Impact of Community Pharmacist Interventions in Hypertension Management on Patient Outcomes: A Randomized Controlled Trial

Final Project Report

Ontario Pharmacists Association and
Green Shield Canada
January 8, 2014

ONTARIO PHARMACISTS ASSOCIATION

gsc green shield canada

Table of Contents

Executive Summary

There is a growing awareness across Canada and internationally that pharmacists are an underutilized resource when it comes to chronic disease management. Hypertension is the most prevalent chronic disease in Canada with over 4 million Canadians afflicted, less than one third of who have their blood pressure under control.

This study aimed to examine the impact of a six-month, pharmacist-led hypertension management program on patient health outcomes. It involved a randomized controlled trial with over 150 patients and 38 community pharmacies across Ontario. The program improved systolic blood pressure by 13.5mm Hg, led to a quadrupling in the number of patients whose blood pressure is under control and increased adherence to medication therapy by 15 per cent. In addition to achieving these positive health outcomes, the program reduced antihypertensive medication costs by over 31 per cent.

Patients reported a very high level of satisfaction with pharmacist services and about a quarter of the employed patients reported being more productive at work as a result of participating in the study.

From an employer perspective, incorporating a pharmacist-led chronic disease management program in their benefit plans can thus not only help contain drug therapy costs in the short term but also lead to healthier, more productive employees.

Background

Hypertension is a significant health problem both in Canada and internationally, with an estimated 1 billion people worldwide,[1] and 4.1 million in Canada[2] afflicted with this disease. In Ontario alone, there are an estimated 1.8 million individuals diagnosed with hypertension.[3] Evidence indicates that there is insufficient hypertension control and prevention at the community level. For instance, blood pressure is controlled in only about 16% of Canadians with diagnosed hypertension.[2] Some of the barriers to effective blood pressure control include patient non-adherence and inadequate access to care.[4] In addition, some evidence shows that management of hypertension by physicians is less than optimal.[5] Research has shown that uncontrolled hypertension can lead to significant morbidity and mortality, accounting for 7 million deaths worldwide each year.[1] At the same time, controlling blood pressure can reduce heart failure by over 50%, strokes by 35-40% and myocardial infarction by 20-25%.[6]
In recent years, numerous strategies have been directed towards improving blood pressure control in the community, including educational campaigns for patients and dissemination of information on guidelines for physicians.[7] However, many of these have shown limited effectiveness.[8,9]

There has been an increasing recognition that pharmacists are an underutilized resource when it comes to chronic disease management, particularly hypertension. This recognition is due in part to the evolution of pharmacy practice from a product-orientation to a patient-orientation. Since the 1990's, pharmacists in Canada and internationally have embraced a philosophy of practice termed pharmaceutical care.[10,11] Through the provision of pharmaceutical care, pharmacists have played a greater role in the management of patients' chronic diseases. In particular, they have been involved in educating patients, improving adherence to drug therapy, monitoring patients' conditions and optimizing drug therapy in collaboration with patients' physicians. More recently, pharmacists in multiple jurisdictions across Canada have been given the authority to practice in an expanded scope of practice that includes the authority to prescribe medication therapy. This has afforded pharmacists additional tools through which they are enabled to manage patient's chronic diseases.

There is a significant and growing body of research evidence that indicates that pharmacists can play a tremendous role in the management of hypertension. This point is most strongly supported by the findings of a 2008 systematic review and meta-analysis that examined the research literature on the impact of pharmacist interventions for hypertension management on patient outcomes.[12] This review identified 28 studies that met their inclusion criteria, the majority of which were randomized controlled trials. The results of the meta-analysis showed that pharmacists' intervention reduced patients' systolic blood pressure by an average of 10.7mm Hg, a finding that is statistically and clinically significant. The systolic blood pressure for patients in the control group, who did not receive pharmacist's intervention, declined an average of only 3.2mm Hg. For comparison purposes, a 5mm Hg reduction in systolic blood pressure has been shown to lower the risk of cardiovascular events and stroke by 25-30%.[13] Similarly, pharmacists' intervention reduced patients' diastolic blood pressure an average of 5.8mm Hg. In comparison, the diastolic blood pressure of patients in the control group declined only 2.4mm Hg. This

illustrates that pharmacists' interventions can reduce patients' blood pressure significantly more than care provided solely by physicians and that such a reduction can significantly lower patient's risk of serious cardiovascular disease.

In addition to clinical outcomes, some studies have shown that pharmacists' intervention can significantly improve humanistic outcomes, such as patient adherence rates, knowledge of medications, and some domains of quality of life. [7,14,15,16,17] Improving patient adherence to medication therapy, in particular, is believed to be essential for effective hypertension control.[18]

Though the research literature provides strong evidence of the effectiveness of pharmacist hypertension management services, the majority of the studies to date have been conducted in team-based settings (hospital outpatient clinic or primary care clinic). Significantly fewer studies were conducted in community pharmacies, and some of these suffer from methodological issues. Community pharmacists face greater challenges in delivering chronic disease management services than those in team-based settings due to their lack of access to patient information and lack of contact with patients' physicians. However, most pharmacists in Ontario and elsewhere work in community settings. Hence, it is important to investigate the degree to which *community* pharmacist interventions can impact patient hypertension. In addition, the majority of studies have focused almost exclusively on elderly patients, with the average age around 64 years. There is clinical evidence that suggests that treating hypertension early can prevent development of cardiovascular disease and associated complications.[19] Hence, this study focused on the impact of community pharmacist hypertension management on a younger patient population.

Study Goal and Objectives

The primary goal of this study was to examine the impact of Ontario pharmacists' interventions in hypertension management on patient health outcomes. Specific study objectives are:

1. To determine the impact of pharmacist intervention on patients' systolic and diastolic blood pressure
2. To determine the impact of pharmacist intervention on patients' overall blood pressure control
3. To determine the impact of pharmacist intervention on patient adherence to medication therapy
4. To determine the impact of pharmacist intervention on patients' lifestyle (smoking status/rate, BMI, frequency of physical exercise)
5. To assess the impact of pharmacist intervention on the number of medications taken by patients
6. To assess the impact of pharmacist intervention on patient drug costs (antihypertensive and all drugs)
7. To examine patient satisfaction with pharmacist hypertension management services
8. To examine the feasibility of implementing a chronic disease management program for a private sector drug plan

Methods

This study consisted of a prospective, randomized controlled trial conducted in the community setting. A total of 38 pharmacies were recruited for this study, eight from each of St. Catharines and Hamilton regions, 10 and 12 respectively from the Windsor and Oshawa regions. Eleven of the 38 pharmacies recruited were independent or banner, while 27 were chain or franchise.

Pharmacies from each region were randomly assigned to either the intervention or control group. The randomization was conducted at the pharmacy level, in order to avoid contamination at the patient level. Randomizing at the pharmacy level ensured that only intervention group patients received pharmacists' intervention. This allowed for causal conclusions to be drawn regarding the effect of pharmacists' intervention on patient outcomes. Neither the patients nor the pharmacists were blinded with respect to their group assignment. Given the transparent nature of pharmacist intervention, blinding was not feasible. Table 1 illustrates the allocation of sample pharmacies by region and format.

Table 1. Pharmacy allocation by region and study group

Region	Pharmacy Format			Group Assignment	
	Independent/Banner	**Chain/Franchise**	**Total**	**Intervention**	**Control**
Hamilton	2	6	8	4	4
St. Catharines	5	3	8	4	4
Windsor	3	7	10	5	5
Oshawa	1	11	12	6	6
Total	11	27	38	19	19

Intervention Group

Pharmacists in the intervention group provided patients with a comprehensive disease management program for hypertension. The 3 major components of pharmacists' intervention are outlined below.

1. Medication review and drug therapy optimization
   Pharmacists comprehensively reviewed patient's medication therapy, with a particular focus on potential interactions, suboptimal dosages, adherence issues, or unnecessary medications. Based on patient need, the pharmacist then develop a pharmaceutical plan, including recommendations for medication and dosage changes, which were shared with the patient's family physician via fax or phone. Physicians were invited to consider the recommendations and reply to the pharmacist. If necessary, the pharmacist conducted a medication review follow-up to address any outstanding drug therapy-related issues.

