Healthy Living Partnerships to Prevent Diabetes in Veterans

(HELP PD Vets)

Pilot Study Protocol

Mara Z. Vitolins, DrPH, MPH, RDN, Principal Investigator, Wake Forest School of Medicine

Kimberly C, Phillips, PhD, BSN, RN, Principal Investigator, Salisbury VAMC

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I. Background, Rationale, and Context

a. Diabetes in the Veteran Population

Type II Diabetes Mellitus (T2DM) is consistently identified as one of the costliest and deadliest public health problems facing the United States today. T2DM accounted for more than $153 billion in medical costs in 2010 and an estimated $65 billion in reduced productivity[1]. An estimated 11.3% of adults in the United States had diagnosed T2DM in 2010[2]. In the population served by the Department of Veteran's Affairs (VA), the estimated prevalence of T2DM in the male population was nearly 25% in 2010[3]. T2DM increases the risk of mortality from all causes, contributing to over 230,000 deaths each year in the US and is a major risk factor for various cardiovascular diseases, renal disease, blindness, neuropathy, lower extremity amputations and depression[4]. As recent research has suggested that nearly 70% of Veterans accessing VA facilities are overweight and at risk for T2DM[5], interventions to address this epidemic are not being utilized effectively within the existing healthcare systems of the VA and continue to be sorely needed. Recent data reported from the MOVE! Program, a weight-management program available to Veterans nationwide, show that access is variable[6], participation rates remain low[7], and weight loss results have varied widely by delivery site[6, 7].

b. Lifestyle Interventions to Prevent Diabetes

Large-scale clinical trials and subsequent translations have demonstrated the potential for the prevention of T2DM through lifestyle change, primarily through interventions focused on weight loss, physical activity and nutrition. The Diabetes Prevention Program (DPP), a behavioral lifestyle intervention targeting modest weight loss and increased physical activity, reduced the incidence of T2DM by 58% among persons with impaired glucose tolerance[8]. The DPP lifestyle intervention produced a mean weight loss of 7% and a decrease of 4 mg/dl in fasting glucose at 2 years[8]. The DPP intervention was delivered through a 16-lesson core curriculum taught by case managers on an individual basis over a 24 week period[9]. Several recent studies have attempted to translate the DPP lifestyle intervention into other settings, including primary care[10-12], churches[13], YMCAs[14], and parks and recreation centers[15, 16]. Taken together, these interventions typically produce approximately 6% weight loss at one year of follow up[17].

The Healthy Living Partnerships to Prevent Diabetes (HELP PD) was designed to translate the DPP approach for use in community settings as a cost-effective intervention led by community health workers (CHWs) with T2DM and administered through a local diabetes education program[18]. Approximately 300 overweight and obese (BMI 25-40 kg/m^2) individuals with prediabetes (fasting blood glucose 95-125 mg/dl) were randomly assigned to either a lifestyle weight loss intervention or an enhanced usual care comparison condition[19]. At 6 months, HELP PD reported significant decreases in biological markers and adiposity comparable to those seen in DPP, including a mean weight loss of more than 7.5% and a mean reduction in fasting glucose of almost 4 mg/dL in intervention participants compared to a weight loss of 1.2% and increase in glucose of 1.1 mg/dL in usual care participants[15]. These results were largely maintained at 12 and 24 months[16] and cost analysis demonstrated that the HELP PD intervention could be delivered for less than one-third the per capita cost of the DPP lifestyle intervention[20].

c. Existing Diabetes Education and Prevention Efforts in the VA

Current clinical practice guidelines developed by the VA include information on screening and therapeutic strategies for the prevention of T2DM. Previous studies in similar care settings have demonstrated that even when this screening is conducted as recommended, follow-up is uncommon and few patients receive information about lifestyle interventions for prevention from their healthcare providers[21]. As managing T2DM is complicated and multifaceted, and requires ongoing education, behavioral interventions, risk factor reduction, health promotion and periodic examination for signs of complications, diabetes self-management education programs can reduce the burden on primary care providers by incorporating comprehensive care, skill training and behavioral strategies that can favorably affect some of the metabolic outcomes for patients with T2DM[22]. Diabetes education programs employ personnel with expertise in lifestyle interventions regarding physical activity and diet and have demonstrated effectiveness for improving patient quality of care[23-28]. While community-based diabetes prevention programs are available[29], they are often expensive, may not be easily accessible in rural areas, and often fail to bridge the divide between a medically-supervised intervention and the community-based resources needed to support a healthy lifestyle long-term.

