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Randomized trial protocol for remote monitoring for equity in advancing the control of hypertension in safety net systems (REACH-SNS) study

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Abstract

Background: Self-measured blood pressure monitoring (SMBP) is essential to effective management of hypertension. This study aims to evaluate effectiveness and implementation of SMBP that leverages: cellular-enabled home BP monitors without a need for Wi-Fi or Bluetooth; simple communication modalities such as text messaging to support patient engagement; and integration into existing team-based workflows in safety-net clinics.

Methods: This study will be conducted with patients in San Francisco who are treated within a network of safety-net clinics. English and Spanish-speaking patients with diagnosed hypertension will be eligible for the trial if they have recent BP readings ≥140/90 mmHg and do not have co-morbid conditions that make home BP monitoring more complex to manage. This study will implement a three-arm randomized controlled trial to compare varying levels of implementation support: 1) cellular-enabled BP monitors (with minimal implementation support), 2) cellular-enabled BP monitors with protocol-based implementation support (text reminders for patients; aggregated BP summaries sent to primary care providers), and 3) cellular-enabled BP monitors and pharmacist-led support (pharmacist coaching and independent medication adjustments).

Results: For the main analysis, we will use mixed effects linear regression to compare the change in primary outcome of systolic BP. Secondary outcomes include BP control (<140/90

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mmHg), medication intensification, patient-reported outcomes, and implementation processes (i.e., engagement with the intervention).

Discussion: This study will design and test a digital health intervention for use in marginalized populations treated within safety net settings, evaluating both effectiveness and implementation to advance more equitable health outcomes.

Keywords

Hypertension; remote patient monitoring; home blood pressure monitoring; self-monitoring of blood pressure; digital health

II. BACKGROUND

Uncontrolled blood pressure (BP) is a leading preventable cause of morbidity and mortality in the US, and a major contributor to disparities in span and quality of life [1,2]. Patients with hypertension who are Black, Hispanic, and Asian; individuals with limited English proficiency; and/or those insured on Medicaid often have higher rates of uncontrolled blood pressure, and its sequelae, including subsequent strokes, myocardial infarctions, heart failure, and other kidney disease [3-5].

Self-monitoring of blood pressure (SMBP) is recommended by evidence-based guidelines and widely recognized as essential for accurate assessment and management of hypertension [6-9]. Yet routine implementation of SMBP remains difficult in primary care practice [10,11]. Furthermore, there are unique barriers to implementation within safety net healthcare systems that provide a substantial proportion of care for marginalized populations [12]. Most existing SMBP programs typically require daily use of a BP device and clear protocols for sharing home readings back to clinicians. At the health system or clinic level, SMBP requires integration into healthcare delivery processes (e.g., active panel management, telehealth clinical encounters, and utilization of non-physician providers such as pharmacists) to ensure timely treatment based on home BP readings, and these implementation steps have been shown to be harder to scale in safety-net clinics [13-15].

Digital strategies such as deploying smart BP monitors can facilitate sharing of data between patients and clinicians, but these devices typically require a smartphone with associated mobile applications (often available only in English) and Bluetooth connection and Wi-Fi at home [16]. Therefore, many of the existing digitally-enabled programs can present challenges for patients who have low digital skills or access or who are non-English speaking – unless we specifically choose strategies that circumvent these barriers and more seamlessly support data sharing between patients and clinicians, such as using cellular-enabled BP monitors [15,17-20]. Consequently, now is the time to study the effectiveness of more sophisticated digitally-enabled SMBP programs that address both patient-facing engagement and clinical system engagement [21]. Furthermore, studies that simultaneously evaluate implementation outcomes of SMBP will advance our scientific understanding of how to spread these programs [22-24]. Explicitly focusing on implementation among marginalized populations with lower access to digital SMBP programs can center the needs of patients and healthcare settings that are often late to receive innovations in chronic disease management, despite

facing the disproportionate burden of hypertension nationwide [25]. Finally, the COVID-19 pandemic has accelerated adoption and implementation of telehealth to increase access and efficiency of care, further emphasizing the need for SMBP technologies within a practical and sustainable workflow [18].