2. Patient education
   Based on each patient's case, pharmacists provided education/counselling on lifestyle changes, including:
   - Nutrition (in particular sodium reduction and the DASH diet)
   - Physical activity
   - Weight loss management
   - Alcohol use
   - Smoking cessation (utilizing Green Shield Canada's smoking cessation program)
     - Initial assessment
     - First follow-up (3-5 days)
     - Second follow-up (7-10 days)
     - Third follow-up (14-21 days)
     - Fourth follow-up (28-56 days)
     - Fifth follow-up (day 90)
     - Final follow-up (day 180)

3. Improving patient adherence
   Pharmacists utilized evidence-based strategies to improve patient adherence to medication therapy.[20] In particular, they were instructed to utilize 6 strategies, summarized by the acronym "SIMPLE"
   - **S**implifying regimen characteristics (e.g. switching to a drug that can be taken once a day instead of twice a day; providing adherence aids such as blister packs)
   - **I**mparting knowledge (ensuring patients understand the purpose of their medications)
   - **M**odifying patient beliefs (about the negative effects of non-adherence, the positive effects of treatment, etc.)
   - **P**atient communication (communicating in a language patients understand, involving patients in decision-making)
   - **L**eaving the bias (not basing interventions on demographic factors such as gender since evidence shows they don't affect adherence)
   - **E**valuating adherence (measuring and evaluating patient adherence reliably)

Control Group

Patients in the control group received standard care pharmacy services, which focused largely on medication dispensing. Control group pharmacists provided these services in accordance with the standards of practice adopted by the Ontario College of Pharmacists.[21] There was no direct effort by the control pharmacists to provide any of the 3 intervention components outlined above, but if the patient specifically requested them, the pharmacist complied. However, data from these patients was excluded from the final analysis.

Study Procedures

Table 2 outlines the study procedures for each of the 2 study groups. All contact with patients was done in-person at the pharmacy, except with regards to smoking cessation counselling where the follow-ups were conducted either over the phone or in-person. Out of the 38 study pharmacies, 34 each had 2 staff pharmacists participate in the study; the remaining 4 pharmacies each had 1 pharmacist participate.

Following the last pharmacist-patient appointment, one of the investigators (NP) conducted exit interviews with one pharmacist from each intervention group pharmacy to examine logistical

issues, the adequacy of compensation and other potential barriers/facilitators for future pharmacist-run chronic disease management programs.

Table 2. Study procedures by group

Appointment # (Elapsed Time)*	Study Procedures	
	Intervention Group	**Control Group**
Enrolment (0 months)	• Patient was assessed for eligibility • If eligible, informed consent was obtained and patient was enrolled in study	

1: Baseline
(1 month)
	• Pharmacist met with the enrolled patient and
	  ○ Conducted a comprehensive medication review, developed a pharmaceutical plan and communicated it to the patient's family physician
	• Obtained baseline measurements, including:
	  ○ Patient demographic information
	  ○ Number of prescription medications currently taken
	  ○ Number of current co-existing diagnosed health conditions
	  ○ Blood pressure (systolic/diastolic)
	  ○ Weight/height (BMI)
	  ○ Adherence score
	  ○ Smoking status/frequency
	  ○ Frequency of physical exercise
	• Recorded the duration of the appointment
		• Pharmacist met with the enrolled patient and obtained baseline measurements, including:
		  ○ Patient demographic information
		  ○ Number of prescription medications currently taken
		  ○ Number of current co-existing diagnosed health conditions
		  ○ Blood pressure (systolic/diastolic)
		  ○ Weight/height (BMI)
		  ○ Adherence score
		  ○ Smoking status/frequency
		  ○ Frequency of physical exercise
		• Recorded the duration of the appointment

2 – 6 (2-6 months)	• Pharmacist measured patient's blood pressure • Implemented intervention(s), as needed, based on each patient's situation • Recorded the duration of the appointment	• Pharmacist measured patient's blood pressure • Recorded the duration of the appointment

7: Final
(7 months)
	Pharmacist met with the enrolled patient and:
	• Provide patient with additional written information on hypertension management
	• Referred patient to their family physician for continuing treatment
	• Obtained final measurements on:
	  ○ Number of prescription medications currently taken
	  ○ Blood pressure (systolic/diastolic)
	  ○ Weight/height (BMI)
	  ○ Adherence score
	  ○ Smoking status/frequency
	  ○ Frequency of physical exercise
	• Recorded the duration of the appointment	

* From the point of patient enrolment

Outcome Measurement
Table 3 outlines how each of the study outcomes were measured.

Table 3. Study outcomes and measures

Outcome	Measure
Blood pressure	Measured by the pharmacist utilizing a digital sphygmomanometer (Thermor Bios Automatic Blood Pressure Monitor 3AL1-3E) • The patient was asked to sit quietly for 5 minutes before their blood pressure was measured • A second measurement was taken 5 minutes after the first one and the average of the 2 measurements computed • Every effort was made to measure blood pressure at the same time of day for each visit to ensure consistency
Adherence to antihypertensive medication therapy	Measured in 2 ways: 1. Through patient self-report (patient completed Morisky 8-Item Medication Adherence Scale;[22] score ≤6 is low adherence[23]) 2. Through Green Shield Canada's prescription claim information • Medication Possession Ratio[24,25] (>80% is adherent; <80% is non-adherent) • Calculated for each antihypertensive medication class and overall mean
Smoking status and frequency	• Assessed by asking the patient: 1. Whether they smoke (yes/no) 2. The average number of cigarettes they smoke per day
Frequency of physical exercise	• Assessed by asking the patient: o The average number of minutes they engage in physical exercise (e.g. running, aerobics, sports, etc.) per week
BMI	• Pharmacist measured patient height and weight and calculated BMI using formula (weight/height^2) • Weight: Measured by a calibrated weight scale • Height: Measured by the pharmacist using a tape measure
Drug costs (antihypertensive and general)	• Obtained through Green Shield Canada's prescription claim information • Antihypertensive drug categories included: o Angiotensin Receptor Blockers (ARBs) o ACE Inhibitors o Direct Renin Inhibitors o Calcium Channel Blocker (CCBs) o Beta Blockers o Alpha Blockers o Diuretics
Intervention costs	• Obtained through study billing data available from Green Shield Canada

Data Collection
During their interaction with the patient, the study pharmacist entered all clinical/demographic patient data collected as part of this research study into paper-based forms. These were then transcribed by the pharmacist into a secure online portal developed by Green Shield Canada (www.providerconnect.ca). Through this portal, data was automatically transmitted to Green Shield's secure servers.

Administrative claims data was collected by Green Shield Canada including medication claim data and intervention service claim data. All reported data was provided to the investigators using an encrypted unique patient identifier to protect the confidentiality of participating patients.

Pharmacist Training

All study pharmacists completed a training/orientation program, consisting of online modules and a live session. The online modules were continuing education programs provided by the Ontario Pharmacists Association on the topics of nutrition and smoking cessation. The live session were conducted by experts in these topic areas, as well as weight management/physical activity and hypertension.

