A Randomized Trial of the Effect of Community Pharmacist and Nurse Care on Improving Blood Pressure Management in Patients With Diabetes Mellitus

Study of Cardiovascular Risk Intervention by Pharmacists–Hypertension (SCRIP-HTN)

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Background: Blood pressure (BP) control in patients with diabetes mellitus is difficult to achieve and current patterns are suboptimal. Given increasing problems with access to primary care physicians, community pharmacists and nurses are well positioned to identify and observe these patients. This study aimed to determine the efficacy of a community-based multidisciplinary intervention on BP control in patients with diabetes mellitus.

Methods: We performed a randomized controlled trial in 14 community pharmacies in Edmonton, Alberta, Canada, of patients with diabetes who had BPs higher than 130/80 mm Hg on 2 consecutive visits 2 weeks apart. Care from a pharmacist and nurse team included a wallet card with recorded BP measures, cardiovascular risk reduction education and counseling, a hypertension education pamphlet, referral to the patient's primary care physician for further assessment or management, a 1-page local opinion leader–endorsed evidence summary sent to the physician reinforcing the guideline recommendations for the treatment of hypertension and diabetes, and 4 follow-up visits throughout 6 months. Control-arm patients received a BP wallet card, a pamphlet on diabetes, general diabetes advice, and usual care by their physician. The primary outcome measure was the difference in change in systolic BP between the 2 groups at 6 months.

Results: A total of 227 eligible patients were randomized to intervention and control arms between May 5, 2005, and September 1, 2006. The mean (SD) patient age was 64.9 (12.1) years, 59.9% were male, and the mean (SD) baseline systolic/diastolic BP was 141.2 (13.9)/77.3 (8.9) mm Hg at baseline. The intervention group had an adjusted mean (SE) greater reduction in systolic BP at 6 months of 5.6 (2.1) mm Hg compared with controls (*P*=.008). In the subgroup of patients with a systolic BP greater than 160 mm Hg at baseline, BP was reduced by an adjusted mean (SE) of 24.1 (1.9) mm Hg more in intervention patients than in controls (*P*<.001).

Conclusion: Even in patients who have diabetes and hypertension that are relatively well controlled, a pharmacist and nurse team–based intervention resulted in a clinically important improvement in BP.

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DIABETES MELLITUS IS A coronary artery disease equivalent: patients with diabetes without prior coronary events have the same risk for myocardial infarction and coronary artery disease–related mortality as nondiabetic patients with prior myocardial infarction.[1] The combination of diabetes and hypertension markedly increases the risk of premature cardiovascular disease.[2-4] Although hypertension is a stronger risk factor for macrovascular cardiovascular events in patients with diabetes than glucose control,[5] control of blood pressure (BP) in patients with diabetes is often suboptimal, with less than 12% achieving the currently recommended target level of 130/80 mm Hg.[6]

Thus, there is a need for a new model of care to improve BP control, particularly in light of increasing problems with access to primary care physicians attributable to labor shortages in most health care systems. Our research group has demonstrated that pharmacists can play a major role in preventive health care in the community.[7] For example, the first Study of Car-
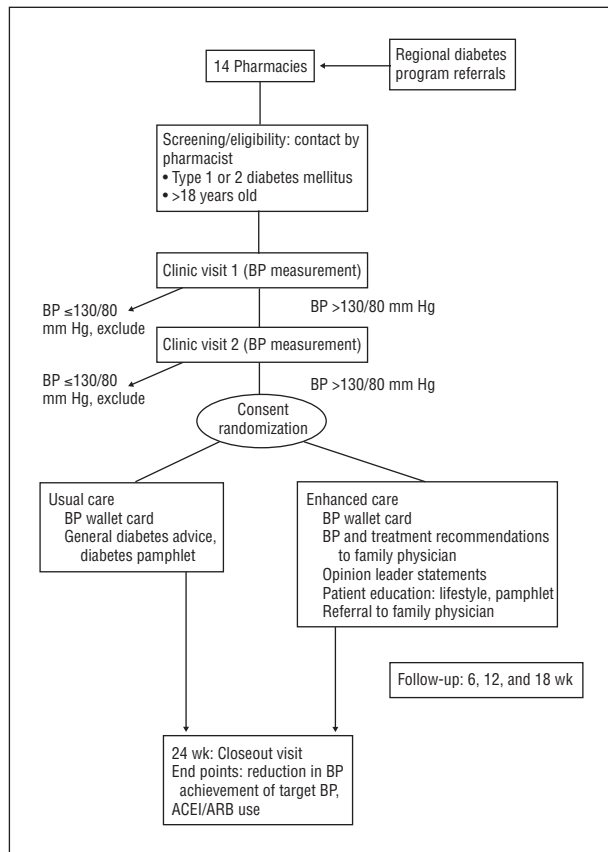
Figure 1. Study design. ACEI/ARB indicates angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BP, blood pressure.

