**Background:** Studies have demonstrated that blood pressure (BP) control can be improved when clinical pharmacists assist with patient management. The objective of this study was to evaluate if a physician and pharmacist collaborative model in community-based medical offices could improve BP control.

**Methods:** This was a prospective, cluster randomized, controlled clinical trial with clinics randomized to a control group (n=3) or to an intervention group (n=3). The study enrolled 402 patients (mean age, 58.3 years) with uncontrolled hypertension. Clinical pharmacists made drug therapy recommendations to physicians based on national guidelines. Research nurses performed BP measurements and 24-hour BP monitoring.

**Results:** The mean (SD) guideline adherence scores increased from 49.4 (19.3) at baseline to 53.4 (18.1) at 6 months (8.1% increase) in the control group and from 40.4 (22.6) at baseline to 62.8 (13.5) at 6 months (55.4% increase) in the intervention group (P=.09 for adjusted between-group comparison). The mean BP decreased 6.8/4.5 mm Hg in the control group and 20.7/9.7 mm Hg in the intervention group (P<.05 for between-group systolic BP comparison). The adjusted difference in systolic BP was −12.0 (95% confidence interval [CI], −24.0 to 0.0) mm Hg, while the adjusted difference in diastolic BP was −1.8 (95% CI, −11.9 to 8.3) mm Hg. The 24-hour BP levels showed similar effect sizes. Blood pressure was controlled in 29.9% of patients in the control group and in 63.9% of patients in the intervention group (adjusted odds ratio, 3.2; 95% CI, 2.0-5.1; P<.001).

**Conclusions:** A physician and pharmacist collaborative intervention achieved significantly better mean BP and overall BP control rates compared with a control group. Additional research should be conducted to evaluate efficient strategies to implement team-based chronic disease management.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00201019


Results of studies 1-5 suggest that antihypertensive medications are frequently not intensified when blood pressure (BP) remains uncontrolled, termed clinical inertia. One strategy to improve BP control is team-based care involving clinical pharmacists. However, many of these investigations were small, single-site studies, did not use an unbiased BP measurement, or did not control for important patient, physician, or clinic variables.
The study was approved by the University of Iowa Institutional Review Board and by the local institutional review boards for the 6 clinics. The recruitment process was identical in control and intervention offices. A research nurse employed by each office reviewed lists and clinic schedules for patients having diagnostic codes for hypertension and approached patients to participate. The research nurse telephoned patients who met the study criteria or approached them during a regular clinic visit.

Patients in the active study groups provided written informed consent. Men or women older than 21 years having a diagnosis of essential hypertension taking 0 to 3 antihypertensive medications were eligible if they did not have diabetes mellitus and their systolic BP (SBP) was between 140 and 179 mm Hg or their diastolic BP (DBP) was between 90 and 109 mm Hg. Patients with diabetes mellitus having an SBP of 130 to 179 mm Hg or a DBP of 80 to 109 mm Hg were eligible. Exclusion criteria included dementia, pregnancy, unstable angina, cognitive impairment, serious renal or hepatic disease, BP of 180/110 mm Hg or higher, poor prognosis (life expectancy <3 years), evidence of hypertensive urgency or emergency, New York Heart Association class III or IV heart failure, myocardial infarction or stroke (6 months before screening), and antihypertensive medication or dosage change within 4 weeks of the baseline visit.

We also performed a medical record audit of patients with hypertension from intervention clinics who met the same inclusion criteria but who did not receive the intervention, termed the passive observation group. The goal of evaluating this group was to determine if BP improved throughout the entire practice. The primary aim was to evaluate if guideline adherence improved more in the intervention group than in the control group using a tool validated for this study. Once the patients completed the trial, the research nurses performed a structured medical record abstraction process for all patients that included all clinic progress notes, laboratory values, and medications and records from hospitalization or emergency department visits. For patients in the passive observation group, an index date was selected, and data were abstracted for 6 months before and 6 months after the index date. One of us (G.A.) visited each clinic and evaluated a sample of the case abstracts against the medical record to ensure that data were being completely abstracted by each research nurse. Guideline adherence was determined by the percentage of 22 eligible criteria met by each patient using a computerized algorithm developed by the investigators.