This protocol outlines a type 1 hybrid effectiveness-implementation randomized trial to compare the effectiveness of a cellular-enabled SMBP intervention with varying levels of implementation support for patient and clinician engagement. We call this intervention the **Remote monitoring for Equity in Advancing Control of Hypertension in Safety Net Systems (REACH-SNS)** study - ClinicalTrials.gov Identifier: NCT05481892.

III. METHODS

Study Aim:

Assess the effectiveness of a cellular-enabled SMBP program with different levels of implementation support among marginalized patients with uncontrolled hypertension in a safety net healthcare system.

Study Population and Setting—We plan to recruit 540 Spanish- and English-speaking adults across four clinics from the San Francisco Health Network (SFHN), which is comprised of 12 safety-net primary care clinics caring for a diverse population of about 59,000 patients (25% Asian, 15% Black, 36% Latinx, 17% White, 7% other)[26]. Among the approximately 8,000 patients with hypertension at the four target SFHN clinic sites with large populations of Black and Latinx/Hispanic patients, there are disparities in BP control, with worse outcomes for Black and Hispanic/Latinx patients compared to white patients within our system. SFHN leaders have implemented multiple programs in recent years to improve population-level BP control within our primary care practices, primarily the use of disease registries and a standard algorithm that provides recommendations for medication intensification/adjustments based on evidence-based guidelines and adapted for the Medicaid medication reimbursement formulary within our setting[27].

Inclusion Criteria.: English- and Spanish-speaking primary care patients aged 18 or older with at least 2 outpatient visits with uncontrolled hypertension (≥140/90mmHg) in the past 12 months will be eligible.

Exclusion criteria.: Prior to enrollment, primary care providers and chart review will exclude patients on dialysis or with end stage liver or renal disease, history of recent acute myocardial infarction, heart failure with reduced ejection fraction (HFrEF), pacemaker use, other serious arrhythmia, pregnancy, dementia, hospice/palliative care patients, and behavioral conditions that would make it difficult to complete care activities (e.g., schizophrenia). In addition, patients with an inability to read in English or Spanish or those with plans for upcoming leave or travel will also be excluded.

Study Design and Randomized Trial Comparator Arms—REACH-SNS is a parallel, individual-level three-arm randomized controlled trial to compare the effectiveness of implementing cellular-enabled home BP monitoring with 1) usual care (distribution of

BP monitors into routine primary care practice with minimal implementation support), 2) protocol-based implementation support (text reminders sent to patients for home BP readings; summaries of home BP readings and suggestions for potential medication intensification based on an algorithm sent to providers), and 3) pharmacist-led support (one-on-one patient-pharmacist coaching and independent medication adjustments). The allocation ratio in the arms will be 0.7:1:1 given larger effect sizes expected in comparisons with the control arm.

Intervention Arms: All study patients will be provided cellular-enabled BP monitors and instructions to check their BP at least 6 times per week in both the morning and evening. These monitors will directly upload all home BP readings into a cloud database via cellular tower transmission. No Bluetooth or other syncing between the home BP cuff is needed for data transmission, given that the BP monitor is paired to the cellular hub from the outset and automatically feeds BP readings into a cloud-based data system using a cellular connection and cellular data plan that is not connected to a cell phone (i.e., covered separately by the study). BP readings will be available to view online, via a mobile application for patients and a companion website dashboard for clinicians. The vendor supplying the devices for this trial is CareSimple device BT106 [28,29]. Study staff will assist patients downloading the companion CareSimple app on their smartphone that allows them to see trends in their home BP readings and receive messages from a clinician or research staff member. Clinicians will also have access to the provider-facing dashboard to see the home BP readings of their patients enrolled into the study.