diovascular Risk Intervention by Pharmacists (SCRIP) was a 675-patient, 54-center randomized trial of community pharmacist intervention vs usual care on cholesterol risk management in patients at high risk for cardiovascular disease events, which was terminated early because of the magnitude of the beneficial effects on lipid management with pharmacist intervention. Registered nurses have a skill set that is complementary to that of pharmacists, are trained in patient assessment and communications skills, and are also well suited to community-based screening and management programs. We designed the current study (SCRIP-Hypertension [SCRIP-*HTN*]) to evaluate the efficacy of a multidisciplinary screening and intervention program by community pharmacists and registered nurses to identify patients with diabetes whose BP control was suboptimal and to collaborate with patients and their primary care physicians on strategies to achieve BP reductions in these patients, thereby addressing the gaps among research evidence, guidelines, and clinical practice for these patients at high risk for cardiovascular events.

METHODS

Detailed methods of this study have been published previously[8] (**Figure 1**). In brief, we conducted a multicenter randomized trial comparing a program of pharmacist and nurse intervention with usual care in 14 community pharmacies in Edmonton, Alberta, Canada. There was no overlap of patients with the SCRIP trial we conducted in 1999-2001 to optimize dyslipidemia monitoring and treatment.[7] Pharmacists and nurses

were trained using a combination of an online learning program and a case-based learning session—both based on the Canadian Hypertension Education Program (CHEP) guidelines (http://www.hypertension.ca). Randomization was at the level of the patient (stratified by pharmacy and using a variable block design); randomization was performed centrally to preserve allocation concealment using a computer-generated sequence over a secure Internet service at the Epidemiology Coordinating and Research (EPICORE) Centre (http://www.epicore.ualberta.ca). Although patients and their pharmacists were not blinded to group allocation, the outcome assessments for this trial were objective.

All adult diabetic patients with BP higher than 130/80 mm Hg on 2 screening visits separated by 2 weeks were identified in participating pharmacies. Diabetes was identified by community pharmacists through the use of diabetes indicator medications in each pharmacy's prescription database (eg, use of insulin or oral hypoglycemic medications for >6 months, excluding those with corticosteroid-induced or gestational diabetes). We measured BP with a commercial BP monitor (Bp-Tru; VSM Medtech, Vancouver, British Columbia, Canada) that was set to report the average of 5 measurements of BP taken 1 minute apart. Patients were excluded from the study if they were currently enrolled in other diabetes or hypertension trials, were institutionalized (or had their medications administered by a professional caregiver), refused consent, or declined attendance at follow-up visits for BP measurements.

