

Real-world Utilization and Treatment Patterns of Spironolactone in Patients with Hypertension

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INTRODUCTION

- Hypertension (HTN) affects nearly half of adults in the United States (US), however less than one-quarter of treated adults achieve blood pressure (BP) control. Uncontrolled HTN is associated with substantial morbidity and mortality.¹⁻⁶
- Dysregulated aldosterone is a key driver of uncontrolled and resistant HTN.⁷ Excess aldosterone may be associated with increased cardiorenal disease risk.^{8,9}
- Spironolactone, a mineralocorticoid receptor antagonist (MRA) is currently recommended for treatment of resistant HTN (rHTN); however, its use may be limited due to tolerability concerns and adverse events (AEs).¹⁰

OBJECTIVE

To describe patient characteristics, treatment patterns, time to treatment initiation, and AEs among patients with HTN initiating spironolactone.

METHODS

Study Design and Data Source

- This was a retrospective cohort study using Optum’s de-identified Market Clarity Data (Optum® Market Clarity) with an identification period from January 1, 2018, through June 30, 2025 (**Figure 1**).

Study Population and Eligibility

- Adults with an HTN ICD-10-CM code (one inpatient or two outpatient) were indexed at spironolactone initiation and required to have ≥365 days continuous pre-index medical and pharmacy enrollment.
- Patients with prior spironolactone or eplerenone use, pregnancy, secondary HTN causes (except primary aldosteronism), acne, hirsutism, or polycystic ovary syndrome during the 1-year baseline were excluded.
- A subgroup analysis was conducted among patients classified as rHTN which was restricted to patients receiving ≥3 other classes of antihypertensive therapies (AHTs) at spironolactone initiation.

Statistical Analysis

- Baseline demographics and clinical characteristics were assessed using descriptive statistics.
- Time-to-event outcomes were assessed using the Kaplan-Meier method.
 - Time to initiation was defined as time from earliest HTN diagnosis in the identification period to spironolactone initiation.
 - Time to discontinuation was defined as having a gap of >30 days from last days of supply to next prescription refill date.
- Adherence was reported among patients with ≥12 months follow-up as the number and proportion of days covered (PDC = number of days when spironolactone was available / 365 days). Patients with PDC ≥80% were considered adherent.
- AE event rates and incidence rates were reported per 100 person-years (PY). Prevalent AE event rates were calculated among all patients. AE incidence rates were calculated among patients without the corresponding AE at baseline. Exact Poisson methods were used to derive 95% CIs.

RESULTS

Baseline Demographics and Clinical Characteristics

- Of patients with HTN, 7% (3,865,090/54,302,519) received spironolactone. Of these, 1% (530,740/54,302,519) met the study inclusion criteria (**Table 1**).
- Median time from earliest HTN diagnosis to spironolactone initiation was 973 days (IQR, 407-1,573).
- Patients had a high burden of cardiometabolic comorbidities, including hyperlipidemia (71%), obesity (45%), heart failure (43%), ischemic heart disease (43%), type 2 diabetes mellitus (42%), and chronic kidney disease (25%) (**Table 2**).

