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ORIGINAL RESEARCH ARTICLE

Real-World Predictors and Patterns of Timely Antihypertensive Treatment Escalation in the United States: A Nationwide Analysis

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Abstract

Background: Hypertension is a leading cause of cardiovascular disease. Despite effective treatments, the burden of hypertension persists. Timely treatment escalation is recommended to achieve blood pressure targets and reduce long-term risks. This study aimed to describe antihypertensive treatment patterns and determine factors associated with timely versus delayed treatment escalation.

Methods: This study was a retrospective, observational secondary data analysis using administrative claims from the Inovalon MORE2 Registry® of Closed Claims and 100% Medicare Fee-for-Service (FFS) databases from 1/1/2019 to 11/30/2022 (Medicare FFS), or 2/28/2024 (MORE2). Eligible patients had ≥ 1 primary inpatient or ≥ 2 outpatient claims with a diagnosis of hypertension (first observed diagnosis = index date), were ≥ 18 years of age, and had ≥ 12 months of continuous database enrollment prior to and ≥ 30 days following the index date. Treatment pattern measures included prescriber specialty, use of combination therapy, antihypertensive class, and timely treatment escalation, defined as escalation to a subsequent line of therapy (LoT) within 3 months. Cardiovascular-Kidney-Metabolic stages were also measured. Logistic regression models were used to evaluate predictors of timely versus delayed treatment escalation to a subsequent LoT, and odds ratios (OR) and 95% confidence intervals (CI) were reported.

Results: The sample (N=19,060,253) were majority female (56.0%) with mean (SD) age of 66.8 (15.3). Antihypertensive medications were predominantly prescribed by primary care providers (71.6%-67.7%) across all LoTs. Use of fixed-dose combinations was low and decreased in subsequent LoTs (14.4% to 9.4%). Of patients with a second LoT, 39.4% and 60.6% LoT experienced timely and delayed treatment escalation, respectively. Real-world predictors of timely escalation within 3 months included primary aldosteronism (OR=1.68, 95% CI 1.62-1.76), cardiovascular disease (OR=1.44, 95% CI 1.44-1.45), age ≥65 years (OR=1.33 95% CI 1.33-1.34), and chronic kidney disease (OR=1.27, 95% CI 1.26-1.27). Predictors of delayed escalation included receipt of angiotensin-converting enzyme inhibitors (OR=0.46, 95% CI 0.46-0.46) or angiotensin receptor blockers (OR=0.56, 95% CI 0.56-0.56).

Conclusions: Many patients experienced treatment escalation more than 3 months after initial therapy, suggesting delayed time to antihypertensive treatment intensification relative to guideline recommendations. Real-world predictors of timely treatment escalation of antihypertensives included primary aldosteronism, cardiovascular disease, chronic kidney disease, and older age. These findings highlight potential gaps in the management of hypertension and opportunities to improve alignment between clinical practice and hypertension treatment guidelines.

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Abbreviations

ACC/AHA: American College of Cardiology/American Heart Association; ACE: Angiotensin-Converting Enzyme; ARB: Angiotensin Receptor Blocker; CCB: Calcium Channel Blocker; CKD: Chronic Kidney Disease; CKM: Cardiovascular-Kidney-Metabolic; CMS: Centers for Medicare & Medicaid Services; CI: Confidence Interval; ECI: Elixhauser Comorbidity Index; FFS: Fee-for-Service; HIPAA: Health Insurance Portability and Accountability Act; ICD-10-CM: International Classification of Diseases, Tenth Revision, Clinical Modification; LoT: Line of Therapy; OR: Odds Ratio

Introduction

The 2025 updates to the American College of Cardiology/American Heart Association (ACC/AHA) clinical guidelines for the prevention, detection, evaluation and management of high blood pressure place greater emphasis on early intervention with lifestyle modification and treatment for all levels of high blood pressure, cognitive protection associated with blood pressure control, and consistent use of guideline-recommended first-line antihypertensive therapies [1]. Importantly, these updates highlight persistent gaps in routine clinical practice, which may limit the population-level impact of guideline-directed hypertension management. With the release of new treatment guidelines, it is timely to revisit the evidence surrounding treatment escalation, especially given the significant clinical burden of hypertension that persists despite available therapeutic options [2,3].

First-line antihypertensive therapies used to manage hypertension include angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), dihydropyridine calcium channel blockers (CCBs), and thiazide diuretics [1]. Additional antihypertensive medication classes are recommended based on an individual's comorbidity profile [1]. Despite robust evidence supporting guideline-recommended first-line antihypertensive therapies, prescribing patterns continue to diverge from these recommendations [4,5]. Thiazide diuretics remain underutilized despite clinical trials and real-world studies demonstrating their effectiveness in improving cardiovascular outcomes relative to newer therapeutics [6,7]. Many patients with hypertension require two or more medications from different classes to achieve blood pressure targets [8,9], and some may experience resistant or refractory hypertension requiring three to five or more antihypertensive medications [10-13].

