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When More Is Not Better
Treatment Intensification Among Hypertensive Patients With Poor Medication Adherence

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Background—Hypertension may be poorly controlled because patients do not take their medications (poor adherence) or because providers do not increase medication when appropriate (lack of medication intensification, or "clinical inertia"). We examined the prevalence of and relationship between patient adherence and provider treatment intensification.

Methods and Results—We used a retrospective cohort study of hypertensive patients who had filled prescriptions for 1 or more blood pressure (BP) medications at Veterans' Affairs (VA) healthcare facilities in a Midwestern VA administrative region. Our sample included all patients who received at least 2 outpatient BP medication refills during 2004 and had 1 or more outpatient primary care visits with an elevated systolic BP >140 but <200 mm Hg or diastolic BP >90 mm Hg during 2005 (n=38 327). For each episode of elevated BP during 2005 (68 610 events), we used electronic pharmacy refill data to examine patients' BP medication adherence over the prior 12 months and whether providers increased doses or added BP medications ("intensification"). Multivariate analyses accounted for the clustering of elevated BP events within patients and adjusted for patient age, comorbidities, number of BP medications, encounter systolic BP, and average systolic BP over the prior year. Providers intensified medications in 30% of the 68 610 elevated BP events, with almost no variation in intensification regardless of whether patients had good or poor BP medication adherence. After adjustment, intensification rates were 31% among patients who had "gaps" of <20% (days on which patients should have had medication but no medication was available because medications had not been refilled), 34% among patients with refill gaps of 20% to 59%, and 32% among patients with gaps of 60% or more.

Conclusions—Intensification of medications occurred in fewer than one third of visits in which patients had an elevated BP. Patients' prior medication adherence had little impact on providers' decisions about intensifying medications, even at very high levels of poor adherence. Addressing both patient adherence and provider intensification simultaneously would most likely result in better BP control. **(*Circulation*. 2008;117:2884-2892.)**

Key Words: hypertension ■ patients ■ adherence ■ treatment intensification ■ quality of care

Many adults with hypertension, including high-risk adults with cardiovascular disease and diabetes, have persistently elevated blood pressures (BP).[1,2] Medications are the cornerstone of effective treatment for hypertension,[3,4] yet when faced with elevated BP, providers often do not appropriately increase medication dose or number of medications: They do not "intensify" the treatment.[5–7] Such failures to intensify medications, often labeled "clinical inertia," are associated with poor BP control.[7–10] Discussions of clinical inertia, however, often neglect another factor that prevents effective treatment: Many adults with hypertension do not take their BP medications as prescribed.[11,12] This poor medication adherence is the cause of up to 50% of treatment failures and is associated with disease progression, avoidable hospitalizations, disability, and death.[11,13] When patients are not taking their medications as prescribed, the appropriate clinical strategy is to address adherence problems rather than to increase doses or numbers of medications. In the words of former US Surgeon General Everett Koop, "Drugs don't work in patients who don't take them." Although both clinical inertia and poor adherence are barriers to achieving BP control, intensifying medications before addressing adherence difficulties is ineffective, costly, and could even be dangerous if patients suddenly start taking all their prescribed BP medications.[11,14]

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To be able to address their patients' poor adherence, providers first need to know that it is a problem.[15,16] A growing number

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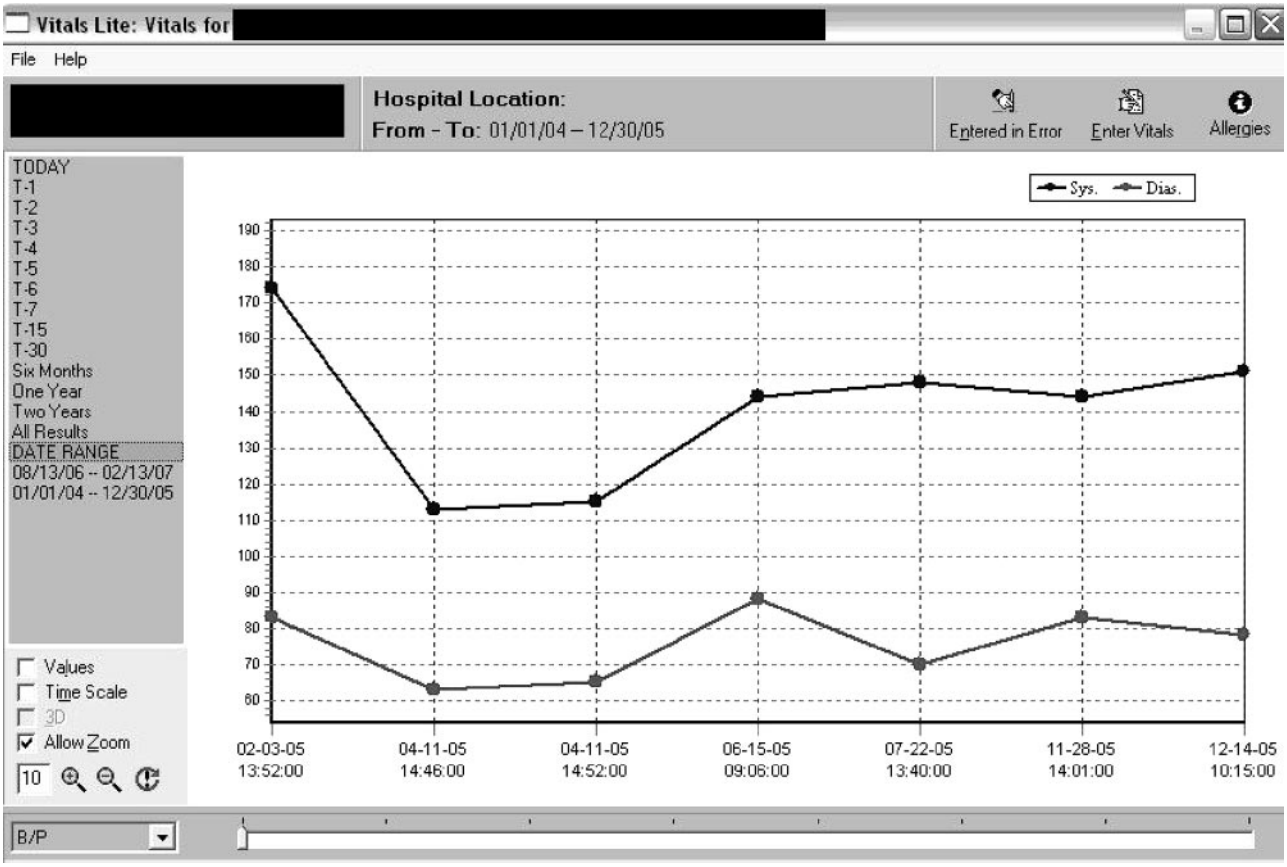

