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The veterans' study to improve the control of hypertension (V-STITCH): Design and methodology

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Abstract

Background: Among the 60 million Americans with hypertension, only approximately 31% have their blood pressure (BP) under control (<140/90 mm Hg). Despite the damaging impact of hypertension and the availability of evidence-based target values for BP, interventions to improve BP control have had limited success.
Objectives: A randomized controlled health services intervention trial with a split-plot design is being conducted to improve BP control. This 4-year trial evaluates both a patient and a provider intervention in a primary care setting among diagnosed hypertensive veterans.
Methods: In a cluster-randomization, 30 primary care providers in the Durham VAMC Primary Care Clinic were randomly assigned to receive the provider intervention or control. The provider intervention is a patient-specific electronically generated hypertension decision support system (DSS) delivering guideline-based recommendations to the provider at each patient's visit, designed to improve guideline-concordant therapy. For these providers, a sample of their hypertensive patients (n=588) was randomly assigned to receive a telephone-administered patient

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intervention or usual care. The patient intervention incorporates patients' need assessments and involves tailored behavioral and education modules to promote medication adherence and improve specific health behaviors. All modules are delivered over the telephone bi-monthly for 24 months. In this trial, the primary outcome is the proportion of patients who achieve a BP ≤140/90 mm Hg at each outpatient clinic visit over 24 months.
Conclusion: Despite the known risk of poor BP control, a majority of adults still do not have their BP controlled. This study is an important step in testing the effectiveness of a patient and provider intervention to improve BP control among veterans in the primary care setting.
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Keywords: Hypertension; Blood pressure control; Clinical trial; Self-management; Adherence

1. Introduction

Heart disease and stroke remain the first and third leading causes of death, respectively, in the US and impose an enormous financial burden (more than US$259 billion in direct and indirect costs in 1996) [1]. Hypertension is the major modifiable risk factor for stroke and one of the major risk factors for coronary heart disease, congestive heart failure, and renal disease [2–4]. Hypertension is particularly prevalent among African-Americans [5], and African-Americans with hypertension are two to three times more likely than whites to have a stroke and seventeen times more likely to progress to end-stage renal disease [6,7].

There are approximately 60 million Americans who have hypertension [8], yet only 31% of all hypertensive patients have their blood pressure (BP) under effective control (<140/90 mm Hg) [9]. Abundant evidence shows that effective BP control lowers the risk of cardiovascular disease [10–13], and the mechanisms for achieving control (e.g., diet, exercise, and pharmacology management) are widely available to all providers. Therefore, an important element to help reduce the burden of hypertension-related disease is to increase the proportion of patients with adequate BP control.

The factors responsible for poor BP control likely reflect deficiencies in addressing at least one of the three levels of disease management [14–16]: patient factors [17–19], provider factors including the medical environment [20,21], and social and cultural factors [16,22,23]. These antecedents of BP control may include patients' psychological/behavioral characteristics, such as perceived risk of hypertension and poor memory; patients' medical care environment, such as problems of access to health care and insurance and provider behavior, and; patients' social/cultural environment. Most interventions have focused on either the patient or medical environment (e.g., patient adherence with medications or provider prescribing behavior). These intervention strategies potentially miss half of the problem and may lead to attenuated results. Although both provider and patient knowledge about hypertension and familiarity with its treatment is necessary, this is insufficient to ensure a high degree of adherence [24–26].

Despite widely published and accepted evidence-based guidelines for pharmacological management of hypertension, providers continue to under-treat elevated BP [27,28]. One component of the providers' role in outcomes of treatment is their medication prescription patterns. In several physician self-report surveys, >70% adherence to the guidelines have been reported, however, actual practice analyses reveal only 50% adherence [29–33]. Moreover, longitudinal studies suggest worsening adherence to hypertension guidelines [32,34–36].