According to 2025 ACC/AHA guidelines, patients with elevated blood pressure should have their antihypertensive treatment regimens reassessed every 3 to 6 months, with any treatment change re-evaluated after 1 month.1 For patients who require treatment escalation, timely escalation can improve health outcomes, whereas undertreatment may exacerbate clinical burden. Although inadequate adherence has consistently posed a barrier to achieving blood pressure control [14], studies demonstrate that treatment escalation can improve blood pressure management and reduce cardiovascular risk even when adherence is suboptimal [15,16]. Prior research has shown that following treatment escalation, blood pressure control did not significantly differ between patients with the highest adherence and those with lower adherence levels [15].

For providers, clinical inertia, defined as the difficulty providers encounter when they initiate or intensify antihypertensive treatment according to guidelines recommendations [17,18], may further impede appropriate treatment escalation for patients whose hypertension is not adequately managed with first-line therapies [19]. A global qualitative study examining barriers to guideline-concordant hypertension care found that providers often reported difficulties managing subgroups of patients perceived as less able to follow recommendations, whether due to unwillingness, low health literacy, or barriers to affording recommended treatment [20]. These perceptions may contribute to clinical inertia and result in delays in appropriate treatment escalation.

Achieving and maintaining blood pressure control remains burdensome for patients, providers, and the healthcare system. Persistent variability in antihypertensive treatment patterns and delays in treatment escalation contribute to widening disparities in hypertension outcomes [20-22]. Nationally, appropriate treatment intensification following an above-target blood pressure reading remains low and has declined in recent years [23,24]. Despite these concerning trends, limited real-world evidence exists on the contemporary predictors of timely treatment escalation, particularly in a large, heterogeneous patient population. Therefore, this real-world analysis aimed to describe the patterns of antihypertensive treatment escalation, defined as progression to the next line of therapy (LoT), and identify factors associated with timely escalation to a subsequent LoT within 3 months compared to delayed escalation occurring after 3 months among adults diagnosed with hypertension.

Methods

Study design and data sources

The Breakthrough Patient Journey Study was a non-interventional, retrospective study that utilized administrative claims from the Inovalon MORE2 Registry® of Closed Claims and the 100% Medicare Fee-for-Service (FFS) databases. The MORE2 Registry® contains claims from all 50 states and is sourced from over 160 health plans, including patients with

commercial, Managed Medicaid, and Medicare Advantage insurance coverage. The 100% Medicare FFS database contains enrollment information and claims for Parts A, B, and Part D Prescription Drug Event data for all Part D plans. The study period began January 1, 2019 and ended on December 31, 2022 among patients appearing in the 100% Medicare FFS database, and on March 31, 2024 among patients appearing in the MORE2 Registry®. The study index date was defined as the first observed diagnosis of hypertension during the study period (Supplemental Figure 1).

These databases are de-identified and in compliance with the confidentiality requirements outlined in the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Therefore, this study was exempt from Institutional Review Board review and the patient consent process.

Study population

Patients at least 18 years of age with (i) ≥ 1 inpatient visit with a primary diagnosis of hypertension or ≥ 2 outpatient visits (> 30 days apart) with an International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) diagnosis code for hypertension in any position of the claim (earliest claim = index date; Supplemental Table 1), and (ii) ≥ 12 months continuous enrolment preceding and ≥ 30 days following the index date were included in the study. LoTs were defined as the first antihypertensive medication class(es) dispensed on or following the index date and continued until initiation of a new treatment or all medications were discontinued. Discontinuation was operationally defined as an absence of pharmacy claims for ≥ 90 days. Dose modifications or substitutions within the same class medication class did not constitute a new LoT. A maximum of four LoTs were examined.

The overall study population was included in a descriptive analysis of demographics, baseline clinical characteristics, and treatment patterns. Patients who escalated from LoT1 to LoT2 were included in an escalation subgroup used for multivariable analysis of predictors of timely versus delayed treatment escalation.

Variables

Demographic variables included age, sex, race/ethnicity, census region, Area Deprivation Index, and payer type. The Area Deprivation Index is a measure of socioeconomic deprivation incorporating indicators of income, education, employment, and housing quality, with percentile rankings from 1 to 100, where higher values represent greater deprivation [25]. Clinical characteristics measured during the 12-month baseline period included general comorbidities, Cardiovascular-Kidney-Metabolic (CKM) stage, which was hierarchical and mutually exclusive [26], and the Elixhauser Comorbidity Index (ECI).

