		Median	1970.81	1701.2						Median	2666.38	1321.24					
		25th percentile	211.12	410.02						25th percentile	340.14	386.57					
		75th percentile	21490.16	17034.94						75th percentile	30808.59	11338.88					
		Interquartile range	21279.04	16624.92						Interquartile range	30468.45	10952.31					
		Period (Post-index vs pre-index)								0.9 5	0.94	0.95					0.00
	Concomitant beta blocker usage (Yes vs No)			0.8 4	0.83	0.85	0.01	Concomitant beta blocker usage (Yes vs No)			1.4 7	1.33	1.62	0.05			
	Concomitant loop diuretic agent usage (Yes vs No)			1.0 7	1.06	1.08	0.01	Concomitant loop diuretic agent usage (Yes vs No)			0.6 2	0.55	0.69	0.06			
	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.2 7	1.26	1.28	0.00	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.3 6	1.24	1.49	0.05			
	75-84	2705, 36.05 %	N (% non-missing)	2154, 79.63%	2426, 89.69%					120, 6.95%	N (% non-missing)	102, 85%	100, 83.33%				
Mean			18827.824	17789.198	Mean						11699.497	9449.808					
Std. Dev			36069.3345	34737.0161	Std. Dev						25408.1033	20250.1445					
Range			(0, 218592.27)	(0, 225834.9)	Range						(0, 155805.91)	(0, 108256.09)					
Median			1491.18	1768.32	Median						2003.57	1392.94					
25th percentile			188.3	439.64	25th percentile						297.54	431.52					
75th percentile			20398.15	18629.8	75th percentile						11780.29	6892.4					

				Interquartile range	20209.85	18190.16						Interquartile range	11482.75	6460.88				
				Period (Post-index vs pre-index)			0.95	0.94	0.95	0.00		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.14	1.13	1.15	0.00		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.15	1.14	1.16	0.00		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.20	1.20	1.21	0.00		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA
		≥85	799, 10.65 %	N (% non-missing)	653, 81.73%	710, 88.86%					29, 1.68%	N (% non-missing)	27, 93.1%	26, 89.66%				
				Mean	15816.067	14477.894						Mean	8108.443	10027.506				
				Std. Dev	28777.1566	28987.3878						Std. Dev	15469.5839	28192.1419				
				Range	(0, 205573.34)	(0, 220439.66)						Range	(0, 76370.28)	(0, 151279.24)				
				Median	1582.24	1557.3						Median	2537.7	1421				
				25th percentile	216.34	440.22						25th percentile	910.02	569.56				
				75th percentile	19443.88	14241.18						75th percentile	6977.81	6232.32				
				Interquartile range	19227.54	13800.96						Interquartile range	6067.79	5662.76				
				Period (Post-index vs pre-index)			0.92	0.91	0.92	0.00		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.14	1.11	1.16	0.01		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			1.27	1.25	1.29	0.01		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.20	1.17	1.22	0.01		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for All-Cause Medical Costs - HFrEF Cohort

			Medicare Advantage								Commercially insured							
Characteristic	Variable	Subgroup	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
All-cause medical costs	Overall cohort		7503, 100%	N (% non-missing)	7310, 97.43%	7310, 97.43%					1727, 100%	N (% non-missing)	1668, 96.58%	1668, 96.58%				
				Mean	41328.589	37409.699						Mean	49785.939	36971.205				
				Std. Dev	50941.2907	49397.8162						Std. Dev	58780.6228	55795.7738				
				Range	(5.8, 292301.72)	(18.56, 309492.08)						Range	(17.98, 291714.53)	(84.1, 304949.88)				
				Median	20682.38	15705.33						Median	25796.25	10743.4				
				25th percentile	7357.65	5632.05						25th percentile	8784.43	3772.32				
				75th percentile	55077.92	49988.35						75th percentile	64821.81	42654.25				
				Interquartile range	47720.27	44356.3						Interquartile range	56037.38	38881.93				
				Period (Post index vs pre index)			0.89	0.85	0.93	0.02		Period (Post index vs pre index)			0.72	0.66	0.80	0.05
				Concomitant beta blocker usage (Yes vs No)			0.99	0.87	1.12	0.06		Concomitant beta blocker usage (Yes vs No)			1.17	0.90	1.53	0.13
				Concomitant loop diuretic agent usage (Yes vs No)			1.09	0.98	1.22	0.06		Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.72	1.22	0.13
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.11	1.00	1.24	0.05		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.15	0.91	1.45	0.12
All-cause medical costs	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17%	N (% non-missing)	959, 97.06%	959, 97.06%					151, 8.74%	N (% non-missing)	139, 92.05%	139, 92.05%				
				Mean	38245.803	41567.707						Mean	45926.674	34877.931				

				Std. Dev	48788.5121	55401.4503					Std. Dev	58293.4871	53165.4666													
				Range	(59.84, 287195.93)	(23.2, 300451)					Range	(176.9, 285750.79)	(84.1, 219446.9)													
				Median	18194.58	16809.99					Median	24770.6	10792.47													
				25th percentile	6691.28	5441.58					25th percentile	7750.65	2249.67													
				75th percentile	49777.21	55888.53					75th percentile	53600.95	36827.76													
				Interquartile range	43085.93	50446.95					Interquartile range	45850.3	34578.09													
				Period (Post-index vs pre-index)							1.08	0.96	1.22					0.06	Period (Post-index vs pre-index)			0.70	0.50	0.99	0.18	
				Concomitant beta blocker usage (Yes vs No)							0.84	0.58	1.22					0.19	Concomitant beta blocker usage (Yes vs No)			1.46	0.60	3.55	0.45	
				Concomitant loop diuretic agent usage (Yes vs No)							1.07	0.79	1.46					0.16	Concomitant loop diuretic agent usage (Yes vs No)			1.47	0.50	4.28	0.55	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							1.10	0.81	1.51					0.16	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.86	0.35	2.08	0.45	
		PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non-missing)	1133, 97%	1133, 97%					249, 14.42 %	N (% non-missing)	238, 95.58%	238, 95.58%												
				Mean	40230.72	41228.234						Mean	48426.718	41934.837												
				Std. Dev	48896.9906	54629.6897						Std. Dev	52181.3086	60543.6237												
				Range	(15.66, 291981.21)	(18.56, 309492.08)						Range	(30.74, 244252.36)	(198.94, 292756.05)												
				Median	20284.34	17031.9						Median	28120.12	11011.23												
				25th percentile	7095	5774.55						25th percentile	10518.19	3474.98												
				75th percentile	56068.04	54873.52						75th percentile	65728.86	58788.08												
				Interquartile range	48973.04	49098.97						Interquartile range	55210.67	55313.1												
				Period (Post-index vs pre-index)								1.01	0.91	1.13					0.06	Period (Post-index vs pre-index)			0.88	0.70	1.12	0.12

				Concomitant beta blocker usage (Yes vs No)			1.14	0.81	1.59	0.17		Concomitant beta blocker usage (Yes vs No)			1.41	0.67	2.97	0.38
				Concomitant loop diuretic agent usage (Yes vs No)			1.02	0.76	1.36	0.15		Concomitant loop diuretic agent usage (Yes vs No)			0.72	0.36	1.44	0.35
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.00	0.75	1.32	0.14		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.77	0.44	1.36	0.29
		PDC ≥ 80%	4721, 62.92 %	N (% non-missing)	4621, 97.88%	4621, 97.88%					1249, 72.32 %	N (% non-missing)	1224, 98%	1224, 98%				
				Mean	41928.841	34642.691						Mean	50644.043	35736.618				
				Std. Dev	51356.5501	45733.2527						Std. Dev	60019.2039	54199.0899				
				Range	(63.22, 292301.72)	(123.16, 293978.37)						Range	(17.98, 291714.53)	(126.44, 304949.88)				
				Median	21470.35	14779.8						Median	25582.28	10407.74				
				25th percentile	7704.64	5521.25						25th percentile	8618.02	3917.97				
				75th percentile	55135.78	45752.48						75th percentile	67128.53	37273.78				
				Interquartile range	47431.14	40231.23						Interquartile range	58510.51	33355.81				
				Period (Post-index vs pre-index)			0.80	0.76	0.85	0.03		Period (Post-index vs pre-index)			0.68	0.61	0.77	0.06
				Concomitant beta blocker usage (Yes vs No)			1.02	0.88	1.19	0.08		Concomitant beta blocker usage (Yes vs No)			1.10	0.81	1.49	0.15
				Concomitant loop diuretic agent usage (Yes vs No)			1.09	0.96	1.25	0.07		Concomitant loop diuretic agent usage (Yes vs No)			0.93	0.69	1.26	0.15
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.18	1.04	1.34	0.07		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.27	0.96	1.66	0.14
All-cause medical costs	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5 %	N (% non-missing)	3836, 97.39%	3836, 97.39%					702, 40.65 %	N (% non-missing)	677, 96.44%	677, 96.44%				
				Mean	45339.99	40588.143						Mean	52181.513	42056.81				

				Std. Dev	52799.1804	51124.3036						Std. Dev	59771.1174	59209.2066				
				Range	(5.8, 291981.21)	(123.16, 308066.64)						Range	(30.74, 291714.53)	(184.44, 278144.85)				
				Median	24441.19	18363.94						Median	27546.29	12570.61				
				25th percentile	8530.91	6550.38						25th percentile	9954.37	4425.28				
				75th percentile	62047.17	55731.27						75th percentile	67988.81	58794.36				
				Interquartile range	53516.26	49180.89						Interquartile range	58034.44	54369.08				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						
				Concomitant beta blocker usage (Yes vs No)								Concomitant beta blocker usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)								Concomitant loop diuretic agent usage (Yes vs No)						
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No diagnosis of T2DM in pre-index period	3564, 47.5 %	N (% non-missing)	3474, 97.47%	3474, 97.47%					1025, 59.35 %	N (% non-missing)	991, 96.68%	991, 96.68%				
				Mean	36899.19	33900.053						Mean	48149.407	33496.983				
				Std. Dev	48430.7327	47177.6165						Std. Dev	58067.7649	53089.4709				
				Range	(15.66, 292301.72)	(18.56, 309492.08)						Range	(17.98, 285750.79)	(84.1, 304949.88)				
				Median	17085.29	13335.3						Median	23947.62	9569.8				
				25th percentile	5994.18	4924.44						25th percentile	7808.87	3514.96				
				75th percentile	47819.34	43770.69						75th percentile	62468.61	32940.9				
				Interquartile range	41825.16	38846.25						Interquartile range	54659.74	29425.94				
				Period (Post-index vs pre-index)								Period (Post-index vs pre-index)						