Figure 1. Example of electronic medical record view of outpatient visit BPs in 2005.

of health systems use electronic pharmacy records that include both prescription orders and information about medication refills, data that can provide objective and readily available refill adherence information.[17–19] Such pharmacy data are more sensitive indicators of medication adherence than physicians' own estimates[20,21] and patients' self-reported measures.[17,22,23] Rates of gaps in prescription refills are an accurate measure of overall adherence in health systems that provide pharmacy services, such as the Veterans Administration (VA) and other integrated systems.[22,24] When automated clinical data also include BP information,[25] they provide an ideal means to study whether medication intensification occurred in response to an elevated BP and whether medications were intensified despite evidence of poor patient adherence (eg, gaps in prescription refills).[10,26]

In prior studies of clinical inertia, providers frequently cited poor patient adherence as the reason they did not intensify medications in response to an elevated BP.[27] Were recognition of patient nonadherence a significant reason for the observed provider behavior, we should find lower rates of medication intensification among hypertensive patients with poor prior medication adherence. On the other hand, if providers did not adequately assess adherence before making a treatment decision, then providers might be as likely to intensify medications for patients with elevated BP and poor adherence as for those with elevated BP and good adherence.

We designed a large retrospective cohort study using VA pharmacy and clinical data to (1) quantify the prevalence of adherence problems and/or lack of intensification among hypertensive patients and (2) explore the relationship between adherence and intensification. The study was approved by the Ann Arbor VA Institutional Review Board.

Methods

Study Population

We identified all patients in 1 VA administrative region covering Michigan, Ohio, Indiana, and Illinois (VISN 11) who received 2 or more outpatient BP medication refills during 2004 and were alive at the end of 2005 (n=113 743). VISN 11 includes 7 facilities, including 3 large academic teaching institutions, and their associated outpatient clinics. Approximately 80% of primary care providers are physicians, and 20% are midlevel providers. During the study period, providers could easily track BPs over the prior year at a clinical encounter through the electronic medical record (see Figure 1 for graphical display providers could view). Providers were also able to examine patients' most recent medication refill records through the electronic medical record. However, as Figure 2 shows, that information was difficult to follow and interpret. We thus hypothesized that providers would appropriately take account of patients' prior BPs in making medication intensification decisions, especially if the encounter BP was only moderately elevated, but not of patients' prior adherence.

We had access to all VISN patient-level data on patient birthdates, outpatient BP values, dates of outpatient and inpatient encounters, International Classification of Diseases, 9th Revision (ICD-9) codes, and pharmacy fills. We excluded patients if they had no BP measurements during either 2004 or 2005, were hospitalized for 180 days or more in 2005, or had no primary care visits in 2005. We studied BP and the use of BP medications among the 82 818 remaining eligible patients during calendar year 2005. Of those

