Study Title: Pilot study to evaluate the feasibility of using a Sequential Multiple Assignment Randomized Trial to Address Food Insecurity in patients with Hypertension (Pilot SMART-FI)

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Background, Rationale and Context

In the US, 47% of adults have hypertension (HTN), and HTN accounts for more cardiovascular disease (CVD) deaths than any other CVD risk factor.[1,2] Despite advances in prevention and treatment, barriers to adherence are common and HTN disparities remain pervasive. Populations that have been socially and economically disadvantaged have a greater prevalence of HTN, worse blood pressure control, and are at higher risk of developing CVD from HTN.[3-6] Food insecurity (FI), the lack of consistent access to nutritionally adequate foods, is an important social need that affects 30 million people in the US, impacts adherence to treatment, and contributes to HTN disparities.[7,8] Increasingly, health systems are investing in interventions to address FI as part of routine care, including lower-cost, low intensity (e.g. providing information about community resources) and higher-cost, high intensity (e.g. using community health workers (CHWs), delivery of medical tailored meals (MTM)) interventions.[9-12] However, individuals often need varying levels of support to address social needs, and, rather than dispensing a fixed intervention, adaptively allocating treatment resources has the potential to more effectively and efficiently improve food security and blood pressure for a greater proportion of patients. Thus, the lack of an adaptive, stepped-care intervention to address FI in patients with HTN is a **critical problem** affecting a large, vulnerable population.

Objectives

The objective of this study is to conduct a pilot sequential multiple assignment randomized trial (SMART) addressing food insecurity in patients with uncontrolled HTN to determine the feasibility of recruitment/retention and the potential impact on blood pressure in anticipation of a larger more definitive trial.

Methods and Measures

Design

We will conduct a longitudinal two-stage, single-site pilot SMART to determine the feasibility and potential impact of the embedded adaptive interventions to improve systolic blood pressure (SBP) among food insecure patients with uncontrolled HTN (see Figure below).[13,14] Patients from 1 clinic within AHWFB with uncontrolled HTN (BP >130/80) who screen positive FI will be eligible for inclusion. We will follow participants for a total of 6 months. We will randomize eligible consenting participants to one of two first-stage interventions: 1) information about local community resources or 2) assistance from a community health worker (CHW). We will assess all participants at 3 months. All participants who do not have a reduction of at least 10mmHg in SBP (suboptimal respondents) will be re-randomized, with equal probability, to receive one of two second-stage interventions: 1) initial or continued assistance with a CHW or 2) weekly medically tailored meals (MTM.) We will assess the feasibility of recruitment (percent of patients who were eligible and who consented) and retention (percent of patients who were enrolled who completed follow up data collection).

Setting

The study will take place in the General Medicine Clinic at Janeway Tower (OPD)

Subjects selection criteria

Inclusion Criteria

Adult patients (≥18 years of age) will be *included* if (1) have a diagnosis of HTN (defined by ICD-10 code) or have been prescribed at least one blood pressure medication (including thiazide diuretic, calcium channel blocker, beta-blocker, angiotensin-converting enzyme inhibitors, or angiotensin receptor blocker); (2) blood pressures at their primary care office was >130/80; (3) experience FI based on the 2-item Hunger Vital Sign; and (5) live in Winston-Salem or Forsyth County.

Exclusion Criteria

Participants will be *excluded* if they are (1) unable to speak English or Spanish; (2) have severe cognitive impairment or major psychiatric illness that prevents consent and participation; (3) lack of safe, stable residence and ability to store meals; (4) pregnant, breastfeeding, or planning to become pregnant in the next year; (5) advance kidney disease (estimated creatine clearance < 30 mL/min); (6) serious medical condition which either limits life expectancy or requires active management (e.g. certain cancers); (7) those planning on moving out of the geographic area within 12 months; (8) lack of a telephone (>80% of patients list a cell phone number in the EHR).