				Concomitant beta blocker usage (Yes vs No)			0.86	0.72	1.03	0.09		Concomitant beta blocker usage (Yes vs No)			1.09	0.77	1.55	0.18
				Concomitant loop diuretic agent usage (Yes vs No)			1.14	0.97	1.34	0.08		Concomitant loop diuretic agent usage (Yes vs No)			1.03	0.72	1.47	0.18
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.14	0.97	1.34	0.08		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.26	0.92	1.72	0.16
All-cause medical costs	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	2799, 96.68%	2799, 96.68%					343, 19.86 %	N (% non-missing)	329, 95.92%	329, 95.92%				
				Mean	51404.106	42223.038						Mean	61938.303	40855.613				
				Std. Dev	56069.488	52544.4526						Std. Dev	63899.6431	57542.4918				
				Range	(59.84, 291961.21)	(93.38, 308023.9)						Range	(19.72, 285750.79)	(156.6, 304949.88)				
				Median	29819.03	19485.1						Median	36269.71	13640.88				
				25th percentile	10395.67	6795.74						25th percentile	15909.71	6089.05				
				75th percentile	73034.4	59570.35						75th percentile	84414.66	50935.02				
				Interquartile range	62638.73	52774.61						Interquartile range	68504.95	44845.97				
				Period (Post-index vs pre-index)			0.80	0.75	0.86	0.03		Period (Post-index vs pre-index)			0.68	0.56	0.83	0.10
				Concomitant beta blocker usage (Yes vs No)			1.11	0.90	1.37	0.11		Concomitant beta blocker usage (Yes vs No)			0.93	0.51	1.70	0.31
				Concomitant loop diuretic agent usage (Yes vs No)			1.05	0.88	1.25	0.09		Concomitant loop diuretic agent usage (Yes vs No)			0.95	0.50	1.79	0.33
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.15	0.97	1.35	0.08		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.69	0.38	1.25	0.31
				No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	4511, 97.89%	4511, 97.89%			1384, 80.14 %	N (% non-missing)	1339, 96.75%	1339, 96.75%				
				Mean	35076.899	34423.103						Mean	46800.034	36016.784				

				Std. Dev	46400.8332	47099.6412						Std. Dev	57083.7881	55338.437				
				Range	(5.8, 292301.72)	(18.56, 309492.08)						Range	(17.98, 291714.53)	(84.1, 292756.05)				
				Median	16014.27	13984.22						Median	23788.23	9881.02				
				25th percentile	5996.89	5133.43						25th percentile	7608.34	3464.91				
				75th percentile	45144.44	44888.84						75th percentile	59397.55	39900.76				
				Interquartile range	39147.55	39755.41						Interquartile range	51789.21	36435.85				
				Period (Post-index vs pre-index)			0.96	0.91	1.02	0.03		Period (Post-index vs pre-index)			0.74	0.66	0.82	0.06
				Concomitant beta blocker usage (Yes vs No)			0.96	0.82	1.12	0.08		Concomitant beta blocker usage (Yes vs No)			1.21	0.90	1.63	0.15
				Concomitant loop diuretic agent usage (Yes vs No)			1.14	0.99	1.31	0.07		Concomitant loop diuretic agent usage (Yes vs No)			0.95	0.72	1.28	0.15
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.10	0.96	1.26	0.07		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.25	0.96	1.61	0.13
All-cause medical costs	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	1242, 98.34%	1242, 98.34%					505, 29.24 %	N (% non-missing)	493, 97.62%	493, 97.62%				
				Mean	37997.999	33799.606						Mean	49654.692	30470.633				
				Std. Dev	47535.3478	43924.5189						Std. Dev	58895.8385	48262.8315				
				Range	(32, 282210.61)	(228.08, 300451)						Range	(19.72, 291714.53)	(205.12, 278144.85)				
				Median	18060.84	15563.83						Median	24263.36	8904.51				
				25th percentile	6959	5610.87						25th percentile	9185.98	3400.54				
				75th percentile	49389.06	46267.94						75th percentile	64792.9	29556.34				
				Interquartile range	42430.06	40657.07						Interquartile range	55606.92	26155.8				
				Period (Post-index vs pre-index)			0.89	0.81	0.99	0.05		Period (Post-index vs pre-index)			0.61	0.51	0.73	0.09

				Concomitant beta blocker usage (Yes vs No)			0.97	0.71	1.32	0.16		Concomitant beta blocker usage (Yes vs No)			0.87	0.54	1.39	0.24
				Concomitant loop diuretic agent usage (Yes vs No)			1.05	0.79	1.39	0.15		Concomitant loop diuretic agent usage (Yes vs No)			1.12	0.69	1.82	0.25
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.93	0.72	1.20	0.13		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.07	0.70	1.62	0.21
		Other	6240, 83.17 %	N (% non-missing)	6068, 97.24%	6068, 97.24%					1222, 70.76 %	N (% non-missing)	1175, 96.15%	1175, 96.15%				
				Mean	42010.295	38148.614						Mean	49841.008	39698.68				
				Std. Dev	51587.9264	50416.3882						Std. Dev	58757.2332	58473.3501				
				Range	(5.8, 292301.72)	(18.56, 309492.08)						Range	(17.98, 290488.63)	(84.1, 304949.88)				
				Median	21376.3	15733.87						Median	26320.09	11652.05				
				25th percentile	7446.92	5636.83						25th percentile	8614.06	3937.84				
				75th percentile	55755.66	51375.31						75th percentile	64789.78	50693.17				
				Interquartile range	48308.74	45738.48						Interquartile range	56175.72	46755.33				
				Period (Post-index vs pre-index)			0.89	0.85	0.93	0.02		Period (Post-index vs pre-index)			0.77	0.69	0.86	0.06
				Concomitant beta blocker usage (Yes vs No)			1.00	0.87	1.14	0.07		Concomitant beta blocker usage (Yes vs No)			1.30	0.95	1.79	0.16
				Concomitant loop diuretic agent usage (Yes vs No)			1.09	0.97	1.23	0.06		Concomitant loop diuretic agent usage (Yes vs No)			0.90	0.66	1.22	0.16
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.15	1.02	1.29	0.06		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.19	0.90	1.58	0.14
All-cause medical costs	Concomitant use of spironolactone	Prescription fills for spironolactone with days of	3179, 42.37 %	N (% non-missing)	3088, 97.14%	3088, 97.14%					880, 50.96 %	N (% non-missing)	849, 96.48%	849, 96.48%				
				Mean	43381.215	40428.291						Mean	50287.813	37967.964				

		supply overlapping with sacubitril/valsartan in the post-index period		Std. Dev	52060.5148	51365.413						Std. Dev	58708.7203	56503.8717													
				Range	(32, 288479.67)	(93.38, 309492.08)						Range	(19.72, 290488.63)	(84.1, 290809.03)													
				Median	22555.4	18136.32						Median	27130.76	10972.58													
				25th percentile	7962.04	6603.77						25th percentile	9954.37	3884.09													
				75th percentile	58258.09	55476.89						75th percentile	63912.31	45881.77													
				Interquartile range	50296.05	48873.12						Interquartile range	53957.94	41997.68													
				Period (Post-index vs pre-index)								0.93	0.87	0.99					0.03	Period (Post-index vs pre-index)							
				Concomitant beta blocker usage (Yes vs No)								1.04	0.87	1.25					0.09	Concomitant beta blocker usage (Yes vs No)							
				Concomitant loop diuretic agent usage (Yes vs No)								1.04	0.89	1.23					0.08	Concomitant loop diuretic agent usage (Yes vs No)							
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	4222, 97.64%	4222, 97.64%						847, 49.04 %	N (% non-missing)	819, 96.69%	819, 96.69%												
				Mean	39827.284	35201.88							Mean	49265.682	35937.935												
				Std. Dev	50059.7871	47793.1324							Std. Dev	58886.422	55067.5819												
				Range	(5.8, 292301.72)	(18.56, 308066.64)							Range	(17.98, 291714.53)	(156.6, 304949.88)												
				Median	19468	14262.65							Median	24304.66	10278.87												
				25th percentile	6961.02	5148.21							25th percentile	7519.87	3682.09												
				75th percentile	52461.44	45599.94							75th percentile	66010.66	37261												
				Interquartile range	45500.42	40451.73							Interquartile range	58490.79	33578.91												
				Period (Post-index vs pre-index)									0.87	0.82	0.92					0.03	Period (Post-index vs pre-index)			0.70	0.61	0.80	0.07

