

Hypertension

ORIGINAL ARTICLE

Importance of Adherence Versus Intensification in Attaining Blood Pressure Control

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BACKGROUND: Understanding the association between improving medication adherence, intensifying antihypertensive medications, or both on blood pressure (BP) control can guide clinical care and quality improvement.

METHODS: Retrospective cohort study of primary care patients with hypertension and 2 uncontrolled BP readings in 2021. Using prescription fills, we classified patients as high ($\geq 80\%$) versus low ($<80\%$) adherence in the 6 months before and after their second uncontrolled reading (aka index visit). We defined intensification as a prescription for a higher dose or a new medication class at that visit. The outcome was BP control ($<130/80 \text{ mm Hg}$) between 30 and 270 days afterward. We identified factors associated with intensification at the index visit. For patients with low adherence before the index visit, we used multilevel logistic regression to measure the association between intensification, postvisit adherence, and subsequent BP control.

RESULTS: Of 27 699 patients with uncontrolled BP, 24% had low adherence before the index visit. Patients with high adherence and prior intensification had the highest adjusted probability of intensification (28% [95% CI, 27%–29%]). Among patients with low previsit adherence, 19% received intensification and 46% transitioned to high adherence. Without intensification or improved adherence, the adjusted probability of control was 23%. Neither intensification alone (24%) nor improved adherence alone (25%) significantly increased the adjusted probability of control. Patients who both received intensification and improved adherence had the highest adjusted probability of control (31%; $P < 0.01$ versus no action).

CONCLUSIONS: Physicians should simultaneously intensify treatment and encourage adherence. Health systems should encourage intensification regardless of adherence status. (*Hypertension*. 2026;83:461–469. DOI: 10.1161/HYPERTENSIONAHA.125.25613.) • **Supplement Material.**

Key Words: blood pressure ■ hypertension ■ physicians ■ prescriptions ■ quality improvement

Uncontrolled hypertension is a leading modifiable cause of cardiovascular and kidney disease.^{1–3} A 10 mm Hg reduction in systolic blood pressure (BP) can reduce all-cause mortality by 13%.^{4–7} Nationwide, BP control rates declined from 54% to 44% between 2013/14 and 2017/18.⁸ In 2017, the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines lowered the target for BP control to $<130/80 \text{ mm Hg}$,⁹ resulting in 19% more individuals being classified as having hypertension.¹⁰ The increased prevalence of hypertension amplifies the burden of addressing it for health systems,¹¹ increasing the need for effective approaches.

Some health systems have implemented quality improvement programs targeting BP control with the hope of reducing future morbidity and premature mortality.^{12–16} In Kaiser Permanente's seminal program in 2013, population-level BP control improved from 44% to 80%.¹⁴ Their interventions included improving knowledge of the importance of hypertension management, ensuring proper BP measurement, appropriately intensifying antihypertensive medications, and enhancing access to care.^{17–19}

During a primary care visit, physicians can address uncontrolled BP by intensifying a medication, stressing adherence, or both. There is already strong evidence that

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NOVELTY AND RELEVANCE

What Is New?

We tracked adherence and intensification in relation to a specific decision point (the index visit) rather than uniformly over the entire study period. This allowed us to evaluate the effects of intensification and changes in adherence on blood pressure control as if they were clinical interventions, and to model how adherence and other factors impacted physicians' decisions on whether to intensify medication.

What is Relevant?

Understanding and quantifying the importance of adherence and intensification is critical to blood pressure control.

Clinical/Pathophysiological Implications

Health systems should increase focus on medication adherence as an often-overlooked but necessary component of blood pressure control, particularly in quality improvement programs. When patients present with uncontrolled blood pressure and low adherence, physicians should simultaneously encourage increased adherence and rigorously intensify medications.

Nonstandard Abbreviation and Acronym

BP	Blood Pressure
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medication intensification improves BP control,²⁰ while therapeutic inertia, or a failure to intensify medications despite an elevated BP reading,²¹ is a known barrier to BP control.