The VA has introduced a personalized, team-based system for providing diabetes education and care in the primary care setting known as Patient Aligned Care Teams (PACTs). This approach, based on the patient-centered medical home model, focuses on providing care that is patient-centered, efficient, and comprehensive by engaging all members of the healthcare team to provide education, preventive care, lifestyle coaching, and other services[30]. PACTs currently provide T2DM screening and self-management education within the VA system, making them the logical home for prevention efforts in the clinical setting. As the PACTs currently providing T2DM self-management education in VA outpatient clinics have the required infrastructure and expertise to provide prevention programming within their existing primary care framework, access to potential CHWs from within their diabetic patient populations, and existing provider referral mechanisms to enroll participants, the HELP PD intervention has great potential for dissemination and sustainability in this environment.

Previous adaptations of the DPP, including HELP PD, have translated specific components of the intervention[15, 16, 18], tested enrollment processes[31-34], or changed the delivery setting[35]-none have attempted to combine all of these individual pieces into a fully integrated program. It is important to note that although HELP PD has been successful at translating the DPP lifestyle weight loss intervention through resources in the local community, further investigation is required to determine whether this model can be effective in other populations and settings. A joint effort with the Salisbury VAMC offers a real-world opportunity to adapt and implement the HELP PD lifestyle intervention in an existing primary care system. Furthermore, current practice paradigms focusing on patient-centered care make VA outpatient clinics well-positioned to test screening and referral procedures and implementation of this lifestyle intervention[30]. This pilot study will allow us to further refine and tailor efforts for use in this population and this setting.

No interventions to date have attempted to use CHWs to deliver diabetes prevention in clinics administered by the VA or to mix lay personnel and healthcare professionals. Ongoing efforts to

implement DPP programming in the VA to-date have been professionally led[36, 37] and, as such, would be expensive to scale up and place a significant burden on the nurses and dietitians already struggling to meet demand. Previous studies have demonstrated the effectiveness of using both non-clinical personnel to deliver weight loss interventions[38, 39] and peer coaches to provide diabetes management assistance[40], but none have used a peer-led model to deliver a behavioral lifestyle intervention. As current legislative and policy initiatives examine potential reimbursement mechanisms for lay-led diabetes prevention programs[29], translating the HELP PD intervention into the VA healthcare system will provide valuable information on potential barriers to delivery and allow us to develop organizational, financial, and attitudinal support for a CHW-led intervention at the program and patient level.

II. Objectives

We have identified three aims to enable us to take the first steps to translate the evidence-based HELP PD intervention to reduce risk for diabetes in the Veteran population served by VA clinics. We will:

1. Adapt the HELP PD intervention specifically for Veterans in collaboration with Salisbury VAMC health care providers and Veterans who have been diagnosed with T2DM;
2. Assess the feasibility of modifying healthcare delivery at an outpatient clinic associated with the Salisbury VAMC to implement the adapted HELP PD Vets program in Veterans with prediabetes;
    a. Aim 2A. Assess our ability to train providers and staff who are currently providing diabetes education to recruit and train veterans with T2DM to serve as CHWs who will administer, implement, and monitor the 6-month HELP PD Vets intervention program.
    b. Aim 2B. Conduct a randomized controlled pilot feasibility study in 50 Veterans with prediabetes.
    c. Aim 2C: Assess our ability to recruit and retain Veterans in the randomized controlled pilot study of HELP PD Vets.
    d. Aim 2D. Obtain preliminary data to estimate variances (means, SD) of measures to be utilized in the larger study. Measures include anthropometrics, blood biomarkers, dietary intake, HRQL and behavioral constructs.

3. Conduct a cost evaluation of the HELP PD Vets program to estimate the relative cost of intervention implementation in the clinical setting.

Upon addressing these aims, we will be prepared to develop a larger grant proposal to implement a full-scale evaluation of the efficacy and practicality of delivering the HELP PD Vets lifestyle intervention within the existing structure of outpatient VA clinics to reduce the risk for T2DM and its complications.