				Concomitant beta blocker usage (Yes vs No)			0.99	0.84	1.16	0.08		Concomitant beta blocker usage (Yes vs No)			1.61	1.10	2.35	0.19
				Concomitant loop diuretic agent usage (Yes vs No)			1.15	1.00	1.34	0.07		Concomitant loop diuretic agent usage (Yes vs No)			0.94	0.64	1.39	0.20
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
All-cause medical costs	Concomitant use of Sodium-glucose transporter-2 inhibitor (SGLT-2)	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237, 3.16 %	N (% non-missing)	233, 98.31%	233, 98.31%					111, 6.43 %	N (% non-missing)	109, 98.2%	109, 98.2%				
				Mean	44231.608	38891.443						Mean	48899.47	44514.448				
				Std. Dev	47388.869	49909.4117						Std. Dev	53592.576	59033.8068				
				Range	(103.24, 242266.64)	(831.14, 300451)						Range	(596.13, 234963.29)	(530.7, 273113.37)				
				Median	25283.26	20590.98						Median	26040.95	14798.81				
				25th percentile	10960.68	8385.15						25th percentile	7611.96	5909				
				75th percentile	63077	49195.38						75th percentile	77347.5	67831.78				
				Interquartile range	52116.32	40810.23						Interquartile range	69735.54	61922.78				
				Period (Post-index vs pre-index)			0.94	0.75	1.17	0.11		Period (Post-index vs pre-index)			0.98	0.71	1.37	0.17
				Concomitant beta blocker usage (Yes vs No)			0.98	0.51	1.91	0.34		Concomitant beta blocker usage (Yes vs No)			0.75	0.29	1.92	0.48
				Concomitant loop diuretic agent usage (Yes vs No)			0.63	0.36	1.11	0.29		Concomitant loop diuretic agent usage (Yes vs No)			0.60	0.24	1.46	0.46
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.70	0.43	1.15	0.25		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.76	0.33	1.77	0.43
		No prescription fills for SGLT-2 inhibitors with days of supply	7266, 96.84 %	N (% non-missing)	7077, 97.4%	7077, 97.4%					1616, 93.57 %	N (% non-missing)	1559, 96.47%	1559, 96.47%				
				Mean	41233.011	37360.915						Mean	49847.918	36443.807				

		overlapping with sacubitril/valsartan in the post-index period		Std. Dev	51054.363	49383.6884						Std. Dev	59141.6406	55543.9719												
				Range	(5.8, 292301.72)	(18.56, 309492.08)						Range	(17.98, 291714.53)	(84.1, 304949.88)												
				Median	20523.3	15563.2						Median	25787.67	10235.69												
				25th percentile	7299.72	5568.09						25th percentile	8876.14	3682.09												
				75th percentile	54909.27	50009.18						75th percentile	64135.56	40333.88												
				Interquartile range	47609.55	44441.09						Interquartile range	55259.42	36651.79												
				Period (Post-index vs pre-index)								0.89	0.85	0.93					0.02	Period (Post-index vs pre-index)			0.71	0.64	0.78	0.05
				Concomitant beta blocker usage (Yes vs No)								0.99	0.87	1.12					0.06	Concomitant beta blocker usage (Yes vs No)			1.20	0.92	1.58	0.14
				Concomitant loop diuretic agent usage (Yes vs No)								1.11	0.99	1.24					0.06	Concomitant loop diuretic agent usage (Yes vs No)			0.96	0.74	1.26	0.14
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								1.13	1.01	1.26					0.05	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.19	0.93	1.51	0.12

All-cause medical costs	Age category	<65	1029, 13.71 %	N (% non-missing)	994, 96.6%	994, 96.6%					1352, 78.29 %	N (% non-missing)	1296, 95.86%	1296, 95.86%												
				Mean	41533.825	42419.304						Mean	52049.459	36605.296												
				Std. Dev	50260.3521	54007.8484						Std. Dev	59960.5923	55311.5975												
				Range	(84.1, 285323.95)	(190.24, 300451)						Range	(17.98, 291714.53)	(84.1, 292756.05)												
				Median	22018.96	19514.95						Median	27131.53	9924.43												
				25th percentile	7325.52	6266.49						25th percentile	9418.37	3580.29												
				75th percentile	56101.8	57975.91						75th percentile	70001.28	43935.89												
				Interquartile range	48776.28	51709.42						Interquartile range	60582.91	40355.6												
				Period (Post-index vs pre-index)								1.00	0.90	1.12					0.06	Period (Post-index vs pre-index)			0.69	0.62	0.77	0.06

				Concomitant beta blocker usage (Yes vs No)			0.85	0.59	1.23	0.19		Concomitant beta blocker usage (Yes vs No)			1.04	0.78	1.39	0.15
				Concomitant loop diuretic agent usage (Yes vs No)			1.38	0.98	1.95	0.18		Concomitant loop diuretic agent usage (Yes vs No)			1.12	0.84	1.50	0.15
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.03	0.77	1.38	0.15		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.04	0.80	1.35	0.13
		65-74	2970, 39.58 %	N (% non-missing)	2878, 96.9%	2878, 96.9%					226, 13.09 %	N (% non-missing)	223, 98.67%	223, 98.67%				
				Mean	42380.536	38160.381						Mean	50945.445	42631.432				
				Std. Dev	51908.6669	50256.8991						Std. Dev	61667.8191	59583.0481				
				Range	(5.8, 291981.21)	(126.44, 309492.08)						Range	(176.9, 290488.63)	(126.44, 278144.85)				
				Median	21179.97	15188.07						Median	27546.29	14065.66				
				25th percentile	7465.49	5711.92						25th percentile	8209.43	5222.09				
				75th percentile	57908.51	52395.56						75th percentile	66573.77	59706.01				
				Interquartile range	50443.02	46683.64						Interquartile range	58364.34	54483.92				
				Period (Post-index vs pre-index)			0.89	0.83	0.95	0.04		Period (Post-index vs pre-index)			0.80	0.62	1.04	0.13
				Concomitant beta blocker usage (Yes vs No)			0.90	0.74	1.10	0.10		Concomitant beta blocker usage (Yes vs No)			1.57	0.78	3.13	0.35
				Concomitant loop diuretic agent usage (Yes vs No)			1.04	0.87	1.23	0.09		Concomitant loop diuretic agent usage (Yes vs No)			0.73	0.35	1.50	0.37
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.20	1.02	1.41	0.08		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.26	0.66	2.41	0.33
		75-84	2705, 36.05 %	N (% non-missing)	2646, 97.82%	2646, 97.82%					120, 6.95 %	N (% non-missing)	120, 100%	120, 100%				
				Mean	41923.343	36660.197						Mean	30732.087	33995.559				

				Std. Dev	52506.3901	48535.953					Std. Dev	38121.455	57561.5018													
				Range	(15.66, 292301.72)	(18.56, 308066.64)					Range	(1246.42, 230979.76)	(252.88, 304949.88)													
				Median	19874.6	15538.69					Median	15101.66	11072.71													
				25th percentile	7414.7	5565.43					25th percentile	8255.93	5062.81													
				75th percentile	54492.98	48682.98					75th percentile	39386.48	32985.66													
				Interquartile range	47078.28	43117.55					Interquartile range	31130.55	27922.85													
				Period (Post-index vs pre-index)							0.85	0.79	0.92					0.04	Period (Post-index vs pre-index)			1.06	0.73	1.56	0.19	
				Concomitant beta blocker usage (Yes vs No)							1.14	0.93	1.40					0.11	Concomitant beta blocker usage (Yes vs No)			0.44	0.07	2.70	0.92	
				Concomitant loop diuretic agent usage (Yes vs No)							1.08	0.90	1.30					0.09	Concomitant loop diuretic agent usage (Yes vs No)			0.48	0.17	1.37	0.54	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							1.06	0.89	1.27					0.09	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			2.48	0.86	7.16	0.54	
		≥85	799, 10.65 %	N (% non-missing)	792, 99.12%	792, 99.12%					29, 1.68 %	N (% non-missing)	29, 100%	29, 100%												
				Mean	35261.383	30898.553						Mean	18557.384	22111.418												
				Std. Dev	41784.8874	41760.0335						Std. Dev	16802.0646	33038.3285												
				Range	(18.56, 287570.99)	(23.2, 308023.9)						Range	(1886.64, 81879.46)	(1156.52, 165431.34)												
				Median	20286.66	14030.57						Median	15903.03	9681.35												
				25th percentile	6967.41	5192.02						25th percentile	6384.64	4328.13												
				75th percentile	48388.62	37641.68						75th percentile	26106.24	23269.07												
				Interquartile range	41421.21	32449.66						Interquartile range	19721.6	18940.94												
				Period (Post-index vs pre-index)								0.85	0.74	0.97					0.07	Period (Post-index vs pre-index)			NA	NA	NA	NA

				Concomitant beta blocker usage (Yes vs No)			102	0.72	1.43	0.17		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			119	0.90	1.58	0.14		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			107	0.77	1.49	0.17		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for All-Cause Pharmacy Costs – HFrEF Cohort

			Medicare Advantage								Commercially insured							
Characteristic	Variable	Subgroup	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error	N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
All-cause pharmacy cost	Overall cohort		7503, 100%	N (% non-missing)	7337, 97.79%	7337, 97.79%					1727, 100%	N (% non-missing)	1669, 96.64%	1669, 96.64%				
				Mean	5128.916	10102.326						Mean	4288.968	10394.466				
				Std. Dev	6506.4349	7364.2616						Std. Dev	6430.1975	7631.1771				
				Range	(3.75, 54450.7)	(1.64, 65940)						Range	(1.45, 51885.73)	(8.59, 61551.41)				
				Median	2845.6	7976.09						Median	1831.33	8203.21				
				25th percentile	947.33	5583.69						25th percentile	494.71	5850.95				
				75th percentile	6556	12308.16						75th percentile	5418.78	12132.14				
				Interquartile range	5608.67	6724.47						Interquartile range	4924.07	6281.19				
				Period (Post index vs pre index)			1.98	1.92	2.05	0.02		Period (Post index vs pre index)			2.41	2.21	2.62	0.04
				Concomitant beta blocker usage (Yes vs No)			0.97	0.88	1.08	0.05		Concomitant beta blocker usage (Yes vs No)			1.06	0.83	1.34	0.12
				Concomitant loop diuretic			0.91	0.83	0.99	0.05		Concomitant loop diuretic			1.09	0.86	1.37	0.12

				agent usage (Yes vs No)							agent usage (Yes vs No)														
				Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			1.0 3	0.95	1.12	0.04	Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)				0.9 4	0.76	1.15	0.11							
All-cause pharmacy cost	Proportion of covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non- missing)	972, 98.38%	972, 98.38%					151, 8.74 %	N (% non- missing)	144, 95.36%	144, 95.36%											
				Mean	3982.871	6591.518					Mean	2863.325	6182.284												
				Std. Dev	5392.4267	5319.0268					Std. Dev	3568.6955	5035.0284												
				Range	(5.19, 41306.26)	(716.71, 50798.06)					Range	(1.65, 17638.41)	(1587.04, 43277.3)												
				Median	1928.4	4851.52					Median	1443.43	4533.52												
				25th percentile	815.5	3424.54					25th percentile	455.27	3117.12												
				75th percentile	5077.94	7843.52					75th percentile	4168.79	7250.24												
				Interquartile range	4262.44	4418.98					Interquartile range	3713.52	4133.12												
				Period (Post- index vs pre- index)							1.6 5	1.49	1.83	0.05					Period (Post- index vs pre- index)			2.1 8	1.69	2.81	0.13
				Concomitant beta blocker usage (Yes vs No)							0.7 9	0.57	1.08	0.16					Concomitant beta blocker usage (Yes vs No)			1.0 3	0.50	2.16	0.38
				Concomitant loop diuretic agent usage (Yes vs No)							0.9 8	0.75	1.28	0.13					Concomitant loop diuretic agent usage (Yes vs No)			1.1 7	0.52	2.64	0.42
				Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)							1.2 1	0.93	1.59	0.14					Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			0.7 7	0.40	1.50	0.34
		PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non- missing)	1154, 98.8%	1154, 98.8%					249, 14.42 %	N (% non- missing)	242, 97.19%	242, 97.19%											
				Mean	4212.545	8199.975					Mean	3350.64	8415.295												
				Std. Dev	5801.2607	6108.9861					Std. Dev	4529.9725	5599.3104												
				Range	(6.56, 53063.96)	(1561.54, 62444.45)					Range	(1.45, 30972.29)	(1883.39, 53980.14)												