There is less focus on adherence, defined as following a physician's recommendations related to lifestyle or anti-hypertensive medications.²² Evidence for the importance of adherence is mixed, with some studies finding an association between adherence and BP control,^{23,24} and others finding no association.^{25,26} One potential explanation for these discrepant results is how adherence is measured. Typically, researchers measure average adherence during the study period (often a year).^{25,27,28} If a patient improved their adherence closer to the time the outcome is measured, it may have improved their BP control despite having low average adherence. A more nuanced approach is to measure changes in adherence around a clinical decision point. To define this decision point, we focus on primary care visits where a patient presented with persistently uncontrolled BP, and the physician documented that they addressed hypertension. Analyzing the events that occur during and after a specific decision point provides an opportunity to compare the importance of improving adherence versus intensifying therapy.

In clinical practice, when physicians identify a patient with uncontrolled BP and poor adherence, they must choose whether to intensify, discuss adherence, or do both. Understanding whether adherence before a visit impacts the physicians' strategy to address uncontrolled BP and how that strategy (eg, intensifying therapy or

improving adherence) affects future BP control can inform quality improvement programs. Our objective was to identify the association between improving adherence, intensifying antihypertensive medications, or both, on BP control. We focused on patients with 2 recent uncontrolled BP measurements and poor adherence. To understand which patients received intensification and which improved their adherence, we also reported the characteristics associated with these outcomes.

METHODS

Data Availability

Data available on request from the authors.

Subjects

This retrospective cohort study included adult primary care patients at a large health system in the Midwest. We only included primary care physicians who had ≥3 eligible patients to ensure we captured routine care patterns. Patients were required to have a diagnosis of hypertension (based on ICD codes)²⁹ either on or before the date of their initial uncontrolled BP reading ($\geq 130/80$ mm Hg)⁹ at a primary care visit in 2021. Since we wanted to ensure that patients had uncontrolled BP, we required a second uncontrolled BP reading between 8 days and 180 days after their initial reading. We defined this second visit as the index visit. We required a documented diagnosis of hypertension on the index visit to ensure the physician discussed hypertension during the visit. Since we were interested in medication adherence, we excluded patients without an anti-hypertensive medication prescription before their index visit or those who had their antihypertensive medications discontinued during their index visit. This structure allowed us to calculate a patient's adherence before and after the index visit.

We also excluded patients who did not have a BP reading at the outcome time point. Finally, similar to our prior work,^{16,30}

we also excluded patients who were pregnant or had end-stage renal disease. A consort diagram describes this process (Figure 1). All data was collected from the electronic health record system.

Outcome Time Point

We classified patients' BP as controlled ($<130/80$ mmHg)⁹ or not based on their closest BP recorded 6 months post the index point. Given that this was an observational study, we allowed a window of 30 to 270 days after their index date to ensure we did not unnecessarily limit the study to a narrower population. We chose this window to allow sufficient time for a change in BP to be attained. If multiple readings were taken during this window, we chose the reading closest to 6 months after the index point.

Medication Intensification

We defined intensification as a new prescription for an increased dose of a current medication or an additional or different class of antihypertensive, regardless of whether the drug from the

initial medication class was stopped. We identified whether intensification occurred within 7 days after the index visit (versus not). We also identified whether intensification occurred in the 6 months before the index visit (prior intensification, yes versus no) as a potential confounding variable.