Providers may impede patients' BP control by providing patients with overly complicated medication regimens or by not addressing adverse effects, which leads to poor patient BP control. Other provider behaviors that can adversely affect patient adherence include the inability to teach and monitor lifestyle changes because of an excessive number of patients, infrequent follow-up appointments, and assuming that elevated values obtained in the office do not reflect the true levels at home (i.e., white-coat effect) [37,38]. Additionally, the information available at the point of care may be inappropriately organized to allow effective decisions.

The inability to achieve adequate BP control seems to arise through a complex interaction of patient and provider behaviors [39]. We posit that proven patient strategies for augmenting BP control, like behavior modification and support, can be enhanced by provider-focused feedback designed to highlight information important for prescribing decisions and to improve sensitivity to patients' issues [40]. Thus, the two primary hypotheses for the study are: (1) The proportion of veterans with BP control who receive *EITHER* the provider-directed decision support *OR* patient health education and behavioral intervention will be increased by 10% as compared to usual care over the 2 years. (2) The proportion of veterans with BP control who receive BOTH the provider-directed decision support *AND* patient health education and behavioral intervention will be increased by 25% as compared to usual care over the 2 years. We seek to test these hypotheses within the context of a busy primary care practice.

2. Trial design and methods

2.1. Overview

The current study incorporates two multilevel interventions that focus on patient and provider behavior, independently, and simultaneously. Some studies have focused on practice-based guideline implementation where compliance was the outcome [41]; however, guideline compliance is not always related to our ultimate outcome of interest, BP control. The few studies that have considered BP control as the outcome have typically involved small sample sizes [42–45], did not include a provider intervention [43,44,46–48], did not examine the intervention sustainability beyond 12 months [42,47], and/or did not focus on more than one factor related to hypertension [49–51]. In summary, our study builds upon the strengths of these prior studies, but also includes both a patient and provider intervention, a large enough sample to examine interactions, a follow-up period of 24 months, and recruitment from a primary care setting where hypertension-related visits are one of the most common reasons to visit the clinic.

2.2. Design, setting, and recruitment

We chose a split-plot in time study design [52] because patients are nested within providers and the interventions occur at the two levels (provider and patient) over time. The provider-level intervention is the "whole plot" factor and the patient-level intervention is the "sub-plot" factor (see Fig. 1). We enrolled 30 continuity care providers (22 attendings, 6 physician assistants and 2 registered nurse practioners) at the Durham VAMC primary care clinic. To prevent contamination between the control and intervention groups, we randomized providers who work closely together to the same intervention group in the following way. We first identified the natural clusters of providers (e.g., physicians who supervise and

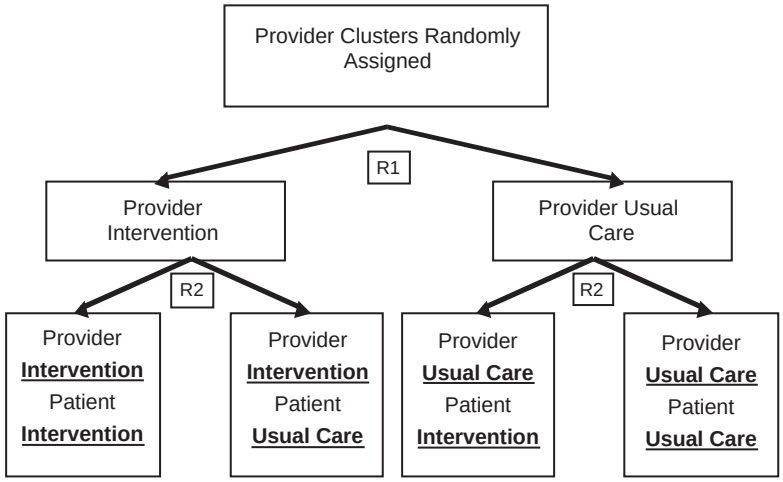

Fig. 1. Study design.

work with physician assistants) where they existed. We enumerated the clusters (some with a single provider) and randomly assigned half the clusters to control and half to the intervention arm. Among the randomized providers, patients were randomly approached and consenting patients who completed baseline interviews were randomized to intervention or usual care. Patients were randomized using consecutively numbered envelopes that contained group assignment based upon a random number computer program. Residents and interns were not included in the study because the study length exceeded their expected clinic rotation length.