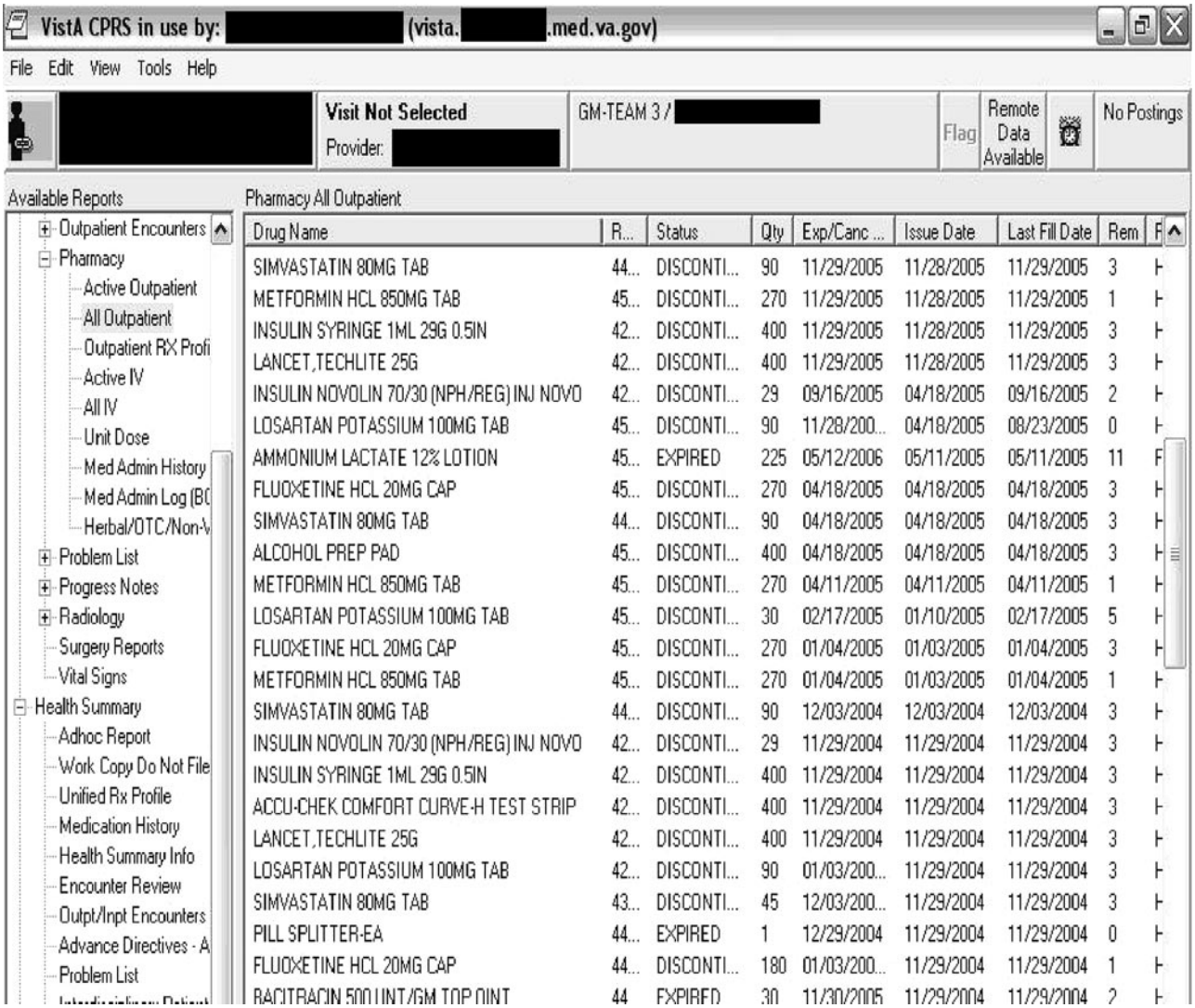

Figure 2. Example of VA electronic medical record pharmacy information available to providers at outpatient visits during study period (2004–2005).

82 818 patients, 38 327 had at least 1 elevated BP event and were eligible for inclusion in the cohort. Those 38 327 patients (46.3%) had a total of 68 610 elevated BP events in 2005. The elevated BP event was the unit of analysis. We identified each elevated BP (systolic BP [SBP] >140 but <200 mm Hg or diastolic BP [DBP] >90 mm Hg) event that occurred on the day of a primary care outpatient encounter during 2005. We excluded events in which SBP was ≥200 mm Hg because these often represent acute events with a different management strategy.

Principal Independent Variable of Poor Medication Refill Adherence

For both adherence and intensification, we categorized BP medications by class. Using automated VA pharmacy data, we used the continuous, multiple interval measure of gaps in therapy (CMG),[17,22] defined as the proportion of days the patient should have been taking medications during which the patient did not have medication available: CMG=total number of days on which patient did not have medications available/total number of days the patient should have been taking medication. Higher proportions indicate worse levels of adherence (ie, larger medication refill gaps). If a patient stopped filling a BP medication during the study period, we assumed that the provider had discontinued the medication and did not include this medication in measurements of refill gaps. Because most medications in the VA are filled for 90-day periods, to gain a more accurate assessment of gaps in refilling medications and account for overstocks of medications from prior fills, we examined adherence over the 12-month period before each encounter with an elevated BP. Details of the algorithms defining this measure and the underlying assumptions are in Appendix I in the online Data Supplement.

For each elevated BP event, we calculated the CMG for each BP medication class in the 12 months before the event. Once the CMG was calculated for each medication class as a continuous variable, we determined the worst CMG, which we will refer to as the "gap," among any class of medication the patient was taking for each elevated BP event. This "worst gap" was used in the analyses. Multiple studies have found significant clinical effects when cumulative days of refill gaps equal or exceed 20%.[24,28,29] We created a final categorical variable of <20% (reference category), 20% to 59%, and ≥60%. For sensitivity analyses, we also created a measure calculating the CMG for the aggregate of all BP medications each patient had filled.[17]

Primary Outcome Measure

Our primary outcome measure was whether or not patients' BP medication regimens were intensified at or within 14 days after a documented elevated BP event at an outpatient clinic visit (primary care, nephrology, endocrinology, or cardiology clinic). Medications

were considered to be intensified if 1 or more of the following changes were made: (1) a new drug class was added; (2) the patient was switched to a new class; (3) the patient was switched to a different medication within the same class; or (4) an increase was made in the daily dosage category of an ongoing medication.

