Statistical Analysis Plan
Title: Veteran Peer Coaches Optimizing and Advancing Cardiac Health
Protocol ID: IIR 14-063
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1. STUDY SUMMARY AND AIMS

A. Study purpose:

The overall goal of this study is to test the effectiveness of a home-visit peer health coach intervention (**Vet-COACH** "**Vet**eran peer **C**oaches **O**ptimizing and **A**dvancing **C**ardiac **H**ealth") to promote health behavior change among Veterans with multiple CVD risk factors with a hybrid type 1 implementation study**.**

B. Study design:

Randomized controlled trial to evaluate the effectiveness of Vet-COACH, a peer health coach home visit program to control hypertension and reduce CVD risk among Veterans.

Randomization
Following baseline assessments, a computerized randomization procedure assigned individuals to either the peer health coach intervention or to the usual care + education control group. Randomization occurred in the order of completed enrollment visits. Randomization lists were constructed using variable length blocks to ensure the groups were not unbalanced at any time. Concealment was used to prevent the study staff from obtaining information on the sequence of assignment.

C. Specific aims:

1. Test the effectiveness of a peer health coach intervention for improving health outcomes for Veterans with multiple CVD risks in a randomized controlled trial.
    a. The **primary outcome** is a reduction in systolic blood pressure (SBP) from baseline to follow-up at 1 year.
    b. **Secondary outcomes** include change in cardiovascular risk, as measured by the Framingham Risk Score, other cardiovascular risks (tobacco use, lipids) and health related quality of life. Using administrative data at 1 year following randomization, we will examine healthcare utilization, hospitalizations, and emergency room visits.
2. Assess the effects of a peer health coach intervention on intermediate outcomes that are intervention targets including social support, patient activation, patient/provider communication and health behaviors (e.g. medication adherence, physical activity, nutrition, alcohol use, and stress management).
3. Assess the cost of the intervention to inform feasibility for future studies.
4. Determine Veteran and staff satisfaction with the intervention and identify barriers and facilitators to adoption. [qualitative study not covered in this analysis plan]

3. STUDY POPULATION

Age up to 70 years; Poorly controlled hypertension (> 150/90 mmHg) in the year prior to enrollment and at least one other CVD risk (overweight or obesity, body mass index (BMI) $\geq$ 25 kg/m^2, tobacco use, hyperlipidemia LDL-c > 130 mg/dL)

Exclusion criteria
Hospitalized in the past 3 months for CV related conditions (IHD, CVA, PVD)
Severe illness that precludes lifestyle program, ESRD on dialysis
Nursing home resident, homeless
Severe cognitive impairment
Receiving home-based primary care or home telehealth services
Presence of suicide and/or behavioral risk flag in CPRS

4. STUDY TIME PERIOD

Enrollment period: 2017 - 2021

5. STUDY OUTCOMES

Primary outcome:
Primary outcome -- continuous change in systolic blood pressure. At baseline and exit (12 months); 3 blood pressure readings were obtained using standard procedures. The average of the 3 blood pressure measurements is used. Blood pressure was assessed at a baseline enrollment visit using standardized protocols, measured by a trained research assistant, using an A&D Medical Ua-767f Multi-User Blood Pressure Monitor blood pressure cuff. Measurements were taken three times. If participant failed to schedule an exit visit, blood pressures were extracted from the medical record for a 3-month period around the date of the exit visit. The lowest value will be used from the CDW for that day.

Secondary outcomes:
Secondary outcome — SBP control. This is a dichotomous outcome in which control is defined as the percentage of respondents meeting pre-specified blood pressure goal (BP $\leq$ 120/80) as based on current VHA/DOD/AHA guidelines.

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120–129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130–139 mm Hg	or	80–89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

All outcomes were measured at baseline and at 12 months. Laboratory examination at both baseline and follow-up includes a non-fasting lipid panel (total, low density lipoprotein [LDL] and high-density lipoprotein [HDL] cholesterol; triglycerides) and are utilized to calculate one of the secondary outcomes, the Framingham Risk Score. Other secondary outcomes include health-related quality of life (HRQOL) measured with the SF-12 and health care utilization.