Medication Adherence

We were interested in whether patients with low adherence before the index visit improved their adherence after the visit. Adherence for the 6 months before and after the index date was measured using prescription fill data. We picked a 6-month time frame for adherence because antihypertensive medications only need to be taken for a week before they are effective in lowering BP³¹ and a narrower window, which is commonly used in the literature,^{32,33} allows us to assess the impact of the index visit on the change in adherence. Adherence was expressed as the number of days filled divided by the number of prescribed days for each time period, across all antihypertensive medications. This adherence data was available to physicians throughout the course of clinical care as a color-coded

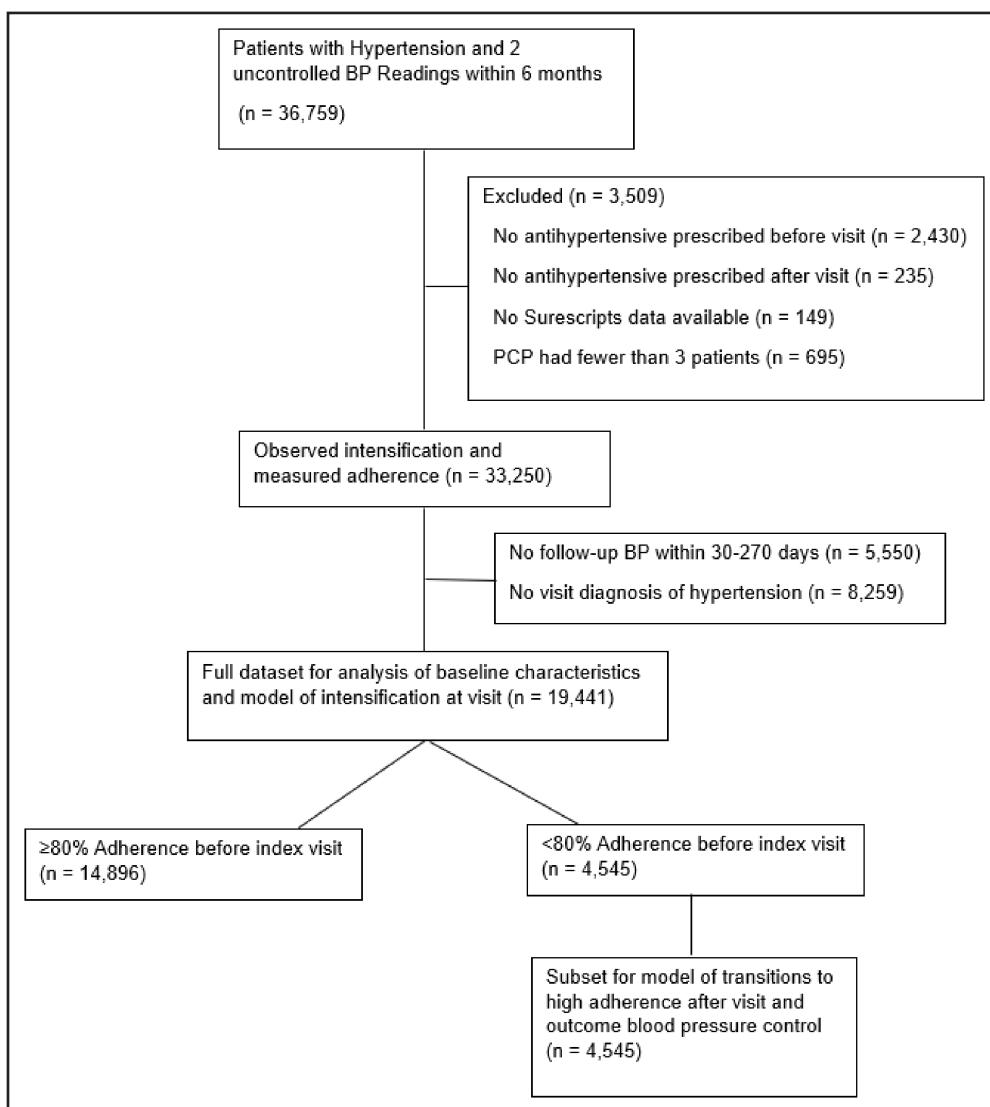


Figure 1. Consort diagram.

hover option within the EPIC electronic health record; however, using this is not part of defined routine workflows. For our analysis, because adherence was right-skewed, we dichotomized it as low (<80%) versus high ($\geq 80\%$) using an accepted threshold.³⁴

Patient Demographic and Health Conditions

We collected patients' age, sex, race, and insurance data from the electronic health record. Due to sample size constraints, we grouped race as White, Black, or other. We collected patients' health conditions via *International Classification of Diseases, Tenth Revision* codes and categorized them based on the Centers for Medicare and Medicaid Service's chronic disease warehouse definitions.³⁵

Statistical Analysis

We reported standard descriptive statistics for the population by adherence status before the index visit. Then, we ran a series of multilevel logistic regression models.

