Once-Daily Antihypertensive Dosing Associated with Better Blood Pressure Control Than Multi-Dose Regimens for Most Medication Classes

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Key Findings:

- Patients prescribed multiple doses per day of ACE inhibitors, ARBs, or calcium channel blockers were less likely to achieve blood pressure control compared to those prescribed once-daily regimens of the same medication classes.
- Differences in blood pressure control between dosing frequencies emerged as early as 30 days after the prescription started and persisted through 180 days.
- Beta blockers, which were the only class commonly prescribed with multiple doses per day, showed slight improvement in early blood pressure control, though no significant difference was seen at 90 to 180 days.

Hypertension affects nearly half of U.S. adults and remains poorly controlled in many cases, which increases cardiovascular risk and healthcare costs.[1] Medication adherence is a critical factor in achieving blood pressure control, and dosing frequency is a known driver of adherence. Studies have demonstrated that patients are significantly more adherent to once-daily cardiovascular medications compared to twice-daily dosing.[2,3] However, the relationship between dosing frequency and blood pressure outcomes by antihypertensive medication class is less understood. We aimed to understand whether the association between dosing frequency and blood pressure control varied across the four major first-line antihypertensive classes: ACE inhibitors, ARBs, calcium channel blockers, and beta blockers.

We studied more than 1 million adults newly treated for essential hypertension between January 1, 2017, and June 30, 2025, after a series of elevated blood pressure readings. We excluded patients with secondary hypertension, those who were pregnant, and those with prior antihypertensive medication use. We compared the likelihood of achieving controlled blood pressure (systolic blood pressure at or below 140 mmHg) at 30 to 59 days, 60 to 89 days, and 90 to 180 days between patients prescribed once-daily versus multi-dose regimens. We accounted for demographics, social vulnerability based on most recent ZIP code, and baseline systolic blood pressure.

Once-daily dosing regimens were most common across all four antihypertensive classes, as shown in Figure 1. Multi-daily dosing accounted for just over 1% of ACE inhibitor, ARB, and calcium channel blocker prescriptions, but 23.8% of beta blocker prescriptions.

Proportion of Prescriptions with One Dose or Multiple Doses Daily

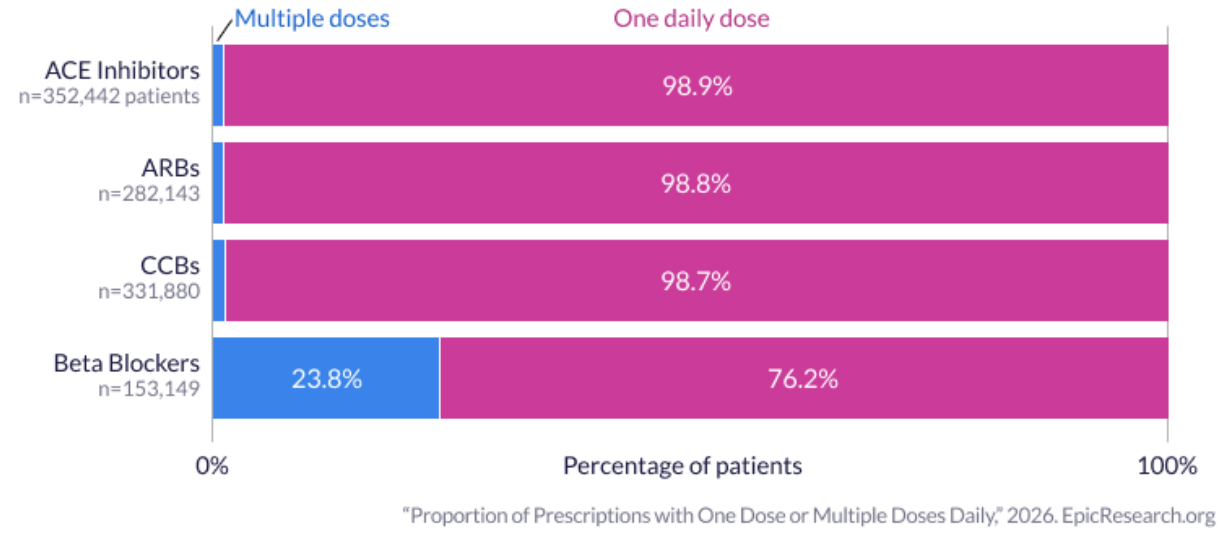

Figure 1. The percentage of prescriptions of each category prescribed once daily or multiple times per day.