The research nurses were trained to measure BP using standardized guidelines and were certified to properly measure BP at baseline and then once yearly. Blood pressure was measured 3 times using an automated device (HEM 907-XL; Omron Corporation, Schaumburg, Illinois). The second and third measurements were averaged and used as the study BP. At the end of the baseline visit, the research nurse placed a 24-hour monitor (90217-A; Spacelabs Medical, Issaquah, Washington) set to measure BP every 20 minutes during the day and every 30 minutes during sleep. These baseline 24-hour results were unavailable to the physician or the clinical pharmacist until the patient completed the trial. Finally, patients in both groups were given written information about hypertension from the National Heart, Lung, and Blood Institute. Clinical pharmacists at control sites abstained from providing care for study patients but continued to answer general treatment questions from physicians. Patients in the control group also received BP measurements at baseline, 3 months, and 6 months. The primary care physician determined when office visits for routine care or BP measurements should occur.

**DATA ANALYSIS**

Data were entered into case report forms by the research nurses. Individual data elements were double entered into a database (Access; Microsoft, Redmond, Washington) and were analyzed by a separate data management team chaired by the biostatistician (J.D.D., C.L.F., or Y.X.).

Power calculations were performed based on a 2-sample t test to compare SBP, assuming mean (SD) effect sizes of 6 to 10 (16-19) mm Hg of SBP. With a sample size of 200 patients per group (400 total), a 2-sided test (α = .05) would have 88% to 100% power. Due to the physician and clinic, this may overstate the power. Descriptive statistics (means [SDs]) were performed on baseline data, and comparisons between groups were made using the t test and Fisher exact test. Preliminary analysis revealed that the response variables were correlated within subjects, but there was no significant clustering within physicians and little clustering within clinics, similar to previous findings in an-

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other study. However, we included clinic as a random effect in our analyses of response variables, consistent with the study design. For continuous responses (BP), likelihood-based mixed models with random patient and clinic effects were fit in a statistical software program (SAS Proc Mixed; SAS Institute, Cary, North Carolina) to incorporate all available data from baseline through 6 months in an intent-to-treat analysis. For BP control, a generalized estimating equation model using the binomial distribution and the logit link was fit in another program (SAS PROC GENMOD) that accommodated the correlations within clinics. For both models (mixed and generalized estimating equation), contrasts were estimated to test for the treatment effect adjusted for the following baseline values: BP, age, sex, race/ethnicity, educational degree, insurance status, annual household income, marital status, smoking status, alcohol intake, body mass index, number of coexisting conditions, number of antihypertensive medications, and medication adherence. Medication adherence was determined using the instrument validated by Morisky et al. Poor medication adherence was defined as answering yes to 3 or more of 5 questions.

### RESULTS

The general operations of all 6 sites were similar, and the office served as the model office for a distinct family medicine residency. All 6 programs met the institutional requirements of the Accreditation Committee for Graduate Medical Education and the program requirements for family practice set out by the Accreditation Committee for Graduate Medical Education and its Residency Review Committee. All faculty physicians were board certified in family practice. The faculty physicians spent 3.4 (mean range and mode range, 2-5) half-days per week seeing patients in their clinic. The scheduled times in the clinic for first-, second-, and third-year family medicine physician residents were 1 to 2 half-days, 2 to 4 half-days, and 3 to 5 half-days per week, respectively. The remainder of the family medicine residents’ time was spent on clinical rotations in the affiliated hospital. Physicians in each office admitted patients to a distinct community hospital that operated and funded a significant portion of each residency program.

### Table 1. Characteristics of the Clinics at Baseline Before the Study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Office</th>
<th>Intervention Office</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Outpatient visits per year</td>
<td>27000</td>
<td>20700</td>
</tr>
<tr>
<td>Faculty physicians</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Resident physicians</td>
<td>17</td>
<td>30</td>
</tr>
<tr>
<td>Clinical pharmacists</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pharmacy residents</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>No. of medical record audits (BP control %)</td>
<td>50 (70.0)</td>
<td>50 (50.0)</td>
</tr>
</tbody>
</table>

*Patient, physician, and pharmacist data were collected in 2000 and blood pressure (BP) data in 2001 as preliminary data for the study grant application.