Treatment pattern variables included prescribing specialist, use of fixed-dose and free-dose combination therapy, receipt of ACC/AHA guideline recommended treatments (i.e., ACE inhibitors, ARBs, dihydropyridine CCBs, and thiazide diuretics), duration of time between LoTs, and treatment escalation. Prescribing specialists included primary care providers (primary care physicians, nurse practitioners, or physician assistants), cardiologists, nephrologists, endocrinologists, and infectious disease specialists. Treatment escalation from LoT1 to LoT2 within 3 months was classified as "timely", and escalation > 3 months after LoT1 initiation was classified as "delayed".

Statistical analysis

Descriptive statistics included means, medians, and standard deviations for continuous variables and frequencies and percentages for binary or categorical variables. Multivariable logistic regression models were used to identify predictors of timely (versus delayed) treatment escalation among patients who escalated to LoT2. Covariates included demographic variables (age group, sex, race/ethnicity, payer type, index year), baseline clinical conditions (complicated hypertension, renal failure, valvular disease, atrial fibrillation, heart failure, primary aldosteronism, renal artery stenosis, type 2 diabetes, arrythmias, coronary artery stenosis, hyperlipidemia, ischemic heart disease), baseline medication use (anticoagulants, antidiabetics, lipid lowering agents), antihypertensive medication classes (ACE inhibitors, ARBs, CCBs, beta blockers), and number of antihypertensive medication classes (monotherapy versus combination therapy with 2, 3, or ≥4 classes). For each covariate, odds ratio (OR) and 95% confidence interval (CI) was reported.

Sensitivity analyses were conducted with analogous models among (i) patients who escalated from LoT2 to LoT3 and from LoT3 to LoT4, (ii) patients who escalated within 6 months, and (iii) patients who escalated to combination therapy.

Results

Patient characteristics

A total of 19,060,253 patients with hypertension were identified for the analysis (Figure 1). Mean (SD) age was 66.8 (15.3) years, and the majority were White (60.6%), female (55.3%), Medicare beneficiaries (61.0%), and lived in urban areas (78.2%) (Table 1). The distribution of the overall study population was balanced across quartiles of the Area Deprivation Index, with a mean (SD) of 49.9 (26.1). Metabolic clinical conditions were common: 29.7% had type 2 diabetes, 9.3% had heart failure, 11.1% had chronic kidney disease, and nearly one fifth had an obesity diagnosis. A majority of patients (62.5%) were classified as CKM Stage 2 (metabolic risk factors or chronic kidney disease), an additional 12.8% were Stage 3 (subclinical cardiovascular disease in

Table 1: Demographic and baseline clinical characteristics of overall study population.

	66.8 (15.3)
Median (IQR)	69.0 (20.0)
Sex, n (%)	
Female	10,543,525 (55.3%)
Race/Ethnicity, n (%)	
White	11,545,196 (60.6%)
Black or African American	2,145,639 (11.3%)
Asian, Native Hawaiian, or Other Pacific Islander	616,230 (3.2%)
Hispanic or Latino	1,207,075 (6.3%)
Unknown	3,546,113 (18.6%)
Census region, n (%)	
Northeast	3,607,879 (18.9%)
Midwest	4,397,059 (23.1%)
South	7,172,552 (37.6%)
West	3,761,622 (19.7%)
U.S. Territory/Unknown	121,141 (0.6%)
Urbanicity, n (%)	
Urban	14,900,276 (78.2%)
Rural	3,390,354 (17.8%)
Unknown	769,623 (4.0%)
Area Deprivation Index,* mean (SD)	49.9 (26.1)
Lowest (least deprived) quartile	4,011,123 (21.0%)
Second quartile	5,267,057 (27.6%)
Third quartile	5,425,696 (28.5%)
Highest (most deprived) quartile	3,696,110 (19.4%)
Unknown	660,267 (3.5%)
Payer type, n (%)	
Medicare †	11,624,296 (61.0%)
Commercial	4,240,310 (22.2%)
Managed Medicaid	3,195,647 (16.8%)
Elixhauser Comorbidity Index (ECI), mean (SD)	3.7 (7.4)
Median (IQR)	0.0 (6.0)
Metabolic clinical conditions, n (%)	
Type 2 Diabetes	5,669,483 (29.7%)
Obesity	3,351,741 (17.6%)
BMI Diagnosis Codes >30	3,604,148 (18.9%)
Non-alcoholic fatty liver disease	439,196 (2.3%)
Cardiorenal clinical conditions, n (%)	
Atrial fibrillation	1,896,916 (10.0%)
Stroke	650,283 (3.4%)
Myocardial infarction	869,888 (4.6%)
Heart failure	1,768,552 (9.3%)
Chronic kidney disease	2,118,858 (11.1%)
CKM stages, n (%)	
Stage 0 (no CKM risk factors)‡	0 (0.0%)
Stage 1 (excess and/or dysfunctional adiposity)§	0 (0.0%)
Stage 2 (metabolic risk factors or CKD)‖	11,912,451 (62.5%)
Stage 3 (subclinical CVD in CKM)¶	2,441,262 (12.8%)
Stage 4 (clinical CVD in CKM)#	4,706,540 (24.7%)
Months of follow-up, mean (SD)	31.1 (17.2)
Median (IQR)	32.3 (31.6)

BMI: Body Mass Index; CKM: Cardiovascular, Kidney, Metabolic; CVD: Cardiovascular Disease; IQR: Interquartile Range; SD: Standard Deviation; U.S.: United States

*Area Deprivation Index is a measure of socioeconomic deprivation that includes factors for the domains of income, education, employment, and housing quality. Percentile rankings range from 1 to 100, with higher values indicating higher levels of deprivation.