The intervention was delivered by pharmacist-nurse teams at various pharmacy sites.[8] Patients randomized to the intervention were assessed by a pharmacist-nurse team. Cardiovascular risk reduction counseling was provided by a nurse-pharmacist team using a hypertension education brochure and cardiovascular risk reduction counseling consisting of (1) reviewing BP as a risk factor, (2) discussing the causes of high BP, (3) describing the importance and consequences of high BP, (4) explaining the effect of diabetes on high BP, and (5) focusing on the lifestyle strategies the patient could undertake to improve BP. The patient was encouraged to make an appointment with his or her primary care physician for further BP and cardiovascular risk assessment. To facilitate this, the nurse-pharmacist team gave the patient a wallet card documenting their BP and faxed a 2-page form to each patient's physician that documented the patient's modifiable and nonmodifiable risk factors, current medications, current BP, and any suggestions for further testing or management based on the CHEP guidelines.[9-11] In addition, a 1-page summary of the evidence for management of BP in patients with diabetes endorsed by 4 local opinion leaders was also included in the fax to the primary care physician. Intervention group patients were seen at 6-week intervals by the study nurse and pharmacist for counseling and measurement of BP, and the study team communicated results of these BP assessments to each patient's primary care physician.

Patients randomized to usual care received the same BP wallet card with their BP measures documented, a pamphlet on diabetes,[12] and general diabetes counseling from the nurse or pharmacist. Usual care patients received telephone follow-up at 12 weeks and no other follow-up until the in-person closeout visit at 24 weeks. Neither of these visits entailed any therapeutic advice to the usual care patients and were merely for the collection of end point data.

Follow-up for the primary outcome in both arms of the trial was similar: an in-person visit to the pharmacy for BP measurement at 24 weeks. The primary outcome was the difference in change in systolic BP between baseline and 24 weeks between study arms. We chose a 24-week follow-up period for our primary outcome to allow comparability with other studies of quality improvement initiatives. Secondary outcomes included the comparison of the following variables in patients randomized to
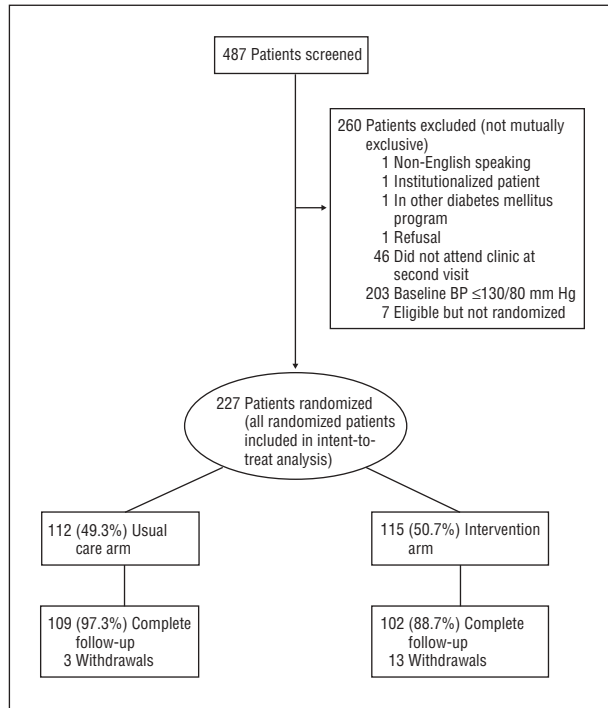
Figure 2. Trial flow. BP indicates blood pressure.

intervention vs usual care: (1) the achievement of BP targets of 130/80 mm Hg or less, (2) the addition, or dosage increase, of antihypertensive drug therapy, (3) the proportion of patients prescribed an angiotensin-converting enzyme inhibitor or angiotensin receptor antagonist, and (4) the difference in change in systolic BP between baseline and 24 weeks in those patients with baseline systolic BP greater than 160 mm Hg. Ethics approval was obtained from the Research Ethics Board of the University of Alberta. Written informed consent was obtained from all participants.