In the minimal support Arm 1, patients will receive these cellular BP systems and their clinicians (i.e., primary care provider, who may also inform other members of the care team) will be notified that they are measuring BP at home. Patients will also receive an online video link and written handout with instructions about how to use the monitor at home, in either English or Spanish, encouraging them to measure their BP at home at least 6 times per week (3 readings in the morning and 3 readings in the evening each week). All patients can request additional instruction on using their BP monitor, such as instructions from a clinician within their primary care clinic (as in standard practice within the SFHN). Clinicians will be notified via EHR in-basket message that home BP readings will be available for their patient on CareSimple dashboard, logging in separately to the dashboard to view the data (i.e., not linked directly to the EHR). Each patient and clinician can then access these data at their own discretion by logging into the online dashboard provided by the cellular BP cuff vendor. Finally, over the course of the study, the CareSimple system will send an automated message to any patient who has not sent BP data for over a week.

Second, in the protocol-based support Arm 2, we will add reminders and feedback to patients and providers. Patients will receive regular text messages to remind them to check their BP at home, general lifestyle advice and tips about managing their hypertension, and recommendations for discussing home BP readings with their provider. Primary care clinicians will also receive an EHR in-basket message with standard information about each patient's home monitoring data 1 time per month: a) a summary of home BP readings (e.g., mean BP, % measurements <140/90 mmHg), b) high and low BP values from readings, and c) a link to the existing SFHN hypertension treatment algorithm [27].

Finally, in the pharmacist-led support Arm 3, our study pharmacists will remotely review the home BP readings and contact patients directly about recommended medication changes. (California law allows pharmacists to make medication adjustments without approval of a physician.[30]) More specifically, for each patient participant, the pharmacists will log on to the online dashboard weekly to review home BP measurements. If there are sufficient home BP readings and >75% of the readings are elevated above BP treatment goal, the pharmacists will contact the patient and consider medication adjustments, driven by the medication intensification protocol. For patients who then start or change a medication, the pharmacists will instruct patients to continue with home BP measurements (twice daily for 7 days) and continue to follow-up with the patient for home monitoring and medication adjustments as appropriate. For patients at their treatment goal, the pharmacists will send regular messages to patients to encourage their progress. Finally, the pharmacists will chart their treatment directly within the EHR throughout the study and send relevant in-basket messages to primary care clinicians with summaries of decision-making and medication changes.

In addition, pharmacists will also engage patients in action planning and lifestyle interventions for managing their hypertension in everyday life. More specifically, the pharmacists will have initial communication with each patient to collaborate on hypertension care management goals and action plans and will continue to follow-up about these goals as the intervention progresses. This pharmacist-patient communication will be digitally enabled as much as possible for enrolled patients, leveraging secure messages via the patient portal when possible.

Recruitment and Follow Up—As this intensive intervention will involve pharmacist-led treatment of hypertension, we will obtain consent from primary care providers who agree to have their patients participate in the study. We will focus our recruitment efforts within 4 clinics in SFHN with high numbers of Latinx and Black patients, given the baseline disparities in hypertension control. Patient recruitment methods will include phone outreach (i.e., phone calls 1-2 weeks before an existing scheduled visit) to identify interested individuals, combined with in-clinic methods to discuss the study with eligible individuals. All patients will provide written informed consent. We plan to recruit up to 25 patients/month for 24-36 months during the randomized controlled trial. We will follow patients over a 6-month intervention period, and a subsequent passive post-intervention period of 6 months will provide secondary clinical outcomes at 12 months post-enrollment. Participants will be incentivized $100 for their participation, split between baseline and follow-up study activities.

Randomization—We will use a computer-generated randomization schema stratified by clinic and BP (≤ or ≥ 150 mmHg of systolic BP). Randomization within each stratum will use random block size allocation to conceal randomization order. The order of the randomization will be concealed until the participant has completed all baseline enrollment steps and is ready to begin the intervention. Patients and clinicians will not be able to be blinded given the nature of the interventions, but all analyses will be completed without knowledge of study arm assignment.