The patient study population for V-STITCH consists of 4017 potential subjects identified through the facility's information system. These individuals had a diagnosis of hypertension by an outpatient ICD 401.0, 401.1, or 401.9 diagnostic code on outpatient encounter forms (primary or secondary), were enrolled in the Durham VAMC primary care clinic, and had a filled prescription for hypertensive medication (ACE inhibitors, beta blockers, calcium channel blockers, diuretics, $alpha_1$ blockers, and/or central $alpha_2$ agonists) in the previous year. The research assistants approached 816 eligible patients to be in the study. Among these patients, 190 refused, 38 were excluded, and 588 were enrolled (76% recruitment rate). The 38 patients were excluded for the following reasons: hospitalized for a stroke, myocardial infarction (MI), coronary artery revascularization, or diagnosis of metastatic cancer in the past 3 months, dementia diagnosis, resident in nursing home or receiving home health care, or severely impaired hearing or speech. Patients enrolled in study are followed for 24 months. The study is approved by the Durham VAMC IRB and meets all IRB and HIPAA regulations.

2.3. Interventions

2.3.1. Patient intervention

The nurse case manager contacts the patients in the intervention arm by telephone within 1 week of randomization and every 2 months for 24 months. At each call, the nurse delivers information in nine educational and behavioral modules: literacy, hypertension knowledge, memory, social support,

patient/provider communication, medication refills, missed appointments, health behaviors, and side effects. The information is both standard and tailored to patients' needs. To ensure that the intervention information is standardized, the nurse uses a computerized database, which contains predetermined scripts and tailoring algorithms. In addition, the database tracks information discussed at each phone call to provide a full understanding of the tailored intervention processes. The database also informs the nurse when each patient needs to be called again as well as what transpired during the past phone conversation. At the conclusion of the study, the database will contain an entire record for each patient describing what occurred (i.e., decisions made, answers to questions) during the intervention. This will enable us to evaluate the specific components of the patient intervention. Patients are also able to telephone the nurse with questions related to their hypertension between scheduled intervention calls, including pharmacological or non-pharmacological management of their disease. Should major emergent health care issues arise during these, or any calls, the nurse can contact the patients' primary care provider. See [53] for more details regarding the patient intervention.

2.3.2. Provider intervention

The Durham VAMC is a site of a larger study of hypertension guideline implementation with providers at three VAMCs (Palo Alto, San Francisco, Durham). The patient and provider interventions were implemented at the same time. The provider intervention includes two major components: [1] audit and feedback ("profiling") of the provider's panel of patients with respect to the guideline-recommended blood pressure targets and medication choices; and [2] recommendations about management of the patient's hypertension presented to the provider at each clinic visit. Each of these is described here briefly [1]. Providers in the intervention group are sent a letter at baseline and every 3 months based on patients they have seen in the previous three months. The letter shows the proportion of patients whose blood pressure control is adequate and the proportion of patients in several clinical categories whose medications include the guideline-recommended drugs. Because most providers do not realize how poor their guideline adherence is, the profiling letter is intended as a priming strategy to increase the provider's receptivity to recommendations. [2] Recommendations about management of the patient's hypertension are computed and presented to the providers using a knowledge-based hypertension guideline automated decision support system known as the ATHENA Decision Support System (DSS) [54–58]. The ATHENA DSS displays recommendations in the computerized patient record system graphical user interface with a pop-up window that appears when the provider opens the record of an appropriate patient near the time of a scheduled primary care clinic visit.