Among patients prescribed ACE inhibitors, ARBs, and calcium channel blockers, those on once-daily regimens were more likely to achieve blood pressure control compared to multiple-dose regimens of the same medication classes. These differences emerged as early as 30 days after the prescription started and persisted through 180 days, as seen in Figure 2. In contrast, beta blockers showed a decrease in early blood pressure control when prescribed once per day, though there was no significant difference at 90 to 180 days.

Likelihood of Blood Pressure Control on Daily Dosing Compared to Multiple Doses Per Day by Medication Class

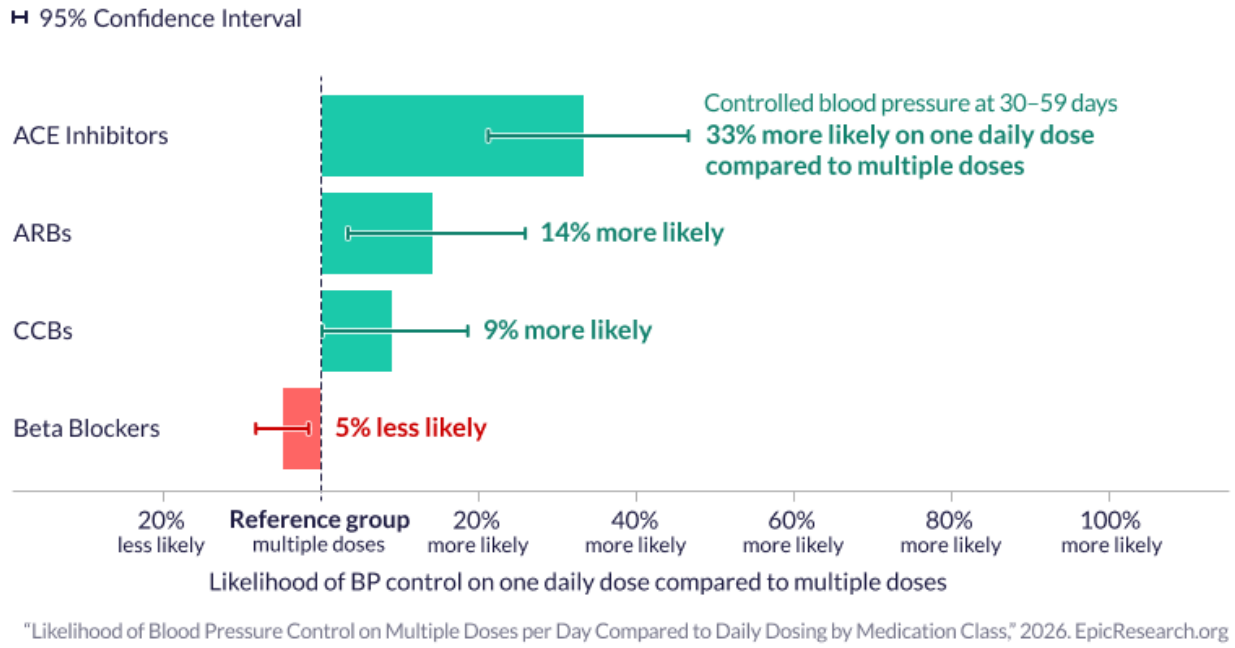

Figure 2a. The likelihood of a patient's systolic BP being ≤ 140 mmHg on once-daily dosing compared to multiple doses per day by medication class at 30 to 59 days.