Table 1: Baseline Demographics and Clinical Characteristics

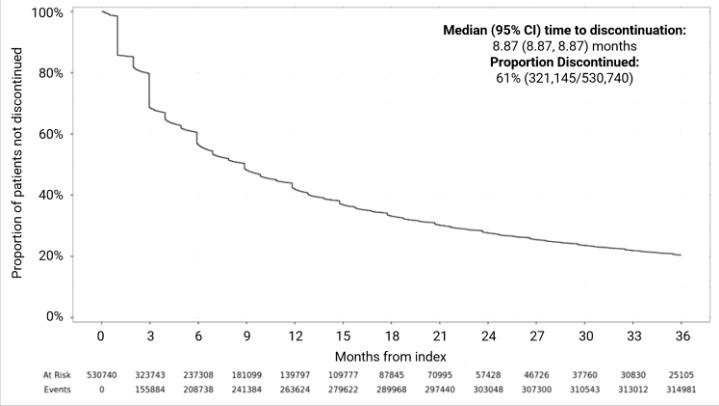
Measure	Overall N=530,740	rHTN n=139,712
Mean age, years (SD)	66 (13)	65 (13)
Female, n (%)	295,278 (56%)	67,309 (48%)
Race/ethnicity, n (%)		
White	334,945 (63%)	81,222 (58%)
Other/Unknown	91,471 (17%)	25,179 (18%)
Black	87,327 (16%)	28,777 (21%)
Asian	16,997 (3%)	4,534 (3%)
Medical coverage payor status, n (%)		
Medicare/Medicare Advantage	291,598 (55%)	70,241 (50%)
Commercial	176,666 (33%)	46,717 (33%)
Medicaid	61,286 (12%)	22,423 (16%)
Other/Missing/Unknown	1,190 (<1%)	331 (<1%)
Prescribing provider for spironolactone, n (%)		
Other or unknown	149,279 (28%)	41,688 (30%)
Primary care physician or internist	145,366 (27%)	37,295 (27%)
Cardiologist	123,446 (23%)	33,650 (24%)
Nurse practitioner or physician assistant	89,646 (17%)	21,091 (15%)
Nephrologist	19,402 (4%)	5,405 (4%)
Endocrinologist	3,601 (1%)	583 (<1%)
Time to spironolactone initiation, days		
Median (IQR)	973 (407 - 1,573)	951 (413 - 1,535)
Number of other background medication classes at spironolactone initiation, n (%)		
0	126,955 (24%)	0 (0%)
1	140,248 (26%)	0 (0%)
2	123,825 (23%)	0 (0%)
3	84,128 (16%)	84,128 (60%)
>3	55,584 (10%)	55,584 (40%)
Concurrent medications, n (%)		
ACE inhibitor	82,358 (16%)	45,585 (33%)
ARB	110,643 (21%)	59,082 (42%)
CCB - dihydropyridines	89,839 (17%)	50,377 (36%)
CCB - non-dihydropyridines	18,673 (4%)	9,087 (6.5%)
Diuretics - thiazide/thiazide-like	87,226 (16%)	46,349 (33%)
Diuretics - loop	151,673 (29%)	71,672 (51%)
Diuretics - potassium-sparing	4,930 (1%)	3,451 (3%)
Beta-blocker	212,206 (40%)	114,859 (82%)
Direct renin inhibitor	83 (<1%)	48 (<1%)
Alpha-blocker	87,136 (16%)	67,982 (49%)
Centrally acting alpha-2-agonist/other AHT	11,825 (2%)	8,318 (6%)
Direct vasodilator	23,497 (4%)	16,254 (12%)

ACE, angiotensin converting enzyme; AHT, antihypertensive; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; IQR, interquartile range; rHTN, resistant hypertension

Table 2: Baseline Comorbidities

Comorbidities, n (%)	Overall N=530,740	rHTN n=139,712
Hyperlipidemia	374,672 (71%)	102,782 (74%)
Obesity	240,534 (45%)	69,484 (50%)
Heart failure	229,604 (43%)	75,165 (54%)
Ischemic heart disease	226,024 (43%)	69,612 (50%)
Type 2 diabetes mellitus	223,001 (42%)	68,318 (49%)
Osteoarthritis	168,584 (32%)	43,059 (31%)
Anemia	154,548 (29%)	43,026 (31%)
Peripheral vascular disease	143,621 (27%)	39,481 (28%)
Atrial fibrillation	133,651 (25%)	36,385 (26%)
Chronic kidney disease	132,562 (25%)	39,950 (29%)
Obstructive sleep apnea	128,306 (24%)	36,085 (26%)
Anxiety	127,923 (24%)	33,430 (24%)
Depression	117,438 (22%)	30,055 (22%)
Myocardial infarction	95,064 (18%)	32,365 (23%)
Cerebrovascular disease	68,685 (13%)	20,248 (14%)
Non-alcoholic fatty liver disease	32,709 (6%)	8,459 (6%)
Dementia	29,468 (6%)	7,683 (6%)
Transient ischemic attack	15,736 (3%)	4,559 (3%)
Any malignancy (excluding skin neoplasm)	11,435 (2%)	2,692 (2%)

Figure 2: TTD



Time to Discontinuation (TTD)

- 61% discontinued spironolactone during follow-up, with a median TTD of 8.87 months (**Figure 2**).
- By 36 months, 80% of patients discontinued spironolactone.
- TTD was similar among the rHTN subgroup.

Adherence

- Among patients with sufficient follow-up, 50% were nonadherent at 12 months (**Table 3**).
- Nonadherence was similar among the rHTN subgroup.