The pop-up window display includes a request for the provider to review and update the blood pressure. The screen provides an assessment of the adequacy of the patient's BP control based on the most recent BP available, and recommendations for the next step in management. Evidence summaries from the medical literature are available for major recommendations. This information is structured so that providers can review the recommendations quickly, but still have the opportunity to assess the scientific justification if they so desire. The purpose is to educate and remind providers about guideline recommendations; however, there are situations in which the provider's knowledge of the patient's clinical condition will call for changes to the BP targets or choice of drugs that are different from the general guideline recommendations. The screen contains a checklist for provider feedback on the recommendations.

Providers not randomized to the intervention receive a control version of the pop-up window that displays the patient's most recent BP and the patient's current antihypertensive drug regimen. The control pop-up window allows for entry of BP data, but does not have any advisories or recommendations. The control pop-up provides a control for the effect of calling the providers' attention to hypertension, rather than to the specific recommendations displayed in the ATHENA intervention window.

3. Study measures

3.1. Baseline

Detailed information about the clinical aspects of hypertension is obtained using computer and medical records review. Such information includes body mass index, dates of visits, diagnostic codes for visits, secondary diagnoses, clinical blood pressure values, and recent changes in antihypertensive medication. Additional data are collected at baseline in-person using a personal digital assistant (PDA) and is used to initiate and inform the nurse intervention. An adapted Hypertension Beliefs Questionnaire [59] is administered to examine the patient's perceived risk associated with hypertension. The Rapid Estimate of Adult Literacy in Medicine (REALM) [60] is used to measure health-related literacy, and immediate recall is measured by reading a brief paragraph that describes a typical interaction involving a provider explaining a hypertension regimen (i.e., take your medication once in the morning and once at night). Smoking habits, alcohol use, diet, and amount of exercise are assessed. Patients are asked to list side effects experienced that are associated with their antihypertensive medication from a standard checklist used in clinical trials. Patients' view of their providers' communication behavior is assessed using the Participatory Decision Making survey [61]. Amount of social support patients receive is assessed using a validated item [62]. Secondary outcome data discuss below is obtained via telephone. See Table 1 for an outline of measures.

3.2. Primary outcome

The primary outcome of the study is BP control measured at each primary care visit and is obtained from patients' medical records. Systolic BP and diastolic BP are obtained from medical records at all of a patient's primary care visits over the study period. These BP values are obtained by nurses prior to each primary care visits. This is also the BP that is entered into the computer for quality monitoring. For each patient's measurement occasion, inadequate BP control is defined as a SBP$\geq$140 mm Hg or a DBP$\geq$90 mm Hg for non-diabetics and SBP$\geq$130 mm Hg or a DBP$\geq$85 mm Hg for diabetics according to the JNC VI guidelines [63]. Using computer retrievals and medical records review, a research assistant abstracts all recordings of subjects' BP for each patient visit to their primary care provider at the Durham VAMC during the 24-month period. When multiple measurements are made during a visit, we use the lowest recorded value for that day's visit. Approximately 80% of BP measures are only recorded once in patient's records for a particular visit. We only use BP recorded in outpatient settings to construct the outcome variable-BP control.

We have chosen a method of hypertension assessment, which relies on computer retrieval and medical record reviews, as opposed to measuring BP at set intervals. If BP was measured at set

Table 1
Summary of measures

Construct	Variable	Location
Independent variable		
	Intervention status	1—nurse intervention, 2—provider intervention, 3—both, 4—usual care
Covariates		
Clinical	Prior 12 month Blood pressure values	Computerized medical records
	Body mass index	Computerized medical records
	Dates of primary care visits	Computerized medical records
	Diagnostic codes for visits	Computerized medical records
	Antihypertensive medications	Electronic pharmacy records
	Comorbidities	Computerized medical records
Demographic	Age	In-person baseline interview
	Marital status	In-person baseline interview
	Education	In-person baseline interview
	Race	In-person baseline interview
Patient	Social support [62]	In-person baseline interview
	Rapid estimate of adult literacy in medicine [60]	In-person baseline interview
	Memory	In-person baseline interview
	Health behaviors	In-person baseline interview
	Side effects	In-person baseline interview
	Participatory decision making [61]	In-person baseline interview
Primary Outcome		
	24-month blood pressure control	Computerized medical records
Secondary Outcomes		
	Hypertension beliefs questionnaire [59]	In-person baseline interview; 6 and 24 via telephone
	Self-efficacy with hypertension regimen	In-person baseline interview; 6 and 24 via telephone
	Pill refill	24 months-pharmacy records

