

## ROKHYT TRIAL PROTOCOL

**The specific aims of this protocol** are to:

1. Develop and pre-test the intervention text messages.
2. Pilot the enrollment, consent, randomization, and data collection procedures at baseline and 3, 6, and 12 months and document participation and completion rates in a randomized pilot study of N=70 per group.
3. Obtain demographic data on potentially eligible participants using an on-line questionnaire.
4. Pilot test the text messaging intervention and document blood pressure control rate in response to the intervention.
5. Pilot test secure data transfer and other data coordinating center (DCC) functions.

The following metrics will be used to decide whether to proceed with a larger trial: **Aim 1.** Successful piloting of text messages including tailored features, based on positive feedback from pilot subjects. **Aim 2.** Successful enrollment, consent, and randomization of N=70/group. **Aim 3.** Completion of  $\geq 80\%$  of all data fields. **Aim 4.** Completion of 12-month follow-up by  $\geq 80\%$  of those randomized; positive signal of intervention effect. **Aim 5.** Successful and secure transfer of all pilot data from higi to the DCC.

The overall goal is to provide pilot data to support an application to conduct a fully powered randomized controlled trial.

### **Structure and organization of the project**

The **clinical coordination function** and overall project leadership is in the Division of General Medicine/Department of Medicine at Columbia (Steven Shea, MD, principal investigator).

The **data coordination function** (Data Coordinating Center, DCC) is in the Department of Biostatistics in the Mailman School of Public Health (John Thompson, PhD, principal investigator).

**higi** is a privately owned company that supports health kiosks with blood pressure devices in Rite Aid pharmacies throughout the United States. [REDACTED]

**Mytonomy** is a privately owned company that makes and hosts educational videos. [REDACTED]

### **Phases of the project**

There are three phases to the project, as follows.

- A. **Pretesting of Text Messages.** We will use formative interviews conducted by telephone to iteratively test the text messages and videos.
- B. **Vanguard.** We will run 10 vanguard or pilot subjects (randomized 7 to intervention and 3 to control) through a compressed 3-month protocol involving the invitation, consent, and baseline data collection, and follow-up data collection at 1, 2, and 3 months (blood pressure only at 1 and 2 months, blood pressure and exit questionnaire at 3 months).
- C. **Trial.** We will conduct the pilot trial (N=70 in each of the two randomized groups).



## **IRB documents**

### **Study Protocol**

#### **A. Pretesting of Text Messages and Formative interviews: N = 40**

1. Invitation (Pretesting)
2. Consent (Pretesting)
3. HIPAA release for higi to give blood pressure data and email to Columbia
4. Text messages – intervention
5. Videos

#### **B. Vanguard: N = 10**

1. Invitation (Vanguard)
2. Consent (Vanguard)
3. HIPAA release for higi to give blood pressure data and email to Columbia
4. Baseline questionnaire (27 items)
5. Text messages – intervention
6. Text messages – reminders to return for 1,2, and 3-month blood pressure measurements
7. Videos
8. Exit questionnaires (one for intervention group and one for usual care group)

#### **C. Trial: N = 140**

1. Invitation (Trial)
2. Consent (Trial)
3. HIPAA release for higi to give blood pressure data and email to Columbia
4. Baseline questionnaire (27 items)
5. Text messages – intervention
6. Text messages – reminders to return for 3, 6, and 12-month blood pressure measurements
7. Videos
9. Exit questionnaires (one for intervention group and one for usual care group)

#### **Notes.**

1. Participants that completed/agreed to ROKHYT consent form but didn't complete the entire enrollment process will be contacted by phone to help them with any issues then and will be sent a text messages with a link to complete the enrollment process. In addition, we will be sending the participants with this or any other issues free text (adhoc messages) on text messages.
2. The baseline and exit questionnaires, the baseline questionnaire, and the higi HIPAA release are the same in all study phases, as are the intervention text messages and videos.
3. Higi will send the Invitation by email in all three phases. The link in the email will pass individuals to the Columbia DCC website where consent will be obtained and the baseline questionnaire will be completed. A link will pass the participant to higi's third party for the HIPAA release. On completion of the HIPAA release, a link will pass the participant back to the Columbia DCC website where participants will be randomized. The text messages will be generated by the Columbia DCC.
4. In addition to the intervention text messages (intervention group only), there will be reminder text messages for both groups to return for the follow-up blood pressure measurements (study endpoints). The email at day 45 (see diagram) will use the same text.
5. The videos will be hosted on the website of Mytonomy. Columbia has a Business Associate Agreement with Mytonomy. The license for use of the Mytonomy website by study participants was purchased through a subcontract from the trial grant.



6. The links to these videos will be embedded in intervention text messages. These links have not yet been created and are not shown in the text messages but will be inserted after they have been created.
7. Mytonomy has given us permission to provide access to the videos to the IRB members and staff.