Covariates

Both the encounter SBP and BPs at previous visits should determine whether treatment is intensified. We, therefore, included both as continuous variables in the model. Prior BP was measured as the mean of SBP in the 12 months that preceded the elevated BP event. Because the response to an elevated BP at a visit might be modified by the degree of past control, we also included an interaction term between current and past SBP. Moreover, because more medications may be associated with worse adherence[12] and affect the likelihood of intensification, the total number of prescribed BP medication classes the patient had filled at the time of the encounter with an elevated BP was included.

We included information on patients' ages (<65 years, 65 to 74, ≥75) and comorbidities obtained from VA electronic databases during the year before cohort entry. We classified morbidities as (1) diabetes mellitus with or without other cardiovascular disease equivalents (CDEs), (2) CDEs but no diabetes, or (3) no diabetes or other CDE. We looked at diabetes separately from other CDEs because we hypothesized that providers might intensify medications for patients with diabetes differently from patients with other CDEs but not diabetes. Patients were categorized as having a CDE not including diabetes if they had 2 outpatient diagnoses or 1 inpatient diagnosis of coronary artery disease, aortic abdominal aneurysm, stroke or transient ischemic attack, peripheral arterial disease, or peripheral vascular disease during 2004 (Appendix II in the Data Supplement). Patients were classified as having diabetes mellitus if they had 2 or more outpatient diagnoses or 1 or more inpatient diagnoses (ICD-9 codes of 250xx, 3572, 3620, or 36641) or if they were taking 1 or more oral antihyperglycemic medications or insulin. Otherwise eligible patients not meeting either of these requirements were classified as not having diabetes or other CDEs.

Data Analyses

To examine all opportunities for provider intensification of medications in response to an elevated BP, our unit of analysis was each elevated BP event. Because many patients had more than 1 elevated BP event, we had to take into account the clustering of BP events within patients. We constructed 2-level models, with the multiple individual BP measurements at level 1 nested within the patient identifier at level 2, using generalized estimating equations with the xtgee logistic regression procedures in STATA 9.2 (StataCorp, College Station, Tex). With this model, as with a single-level logistic regression, predicted probabilities are marginal probabilities that reflect responses to an elevated BP averaged across the population of patients sampled, conditional on the covariates. The model is robust to misspecification of the correlation structure within patients and furthermore allows for use of a robust Huber/White/sandwich estimator of variances of the predictors.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Descriptive Statistics

There were 38 327 eligible patients with 1 or more primary care outpatient clinic encounters with elevated BPs in 2005. The mean age of eligible patients was 67.5 years, and 97% were men. The mean number of elevated BP events was 1.79 per person (SD 1.27).

These 38 327 eligible patients had a total of 68 610 elevated BP events. Mean BPs for the elevated BP events was 151.7 mm Hg (SD 12.3 mm Hg) for SBP and 78.3 mm Hg (SD 12.4) for DBP. In 80% of the elevated BP events, only the SBP was elevated, in 4% only the DBP was elevated, and in 16%, both were elevated. Intensification was more likely to occur in encounters in which both SBP and DBP were elevated than if only 1 of these was elevated. The number of BP medications being taken at the time of elevated BP events was, on average, 2.4. The mean worst refill gap before an elevated BP event was 21% of prescribed days during the 12-month period before the date of the elevated BP event. A total of 42% of elevated BP events were preceded by poor refill adherence (gaps ≥20%). In 41% of elevated BP events with good refill adherence (gaps <20%), however, there was no medication intensification. Thus, in 83% of elevated BP events, either poor patient adherence or lack of provider medication intensification in the face of good patient refill adherence was present. In the face of poor adherence, providers ideally would address adherence problems before intensifying medications. In the face of good adherence, the appropriate response would be to intensify medications.

Table 1 shows the unadjusted mean refill gaps and intensification rates at clinic visits with elevated BPs according to the characteristics of the patients at the clinic visits. Poor adherence (refill gap of ≥20%) was present in 42% of elevated BP events. Of the 68 610 elevated BP events, intensification took place in 30%. Of those who had their medication regimen intensified, 29% had medication gaps <20%, 32% had medication gaps of 20% to 59%, and 30% had medication gaps of 60% or more.