† Includes the combined Medicare Fee-for-Service and Medicare Advantage populations.

‡ No diagnosis of any of the following: obesity, BMI diagnosis codes > 30, type 2 diabetes, hyperlipidemia, hypertension, metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), chronic kidney disease (CKD), cardiovascular disease (CVD), ischemic heart disease, coronary artery disease, peripheral vascular disease, valvular disease.

§ Diagnosis of obesity or BMI diagnosis codes > 30 and no diagnosis of any of the following: type 2 diabetes, hyperlipidemia, hypertension, metabolic syndrome, NAFLD, CKD, CVD, ischemic heart disease, coronary artery disease, peripheral vascular disease, valvular disease.

‖ Diagnosis of type 2 diabetes, hyperlipidemia, hypertension, metabolic syndrome, NAFLD, CKD and no diagnosis of any of following: CVD, ischemic heart disease, coronary artery disease, peripheral vascular disease, valvular disease.

¶ Diagnosis of ischemic heart disease, coronary artery disease, peripheral vascular disease, valvular disease and no diagnosis of CVD.

Diagnosis of heart failure, myocardial infarction, stroke, atrial fibrillation, arrhythmia.

CKM), and 24.7% were Stage 4 (clinical cardiovascular disease in CKM). Mean (SD) follow-up time was 31.1 (17.2) months, indicating that treatment patterns were observed over more than two and a half years.

Treatment patterns

A total of 17,077,696 patients (89.6%) received at least one antihypertensive treatment LoT, and the mean (SD) time from diagnosis to first LoT was 1.8 (4.7) months (Figure 2). Approximately half (51.0%; N = 9,724,029) escalated to LoT2, on average 15.0 (15.1) months after initiating LoT1. One-third (33.1%; N = 6,317,768) escalated to LoT3 9.0 (11.4) months after LoT2, and 23.0% (N = 4,378,963) escalated to LoT4 7.3 (9.9) months after LoT3 (Figure 2). Patients progressing to a third or fourth LoT escalated more rapidly through treatments compared to the overall sample (Supplemental Table 2).

Antihypertensive medications were predominantly prescribed by primary care providers (71.6%-67.7% across all LoTs), primarily primary care physicians (54.5%-51.1%), followed by nurse practitioners and physician assistants (17.1%-16.7%) (Table 2). Cardiologists were the next most common prescriber type, and cardiologist prescribing increased from 9.2% at LoT1 to 15.0% at LoT4. Overall, the percentage of patients receiving combination therapy (≥ 2 antihypertensive classes) increased from 46.9% at LoT1 to 57.2% at LoT4. Use of fixed-dose combinations decreased (14.4% to 9.4%), while free-dosing combinations increased (32.6% to 47.7%) (Table 2).

As patients progressed through LoTs, the proportion receiving at least one guideline-recommended antihypertensive class (i.e., ACE inhibitors, ARBs, dihydropyridine CCBs, or thiazides) decreased slightly from 79.2% during LoT1 to 72.7% during LoT4 (Table 2). During LoT1, when guideline-concordant treatment was highest, only 36.1% of patients on monotherapy received one of the four recommended classes. Among those on two-class combination therapy in LoT1, 47.9% received two of the four recommended classes. Among