First, to understand who received intensification at the index visit, we modeled the association between previous adherence and prior intensification with intensification at the index visit. Our independent variables were previsit adherence (low versus high), prior intensification (yes versus no), and their interaction. For ease of understanding, we reported the predicted probability of receiving intensification at the visit.

The subsequent 2 models focused on patients with low previsit adherence. This approach allows us to account for the temporal sequencing between the physician's actions during the index visit and a patient's subsequent BP control. The appendix figure illustrates how medication intensification or discussions would have impacted BP control. Among patients with low adherence in the 6 months before the index visit, we modeled the association between patient characteristics at the index visit and high adherence in the subsequent 6 months. Finally, we modeled the association between postvisit adherence, medication intensification at the index visit, and subsequent BP control. Our independent variables were postvisit adherence (low versus high), intensification (yes versus no), and their interaction. For ease of understanding, we reported the predicted probability of BP control.

This last model was limited to patients with low previsit adherence to focus on decision-making at our core clinical scenario of patients presenting with uncontrolled BP and low adherence. For a sensitivity analysis, we also fit an analogous model among patients with high previsit adherence. Results of this may be found in Table S1.

In all models, we included age, sex, race, insurance, years with hypertension, diabetes status (yes versus no), and the patient's systolic BP reading at the index visit as fixed variables and physician ID as a random variable. All analysis was conducted using Stata 18.0 and R Studio.

Figure S2 shows our logical model of how physician's actions at the index visit impact measured variables and eventual BP control, in the form of a directed acyclic graph.

This study was approved by the Cleveland Clinic's institutional review board (No. 17-139).

RESULTS

We identified 19 441 patients who met the inclusion criteria. Their median age was 68 (interquartile range, 58–76), 56% were female, 71% were White, and 23% were Black. The primary insurance was as follows: 50% Medicare, 42% Commercial, and 8% Medicaid. On average, patients were diagnosed with hypertension 8 years before the index date. At the index visit, patients' mean systolic BP was 140 mmHg, and mean diastolic BP was 79 mmHg. Before the index visit, patients were prescribed an average of 2.11 antihypertensives. Table 1 shows descriptive statistics by adherence status before the index visit.

Intensification Before or at the Index Visit

During the 6 months before the index visit, 50% (n=9638) of patients had an intensification. At the index visit, 24% (n=4635) received medication intensification. Patients who did not receive intensification before the index visit had the lowest predicted probability of intensification, regardless of adherence status (21% for those in both the low adherence and high adherence groups). Patients who had low adherence and received a prior intensification had a predicted probability of 26% (95% CI, 23%–27%), and patients who had high adherence and received a prior intensification had the highest predicted probability of intensification (28% [95% CI, 27%–29%]; Figure 2).

Of patients who had an intensification at the index visit, 50% received a higher dose (n=2330), 47% received a new or additional class (n=2186), and 3% received both (n=119).

Change in Adherence

Seventy-seven percent of patients (n=14 896) had $\geq 80\%$ adherence before the index visit. Among patients who had low adherence before the index visit, 47% (n=2129) became highly adherent after the index visit. Patients who received a medication intensification at the index visit were more likely to become highly adherent (adjusted odds ratio [AOR], 1.20 [95% CI, 1.03–1.38]; Table 2).

Outcome Point and Blood Pressure Control

Patients had a mean of 1.02 visits (SD, 1.2) between the index visit and the outcome time point (ie, the closest reading to 6 months after the index visit). Just over a quarter of patients (28%, n=5497) had a controlled BP reading at the outcome time point.