Multivariate Analyses

In multivariate analyses, higher SBP was the factor most associated with probability of medication intensification (Table 2). Both higher SBP at the clinic visit (adjusted OR 1.34 per 10 mm Hg, $P<0.001$) and average SBP over the prior year (adjusted OR 1.14 per 10 mm Hg, $P<0.001$) were associated with higher odds of intensification. As indicated by the significant coefficient of the interaction term (encounter SBP×average prior SBP) in Table 2, at higher encounter SBPs, there was less influence of average prior SBPs on the treatment intensification decision: Patients with higher SBPs at the clinic visit were more likely to be prescribed intensified treatment regardless of their prior SBP readings. For example, for those patients with a mean of prior BPs of 140 mm Hg, the OR of intensification was 1.35 (95% CI 1.32 to 1.38) for each 10-mm Hg increase in the encounter SBP. The interaction term coefficient indicated that as hypothesized, when the prior BPs had been elevated, intensification was less sensitive to the encounter BP, and when prior BPs had been lower, providers placed more weight on the encounter SBP in making intensification decisions (so for a mean of prior BPs of 120 mm Hg, the OR for encounter SBP was 1.42 [95% CI 1.38 to 1.47] per 10-mm Hg, and for a mean of prior BPs of 160 mm Hg, it was 1.28 [95% CI 1.26 to 1.31]). In alternative analyses, higher encounter DBP but not mean prior DBP was also associated with intensification, after controlling for encounter SBP and prior mean SBP (analyses not shown).

In adjusted analyses, there continued to be little variation in intensification rates regardless of whether patients had good or poor BP medication adherence. Medication refill gaps

Table 1. Unadjusted Refill Gaps and Intensification Rates at Visits With Elevated BPs, by Patient Characteristics

Visits With Elevated BP by Patient Characteristics	Mean Worst Refill Gap,* %	Intensification Rate,† %
All visits (n=68 610)	21	30
Level of SBP, mm Hg		
<160 (n=52 726)	20	27
160–179 (n=13 225)	23	40
180–199 (n=2659)	26	47
Age, y		
<65 (n=28 777)	22	31
65–74 (n=18 294)	21	31
≥75 (n=21 539)	20	29
Diagnoses		
Neither DM or CDE (n=33 394)	20	30
CDE but no DM (n=8305)	22	27
Diabetes with or without other CDE (n=26 911)	22	31
Gender		
Female (n=1918)	20	26
Male (n=66 692)	21	30
No. of active BP medication classes (at encounter)		
0 (n=2508)	15	21
1 (n=15 854)	17	30
2 (n=20 312)	20	30
3 (n=16 963)	22	31
4–5 (n=11 817)	25	31
≥6 (n=1156)	31	32
Worst refill gap (% of Rx days)		
<20 (n=39 734)	8	29
20–60 (n=25,492)	35	32
≥60 (n=3384)	70	30

DM indicates diabetes mellitus.

*Gaps in medication refills for each BP medication class were calculated with the CMG measure, defined as the proportion of days the patient should have been taking medications during which the patient did not have medication available. Higher proportions indicate worse levels of adherence (ie, larger medication refill gaps). For each patient visit with an elevated BP, the highest (worst) gap among the patient's BP medications was used to generate the mean worst refill gap.

†Intensification included any of the following actions within 14 days of the visit with an elevated BP: (1) adding a new class; (2) switching to a new class; (3) switching to a different medication within the same class; or (4) increasing the dosage category of an ongoing medication.

from 20% to 59% were associated with slightly higher odds of intensification than gaps <20% (adjusted OR 1.07, $P<0.001$), with adjusted intensification rates of 31% among patients with medication refill gaps <20%, 34% among patients with gaps of 20% to 59%, and 32% among patients with gaps of 60% or more.

Because we hypothesized that providers might be more likely to consider patients' prior medication adherence in making intensification decisions when BP was only marginally elevated, we included an interaction term between encounter SBP and adherence gaps. This interaction term was significant but in the opposite direction of our hypothesis; however, the effect was small and clinically insignificant (as can be seen in Figure 3). There were also no significant differences in the independent effect of medication adherence on the likelihood of medication intensification across age and clinical diagnosis groups. In sensitivity analyses using an aggregate measure of adherence across all medication classes that patients were taking, there continued to be almost no variation in intensification based on patients' prior adherence levels. Intensification rates for each category of adherence (<20%, 20% to 59%, and ≥60% of prescription days) differed from the intensification rates for each category of adherence with the medication class-specific measure by only 1% to 2%.

What specific effect did adherence have on the likelihood of intensification? Figure 3 shows data for patients with diabetes, younger than 75 years, taking 2 medication classes, with adjustment for prior SBP. Figure 3 shows the association of each level of adherence on adjusted predicted probabilities of intensification at different levels of office visit SBPs and illustrates that different levels of medication refill adherence have relatively little effect on the probability of undergoing medication intensification for an elevated BP event. Across all adherence categories, the likelihood ranged from a mean intensification rate of ≈25% in office visits with SBPs ≈140 mm Hg to a mean intensification rate of ≈50% in office visits with SBPs >170 mm Hg. Overall adjusted probabilities of intensification were similar across adherence categories: 31% among adherent patients compared with 34% among patients with moderate medication refill gaps (20% to 59%) and 32% among patients with refill gaps ≥60%.