intervals, patients assigned to the control group might alter their behavior and subsequently influence their adherence efforts. In addition, it is likely that those who are the least compliant would drop out of the study and introduce bias in the results. Abstracting patients' BP when they visit the primary care clinic ensures a higher level of participation. In addition, these blood pressures are what the physicians use to make clinical decisions and they guide the ATHENA recommendations. Finally, we are using the BP measurements that the regular clinic staff take in their usual environment, and these BP measurements are not related to any observer bias associated with the study.

3.3. Secondary outcomes

Knowledge and perceived risks associated with hypertension and ability to continue hypertension regimen is assessed via telephone at baseline, 6 and 24 months after baseline. Medication adherence, the

third secondary outcome, is assessed from pharmacy records for the entire 24-month period. The specific operationalization of these three variables are:

Knowledge and perceived risks associated with hypertension. The modified hypertension beliefs questionnaire is used to assess knowledge and perceived risks [59].
Ability to continue hypertension regimen. Patients are asked to rate their confidence and ability to continue their recommended hypertension regimen and maintain BP control.
Adherence to hypertension regimen. Pill refill based upon computerized pharmacy records is used to measure adherence. Pill refills are an accurate, easily operationalized, commonly used, and conservative measure of medication adherence. Pharmacy refill records is used because veterans enrolled in the Primary Care Clinic have a strong financial incentive to obtain their medication from the VAMC pharmacy. For each patient, the number of days of non-adherence is calculated using "pill fill/re-fill dates", "quantity dispensed" and "days' supply" data on all antihypertensive prescriptions filled within the VA. Days spent in the hospital are counted as days of full adherence. This is a similar to the method used in other studies of medication adherence [64,65].

3.4. Patient sample

Patients mean age is 63 years, 98% are male, 41% are African-American, and 57% are white. A majority of the sample (67%) is married and 22% live alone. Half the sample (50%) has a high school education or less, 22% reported having inadequate incomes, and 25% are employed (see Table 2).

In terms of clinical information, 62% of the sample have been taking medications for 5 or more years, 66% have at least one parent with hypertension. A significant percent of the sample did not report any exercise (47%) in the last week and 33% currently smoke. Diabetes is prevalent with 38% having a diagnosis (self-report). Baseline mean systolic blood pressure obtained from patients' medical records is 139.2 mm Hg (SD=18) and the mean diastolic blood pressure is 75.6 (SD=12). Using cut-offs suggested by JNC VI, 43% of the sample have their BP under control at baseline (<140/90 mm Hg non-diabetic, and <130/85 mm Hg diabetic).

3.5. Sample size and power considerations

The base rate of BP control in our clinic population is about 40%. One of the Healthy Year 2010 goals is to increase the proportion of hypertensive adults who are below target values to 50% BP control [5]; therefore, for the purpose of power calculations, we hypothesized that either the patient or the provider intervention will result in 50% of the study sample with controlled BP at the conclusion of the study.

The primary outcome variable (BP control) is measured at each patient's primary care visit over the 2-year follow-up period. Simply fitting a model for this type of outcome variable presents several computational challenges [66]. Not surprisingly, there are no closed form sample size or power formulas based on hypotheses for these models. Therefore, we used a simulation study to estimate a required sample size. In the simulation study, datasets of a specific sample size were generated under the alternative model (i.e. achieving 50% control in the treatment group) and fit under both the alternative and null models using PROC NLMIXED (SAS Version 8). For each dataset, power was then derived from the non-central chi-square distribution with twice the difference in log-likelihood statistics as the non-centrality parameter. Overall power for a specific sample size was estimated by the mean power. All