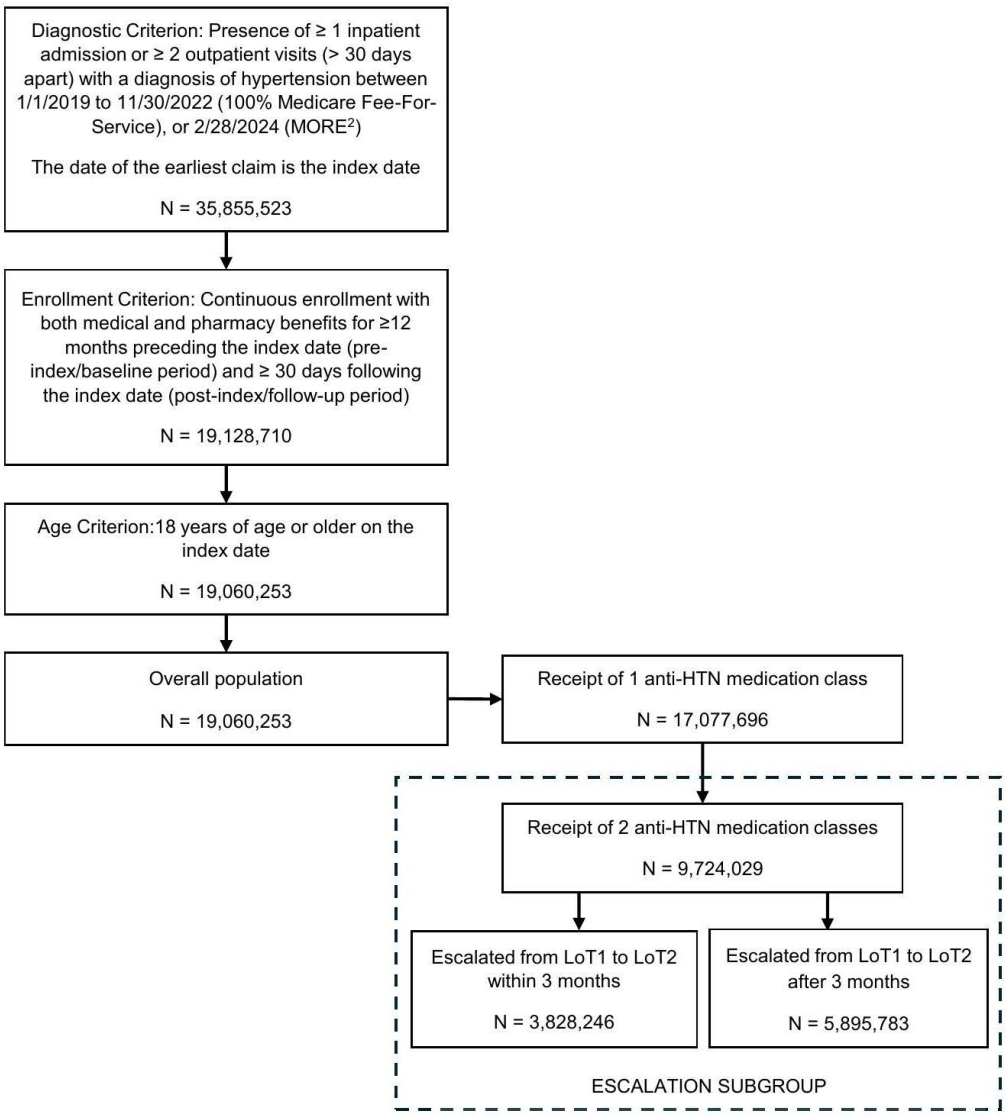

Figure 1: Patient selection.

Abbreviations: anti-HTN: antihypertensive; FFS, Fee-for-Service; LoT, line of therapy

