Official Title: Short Message Service System for Patients With Uncontrolled Hypertension
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Project Title: “SMS patient-centric system for patients with uncontrolled hypertension: a pilot study.”

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Background, Rationale and Context

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The successful implementation of the new AHA/ACC hypertension (HTN) guidelines based on the SPRINT trial findings will reduce risks posed by heart disease and stroke. Heart disease is the United States’ leading cause of death.[1,2] Low patient adherence to antihypertensive medication is the most significant modifiable patient-related barrier to achieving controlled blood pressure[3]. Vulnerable patients have higher blood pressure (BP) and lower adoption rates of mobile health (myHealth) technologies. This is particularly prevalent in African Americans, low literacy, and older patients (our definition of “vulnerable” populations for this proposal).[3-7] Developing and evaluating myHealth tools to implement clinical guidelines is essential and particularly relevant in settings like our clinic, where uncontrolled HTN, poor adherence to medications, and no-show rates are exceptionally high. Using SMS to improve adherence is logical because of its low cost and widespread use: more than six billion people worldwide have access to mobile phones.[8]

Medication non-adherence contributes to poor blood pressure control, which can lead to further cardiovascular complications including coronary heart disease and heart failure.[3,7] Hospitalization rates are significantly higher in patients with poor medication adherence.[9] Supporting adherence to medical regimens requires insight into patient’s medication-taking behavior and their reasons for non-adherence.[3,10] Subjective measures of adherence include physician reports, self-report, and adherence scales. More objective measures of adherence, e.g. electronic monitoring of medication administration, prescription records and dose counts, all are expensive, labor-intensive and difficult to incorporate in clinic work flows. However, for this project we will use the Medication Adherence Questionnaire (MAQ) because it has been well-validated to identify adherence among those with HTN, and scores correlate well with a range of objective adherence measures.[11,12] compliance

Home blood pressure monitoring (HBPM) appears to reduce BP in patients with HTN, but important questions remain regarding effective implementation and which groups may benefit most.[13,14] In addition, non- with clinic appointments (“no shows”) is a widespread health care problem and a missed opportunity for medication adjustment and BP control.[3]

Our study team has developed an SMS system based on the input of three focus groups composed of minority patients with hypertension. Our goal is to test the patient-centric SMS tool to support hypertension management in vulnerable patients seen in the WFBH Internal Medicine and Nephrology Clinics. Adopting these new clinical guidelines is imperative to achieving better healthcare outcomes.

The proposed study is distinctive in its ability to recruit and test the implementation in a population particularly affected by non- adherence and uncontrolled HTN. To engage patients in healthcare is considered a key strategy to improve patients' adherence, clinical outcomes, and satisfaction about care received.[5,15,16]

If it is determined that our system is feasible and efficacious, it could be applied for better care of patients with other chronic medical conditions, such as depression or diabetes.

Research Plan

Objectives

Our pilot will evaluate the feasibility of implementing an SMS system and HBPM at Wake Forest Baptist Health. Implementing a new text messaging service will improve the health delivery system in three ways. 1) Increasing patient engagement: SMS and HBPM requires the patients to be highly involved and committed to improving their health and results in a marked improvement in the adherence to medication. BP measurements has also been reported to improve BP control. 2) Supporting patients outside of the office visits by identifying and resolving barriers to medication adherence earlier on (i.e. if patients are unable to get their prescriptions or are having significant side effects). 3) Adopting clinical guidelines to improve BP control in a vulnerable population.

Specific Aims

Given the high prevalence of uncontrolled hypertension (HTN), testing novel interventions that support the implementation of hypertension guidelines may improve access, quality, and health outcomes. Although mobile health and text messaging shows promise in other health promotion settings, the best strategy to support HTN management in minority non-adherent patients is still unknown. [13,14] Thus, the goal of this pilot is to test a patient centric SMS-based text message intervention and ensure that it is feasible and acceptable in a sample of minority non-adherent patients with hypertension, currently seen in the internal medicine and nephrology clinics at WFBH.

Our long-term goal is to test an automated SMS intervention that can be disseminated and implemented to encourage adoption of hypertension guidelines by lowering blood pressure and incorporating home blood pressure monitoring in the care of vulnerable patients with uncontrolled hypertension.