III. Methods and Measures

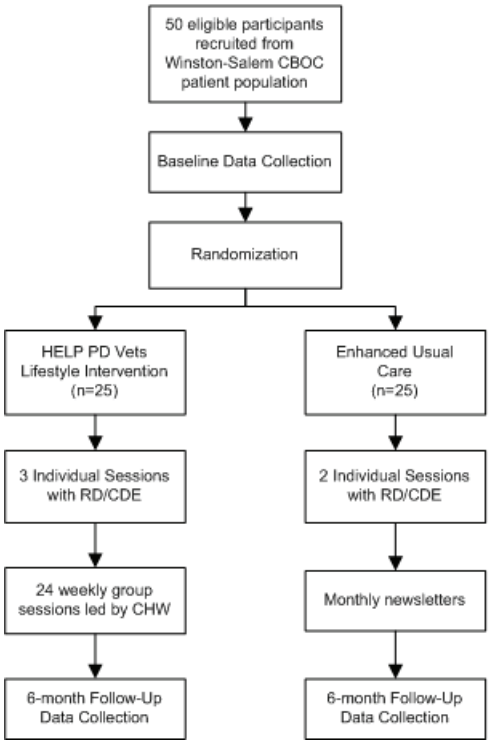
a. Design

The Healthy Living Partnerships to Prevent Diabetes in Veterans (HELP PD Vets) is a two-armed randomized controlled feasibility pilot study. One arm will consist of the HELP PD Vets intensive lifestyle intervention aimed at promoting healthy eating, increasing physical activity and attaining modest, yet achievable (5-7%) weight loss and the comparison intervention will be an education program consisting

of 2 visits with an RD, health education materials and monthly newsletters. The HELP PD Vets intervention will be implemented and monitored by staff members at the Kernersville Health Care Center, who will recruit, train, and supervise community health workers (CHWs), to facilitate the delivery of the lifestyle intervention.

Participants will be community dwelling Veterans with prediabetes who are overweight or obese seen at a local facility for primary care. Following baseline assessments, participants will be randomized to the intervention or control arm with 1:1 allocation (see Figure 1). Study measures will be collected at baseline and 6 months to assess feasibility and to provide data to inform the larger R18 application (i.e., anthropometric measures, blood biomarkers, psychosocial measures).

Figure 1. Schema of Study Participation



b. Setting

The VA operates 23 distinct Veterans Integrated Service Networks (VISNs) across the United States, providing a wide array of healthcare services including inpatient facilities, outpatient and primary care, and allied health services. The Salisbury VAMC is one of 8 medical centers housed within VISN 6: the VA Mid-Atlantic Health Care Network and provides service to the central and Piedmont portions of North Carolina. In addition to the Medical Center, there are 3 community clinics affiliated with Salisbury VAMC located in Kernersville and Charlotte. In this pilot feasibility study, we intend to target Veterans seen in the Kernersville Health Care Center because of the large number of visits conducted each year (145,653 in the previous fiscal year at the 2 previous Winston-Salem locations) and the population served and services offered are representative of clinics throughout the VA system. In a future, full-scale pragmatic trial we anticipate including all clinics affiliated with Salisbury VAMC to deliver the HELP PD Vets intervention.

The screening activities, data collection, and individual sessions will take place in the Kernersville Health Care Center. The CHW led intervention meetings and contacts will take place in designated community facilities (e.g., recreation facilities, libraries, churches or schools). We will enroll 50 adult (21 and older) Veteran participants in the greater Winston-Salem, Forsyth County, NC area to participate in this study. Based on recent data from the National Center for Veterans Analysis and Statistics, there are more than 775,000 living Veterans in NC of which 73.0% are non-Hispanic white, 21.7% black/African-American, and 2.7% Latino. Roughly 10% of the total Veteran population in NC is female. There are approximately 25,000 living Veterans in Forsyth County alone. As the demographics of the Veteran population in NC closely resemble national averages, we anticipate recruiting a study population that closely resembles the larger population of Veterans seen at VA facilities across the country.

c. Subject Selection Criteria

The principles guiding the selection of the following inclusion and exclusion criteria are to ensure the enrollment of participants who meet 4 major criteria: 1) high risk for developing Type 2 Diabetes Mellitus (T2DM), 2) no medical contraindications to participate in a lifestyle intervention including unsupervised physical activity and weight loss, 3) ethical randomization, i.e., there are no compelling reasons that potential participants should be referred for immediate weight loss, and 4) willingness to accept the randomized arm.

i. Inclusion Criteria

Demographics: Men and women (21 years of age and older) of all races/ethnicities seen as patients at the Kernersville Health Care Center.

BMI: 25 kg/m^2 < BMI < 40 kg/m^2. We plan to use the widely accepted BMI cut point for overweight (25 kg/m^2) as the threshold for eligibility. The maximum BMI will be 40 kg/m^2, as current recommendations indicate that intensive weight loss management is appropriate for persons with BMI values greater than that, even including consideration of surgery. Hence, randomization might raise ethical concerns in this group.