*One resident per year spent 5 weeks in this office.*

### Figure

Flowchart of patients through the study protocol. BP indicates blood pressure.
The first patient was enrolled on August 16, 2005, and the last patient completed the trial on April 9, 2008. In the control group, 173 of 210 patients (82.4%) completed the 3-month visit, and 174 of 210 patients (82.9%) completed the 6-month visit; in the intervention group, 173 of 192 patients (90.1%) completed the 3-month visit, and 158 of 192 patients (82.3%) completed the 6-month visit (Figure). Pharmacists made a mean (SD) of 1.6 (1.4) additional visits or contacts per patient, including 83.9% of the specified 1-month telephone calls, and these contacts were controlled for in the analyses. When adjusted for the intervention effect, the within-clinic interclass correlation coefficients at 6 months were 1.7% for SBP, 11.3% for DBP, and 10.4% for guideline adherence scores.

At baseline, patients in the control group were significantly less likely to be married (P <.001) and were more likely to have diabetes mellitus (P <.001), self-pay for their care (P <.001), have more coexisting conditions (P <.001), and have a history of myocardial infarction (P =.002) or angina (P =.003) (Table 2). These variables were covariates in the analyses.

**PRIMARY OUTCOMES**

The mean (SD) guideline adherence scores improved modestly (8.1%) in the control group from 49.4 (19.3) at baseline to 53.4 (18.1) at 6 months (Table 3). The mean (SD) guideline adherence scores improved 55.4% in the intervention group from 40.4 (22.6) at baseline to 62.8 (13.5) at 6 months (P =.04 for unadjusted and P =.09 for adjusted between-group comparisons). After adjustment for the covariates, the mean difference between groups for the improvement in guideline adherence scores was 9.6 (95% confidence interval [CI], −2.3 to 21.5) (Table 4).

Blood pressure was controlled among significantly more patients in the intervention group (63.9%) than in the control group (29.9%) (P <.001), with an odds ratio of 3.2 (95% CI, 2.0-5.1) after adjustment for covariates (Table 4). Blood pressure was controlled in 32.4% of patients without diabetes mellitus in the control group and in 68.8% of patients without diabetes mellitus in the intervention group (adjusted odds ratio, 3.9; 95% CI, 3.1-5.0; P <.001). Blood pressure was controlled in 26.1% of patients with diabetes mellitus in the control group and in 45.5% of patients without diabetes mellitus in the intervention group (adjusted odds ratio, 4.7; 95% CI, 1.7-13.1; P =.003).

The mean BP was reduced by 6.8/4.5 mm Hg in the control group and by 20.7/9.7 mm Hg in the intervention group (P <.05 for between-group SBP comparison). The adjusted mean difference (control group minus intervention group) in 6-month SBP was −12.0 (95% CI, −24.0 to 0.0) mm Hg, while the adjusted mean difference in 6-month DBP was −1.8 (−11.9 to 8.3) mm Hg (Table 4). The mean difference in 24-hour BP was −10.3 (−23.7 to 3.1) mm Hg for SBP and −3.1 (−9.0 to 2.8) mm Hg for DBP.

We performed a sensitivity analysis to determine the robustness of our findings in the presence of informative dropout. We repeated our analysis under a scenario that all 70 subjects who dropped out had uncontrolled BP at the end of the study and found that BP control rates in the intervention and control groups would be 52.6% and 24.8%, respectively (adjusted odds ratio, 3.2; 95% CI, 2.0-5.2; P <.001). More pessimistically, we considered the scenario in which all 34 dropouts in the intervention group had uncontrolled BP and all 36 dropouts in the control group had controlled BP. In this situation, the respective BP control rates would be 52.6% and 41.9% (adjusted odds ratio, 3.0; 95% CI, 2.0-4.5; P <.001).

**SECONDARY OUTCOMES**

We identified 197 patients for the passive observation group from the 3 intervention clinics. We did not compare this group statistically with the active intervention group because the outcome measures were different (research nurse-
measured BP in study patients vs medical record–recorded BP in the passive observation group). At baseline, the mean (SD) SBP in the passive observation group (149.2 [15.8] mm Hg) was lower than that in the active control group (150.6 [14.1] mm Hg) and the active intervention group (153.6 [12.7] mm Hg). By 6 months, the mean (SD) SBP in the passive observation group was 139.3 (16.9) mm Hg compared with 143.8 (20.5) mm Hg in the active control group and 132.9 (15.4) mm Hg in the active intervention group. Blood pressure control rates at 6 months were 29.9% in the active control group, 39.1% in the passive observation group, and 63.9% in the active intervention group, which supports the initial hypothesis that BP control within intervention sites could be improved more broadly in patients who did not receive the intervention.