[use browser other than IE to access]

### **Approach to Accomplishing the Specific Aims**

**Aim 1. Develop and pre-test the intervention text messages.** We will draft sample messages (table 2) based on the Health Belief Model<sup>1,2</sup> in English and Spanish for each component of the messaging loop, with alternatives. Based on our previous formative work, messages will be

personalized and interactive. The level of personalization may change based on the pre-testing as below but preliminarily will include first name, preferred gender and language (Spanish or English).

Additionally, messages will be different based on blood pressure elevation.

**Table 2. Focus of Intervention Text Messages**

- |   |
|---|
| <ul style="list-style-type: none"><li>• High BP level should be followed up</li><li>• High BP can lead to health problems unless it is treated</li><li>• A health care provider should be seen to provide treatment for high BP</li><li>• Medications lower blood pressure</li><li>• Taking blood pressure medication daily is necessary for the medication to be effective</li></ul> |
|---|

Overall, there will be three types of messages. The first will be educational messages that are sent to all participants. Under the health literacy paradigm of “universal precautions” these will include key educational information that would be helpful for all participants to know. The second set of messages will be interactive and will allow participants to self-tailor messages by selecting areas about which they would like to receive more information. The third set are reminder messages which act as cues to action to come in and get a blood pressure reading taken.

**Pretesting.** Email messages will be sent to randomly selected high users who meet eligibility criteria for the trial, inviting participation. There will be a financial incentive of \$50 in Bank of America pay card for the pre-test component. Those who participate will not be eligible for the pilot. We will obtain consent for the pretesting as for the pilot. For those who consent, we will arrange in depth interviews to be conducted by telephone to pre-test the text messages and videos and to receive feedback. We will purposefully sample to include participants from all four regions of the country. We considered focus groups rather than interviews but focus groups would limit us logistically rather than allowing random selection for this phase, and would create a time and travel barrier to participation, introducing further selection. While focus groups are helpful to explore what content areas may be helpful, the goal of this pretesting phase is to obtain specific feedback on the message structure and timing. This goal is better suited to one on one interviews.

We will pre-test the messages following the protocol Dr. Stockwell has previously used for field-testing messages. An important focus of pre-testing will be understandability to low literacy individuals. Under the oversight of Dr. Stockwell, the project coordinator will text participants in real-time over the phone the proposed messages and using a semi-structured interview guide ask the individual to say back in his/her own words what the message means to him or her as well as to text back a response (if appropriate; interactive text message). The interviewer will then ask participants about any problems or suggested changes. This will include all proposed messages. Participants will also be asked their opinion on timing of reminder messages for upcoming as well as missed (separately) blood pressure checks. This process will be iterative with changes made after each set of 10 interviews until no new message changes are made. We expect to conduct 40 interviews and believe that by then we will have reached saturation. All



of the research conducted by Dr. Shea and Dr. Stockwell described in section C.2 was conducted in English and Spanish, as will this trial.

**Aim 2. Pilot the enrollment, consent, randomization, and data collection procedures at baseline and 3, 6, and 12 months, and document participation and completion rates.**

Enrollment, consent, randomization, and data collection will be done using a web-based trial management approach interacting with the kiosk and its associated informatics infrastructure. Kiosks are installed in all 50 states, and sampling will include all kiosk locations in the U.S.

**Enrollment** will be accomplished by randomly selecting potentially eligible individuals from the highi database to receive email messages prompting them to log into highi's HIPAA-compliant, FDA approved, secure web portal. The e-mail messages will inform these individuals that they are potentially eligible for a research study on BP and that more information is available on the

portal if they are interested in participating. Individuals will in this way be able to access a short description of the study, which is that it is a randomized trial of text messaging in patients with high blood pressure, that if they participate they will need to give consent, provide a cell phone number, and have their BP measured at time the study starts and at 3, 6, and 12 months. There will be a financial incentive of \$200 in Bank of America pay card for participation divided for 3 follow-up blood pressure checks at a highi kiosk and final survey. Compensation will be as follow at each completion:

