U.S. FOOD & DRUG ADMINISTRATION

Utilization of Sacubitril/Valsartan in Real-World Settings

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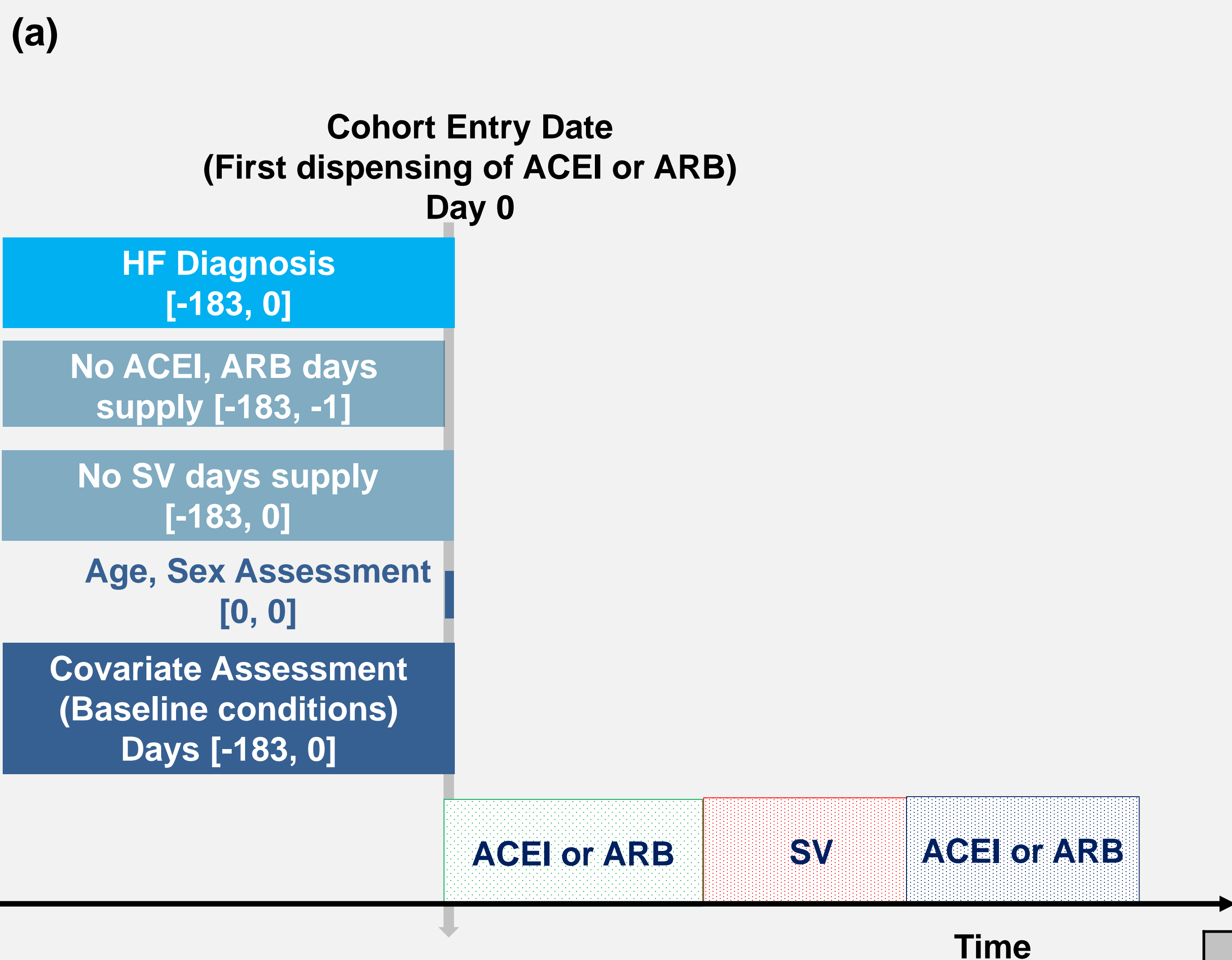
Background and Objective

- Sacubitril/Valsartan (SV) is a first-in-class angiotensin-neprilysin-receptor-inhibitor (ARNI) and angiotensin-receptor-blocker (ARB) approved for the treatment of patients with Heart Failure with Reduced Ejection Fraction (HFrEF).

- In 2016, the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on clinical practice guidelines recommended replacing use of angiotensin-converting-enzyme inhibitors (ACEI) or ARB with an ARNI for chronic symptomatic HFrEF to further reduce morbidity or mortality. Real-world utilization of SV is unknown.