Pharmacists in the intervention group were trained on the following topics:

- Patient recruitment and enrolment procedures
- Blood pressure measurement
- Hypertension guidelines and treatment
- Lifestyle counselling and education
- Smoking cessation counselling
- Strategies to improve adherence to medication therapy
- Data recording

Pharmacists in the control group were trained on the following topics:

- Patient recruitment and enrolment procedures
- Blood pressure measurement
- Data recording

Participants

The study participants were 118 patients with hypertension. The patients were selected based on the following criteria:

Inclusion criteria:

- Provided written consent
- Green Shield Canada cardholder (or their dependent)
- Indicated intent to refill all prescriptions at the study pharmacy
- 18 to 64 years of age
- On antihypertensive medication therapy for which the dose and/or medication has remained unchanged for 3 months
- Uncontrolled blood pressure (non-diabetic patients): systolic blood pressure 140 Hg or higher or diastolic blood pressure 90mm Hg or higher (as determined by the average of 2 measurements taken by a pharmacist during enrolment)
- Uncontrolled blood pressure (diabetic patients): systolic blood pressure 130 Hg or higher or diastolic blood pressure 80mm Hg or higher (as determined by the average of 2 measurements taken by a pharmacist during enrolment)

Exclusion Criteria:

- Pregnant women
- Unable or unwilling to return to the pharmacy for scheduled visits
- Terminal illness or poor prognosis (life expectancy less than 3 years)
- Stage 3 hypertension: blood pressure equal to or greater than 180/110mm Hg (pharmacist to refer the patient to their physician)
- History of alcoholism or drug abuse
- Comorbidities/health issues:
    - Recent myocardial infarction or stroke (6 months prior to enrolment)
    - Congestive heart failure (New York Heart Association Class III or IV)
    - Unstable angina
    - Ventricular arrhythmia,
    - Renal or hepatic disease
    - Cancer (in the past 5 years preceding enrolment)
    - Organ transplantation
    - Dementia, cognitive impairment or other psychiatric disorder (Cognitive Impairments such as those found under the DSM-IV-TR common Axis I and Axis II disorders)
- Secondary cause of hypertension (e.g. Cushing's syndrome, primary aldosteronism, pheochromocytoma, etc.)
- Enrolled in an Employee Assistance Program for disease management (e.g. Ceridian Cardiovascular Health Management Program), within 6 months preceding the study enrolment date OR planning to enrol in the next 6 months
- Enrolled in a smoking cessation program (pharmacy-based or other) within 6 months preceding the study enrolment date OR planning to enrol in the next 6 months
- Had an Annual MedsCheck done within the 6-month period preceding the anticipated date of the first study appointment

Recruitment

Pharmacies:

Green Shield Canada provided the Ontario Pharmacists Association with a list of pharmacies in each of the 4 regions that had the highest number of antihypertensive medication claim submissions. This was considered a reliable estimate of the number of potentially eligible patients at each pharmacy. The chain and franchise pharmacies were recruited by members of the study steering committee who were representatives of these organizations. Independent pharmacies were recruited by the study project manager.

Patients:

Pharmacists recruited patients for participation in this study either at the point of medication dispensing or through a review of their pharmacy records.

1. When a patient came in for a refill of an antihypertensive medication, the pharmacist informed them of the study and determined their interest in participating. If the patient expressed interest, the pharmacist assessed them for eligibility by
    - Asking the patient to complete an eligibility screening questionnaire
    - Measuring the patient's blood pressure to determine whether it is in the eligible range

2. The pharmacist screened their pharmacy records for patients who had at least 1 antihypertensive medication dispensed in the previous 6-month period. The pharmacist targeted patient groups that have a higher prevalence of high blood pressure and were more likely to meet the eligibility criteria.[26]
    - Over 50 years of age
    - Taking statins
    - Without a family physician
    - Have poor refill adherence

    The pharmacist phoned these patients in order to gauge their interest in participating in the study. If interested, patients were invited to visit the pharmacy to be screened for eligibility.

Sample Size Justification

The study sample size was calculated based on the following factors:

- Detecting a 5mm Hg mean difference in systolic blood pressure between the intervention group and the control group at study endpoint
- Estimated standard deviation of 10mm Hg in systolic blood pressure
- 5% chance of type I error (α level = 0.05, 2-sided)
- Statistical power of 80%
- Estimated intracluster correlation coefficient of 0.01 (to account for cluster design)[27]

The following formula [28] was utilized to calculate the required sample size:

$$n = [2\sigma^2(z_{\alpha/2} + z_{\beta/2})^2] / (\mu_1 - \mu_2)$$

Utilizing the above formula and parameters, it was estimated that the required sample size was 64 patients per group for a total of 128 patients. Accounting for an estimated 30% patient dropout rate,[29,30,31] the total sample size was adjusted to 184 patients.

Because this study utilized a cluster sampling technique (with each cluster being a pharmacy), the above sample size was then adjusted for the variance inflation factor, using the following formula:

Inflation factor = [1 + (m-1)X)
m= number of patients per cluster (10 in this study)
X = intracluster correlation coefficient (estimated 0.01 based on other studies)

Adjusting for this factor generated a total sample size of 204 patients. With equal assortment to the 2 study groups, this translated to 102 patients per group.

Data Analysis Procedures

All data was analyzed using SAS software (version 9.3). Significance level was set at 0.05. Pharmacy level descriptive characteristics, including mean and standard deviation for the number of patients were reported.

For age, the number of diagnosed health conditions, number of prescription medications taken, body mass index, blood pressure, adherence to medication therapy, and frequency of physical exercise per week, baseline (appointment #1) descriptive statistics were reported by treatment arm including mean, median, range and upper and lower quartiles. For education, income, gender and smoking status the frequencies and percentages were reported.

End of study comparisons (appointment #7) for continuous outcomes (blood pressure, adherence to medication therapy, body mass index, and frequency of physical exercise per week) were reported using a mixed effects regression mode for between-group comparisons.[32] Prediction variables in the mixed models included treatment group and the baseline value (Appointment #1) corresponding to the end of study outcome. Adjustment was made in these models for the intra-cluster correlation within pharmacies by allowing pharmacies to be modeled as a random effect. In addition, for each end of study outcome, the mean difference from baseline was calculated with between-group comparisons again made using a mixed effects regression model.

Frequencies and percentages for the blood pressure control outcome, defined as 140/90 mm Hg or lower for non-diabetics and 130/80 mm Hg or lower for diabetics, were provided. The method of generalized estimating equations (GEE) was used to conduct between-group comparisons, adjusting for baseline blood pressure control.[32]

For the number of prescription medications taken, an ordinal endpoint, a Wilcoxon rank sum test adjusting for clustering was used to compare the groups.[33]

There were 13 smokers in the control group and 10 in the intervention group with only three 'quitters', one in the control group and two in the intervention group. A descriptive comparison for this outcome variable was deemed adequate.

In addition to the mixed effects regression models used for the between-group comparisons with respect to adherence level (self-reported), the percentage of patients having compliance greater than 80% was reported. Statistical tests for between-group differences with respect to the proportion greater than 80% were not reported due to the small number for whom compliance was less than 80%.

Adherence rates were calculated using Green Shield Canada's prescription claims data, using a method known as the modified Medication Possession Ratio (MPR). An MPR of 80% or greater was considered adherent based on previous research. [24,25] Medication possession ratios for each study participant were calculated for each class of antihypertensive drugs they were taking and a mean MPR across the drug classes was computed. Antihypertensive drug classes included in the analysis included angiotensin converting enzyme (ACE) inhibitors, angiotension II receptor blockers (ARBs), direct renin inhibitors, calcium channel blockers, beta blockers, alpha blockers, and diuretics. MPR was measured for the period 6 months preceding the baseline assessment, and for 6 months after the baseline assessment.

Drug costs (excluding dispensing fees) for all antihypertensive drug claims, and all drug claims were summed for six months before and six months after the date upon which each study participated had their baseline study assessment. For drug claims incurred prior to the baseline study assessment, but for which a portion of the medication would have been consumed after the baseline assessment, a portion of the claim was assigned to the post-intervention period based on the proportion of days supplied that would have been taken after the baseline assessment, assuming that the plan member would have started consuming the tablets on the date they were filled.

Compensation

The *pharmacies* participating in this study were compensated on a per-service basis. Claims were submitted electronically to Green Shield Canada, except for an annual MedsCheck where the claim was submitted to the Ontario Public Drug Programs.

The individual *pharmacists* participating in this study received honoraria for completing the training program, enrolling at least 1 patient and completing exit interviews.

Ethical Considerations

The Ontario Pharmacists Association and Green Shield Canada took every precaution to ensure this study was conducted in an ethical manner, including protecting patient confidentiality and anonymity. This study was reviewed and approved by the Institutional Review Board Services (IRB) research ethics board.

Results

Out of the 38 pharmacies originally recruited for this study, 11 dropped out due to their inability to recruit any patients and/or staffing issues. The remaining 27 pharmacies had at least 1 patient complete the entire study. A mean of 4.4 patients per pharmacy completed the study in the control group and a mean of 4.3 patients per pharmacy completed the study in the intervention group (Table 4). Majority of the patients completing the study were in the control group (79/118).