- \$50 at 3-month blood pressure check
- \$50 at 6-month blood pressure check
- \$100 at 12-month blood pressure check and final survey. All highi communications are available in English or Spanish as selected by the individual. **Eligibility** criteria are shown in table 3. **Consent** will be obtained electronically, also in English or Spanish. **Randomization** will be stratified by sex, age (18-55, 56-85 years), and region of the country (northeast, southeast, north central/west, south central/west), assigned 1:1, and performed by the DCC using the web-based trial management system. Participants will receive email informing them that they have been enrolled and which group has been assigned. **Data collection** for Aim 3 will be accomplished using an electronic form with multiple-choice or numeric response sets on the secure web portal, to be completed as part of the consent process. We will obtain BP measurements at the kiosk at time of enrollment and at 3, 6, and 12 months post randomization. For follow-up measurements, subjects will receive email messages prompting them that it is time to obtain a study BP measurement at a kiosk along with instructions about how to take the BP, specifically to take all of their usual medications the day they take the BP, to log in at the kiosk using their account identifier (email address) when they take the BP, and to take the BP three times at intervals of about one minute. Subjects will receive up to \$200 in Bank of America pay card by mail when completing each blood pressure check points. **Participation rate** will be calculated as the proportion of those invited to participate and eligible who consent and complete the baseline questionnaire and BP measurement. **Completion rate** will be calculated as the proportion of those randomized who complete the 12-month follow-up BP measurement. We do not propose to replace randomized individuals who die, drop out, or are lost to follow-up in either the pilot or the full scale study.

**Table 3. Eligibility Criteria**

- $\geq 3$  systolic blood pressure measurements  $\geq 140/90$  mmHg (in the previous 12 months including one in the 3 months prior to invitation to participate)
- Age 18-85 years
- Weight <300 pounds
- Has a cell phone
- Consent

**Aim 3. Obtain demographic and other data on potentially eligible participants using an on-line questionnaire.** We will collect demographic data at time of enrollment including date of birth, sex, race/ethnicity, zip code of residence, country of birth, years of residence in the U.S., years of education completed, family income in wide categories to avoid non-response, current health insurance (Medicare [including managed care plans], Medicaid, VA/Tricare, commercial,

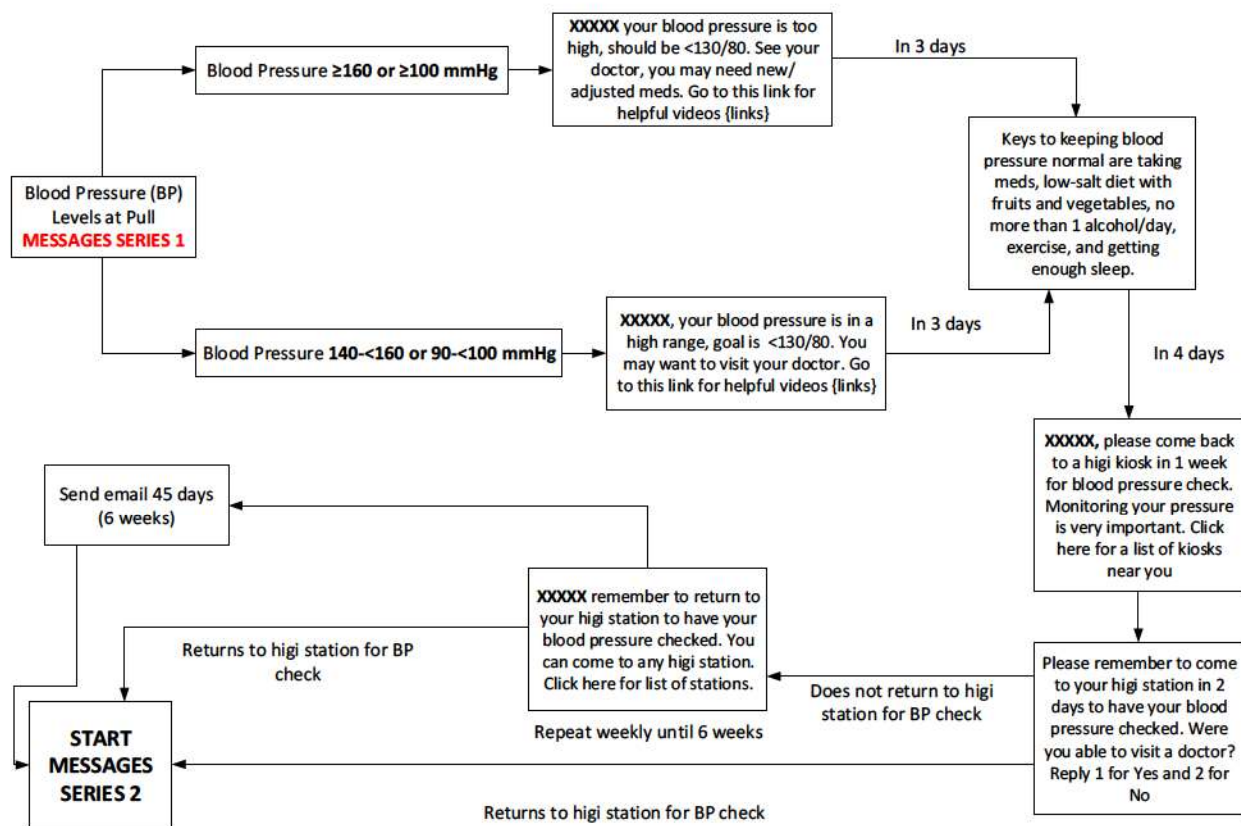


none), and whether the individual has a regular health care provider. In addition, we will collect data on other potential confounding variables including smoking, alcohol and caffeinated beverage consumption, smoking, exercise, height, weight, and baseline BP medications. We will also collect data on health care utilization, specifically physician/RNP office and emergency department/urgency-care visits. We will base the data collection instrument on forms used in the MESA study, where these variables have been collected<sup>3,4</sup> among participants of varying levels of health literacy. These forms are available in Spanish and English.