Sample Size

The goal of this study is to determine the feasibility of testing the SMART design, recruitment and retention, data collection, and to provide information to refine the study protocol for a larger study powered to determine differences in the future. Our goal is to recruit 60 participants. A sample size of 60 participants will provide a >90% chance of having at 4 participants in each subgroup assuming 20% attrition (12 people lost to follow up).

Interventions and Interactions

First-stage treatment options:

1. Resource information: Participants randomized to the resource referral arm will receive a tailored list of information about community resources. The list will include information about local emergency food resources (e.g. local food pantries) and government programs to address FI (e.g. SNAP).

2. CHW assistance: The CHW will assist participants in addressing FI and supporting them in their blood pressure management. Participants randomized to the CHW intervention will have an initial baseline visit scheduled at a mutually convenient location. The purpose of the baseline visit is to build rapport and trust with the patient and being able to identify and address social and structural factors that affect the participant's health and healthcare. Follow-up visits will occur at home, over the telephone, and in-person at participant's regularly scheduled patient visits based on the needs of the participant. During the follow-up visits, the CHW will monitor the participants' progress with care plans, elicit and address additional barriers, reinforce health education, and facilitate patient and family empowerment.

Tailoring variable: We will assess all participants at 3 months. Participants who do not have at least a 10mmHg decrease in SBP at 3 months (suboptimal respondents) will be re-randomized to one of two second-stage interventions.

Second-stage treatment options:

1. CHW assistance: The CHWs will provide the same assistance as described above. Participants randomized to resource information in the first-stage and will be new to receiving CHW assistance, will have an initial baseline visit scheduled to build rapport and trust with the patient. Participants who had been randomized to the CHWs in the first-stage intervention will continue to work with the same CHW for an additional 3 months. We are including an additional 3 months of working with a CHW as a treatment option for participants because the optimal time individuals need to work with a CHW is unclear.

2. MTM: The MTM will consist of weekly home meal delivery and will be provided by Providence Community Kitchen, which is a program of Second Harvest Food Bank of Northwest NC. During the 3 months of meal provisions, participants will receive 10 medically tailored refrigerated or frozen meals (5 lunches and 5 dinners) delivered to the participant's home weekly. Meals are refrigerated or frozen, have minimal preparation time, and can be heated by stove, oven, or microwave.

Outcome Measure(s)
The goal of this aim is to determine the feasibility of testing the SMART design, recruitment and retention of participants, data collection, and to provide information to refine the future study protocol. We will assess blood pressure (using ambulatory blood pressure cuffs) and surveys at baseline, 3 months, and 6 months. Additionally, we will extract demographic data from the electronic health record including age, sex, race/ethnicity, health insurance, medications, neighborhood socioeconomic characteristics, and Charlson Comoribidity Index. We are collecting insurance to see if response varies by insurance coverage as many private and public insurers are considering including food insecurity interventions as part of their benefits coverage. We will also collected data on which services were provided from the CHW through data extraction from the EHR.

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 or ANOVA procedures for continuous variables. Regression analysis will be performed to identify independent outcome predictors. Other inferential statistical analysis will be conducted as appropriate. We will use descriptive statistics to summarize the feasibility of recruitment and retention. We will used repeated measure ANOVA to evaluate change in blood pressure over time to estimate measures of variance to assist in sample size calculations for a future large randomized trial.

Human Subjects Protection

Subject Recruitment Methods
We will identify patients living with HTN whose blood pressure at their last primary care visit was >130/80 through review of the clinic schedule and EHR. Patients that could be eligible will be contacted by phone prior to their scheduled visit to briefly discuss the study goals and gauge interest in participating. We are requesting a limited waiver of HIPAA authorization as potential subjects will be assessed prior to interacting with the study. We will collect he potential subject's name, telephone number, age (in years), problem list (to see if they have a diagnosis of hypertension), and most recent blood pressure to determine if they meet eligibility requirements. Confidentiality and privacy will be protected by collecting only information needed to assess study eligibility, stored on a secure password protected data file, and data access will be limited to study staff only. For potential participants that decline, name, telephone number, and problem list will be immediately destroyed. Age and reason for declining (if provided) will be destroyed 3 years after study completion.