Table 4. Pharmacy characteristics by group

Characteristic	Control Group	Intervention Group
Number of pharmacies	18	9
Average number of prescriptions dispensed per day	351	459
Patients completed study	79	39
Mean per pharmacy (SD)	4.4 (3.0)	4.3 (1.7)
Median per pharmacy	3.0	4.0
Range	1-11	2-7

A total of 74 pharmacists took part in this study. The demographic characteristics of the participating study pharmacists are illustrated Table 5.

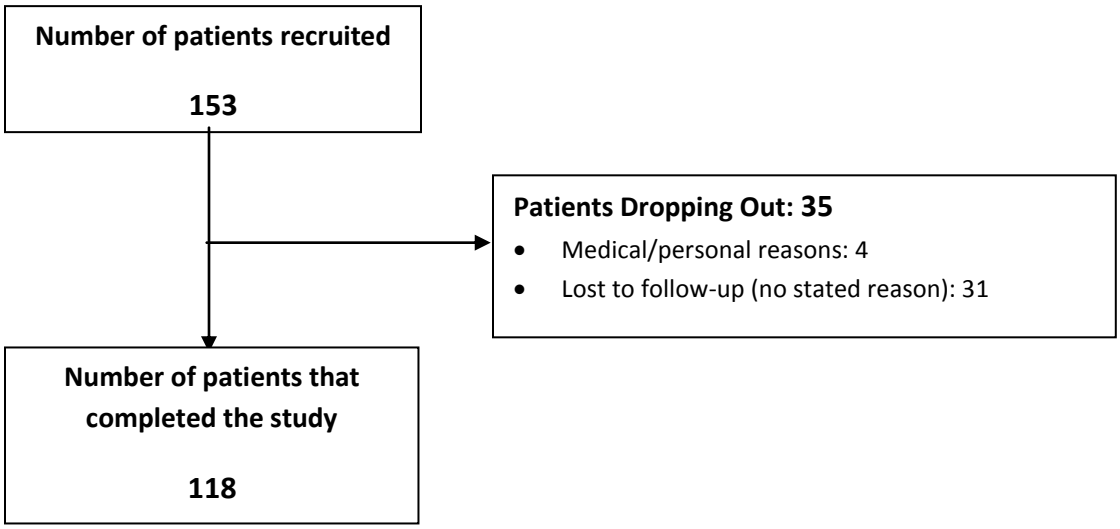
Table 5. Participating study pharmacist demographic characteristics

Characteristic	Control Group	Intervention Group
Number of pharmacists*	27	25
Position		
Staff pharmacist	16	10
Manager/owner	7	10
Franchisee	4	1
Freelance/Relief pharmacist	0	2
Other	0	2
Gender		
Male	11	9
Female	16	16
PharmD Training	2	0
Additional Post-Certification Training (e.g. Certified Diabetes Educator)	9	14

* 52 of the 74 pharmacists who took part in the study completed the demographic survey

A total of 153 patients were recruited, of which 118 completed the entire study. Figure 1 below illustrates the reasons for patient drop-out.

Figure 1. Patient recruitment and drop out



The patients in the 2 study groups were similar at baseline with respect to all demographic and clinical characteristics, except income for which a slightly larger proportion of control group patients were in the higher income brackets (Table 6). In addition, patients in the control group had a higher frequency of physical exercise per week and took slightly fewer medications.

Table 6. Patient demographic and baseline characteristics by group

Demographic / Baseline Characteristic	Control Group (n=79)	Intervention Group (n=39)
Age		
Mean	55.4	56.5
Median (Q1, Q3)	57.0 (52, 61)	57.0 (54,61)
Range	32-64	41-64
Gender – Male (%)	44 (55.7%)	24 (61.5%)
Education (%)		
Elementary	5 (7.1%)	2 (5.4%)
High School	32 (45.7%)	20 (54.0%)
College/University	29 (41.4%)	14 (37.8%)
Graduate	4 (5.7%)	1 (2.7%)
No answer	9	2
Income (%)		
$25,000 - $45, 000	9 (16.3%)	12 (33.3%)
$45,001 - $65,000	13 (23.6%)	10 (27.8%)
$65,001 - $85,000	12 (21.8%)	4 (11.1%)
$85,000 +	18 (32.7%)	9 (25.0%)
Declined to Answer	24	3
Number of Health Conditions		
Mean	1.68	1.69
Median (Q1,Q3)	1.5 (1,2.5)	1.0 (1,3)
Range	0-4	0-4
Diabetics (%)	8 (10.0%)	3 (7.7%)
Number of Prescription Medications (%)		
Mean	3.6	4.1
Median (Q1,Q3)	4.0 (2,5)	4.0 (2,6)
Range	1-7	1-7
Body Mass Index		
Mean	32.3	32.8
Median (Q1,Q3)	31.2 (28.1,35.4)	31.6 (26.8,35.6)
Range	22-51	24-56
Systolic Blood Pressure (mm Hg)		
Mean	143.1	142.7
Median (Q1,Q3)	142.0 (135.5,150)	143.0 (137,149)
Range	103-190	122-166
Diastolic Blood Pressure (mm Hg)		
Mean	85.8	84.1
Median (Q1,Q3)	85.5 (78.5,93)	85.0 (78,91)
Range	59-112	62-114
Controlled Blood Pressure	29 (36.3%)	10 (25.6%)
Adherence (Self Report)		
Mean	6.4	5.7
Median (Q1,Q3)	7.0 (5,8)	7.0 (4,8)
Range	1-8	1-8

Table 6 continued. Patient demographic and baseline characteristics by group

Demographic / Baseline Characteristic	Control Group (n=79)	Intervention Group (n=39)
Adherence (Claims Data) (MPR)		
Mean	100.1	98.5
Median (Q1,Q3)	100.0 (97, 103)	99.5 (97, 101)
Range	75-124	66-117
Proportion adherent	94.9	94.7
Physical Exercise (minutes per week)		
Mean	91.4	66.6
Median (Q1,Q3)	60.0 (22.5,120)	35.0 (5,75)
Range	0-600	0-480
Smokers (%)	13 (16.3%)	10 (25.6%)
Antihypertensive Medication Costs (6 month time period)		
Mean	171.3	177.2
Median (Q1,Q3)	141.4 (60,245)	130.2 (51,235)
Range	0-605	2-841
All Medication Costs (6 month time period)		
Mean	831.5	730.6
Median (Q1,Q3)	476.1 (247,703)	407.2 (228,809)
Range	0 - 10,636	9 - 5,966

Table 7 illustrates patient health outcomes at the end of the study (6 months later) and the mean difference from baseline for each outcome measure. Patients in the intervention group had better outcomes than control group patients for all measures, though only systolic blood pressure and proportion with overall blood pressure control were statistically significant. Self-reported adherence and adherence based on claims data approached statistical significance (p=0.08 and p=0.074, respectively).