**Aim 4. Pilot test the text messaging intervention and document BP control rate in response to the intervention in a pilot study of N=70 per group.** Once the intervention messages have been developed, pre-tested, and approved by our IRB, we will conduct a pilot of the study procedures using 5-10 volunteers, specifically of the enrollment, intervention, and data collection procedures. Once we are satisfied that the procedures are working as expected, we will conduct a pilot study randomizing 70 individuals to each group. We chose this sample size for the pilot as 10% of the planned full scale trial and therefore sufficient to demonstrate that all study procedures including recruitment are feasible and realistic and to provide a preliminary signal of the intervention effect. The intervention group will receive text messages as described below. The comparison group will receive usual care. Blood pressure measures will be obtained in both groups at baseline and at 3, 6, and 12 months. A reduced questionnaire will be administered at 12 months to ascertain insurance and health care provider status at that time. Compensation (up to \$200 by Bank of America pay card) will be sent by mail to all individuals who complete the blood pressure checks at 3, 6 and 12 months follow up.

**Intervention.** Individuals randomized to intervention will receive usual care (see below) plus intervention. The intervention will consist of additional communication via interactive text messaging. If the blood pressure is  $\geq 140/90$  mm Hg at a measurement occasion including baseline, individuals will receive a text message advising them to see a health care provider to receive care for high blood pressure, that the minimal goal is  $<140/90$  mmHg for people with hypertension, and asking them to return to a high kiosk in 2 weeks to have the blood pressure taken. A reminder to return will be sent both one week and two days prior to the 2-week due date. For the reminder 2 days before, individuals will be asked to respond whether they saw or spoke to a health care provider for their elevated blood pressure. Regardless of response they will be asked to return to a high kiosk to have their blood pressure checked. If the individual does not return to the high kiosk, he or she will be sent a text message weekly gently urging them to come in to have their blood pressure assessed. These messages will also include other educational information as outlined in section C.5 (table 2). In addition, these messages will include advice to see a health care provider for further assessment and treatment of high blood





pressure. If the kiosk blood pressure level remains elevated, these individuals will continue in the text message loop, with additional educational and interactive message options. The figure above is an example of such a loop. If their blood pressure is  $<140/90$  mm Hg, they will be congratulated on improving their blood pressure, reminded to maintain contact with their health care provider for blood pressure management, and asked to return in 1 month for a recheck. Reminders for this blood pressure check will be sent one week and 2 days before and will continue to be sent weekly if they do not return.

**Usual Care.** Individuals randomized to usual care will receive the health information currently provided to individuals measuring their BP at a highi health kiosk, who are informed on the screen that their BP level falls into one of five categories, with advice for those in the highest category ( $\geq 180$  systolic or  $110$  mmHg diastolic) to seek emergency medical care. The screen seen by individuals with systolic  $\geq 140$  mmHg is shown in the graphic.

**Aim 5. Pilot test secure data transfer and other DCC functions.** All study-specific data will be managed by the DCC. Blood pressure measurements obtained at kiosks will be securely transferred to the DCC via an automated web service employing a secure sockets layer (SSL) over encrypted https. The DCC will host a secure website on which consent and questionnaire data will be obtained and also the messaging server for the intervention. Enrollment, follow up blood pressure measurements, and intervention messaging will be monitored weekly by the investigators though reports created by the DCC. The DCC will perform statistical analysis of the study data.



The main approach will be data summarization as we do not expect statistical significance in the pilot study. The DCC will also provide reports to the DSMB.

## References

1. Becker MH. The health belief model and personal health behavior: Slack; 1974.
2. Rosenstock IM, Strecher VJ, Becker MH. Social learning theory and the health belief model. *Health Education & Behavior* 1988;15:175-83.
3. Bild DE, Bluemke DA, Burke GL, et al. Multi-Ethnic Study of Atherosclerosis: objectives and design. *Am J Epidemiology* 2002;156:871-81.
4. Shea S, Lima J, Diez-Roux A, Jorgensen NW, McClelland RL. Socioeconomic status and poor health outcome at 10 years of follow-up in the Multi-Ethnic Study of Atherosclerosis. *PloS one* 2016;11:e0165651.