- The objective of this study was to evaluate SV use among patients with heart failure (HF) and describe patient characteristics in the United States.

Methods

- Study design: retrospective new user cohort study in the Sentinel Distributed Database (January 1, 2015 to July 31, 2019)
- New user definitions used in the study:
  1. ACEI and ARB new users: each with no evidence of baseline (183 days prior to index dispensing) ACEI, ARB, or SV use
  2. New SV users: with no evidence of baseline SV use and no evidence of ACEI or ARB use
  3. SV cohorts (Figure): (a) new ACEI or ARB users switched to SV (new-ACEI-SV or new-ARB-SV switchers) (b) new SV users with prior ACEI or ARB use (ACEI-SV or ARB-SV new users)
- Statistical analysis: descriptive summary on the number of new users each month, time to switch, and patient characteristics, performed using Sentinel Query Request Package, Cohort Identification and Descriptive Analysis v8.1.1

(a)

Cohort Entry Date (First dispensing of ACEI or ARB) Day 0

| HF Diagnosis [-183, 0] |
| No ACEI, ARB days supply [-183, -1] |
| No SV days supply [-183, 0] |
| Age, Sex Assessment [0, 0] |
| Covariate Assessment (Baseline conditions) Days [-183, 0] |

ACEI or ARB — SV — ACEI or ARB

Time

(b)

Cohort Entry Date (First dispensing of SV) Day 0

| HF Diagnosis [-183, 0] |
| ACEI or ARB days supply [-183, -1] |
| No SV days supply [-183, -1] |
| ACEI (ACE-SV) or ARB Dispensing (ARB-SV) Exclusion [0, 0] |
| Age, Sex Assessment [0, 0] |
| Covariate Assessment (Baseline conditions) Days [-183, 0] |

SV — ACEI or ARB

Results

- We identified 703,848 and 318,588 new ACEI and ARB users, compared to 30,557 and 30,547 new SV users with no prior ACEI and ARB respectively; 58,141 and 41,351 ACEI-SV and ARB-SV new users; and 6,622 and 3,361 new-ACEI-SV and new-ARB-SV switchers.

- Over time, the use of SV increased in all cohorts, with the ACEI-SV new user cohort consistently being the largest: 2.4 users per 1,000 eligible members as of March 2019.

- Baseline characteristics were comparable across all SV cohorts (Table). The proportion of SV users who switched to ACEI or ARB was generally low but switching to ARB was more frequent (5.7%).

- The shortest time to switch (median [Q1-Q3]: 42 [20-99] days) was observed among new SV users who switched to ACEI.