Our sample size was based on the following assumptions: we wanted to detect (or rule out) a 10-mm Hg change in systolic BP, assuming an SD of 20 mm Hg, with a 2-sided α of .05 and 90% power. To account for dropouts or loss of patients to follow-up, the sample size was adjusted upward from 85 to 110 per group. All analyses were conducted according to the intent-to-treat principle with the P value set at .05. The mean change in systolic BP from baseline was calculated for each study arm and compared using analysis of covariance. Multivariate linear regression with change in systolic BP as the dependent variable was calculated to adjust for baseline imbalances between treatment groups (those values with $P < .20$). We adjusted for age, sex, heart rate at visit 1, arm used for BP measurement, myocardial infarction, stroke, and family history of cardiovascular disease. Missing data at the 24-week follow-up assessment were imputed with a last-observation carried forward strategy. This approach conservatively assumes that all patients lost to follow-up have no change in their BP. All analyses were conducted using a commercially available software program (SPSS, version 13.0; SPSS Inc, Chicago, Illinois).

RESULTS

Between May 5, 2005, and September 1, 2006, we screened 487 patients with diabetes and randomized 227 patients (115 to the intervention and 112 to usual care) (**Figure 2**). Of the 260 patients who were not randomized, 203 were

Table 1. Patient Characteristics[a]

Variable	Usual Care (n=112)	Intervention (n=115)
Demographics		
Male sex	61 (54.5)	75 (65.2)[b]
Age, mean (SD), y	63.7 (12.7)	66.2 (11.3)
Cardiovascular risk factors		
Systolic/diastolic BP at baseline, mean (SD), mm Hg	139.9 (11.9)/ 78.2 (8.6)	142.5 (15.5)/ 76.4 (9.2)
Premature atherosclerotic event, MI, or stroke in first-degree relative	71 (63.4)	66 (57.4)
Hyperlipidemia, self-reported	69 (61.6)	64 (55.7)
Smoking		
Current	12 (10.7)	11 (9.6)
Ex-smoker	48 (42.9)	55 (47.8)
BMI, mean (SD)	31.6 (7.9)	31.7 (6.0)
Waist circumference, mean (SD), cm	106.1 (17.8)	108.0 (13.9)
Elevated waist circumference (>102 cm in men and >88 cm in women)	78 (69.6)	89 (77.4)
Alcohol consumption		
One or more servings per day	5 (4.5)	18 (15.7)[c]
Occasional	58 (51.8)	49 (42.6)
Sedentary lifestyle, <30 min of moderate exercise 4 times per week	64 (57.1)	62 (53.9)
Self-reported cardiovascular comorbidities[c]		
CAD, including prior MI, angina, or coronary revascularization	26 (23.2)	23 (20.0)
Heart failure	5 (4.5)	4 (3.5)
Atrial fibrillation	25 (22.3)	20 (17.4)
Prior stroke, TIA, or carotid revascularization	4 (3.6)	13 (11.3)[c]
Chronic kidney disease	13 (11.6)	19 (16.5)
Peripheral arterial disease, including prior revascularization	14 (12.5)	13 (11.3)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BP, blood pressure; CAD, coronary artery disease; MI, myocardial infarction; TIA, transient ischemic attack.
[a] All data are given as numbers (percentages) unless otherwise indicated.
[b] Variable indicates baseline imbalances between treatment groups at $P < .10$.
[c] Not mutually exclusive.

ineligible on the basis of having a BP lower than 130/80 mm Hg and 46 did not return for a second BP screening measurement. There were a total of 16 early withdrawals from the study (Figure 2), and 25 patients did not return for their final BP measure (but their final values were imputed using the method of the last observation carried forward).

At baseline, no appreciable differences were found between the patients in the intervention and usual care arms (**Table 1**). As expected, most patients in both arms had multiple cardiovascular risk factors. Of the 227 trial participants, 192 (84.6%) were aware that they had hypertension. Among these 192 patients, 81 (42.2%) were taking 1 antihypertensive agent at baseline, 55 (28.6%) were taking 2 agents, and 16 (8.3%) were taking 3 or more antihypertensive drugs; only 4 (2.1%) reported that they had seen a hypertension specialist.