Discussion

In this large cohort of hypertensive patients followed up over 2004 to 2005, whether or not patients had been adherent to their BP medications had little effect on providers' decisions about intensifying therapy in response to an elevated BP. Where there was very poor adherence in the 12 months before an elevated BP event, as evidenced by large BP medication refill gaps (≥60%), medications were as likely to be intensified as when events were preceded by no or small medication refill gaps. These findings were robust whether we examined medication refill gaps in individual medication classes or across all prescribed antihypertensive medications. One possible explanation for the lack of variation in intensification among patients with different levels of adherence is that nonadherent patients also have higher prior BPs, thus increasing the likelihood that providers will intensify medication. Our models controlled for the previous level of BP control, and thus, this is unlikely to be an explanation. In some cases of observed BP medication changes (ie, switching to another medication), providers may be appropriately changing medications in response to patient side effects. However, the lack of significant differences in both unadjusted and adjusted predicted rates of intensification among patients with good and very poor prior medication adherence suggests that providers are simply not taking patients' prior

Table 2. Adjusted ORs of Undergoing BP Medication Intensification

	Model 1: Base (95% CIs)	Model 2: Age and Diagnosis (95% CIs)	Model 3: No. of BP Meds at Encounter (95% CIs)	Model 4: % Worst Refill Gap* (95% CIs)
Encounter SBP	1.31 (1.29–1.33)	1.32 (1.30–1.34)	1.32 (1.30–1.34)	1.34 (1.32–1.37)
Average prior SBP	1.13 (1.12–1.15)	1.13 (1.12–1.15)	1.14 (1.12–1.15)	1.14 (1.12–1.15)
SBP×average prior SBP†	0.97 (0.97–0.98)	0.97 (0.97–0.98)	0.97 (0.97–0.98)	0.97 (0.97–0.98)
Age <65 y		Reference	Reference	Reference
Age 65–74 y		0.98 (0.93–1.02)	0.98 (0.93–1.02)	0.98 (0.94–1.02)
Age ≥75 y		0.85 (0.81–0.88)	0.85 (0.81–0.88)	0.85 (0.81–0.88)
Neither diabetes or CDE		Reference	Reference	Reference
CDE with no diabetes		0.84 (0.79–0.89)	0.85 (0.80–0.90)	0.85 (0.80–0.90)
Diabetes with or without other CDE		0.97 (0.94–1.01)	0.99 (0.96–1.03)	0.99 (0.96–1.03)
Male gender		1.24 (1.11–1.40)	1.25 (1.11–1.41)	1.25 (1.11–1.40)
No. of BP medications at encounter			Reference	Reference
1			1.62 (1.45–1.80)	1.60 (1.44–1.78)
2			1.54 (1.39–1.71)	1.52 (1.37–1.69)
3			1.46 (1.31–1.63)	1.44 (1.30–1.61)
4 or 5			1.34 (1.20–1.49)	1.31 (1.18–1.47)
≥6			1.18 (0.99–1.42)	1.17 (0.97–1.40)
<20% Worst refill gap†				Reference
20% to 59% Worst refill gap				1.07 (1.03–1.11)
≥60% Worst refill gap				0.95 (0.87–1.04)
Encounter SBP ×20% to 59% refill gaps				0.96 (0.93–0.99)
Encounter SBP ×≥60% refill gaps				0.98 (0.92–1.04)
Observations	68 610	68 610	68 610	68 610

All models included the same number of observations (68 610 BP elevated events). Exponentiated coefficients (95% CIs).

*Gaps refer to the maximum gap in coverage days for a medication in the prior 6 months.

†The interaction term coefficient indicates that when the prior BPs have been elevated, intensification is less sensitive to the encounter BP, and when prior BPs have been lower, providers place more weight on the encounter SBP in making intensification decisions (so for a mean of prior BPs of 120 mm Hg, the OR for encounter SBP is 1.42 [1.38 to 1.47] per 10 mm Hg, and for a mean of prior BPs of 160 mm Hg, it is 1.28 [1.26 to 1.31]). For example, for those patients with a mean of prior BPs of 140 mm Hg, the OR of intensification is 1.35 (1.32 to 1.38) for each 10-mm Hg increase in the encounter SBP.

medication adherence into account in making medication management decisions.

In the study health system (VA VISN 11), during 2005, providers could easily track BPs over the prior year at the time of clinical encounters through the electronic medical record (Figure 1). Indeed, we found that both the actual level of the SBP at the time of the office visit and prior BP levels independently had a large influence on the likelihood of intensification. As we hypothesized, when the SBP at the office visit was elevated only marginally, higher prior SBPs more significantly influenced providers' decisions. This finding further suggests that providers were appropriately taking account of both the current and prior BP levels in determining whether or not to intensify BP medications.

The present study findings suggest that providers were less vigilant—or less successful—in assessing patients' medication adherence to already prescribed BP medications before further intensifying their medication regimens. Multiple studies have documented inaccuracies and biases in providers' assessments of individual patients' adherence levels.[20,30,31] As noted, at the time of the present study, although providers were able to examine patients' most recent medication refill records through the electronic medical record at the time of a visit, the information was difficult to follow and interpret (Figure 2). Since early 2006, however, the VA's electronic medical record has begun to display patients' medication refill gaps for each prescribed medication in a more visually accessible, clear, graphical format (Figure 4). Although this information does not account for hospitalizations or prior overstocks due to dosage changes, as the algorithm in the present study did, this type of easily accessible, objective information at the time of prescribing or renewing prescriptions is an important first step in ensuring that assessment of current adherence becomes an integral part of outpatient clinical decision making.