Outcomes—We will use several data sources to collect data to evaluate effectiveness and implementation of the intervention:

Clinical outcomes

1. *Primary outcome: systolic BP (SBP).* We will use clinic-based assessment of SBP as the primary outcome of interest, using all SBP measurements during any outpatient encounter in the 6 months prior to enrollment in the study and the 6 months during the active intervention period. BP is collected routinely during all patient encounters in our system, using a standardized BP measurement protocol that requires the use of automated BP machines at primary clinics broadly implemented as part of ongoing, previously described, qualify improvement efforts [27]. While different measures of BP can produce different results, we will use clinic BP readings as the primary outcome to ensure the analysis will include patients without sufficient engagement in home monitoring. Improvements in SBP will be our focus given that SBP is more predictive of cardiovascular disease than diastolic BP [31-35].
2. *Secondary outcome: BP control.* Also using clinic-based measurements, we will define BP control as SBP <140mmg and DBP <90mmHg in secondary analyses [36]. This BP control analysis will also use all available BP readings and treat every clinic BP reading as separate repeated binary assessments.
3. *Secondary outcome: Medication intensification*. We will review prescribing patterns for anti-hypertensive medications for each patient in the trial. This will be measured as total proportion of patients with medication intensification (new drug or increased dosage) over the study period [37].
4. *Secondary outcome: Change in Home BP.* We will also examine change in BP (systolic and diastolic) based on the Home BP measurements from the cellular monitors [31].

Patient-reported outcomes: In addition, we will collect patient-reported outcomes on a baseline survey at onboarding, with a repeat follow-up survey at 6 months when they exit the study. The two primary patient-reported outcomes for this study will be 1) the Patient Assessment of Chronic Illness Care (PACIC) and 2) the Krousel-Wood Adherence Scale for medication adherence [38,39].

Implementation Outcomes: Using CareSimple app/device and EHR data, we will measure how the intervention was utilized by patients and clinicians. Implementation outcomes will focus on engagement at both the patient and primary care clinician levels [40].

1. *Main implementation outcome: Patient engagement with SMBP.* Patient engagement with SMBP will be measured continuously as number of SMBP readings over the active intervention period. We will compare this engagement across intervention arms to determine how the implementation support impacted patient engagement.

2. *Patient engagement with mobile app.* Next, we will measure how patients interacted with the mobile app to review their home BP readings over the study. Total number of unique days with one or more logins will be extracted from the CareSimple app data.

3. *Primary care clinician engagement with SMBP data.* Finally, we will measure clinician adoption of the SMBP program into their routine practice. Specifically, we will assess the proportion of clinicians that view home BP data, assessed by 1) number of read EHR in-basket messages for Arm 2 and Arm 3 participants and 2) number of unique days with one or more logins to the CareSimple clinician dashboard overall (given that this is the primary pathway for data sharing for Arm 1 participants).

We will also collect qualitative data and cost outcomes for our intervention to determine a more nuanced understanding of implementation. Qualitative data will be collected via interviews with participants, clinicians, and observations of clinical practice within the primary care sites. We will evaluate the cost of implementing each arm of the trial using time-drive activity-based costing. This will include the costs of consumables (e.g., BP monitor and medications) and labor costs for healthcare providers (e.g., pharmacists) for delivering the intervention. Both separate analyses will be outlined in more detail in separate publications.

IV. RESULTS

Primary Hypotheses:

1. Cellular-enabled home BP monitoring with pharmacist-led support will lead to greater reductions in SBP compared to protocol-based support alone (Arm 3 vs Arm 2). 2. The pharmacist-led and protocol-based support will each lead to greater reductions in SBP compared to minimal support (Arm 3 vs Arm 1 and Arm 2 vs Arm 1).