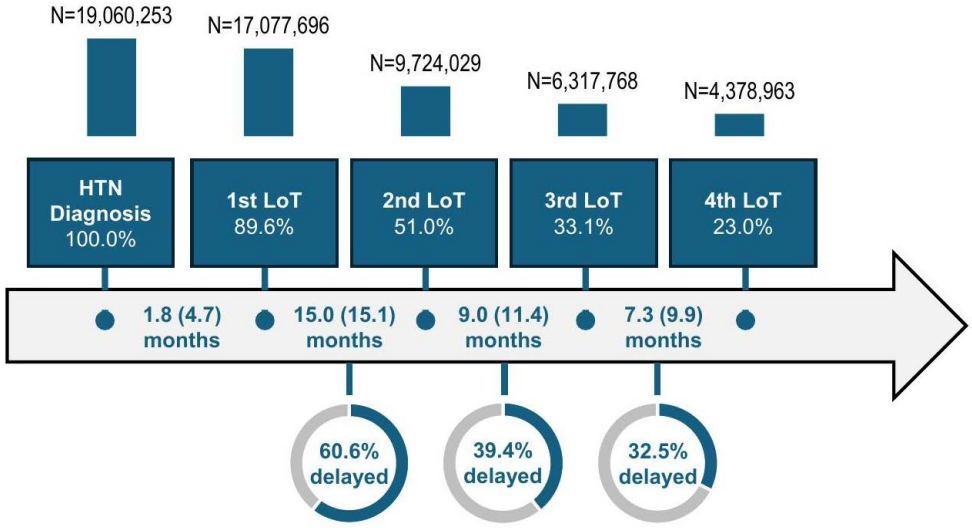

Figure 2: Hypertension patient journey

Abbreviations: HTN: Hypertension; LoT: Line of Therapy

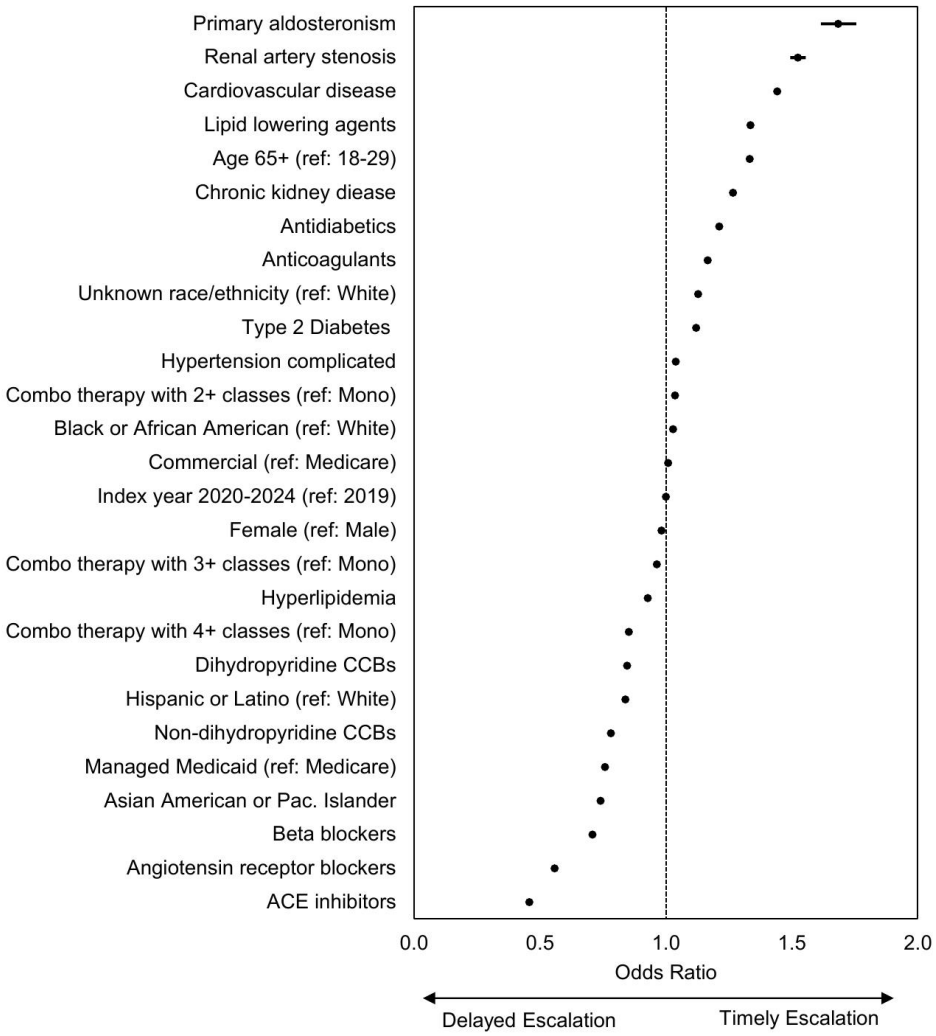

Figure 3: Predictors of treatment escalation within or after 3 months (N = 9,724,029).

Note: Error bars are 95% Cis

Abbreviations: ACE: Angiotensin-Converting Enzyme; CCB: Calcium Channel Blocker

Table 2: Treatment patterns.

	LoT1 N = 17,077,696	LoT2 N = 9,724,029	LoT3 N = 6,317,768	LoT4 N = 4,378,963
Prescribing specialist,* n (%)				
Primary care provider	12,220,654 (71.6%)	6,732,749 (69.2%)	4,364,404 (69.1%)	2,965,790 (67.7%)
Primary care physician	9,302,461 (54.5%)	4,995,425 (51.4%)	3,278,823 (51.9%)	2,236,060 (51.1%)
Nurse practitioner / physician assistant	2,918,193 (17.1%)	1,737,324 (17.9%)	1,085,581 (17.2%)	729,730 (16.7%)
Cardiologist	1,566,008 (9.2%)	1,130,709 (11.6%)	836,051 (13.2%)	656,771 (15.0%)
Nephrologist	237,303 (1.4%)	189,872 (2.0%)	141,888 (2.2%)	114,659 (2.6%)
Endocrinologist	87,208 (0.5%)	47,264 (0.5%)	30,778 (0.5%)	21,296 (0.5%)
Infectious disease specialist	34,361 (0.2%)	16,997 (0.2%)	10,368 (0.2%)	6,721 (0.2%)
Other	676,222 (4.0%)	476,781 (4.9%)	266,515 (4.2%)	177,957 (4.1%)
Specialist not specified	2,255,940 (13.2%)	1,129,657 (11.6%)	667,764 (10.6%)	435,769 (10.0%)
Combination therapy with 2+ classes, n (%)	8,012,319 (46.9%)	5,254,610 (54.0%)	3,620,098 (57.3%)	2,504,016 (57.2%)
Fixed-dose combination	2,453,370 (14.4%)	1,131,719 (11.6%)	683,444 (10.8%)	413,716 (9.4%)
Free-dose combination	5,558,949 (32.6%)	4,122,891 (42.4%)	2,936,654 (46.5%)	2,090,300 (47.7%)
Number of patients receiving guideline-recommended antihypertensive classes,† n (%)				
Using at least 1 of the classes	13,519,507 (79.2%)	7,299,206 (75.1%)	4,743,062 (75.1%)	3,183,325 (72.7%)
Monotherapy using only the classes	6,158,723 (36.1%)	2,655,685 (27.3%)	1,564,670 (24.8%)	1,023,128 (23.4%)
Combination therapy with 2+ classes using 2 of the 4 classes	3,840,964 (47.9%)	2,169,261 (41.3%)	1,435,466 (39.7%)	927,950 (37.1%)
Combination therapy with 3+ classes using 3 of the 4 classes	647,436 (24.3%)	419,322 (21.4%)	288,133 (20.2%)	188,851 (18.6%)
Combination therapy with 4+ classes using 3 of the 4 classes	257,224 (40.3%)	182,109 (34.7%)	131,182 (33.4%)	92,084 (31.7%)