Systolic BP decreased in both arms of the trial during 6 months (**Figure 3**), but the reduction in the intervention group of 10.1 mm Hg was greater than that in the usual care group of 5.0 mm Hg. After adjusting for baseline systolic BP and imbalances in baseline covariates (as described in the "Methods" section), the mean (SE) between-group difference in systolic BP was 5.6 (2.1)
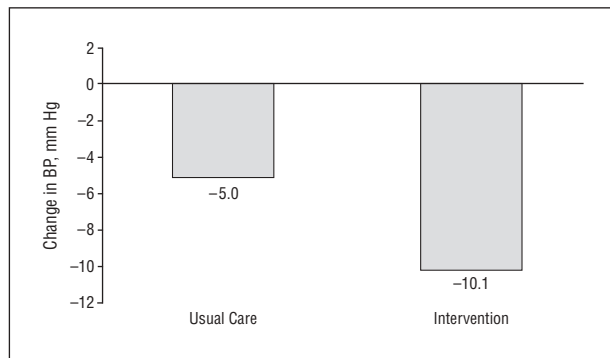
Figure 3. Adjusted difference in systolic blood pressure (BP) during 6 months. Differences were adjusted for age; sex; heart rate at visit 1; arm on which the BP was measured; myocardial infarction; stroke; first-degree relative with myocardial infarction, angina, and high cholesterol levels; and baseline systolic BP. The mean (SE) between-group difference in systolic BP was 5.6 (2.1) mm Hg (*P*=.008).
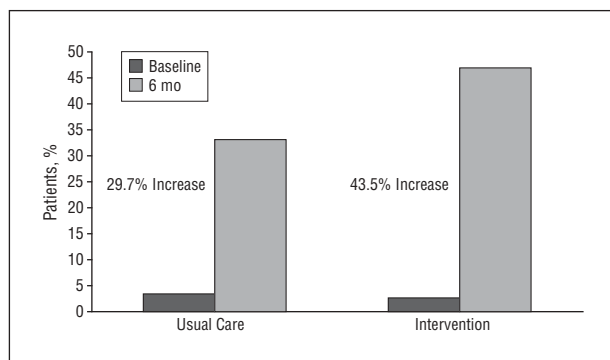

Figure 4. Proportion of patients who achieved the goal blood pressure of less than or equal to 130/80 mm Hg. For the between-group difference in patients achieving the goal blood pressure, *P*=.02.

mm Hg, a finding that was statistically significant (*P*=.008). In the subgroup of patients with a systolic BP higher than 160 mm Hg at baseline, the effects of the intervention were even more marked: a 27.4-mm Hg reduction in the intervention group compared with a 3.3-mm Hg reduction in the usual care group; after adjustment for baseline BP, the adjusted mean (SE) difference of 24.1 (1.96) mm Hg was statistically significant (*P*<.001).

The proportion of patients who met guideline-recommended BP targets (ie, ≤130/80 mm Hg) increased in both arms of this trial (**Figure 4**): from 3 of 115 (2.6%) to 54 (47.0%) (*P*<.001) in patients randomized to the intervention and from 4 of 112 (3.6%) to 37 (33.0%) (*P*<.001) in usual care patients. Thus, the intervention was associated with a statistically significant 14% absolute improvement (46% relative improvement) in the proportion of diabetic patients achieving BP targets compared with controls (*P*=.02). Changes in antihypertensive medication use are given in **Table 2**. Notably, the use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers did not change in either group.

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COMMENT

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Even in a relatively well-controlled group of patients with diabetes and elevated BP, we found that a community pharmacist and nurse–based intervention that empowered patients to take charge of their BP, educated them about dietary and exercise approaches to lower BP, and communicated BP measurements and opinion leader–endorsed and guideline-based recommendations to family physicians conferred a 5.6-mm Hg greater reduction in systolic BP after 6 months compared with usual care. Of particular note, in patients with the poorest BP control at baseline (systolic BP >160 mm Hg), our intervention was extremely efficacious, resulting in a 24.1-mm Hg greater reduction in systolic BP.