Table 2
Veterans study to improve the control of hypertension: baseline sample characteristics (N=588)

Characteristic	Percent
Mean age	63 years (SD=11.24, Range=30–87)
Male	98%
Married	67%
Lives alone	22%
High school or less	50%
Employed	25%
Inadequate income	23%
Race	
White	56%
African American	41%
Medical	
Taking BP meds for ≥5 years.	62%
Parent with hypertension	66%
No exercise	47%
Currently smoke	33%
Diabetic	38%
Baseline blood pressure	
Mean systolic (SD)	139.2 mm Hg (SD=18)
Mean diastolic (SD)	75.6 (SD=12)
BP control[a]	43%

[a] Control based upon Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 6 Report guidelines [63].

of the parameters for the simulation study were derived from a pilot study of Durham VAMC hypertensive patients. Using a simulation study gave us the additional flexibility to naturally incorporate dropout into the power calculations. Instead of simply inflating the sample size estimate for dropout, we imposed dropout into the simulated datasets and investigated the impact of varying levels of dropout on power. Finally, we accounted for clustering of patients within provider using formulas given by Donner [67]. In this calculation, based upon pilot data, we assumed an Interclass correlation of 0.01. With these methods, we arrived on a final sample size of 544 patients—136 in each of the four provider by patient intervention groups.

3.6. Primary analyses

Measuring BP control as part of the natural clinic setting leads to many analytic challenges. BP control is dichotomous and multiple values for each patient is recorded over 24 months. BP control is obtained from patients' medical records. Because the BP measurements is taken at the patient's regular primary care visit, the actual number of measurements will vary between patients and these measurements are not taken at equally spaced intervals over the 24-month study period (Fig. 2). In addition, there may be a lack of independence between patients seen by the same provider or cluster of providers. A hierarchical logistic regression with random effects is a way to address the main