Of the 4545 patients who had low adherence before the index visit, 25% (n=1146) had controlled BP at the outcome point. Patients who received intensification and became highly adherent had the highest predicted

Table 1. Descriptive Statistics

	Overall	Previsit adherence ≥80%	Previsit adherence <80%	P value
n (%)	19 441	14 896 (76.6%)	4545 (23.4%)	
Age, median (IQR)	67.82 (58.11–76.42)	68.26 (58.49–76.68)	66.47 (57.06–75.68)	<0.001
Sex (% Female)	56.5%	56.5%	56.3%	0.900
Race				<0.001
Black	22.8%	20.6%	30.2%	
White	71.0%	73.7%	62.3%	
Other	6.2%	5.7%	7.5%	
Insurance				<0.001
Commercial	42.5%	42.3%	42.9%	
Medicaid	8.0%	7.2%	10.6%	
Medicare	49.6%	50.5%	46.5%	
Years since hypertension Dx, median (IQR)	8.07 (3.81–13.27)	8.09 (3.77–13.36)	8.02 (3.98–12.97)	0.907
Systolic BP at index visit, mean (SD)	139.64 (13.89)	139.18 (13.61)	141.14 (14.70)	<0.001
Diastolic BP at index visit, mean (SD)	78.80 (10.17)	78.50 (10.11)	79.77 (10.29)	<0.001
No. of antihypertensives prescribed before the index visit, mean (SD)	2.11 (1.12)	2.04 (1.09)	2.33 (1.19)	<0.001
Intensified at index visit (%)	23.8%	23.7%	24.5%	0.267
Dose increase	12.0%	12.3%	11.0%	0.001
New class	11.2%	10.8%	12.7%	
Both	0.6%	0.6%	0.7%	
Intensified before index visit (%)	49.6%	49.3%	50.4%	0.232
Postvisit adherence score, median (IQR)	0.98 (0.80–1.00)	1.00 (0.88–1.00)	0.77 (0.50–0.98)	<0.001
Postvisit adherence ≥80 (%)	75.2%	83.9%	46.8%	<0.001
Systolic BP at outcome, mean (SD)	133.72 (14.69)	133.24 (14.32)	135.31 (15.74)	<0.001
Diastolic BP at outcome, mean (SD)	76.01 (10.17)	75.69 (10.02)	77.09 (10.57)	
BP controlled at outcome (%)	28.3%	29.2%	25.2%	<0.001

BP indicates blood pressure; and IQR, interquartile range.

*P values reflect comparison between patients who had ≥80% adherence before the index visit vs patients who had <80% adherence before the index visit using the following statistical tests: χ^2 (sex, race, insurance, intensification, adherence ≥80%, BP controlled), 2-tailed *t* test of means (systolic BP, diastolic BP), Wilcoxon rank-sum (age, years since HTN Dx, adherence score).

probability of control (31% [95% CI, 27%–35%]), and this was significantly higher than patients who remained at low adherence and did not receive intensification ($P<0.01$) and patients who remained at low adherence and received intensification ($P=0.02$; Figure 3). Patients who either increased adherence or received intensification alone were not more likely to attain BP control than those who did neither.

In our sensitivity analysis focused on patients with high adherence in the preindex period, we found similar results. Patients who received intensification and maintained high adherence had the largest predicted probability of BP control (34% [95% CI, 32%–36%]), followed by patients who received an intensification and changed to low adherence (30% [95% CI, 27%–34%]; Table S1).

DISCUSSION

In this large cohort study of patients with uncontrolled hypertension, we observed physician and patient behavior following the second visit with uncontrolled BP.

Despite patients having uncontrolled BP on 2 visits, physicians intensified therapy for only 24% of patients within 7 days. Patients who were already highly adherent and had prior medication intensification were most likely to have their medication intensified, but even then, only a quarter of those patients received intensification. Almost half of nonadherent patients reached the threshold of at least 80% adherence after the index visit. Few patient characteristics were associated with improved adherence, but patients who received intensification at the index visit had greater odds of increasing their adherence. For patients who had low adherence before the index visit, both improving adherence and intensifying treatment were necessary to improve the probability of BP control. Neither intervention alone was sufficient to improve BP control. However, even when patients both increased adherence and had their medication intensified, less than one-third attained BP control at follow-up.