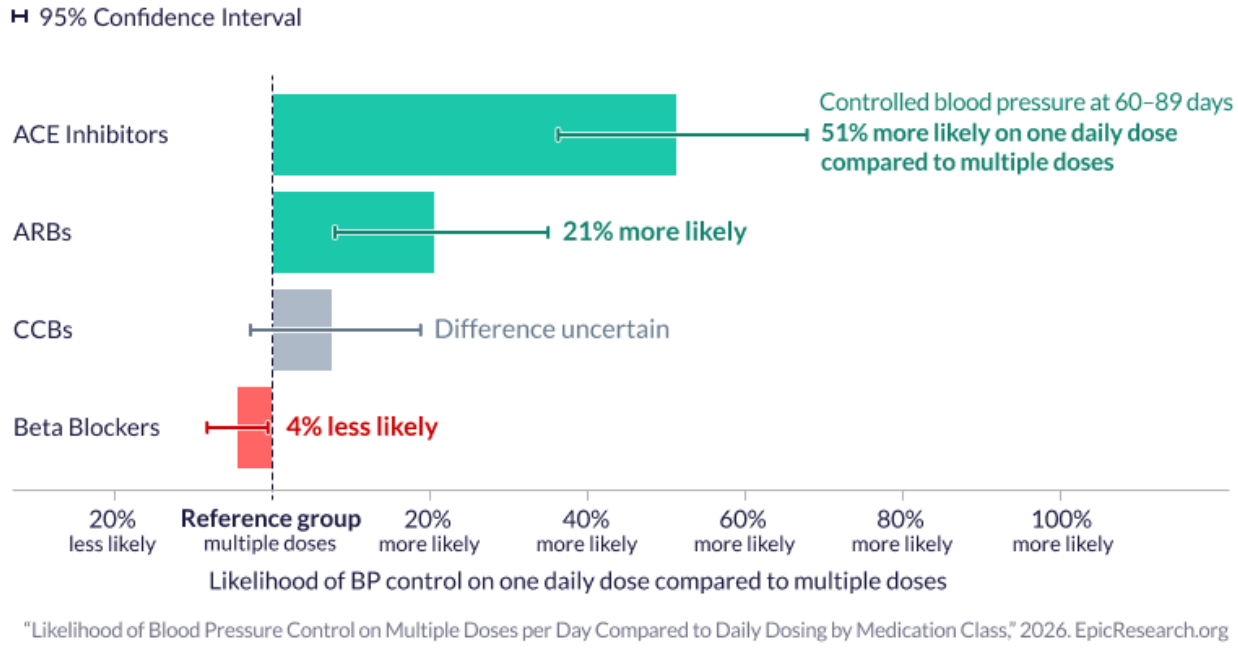

Figure 2b. The likelihood of a patient's systolic BP being ≤ 140 mmHg on once-daily dosing compared to multiple doses per day by medication class at 60 to 89 days.