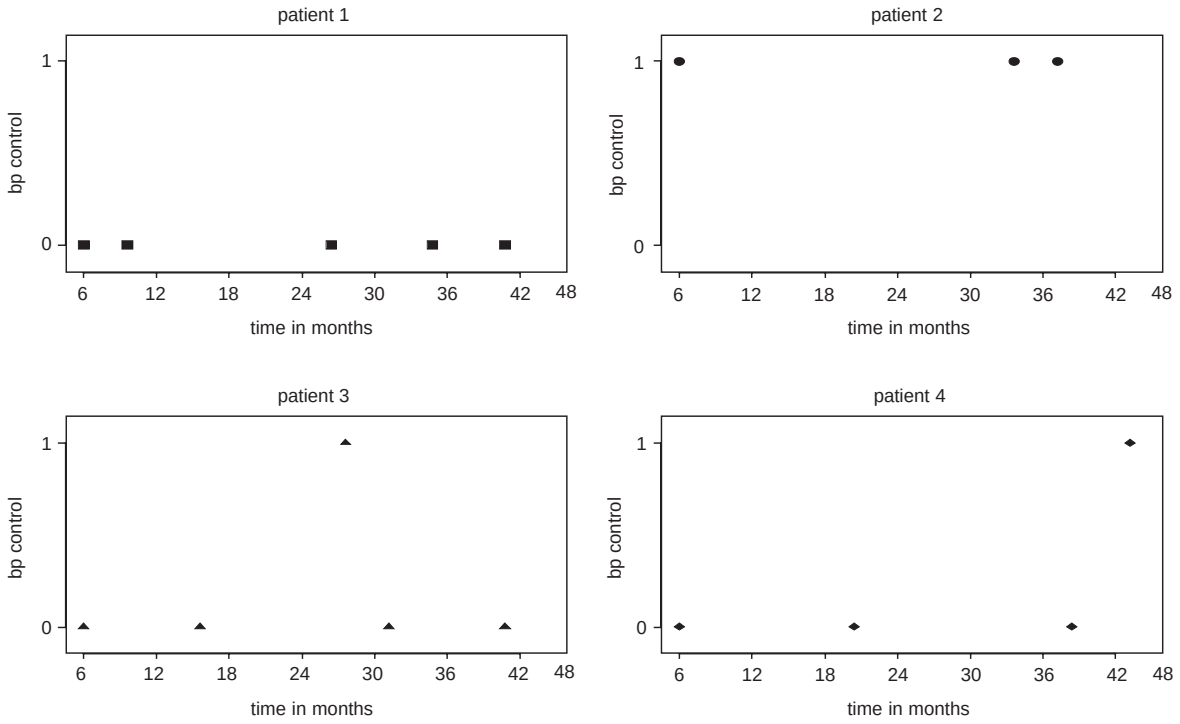

Fig. 2. Four patterns of longitudinal BP control. Each patients' observed SBP and DBP is converted to the outcome variable of BP control. In this figure, a "1" represents BP control and a "0" represents BP out of control.

study hypotheses [68] and address these challenges. From this model, we obtain the patient-specific expected probability of BP control over time. Time is defined as the number of days from baseline and is treated as a continuous predictor in the models. Including random effects in the model implicitly accounts for two sources of variation that arise from the study design: (1) the correlation between a patient's repeated BP measurements over time; and (2) the correlation between patients who are being treated by the same primary care provider. In addition to intervention group as our main independent variable, we will also include several important baseline covariates in our models that we chose based upon the literature including comorbid diseases, gender, age, race, length of disease, and prior BP control status.

3.7. Secondary analyses

We also plan to determine if the intervention influenced several important intermediary hypertension outcomes. Knowledge, perceived risks, medication adherence, and self-efficacy of hypertension regimen are all continuous, longitudinal measures. The analyses of these variables will also need to account for patients nesting within providers. That is, patients with the same primary care provider may have more similar outcomes as compared to patients with a different primary care provider. In addition, each provider (and, consequently, each treatment-intervention group) may have a different number of patients. For these reasons, we plan to use a hierarchical linear model with random effects for our analysis of these secondary outcomes.

4. Discussion

This study uses a comprehensive model that includes both a novel patient and provider intervention in an attempt to improve the overall BP control among hypertensive adults. In addition, the study involves a large enough sample to examine interactions, a follow-up period of 2 years and recruitment from a primary care setting where hypertension-related visits are one of the most common reasons to visit a primary care clinic. BP control was chosen as the outcome because it is a valid, reliable, measure that has clear biological implications and is readily understood by providers, patients and administrators.

Elevated BP is one of the most common reasons for adults to visit the primary care clinic, and it is one of the major risk factors for CHD and cerebrovascular disease. Investigators have shown that improving hypertension diagnosis, treatment, and control levels will lead to further declines in stroke incidence and mortality [69,70]. Despite knowledge of the risks and acceptable evidence, a large number of adults still do not have their BP under effective control. This study is an important step in defining two explicit interventions to improve BP control. The product of our research will be recommendations for health services interventions that will allow primary care clinic managers to achieve an improved rate of BP control for their patients with hypertension. Translation of our findings into practice is enhanced by the pragmatic design of each intervention.

At present, we count as our initial successes with the patient intervention our methods for identifying and our ability to maintain patient enrollment. We have a 96.5% retention rate at six-month post randomization. With the provider intervention, we have seen that the providers are interacting with the automated decision support extensively, suggesting that they find it useful and usable. Interventions attempting to improve provider adherence to guidelines are associated with modest improvements. Interventions with only small improvements, however, are reasonable to implement if the cost is small. The costs associated with automated decision support systems such as the ATHENA DSS are primarily the start-up costs of initial deployment of the system, with a very low marginal cost for each additional provider and no difference in the costs for a provider with a small panel of patients versus a large panel of patients.

5. Conclusion

The lessons learned in implementing this trial may be instructive to others planning similar work. With 60 million of the US population having hypertension and only approximately a third of them have their BP under control, there is a great need to develop effective means of reducing the impact of high blood pressure.

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