The rationale for the proposed pilot is that evaluating an SMS system that considers patients' preferences and identifies barriers to adherence, is of critical importance in a learning health care system to transform health delivery, particularly for vulnerable populations. Minority populations are usually low adopters of mobile health tools and are most affected by uncontrolled hypertension.[4,6,17]

Aim 1: Feasibility will be assessed through examination of participant recruitment, retention and engagement. Specifically, we will look at the number of participants who refuse to participate in the pilot at the time of recruitment and the reason they declined participation. Secondary impacts of interest include: medication adherence as measured by the four-item MA Questionnaire (MAQ) and change in systolic and diastolic blood pressure at 3 months.

Aim 2: To test the acceptability of a 3-month SMS-based intervention in adults with uncontrolled hypertension. One cohort of 24 participants will be recruited for the SMS intervention. Acceptability will be assessed using the systems usability scale (a validated questionnaire that measures usability reliably in small samples)[18] and eliciting free comments after the survey.

At the end of this pilot project, we will have preliminary data essential for a future formal efficacy trial, to be proposed in a subsequent application to the AHRQ.

Our **first hypothesis** is that over 50% of contacted patients will respond to SMS messages and over 50% will check HBPM. This estimate is based on previous study by Bobrow and

colleagues in a similar patient population.[3] Our **second hypothesis** will be that > 75% will be satisfied with the service (OK or above on the usability survey).[9]

Methods and Measures

Design

A randomized control trial of 24 non-adherent participants will be monitored and followed for 3 months; An ambulatory BP arm device will be provided to all participants with printed instructions in English or Spanish (from the American Heart Association) on how to measure BP at home (HBPM). Patients will be instructed on checking their BP at least twice a week.[14,19] Text messages will be generated by Twillio platform, keeping a record of participants contacted, sent and received texts. Participants in the control arm will receive standard of care education for controlling high blood pressure in clinic by their healthcare providers. They will be followed to monitor any changes in their BP throughout the duration of the study.

Study team members will identify patients with uncontrolled hypertension during clinic visits. Study team members will approach patients 18 years or older who have uncontrolled HTN (SBP>130 or DBP >80) and have 2 or more BP medication(s)on their medication list. Participants will be interviewed by the study team and those with a MAQ score of 1 to 4 will be classified as non-adherent will be invited to participate. The study team member will assess the potential participant's phone ownership, text messaging ability, text messaging willingness, and receptivity to the intervention (and record all this information).The MAQ cut-off was chosen for the study because it has been used in the literature in previous studies,[20-22] and the cut-off at this value provides a highly sensitive tool for identifying medication non-adherence. [22,23]

Participants will be randomized into one of two groups: intervention SMS arm or the control arm. If enrolled in the intervention arm, the subjects will be contacted by phone via SMS and phone call. To ensure equal access to participation among women and minorities we will translate all materials and questions to Spanish. The privacy of potential subjects during recruitment will be protected by collecting only necessary identifiers and using a private room during the interview process.

As part of routine care, patients who present to the office with uncontrolled HTN receive instructions from their clinician on medication changes and are advised to return for a nurse visit in 2 weeks and a clinician visit in 3 months. During follow-up, the nurse checks the patient's blood pressure and contacts the clinician for further management if the BP is not controlled. Participants in the SMS arm will receive SMS messages to monitor their blood pressure in addition to this routine care whereas the control arm will only receive the standard provider education and monitoring for controlling blood pressure.

Baseline demographic characteristics of the participants will be collected. Participants will be followed with office (or phone if they no show for their visit) interviews at 2 weeks or 3 months to complete 2 validated scales: the MAQ, and SUS+ free comments

Study intervention participants will be provided with a blood pressure monitor to be used for measurement and extraction of HBPM information. Clinicians will be alerted through an in-basket message in the electronic medical record (Wake One) if the participants report BP outside the threshold range, and the patient will be sent an SMS and prompted to contact their clinic. The threshold range set for SBP is between 90 and180 mm Hg and between 60 and 110 mm Hg for DBP for one-time measurements, These thresholds are made based on the

recommendations by HTN guidelines, which designate a hypertensive urgency to be 180/110 mm Hg or higher and hypotension 90/60 or lower.[2]

Patients who no show to the follow up visits will be telephoned to assess adherence barriers. The study team member will create a telephone encounter in the electronic health record to document their discussion and route it to the patient's PCP. Patients who refuse participation in the study will be asked for the reason and their responses will be recorded to determine any barriers to participation. Study team members will attempt to contact patients who miss follow up visits every week up to 3 times, if after the 3rd time the patient is still not able to be reached, the patient will be lost to follow up.