Table 7. End of study comparisons for outcomes measures

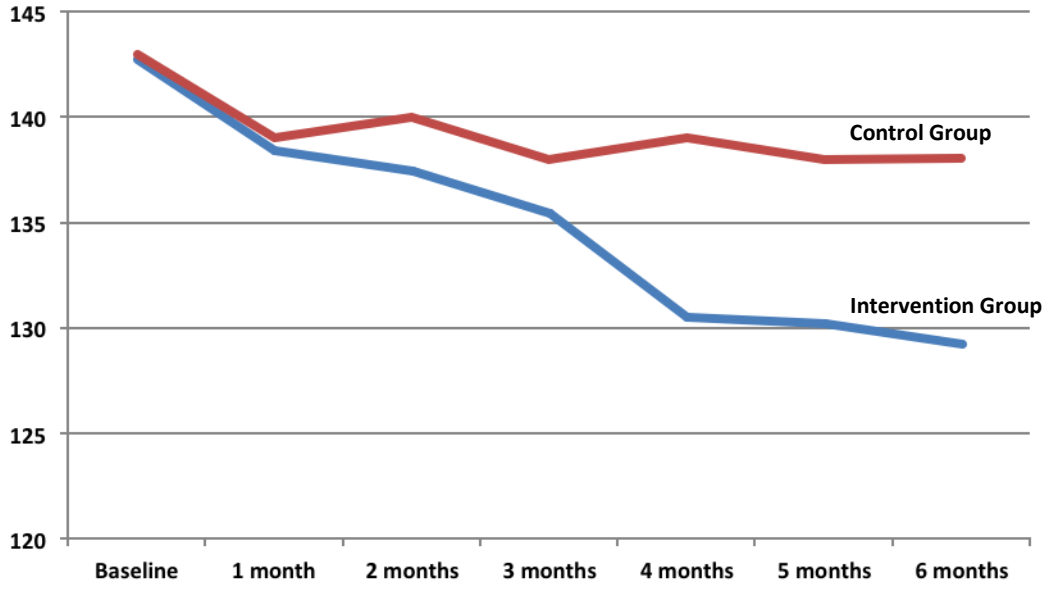
Measure	Control Group (n=79)	Intervention Group (n=39)	p value*
Systolic Blood Pressure (mm Hg)			
Mean	138.1	129.2	
Median (Q1,Q3)	136.0 (128,144)	128.0 (122,135)	
Range	104-208	99-163	
Mean difference from baseline	-5.0	-13.5	**.005**
Diastolic Blood Pressure (mm Hg)			
Mean	81.5	78.2	
Median (Q1, Q3)	81.0 (76,88)	77.0 (72,84)	
Range	53-104	61-94	
Mean difference from baseline	-4.2	-5.9	.511
Controlled Blood Pressure	43 (53.8%)	32 (82.1%)	**<.001**
Adherence Score (Self Report)			
Mean	6.6	6.5	
Median (Q1, Q3)	7.0 (5,8)	7.0 (5,8)	
Range	3-8	3-8	
Mean difference from baseline	+0.14	+0.85	.080
Adherence (Claims Data) (MPR)			
Mean	99.1	98.5	
Median (Q1,Q3)	99.6 (97, 102)	99.5 (96, 100)	
Range	71-129	78-109	
Proportion adherent	96.2	97.3	
Mean difference from baseline	-1.3	+0.3	.074
Body Mass Index			
Mean	32.7	31.3	
Median (Q1, Q3)	30.5 (27.6,35.5)	31.1 (25.7,35.5)	
Range	23-58.6	23-49.3	
Mean difference from baseline	+0.5	-1.2	0.125
Number of Prescription Medications			
Mean	3.59	4.0	
Median (Q1,Q3)	3.5 (2,5)	4.0 (2,6)	
Range	1-7	1-7	
Mean difference from baseline	0	-0.1	0.836
Smokers (%)	12 (15%)	8 (20.5%)	-----
Difference from baseline	- 1	-2	
Physical Exercise (minutes per week)			
Mean	143.6	131.2	
Median (Q1,Q3)	100 (30,205)	110 (45,180)	
Range	1-840	1-500	
Mean difference from baseline	+52.3	+64.7	0.653
Antihypertensive Medication Costs (6 month time period)			
Mean	162.3	121.9	
Median (Q1,Q3)	129.7 (60,226)	94.2 (50,168)	
Range	0-939	3-435	
Mean difference from baseline	- 9.0	- 55.4	0.055

Blood Pressure

Both the intervention and control groups experienced a reduction in systolic blood pressure from baseline to study end point, with a much more pronounced difference in the intervention group (Figure 2). The reduction in the intervention group was significantly greater than the reduction in the control group (13.5mm Hg vs. 5mm Hg, $p<0.01$). The 8.5mm Hg greater improvement in the intervention group versus the control group is consistent with the findings of a 2007 meta-analysis of pharmacist hypertension management which showed an average 6.9mm Hg greater improvement in the intervention group.[12] However, the average patient age for the studies included in that meta-analysis was 63, while the average age of patients in this study was just under 56 years. Evidence indicates that earlier intervention to reduce blood pressure can produce significantly better long-term outcomes for patients.[34] This study has demonstrated that pharmacists can effectively decrease "younger" patients' blood pressure thus improving their outcomes.

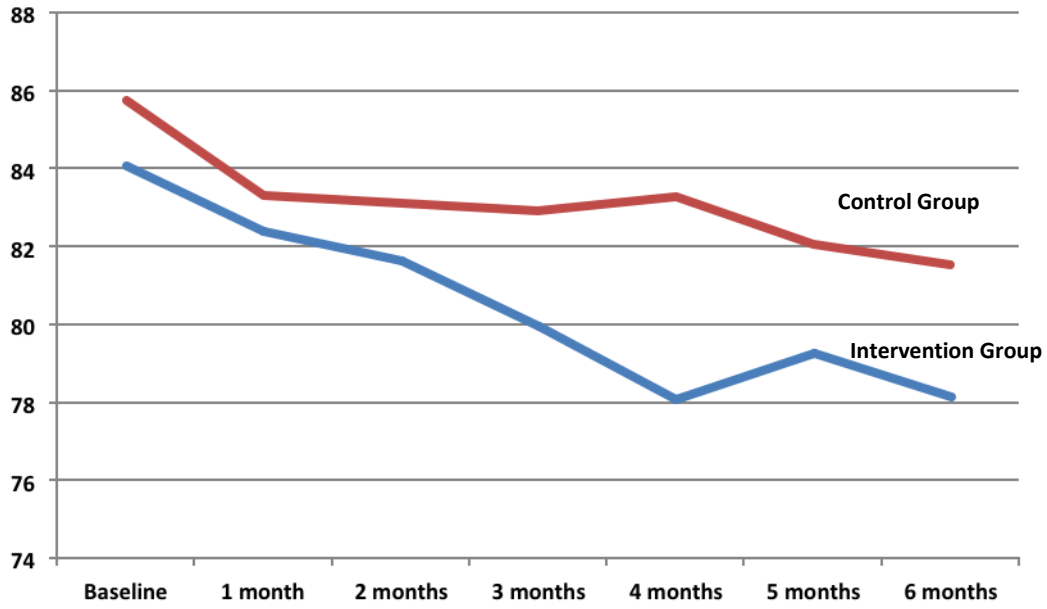
Studies have shown that a reduction of 10-12mm Hg could reduce chances of cardiovascular events and stroke of up to 50%.[35] A 13.5mm Hg decrease in blood pressure evidenced in this study could thus produce a substantial positive impact on patient health and reduce chances of developing cardiovascular disease. This is assuming that pharmacist intervention is continuously maintained – it is likely that when pharmacist intervention ceases, patients relapse towards unhealthy behaviours, and their blood pressure rises accordingly. Hence, future pharmacist-run chronic disease management programs should be structured to include pharmacist intervention throughout the year to ensure that patients receive the support they need to maintain controlled blood pressure.

Figure 2. Patient systolic blood pressure by study group



In contrast to systolic blood pressure, the reduction in diastolic blood pressure was not significantly greater for the intervention group compared to the control group (5.9mm Hg vs. 4.2mm Hg, p=0.511) (Figure 3). This is not unexpected given that both intervention and control group had fairly well controlled diastolic blood pressure to begin with (84.1 and 85.8mm Hg respectively). Hence, the impact that a pharmacist intervention could possibly have on these patients' diastolic blood pressure was limited.

Figure 3. Patient diastolic blood pressure by study group



The percentage of intervention group patients who had controlled blood pressure increased from 26% at study baseline to 82% at study end point, while the proportion in the control group increased from 36% to 54% over the same timeframe. This differences between the two groups was statistically significant ($p<0.001$). This result illustrates that patients who receive a comprehensive hypertension management program from pharmacists are significantly more likely to reach blood pressure targets than patients who receive care solely from physicians. As noted in the Methods section, one of the patient inclusion criteria was uncontrolled blood pressure, yet 26% of the intervention patients and 36% of the control patients had controlled blood pressure at baseline. This discrepancy was due to the fact that patient screening was done prior to the baseline appointment. Hence, some of the patients whose blood pressure was uncontrolled at screening, and who were thus enrolled in the study, had controlled blood pressure at baseline.

One of the interesting findings from this study was the control group's relative improvement in blood pressure and other outcome measures across the 6 months of study. Since control group patients received no pharmacist intervention, these improvements were not expected. However, control group patients still met with their pharmacists on a monthly basis, received information about their elevated blood pressure and were encouraged to speak with their physician about

their condition. These factors likely acted as a motivator for patients to engage in healthier behaviours that then translated into improvements in blood pressure. In real world conditions, however, patients do not have these motivators and are unlikely to change their behaviours in the absence of an intervention (e.g. from a pharmacist).