Evidence of Pre-Diabetes: As we plan to identify participants in a clinical setting, all participants will be required to qualify based on evidence of prediabetes from fasting plasma glucose, oral glucose tolerance test, or HbA1c taken in the three months. The appropriate ranges for each test are 1) HbAlc: 5.7 to 6.4%; 2) Fasting Plasma Glucose: 95-125 mg/dL; 3) Oral Glucose Tolerance Test: 140-200 mg/dL. Blood measures will be collected from the medical record.

Willingness to Accept Randomization: Prospective participants must be willing to accept randomization to either the intensive lifestyle intervention or the comparison intervention condition.

ii. Exclusion Criteria

Weight Loss: Currently involved in a supervised program for weight loss.

Diabetes: Clinical history of diabetes.

Recent History of Cardiovascular Disease: Clinical history of cardiovascular disease (CVD) occurring within the past 6 months, including myocardial infarction, angina, coronary revascularization, stroke, TIA, carotid revascularization, peripheral arterial disease, and congestive heart failure. All persons with recent CVD should be participating in cardiac rehabilitation (with appropriate supervision as indicated) to reduce their risk of recurrence; hence, randomization might raise ethical concerns.

Hypertension: Uncontrolled high blood pressure: BP > 160/100 mmHg. Potential participants can be re-screened after controlled.

Pregnancy, planning pregnancy and breast feeding (self-report) during screening: Pregnancy, breast feeding, or planning pregnancy within the next year.

Other Chronic Conditions: Other chronic disease likely to limit lifespan to less than 2-3 years, including any cancer requiring treatment in past 5 years except non-melanoma skin cancer.

Medication: Chronic use of medicine known to significantly affect glucose metabolism (e.g., corticosteroids, protease inhibitors).

Other: Conditions/criteria likely to interfere with participation and acceptance of randomized assignment, including the following: inability/unwillingness to give informed consent, another household member already randomized to HELP PD Vets, major psychiatric or cognitive problems (schizophrenia, dementia, self-reported active illegal substance or alcohol abuse), participation in another research study that would interfere with HELP PD Vets.

d. Sample Size

This is a pilot study and is not powered to test the effect of the HELP PD Vets intervention on any outcome. The sample size of 50 for this pilot study was selected to provide reasonably tight estimates of the treatment effect, allowing us to estimate treatment differences in continuous outcomes to within ± 0.6 SD with 95% confidence (assuming a dropout of 16%). Retention can be estimated to within ± 14% and successful adherence within the intervention to within ± 20%. The estimates obtained in this study will be used to design a fully powered randomized controlled trial assessing the effect of the HELP PD Vets intervention on blood glucose. Estimates of the variability of the outcome measures obtained in this study will be used to determine the required sample size in the subsequent trial. Effect estimates will inform us if desired effects are feasible. Estimates of retention and adherence will be used to modify the sample size to account for dropouts and poor adherence. Estimates of the participation and accrual rates will be used to judge the feasibility of the subsequent trial given the required sample size relative to patient availability and our ability to recruit them into our trial.

IV. Interventions and Interactions

a. Intensive Lifestyle Intervention

The intensive lifestyle intervention used in HELP PD was a modification of the DPP core curriculum adapted for use in groups. The 16-session core curriculum used in DPP, covering key concepts related to energy balance, nutrition, and physical activity, was expanded to include regular sessions focused on group problem-solving of barriers and issues specific to the members and to incorporate presentations from local community groups on topics relevant to weight-loss and healthy living (exercise resources, food shopping, etc.) The same intervention will be used in HELP PD Vets and will target decreased caloric intake (reduction of 500-1000 kcal/day) and increased caloric expenditure through moderate intensity physical activity (goal ≥180 min/wk). The primary objective will be to produce a total weight loss of 5-7% from baseline during the 6-month intervention. A DVD series was developed in HELP PD to standardize this core content, improve fidelity of intervention delivery, and to allow the CHWs to focus on group facilitation and problem-solving. This DVD series will also be used in HELP PD Vets.