For those interested, we will approach eligible participants in the clinic after their routine visit with the clinician. All potential patients will be assessed using the screening questionnaire. We will further discuss with eligible, interested participants the study goals, objectives, and procedures and obtained informed consent. After consent is obtained, we will collect baseline data and teach participants how to properly use the ambulatory blood pressure monitors. After baseline data collection is obtained, participants will be randomized to one of the two first-stage interventions.

Informed Consent
Signed informed consent will be obtained from each subject who is recruited in person. A study team member (e.g. PI, co-investigators, study coordinator, or other study team member) will obtained informed consent. A study team member will obtain consent in a quiet area within the primary care clinic.

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, store 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 three years after closure of the study 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.

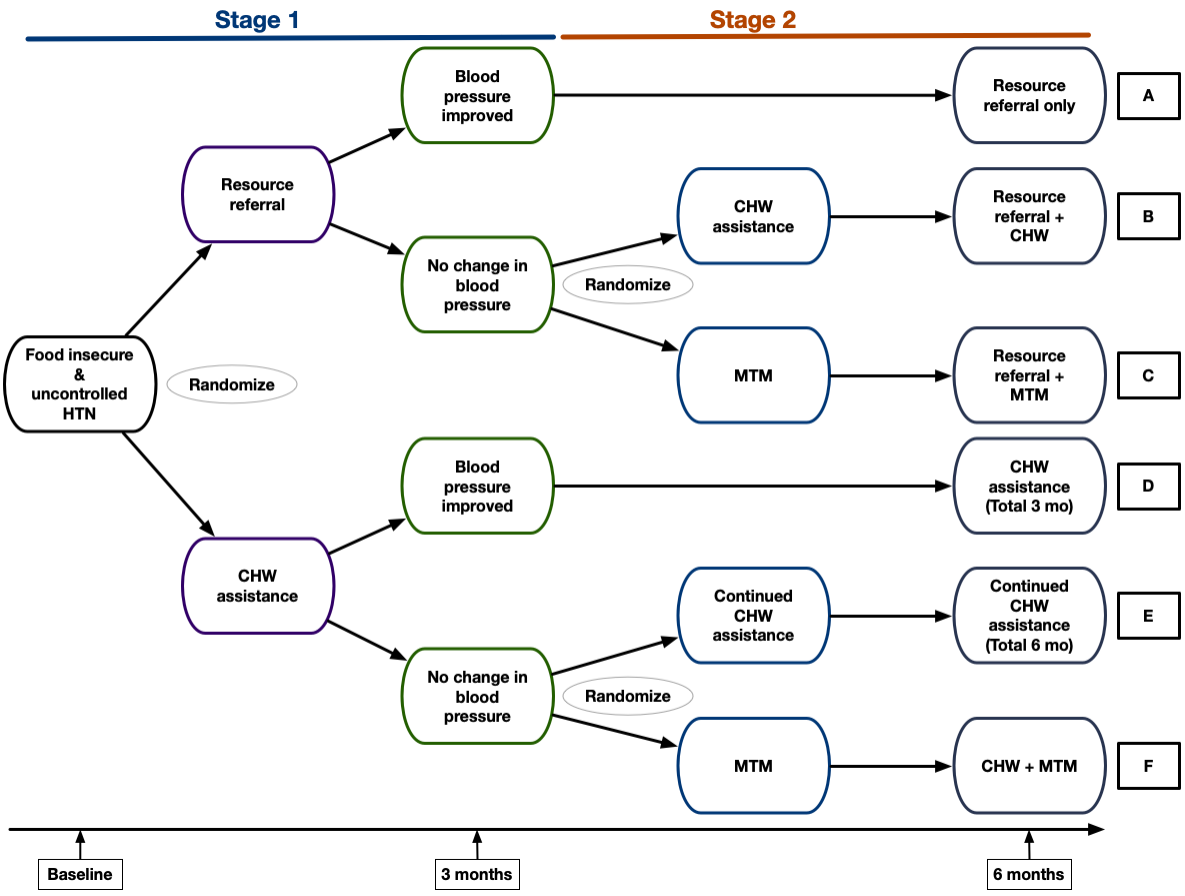
Data and Safety Monitoring

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 or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

Figure: SMART-FI Pilot Design



Appendix

1. Screening questionnaire
2. Baseline questionnaire
3. Follow up questionnaires
4. Data collection form
5. Consent form

References:

1. Carey RM, Moran AE, Whelton PK. Treatment of Hypertension: A Review. *JAMA : the journal of the American Medical Association.* 2022;328(18):1849-1861.
2. Services USDoHaH. The Surgeon General's Call to Action to Control Hypertension. In: Department of Health and Human Services OoSG, ed. Washington, DC2020.
3. Mahdavi R, Bagheri Asl A, Abadi MAJ, Namazi N. Perceived Barriers to Following Dietary Recommendations in Hypertensive Patients. *J Am Coll Nutr.* 2017;36(3):193-199.
4. Soltani S, Arablou T, Jayedi A, Salehi-Abargouei A. Adherence to the dietary approaches to stop hypertension (DASH) diet in relation to all-cause and cause-specific mortality: a systematic review and dose-response meta-analysis of prospective cohort studies. *Nutr J.* 2020;19(1):37.