Adherence to Medication Therapy

Patients in the intervention group reported a 15% increase in adherence to antihypertensive medication therapy from baseline to study end point, while control group patients reported a 2.2% increase. The difference between the groups approached statistical significance (p=0.08). Analysis of prescription refill data from Green Shield Canada also showed a greater improvement in the intervention group compared to the control group, however, the overall improvement was not as substantial (0.8% increase vs. 1% decrease respectively, p =0.07).

The discrepancy between the findings based on patient self-report and prescription refill data could be due to the short time frame (6 months pre and post first consultation with the pharmacist) for which refill data was obtained. With most drug plans requiring 90-day refills of chronic medications, study patients would have only had 2 refills during each of the pre and post time periods. This represents a very small sample from which to draw conclusions about the impact of pharmacist interventions on refill adherence. With this limitation, the self-report data might offer a more reliable estimate of adherence, particularly given that this study used a validated MMAS scale to measure adherence. Furthermore, self-report data provides a better picture of the actual medication taking behaviour, which refill data does not capture.

Previous studies of pharmacist interventions in hypertension management have shown mixed results with respect to adherence. A 2007 systematic review identified 13 studies, only 5 of which showed significantly greater improvement in adherence in the intervention group compared to the control group.[12]

Evidence indicates that there is a strong relationship between adherence to medication therapy and overall health outcomes. A systematic review of 57 studies, showed that 86% demonstrated a positive association, meaning that as adherence increased clinical health outcomes improved as well.[36] This relationship was demonstrated for multiple disease states including hypertension, diabetes, depression and asthma. Hence, it could be expected that, if maintained, the 15% improvement in adherence in the intervention group would ultimately lead to better long-term patient health outcomes, further to what was already demonstrated in the 6-month study time period.

Recent research has also shown a strong association between adherence to medication therapy and absenteeism in the workplace. A 2012 study of administrative health care claims data for over 100,000 employees at 16 medium to large size organizations, showed that employees who were adherent to medication therapy were significantly less likely to be absent from the workplace.[37] The strength of the relationship varied by chronic disease condition, with adherent hypertensive patients having 5.2 fewer absent days and 3.5 fewer short-term disability days annually. Considering that most of the patients in this study were employed full time, their

improvement in adherence would not only translate into improved long-term health outcomes but also fewer days of absence from the workplace in the near-term. From an employer perspective, a pharmacist-led hypertension management program, provided as a benefit to employees could be a cost-effective return on investment that produces healthier, more productive employees.

Increasingly, health care leaders are calling for employer drug plans to institute more chronic disease management program as benefits for their employees. In a 2011 white paper on the strategies employer drug plans should implement to manage their costs, the former executive officer of the Ontario Public Drug Programs, Helen Stevenson makes the following argument:[38]

> *"Finally, employer health and drug plans should provide comprehensive clinical programs to help employees better manage chronic conditions, and particularly as it relates to prescription drugs and adherence. Programs such as a diabetes care program or a pain management program, among others, will drive better outcomes for employees and help manage prescription costs."*

Body Mass Index (BMI)

Intervention group patients had a 4.6% decrease in their body mass index (BMI) from baseline to study endpoint , while control group patients actually had a 1.4% increase in their BMI. While the difference between the two groups was not statistically significant (p=0.125), the trend was clearly favourable for the intervention group. This improvement in BMI in the intervention group is likely due to a number of factors, including changes in diet and frequency of physical exercise (report below). In particular, all study pharmacists reported that the enrolled patients had greater awareness of the sodium levels in products and made healthier dietary choices as a result of pharmacist counselling.

> *"Patient B. is continuing to exercise and count calories to try to achieve a healthy BMI. He is careful to read labels for sodium content when purchasing food. He continues to golf 4x weekly for 30-60 min sessions of walking. Both Patient B. and his Dr. are happy with his blood pressure"*

> *"Patient is doing well with maintaining his exercise program. He is also reading labels to check sodium level before purchasing foods at the grocery store. He is dealing with stress at work and is trying to find a way to minimize these stressors."*

Frequency of Physical Exercise

Control group patients had a much higher frequency of physical exercise per week than intervention group patients at study baseline (94.4 minutes/week vs. 66.6 minutes/week). By study end, the frequency of physical exercise increased by 57%, in the control group and 97% in the intervention group. While the difference between the 2 groups was not statistically significant (p=0.653), there was a clear tendency for the intervention group to engage in more physical exercise as the study progressed. This finding was not surprising as one of key aspects of pharmacist counselling on lifestyle modification, involved convincing patients of the importance of physical exercise in the control of their hypertension.

Smoking Status

At baseline there were 13 smokers in the control group and 10 in the intervention group and at study end (appointment seven) one smoker in the control and 2 in the intervention group quit. Given that there were so few smokers in both groups, no statistical analyses were performed on this variable. However, previous research has shown that pharmacists are effective in helping patients successfully quit smoking, with quit rates ranging from 5-36%.[39] Recognizing the value of pharmacists in this capacity, Green Shield Canada offers a pharmacy-based smoking cessation program that employers can incorporate in their benefit plans. Early evaluation of that program has shown promising results with an average quit rate of 37.5%.[40] The Ontario government similarly introduced the Pharmacy Smoking Cessation program in 2011 through which pharmacists are compensated for counselling ODB patients on strategies to quit smoking.[41]

Number of Prescription Medications

There was no change from baseline to study endpoint in the mean number of prescription medications patients in the control group were taking, while intervention group patients had a mean 2.4% decline. The difference between the two groups was not statistically significant (p=0.836). This is consistent with the findings of other research studies of pharmacist interventions which have typically shown no impact on the number of medications patients take.[42]

Drug Therapy Costs (Antihypertensive Drugs)

Intervention group patients' average cost of all antihypertensive drug therapy *decreased* from $177.20 in the 6-month time period preceding their enrolment in the study to $121.90 in the 6-months study period. This represents a decrease of 31.2%. In comparison, control group patients had a 5.2% decline in their average antihypertensive drug costs in the same time period ($171.30 and $162.30, respectively). The difference between the two groups approached statistical significance (p=0.055).

This reduction in antihypertensive medication costs in the intervention group could be attributable to the significant improvement in patient's blood pressure control. As patients reached blood pressure control, their physicians may have altered their drug therapy regimen to eliminate certain medications or reduce the frequency of usage of others. Alternatively, the reduction in drug costs may also be attributable to change to more cost-effective drug therapy. In other words, pharmacists may have made recommendations to prescribers to utilize more cost-effective antihypertensive therapeutic options. Interestingly, however, pharmacists were not specifically instructed during the training sessions, or any follow-up communications, to look for ways to optimize drug therapy costs.

From a private drug plan perspective, this finding is important in that it demonstrates that pharmacists can play a key role in containing rapidly escalating drug therapy costs. Being knowledgeable not only about the effectiveness of various drug therapy options but also their relative cost-effectiveness, pharmacists are ideally positioned to optimize drug therapy in a way

that maximizes therapeutic benefit at the lowest possible cost. Incorporating a pharmacist-led chronic disease management program into an employer-sponsored benefit plan can thus serve the dual purpose of containing costs while improving employee health.

Drug Therapy Costs (All Drug Categories)
Looking at the average drug costs for all drug categories, the intervention group declined about 6% from the 6-month pre-study period to the 6-month study period ($730.60 and $684.30, respectively). Control group patients had a similar 8% cost decrease from the pre-study to study period ($821.5 and $762.5, respectively). The difference in the relative cost declines between the two study groups was not statistically significant (p=0.909).

In contrast to antihypertensive medication costs, pharmacist intervention did not appear to have an impact on the overall drug therapy costs. This is logical in that pharmacist intervention was focused on hypertension and the medications to treat that condition. The study pharmacists did review the patient's entire medication regimen, with a focus on optimizing drug therapy to achieve best possible health outcomes.