Setting

The study team will recruit patients who fall within the eligibility criteria from Wake Forest Baptist Medical Center.

Subjects selection criteria

Eligibility and recruitment

Inclusion criteria

Patients 18 years and older who have SBP>130 or DBP >80 during an office visit encounter in the past 6 months and have BP medication(s) on their medication list.

- Own a phone with SMS capability
- Non-adherent-MAQ score of 1 to 4
- Vulnerable population (Black, Hispanic or education level < or equal high school (as an indicator of low SES)

Exclusion Criteria

- End-stage renal disease (on hemodialysis or peritoneal dialysis)
- Kidney transplant recipients
- Unable to afford BP medications or lack transportation to clinic visits
- Hospice or nursing home care
- Dementia or cognitive impairment on the problem list

Sample Size

24 patients –We will randomize 12 patients into 2 groups

Interventions and Interactions

Pilot randomized controlled study.

Participants in the SMS intervention arm will receive usual care and SMS texting and phone calls. Study team members will send secure SMS messages to participants weekly for four weeks and then every other week until their next appointment.

The secure messaging system will be as follows

Introductory message:

Welcome to managing your blood pressure with the Nephrology/ Internal medicine clinics at Wake Forest. Try to take your BP meds at the same time every day to keep your BP under control! Make it part of your daily routine:

First week

Adherence checkpoint:

1. *Good morning! Did you take your blood pressure medications today?*

"No" Response:

1. *Let's try to stay on top of taking them daily! You can do this!*

Additional prompts:

Did you fill your prescription?

- -If no -> phone call to determine barrier to filling BP meds "Mr./Mrs. (X). My name is (Y), we met when you were in the 7th Janeway clinic. I am calling you to find out if you are having difficulties filling your prescriptions. I will let Dr. (Name) know. Have you tried our pharmacy?" Message clinician in Wake One.
- If yes
- *Did you have any side effects from your blood pressure medication?*
- -If yes -> phone call to determine side effects
- Mr./Mrs. (X). My name is (Y), we met when you were in the 7th Janeway clinic. I am calling you to find out if you are having side effects from your blood pressure medications. I will let Dr. (Name) know. Message clinician in Wake One.
- - If No, no action

"Yes" Response:

1. *Keep it up! Plus thumbs up emoji*

Self-monitoring phase:

1. *Have you been checking your BP? We'll be checking in tomorrow for results!*

"Yes" Response:

1. *Nice work!*

Additionally:

What was the top number (SBP)?

What was the bottom number (DBP)?

"No" Response:

1. *Never too late to start! Try checking your BP in the AM and PM every day for the next few days and we'll check back again later.*

Data Response/Gamification:

1. *BP measurements received. You're doing great! Keep it up – you're currently in X place among texters.*

An adapted version of the System Usability Scale (SUS) by Bangor[9] will be administered either in person or the phone after the follow up clinic visit or at the end of week 12 (if patient misses follow up appointment).

Study team members will perform the following tasks to track study participants progress:

1. Weekly tracking of number of patients contacted and who responded to SMS, number of SMS questions answered, and number of office visits completed
2. Monthly tracking of patient satisfaction surveys
3. Monthly reports distributed via email to the team providing ongoing feedback on performance related to patient outreach and patient satisfaction
4. When high or low BP is reported SBP > 180 or <90 and or DBP > 110 or <60, a study team member will send a message in Wake One to the clinic triage nurses. The triage nurse will contact the patient to arrange a clinician office visit or a nurse blood pressure check appointment based on additional information on clinical symptoms.

Outcome Measure(s)

A- Feasibility

Feasibility will be assessed consistent with the recommendations of Leon and colleagues.[24]

Specifically, we will examine:

1. Screening: we will track the number of patients screened per month, the number enrolled per month, the proportion that are eligible who enroll.
2. Recruitment: number of participants who refuse to participate in the pilot at the time of recruitment and the reason why. Proportion of vulnerable patients screened but excluded because they did not own a phone with SMS capability.
3. Retention: the proportion of participants who continue to use the myHealth tool per month through three months will be tracked for the intervention.
4. Engagement: 12- SMS rate response of at least one home BP measurement. We will use 44% as our cut off based on an SMS study by Peters and colleagues[25].