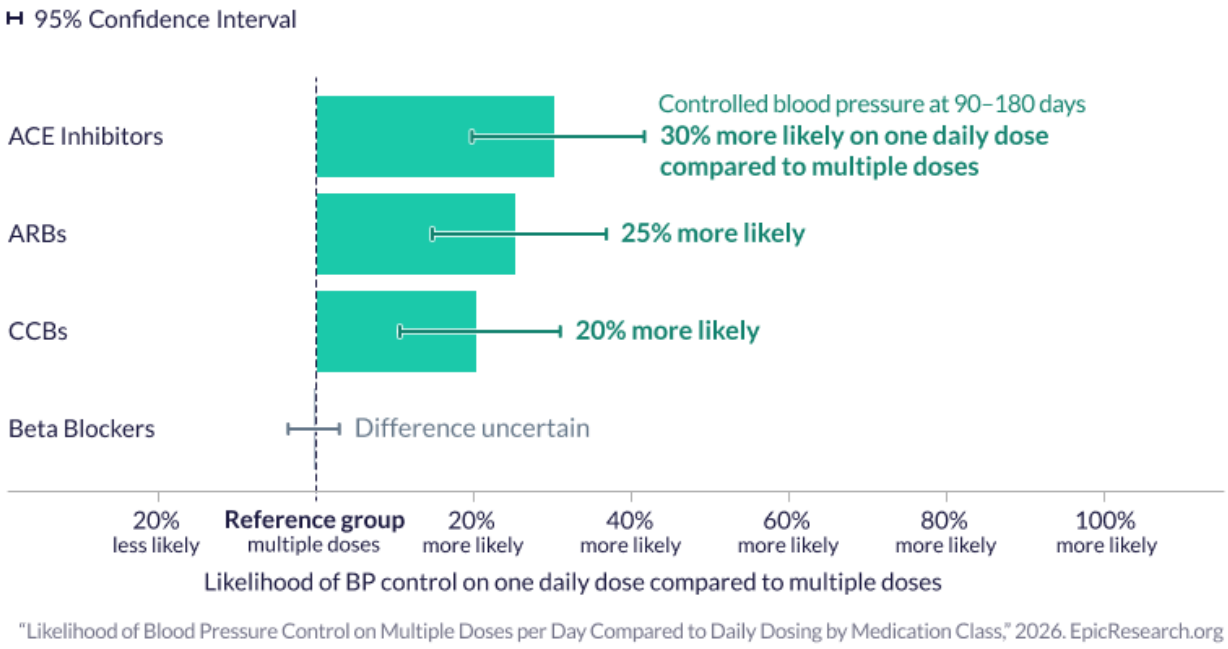

Figure 2c. The likelihood of a patient's systolic BP being ≤ 140 mmHg on once-daily dosing compared to multiple doses per day by medication class at 90 to 180 days.

Multi-dose prescribing for newly hypertensive patients is uncommon among most of the medications studied. The patients who did receive multi-dose regimens might have other factors that influenced the prescribing pattern that were not accounted for. Observed associations represent prescribing patterns rather than confirmed medication exposure or use.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 2,000 hospitals and more than 47,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientist. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Lee JS, Segura Escano R, Therrien NL, et al. Antihypertensive Medication Adherence and Medical Costs, Health Care Use, and Labor Productivity Among People With Hypertension. J Am Heart Assoc. 2024;13(21):e037357. doi:10.1161/JAHA.124.037357
2. Srivastava K, Arora A, Kataria A, Cappelleri JC, Sadosky A, Peterson AM. Impact of reducing dosing frequency on adherence to oral therapies: a literature review and meta-analysis. Patient Prefer Adherence. 2013;7:419-434. Published 2013 May 20. doi:10.2147/PPA.S44646
3. Laliberté F, Bookhart BK, Nelson WW, et al. Impact of once-daily versus twice-daily dosing frequency on adherence to chronic medications among patients with venous thromboembolism. Patient. 2013;6(3):213-224. doi:10.1007/s40271-013-0020-5

Data Definitions

Term	Definition
Study period	1/1/2017 to 6/30/2025
Study population: inclusion	Adult patients: • Newly diagnosed with **essential hypertension** • Prescribed a **first-line antihypertensive medication** (excluding those from an emergency department visit or hospital admission) after a hypertension diagnosis or within 30 days prior to their initial hypertension diagnosis, with no changes to the frequency or type through the follow-up period. This initial prescription must be during the **study period**. • With a systolic blood pressure reading ≥130 mmHg not taken during an admission between two weeks before and three days after their prescription • With at least two additional elevated BP readings not taken during an admission in the 12 months prior to the prescription separated by at least a week each • With at least one **outpatient face-to-face visit** at least a year prior to the prescription
Study population: exclusion	Patients with: • Patients with any **antihypertensive medication** prescribed more than 30 days prior to their diagnosis of **essential hypertension** • **Evidence of pregnancy** during the year following the start of the medication • A diagnosis that **causes secondary hypertension** on or prior to the prescription date
Censoring	When: • The prescription ended without another prescription documented • There was a prescription gap longer than 10 days • The patient switched to or added another type of **antihypertensive medication**
Exposures	Antihypertensive prescription medication: • ACE inhibitors: a medication with ATC code C09A* • ARBs: a medication with ATC code C09C* • Calcium channel blockers: a medication with ATC code C08* • Beta blockers: a medication with ATC code C07AA* or C07AB* • Frequency: daily or more than daily
Outcomes	Systolic BP ≤ 140 at 30 to 59 days, 60 to 89 days, and 90 days to 6 months Blood pressures were taken from non-admission encounter, using the lowest reading per day and each outcome evaluating the day closest to the end of the window
Confounders	**Race and ethnicity** Age: 0-17, 18-29, 30-54, 55-64, 65-79, 80+ Evaluated sex Social Vulnerability Index quintile Age at time of **hypertension** diagnosis Baseline systolic BP • 130-139 • 140-154