Analysis Plan—For our primary analyses, we will conduct mixed effects linear regression, including random effects for patients to account for within-patient correlation of repeated measurements and fixed effects for participating clinicians to account for clustering at the clinic and provider levels [41]. The primary comparison will be between the pharmacist-led vs. protocol-based arm (Arm 3 vs Arm 2), with subsequent comparisons between the pharmacist-led and protocol-based arms vs. the minimal support arm (Arms 3 vs 1 and Arms 2 vs 1). These primary comparisons will be assessed by a test of the interaction of treatment arm by time to assess changes in SBP. We will check assumptions of linearity in time and normality of the SBP measurements to determine appropriate fit of the model and will not plan to adjust for baseline characteristics unless we observe imbalance in the study arms by key participant characteristics such as age, gender, and race/ethnicity. While we expect all participants to have ambulatory clinic BP readings during the 6-month active intervention period, we will complete multiple imputation of SBP values if missingness greater than 10% arises. We will consider adjustment for total number of pharmacist visits, to account for overall pharmacist care for participants outside of the REACH-SNS intervention.

For analyses of continuous secondary outcomes (BP readings from the cellular devices and patient-reported measures), we will use the same analytic approach. For secondary analyses of dichotomized outcomes (BP control and medication intensification), we will use mixed effects logistic regression, treating the BP control outcome as repeated assessments of a binary outcome and adjusting for length of follow-up. Finally, for medication intensification, we will use logistic regression to determine significant differences in this outcome by arm over the entire follow-up period.

Finally, for patient engagement outcomes, we will run mixed effect Poisson regression models with robust standard errors at the clinician level to account for clustering and overdispersion. We will adjust for baseline characteristics that are imbalanced after randomization. For clinician engagement we will conduct descriptive analyses to report the proportion of SMBP in-basket messages opened by the clinician and mean of days with one or more log-ins by clinicians to the CareSimple dashboard.

Power calculation and sample size.: We have used t-test formulae based on a BP change score between two time points to conservatively calculate our sample size; the hierarchical model analysis will use all available time points (typically more than two SBP measures that will increase our power). Using a two-tailed alpha of 0.05 and power of 0.8, we would need to enroll 200 patients each in Arm 2 and Arm 3 to detect a clinically meaningful 5 mmHg change in BP between study arms, assuming a standard deviation of the change in BP of 15 mmHg [42]. For the additional primary comparisons between Arm 2 vs Arm 1 and Arm 3 vs 1, we are powered to detect a difference in BP of 6 mmHg with 140 participants in the minimal support Arm 1. Since we have pre-specified our primary comparison of interest, we will not adjust our p-value threshold for multiple hypothesis testing. While we anticipate drop-out among n=540 study participants, we expect to have virtually complete outcome ascertainment of the primary outcome of clinic SBP given that we will be recruiting active primary care patients within SFHN into the study. For any outcome variable with >10% missingness (particularly survey data, given that previous trials in our setting have resulted in 10-15% missingness in follow-up survey data completion), we will explore multiple imputation using chained equations [43].

Test for heterogeneity of treatment effects (HTE) and subgroup analyses: Because of the unique nature of the patient population enrolled in our study, we plan to compare intervention effects across *a priori* specified sub-groups (Table 3): self-reported digital literacy, language, race/ethnicity, baseline SBP, and clinic site by testing the interaction of time by subgroup by intervention arm within the mixed-effect models described above [44]. If heterogeneity of effect is detected, we will conduct subgroup analyses to examine the intervention effect within each subgroup. Given our projected sample sizes, we anticipate a detectable effect size of larger >10mmHg change in SBP within racial/ethnic groups if they represent at least 50% of the total participant sample. Since the detectable effect size would be even larger for testing interaction between intervention and racial/ethnic groups, we do not anticipate sufficient sample size to assess the intervention's effect in reducing racial disparities.

Data source, collection, management, and safety: We will use existing data (primarily EHR and cellular BP monitor data) to assess intervention implementation and outcomes. All three arms within this study are consistent with and integrated into standard of care, with minimal risk to patients. We will monitor adverse events and serious adverse events with our Data and Safety Monitoring Board throughout the trial, directly outreaching to participants with extremely high or low home BP readings (>180/105mmHg or <90/55mmHg) to seek appropriate care.