LoT: Line of Therapy

* Measured 30 days prior or on the start date of the anti-hypertensive medication class and provider assigned using a hierarchy of cardiologist, nephrologist, endocrinologist, primary care, nurse practitioner/physician assistant, other, unknown.

† Angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) plus dihydropyridine calcium channel blocker (DHP-CCB) and thiazide-like diuretic (thiazide)

those on three and four or more class combination therapy, 24.3% and 40.3%, respectively, were treated with three of the four recommended classes.

Predictors of timely versus delayed treatment escalation

The 9,724,029 patients who escalated to LoT2 were included in the escalation subgroup and analyzed in the multivariate analysis of predictors of delayed escalation. Among these patients, 39.4% (N = 3,828,246) received timely treatment escalation, while 60.6% (N = 5,895,783) received delayed treatment escalation. Demographic characteristics for this subgroup are shown in supplemental table 3.

The real-world predictors most strongly associated with timely escalation included primary aldosteronism (OR = 1.68, 95% CI 1.62-1.76), cardiovascular disease (OR = 1.44, 95% CI 1.44-1.45), age ≥ 65 years (OR = 1.33 95% CI 1.33-1.34), and chronic kidney disease (OR = 1.27, 95% CI 1.26-1.27) (Figure 3). The predictors most strongly associated with delayed escalation included receipt of ACE inhibitors (OR = 0.46, 95% CI 0.46-0.46) or ARBs (OR = 0.56, 95% CI 0.56-0.56) (Supplemental Table 4).

Sensitivity analysis showed consistent findings for escalation to LoT3 and LoT4, escalation within 6 months, and escalation to combination therapy (Supplemental Tables 5, 6, and 7, Supplemental Figure 2).

Discussion

In this retrospective, claims-based study of patients with hypertension, 60.6% of patients experienced delays in treatment escalation. These findings highlight opportunities to overcome clinical inertia and escalate antihypertensive therapy in a timely manner to improve population-level cardiovascular outcomes for patients with hypertension.

The prolonged intervals between treatment escalations, ranging between nearly 6 and 15 months, suggest that many patients are not receiving guideline-concordant treatment escalation. Given that antihypertensives were predominantly prescribed by primary care providers, these providers represent a critical leverage point in overcoming clinical inertia. However, both primary care providers and specialists face similar pressures, including evolving clinical guideline recommendations, concerns about

polypharmacy, rising medication costs, and challenges with patient adherence and engagement with the healthcare system [17,27]. Despite these barriers, prior evidence demonstrates that interventions such as physician and patient educational programs and clinical reminders as well as pharmacist led interventions can meaningfully improve blood pressure control [17,28].

Patterns of antihypertensive use in this study further highlight opportunities to enhance hypertension management. As expected, the four guideline-recommended first-line antihypertensive classes remain the cornerstone of first-line treatment strategies, with more frequent use during first-line therapy compared with subsequent LoTs. A similar pattern was observed for fixed-dose combinations, therapies designed to reduce pill burden and increase adherence [29-31], which were most common during the first LoT but declined in subsequent LoTs as patients transitioned to free-dose combinations. These shifts may indicate that, as patients progress through treatments, providers increasingly prefer more flexible dosing strategies (i.e., free-dose combinations) or tailored regimens using alternative antihypertensive classes (e.g., beta blockers, loop diuretics, vasodilators).