The low rate of intensification among patients with low adherence is concerning. It may reflect providers' beliefs that improving adherence is necessary before intensifying

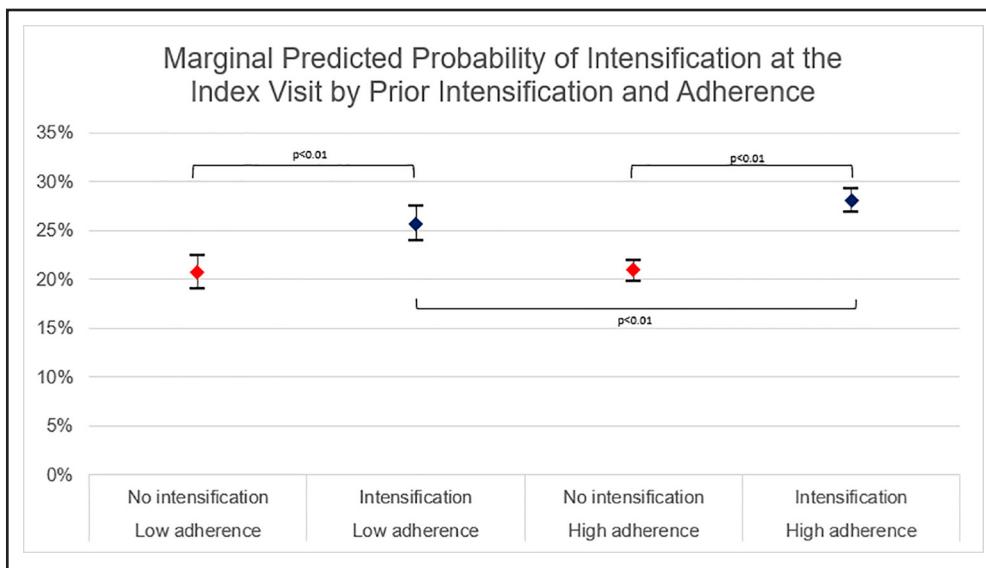


Figure 2. Marginal predicted probability of intensification at the index visit by prior intensification and adherence.

We defined low adherence as having <80% adherence rates. Intensification was defined as a new prescription for an increased dose of a current medication or a new prescription for an additional or different class of antihypertensive medication within the 6 months preceding the index visit. Patients in the no intensification group did not receive antihypertensive intensification in the 6 months before the index visit, and those in the intensification group did. Thus, moving from left to right, the first group received no intensification and had low adherence in the 6 months before the index visit. The second group received intensification and had low adherence in the 6 months before the index visit. The third group received no intensification and had higher adherence in the 6 months before the index visit. The fourth group received intensification and had high adherence in the 6 months before the index visit. We ran a multilevel logistic regression model with age, sex, race, insurance, years with hypertension, an indicator for diabetes, and systolic blood pressure measurement at the index visit as fixed variables and primary care provider as a random variable. Stata's margins command was used to identify the predicted probability of intensification at the index visit using the interaction of previsit adherence and previsit intensification as predictor variables.

medications,³⁶ a contributor to therapeutic inertia.²¹ After all, if a patient does not take a medication, it is hard to understand how adding another prescription could improve BP. However, our findings do not support this logic. Patients who improved their adherence without intensification did not have better BP control than those who did not improve adherence, so simply encouraging adherence without intensifying medications is unlikely to be sufficient. Further, our sensitivity analysis focused on patients with high adherence in the preindex period and found that the effect of medication intensification was strong and significant when high adherence was maintained, but was not statistically significant among patients who transitioned from high to low adherence, further reinforcing the importance of both medication intensification and high adherence.