				Median	2289.59	6318.04						Median	1226.89	6922.09				
				25th percentile	830.43	4857.25						25th percentile	424.11	4550.75				
				75th percentile	5361.9	9208.49						75th percentile	5178.79	10361.83				
				Interquartile range	4531.47	4351.24						Interquartile range	4754.68	5811.08				
				Period (Post-index vs pre-index)			1.94	1.76	2.13	0.05	Period (Post-index vs pre-index)			2.48	2.04	3.02	0.10	
				Concomitant beta blocker usage (Yes vs No)			1.10	0.82	1.47	0.15	Concomitant beta blocker usage (Yes vs No)			1.31	0.70	2.46	0.32	
				Concomitant loop diuretic agent usage (Yes vs No)			0.83	0.65	1.07	0.13	Concomitant loop diuretic agent usage (Yes vs No)			1.04	0.58	1.85	0.30	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.15	0.90	1.46	0.12	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.91	0.56	1.46	0.24	
		PDC ≥ 80%	4721.62.92 %	N (% non-missing)	4596, 97.35%	4596, 97.35%					1249.72.32 %	N (% non-missing)	1209, 96.8%	1209, 96.8%				
				Mean	5755.066	11975.551					Mean	4631.491	11447.405					
				Std. Dev	7002.4276	7477.0653					Std. Dev	6966.0158	7889.8315					
				Range	(3.75, 54450.7)	(1765.1, 65940)					Range	(2.69, 51885.73)	(3122.4, 61551.41)					
				Median	3399.74	9979.45					Median	1902.38	9265.51					
				25th percentile	1032.79	6837.43					25th percentile	508.56	6460.51					
				75th percentile	7472.97	14109.18					75th percentile	5656.61	12951.12					
				Interquartile range	6440.18	7271.75					Interquartile range	5148.05	6490.61					
				Period (Post-index vs pre-index)			2.10	2.02	2.19	0.02	Period (Post-index vs pre-index)			2.44	2.22	2.69	0.05	
				Concomitant beta blocker usage (Yes vs No)			0.97	0.86	1.09	0.06	Concomitant beta blocker usage (Yes vs No)			1.07	0.82	1.41	0.14	

				Concomitant loop diuretic agent usage (Yes vs No)			0.92	0.83	1.02	0.05		Concomitant loop diuretic agent usage (Yes vs No)			1.06	0.82	1.38	0.13
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.99	0.89	1.09	0.05		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.97	0.76	1.24	0.12
All-cause pharmacy cost	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5 %	N (% non-missing)	3867, 98.17%	3867, 98.17%					702, 40.65 %	N (% non-missing)	679, 96.72%	679, 96.72%				
				Mean	6723.856	11752.908						Mean	6366.052	12872.721				
				Std. Dev	7489.8068	8319.9877						Std. Dev	7282.1019	8674.7408				
				Range	(4.54, 54450.7)	(210.46, 65940)						Range	(2.69, 49289.88)	(42.25, 59133.72)				
				Median	4309.8	9452.37						Median	4093.47	10693.76				
				25th percentile	1546.82	6241.51						25th percentile	1006.56	6910.58				
				75th percentile	8951.03	14775.17						75th percentile	8447.62	16281.11				
				Interquartile range	7404.21	8533.66						Interquartile range	7441.06	9370.53				
				Period (Post-index vs pre-index)			1.77	1.69	1.84	0.02		Period (Post-index vs pre-index)			2.02	1.82	2.24	0.05
				Concomitant beta blocker usage (Yes vs No)			1.04	0.90	1.19	0.07		Concomitant beta blocker usage (Yes vs No)			1.03	0.76	1.39	0.15
				Concomitant loop diuretic agent usage (Yes vs No)			0.83	0.74	0.93	0.06		Concomitant loop diuretic agent usage (Yes vs No)			1.00	0.75	1.32	0.14
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.03	0.92	1.14	0.05		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.00	0.77	1.30	0.14
		No diagnosis of T2DM in pre-index period	3564, 47.5 %	N (% non-missing)	3470, 97.36%	3470, 97.36%					1025, 59.35 %	N (% non-missing)	990, 96.59%	990, 96.59%				
				Mean	3351.5	8262.901						Mean	2864.382	8694.734				
				Std. Dev	4583.8253	5578.6387						Std. Dev	5327.9995	6286.4743				
				Range	(3.75, 53113.46)	(1.64, 60824.11)						Range	(1.45, 51885.73)	(8.59, 61551.41)				

				Median	1631.52	6878.93						Median	1110.35	7009.68														
				25th percentile	639.86	5015.69						25th percentile	391.28	5599.41														
				75th percentile	4696.01	10434.48						75th percentile	3379.67	10282.3														
				Interquartile range	4056.15	5418.79						Interquartile range	2988.39	4682.89														
				Period (Post-index vs pre-index)								2.46	2.33	2.59					0.03	Period (Post-index vs pre-index)			2.98	2.62	3.39	0.07		
				Concomitant beta blocker usage (Yes vs No)								0.96	0.83	1.11					0.07	Concomitant beta blocker usage (Yes vs No)			1.14	0.79	1.64	0.19		
				Concomitant loop diuretic agent usage (Yes vs No)								1.03	0.91	1.17					0.07	Concomitant loop diuretic agent usage (Yes vs No)			1.15	0.80	1.66	0.19		
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								1.03	0.91	1.18					0.07	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.89	0.65	1.22	0.16		
All-cause pharmacy cost	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58 %	N (% non-missing)	2837, 98%	2837, 98%					343, 19.86 %	N (% non-missing)	334, 97.38%	334, 97.38%														
				Mean	6251.75	11075.458						Mean	5913.205	11593.681														
				Std. Dev	7389.4248	8119.5275						Std. Dev	7315.3729	8216.4651														
				Range	(3.75, 54442.78)	(33.72, 62393.2)						Range	(5.83, 38665.36)	(1698.17, 58919.69)														
				Median	3925.86	8841.79						Median	3061.08	9497.24														
				25th percentile	1328.28	5884.23						25th percentile	774.4	6451.64														
				75th percentile	8145.3	13600.15						75th percentile	7630.77	13595.86														
				Interquartile range	6817.02	7715.92						Interquartile range	6856.37	7144.22														
				Period (Post-index vs pre-index)								1.79	1.70	1.89					0.03	Period (Post-index vs pre-index)				1.99	1.70	2.32	0.08	
Concomitant beta blocker usage (Yes vs No)			0.92	0.77	1.10	0.09	Concomitant beta blocker usage (Yes vs No)				0.82	0.50	1.35	0.25														

				Concomitant loop diuretic agent usage (Yes vs No)			0.85	0.74	0.99	0.07		Concomitant loop diuretic agent usage (Yes vs No)			1.15	0.69	1.91	0.26
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.04	0.91	1.20	0.07		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.84	0.51	1.38	0.26
		No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)	4500, 97.66%	4500, 97.66%					1384, 80.14 %	N (% non-missing)	1335, 96.46%	1335, 96.46%				
	Mean			4421.031	9488.82	Mean						3882.604	10094.438					
	Std. Dev			5771.6889	6774.886	Std. Dev						6124.982	7450.7036					
	Range			(4.3, 54450.7)	(1.64, 65940)	Range						(1.45, 51885.73)	(8.59, 61551.41)					
	Median			2246.39	7548.03	Median						1596.89	7900.9					
	25th percentile			804.93	5413.33	25th percentile						454.4	5723.25					
	75th percentile			5777.38	11732.32	75th percentile						4920.77	11809.38					
	Interquartile range			4972.45	6318.99	Interquartile range						4466.37	6086.13					
	Period (Post-index vs pre-index)				2.15	2.05	2.25	0.02	Period (Post-index vs pre-index)			2.56	2.32	2.82	0.05			
	Concomitant beta blocker usage (Yes vs No)				1.01	0.89	1.14	0.06	Concomitant beta blocker usage (Yes vs No)			1.11	0.85	1.47	0.14			
	Concomitant loop diuretic agent usage (Yes vs No)				0.95	0.85	1.06	0.06	Concomitant loop diuretic agent usage (Yes vs No)			1.08	0.83	1.40	0.13			
	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				1.03	0.92	1.15	0.06	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.96	0.76	1.21	0.12			
						</												