5. Epstein DE, Sherwood A, Smith PJ, et al. Determinants and consequences of adherence to the dietary approaches to stop hypertension diet in African-American and white adults with high blood pressure: results from the ENCORE trial. *Journal of the Academy of Nutrition and Dietetics.* 2012;112(11):1763-1773.
6. Choudhry NK, Kronish IM, Vongpatanasin W, et al. Medication Adherence and Blood Pressure Control: A Scientific Statement From the American Heart Association. *Hypertension.* 2022;79(1):e1-e14.
7. Coleman-Jensen A, Rabbitt MP, Gregory CA, Singh A. Household Food Security in the United States in 2020, ERR-298. In: U.S. Department of Agriculture ERS, ed2021.
8. Gregory C, Coleman-Jensen A. Food Insecurity, Chronic Disease, and Health Among Working-Age Adults, ERR-235. In: Agriculture USDo, ed. Economic Research Service2017.
9. De Marchis EH, Torres JM, Benesch T, et al. Interventions Addressing Food Insecurity in Health Care Settings: A Systematic Review. *Annals of family medicine.* 2019;17(5):436-447.
10. De Marchis EH, Torres JM, Fichtenberg C, Gottlieb LM. Identifying Food Insecurity in Health Care Settings: A Systematic Scoping Review of the Evidence. *Family & community health.* 2019;42(1):20-29.
11. De Marchis EH, Hessler D, Fichtenberg C, et al. Part I: A Quantitative Study of Social Risk Screening Acceptability in Patients and Caregivers. *American journal of preventive medicine.* 2019;57(6S1):S25-S37.
12. Byhoff E, De Marchis EH, Hessler D, et al. Part II: A Qualitative Study of Social Risk Screening Acceptability in Patients and Caregivers. *American journal of preventive medicine.* 2019;57(6S1):S38-S46.
13. Kidwell KM, Almirall D. Sequential, Multiple Assignment, Randomized Trial Designs. *JAMA : the journal of the American Medical Association.* 2023;329(4):336-337.
14. Bigirumurame T, Uwimpuhwe G, Wason J. Sequential multiple assignment randomized trial studies should report all key components: a systematic review. *Journal of clinical epidemiology.* 2022;142:152-160.