Physicians commonly cite other rationales for delaying intensification, such as promoting lifestyle changes or concerns that the BP reading is not representative. That is why we required at least 2 uncontrolled BP readings. Even so, intensification was rare. This may be in part due to our choice of using the updated BP control rate of 130/80 mm Hg. Recent evidence suggests there is a gap between guideline-recommended BP control targets and clinical practice.³⁷ Unfortunately, this inertia limits patients' ability to attain BP control.³⁸ In contrast, physicians in the SPRINT trial were directed to follow strict intensification protocols. In this context, patient-reported

adherence was not associated with therapeutic inertia.³⁹ Thus, adopting strong protocol-driven care may reduce therapeutic inertia. The next step may be to incorporate interventions to improve adherence into these protocols.

Table 2. Adjusted Odds Ratios of Improvement in Adherence After the Index Visit*

	Improvement in adherence after the index visit		
	AOR	95% CI	P value
Intensification at the index visit	1.20	1.03–1.38	0.02
Age (per 10 y)	1.03	0.97–1.09	0.30
Female (vs male)	1.00	0.88–1.13	0.94
Race			
Black (vs White)	0.79	0.38–0.92	<0.01
Other (vs White)	0.87	0.68–1.10	0.25
Insurance			
Medicare (vs commercial)	1.26	1.08–1.47	<0.01
Medicaid (vs commercial)	1.12	0.91–1.38	0.30
Years with a hypertension diagnosis	1.00	0.99–1.01	0.48
Diabetes (yes vs no)	0.98	0.86–1.12	0.80
Systolic BP at the index visit	1.00	1.00–1.01	0.66

BP indicates blood pressure.

*The population for this model is patients with uncontrolled BP and low (<80%) adherence before the index visit, with the outcome as an improvement in adherence to high (≥80%) after the index visit.

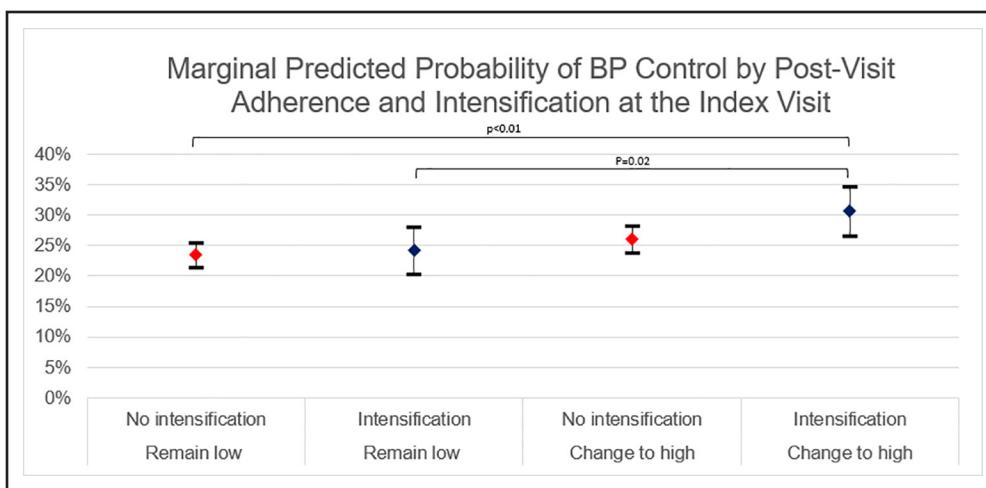


Figure 3. Marginal predicted probability of blood pressure (BP) control by postvisit adherence and intensification at the index visit.