Future studies should assess whether and how the availability of such medication adherence information to providers through the electronic medical records will influence clinical decision making. Prior studies, however, suggest that simply providing adherence and treatment intensification information to physicians is not likely to be successful.[32,33] Physicians and other primary care providers face multiple competing demands in the limited time available in clinic visits. This combination of multiple demands and lack of time makes it

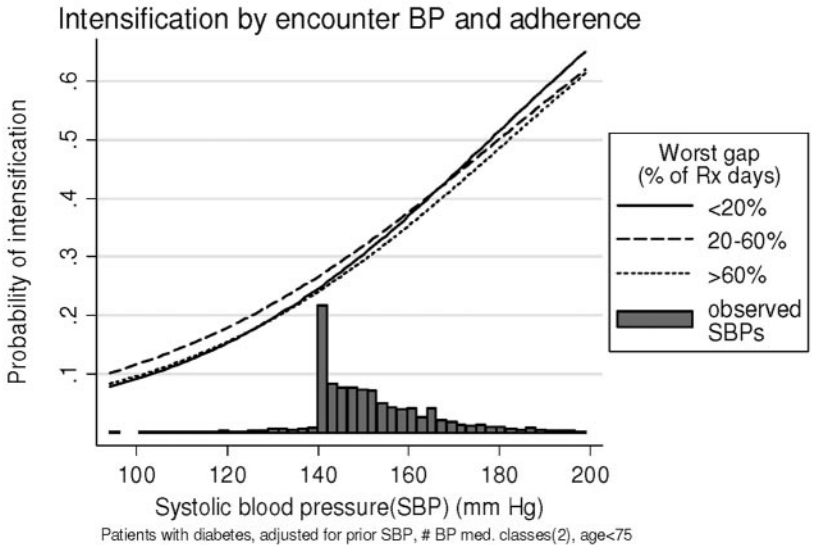

Figure 3. Intensification by encounter BP and adherence. Rx indicates prescription.

difficult, if not impossible, to adequately assess adherence and address identified adherence problems in brief office visits. Instead of using adherence information post hoc as we did here, we need to provide readily usable adherence information at visits combined with effective approaches to addressing medication adherence problems and clinical inertia. We need to integrate the use of electronic data to proactively identify adherence and treatment intensification problems into a team-based approach that will enable that information to be adequately acted on and followed up with evidence-based behavioral approaches, standardized treatment algorithms, and collaboration across providers.[33–36]

The findings of the present study should be interpreted in the face of several limitations. First, medication refill data