Because medical management is the cornerstone of the treatment of hypertension, it makes sense that pharmacists, who are accessible drug therapy experts, should be engaged in the battle to control this important public health problem. In 2003, Chabot et al[13] conducted a 9-month nonrandomized pilot study that involved 9 community pharmacies located in Québec City, Québec, Canada. That study reported similar reductions in systolic BP (–7.8 vs 0.5 mm Hg; *P*=.01) with a pharmacist-based intervention that involved a computerized decision-aid BP management software program integrated into pharmacy prescription management systems. Pharmacists were prompted each time the patient refilled a prescription for antihypertensive agents to perform BP measurements, evaluate adherence, and propose written and verbal interventions. The Hypertension Outcomes Through BP Monitoring and Evaluation by Pharmacists (HOME) Study[14] was a randomized controlled trial of a high-intensity vs low-intensity intervention in 125 patients to evaluate the effectiveness of a community pharmacist–based home BP monitoring program in 12 community pharmacies for 3 months. The high-intensity intervention included 4 face-to-face visits with a trained pharmacist who provided patient-specific education about hypertension. After the first and third visits, patients were required to take home BP measurements once a day for 1 month. Home BP measurements were used by the pharmacists to develop treatment recommendations for the patient's physician. In the low-intensity intervention, pharmacists measured patients' BP in the pharmacy and referred them to their physician for evaluation. At the final visit, the difference in systolic BP change between the high- and low-intensity groups was –4.5 mm Hg (*P*=.12), similar to our findings. Our current study took this work a step further by studying more patients, using the patient as the unit of randomization, including higher-risk patients regardless of drug treatment with a longer duration of follow-up, and, importantly, adding in the complementary skills of nurses in a team-based approach.

The degree of BP control in patients with diabetes in our community was greater than expected at baseline, with 41.7% of those screened excluded for having BP lower than 130/80 mm Hg; this proportion is much higher than that reported in older studies,[5] which suggested control rates of approximately 12%. Furthermore, the baseline BP of eligible patients was lower than expected. This finding may reflect a volunteer bias in that those patients most interested in control of BP may have been more likely to agree to participate in this trial (indeed, >80% of trial participants were aware that hypertension is a risk factor for cardiovascular disease). It may also explain why the intensity of drug therapy was not significantly improved and

Table 2. Use of Antihypertensive Medications

Medication	Usual Care, No. (%) (n=112)		Intervention, No. (%) (n=115)	
	Baseline	6 mo	Baseline	6 mo
Diuretics	14 (12.5)	17 (15.2)	10 (8.7)	11 (9.6)
β-Blockers	15 (13.4)	15 (13.4)	25 (21.7)	27 (23.5)
Calcium channel blockers	25 (22.3)	26 (23.2)	28 (24.3)	27 (23.5)
ACE inhibitors	48 (42.9)	48 (42.9)	46 (40.0)	45 (39.1)
Angiotensin receptor blockers	30 (26.8)	33 (29.5)	35 (30.4)	37 (32.2)
ACE inhibitor or angiotensin receptor blocker	73 (65.2)	75 (67.0)	71 (61.7)	68 (59.1)
Other	1 (0.9)	1 (0.9)	2 (1.7)	2 (1.7)
Use of any antihypertensive medications	81 (72.3)	81 (72.3)	85 (73.9)	76 (66.1)

Abbreviation: ACE, angiotensin-converting enzyme.

why only 47.0% of our trial participants achieved their target BP after the intervention; a similar ceiling effect has been seen in randomized trials evaluating intensive antihypertensive therapy in diabetic patients (eg, recent antihypertensive trials have demonstrated the difficulties of achieving currently recommended targets in diabetic patients, with less than half of diabetic trial participants in the Hypertension Optimal Treatment [HOT] trial,[15] UK Prospective Diabetes Study 38 [UKPDS 38],[16] Valsartan Antihypertensive Long-term Use Evaluation [VALUE],[17] Anglo-Scandinavian Cardiac Outcomes Trial [ASCOT],[18] Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial [ALLHAT],[19] and Action in Diabetes and Vascular Disease [ADVANCE][20] attaining a systolic BP of <130 mm Hg at 6 months). Of course in the real-world setting, physicians may choose not to uptitrate therapy in all patients if they have competing comorbidities or adverse reactions, and a qualitative study to examine reasons behind physician decision making in antihypertensive therapy is needed rather than merely assuming it represents clinical inertia. Interestingly, we observed a significant reduction in systolic BP without large changes in the use of antihypertensive therapy, which suggests that improvements in adherence with patients' prescribed drug therapy and/or lifestyle maneuvers may have contributed to the benefits we observed. However, because we did not collect data on these factors, we cannot be certain which element of our multicomponent intervention was responsible for the improved BP control.