	• 155-169 • 170+
Essential hypertension	An encounter or billing diagnosis with ICD-10-CM code I10
Causes of secondary hypertension	An encounter, billing, or problem list diagnosis of any of the following ICD-10-CM codes. Renal • Chronic kidney disease (CKD), unspecified: N18.9 • Chronic glomerulonephritis, unspecified: N03.9 • Polycystic kidney disease, autosomal dominant: Q61.2 • Diabetic nephropathy: E11.21 or E10.21 • Renal artery stenosis (renovascular hypertension): I15.0 • Hypertensive renal disease (secondary hypertension due to renal disorder): I12.9 Endocrine • Primary aldosteronism (Conn's syndrome): E26.01 • Cushing's syndrome: E24.9 • Pheochromocytoma: C74.10, C74.11, or D35.00 • Paraganglioma, benign: D35.6 • Hyperthyroidism (thyrotoxicosis): E05.90 • Hypothyroidism: E03.9 • Hyperparathyroidism: E21.3 Cardiovascular • Coarctation of the aorta: Q25.1 • Hypertensive heart disease due to secondary cause: I15.2 Pulmonary • Sleep-related hypoventilation: G47.36 Medication- or substance-induced • Drug-induced hypertension: I15.8 Genetic & rare disorders • Liddle's syndrome: E26.89 • Apparent mineralocorticoid excess: E26.09 • 11β-hydroxylase deficiency: E25.0 • 17α-hydroxylase deficiency: E25.8 Other/unspecified secondary hypertension • Secondary hypertension: I15.9 • Hypertension due to endocrine disorder: I15.2 • Hypertension due to renal disease: I15.1
Outpatient face-to-face visit	An encounter of type "Office Visit," "Emergency," "Well Child," "Follow-up," "Telemedicine," "Urgent Care," "Walk-in," "Routine Prenatal," "Postpartum Visit," "Fetal Care Consult," "Emergency to Inpatient," "Hospital Outpatient Visit," or "Hospital Outpatient Visit to Inpatient"
Race and ethnicity	Patients were classified into one of Hispanic, White, Black, Asian, Multiracial, Other, and Unknown based on self-reported race & ethnicity that were mapped to standards
Model specifications	Binomial logistic regression
Limitations	Medication order data do not reflect actual dispensing or adherence behavior, and dosage was not captured. Patients could switch frequency after original frequency was ordered without needing a new prescription.

Table 1. Proportion of Prescriptions with One Dose or Multiple Doses Daily

Population	Patients	Daily	More Than Daily	More Than Daily Rate	Daily Rate
ACE Inhibitors	352,442	348,426	4,016	1.1%	98.9%
ARBs	282,143	278,636	3,507	1.2%	98.8%
CCBs	331,880	327,519	4,361	1.3%	98.7%
Beta Blockers	153,149	116,703	36,446	23.8%	76.2%

Table 2. Likelihood of Blood Pressure Control on Multiple Doses per Day Compared to Daily Dosing by Medication Class

Medication	Follow-Up Period	Odds Ratio	Lower CI	Upper CI
	30 to 59 days	1.333	1.466	1.212
	60 to 89 days	1.513	1.678	1.362
ACE inhibitors	90 to 180 days	1.302	1.416	1.198
	30 to 59 days	1.142	1.259	1.034
	60 to 89 days	1.206	1.350	1.079
ARBs	90 to 180 days	1.253	1.368	1.147
	30 to 59 days	1.089	1.186	1.001
	60 to 89 days	1.075	1.189	0.972
CCBs	90 to 180 days	1.203	1.309	1.106
	30 to 59 days	0.951	0.984	0.917
	60 to 89 days	0.956	0.995	0.918
Beta Blockers	90 to 180 days	0.997	1.030	0.964