				Median	2888.27	8574.46					Median	1545.94	8201.48																									
				25th percentile	911.36	6129.13					25th percentile	356.76	5954.97																									
				75th percentile	6872.78	13220.26					75th percentile	5221.98	12046.21																									
				Interquartile range	5961.42	7091.13					Interquartile range	4865.22	6091.24																									
				Period (Post-index vs pre-index)								2.0 3	1.87					2.22	0.04	Period (Post-index vs pre-index)			2.5 1	2.14	2.94	0.08												
				Concomitant beta blocker usage (Yes vs No)								0.9 5	0.73					1.23	0.13	Concomitant beta blocker usage (Yes vs No)			1.0 1	0.66	1.54	0.22												
				Concomitant loop diuretic agent usage (Yes vs No)								0.8 9	0.70					1.12	0.12	Concomitant loop diuretic agent usage (Yes vs No)			0.9 8	0.65	1.49	0.21												
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								1.0 6	0.86					1.31	0.11	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.9 2	0.64	1.32	0.18												
				Other	6240, 83.17 %	N (% non-missing)					6096, 97.69%	6096, 97.69%									1222, 70.76 %	N (% non-missing)	1182, 96.73%	1182, 96.73%														
						Mean					5068.641	9927.338										Mean	4353.08	10446.035														
						Std. Dev					6389.5427	7258.93										Std. Dev	6427.623	7988.3256														
						Range					(3.75, 54442.78)	(1.64, 62444.45)										Range	(1.45, 51847.55)	(8.59, 61551.41)														
						Median					2837.09	7868.96										Median	1879.75	8208.51														
						25th percentile					956.69	5458.01										25th percentile	552.89	5846.71														
						75th percentile					6519	12212.21										75th percentile	5454.67	12138.76														
						Interquartile range					5562.31	6754.2										Interquartile range	4901.78	6292.05														
						Period (Post-index vs pre-index)																		1.9 7					1.90	2.05	0.02	Period (Post-index vs pre-index)			2.3 7	2.14	2.61	0.05
						Concomitant beta blocker usage (Yes vs No)																		0.9 8					0.87	1.09	0.06	Concomitant beta blocker usage (Yes vs No)			1.0 8	0.81	1.44	0.15

				Concomitant loop diuretic agent usage (Yes vs No)			0.92	0.83	1.01	0.05		Concomitant loop diuretic agent usage (Yes vs No)			1.13	0.85	1.48	0.14
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.03	0.93	1.13	0.05		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.94	0.73	1.22	0.13
All-cause pharmacy cost	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	3118, 98.08%	3118, 98.08%					880, 50.96 %	N (% non-missing)	851, 96.7%	851, 96.7%				
				Mean	5250.459	10393.612						Mean	3850.212	10218.997				
				Std. Dev	6748.2312	7613.7149						Std. Dev	5611.6513	7410.3523				
				Range	(4.54, 54442.78)	(33.72, 62444.45)						Range	(1.45, 38572.64)	(234.56, 61551.41)				
				Median	2803.93	8244.83						Median	1551.72	7994.77				
				25th percentile	944.46	5640.2						25th percentile	472.12	5810.22				
				75th percentile	6666.52	12672.14						75th percentile	5033.41	11846.06				
				Interquartile range	5722.06	7031.94						Interquartile range	4561.29	6035.84				
				Period (Post-index vs pre-index)			2.00	1.89	2.11	0.03		Period (Post-index vs pre-index)			2.65	2.36	2.97	0.06
				Concomitant beta blocker usage (Yes vs No)			1.00	0.85	1.16	0.08		Concomitant beta blocker usage (Yes vs No)			0.92	0.67	1.27	0.16
				Concomitant loop diuretic agent usage (Yes vs No)			0.92	0.80	1.05	0.07		Concomitant loop diuretic agent usage (Yes vs No)			1.09	0.81	1.46	0.15
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
		No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsar	4324, 57.63 %	N (% non-missing)	4219, 97.57%	4219, 97.57%					847, 49.04 %	N (% non-missing)	818, 96.58%	818, 96.58%				
				Mean	5039.091	9887.054						Mean	4745.424	10577.014				
				Std. Dev	6321.1055	7167.6421						Std. Dev	7158.4821	7854.7065				
				Range	(3.75, 54450.7)	(1.64, 65940)						Range	(1.65, 51885.73)	(8.59, 58919.69)				

		tan in the post-index period		Median	2874.33	7805.46						Median	2066.18	8341.93				
				25th percentile	948.56	5567.18						25th percentile	538.88	5922.41				
				75th percentile	6512.74	12145.34						75th percentile	5958.5	12351.56				
				Interquartile range	5564.18	6578.16						Interquartile range	5419.62	6429.15				
				Period (Post-index vs pre-index)			1.98	1.90	2.07	0.02		Period (Post-index vs pre-index)			2.18	1.93	2.45	0.06
				Concomitant beta blocker usage (Yes vs No)			0.96	0.84	1.09	0.07		Concomitant beta blocker usage (Yes vs No)			1.18	0.85	1.66	0.17
				Concomitant loop diuretic agent usage (Yes vs No)			0.91	0.81	1.02	0.06		Concomitant loop diuretic agent usage (Yes vs No)			1.11	0.79	1.56	0.17
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
All-cause pharmacy cost	Concomitant use of Sodium-glucose transporter-2 (SGLT-2) inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	237,316 %	N (% non-missing)	229, 96.62%	229, 96.62%					111, 6.43 %	N (% non-missing)	108, 97.3%	108, 97.3%				
				Mean	10235.989	18343.828						Mean	9748.148	18275.526				
				Std. Dev	8431.1628	10179.3042						Std. Dev	8381.0713	8832.679				
				Range	(12.48, 43731.67)	(3055.35, 62444.45)						Range	(7.43, 40175.07)	(3587.79, 50554.87)				
				Median	7701.25	16470.53						Median	7385.39	16281.11				
				25th percentile	4213.13	10728.17						25th percentile	3428.29	11529.35				
				75th percentile	14134.12	22758.54						75th percentile	14101.89	22782.49				
				Interquartile range	9920.99	12030.37						Interquartile range	10673.6	11253.14				
				Period (Post-index vs pre-index)			1.82	1.59	2.08	0.07		Period (Post-index vs pre-index)			1.90	1.56	2.31	0.10
				Concomitant beta blocker usage (Yes vs No)			0.94	0.62	1.42	0.21		Concomitant beta blocker usage (Yes vs No)			0.88	0.51	1.55	0.28

				Concomitant loop diuretic agent usage (Yes vs No)			0.81	0.58	1.13	0.17		Concomitant loop diuretic agent usage (Yes vs No)			0.98	0.58	1.66	0.27
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.07	0.79	1.44	0.15		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.98	0.60	1.61	0.25
		No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	N (% non-missing)	7108, 97.83%	7108, 97.83%					1616, 93.57 %	N (% non-missing)	1561, 96.6%	1561, 96.6%				
				Mean	4964.38	9836.807						Mean	3911.267	9849.204				
				Std. Dev	6367.8729	7099.0522						Std. Dev	6098.0357	7233.111				
				Range	(3.75, 54450.7)	(1.64, 65940)						Range	(1.45, 51885.73)	(8.59, 61551.41)				
				Median	2759.43	7802.67						Median	1600.31	7812.4				
				25th percentile	924.27	5523.97						25th percentile	468.17	5738.97				
				75th percentile	6370.68	12025.26						75th percentile	5013.3	11627.05				
				Interquartile range	5446.41	6501.29						Interquartile range	4545.13	5888.08				
				Period (Post-index vs pre-index)			2.00	1.93	2.07	0.02		Period (Post-index vs pre-index)			2.49	2.28	2.72	0.05
				Concomitant beta blocker usage (Yes vs No)			0.98	0.88	1.08	0.05		Concomitant beta blocker usage (Yes vs No)			1.08	0.84	1.39	0.13
				Concomitant loop diuretic agent usage (Yes vs No)			0.92	0.84	1.01	0.05		Concomitant loop diuretic agent usage (Yes vs No)			1.10	0.86	1.40	0.13
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.02	0.93	1.11	0.04		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.94	0.75	1.17	0.11
All-cause pharmacy cost	Age category	<65	1029, 13.71 %	N (% non-missing)	995, 96.7%	995, 96.7%					1352, 78.29 %	N (% non-missing)	1304, 96.45%	1304, 96.45%				
				Mean	7315.329	12746.596						Mean	3890.348	9966.584				
				Std. Dev	8770.8296	9950.0444						Std. Dev	6238.1867	7244.1014				
				Range	(25.24, 54450.7)	(289.68, 62444.45)						Range	(1.45, 51885.73)	(8.59, 61551.41)				

				Median	4233.24	9590.13					Median	1500.6	7641.88																							
				25th percentile	1381.79	5970.02					25th percentile	406.36	5666.27																							
				75th percentile	9717.07	16095.24					75th percentile	4892.41	11770.82																							
				Interquartile range	8335.28	10125.22					Interquartile range	4486.05	6104.55																							
				Period (Post-index vs pre-index)							1.75	1.60	1.92					0.05	Period (Post-index vs pre-index)			2.54	2.30	2.81	0.05											
				Concomitant beta blocker usage (Yes vs No)							1.08	0.78	1.49					0.17	Concomitant beta blocker usage (Yes vs No)			1.06	0.80	1.40	0.14											
				Concomitant loop diuretic agent usage (Yes vs No)							0.96	0.72	1.29					0.15	Concomitant loop diuretic agent usage (Yes vs No)			1.11	0.84	1.46	0.14											
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.92	0.72	1.18					0.13	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.91	0.71	1.16	0.12											
				65-74	2970, 39.58 %	N (% non-missing)					2903, 97.74%	2903, 97.74%									226, 13.09 %	N (% non-missing)	219, 96.9%	219, 96.9%												
						Mean					5231.381	10226.567										Mean	5794.2	12390.042												
						Std. Dev					6874.0708	7556.6507										Std. Dev	7543.5693	9327.3956												
						Range					(4.3, 53113.46)	(119.59, 65940)										Range	(5.83, 51847.55)	(1587.04, 59133.72)												
						Median					2752.31	7939.3										Median	3076.84	10186.68												
						25th percentile					895.48	5603.32										25th percentile	828.27	6865.37												
						75th percentile					6581.62	12443.12										75th percentile	7032.26	14255.46												
						Interquartile range					5686.14	6839.8										Interquartile range	6203.99	7390.09												
						Period (Post-index vs pre-index)																1.97	1.86	2.09					0.03	Period (Post-index vs pre-index)			2.07	1.68	2.54	0.11
						Concomitant beta blocker usage (Yes vs No)																0.89	0.75	1.05					0.08	Concomitant beta blocker usage (Yes vs No)			1.26	0.69	2.31	0.31