The intervention pharmacists made 771 recommendations, of which 742 (96.2%) were accepted by physicians. The mean increase in the number of antihypertensive medications from baseline was higher in the intervention group than in the control group (1.1 vs 0.3, P < .001). There were 1139 documented antihypertensive medication changes in 402 subjects (mean age, 58.3 years), of which 562 (49.3%) were new medications, 333 (29.2%) were dosage increases, 195 (17.1%) were cessation of current medications, and 49 (4.3%) were decreases in dosage. The mean of overall changes was higher in the active intervention group (3.6 vs 2.2 changes per subject, P < .001), as was the number of new antihypertensive medications (1.9 vs 1.0, P < .001) and possibly the number of discontinued antihypertensive medications (0.6 vs 0.3, P < .05). The number of dosage changes did not vary significantly between groups. The mean (SD) number of antihypertensive medications was not different between the intervention group (2.4 [1.1] medications) and the control group (2.2 [1.1] medications) at the end of the study (P = .22).

The mean (SD) percentage of patients with poor self-reported medication adherence declined from 18.7% (22.0%) to 14.7% (20.9%) in the control group (P = .60). The mean (SD) percentage of patients with poor self-reported medication adherence declined from 17.3% (27.5%) to 14.6% (25.4%) in the intervention group (P = .98).

The mean (SD) symptom scores were higher at baseline in the control group (score, 42.1 [24.2]) compared with the intervention group (score, 28.0 [23.0]) (P < .001). Despite the increase in antihypertensive medications in both groups, the mean (SD) symptom scores declined at 6 months to 39.2 (24.2) in the control group (P = .07 vs baseline) and 16.6 (12.5) in the intervention group (P < .001 vs baseline or between groups at 6 months).

### Table 3. Clinic Blood Pressure (BP), 24-Hour BP, BP Control, and Guideline Adherence Scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP, mean (SD), mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>150.6 (14.1)</td>
<td>146.1 (19.6)</td>
<td>143.8 (20.5)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>83.6 (12.3)</td>
<td>81.5 (14.0)</td>
<td>78.1 (14.3)</td>
</tr>
<tr>
<td>BP control, %</td>
<td>0</td>
<td>25.4</td>
<td>29.9</td>
</tr>
<tr>
<td>24-h BP, mean (SD), mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>137.9 (15.8)</td>
<td>...</td>
<td>131.5 (17.7)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>77.2 (10.7)</td>
<td>...</td>
<td>73.7 (10.7)</td>
</tr>
<tr>
<td>Total guideline adherence score, % criteria met, mean (SD)</td>
<td>49.4 (19.3)</td>
<td>...</td>
<td>53.4 (18.1)</td>
</tr>
</tbody>
</table>

| Intervention (n=192) | | | |
| BP, mean (SD), mm Hg | | | |
| Systolic | 153.6 (12.8) | 134.8 (14.6) | 132.9 (15.5) |
| Diastolic | 87.4 (11.9) | 79.9 (11.3) | 77.7 (11.2) |
| BP control, % | 0 | 49.7 | 63.9 |
| 24-h BP, mean (SD), mm Hg | | | |
| Systolic | 136.2 (14.6) | ... | 121.1 (13.7) |
| Diastolic | 78.5 (11.7) | ... | 70.2 (8.7) |
| Total guideline adherence score, % criteria met, mean (SD) | 40.4 (22.6) | ... | 62.8 (13.5) |

### Table 4. Unadjusted and Adjusted Effects of Intervention vs Control at 6 Months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Unadjusted Effect (95% CI)</th>
<th>Adjusted Effect (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP, mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>-11.9 [-21.6 to -2.2]</td>
<td>-12.0 [-24.0 to 0.0]</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-3.6 [-10.7 to 3.4]</td>
<td>-1.8 [-11.9 to 8.3]</td>
</tr>
<tr>
<td>BP control odds ratio</td>
<td>4.2 [2.6 to 6.7]</td>
<td>3.2 [2.0 to 5.1]</td>
</tr>
<tr>
<td>24-h BP, mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>-8.0 [-17.8 to 1.9]</td>
<td>-10.3 [-23.7 to 3.1]</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-3.9 [-9.7 to 1.8]</td>
<td>-3.1 [-9.0 to 2.8]</td>
</tr>
<tr>
<td>Total guideline adherence score odds ratio</td>
<td>11.1 [4.0 to 21.7]</td>
<td>9.6 [-2.3 to 21.5]</td>
</tr>
</tbody>
</table>