- The longest time to switch (75 [39-169] days) was observed among new-ACEI-SV switchers who switched back to ACEI.
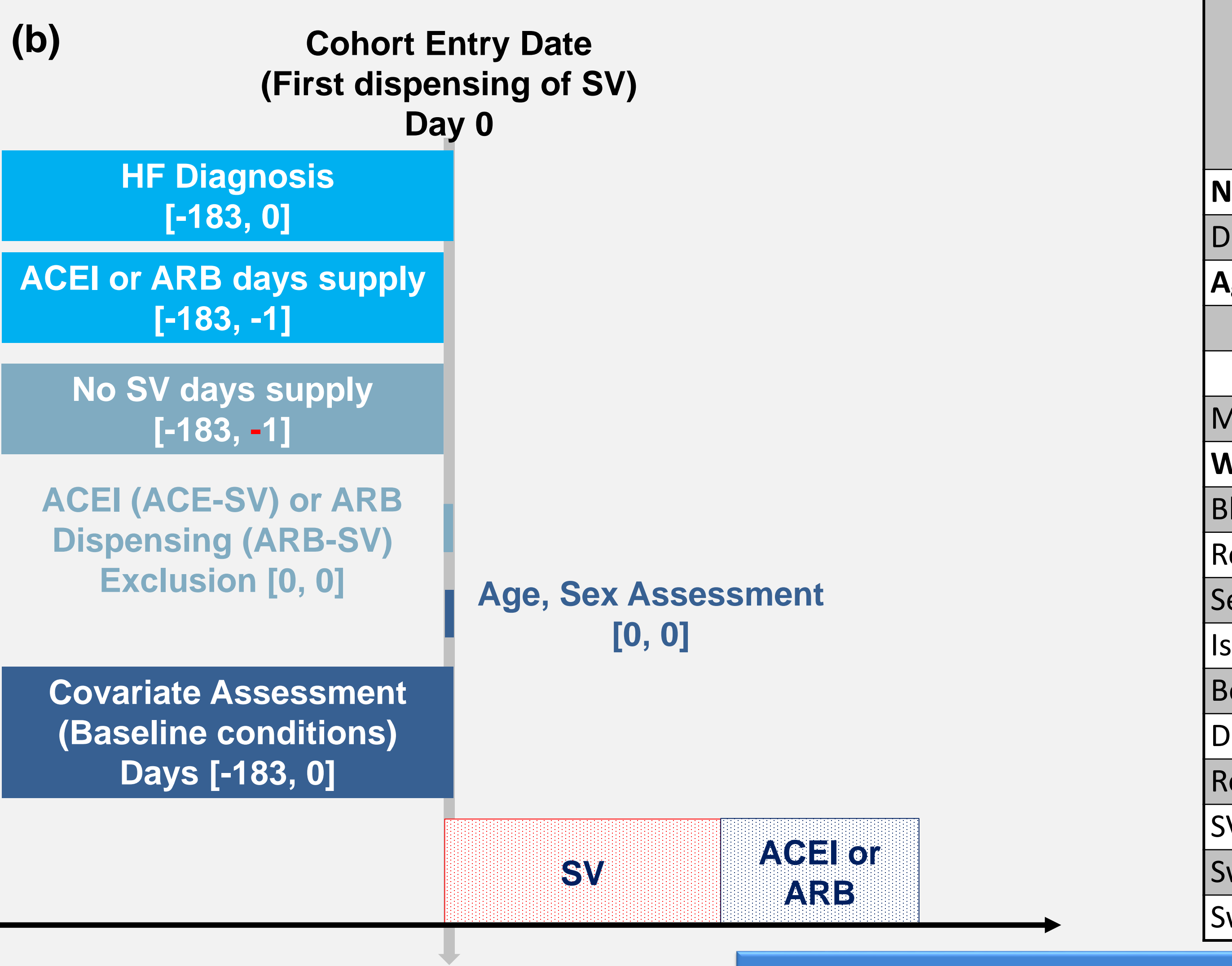
	SV Cohorts							
	ACEI-SV New Users	ARB-SV New Users	No ACEI new SV Users	No ARB new SV Users	New-ACEI-SV Switchers	New-ARB-SV Switchers	New ACEI Users	New ARB Users
Number of unique patients	58,141	41,351	30,557	30,547	6,622	3,361	703,848	318,588
Demographics, %								
Age (years), mean±std	70.1±11.2	72.3±10.8	71.9±11.8	71.9±11.8	69.0±11.8	71.3±11.5	72.6±12.7	73.8±12.1
55-64	16.4	12.5	13.4	13.4	16.1	13.6	14.3	12.1
65+	72.6	79.5	76.4	76.4	69.1	75.9	75.5	79.8
Male	69.2	61.3	64.8	64.8	66.0	60.5	50.7	44.0
White	69.7	67.7	70.5	70.5	68.2	65.9	70.9	66.6
Black or African American	13.6	14.6	13.9	13.9	10.5	13.7	13.5	16.7
Recorded History, %								
Serious allergy	11.6	13.1	13.2	13.2	12.4	14.8	15.5	15.6
Ischemic heart disease	79.2	78.6	76.7	76.7	75.7	77.5	62.4	60.6
Beta blockers	96.1	94.9	86.6	86.6	95.9	94.5	75.4	73.1
Diabetes	50.8	53.8	47.4	47.4	40.6	47.2	46.9	52.0
Renal disorders	39.6	43.5	44.9	45.0	36.5	43.5	41.3	45.8
SV Switching Patterns, %								
Switch to ACEI	4.1	--	1.9	--	3.8	0.9	--	--
Switch to ARB	--	5.7	--	2.5	2.4	5.0	--	--

Conclusions

- The use of SV for HF remains low with no impact from the recent ACC/AHA recommendation

- Low frequency of switching after SV initiation suggest high persistence to SV following new initiation of SV. Similarly high levels of persistence and compliance post-SV have been previously reported.[1]

- Barriers to utilization of SV need to be further assessed.

Funding, Disclaimer and Acknowledgements

[1]Wachter R, Fonseca AF, Balas B, et al. Real-world treatment patterns of sacubitril/valsartan: a longitudinal cohort study in Germany. *European Journal of Heart Failure.* 2019;21(5):588-597.