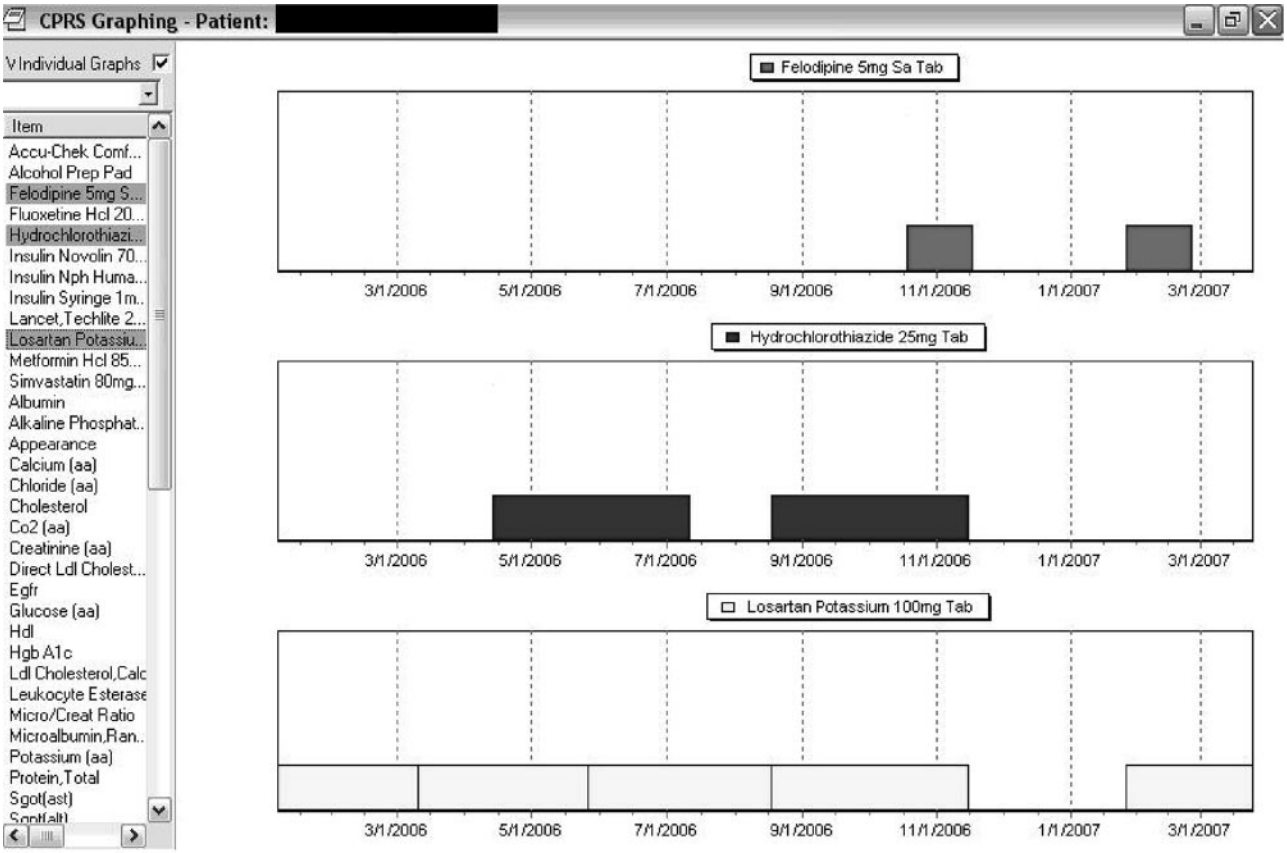

Figure 4. Example of VA electronic medical record graph of medication-specific refill patterns available to providers at outpatient visits since 2006.

provide a measure of medication availability and could overestimate actual pill taking. In other respects, however, our methods for measuring adherence overestimate adherence. For example, if patients completely stopped filling prescriptions for a medication ("nonpersistence"), we assumed that the provider had discontinued that medication, thereby not including nonpersistence in our adherence calculations. Second, our measures required that medications be obtained within the VA pharmacy system. With the advent of electronic prescribing systems with links to outside pharmacy data, however, such pharmacy data will become increasingly available without necessitating within-system pharmacy services. Third, although our measure provides information on the magnitude of refill gaps during the 12 months before each elevated BP, we did not account for timing of the refill gaps in our analysis. Ideally, for clinical decision making and adherence counseling, adherence measures would provide information on both the magnitude and exact timing of refill gaps (such as that shown in Figure 4). Finally, as with any study using large administrative and clinical data sets, we have sufficient sample size to examine patterns of care in different patient subsamples but cannot account for unmeasured confounding or explore in-depth mechanisms for observed patterns.

The present study builds on prior research in several ways. In the present study sample, 83% of elevated BP events occurred in the context of either poor prior patient refill adherence or lack of provider intensification. In a recent study in The Netherlands, the authors did not examine intensification and poor adherence in the face of elevated BPs. Instead, they examined all medication changes (including dose decreases). Although only 4% to 5% of the patients had medication refill gaps ≥20%, poor medication adherence was positively associated with modification of BP medications.[37] Grant et al[38] measured antihyperglycemic medication adherence among health maintenance organization patients with diabetes mellitus who had just started taking medication or had recently begun medication intensification within 12 months of the patients' next elevated glycosylated hemoglobin (A_{Ic}). Patients with the worst baseline adherence had lower rates of medication intensification than those in the highest quartile of adherence (27% versus 36%). Grant and colleagues interpreted providers' lower rates of medication intensification among patients with the worst medication adherence as "clinical inertia." Instead, this could represent rational clinical decision making: an effort to improve medication adherence to prescribed medications, rather than inappropriately intensifying medications among patients not taking their current prescriptions. In the present study, 42% of the elevated BP events in which providers did not intensify medication were events preceded by refill gaps ≥20%, cases that indeed may have represented efforts by the providers to address adherence problems first before intensifying medications.

In conclusion, most patients who presented with elevated BPs had either poor medication adherence or failed to have their medication intensified. Indeed, patients with large BP medication refill gaps were intensified at rates similar to or slightly higher than those for patients with good medication adherence, which suggests that providers did not consider patients' adherence before intensifying medication. This failure could lead to polypharmacy, ineffective treatment, and increased costs. A growing number of health systems have the capacity to use electronic pharmacy data to alert providers to possible medication-specific adherence problems at clinic visits; however, as shown in prior studies,[39] an exclusively primary care provider–based intervention is unlikely to succeed. To be effective, an ideal health system–level intervention to improve BP and other risk factor control among patients must address 3 key elements. First, electronic pharmacy data with links to patient biomedical data should be used to identify and proactively target patients with poor BP (and other risk factor) control who are not taking medications as prescribed or require medication intensification. Second, an intervention must address sequentially the complexity of both adherence and intensification. This requires a provider trained in both behavioral approaches and pharmacological management. Third, there needs to be follow-up once a behavioral or pharmacological change has been initiated. This requires that the care organization provide contacts at appropriate intervals with appropriate providers. Interventions combining these 3 components are within the reach of many health systems, and if properly constructed, they may be cost-effective or even cost-saving. Interventions that address both adherence and intensification may be critical to improving BP control and decreasing morbidity and mortality from cardiovascular disease.

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Disclosures

None.

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CLINICAL PERSPECTIVE

It is important for clinicians to determine whether patients are taking already prescribed medications before increasing doses or numbers of medications ("intensifying" medications). Intensifying medications before addressing adherence difficulties is ineffective, costly, and could even be dangerous if patients suddenly start taking all their prescribed medications. In a large cohort of patients with hypertension, we investigated the extent to which providers increased medications in the face of poor patient blood pressure control when there was evidence of poor patient medication adherence. We conclude with recommendations for effective approaches to assess and address medication adherence problems.