Pharmacist Intervention Costs
The average cost of all of the services delivered by pharmacists (across the 6 months of study) in the intervention group was $421.10. This figure does not include the cost of the medication reviews, as these were billed directly to the Ontario Ministry of Health and Long-Term Care through the MedsCheck program. The figure does include the reimbursement paid to pharmacists for collecting study data (e.g. patient demographic information, etc.). The average cost of all of the services in the control group was $183.10. Since the control group pharmacists provided no clinical services to patients, this figure reflects only the reimbursement paid for collecting study data and measuring blood pressure. If this amount ($183.10) is subtracted from the average service costs in the intervention group, the remainder ($238) reflects only the cost of the clinical services delivered by pharmacists.

Control group pharmacists reported spending an average total of 52 minutes across all 7 appointments with the patient, while intervention group patients reported spending 199 minutes (Table 8). If the control group total time is subtracted from the intervention group total time, the remainder (147 minutes or about 2.5 hours) represents time spent by the pharmacist in direct patient care (not including blood pressure measurement). Therefore, to achieve the level of patient improvement evidenced in this study requires about 2.5 hours of pharmacist time. In total, pharmacists in this study were compensated $238 for 147 minutes of their time or $1.60/minute for providing direct patient care services. This level of compensation is lower than the standard reimbursement rate of $2/minute for professional pharmacy services, as established in the Medsheck program ($60 for a 30 minute consultation).

Table 8. Average reported appointment duration

Group	Average Appointment Duration (minutes)							
	1 (Baseline)	2	3	4	5	6	7 (Final)	Total
Control Group	28	13	12	12	11	11	23	52
Intervention Group	57	27	22	22	21	20	29	199

Patient Satisfaction

All intervention group patients were asked to complete a service satisfaction survey following their last appointment with the pharmacist. Twenty-seven out of the 39 intervention group patients completed the survey for a response rate of about 69%. Patients were generally very satisfied with pharmacist services, perceiving that pharmacists helped them understand their medications and control their blood pressure (Table 9).

Patients were also very satisfied with the study itself, with 100% perceiving it to be of value to them. A few patients (4%) were inconvenienced by the monthly appointments with the pharmacist and several others (11%) felt that some aspects of the study could have been better.

Table 9. Patient satisfaction with pharmacist services

Statement	Satisfaction		
	Agree	Disagree	Neutral
Overall, this study provided a valuable service to me	**100%**	0%	0%
The quality of information provided to me by the pharmacist was excellent	**100%**	0%	0%
My participation in this study helped me understand high blood pressure better	**89%**	0%	11%
I felt comfortable talking with the pharmacist about my health problems	**96%**	0%	4%
The pharmacist was able to help me control my high blood pressure	**85%**	0%	15%
The pharmacist helped me understand my high blood pressure medications better	**100%**	0%	0%
I was inconvenienced by the monthly appointments with the pharmacist	4%	**78%**	15%
There are some aspects of the hypertension study that could be better	11%	**52%**	37%
I think the pharmacist should provide this type of service for everyone	**81%**	0%	15%
I think the pharmacist should be paid for this type of service	**78%**	4%	15%

The narrative comments offered by study patients also illustrate their satisfaction with the study and the impact that pharmacist interventions had on their health.

> *This study has made me aware of the severity of hypertension and the damage it can do not only to the heart but other organs of the body as well. I am now eating healthier and exercising daily. Lots of fruits, vegetables, grains and water have become part of my daily diet. Thank you all for this opportunity.*
>
> *I found the hypertension study very informative. I changed many bad habits. The pharmacist was very helpful in helping me with eating habits and I quit smoking*
>
> *The pharmacist was very knowledgeable and friendly. It was a very pleasant experience and felt that I greatly benefited from this study.*
>
> *Study was very helpful - appreciative of the assistance, suggestions, and information offered by the pharmacist. He was very informative and encouraging. I learned several new things related to hypertension.*

Patients were also asked to comment on how the study may have impacted their workplace absenteeism and performance. Nine out of the 27 patients were retired and were thus unable to respond to these questions and one additional patient did not complete the question. Out of the remaining 17 patients, four (24%) reported being more productive at work now than they were before enrolling in the study, and one (6%) reported missing fewer days of work. With respect to absenteeism, most patients reported not missing any days of work at the outset and as such, the study had no impact on their absenteeism. Furthermore, with hypertension being largely asymptomatic, it is unlikely that patients would have missed work due to this condition, until such a time when it progressed into a more severe health issue (i.e. serious event such as cardiac arrest or the onset of cardiovascular disease).

Pharmacist Perceptions

Following the completion of the study, 10 intervention group pharmacists participated in one-on-one semi-structured interviews regarding their experiences participating in the study and providing the structured hypertension management services. The interviews lasted an average of 19 minutes.

The primary motivation for pharmacists in participating in the study was to have an opportunity to provide more direct patient care services. All of the pharmacists commented that providing clinical, patient-focused services increased their job satisfaction and was strongly preferred over dispensing medications. Other pharmacists commented that their motivation for participating in the study was to help promote the value of pharmacists to government and private payers.

Two of the biggest challenges encountered by participating pharmacists included finding enough time to deliver the hypertension management services and ensuring patients show up for their appointments. They noted that a change in workflow will be necessary in order to continue providing these services, with pharmacist overlap noted as a potential solution. Pharmacists noted multiple instances where patients did not keep their scheduled appointments

due to a lack of time and conflicting work schedule. They found success in scheduling appointments outside of work hours – either very early in the morning or late afternoons.

When asked about which aspect of their interventions had the greatest impact on patient health outcomes, all pharmacists noted lifestyle counselling. In particular, the pharmacists felt that nutrition-related counselling was well received by patients and led to dramatic changes in patients' diets and ultimately improved outcomes. Interestingly, only two pharmacists noted that drug therapy optimization played a substantial role in achieving the demonstrated health outcomes. Some pharmacists felt frustrated by their inability to reach the patient's doctors and by the lack for response from them regarding pharmacist-suggested drug therapy changes.

All but two of the participating pharmacists indicated they would unequivocally take part in a similar employer-sponsored hypertension-management program once it is rolled out. The two remaining pharmacists also expressed strong interest in participating but qualified their statement by stating that they would need to implement workflow changes to ensure they could accommodate additional patients.

Pharmacists generally felt that the study provided a tremendous experience and a great learning opportunity. They expressed a strong desire to see the study expand into other chronic conditions, including hyperlipidemia and asthma. Potential areas of improvement for future studies included greater involvement of physicians from the outset in order to ensure their support, and more support from study investigators in keeping patients enrolled in the study and reducing dropout.

Conclusions

This study has demonstrated that a pharmacist-led hypertension management program can significantly improve patient blood pressure and adherence to medication therapy in a very short, six-month time frame. Perhaps more importantly, the improvements in health outcomes were observed for a younger patient population than has traditionally been the subject of research in this area. Improving blood pressure control in this population can translate into a significant reduction in the risk for cardiovascular disease and stroke and better long-term outcomes.

In addition to improving patient health outcomes, the hypertension management program led to a reduction in the overall cost of anti-hypertensive medication therapy by about a third. Patient satisfaction with pharmacist services was uniformly high and there was evidence of greater productivity amongst a quarter of employed study patients.

Hence, from an employer perspective, incorporating a pharmacist-led chronic disease management program in their benefit plans can not only help contain drug therapy costs in the short term but also lead to healthier, more productive employees.

Acknowledgements

The Ontario Pharmacists Association (OPA) and Green Shield Canada (GSC) would like to express their appreciation to the study sponsors, including Servier Canada, the Canadian Foundation for Pharmacy, Thermor Canada and the Heart and Stroke Foundation.

OPA and GSC would also like to thank all of the pharmacists and patients that participated in this study as well as Shoppers Drug Mart, Dell Pharmacies (now part of Rexall), Medical Pharmacies, Lovell Drugs, Loblaws and Metro for facilitating their pharmacies' involvement in the study and assisting with patient recruitment.

References

[1] World Health Report 2002. *Reducing risks, promoting healthy life.* World Health Organization. Geneva, Switzerland: 2002. Available at: http://www.who.int/whr/2002/

[2] Joffres MR, Ghandirian P, Fodor JG et al. Awareness, treatment, and control of hypertension in Canada. *American Journal of Hypertension* 1997;10(Pt 1):747-749.