Finally, we will monitor time needed for assessments and gather feedback on the participant burden.

B-Acceptability

Participants will complete the SUS in person on an I-Pad or over the phone. They will also be offered the opportunity to comment in their questionnaires about their experiences of taking part in the pilot. The SUS yields a single score on a scale of 0–100. A SUS score above a 68 would be considered above average. We will consider acceptable when >70 % of participants score the SUS above 68.[26]

Secondary measures of interest

Medication adherence (MA) will be measured by administrating the four-item MAQ by the study coordinator during enrollment and at 3 months follow up visit. The MAQ was selected because it has been well-validated to identify adherence in HTN and scores have been shown to correlate well with a range of objective adherence measures.[11,12]

SBP and DBP change at 3 months. BP will be measured during initial and follow up office visits by nurses or clinicians while patient is seated with automated arm devices according to standard office procedures. We will extract from the electronic medical record, SBP and DBP at enrollment and at 12 weeks follow up. The average change will be calculated and reported in mmHg.

No-show rate at 3 months' follow-up (f/u) clinic visits. If participants fail to come to their f/u visits within 7 days of their scheduled follow-up appointment, they will be considered as "no- shows". Our current clinic no-show rate is 30%, therefore if the study participants no-show rate is less than 30% we will consider our tool a feasible intervention.

Analytical Plan

Results will be analyzed initially using descriptive statistics. Comparison between groups will be done using chi square tests for proportions, and t-tests for continuous variables. Regression analysis will be performed to identify independent outcome predictors. RedCap will be utilized to collect all patient data. Participant's demographics (including education level), co-morbidities, number of medications, number of blood pressure medications and BP numbers will be extracted from Wake One when available. Level of education will be confirmed verbally with each participant during consent process. Only one participant identifier will appear in the data collection forms.

The full analysis set will include participants who have responded to at least one SMS message post-randomization. Descriptive statistics will be computed for each treatment group; medians and percentiles will be reported for skewed continuous variables. For primary and secondary outcomes, descriptive statistics and 95% confidence intervals will be used to summarize the differences between groups. The secondary outcome of BP and other continuous variables will be assessed with a repeated-measures analysis using a mixed linear model approach. The Wilcoxon rank sum test will be used to compare MA between groups. Hypothesis tests will be 2-sided using the 0.05 significance level. Bonferroni-type adjustments for multiple testing will be implemented to control type I errors. Statistical analysis will be performed using SAS software (SAS Institute, Cary, NC).

Treatment assignment will be determined using blocked randomization

The primary analysis will consist of all subjects who responded with at least one BP measurement

Human Subjects Protection

Subject Recruitment Methods

Subjects will be identified when they come to an office visit and their blood pressure is not well controlled. The PI clinician (internal medicine preceptors or residents) will verbally alert the study coordinator on site of possible participants based on BP >140/90. The study team member will meet the patient in a private room in 7th Janeway, determine eligibility, and signed informed consent will be obtained from each subject. Once enrolled, the subjects will be contacted by phone via SMS and phone call. To ensure equal access to participation among women and minorities we will translate all materials and questions to Spanish. The privacy of

potential subjects during recruitment will be protected by collecting only necessary identifiers and using a private room during the interview process.

Informed Consent

The study team will recruit patients in the renal and internal medicine clinics. Signed informed consent will be obtained from each subject. Participants will be consented in a private room in the clinic. Group assignment will be determined using blocked randomization.

Participants will either receive an educational pamphlet or use their own mobile phone to communicate with the study coordinator via SMS. HIPAA-compliant SMS text messages will be sent to participants through any of the local mobile phone network providers.

Confidentiality and Privacy

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, stored separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed after three years using a shredder, consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured, with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study. To prevent breach of confidentiality on subject's cell phone device the study team will ensure the subject is aware of the configuration feature on the device to only show text messages upon unlocking the phone.

Data and Safety Monitoring

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

Reporting of Unanticipated Problems, Adverse Events or Deviations

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator to the IRB and sponsor.

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