This analysis was restricted to the population that had low adherence before the index visit. We defined low adherence as having <80% adherence rates. The group remained low, had <80% adherence before and after the index date. The group changed to high had <80% adherence before the index date and ≥80% adherence after the index date. Patients in the no intensification group did not receive antihypertensive intensification at the index visit, and those in the intensification group did. Thus, going from left to right, the first group received no intensification at the index visit, and adherence remained low. The second group received intensification at the index visit, and adherence remained low. The third group received no intensification at the index visit, but adherence increased to high in the 6 months after the index visit, and the fourth group received intensification at the index visit, and adherence increased to high in the 6 months after the index visit. We ran a multilevel logistic regression model with age, sex, race, insurance, years with hypertension, an indicator for diabetes, and systolic blood pressure measurement at the index visit as fixed variables and primary care provider as a random variable. Stata's margins command was used to identify the predicted probability of blood pressure control after the index visit using the interaction of change in adherence and index-visit intensification as predictor variables. Pairwise comparisons without an indicated significance level were not significant.

Quality improvement efforts have generally focused on medication intensification,^{16,18,19} with less attention to adherence. The American Heart Association's toolkit¹⁷ suggests talking openly about expectations and goals related to adherence. Physicians may review adherence data before a patient's visit. When available, Surescripts pharmacy fill information may offer a more reliable assessment of antihypertensive adherence than patient reports,⁴⁰ which may overestimate adherence.⁴¹ However, improving adherence is not enough. One trial of personalized adherence feedback improved medication adherence in patients with resistant hypertension, but it did not improve BP control.⁴² Another found that providing information on patients' adherence increased discussions regarding goals of care, but did not improve BP control.⁴³ Our findings suggest that such discussions must be paired with intensification.

Primary care physicians are busy,⁴⁴ and discussing adherence requires time.⁴⁵ Reviewing antihypertensive medication history, discussing adherence, and addressing reasons for nonadherence may not all be feasible in the setting of a busy primary care visit. Physicians often prioritize other issues and may defer addressing an uncontrolled BP. Given the worsening of BP control over time, health care systems may need to help physicians prioritize adherence counseling and treatment intensification through written protocols.

Even when physicians intensified therapy and improved adherence, patients usually did not attain BP

control at 6 months. This highlights the difficulty of attaining BP control in this population. Unlike patients with newly diagnosed hypertension, patients in this study had longstanding hypertension, and their BP was uncontrolled at baseline. This may represent a population with difficult-to-control BP. Patients, on average, took 2.11 medications. In SPRINT, patients required an average of 3 medications to achieve tight BP control.⁴⁶

The limitations of this study include the fact that it was an observational study conducted at a single integrated health system. Thus, there may be other factors we cannot control that could have impacted BP control (eg, changes in diet or stress levels). To mitigate this concern, we created a clinically meaningful scenario that allowed us to assess physicians' actions for patients with hypertension who had consistently uncontrolled BP, and provided a diagram to understand the temporal relationship between actions at the index visit and subsequent BP control. Another limitation is that we measured adherence using prescription fill data, which is generally accurate⁴⁰ but may not reflect whether a patient took the medication, particularly on the day of the visit. For medication intensification, we focused on the physician's action of prescribing a new class or higher dose of medication. It is possible that the physician might have simultaneously discontinued another class of medication due to the side effects. In that case, we would have overestimated intensification. Given that medication discontinuation is not

reliably captured within the electronic health record, we were unable to calculate changes in medication burden. Further, we cannot determine the true clinical rationale behind a physician's actions regarding medication intensification or whether they discussed adherence. Finally, it is possible that external generalizability could be limited since this study was conducted in Northeast Ohio. However, this health system serves a large population of primary care patients from diverse geographic and socio-economic backgrounds.

PERSPECTIVES

In sum, our findings suggest the importance of simultaneously intensifying medication and improving adherence for patients with hypertension and uncontrolled BP at primary care visits, with both factors necessary to improve BP control. Only a small portion of patients presenting with low adherence had their medication intensified. The patients who were intensively treated had higher rates of adherence after the index visit. To achieve BP control, physicians and health systems should continue to appropriately intensify medication, even in situations where patients are poorly adherent. In these circumstances, physicians should address both adherence and intensification together.

ARTICLE INFORMATION

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None.

Disclosures

None.

Supplemental Material

Table S1

Figure S1

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