There will be 24 sessions delivered over the course of 6 months; materials consist of CHW lesson plans, participant workbooks, and the DVD series. These materials will be adapted for use in HELP PD Vets and

may include information on mental health resources available to Veterans for common illnesses like depression and post-traumatic stress disorder and modifying physical activity recommendations for Veterans with limited mobility. We will conduct an initial round of modifications to the materials prior to training community health workers and will modify the materials again based on feedback received during that training. Final adaptations to the materials will be made (for the subsequent larger trial) based on feedback collected from the participants at their 6-month close out visit.

The training programs for staff and lay personnel will be adapted from HELP PD and designed with the understanding that staff delivering diabetes education services as part of a PACT in the Kernersville Health Care Center will be trained by investigators and staff from Wake Forest School of Medicine to screen and enroll participants, recruit and train community health workers, and administer, implement, and monitor the HELP PD Vets 6-month weight-loss program. The training program will focus on study specific material and consist of a) study protocol; b) program philosophy, goals, and procedures; c) weight loss (energy balance); d) physical activity basics; e) group facilitation; f) cognitive-behavioral principles; g) participant monitoring; and h) use of the study website for data entry.

Table 1. Weekly Session Topics from HELP PD

Session #	Session Title
1	Welcome to HELP PD
2	Nutrition 101
3	Physical Activity 101
4	Footwear
5	Troubleshooting
6	Calorie Balance
7	Mindfulness
8	Portion Sizes
9	Troubleshooting
10	Community Exercise/Nutrition Resources
11	Problem Solving
12	Physical Activity Hands On
13	Troubleshooting
14	Emotions and You
15	Healthy Eating
16	Stretching/Injury Prevention/Strength Training
17	Troubleshooting
18	More about Healthy Eating
19	Food shopping/eating out
20	Creating an Environment for Success
21	Troubleshooting
22	Wt. loss maintenance
23	Preparation for Independence
24	Transition

Staff from the Kernersville Health Care Center will then recruit and train 3 CHWs. These CHWs will be recruited from the existing patient population seen for diabetes care at the Kernersville Health Care Center. All potential CHWs will be required to be members of the local Veteran community and will be expected to maintain good control of their diabetes, have the ability to devote ten hours per week to the study, and to maintain a regular exercise program. The CHWs will be responsible for facilitating participant group meetings, conducting calls to remind study participants of the group meetings, completing make-up sessions for missed group meetings, providing regular updates to the CBOC staff, and attending required training sessions. At the end of the training program, each CHW will undergo a formal certification process adapted from HELP PD for this pilot study.

Participants will meet weekly for CHW-led group sessions for 6 months. The core content will be delivered via DVD series to allow the CHW to focus on facilitating the group. The physical activity program will

focus on walking and other large muscle activities. Within 3 months of study onset, the goal will be to have participants engaging in 30 minutes or more of moderate intensity activity for most, if not all, days of the week for a total weekly accumulation of 180 minutes. Physical activity bouts of ten minutes and longer will be counted toward the physical activity goal, but occupational activity will not be counted towards the physical activity goal. The physical activity goals and methods of HELP PD and this pilot are consistent with the recommendations of the Surgeon General and the American College of Sports Medicine[41]. We will use pedometers to enable participants to self-monitor their physical activity and to set goals for progressively increasing their activity level. As a component of the community-based design, some sessions may be presented by community representatives, including sessions on selecting appropriate footwear for walking or running, community exercise resources, safe exercise practices, and food shopping. An outline of the sessions used in HELP PD is included in Table 1.

As the intervention is based on social cognitive theory, each group session will begin with a review of the participants' progress in implementing the strategies recommended for changing their eating or physical activity in the previous session. After a private weigh-in with the CHW, participants will describe the progress they have achieved and they will identify any problems they might have encountered. Difficulties encountered by participants will be dealt with through group support and advice. The session will then focus on skill training related to self-management skills (e.g., goal setting, self-monitoring), nutrition training (e.g., recognizing the caloric and fat contents of food), or exercise science (e.g., minimizing the risk of injuries). The final component of each session will consist of a discussion of the next week's goals. Each participant will be asked to identify specific behavioral goals for the next period and will receive feedback and encouragement from the group. Each participant will also receive individual counseling sessions with a study nutritionist during months 1 and 3.

b. Enhanced Usual Care (EUC)

Our comparison intervention is designed to exceed the usual care provided to Veterans diagnosed with prediabetes. The EUC will consist of an individual education program that builds on an increased awareness of existing community resources. Comparison participants will receive two individual nutrition counseling sessions with a study nutritionist during the first 3 months. In these sessions, she will cover basic aspects of healthy eating and activity to support weight loss, and discuss existing resources (e.g., fitness facilities, weight loss programs, parks, walking trails, etc.) that may fit the individual needs of comparison participants as they pursue dietary change, increased physical activity and weight loss. In addition, comparison participants will receive monthly newsletters with topics related to healthy lifestyle. In order to maximize retention of participants in this group, participants will be allowed to enroll in any existing wellness programs provided by the VA including MOVE! and other diabetes prevention programs and we will track their participation via documentation in the electronic medical record and participant self-report.