Given that nearly two-thirds of patients did not receive timely treatment escalation, identifying patient-level predictors of treatment escalation is essential for informing strategies to improve clinical care. In this analysis, comorbidities, age, race/ethnicity, and antihypertensive classes were significantly associated with either timely or delayed treatment escalation. Although prior research suggested that the number of comorbidities was not significantly associated with treatment intensification [24], our analysis revealed that specific comorbidities may play a role. Most of the top seven predictors of timely anti-HTN treatment escalation within 3 months were aldosterone-related conditions such as primary aldosteronism, cardiovascular disease and chronic kidney disease. Primary aldosteronism, cardiovascular disease, and chronic kidney disease, each pathophysiological consequences of aldosterone dysregulation [32], were found to be significantly associated with timely treatment escalation. These results suggest clinicians may respond more urgently when managing hypertension in the context of select comorbidities with underlying aldosterone-related pathophysiology, which conveys higher cardiovascular risk.

Importantly, these findings align with key guideline-recommendations for patients with primary aldosteronism, cardiovascular disease, and chronic kidney disease. The ACC/AHA guidelines emphasize rapid evaluation and management of patients with secondary hypertension, including primary aldosteronism, and for those at high risk for cardiovascular disease [1]. Endocrine Society guidelines similarly underscore the importance of prompt management in primary aldosteronism [33]. For patients with chronic kidney disease, specifically those not receiving dialysis, the 2021 KDIGO Guideline on the Management of Blood Pressure in CKD recommends urgent treatment and tight blood pressure control, with a target blood pressure < 120 mmHg for appropriate candidates [34].

Age was also a meaningful predictor. Patients ≥ 65 years were more likely to receive timely treatment escalation compared to younger patients. This pattern is consistent with evidence that, when guided by individualized assessments of frailty and orthostatic hypotension risk, older adults benefit from blood pressure control through reductions in major cardiovascular events and kidney failure [1,35]. Timely treatment escalation among older adults may also be a consequence of increased contact with the healthcare system. This may also occur if clinicians underestimate cardiovascular risk in younger patients that may result in less urgency to escalate.

In contrast, several factors were associated with delayed escalation. The top seven predictors of delayed treatment escalation were either disparities of care (Asian Americans, Hispanics, Medicaid) or treatment inertia related (receipt of ACE inhibitors, ARBs, beta blockers and non-dihydropyridine CCBs), which can inform quality improvement efforts. Patients receiving ACE inhibitors or ARBs, cornerstones of guideline-recommended first-line treatment, showed slower intensification, which may indicate clinician reluctance to deviate from guideline-preferred therapies even when additional agents are warranted. Reliance on non-first line treatments like beta blockers and non-dihydropyridine CCBs as being associated with longer time to intensification may reflect clinical inertia to deviate from engrained prescribing habits. Concerns for side effects such as hyperkalemia that can arise from additional anti-HTN classes may also result in more delayed escalations. Hispanic ethnicity or Asian race were associated with delayed escalation relative to White patients. These findings align with prior evidence that Hispanic patients were less likely to receive hypertension treatment escalation,36 but differ from a previous study suggesting Asian patients had higher intensification scores relative to White patients [37]. Moreover, the finding that Black patients had similar odds of timely escalation compared to White patients differs from an earlier study reporting that Black patients had lower treatment intensification scores [37]. Collectively, these inconsistencies highlight the need for further research to clarify the racial and ethnic disparities in hypertension management and to inform interventions that promote equity.

Limitations

This study has limitations inherent to claims-based research. First, as blood pressure measurements were

not available to quantify the level of uncontrolled hypertension as patients progress through LoTs, the longer time intervals may have been appropriate because patients already achieved blood pressure targets. Second, as is common with claims-based studies, medication usage was based on filled outpatient prescriptions and patients were assumed to take the medications as prescribed, though this could not be confirmed for all patients. Third, clinical measures necessary for CKM staging require claims-based proxies, which may introduce misclassification of CKM stage.

Conclusion

In conclusion, this study demonstrated prolonged time to antihypertensive treatment escalation as compared to timeframes recommended in 2025 American College of Cardiology/American Heart Association (ACC/AHA) clinical guidelines and identified important real-world predictors of timely escalation, including primary aldosteronism, cardiovascular disease, chronic kidney disease, and older age. These findings highlight potential gaps in the real-world management of hypertension and reinforce the need for timely treatment escalation. As the primary prescribers of antihypertension therapeutics, primary care providers are uniquely positioned to close these gaps by optimizing timely and guideline-concordant treatment escalation. Since primary care providers play a key role in escalating therapy, interventions aimed at improving clinical inertia should include primary care providers.

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Conflicting and Competing Interests

TD and CB are paid external medical consultants for AstraZeneca. AA, SL, and JH are employees and stockholders of AstraZeneca. KW, EP and ZP are employees of Inovalon, which received funding from AstraZeneca to conduct the study. JT was an employee of Inovalon at the time the study was conducted.

Authors' Contributions

AA, JT, SL, and JH contributed to study conception and design. KW, EP, JT, and ZP conducted the data analysis. All authors contributed to interpretation of results, critically revised the manuscript, and approved the final version for submission.

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