[3] Tu K, Zhongliang C, Lipscombe L. Prevalence and incidence of hypertension from 1995 to 2005: a population based study. *Canadian Medical Association Journal* 2008;178(11):1429-1435.

[4] Carter BL, Zillich AJ. Pharmaceutical care services for patients with hypertension. *The Annals of Pharmacotherapy 2003*;37:1335-1337.

[5] Oliviera SA, Lapuerta P, McCarthy BD, L'Italien GJ, Berlowitz DR, et al. Inadequate management of blood pressure in a hypertensive population. *New England Journal of Medicine* 1998;339:1957-1963.

[6] Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003;42:1206-1252.

[7] Carter BL, Bergus GR, Dawson JD, Farris KB, Doucette WR, et al. A cluster-randomized trial to evaluate physician/pharmacist collaboration to improve blood pressure control. *Journal of Clinical Hypertension* 2008;10(4):260-271.

[8] Milchak JL, Carter BL, James PA, Ardery G. Measuring adherence to practice guidelines for the management of hypertension: an evaluation of the literature. *Hypertension* 2004;44:602-608.
[9] Walsh JM, McDonald KM, Shojania KG, et al. Quality improvement strategies for hypertension management. *Medical Care* 2006;44:646-657.
[10] Hepler CD, Strand LM. Opportunities and responsibilities in pharmaceutical care. *American Journal of Health-System Pharmacy* 1990;47(3):533-543.
[11] Task Force on a Blueprint for Pharmacy. *Blueprint for pharmacy: the vision for pharmacy.* Ottawa (ON): Canadian Pharmacists Association; 2008. Available at: http://www.pharmacists.ca/content/about_cpha/whats_happening/cpha_in_action/pdf/BlueprintVision.pdf
[12] Machado M, Bajcar J, Guzzo GC, Einarson TR. Sensitivity of patient outcomes to pharmacist interventions. Part II: systematic review and meta-analysis in hypertension management. *The Annals of Pharmacotherapy* 2007;41:17701-1781.
[13] Staessen JA, Wang JG, Thijs L. Cardiovascular prognosis of "masked hypertension" detected by blood pressure self-measurement in elderly treated hypertensive patients. Journal of the American Medical Association 2004;291:1342-1349.
[14] Blenkinsopp A, Phelan M, Bourne J, Dakhil N. Extended adherence support by community pharmacists for patients with hypertension: a randomized controlled trial. *International Journal of Pharmacy Practice* 2000;8:165-175.
[15] Sookaneknun P, Richards RME, Sanguansermsri J, Teerasut C. Pharmacist involvement in primary care improves hypertensive patient clinical outcomes. *Annals of Pharmacotherapy* 2004;38:2023-2028.
[16] Wang J, Wu J, Yang J, Zhuang Y, et al. Effect of pharmaceutical care interventions on blood pressure and medication adherence of patients with primary hypertension in China. *Clinical Research and Regulatory Affairs* 2011;1:1-6.
[17] Robinson JD, Segal R, Lopez LM, Doty RE. Impact of pharmaceutical care intervention on blood pressure control in a chain pharmacy practice. *The Annals of Pharmacotherapy* 2010;44:88-96.
[18] Burt VL, Whelton P, Roccella EJ, et al. Prevalence of hypertension in the U.S. population: results from the third national health an nutrition examination survey, 1988-1991. Hypertension 1995;25:305-313.
[19] Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. *Journal of the American Medical Association* 1999;272(20):1557-62.
[20] Atreja A, Bellam N, Levy SR. Strategies to enhance patient adherence: making it simple. Medscape General Medicine 2005;7(1):4.
[21] National Association of Pharmacy Regulatory Authorities. Model Standards of Practice for Canadian Pharmacists. National Association of Pharmacy Regulatory Authorities; 2010. Available at: http://www.ocpinfo.com/Client/ocp/OCPHome.nsf/object/Model_Standards/$file/Model_Standards.pdf
[22] Morisky DE, Ang A, Krousel-Wood M, Ward HJ. Predictive validity of a medication adherence measure in an outpatient setting. The Journal of Clinical Hypertension 2008;10(5):348-354.
[23] Gatti ME, Jacobson KL, Gamararian JA, Schmotzer B, Kripalani S. Relationship between beliefs about medications and adherence 2009; American Journal of Health-System Pharmacy 2009;66(1):657-664.
[24] Krousel-Wood M, Islam T, Webber LS, Re RN, Morisky DE, Muntner P. New medication adherence scale versus pharmacy refill rates in seniors with hypertension. The American Journal of Managed Care 2009;15(1):59-66.
[25] Stroupe KT, Teal EY, Wanzhu T, Weiner M, Murray MD. Association of refill adherence and health care use among adults with hypertension in an urban health care system. Pharmacotherapy 2006;26(6):779-789.
[26] Kassamali A, Houle S, Rosenthal M, Tsuyki RT. Case finding: the missing link in chronic disease management. *Canadian Pharmacists Journal* 2011;144:4: 170-172.
[27] Pavlik VN, Greisinger AJ, Pool J, Haidet P, Hyman DJ. Does reducing physician uncertainty improve hypertension control: rationale and methods. *Circulation: Cardiovascular Quality and Outcomes* 2009;2(3):257-263.
[28] Fless JL. The Design and Analysis of Clinical Experiments. New York (NY): John Wiley and Sons; 1999.
[29] Robinson JD, Segal R, Lopez LM, Doty RE. Impact of pharmaceutical care intervention on blood pressure control in a chain pharmacy practice. *The Annals of Pharmacotherapy* 2010;44:88-96.
[30] Chabot I, Moisan J, Gregorie JP, Milot A. Pharmacist intervention program for control of hypertension. *Annals of Pharmacotherapy* 2003;37:1186-1193.

[31] Zillich AJ, Sutherland JM, Kumbera PA, Carter BL. Hypertension outcomes through blood pressure monitoring and evaluation by pharmacists (HOME Study). *Journal of General Internal Medicine* 2005;20:1091-1096.
[32] Donner A, Klar N. *Design and Analysis of Cluster Randomization Trials in Health Research*. 2000.
[33] Rosner B, Glynn RJ, Ting Lee ML. Incorporation of Clustering Effects for the Wilcoxon Rank Sum Test: A Large Sample Approach. *Biometrics* 2003;59: 1089-1098.
[34] O'Connor PJ, Vazquez-Benitez G, Schmittdiel JA, Parker ED, et al. Benefits of early hypertension control on cardiovascular outcomes in patients with diabetes. *Diabetes Care* 2013;36(2):322-327.
[35] Mancia G. Blood pressure reduction and cardiovascular outcomes: past, present, and future. *American Journal of Cardiology* 2007;100(suppl):3J-9J
[36] Harris BL, Stergachis A, Ried LD. The effect of drug copayments on utilization and cost of pharmaceuticals in a health maintenance organization. *Medical Care* 1990;28:907-917.
[37] Carls GS, Roebuck C, Brennan TA, Slezak JA, et al. Impact of medication adherence on absenteeism and short-term disability for five chronic diseases. *Journal of Occupational and Environmental Medicine* 2012;54(7):792-805.
[38] Stevenson H. *An end to blank cheques: getting more value out of employer drug plans.* Toronto (ON): Reformulary group 2011; Available at: http://www.reformulary.com/files_docs/content/pdf/en/An_End_to_Blank_Cheques-May_2011_ENr.pdf
[39] Dent LA, Harris KJ, Noonan CW. Tobacco interventions delivered by pharmacists: a summary and systematic review. *Pharmacotherapy* 2007;27(7):1040-1051.
[40] Jackson M, Gaspic-Piskovic M, Cimino S. Description of a Canadian employer-sponsored smoking cessation program utilizing community pharmacy-based cognitive services. *Canadian Pharmacists Journal* 2008;141(4):234-240.
[41] Ontario Ministry of Health and Long-Term Care. Pharmacy smoking cessation program. 2013. Available from: http://www.health.gov.on.ca/en/pro/programs/drugs/smoking/
[42] Sellors J, Kaczorowski J, Sellors C, Dolovich L, et al. A randomized controlled trial of pharmacist consultation program for family physicians and their elderly patients. *Canadian Medical Association Journal* 2003;169(1):17-22.