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Background

Existing knowledge

- Four foundational drug classes (ARNI/ACEi/ARB, evidence-based β -blocker, MRA, and SGLT2i) are recommended for all eligible patients with heart failure with reduced ejection fraction (HFrEF) and provide reductions in death and hospitalization.
- Rapid initiation of these therapies is advocated to capture early clinical benefit (often within weeks).
- Despite strong evidence and guidelines, quadruple therapy remains underused in real-world practice.

Objective

- To quantify 2020–2024 trends in prescribing and dispensing of quadruple therapy among adults with HFrEF (index LVEF 10–40%).

Methods

Data

- A subset of Truveta Data: real-world US electronic health record (EHR) data, which is aggregated, normalized, and de-identified from US health care systems comprising clinics and hospitals.
- Therapies assessed (quadruple therapy): evidence-based β -blocker (carvedilol/metoprolol succinate/bisoprolol), ACEi/ARB/ARNI, MRA, and SGLT2i.

Population

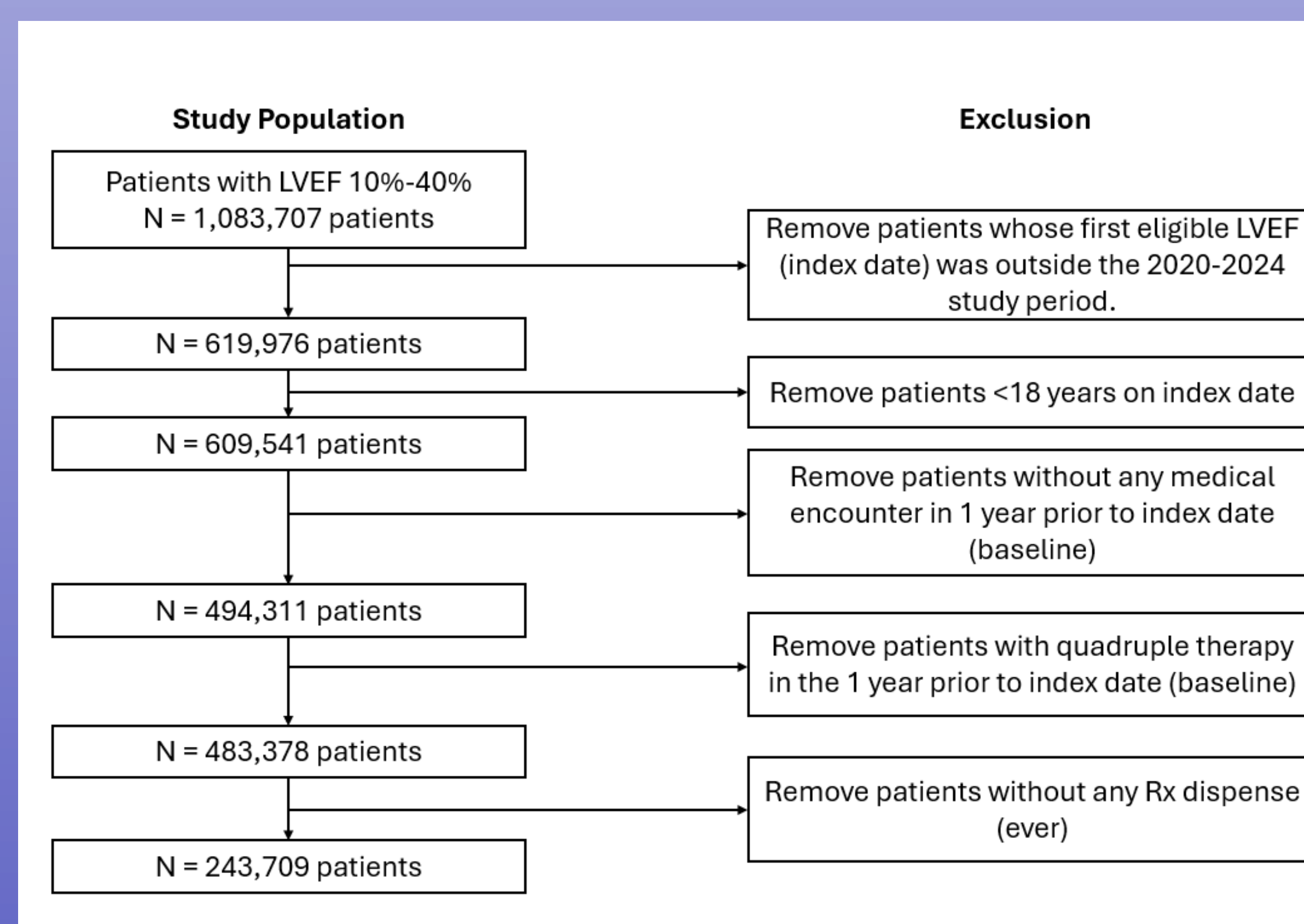
- Adults (≥ 18 years) with first qualifying LVEF (index date) of 10–40% between 2020–2024.
- **Inclusion criteria:** required ≥ 1 encounter in the year prior to the index date and ≥ 1 medication dispense ever.
- **Exclusion criteria:** prior quadruple therapy during the 1-year baseline.

Statistical Analysis

- Rapid prescribing/dispensing was defined as prescribing/dispensing of all four medication classes within 30 days of the index date.
- Annual prescribing and dispensing rates (2020–2024) were analyzed.
- Multivariable logistic regression for rapid dispensing, adjusted for age, sex, race/ethnicity, urban/rural status, BMI, LVEF group, and Elixhauser comorbidity index.