Pharmacists and nurses who participated may be different from those who did not participate, an investigator volunteer bias that may limit generalizability of the program. However, pharmacists were selected on the basis of a partnership with Medicine Shoppe Canada rather than any prior involvement with quality improvement programs or research studies. Furthermore, the activities of the pharmacists and nurses were in accordance with recently published profession-specific guidelines for the management of hypertension by CHEP.[11,21]

Another potential limitation is that our intervention involved substantial in-person contact time between patients and study personnel, and future studies will need to define whether less intensive interventions are as efficacious. However, our previous study[7] of a pharmacist intervention on dyslipidemia practices did not demonstrate any increase in primary care physician time related to the study intervention.

By necessity, the participants and investigators could not be blinded to the intervention. The outcome measures were, however, objective. We used a well-validated automated device for accurate BP measurements (BpTru). It is possible that the more frequent contact with the pharmacist-nurse team reduced the anxiety of patients and any "white coat effect" on their BP measurements (ie, elevated BP in the office but not at home). However, patients in both groups had their BP measured with the same device, which takes 6 readings, discards the first, and takes an average of the subsequent 5 measures. This approach may reduce the white coat effect because of the multiple measurements and because the machine takes the BPs automatically without a health care professional in the room. The use of a randomized controlled study design, however, gives our study a high degree of causal inference, and, to our knowledge, this is the largest such trial conducted to date.

The results of our study should be interpreted in light of the recently published ADVANCE trial.[20] In that randomized trial, more than 11 000 patients with diabetes and mildly elevated BP received a combination of perindopril erbumine and indapamide or placebo. After 4.3 years of follow-up, a 9% reduction was seen in risk of major macrovascular or microvascular events and an 18% reduction in cardiovascular death. Of note, the baseline BPs (approximately 145/81 mm Hg) and degree of BP lowering (5.6 mm Hg) achieved in ADVANCE were nearly identical to the values in our study. This reinforces the fact that lowering even mildly elevated BP by as little as 5 to 6 mm Hg in patients with diabetes is beneficial, and it is worth noting that our intervention was not tested against placebo but against usual care in which almost three-quarters of patients were receiving antihypertensive therapy. In fact, a 5.6-mm Hg reduction in systolic BP is what would be expected from the addition of another antihypertensive agent to a treatment regimen.[22]

The results of our study demonstrate the value of community pharmacist and nurse teams working in collaboration with patients and physicians to achieve better BP control. Because many patients with hypertension do not present to their physician and because primary care physicians are already overwhelmed,[23,24] such approaches

should be seriously considered. What is needed now are systems of remuneration for chronic disease management that will allow patients to have access to these multidisciplinary services. This responsibility rests with health care policymakers.

In conclusion, SCRIP-*HTN* provides strong evidence that a community pharmacist and nurse team, working collaboratively with patients and primary care physicians, can have a major effect on hypertension management in patients with diabetes mellitus and suboptimal BP control in the community. Extrapolating our findings on the basis of previous long-term trials with clinical end points and large population-based epidemiologic studies, a sustained 5–mm Hg reduction in systolic BP would be expected to reduce long-term incidence of strokes by 30%, coronary events by 23%, and mortality by 13%.[20,25,26] This potential benefit is particularly important given the magnitude of the care gap for diabetic hypertensive individuals, the prevalence of both conditions, and the increasing difficulties in accessing primary care physicians in North America.

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