				Concomitant loop diuretic agent usage (Yes vs No)			0.95	0.82	1.10	0.07		Concomitant loop diuretic agent usage (Yes vs No)			1.16	0.64	2.08	0.30	
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.03	0.90	1.19	0.07		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.07	0.62	1.82	0.27	
75-84	2705, 36.05 %	N (% non-missing)	2650, 97.97%	2650, 97.97%					120, 6.95 %	N (% non-missing)	117, 97.5%	117, 97.5%							
		Mean	4594.575	9469.779						Mean	5905.82	11105.484							
		Std. Dev	5244.1106	6262.1226						Std. Dev	6230.6685	6528.8176							
		Range	(8.55, 52862.22)	(33.72, 62393.2)						Range	(13.52, 38572.64)	(208.47, 46622.87)							
		Median	2742.33	7818.78						Median	4169.54	9992.43							
		25th percentile	928.28	5540.77						25th percentile	1229.49	7191.7							
		75th percentile	6247.57	11849.86						75th percentile	8007.43	12668.51							
		Interquartile range	5319.29	6309.09						Interquartile range	6777.94	5476.81							
		Period (Post-index vs pre-index)			2.07	1.97	2.18	0.03	Period (Post-index vs pre-index)			1.89	1.50	2.37	0.12				
		Concomitant beta blocker usage (Yes vs No)			1.04	0.90	1.21	0.08	Concomitant beta blocker usage (Yes vs No)			0.60	0.17	2.05	0.63				
		Concomitant loop diuretic agent usage (Yes vs No)			0.87	0.76	0.99	0.07	Concomitant loop diuretic agent usage (Yes vs No)			0.97	0.51	1.82	0.32				
		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.05	0.93	1.20	0.06	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.12	0.55	2.27	0.36				
		≥85	799, 10.65 %	N (% non-missing)	789, 98.75%	789, 98.75%					29, 1.68 %	N (% non-missing)	29, 100%	29, 100%					
Mean	3789.327			8435.062	Mean	4322.853						11695.783							
Std. Dev	4666.2082			4986.3273	Std. Dev	3501.9323						11383.6774							

				Range	(3.75, 48121.49)	(1.64, 46779.38)						Range	(98.99, 15962.1)	(2469.77, 58919.69)				
				Median	2192.93	7240						Median	3539.85	7684.74				
				25th percentile	837.02	5287.61						25th percentile	1439.56	5949.53				
				75th percentile	5290.27	11013.72						75th percentile	6151.15	12139.01				
				Interquartile range	4453.25	5726.11						Interquartile range	4711.59	6189.48				
				Period (Post-index vs pre-index)			2.19	1.98	2.43	0.05		Period (Post-index vs pre-index)			NA	NA	NA	NA
				Concomitant beta blocker usage (Yes vs No)			1.05	0.81	1.36	0.13		Concomitant beta blocker usage (Yes vs No)			NA	NA	NA	NA
				Concomitant loop diuretic agent usage (Yes vs No)			0.98	0.79	1.22	0.11		Concomitant loop diuretic agent usage (Yes vs No)			NA	NA	NA	NA
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.15	0.90	1.48	0.13		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			NA	NA	NA	NA

*NA: Not applicable. Statistics not calculated due to small sample size.

Results for All-Cause Total Costs of Care – HFrEF Cohort

			Medicare Advantage								Commercially insured							
			N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation					N	Statistic	12 months pre-sacubitril/valsartan initiation	12 months post-sacubitril/valsartan initiation				
Characteristic	Variable	Subgroup			N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error			N	N	Cost ratio	95% CI Lower	95% CI Upper	Standard Error
All-cause total cost of care	Overall cohort		7503, 100%	N (% non-missing)	7340, 97.83%	7340, 97.83%					1727, 100%	N (% non-missing)	1675, 96.99%	1675, 96.99%				
				Mean	47152.243	48540.02						Mean	55051.299	48295.613				
				Std. Dev	53074.7301	52413.4574						Std. Dev	61004.1519	58603.4321				
				Range	(4.54, 307762.19)	(127.1, 324275.98)						Range	(17.98, 305289.23)	(42.25, 322582.44)				
				Median	26651.69	27213.85						Median	29822.85	22458.44				

				25th percentile	11155.11	14173.31					25th percentile	13119.78	12321.97				
				75th percentile	62973.68	64080.63					75th percentile	72434.82	59105				
				Interquartile range	51818.57	49907.32					Interquartile range	59315.04	46783.03				
				Period (Post index vs pre index)			1.02	0.98	1.06	0.02	Period (Post index vs pre index)			0.85	0.79	0.93	0.04
				Concomitant beta blocker usage (Yes vs No)			1.00	0.90	1.12	0.05	Concomitant beta blocker usage (Yes vs No)			1.16	0.93	1.46	0.11
				Concomitant loop diuretic agent usage (Yes vs No)			1.03	0.94	1.13	0.05	Concomitant loop diuretic agent usage (Yes vs No)			0.96	0.77	1.20	0.11
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.10	1.00	1.20	0.05	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.15	0.94	1.40	0.10
All-cause total cost of care	Proportion of days covered (PDC)	PDC ≥ 40% & < 60%	988, 13.17 %	N (% non-missing)	964, 97.57%	964, 97.57%					151, 8.74%	N (% non-missing)	140, 92.72%	140, 92.72%			
				Mean	42831.274	48661.498					Mean	49119.403	41043.655				
				Std. Dev	50367.1675	57750.7623					Std. Dev	59237.1243	55750.8992				
				Range	(127.6, 307699.39)	(1000.68, 316114.24)					Range	(19.87, 287390.35)	(2882.52, 284905.51)				
				Median	22812.74	24915.13					Median	27425.01	16884.41				
				25th percentile	9606.36	10824.43					25th percentile	10867.3	7395.86				
				75th percentile	56380.34	65584.32					75th percentile	59214.79	39764.56				
				Interquartile range	46773.98	54759.89					Interquartile range	48347.49	32368.7				
				Period (Post-index vs pre-index)			1.13	1.01	1.26	0.06	Period (Post-index vs pre-index)			0.79	0.58	1.08	0.16
				Concomitant beta blocker usage (Yes vs No)			0.83	0.59	1.16	0.17	Concomitant beta blocker usage (Yes vs No)			1.34	0.60	2.99	0.41
				Concomitant loop diuretic			1.07	0.81	1.42	0.14	Concomitant loop diuretic			1.33	0.51	3.43	0.48

				agent usage (Yes vs No)							agent usage (Yes vs No)								
				Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)							Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)								
PDC ≥ 60% & < 80%	1168, 15.57 %	N (% non- missing)	1141, 97.69%	1141, 97.69%					249, 14.42 %	N (% non- missing)	239, 95.98%	239, 95.98%							
		Mean	44460.434	49723.816						Mean	52345.262	49566.436							
		Std. Dev	50523.8016	57104.4281						Std. Dev	54859.3838	60642.6226							
		Range	(12.48, 303699.84)	(2528.76, 324275.98)						Range	(30.74, 251940.59)	(3504.37, 298360.12)							
		Median	24898.78	25615.12						Median	32664.05	20418.43							
		25th percentile	10311.88	12729.01						25th percentile	12857.24	10291.06							
		75th percentile	60895.56	66474.28						75th percentile	68098.78	66471.22							
		Interquartile range	50583.68	53745.27						Interquartile range	55241.54	56180.16							
		Period (Post- index vs pre- index)			1.1 1	1.01	1.23	0.05	Period (Post- index vs pre- index)				0.9 6	0.77	1.18	0.11			
		Concomitant beta blocker usage (Yes vs No)			1.1 1	0.82	1.51	0.15	Concomitant beta blocker usage (Yes vs No)				1.4 2	0.73	2.76	0.34			
		Concomitant loop diuretic agent usage (Yes vs No)			0.9 7	0.75	1.26	0.13	Concomitant loop diuretic agent usage (Yes vs No)				0.7 7	0.42	1.43	0.31			
		Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)			1.0 1	0.78	1.30	0.13	Concomitant Mineralocortic oid Receptor Antagonist usage (Yes vs No)				0.8 1	0.49	1.35	0.26			
		PDC ≥ 80%	4721, 62.92 %	N (% non- missing)	4633, 98.14%	4633, 98.14%					1249, 72.32 %	N (% non- missing)	1228, 98.32%	1228, 98.32%					
				Mean	48667.658	47974.626						Mean	56389.107	48541.016					
Std. Dev	53805.4841			49431.3852	Std. Dev	62261.3949						57447.3844							
Range	(4.78, 307762.19)			(2956.86, 321182.99)	Range	(17.98, 305289.23)						(5116.22, 322582.44)							

				Median	28503.53	27999.65						Median	30081.98	23358.49				
				25th percentile	12140.76	15648.59						25th percentile	13679.78	13495.23				
				75th percentile	64231.72	62606.74						75th percentile	75182.47	56065.47				
				Interquartile range	52090.96	46958.15						Interquartile range	61502.69	42570.24				
				Period (Post-index vs pre-index)			0.97	0.92	1.01	0.02		Period (Post-index vs pre-index)			0.83	0.76	0.92	0.05
				Concomitant beta blocker usage (Yes vs No)			1.04	0.91	1.18	0.07		Concomitant beta blocker usage (Yes vs No)			1.12	0.87	1.45	0.13
				Concomitant loop diuretic agent usage (Yes vs No)			1.02	0.91	1.14	0.06		Concomitant loop diuretic agent usage (Yes vs No)			0.95	0.74	1.22	0.13
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.14	1.03	1.27	0.06		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.25	0.99	1.57	0.12
All-cause total cost of care	Presence of Type 2 Diabetes Mellitus (T2DM)	Diagnosis of T2DM in pre-index period	3939, 52.5%	N (% non-missing)	3844, 97.59%	3844, 97.59%					702, 40.65%	N (% non-missing)	678, 96.58%	678, 96.58%				
				Mean	52767.106	53398.154						Mean	59791.809	55653.817				
				Std. Dev	54788.3349	54128.7519						Std. Dev	62255.8922	61795.6068				
				Range	(4.54, 307762.19)	(190.82, 323030.28)						Range	(30.74, 305289.23)	(42.25, 322582.44)				
				Median	32576.31	31993.63						Median	33686.02	27457.17				
				25th percentile	14479.06	16738.94						25th percentile	17626.58	15333.64				
				75th percentile	71392.49	72160.61						75th percentile	82928.46	76128.65				
				Interquartile range	56913.43	55421.67						Interquartile range	65301.88	60795.01				
				Period (Post-index vs pre-index)			1.00	0.95	1.05	0.02		Period (Post-index vs pre-index)			0.91	0.81	1.03	0.06
				Concomitant beta blocker usage (Yes vs No)			1.12	0.97	1.30	0.08		Concomitant beta blocker usage (Yes vs No)			1.32	0.94	1.85	0.17

				Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.87	1.12	0.06		Concomitant loop diuretic agent usage (Yes vs No)			0.87	0.64	1.20	0.16
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.08	0.96	1.22	0.06		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.10	0.82	1.48	0.15
		No diagnosis of T2DM in pre-index period	3564, 47.5%	N (% non-missing)	3496, 98.09%	3496, 98.09%					1025, 59.35%	N (% non-missing)	997, 97.27%	997, 97.27%				
				Mean	40978.464	43198.296						Mean	51827.562	43291.739				
				Std. Dev	50415.2046	49925.0255						Std. Dev	59955.559	55809.0532				
				Range	(4.78, 305142.13)	(127.1, 324275.98)						Range	(17.98, 297646.16)	(261.47, 318954.63)				
				Median	21213.05	22658.35						Median	27052.55	19101.01				
				25th percentile	8643.67	12169.25						25th percentile	10584.8	10705.9				
				75th percentile	51859.91	54448.48						75th percentile	67542.53	45149.03				
				Interquartile range	43216.24	42279.23						Interquartile range	56957.73	34443.13				
				Period (Post-index vs pre-index)			1.04	0.98	1.10	0.03		Period (Post-index vs pre-index)			0.81	0.72	0.90	0.06
				Concomitant beta blocker usage (Yes vs No)			0.93	0.79	1.08	0.08		Concomitant beta blocker usage (Yes vs No)			1.10	0.81	1.49	0.16
				Concomitant loop diuretic agent usage (Yes vs No)			1.10	0.95	1.26	0.07		Concomitant loop diuretic agent usage (Yes vs No)			1.03	0.75	1.40	0.16
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.11	0.97	1.28	0.07		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.18	0.90	1.55	0.14
All-cause total cost of care	Prior history of Chronic Kidney Disease (CKD)	Evidence of CKD in the pre-index period	2895, 38.58%	N (% non-missing)	2809, 97.03%	2809, 97.03%					343, 19.86%	N (% non-missing)	329, 95.92%	329, 95.92%				
				Mean	58642.999	54542.193						Mean	68620.591	52282.437				
				Std. Dev	58579.0743	55851.6599						Std. Dev	66675.7185	58708.9136				

				Range	(12.48, 307762.19)	(127.1, 323030.28)					Range	(595.8, 305289.23)	(3251.68, 316787.55)																						
				Median	37117.92	31839.11					Median	41864.02	28702.47																						
				25th percentile	16409.09	16529.25					25th percentile	21854.12	15858.31																						
				75th percentile	82215.16	73446.13					75th percentile	91348.1	66044.94																						
				Interquartile range	65806.07	56916.88					Interquartile range	69493.98	50186.63																						
				Period (Post-index vs pre-index)									Period (Post-index vs pre-index)																						
				Concomitant beta blocker usage (Yes vs No)																				Concomitant beta blocker usage (Yes vs No)											
				Concomitant loop diuretic agent usage (Yes vs No)																				Concomitant loop diuretic agent usage (Yes vs No)											
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)											
				No evidence of CKD in the pre-index period	4608, 61.42 %	N (% non-missing)					4531, 98.33%	4531, 98.33%							1384, 80.14 %	N (% non-missing)	1346, 97.25%	1346, 97.25%													
							Mean	40028.533	44818.964	Mean				51734.585	47321.121																				
							Std. Dev	47999.5486	49808.1359	Std. Dev				59090.0273	58558.1733																				
							Range	(4.54, 303699.84)	(838.36, 324275.98)	Range				(17.98, 297646.16)	(42.25, 322582.44)																				
							Median	21685.3	24468.68	Median				27449.95	21447.76																				
							25th percentile	9454	13182.29	25th percentile				11363.54	11673																				
							75th percentile	50913.9	57954.53	75th percentile				65145.29	56577.3																				
							Interquartile range	41459.9	44772.24	Interquartile range				53781.75	44904.3																				
							Period (Post-index vs pre-index)								Period (Post-index vs pre-index)																				
							Concomitant beta blocker																									Concomitant beta blocker			

				usage (Yes vs No)								usage (Yes vs No)															
				Concomitant loop diuretic agent usage (Yes vs No)			1.0 9	0.97	1.23	0.06		Concomitant loop diuretic agent usage (Yes vs No)			0.9 7	0.76	1.24	0.13									
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.0 9	0.97	1.22	0.06		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.2 1	0.97	1.51	0.11									
All-cause total cost of care	Sacubitril/valsartan dosing regimen at last prescription	97-103mg (Twice daily)	1263, 16.83 %	N (% non-missing)	1244, 98.5%	1244, 98.5%					505, 29.24 %	N (% non-missing)	494, 97.82%	494, 97.82%													
				Mean	43923.502	45354.722						Mean	54842.229	41180.721													
				Std. Dev	48734.4187	45736.4517						Std. Dev	61254.4897	51826.3982													
				Range	(48.66, 289304)	(2554.77, 308951.89)						Range	(170.09, 305289.23)	(2266.27, 322582.44)													
				Median	24781.32	28069.71						Median	28359.61	19924.43													
				25th percentile	11108.31	14891.62						25th percentile	13573.91	11262.13													
				75th percentile	58244.03	60188.93						75th percentile	72896.76	42370.05													
				Interquartile range	47135.72	45297.31						Interquartile range	59322.85	31107.92													
				Period (Post-index vs pre-index)								1.0 4	0.95	1.13					0.04	Period (Post-index vs pre-index)				0.7 5	0.64	0.88	0.08
				Concomitant beta blocker usage (Yes vs No)								0.9 7	0.75	1.25					0.13	Concomitant beta blocker usage (Yes vs No)				0.9 3	0.62	1.40	0.21
				Concomitant loop diuretic agent usage (Yes vs No)								1.0 3	0.81	1.30					0.12	Concomitant loop diuretic agent usage (Yes vs No)				1.0 4	0.69	1.57	0.21
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								0.9 4	0.76	1.16					0.11	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				1.0 5	0.73	1.49	0.18
		Other	6240, 83.17 %	N (% non-missing)	6096, 97.69%	6096, 97.69%						1222, 70.76 %	N (% non-missing)	1181, 96.64%	1181, 96.64%												
				Mean	47811.127	49190.038							Mean	55138.751	51271.698												
				Std. Dev	53897.5315	53654.2434							Std. Dev	60924.9321	60990.8936												

				Range	(4.54, 307762.19)	(127.1, 324275.98)						Range	(17.98, 297646.16)	(42.25, 318954.63)				
				Median	27055.69	27011.14						Median	30750.81	23476.1				
				25th percentile	11208.22	14058.45						25th percentile	12914.52	12778.22				
				75th percentile	63805.23	65234.76						75th percentile	72417.26	66565.7				
				Interquartile range	52597.01	51176.31						Interquartile range	59502.74	53787.48				
				Period (Post-index vs pre-index)			1.01	0.97	1.06	0.02		Period (Post-index vs pre-index)			0.90	0.81	0.99	0.05
				Concomitant beta blocker usage (Yes vs No)			1.01	0.90	1.14	0.06		Concomitant beta blocker usage (Yes vs No)			1.28	0.97	1.68	0.14
				Concomitant loop diuretic agent usage (Yes vs No)			1.03	0.93	1.14	0.05		Concomitant loop diuretic agent usage (Yes vs No)			0.93	0.71	1.21	0.13
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.13	1.02	1.25	0.05		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.20	0.95	1.53	0.12
All-cause total cost of care	Concomitant use of spironolactone	Prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	3179, 42.37 %	N (% non-missing)	3094, 97.33%	3094, 97.33%					880, 50.96 %	N (% non-missing)	852, 96.82%	852, 96.82%				
				Mean	49404.525	51690.238					Mean	55513.761	49728.056					
				Std. Dev	54175.5286	53857.1184					Std. Dev	61125.1602	60255.585					
				Range	(4.54, 307762.19)	(127.1, 322692.67)					Range	(30.74, 305289.23)	(1994.71, 322582.44)					
				Median	28985.59	30203.82					Median	31487.62	21863.72					
				25th percentile	11636.56	15641.69					25th percentile	13591.13	12362.46					
				75th percentile	67391.64	69357.31					75th percentile	70968.36	66400.73					
				Interquartile range	55755.08	53715.62					Interquartile range	57377.23	54038.27					
				Period (Post-index vs pre-index)			1.04	0.99	1.10	0.03		Period (Post-index vs pre-index)			0.90	0.80	1.01	0.06
				Concomitant beta blocker			1.05	0.90	1.23	0.08		Concomitant beta blocker			0.90	0.66	1.22	0.16

				usage (Yes vs No)								usage (Yes vs No)													
				Concomitant loop diuretic agent usage (Yes vs No)			1.00	0.87	1.15	0.07		Concomitant loop diuretic agent usage (Yes vs No)			1.04	0.78	1.39	0.15							
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)													
No prescription fills for spironolactone with days of supply overlapping with sacubitril/valsartan in the post-index period	4324, 57.63 %	N (% non-missing)	4246, 98.2%	4246, 98.2%						847, 49.04 %	N (% non-missing)	823, 97.17%	823, 97.17%												
		Mean	45511.037	46244.5							Mean	54572.541	46812.695												
		Std. Dev	52203.2304	51220.4033							Std. Dev	60912.09	56841.0989												
		Range	(4.78, 307699.39)	(190.82, 324275.98)							Range	(17.98, 297646.16)	(42.25, 316787.55)												
		Median	25206.29	25181.43							Median	28317.63	23180.47												
		25th percentile	10835.36	13324.24							25th percentile	12525.9	12190.75												
		75th percentile	59510.53	59474.07							75th percentile	74179.56	54340.97												
		Interquartile range	48675.17	46149.83							Interquartile range	61653.66	42150.22												
		Period (Post-index vs pre-index)									1.01	0.96	1.06					0.03	Period (Post-index vs pre-index)			0.82	0.73	0.92	0.06
		Concomitant beta blocker usage (Yes vs No)									1.00	0.87	1.15					0.07	Concomitant beta blocker usage (Yes vs No)			1.52	1.11	2.10	0.16
		Concomitant loop diuretic agent usage (Yes vs No)									1.07	0.95	1.22					0.06	Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.72	1.38	0.17
		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)																	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)						
AIK-cause total cost of care	Concomitant use of Sodium-glucose transporter-2 inhibitor	Prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsar	237, 3.16%	N (% non-missing)	234, 98.73%	234, 98.73%					111, 6.43%	N (% non-missing)	109, 98.2%	109, 98.2%											
			Mean	55910.904	58625.594	Mean						58921.381	63052.835												
			Std. Dev	49693.7331	54157.3856	Std. Dev						56138.9427	60925.5449												