Table 1. Trends in dispensing and prescribing of quadruple therapy, N = 243,709

	2020 N = 37,656	2021 N = 46,827	2022 N = 49,039	2023 N = 54,108	2024 N = 56,079
	n (%)				
Dispensing					
Quadruple therapy initiation at follow-up					
Filled all 4 meds during first 30 days	139 (0.4%)	763 (1.6%)	2,197 (4.5%)	3,639 (6.7%)	4,528 (8.1%)
Filled all 4 meds, not during first 30 days	779 (2.1%)	2,121 (4.5%)	3,468 (7.1%)	4,416 (8.2%)	4,709 (8.4%)
Never filled all 4 meds at follow-up	36,738 (97.6%)	43,943 (93.8%)	43,374 (88.4%)	46,053 (85.1%)	46,842 (83.5%)
Filled ACE, ARB, ARNI within 30 days	16,668 (44.3%)	20,869 (44.6%)	22,394 (45.7%)	24,650 (45.6%)	25,437 (45.4%)
Filled beta blockers within 30 days	22,768 (60.5%)	28,251 (60.3%)	30,138 (61.5%)	32,800 (60.6%)	33,400 (59.6%)
Filled MRA within 30 days	5,720 (15.2%)	7,436 (15.9%)	8,651 (17.6%)	10,148 (18.8%)	11,223 (20.0%)
Filled SGLT2i within 30 days	462 (1.2%)	1,693 (3.6%)	4,587 (9.4%)	8,409 (15.5%)	10,905 (19.4%)
Prescribing					
Quadruple therapy prescribing at follow-up					
Prescribed all 4 meds during first 30 days	1,351 (3.6%)	1,865 (4%)	3,676 (7.5%)	6,029 (11.1%)	7,372 (13.1%)
Prescribed all 4 meds not during first 30 days	2,374 (6.3%)	3,803 (8.1%)	5,948 (12.1%)	7,133 (13.2%)	8,574 (15.3%)
Never prescribed all 4 meds at follow-up	33,931 (90.1%)	41,159 (87.9%)	3,9415 (80.4%)	4,0946 (75.7%)	40,133 (71.6%)
Prescribed ACE, ARB, ARNI within 30 days	18,899 (50.2%)	23,622 (50.4%)	25,071 (51.1%)	27,640 (51.1%)	28,449 (50.7%)
Prescribed beta blockers within 30 days	24,959 (66.3%)	31,122 (66.5%)	33,237 (67.8%)	36,364 (67.2%)	37,993 (67.7%)
Prescribed MRA within 30 days	8,936 (23.7%)	12,229 (26.1%)	13,172 (26.9%)	16,141 (29.8%)	18,692 (33.3%)
Prescribed SGLT2i within 30 days	2,743 (7.3%)	4,109 (8.8%)	9,725 (19.8%)	15,725 (29.1%)	19,351 (34.5%)



Results

- Adoption of quadruple therapy increased rapidly from 2020–2024
 - Prescribing increased from 3.6% \rightarrow 13.1%.
 - Dispensing increased from 0.4% \rightarrow 8.1%.
 - SGLT2i rose sharply (prescribed 7.3% \rightarrow 34.5%; dispensed 1.2% \rightarrow 19.4%). ARNI/ACEi/ARB, β -blocker, and MRA changed modestly.
 - Rapid dispensing of quadruple therapy was higher for:
 - Rural residents (compared to urban)*
 - Patients with obesity (compared to underweight)*
 - Lower LVEF*
- *(p<0.001)

Conclusions

- Rapid quadruple therapy prescribing and dispensing improved from 2020–2024, but it remains underutilized (8.1% in 2024).
- Uptake gains were driven largely by SGLT2i, with smaller changes in ARNI/ACEi/ARB, β -blocker, and MRA use.

Table 2. Multivariable logistic regression of quadruple therapy dispensing

	Filled all quadruple therapy during first 30 days		
	OR	95% CI	p-value
LVEF value on index date			
10% to 19.9%	3.70	3.47, 3.95	<0.001
20% to 29.9%	2.39	2.27, 2.52	<0.001
30% to 39.9%	1.00	—	
Age group (years) on index date			
18-34	1.00	—	
35-49	1.37	1.15, 1.63	<0.001
50-64	1.11	0.94, 1.31	0.200
65+	0.77	0.65, 0.91	0.002
Sex			
Female	1.00	—	
Male	0.94	0.90, 0.99	0.011
Unknown	4.20	0.87, 20.4	0.075
Race			
Asian	1.00	—	
Black	1.18	1.02, 1.38	0.031
White	1.03	0.89, 1.19	0.700
Other	1.18	0.99, 1.40	0.071
Unknown	1.37	1.14, 1.64	<0.001
Hispanic ethnicity			
Not Hispanic	1.00	—	
Hispanic	0.79	0.72, 0.87	<0.001
Unknown	0.81	0.69, 0.94	0.006
Urban/rural status			
Urban	1.00	—	
Rural	1.24	1.15, 1.33	<0.001
Unknown	1.08	1.01, 1.14	0.019
BMI at baseline (most recent)			
Underweight	1.00	—	
Normal weight	1.18	1.00, 1.40	0.057
Overweight	1.42	1.19, 1.68	<0.001
Obesity	1.73	1.47, 2.05	<0.001
Unknown	1.24	1.02, 1.50	0.027
Elixhauser comorbidity index			
None	1.00	—	
1-2	1.22	1.06, 1.40	0.004
3-4	1.25	1.09, 1.42	0.001
5+	1.15	1.02, 1.31	0.025

From 2020–2024, adoption of all four classes in HFrEF rose markedly, yet timely quadruple therapy prescribing and dispensing remain uncommon