Abbreviations: BP, blood pressure; CI, confidence interval.

a P values are based on between-group differences adjusted for baseline age, sex, race/ethnicity, educational degree, insurance status, annual household income, marital status, smoking status, alcohol intake, body mass index, number of coexisting conditions, number of antihypertensive medications, and medication adherence. Blood pressure control is defined as less than 130/80 mm Hg for patients without diabetes or chronic kidney disease, and less than 130/80 mm Hg for patients with diabetes or chronic kidney disease and as less than 140/90 mm Hg for patients without diabetes or chronic kidney disease.

b P < .05.

c P < .001.

d P = .04 (unadjusted) and P < .09 (adjusted).

This team-based approach to the management of BP was highly effective. Studies involving pharmacists have found control rates of 45% to 70% and a difference of approximately 8 to 14 mm Hg in SBP. The present pragmatic study achieved BP control (63.9%) and SBP (12 mm Hg) at the higher end of this range but lower BP control than that in a previous efficacy study (89.1%). However, that study used a 9-month intervention with more required visits with the pharmacist than the present study. The 6-month BP control in that study was 73% compared with 63.9% in the present trial. These differences could be owing to incomplete implementation of the intervention, a less potent intervention, differences in the
taining. As in the previous study, there were more antihypertensive medication additions herein in the intervention group (1.1 additions) than in the control group (0.3 addition), which is a likely reason for better BP control in the intervention group because medication adherence did not differ.

The changes in 24-hour BP values showed reductions similar to those of the clinic BP values. However, the large difference between groups was not statistically significant because of the large number of patients who refused the second 24-hour monitoring in this pragmatic trial. Therefore, the power was low for the 24-hour results.

There was greater improvement in guideline adherence scores in the intervention group (55.4%) than in the control group (8.1%), which was significant in unadjusted analyses but not significant in adjusted analyses. This may be due to the notable within-clinic clustering of guideline adherence scores, which would tend to compromise power in our cluster randomized design and may have been compounded by adjusting for so many baseline covariates. Both groups still had room for improvement, with more than one-third of the eligible criteria not met in the intervention group and almost half of the eligible criteria not met in the control group at the end of the study.

The patients in the control group did not receive usual care. Instead, they were informed of their BP and the goal BP they needed to achieve, and they were given written information about managing BP. In addition, all physicians received educational sessions on strategies to improve BP control. These approaches, along with increased surveillance by the research nurses, achieved BP control in 29.9% of patients with previously uncontrolled BP in the control group.

This study had several strengths, including the use of standardized research BP measurements, intent-to-treat analyses, and control of numerous baseline covariates. In addition, this was only the second study (to our knowledge) of team-based care to use 24-hour BP monitoring. This study was randomized by clinic, which avoided contamination that might occur with randomization by patient or physician, and had one of the largest sample sizes of team-based care for BP.

There were several limitations of the study, including few randomized clinics, which may have compromised power for guideline adherence scores and BP levels. As an additional concern, the control group had greater nonwhite race/ethnicity, lower income, higher body mass index, and more coexisting conditions, including diabetes mellitus, which could have made it more difficult to achieve improvements in BP or led to lower medication adherence. However, we adjusted for all these variables in our analyses. Blood pressure was controlled in 45.5% of patients with diabetes mellitus in the intervention group and in 26.1% of patients with diabetes mellitus in the control group, suggesting that at least the imbalance of patients with diabetes between groups probably did not influence the findings. Our study findings are generalizable only to community-based family medicine offices. Blood pressure control rates might be different in other practice settings or when patients are not required to attend specific research visits. Also, this study had a higher drop-out rate than a previous efficacy study. Even so, the BP reductions were still significantly greater in the intervention group, and our sensitivity analysis suggests that inclusion of the dropouts would not have changed the conclusions. Finally, because the study enrolled only patients with diagnosed hypertension, the intervention strategy and results are not generalizable to patients who are unaware of their hypertension or those yet to receive a diagnosis of hypertension.

In conclusion, this study used an intervention involving physician and pharmacist collaboration and found significant improvement in BP control compared with the control group. The results of this study suggest that clinics or health systems with clinical pharmacists should consider reallocation of duties to provide more direct patient management to significantly improve BP control. Future studies of this model should include more clinics with greater geographic, racial/ethnic, and socioeconomic diversity because these populations are likely to respond differently to the intervention.

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