Intermediate outcomes:
Self-management behaviors were measured at baseline and 12-months that are intermediate outcomes, such as nutrition, physical activity and medication adherence. The nutritional assessment includes a self-reported assessment of dietary intake "Starting the conversation" an eight-item validated, simplified food frequency instrument designed for use in primary care and health-promotion settings. Level of physical activity at baseline and follow-up is assessed using the International Physical Activity Questionnaire (IPAQ), a validated and reliable measure of physical activity (PA) level that classifies participants as high (e.g. over 60 minutes of moderate-intensity PA per day), moderate (e.g. 30 minutes of at least moderate-intensity PA on most days), or low. Medication adherence is assessed using a standardized participant interview.

Covariates:
Key covariates include those that have been shown in previous studies to be associated with hypertension control and self-care. Self-reported demographic covariates include age, gender, marital status, education, annual income and race/ethnicity. Self-reported race and ethnicity questions were taken from the Behavioral Risk Factor Surveillance System (BRFSS) Questionnaire. Race responses were then classified as American Indian American Indian or Alaskan Native, Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, Native Hawaiian, Guamanian or Chamorro, Samoan, Black or African-American, White or other. We ask them separately to define their ethnicity as Hispanic, Latino or Spanish origin. We include questions to measure health literacy in adults. We assess alcohol consumption using the Alcohol Use Disorders Identification Test (AUDIT-C), a 3-item screening test for heavy drinking and/or abuse. Because of the strong link between depression and poor self-care, depressive symptoms are assessed using the Patient Health Questionnaire-8 (PHQ-8). We also collect data on costs and utilization obtained from VHA administrative data.

Outcome Measures; measured at baseline and 12 months		
	Measurement domain	**Measurement instrument**
Primary outcome		
Blood pressure	Systolic blood pressure (SBP)	Standard protocols
Secondary outcomes		
Cardiovascular risk	Framingham risk score (FRS)	FRS algorithms
Individual Cardio-metabolic risks	Body Mass Index (BMI)	Standard protocols for height and weight
	Low density lipoprotein cholesterol (LDL-c)	Laboratory data from CPRS if within 12 months of enrollment, otherwise drawn at enrollment, and within 3 months of the exit visit
	Tobacco use	Self-report from BRFSS questions
Health Care Utilization	Outpatient (including specialty care visits) and ER visits, hospitalizations utilization.	Self-report and VA administrative data
Health-related quality of life	Role limitations caused by physical health, emotional problems, physical functioning, and general health	SF-12

Outcome Measures; measured at baseline and 12 months		
Intermediate outcomes		
Patient activation, Self-efficacy	Self-rated ability to take preventive actions, manage symptoms of medical problems, find and use appropriate medical care, and work with their health care providers	Consumer Health Activation Index (CHAI)
Social Support	Domains of Social support	8-item Medical Outcomes Study (MOS) Social Support Survey Instrument & Behavioral Risk Factor Surveillance System (BRFSS) Questionnaire
Self-management Behaviors – Measure of behavioral enactment	Physical activity Nutrition – eating behavior, food frequency Medication adherence Alcohol use Stress Management	IPAQ "Starting the conversation," FFQ Voils et al Medication BRFSS AUDIT-C
Patient provider communication	Communication with physician and health care team	Consumer assessment of health plans (CAHPS)-patient provider communication

6. STATISTICAL ANALYSES AND DESCRIPTION OF MAIN TABLES

The primary outcomes are changes from baseline to one year in systolic blood pressure. We will test the primary hypothesis that among Veterans with poorly controlled hypertension and at least one other CVD risk, the **Vet-COACH** intervention targeting behavior change and disease self-management will decrease SBP by 4 mmHg compared to a usual care + education control group. Primary analyses will be conducted on an intent-to-treat basis; participants will be analyzed in the group to which they were assigned, regardless of intervention adherence, using all follow-up data or up to last available measurement prior to exclusion or dropout.