Table 3: Adherence

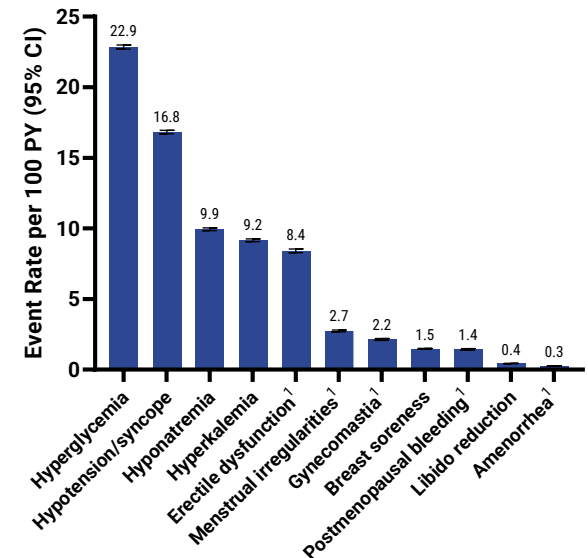
Measure	Overall N=530,740
Patients with 12+ mo. follow-up	334,478
Days covered at 12 mo.	
Mean (SD)	244.15 (124.33)
Proportion of Days Covered at 12 mo.	
Mean (SD)	0.67 (0.34)
Adherent at 12 mo., n (%)	168,360 (50%)

Mo., months; rHTN, resistant hypertension

Adverse Events (AEs)

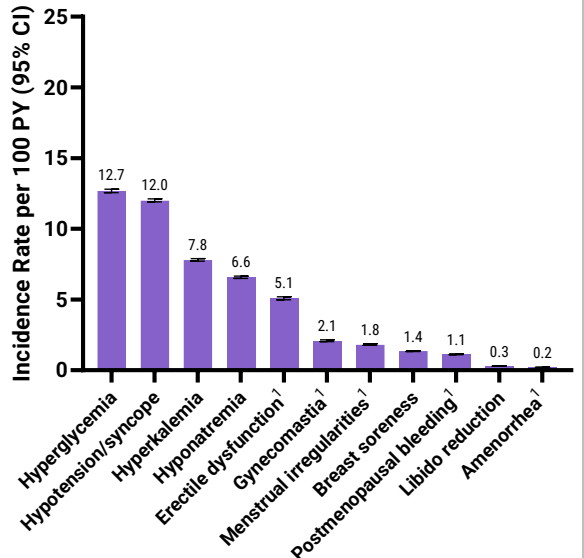
- AE rates for prevalent AEs (**Figure 3**) and incident AEs (**Figure 4**) were highest for hyperglycemia, hypotension or syncope, hyperkalemia, and hyponatremia.
- AE rates were similar among the rHTN subgroup.

Figure 3: Prevalent AEs



¹Sex-specific denominators were used given the conditions were sex-specific.

Figure 4: Incident AEs



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Limitations

- In claims/electronic health record data the reasons for spironolactone discontinuation cannot be directly ascertained. However, the occurrence of AEs can serve as a proxy to contextualize discontinuation patterns, given that treatment-emergent AEs can contribute to treatment discontinuation in clinical practice.
- AEs may be subject to underdiagnosis or under-coding, resulting in missed cases and lower rates than observed in clinical trials.¹¹

CONCLUSIONS

- In this real-world cohort of US adults with hypertension, spironolactone was infrequently initiated and often after prolonged periods following hypertension diagnosis.
- Use of spironolactone was also characterized by high rates of nonadherence, discontinuation, and AEs.
- This potentially delayed treatment intensification may in part be due to clinical inertia and/or tolerability concerns with spironolactone. Delaying treatment may increase time spent outside BP target range and may increase risk for cardiovascular and cardiorenal events.
- Together these results highlight an unmet need for novel, well-tolerated therapies targeting aldosterone which may support earlier intervention for patients with uncontrolled and resistant hypertension.

Disclosures

FR: Reports receiving consulting fees from Bristol Myers Squibb, Cytokinetics, AstraZeneca, Mineralys Therapeutics, Idorsia, Medtronic, and ReCor Medical.

SK, TW, AC, and AD: Employees of Genesis Research Group, which received funding from Mineralys Therapeutics.

KS: Employee of Mineralys Therapeutics.

JML: Reports receiving consulting fees from Mineralys Therapeutics, Idorsia, Corcept, and Novo Nordisk.



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