V. DISCUSSION

In this study, we propose to leverage newer digitally enabled SMBP platforms with cellular capability that upload to a central database passively without a need for Bluetooth or Internet connection, removing digital barriers for patients [23,45]. We also specify varying implementation strategies (protocol-based and pharmacist-led,) to assess how the rollout of the SMBP program impacts outcomes. We will conduct a randomized controlled trial to compare effectiveness of these varying levels of implementation support, and to understand implementation processes that could inform scalability and sustainability in safety-net health systems.

Prior to the COVID-19 pandemic, there was extensive literature about barriers to hypertension management, including the need for greater patient engagement in hypertension self-management, and missed opportunities for treatment during short, infrequent doctor visits with often inadequate BP measurements [46-48]. The rapid deployment of telehealth during the pandemic emphasizes these existing barriers and simultaneously underscores the need for remote monitoring approaches to reach diverse populations [49]. Increasing telehealth adoption during the pandemic may facilitate uptake of remote monitoring [48]. Moving forward post-pandemic, digital/remote interventions like REACH-SNS that emphasize implementation within safety net settings serving marginalized communities must be core to chronic disease research, rather than adapting programs at a later date in an attempt to reduce disparities [49-51]. This study will tackle the important task of designing a digitally enabled SMBP for use in safety net settings and available to both English- and Spanish-speaking patients.

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Table 1.

Cellular Home BP Monitoring intervention arms

	Usual care w cellular BP monitor	**+ automated support**	**+ pharmacist support**
Cellular-enabled BP Monitoring system, both devices as well as patient and provider dashboards for reviewing data	Yes	Yes	Yes
Timely summarized HBP measurements sent to PCPs	No	Yes	Yes
Automated text reminders to patients	No	Yes	Yes
Pharmacist intensify meds directly with patients	No	No	Yes
Patient digital coaching using the EHR patient portal	No	No	Yes

Table 2.

Variables, outcomes, and process measures with definitions

Outcomes	Definition	Data Source	Timepoints for data collection
Clinical			
Systolic BP* (*primary outcome)	All available clinic SBP readings from any outpatient encounter	Epic EHR	All measures 6 months prior to enrollment and 6 months during active intervention; Extended to 12 months post-enrollment in secondary analyses
Blood pressure control	Using all available clinic BP readings, dichotomize BP control as SBP <140mmg and DBP <90mmHg	Epic EHR	All measures 6 months prior to enrollment and 6 months during active intervention; Extended to 12 months post-enrollment in secondary analyses
Medication intensification	Proportion of participants with 1) increased number of classes of anti-hypertensive medications and/or 2) increased doses of anti-hypertensive medications, from baseline to follow-up	Epic EHR	Assessed within 6-month active intervention period
Blood pressure readings	All available home SBP and DBP readings	CareSimple BP device	Assessed during 6-month active intervention period
Patient-reported			
Patient Assessment of Chronic Illness Care (PACIC)	Patient-reported experiences with chronic disease healthcare treatment, scored continuously on validated scale	Study survey	Assessed at baseline and 6-month follow-up
Krousel-Wood Adherence Scale (K-Wood-MAS-4)	Self-reported medication adherence, scored continuously on validated scale	Study survey	Assessed at baseline and 6-month follow-up
Implementation			
Patient engagement in SMBP	Number of SMBP readings	CareSimple BP device data	Assessed during 6-month active intervention period
Patient app engagement	Number of days with ≥1 logins to the CareSimple app	CareSimple app usage data	Assessed during 6-month active intervention period
Primary care clinician engagement in SMBP	Primary care clinician review home BP data, assessed by a) proportion of EHR in-basket messages viewed by the clinician for Arm 2 and Arm 3 participants, and b) mean number of days with ≥1 logins to the CareSimple dashboard	Epic EHR data and CareSimple dashboard	Assessed over entire 6-month active intervention period

Table 3.

Subgroups for HTE analysis

Race/ethnicity: NH White, NH Black, NH Asian, Hispanic/Latinx (any race), Other
Digital literacy
Language (English vs Spanish)
Baseline SBP >150 mmHg
Clinic site

HTE – Heterogeneity of treatment effects

NH – Non-Hispanic

SBP – systolic blood pressure