Primary Effectiveness Analyses for Specific Aims 1 & 2

Since there are multiple patients enrolled per physician and multiple patients enrolled per peer health coach, a physician-level and peer health coach random effect will be included in the primary analytic model to take this correlation into account. For the Aim 1 primary outcome analysis, we will evaluate change in systolic blood pressure, from baseline to 12 months, in the intervention versus controls using the following random effects model:

$$\boldsymbol{Y_{ij} = \mu + \beta_1 Group_{ij} + \beta_2 Baseline_{ij} + \beta_3 x_{ij} + \alpha_j + Group_{ij} * \tau_k + \epsilon_{ijk}}$$

where Y_{ij} is the change in blood pressure from baseline to 12 months for subject i having provider j (and k for peer coach intervention participants); μ is the overall mean; Group_{ij} is group assignment (intervention vs. control); $\mathrm{Baseline}_{ij}$ is the baseline BP value; x_{ij} are baseline covariates that could affect the outcome ; α_j is the random effect for provider cluster j and τ_k is the random effect for peer coach cluster k (note that τ_k is multiplied by the intervention indicator Group_{ij} so that the added peer coach correlation is accounted for only amongst intervention participants, as suggest by Roberts et al). Our main goal is to test whether $\beta_1 = 0$ which is the difference in BP change (from baseline to 12 months) between the intervention and control groups.

The main conclusions drawn from this trial will be based on the pre-specified primary hypothesis tested with two-sided p-values at the standard 0.05 level with associated effect size differences and confidence intervals.

MAIN ANALYSIS:
Unadjusted
Secondary: Prespecified variables will include sex, age, and race
All Aim 1 secondary outcomes and Aim 2 intermediate outcomes will be compared between intervention and control participants using the same model above for continuous outcomes and using a logit link for the same model for binary outcomes.

Sensitivity analyses
We will include a sensitivity analysis that will explore whether intervention fidelity influences the effect of the intervention on primary outcomes, treatment receipt ("dose" of intervention: number of visits, phone calls, proportion of required modules delivered). This approach will allow for testing whether greater participation in the intervention was associated with a greater impact on SBP, and if that impact was different for those with different SBP at baseline {include baseline blood pressure in the primary analysis). We will also add a sensitivity analysis among patients enrolled after the COVID pandemic, when all study activities were moved to remote/virtual.

Exploratory Analysis:

1. Restrict ample was restricted to patients who met criteria for uncontrolled hypertension (BP ≥ 140/90 mmHg)
2. Pre- vs. During pandemic
    a. Demographics of Veterans enrolled post-COVID versus pre-COVID – are the Veterans enrolled post-COVID different than Veterans enrolled pre-COVID?
    b. Separate analysis of primary/secondary outcomes for (1) Veterans with 12 month outcome collected pre-COVID and (2) Veterans with 12 month outcome collected post-COVID – are treatment effects different post-COVID?
3. Secondary analyses to adjust for important baseline covariates in our models. Prespecified variables age, race [others to consider diabetes status because there is a different goal blood pressure for patients with diabetes]

Missing data analyses
If outcome is missing (e.g. exit blood pressure) then will use value in CPRS on the date closest to the exit date (must be +/- 3 months around the date of the exit visit).

- Use outpatient blood pressure as defined by EPRP (EPRP documentation in Teams)

For key analysis variables that have 15% or more missing values, we will analyze patient and clinical factors that are associated with having a missing value. We will then perform analyses using multiple imputations to impute these key variables to allow analysis for all subjects and reduce any bias associated with the missing data. We will perform a sensitivity analysis to determine if missing values have an effect on study outcomes.

Baseline Analysis and descriptive statistics
Equivalence of participants in the intervention and control arms will be assessed on demographic and clinical variables, including outcomes, health status, co-morbidity, and utilization variables. Unadjusted comparisons between intervention groups will be calculated using t-tests and chi-square tests for continuous and categorical outcomes, respectively. Because this is a randomized controlled trial, no systematic bias is anticipated. However, we will conduct adjusted analyses and use as covariates those

factors that are thought *a priori* to be related to the primary and secondary outcomes. We will report summary statistics for all baseline covariates and outcomes (means, standard deviations, and quartiles for continuous variables; frequencies and percentages for categorical variables) by randomized group.

Cost of intervention

We will calculate intervention costs per patient. These costs will include all labor and materials (pamphlets, home blood pressure monitors, etc.) used in the intervention divided by the number of participants.