		tan in the post-index period		Range	(12.48, 281254.37)	(6840.33, 315898.22)					Range	(3071.11, 251940.59)	(6678.67, 299324.35)															
				Median	39596.6	38692.65					Median	39757.65	34125.77															
				25th percentile	19608.07	24924.59					25th percentile	18082.29	22955.13															
				75th percentile	75427.58	74245.34					75th percentile	88047.05	89602.99															
				Interquartile range	55819.51	49320.75					Interquartile range	69964.76	66647.86															
				Period (Post-index vs pre-index)							1.10	0.93	1.31					0.09	Period (Post-index vs pre-index)			1.14	0.88	1.48	0.13			
				Concomitant beta blocker usage (Yes vs No)							1.03	0.63	1.70					0.25	Concomitant beta blocker usage (Yes vs No)			0.80	0.38	1.69	0.38			
				Concomitant loop diuretic agent usage (Yes vs No)							0.64	0.42	0.99					0.22	Concomitant loop diuretic agent usage (Yes vs No)			0.71	0.35	1.44	0.36			
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							0.81	0.55	1.18					0.19	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			0.83	0.43	1.61	0.34			
				No prescription fills for SGLT-2 inhibitors with days of supply overlapping with sacubitril/valsartan in the post-index period	7266, 96.84 %	N (% non-missing)					7106, 97.8%	7106, 97.8%									1616, 93.57 %	N (% non-missing)	1566, 96.91%	1566, 96.91%				
						Mean					46863.821	48207.903										Mean	54781.925	47268.45				
						Std. Dev					53161.1534	52325.9209										Std. Dev	61335.9525	58319.6275				
		Range	(4.54, 307762.19)			(127.1, 324275.98)	Range	(17.98, 305289.23)	(42.25, 322582.44)																			
		Median	26315.55			26717.64	Median	29702.92	21527.49																			
		25th percentile	10973.91			13966.23	25th percentile	12571.58	11867.89																			
		75th percentile	62407.72			63590.61	75th percentile	71464.82	56701.67																			
		Interquartile range	51433.81			49624.38	Interquartile range	58893.24	44833.78																			
		Period (Post-index vs pre-index)					1.01	0.98	1.05	0.02	Period (Post-index vs pre-index)				0.83	0.76	0.91					0.04						
		Concomitant beta blocker					1.00	0.90	1.12	0.06	Concomitant beta blocker				1.20	0.95	1.51					0.12						

				usage (Yes vs No)								usage (Yes vs No)														
				Concomitant loop diuretic agent usage (Yes vs No)			1.05	0.95	1.15	0.05		Concomitant loop diuretic agent usage (Yes vs No)			0.98	0.77	1.23	0.12								
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.11	1.01	1.22	0.05		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.18	0.96	1.46	0.11								
All-cause total cost of care	Age category	<65	1029, 13.71 %	N (% non-missing)	998, 96.99%	998, 96.99%					1352, 78.29 %	N (% non-missing)	1303, 96.38%	1303, 96.38%												
				Mean	49994.672	57091.553						Mean	56705.37	47231.297												
				Std. Dev	53272.3736	58392.7089						Std. Dev	62294.1481	57659.6551												
				Range	(109.34, 307699.39)	(838.36, 316114.24)						Range	(17.98, 305289.23)	(42.25, 318954.63)												
				Median	31678.72	35788.24						Median	30864.82	21527.66												
				25th percentile	12718.92	16672.15						25th percentile	13147.08	11310.75												
				75th percentile	67364.76	76303.7						75th percentile	75627.85	57256.25												
				Interquartile range	54645.84	59631.55						Interquartile range	62480.77	45945.5												
				Period (Post-index vs pre-index)								1.12	1.02	1.24					0.05	Period (Post-index vs pre-index)			0.81	0.74	0.89	0.05
				Concomitant beta blocker usage (Yes vs No)								0.94	0.69	1.28					0.16	Concomitant beta blocker usage (Yes vs No)			1.07	0.84	1.38	0.13
				Concomitant loop diuretic agent usage (Yes vs No)								1.27	0.95	1.69					0.15	Concomitant loop diuretic agent usage (Yes vs No)			1.10	0.86	1.42	0.13
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)								1.03	0.81	1.32					0.13	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.02	0.81	1.27	0.11
		65-74	2970, 39.58 %	N (% non-missing)	2890, 97.31%	2890, 97.31%					226, 13.09 %	N (% non-missing)	223, 98.67%	223, 98.67%												
				Mean	48307.551	48819.459						Mean	58456.718	56958.916												
Std. Dev	54311.8983			52109.4614	Std. Dev	63637.522						65119.124														

				Range	(4.54, 307762.19)	(1126.6, 322692.67)					Range	(297.54, 294323.46)	(3047.17, 322582.44)															
				Median	27089.1	27272.45					Median	35294.25	25472.94															
				25th percentile	11044.72	14066.84					25th percentile	12399.32	15156.85															
				75th percentile	65663.93	65547.93					75th percentile	78576.77	78656.05															
				Interquartile range	54619.21	51481.09					Interquartile range	66177.45	63499.2															
				Period (Post-index vs pre-index)							1.00	0.94	1.06					0.03	Period (Post-index vs pre-index)			0.93	0.75	1.16	0.11			
				Concomitant beta blocker usage (Yes vs No)							0.91	0.77	1.08					0.09	Concomitant beta blocker usage (Yes vs No)			1.47	0.82	2.66	0.30			
				Concomitant loop diuretic agent usage (Yes vs No)							1.02	0.88	1.18					0.08	Concomitant loop diuretic agent usage (Yes vs No)			0.77	0.42	1.43	0.31			
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)							1.18	1.02	1.36					0.07	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.35	0.78	2.34	0.28			
				75-84	2705.36.05 %	N (% non-missing)					2658, 98.26%	2658, 98.26%									120, 6.95%	N (% non-missing)	120, 100%	120, 100%				
				Mean	47069.846	47607.406					Mean	38537.11									47254.363							
				Std. Dev	54141.521	52493.6318					Std. Dev	41050.0371									59700.0858							
				Range	(12.48, 303699.84)	(127.1, 324275.98)					Range	(1259.94, 231781.34)									(5055.03, 316787.55)							
				Median	25003.62	26051.09					Median	22048.84									25344.01							
				25th percentile	11119.91	14061.74					25th percentile	13793.13									15184.57							
				75th percentile	60914.37	60656.67					75th percentile	50044.49									49483.07							
				Interquartile range	49794.46	46594.93					Interquartile range	36251.36									34298.5							
						Period (Post-index vs pre-index)							1.00					0.94	1.06	0.03	Period (Post-index vs pre-index)			1.13	0.84	1.52	0.15	
						Concomitant beta blocker							1.14					0.96	1.37	0.09	Concomitant beta blocker			0.86	0.21	3.60	0.73	

				usage (Yes vs No)								usage (Yes vs No)						
				Concomitant loop diuretic agent usage (Yes vs No)			0.99	0.84	1.16	0.08		Concomitant loop diuretic agent usage (Yes vs No)			0.65	0.28	1.50	0.43
				Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.04	0.90	1.22	0.08		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			2.92	1.27	6.73	0.43
≥85	799, 10.65 %	N (% non-missing)	794, 99.37%	794, 99.37%					29, 1.68%	N (% non-missing)	29, 100%	29, 100%						
		Mean	39650.265	39896.287						Mean	22880.237	33807.201						
		Std. Dev	43156.8564	42919.959						Std. Dev	17779.9338	33002.7991						
		Range	(24.28, 305142.13)	(1444.55, 315483.38)						Range	(5426.49, 85413.82)	(7534.67, 174785.68)						
		Median	24521.3	23607.91						Median	19558.15	20976.65						
		25th percentile	10583.85	13117.67						25th percentile	9764.15	15936.73						
		75th percentile	52721.01	48404.14						75th percentile	28300.41	35639.67						
		Interquartile range	42137.16	35286.47						Interquartile range	18536.26	19702.94						
		Period (Post-index vs pre-index)			0.98	0.88	1.10	0.06	Period (Post-index vs pre-index)				NA	NA	NA	NA		
		Concomitant beta blocker usage (Yes vs No)			1.01	0.76	1.35	0.15	Concomitant beta blocker usage (Yes vs No)				NA	NA	NA	NA		
		Concomitant loop diuretic agent usage (Yes vs No)			1.13	0.89	1.44	0.12	Concomitant loop diuretic agent usage (Yes vs No)				NA	NA	NA	NA		
		Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)			1.07	0.81	1.42	0.14	Concomitant Mineralocorticoid Receptor Antagonist usage (Yes vs No)				NA	NA	NA	NA		

*NA: Not applicable. Statistics not calculated due to small sample size.

Safety Results

No adverse event data was collected for this study. As this is a study based on secondary use of data.

Other Relevant Findings

NA

Conclusion

This retrospective study evaluated the association between sac/val utilization and HRCU and costs of care within 12 months following initiation of sac/val commercially insured and Medicare Advantage in U.S. adult patients with HFrEF and CHF. The HFrEF and CHF cohorts both exhibited significantly lower HRCU and costs of care following 12-months post-initiation of sac/val compared to 12-months prior to initiation, with consistent results across patient sub-groups including those with comorbidities and on concomitant medications. The results of this study demonstrate the clinical and economic benefits of sac/val initiation for up to 12 months, indicating an opportunity to increase utilization of sac/val in diverse patient populations.

Date of Clinical Study Report

07 February 2022