V. Study Measures

We will collect information regarding demographics, anthropometry (height, weight, and waist circumference), blood pressure, medical history, health behaviors and behavioral constructs and health-

related quality of life (HRQL). The frequency with which study measures will be collected is outlined in Table 2.

a. Demographics

Age (date of birth), gender, race and ethnicity (US Census Definition), and names and contact information will be collected.

b. Blood pressure and anthropometry

Blood pressure, height, and weight will be collected from the most recent clinical encounter in the participant's existing medical record within the VA. This data will be used to both confirm eligibility for the trial and to serve as baseline and follow-up data.

c. Medical history and current medications

During screening, medical history of T2DM, cardiovascular disease and other medical conditions described above will be obtained to implement the inclusion and exclusion criteria. Medications that have the potential to impact blood glucose, lipid levels and body weight will be collected. This information will be obtained from the electronic medical record. Throughout the study, adverse and serious adverse events will be tracked.

d. Laboratory measures

Based on the current standard of care provided to patients in VA CBOCs, participants who are diagnosed with prediabetes are seen every 6 months and fasting blood is collected at those visits. Staff at the Kernersville Health Care Center will be able to obtain laboratory values to verify eligibility for participation and to serve as baseline and follow-up data from the participant's existing electronic medical record including hemoglobin A1c, fasting glucose, lipids and lipoproteins.

e. Physical activity

We will use the International Physical Activity Questionnaire (IPAQ), a reliable and valid instrument for assessing physical activity[42]. The IPAQ short form is a 7-item index that asks respondents the number of days per week and the amount of time per day spent in vigorous- and moderate-intensity

Table 2. Pilot Study Data Collection: Measures and Frequency

	Screening	Baseline	6-months
Informed Consent and HIPAA Authorization	X		
Demographics	X		
*Medical History	X		X
*Blood Pressure	X		X
*Height, Weight	X		X
*Current Medication Use		X	X
*HbA1c, *Fasting Glucose, *Lipids		X	X
3-day food records		X	X
International Physical Activity Questionnaire (IPAQ)		X	X
Veterans RAND36 (VR-36)		X	X

**Measure obtained from medical record*

activities and walking, during the seven days prior to the interview. Different levels of physical activity are assigned metabolic equivalent (MET) scores based on the Compendium of Physical Activity and, using MET-minutes, can be converted to both continuous and categorical values. Using the IPAQ in HELP PD Vets will enable us to compare changes in physical activity with other trials, including the original HELP PD study.

f. Health-related quality of life (HRQL)

The Veterans RAND 36 (VR-36) Item Health Survey will be collected[43, 44]. The VR-36 differs from the RAND 36 in the use of 5-point response choices for two of the eight scales, role limitations due to physical and emotional problems. The eight domains of the VR-36 include physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems and mental health. The eight scales are summarized into physical and mental summary scores. The summaries are standardized using a t-score transformation and are normed to a U.S. population at a score of 50 and a standard deviation of 10[45].

g. Diet records

During screening, potential participants will be instructed to write down all foods and beverages consumed during the day prior to their baseline visit. A reminder call will be made to candidates two days prior to their visit to remind them of the visit and to remind them to start documenting their intake the next day. These diet records will serve two purposes: 1) to provide the study dietitian with baseline diet information to allow for tailored nutrition counseling, and 2) to assess changes in dietary intake pre- and post- intervention and compare dietary intake between intervention and EUC group participants. These food records will be analyzed using the Nutrition Data System for Research (Minneapolis, MN).

h. Cost estimation

We will conduct a preliminary cost estimation of HELP PD Vets. Direct medical cost is a close proxy for what the intervention delivery would cost a large healthcare provider, such as the Veteran's Administration, a hospital, or insurance company. These direct costs will include the implementation of the lifestyle intervention and side effects of the intervention. We will estimate cost by relying on records of personnel and material costs and records of the number of participants attending intervention sessions; this information will be jointly collected by Wake Forest and staff from the Kernersville Health Care Center. Since this is a feasibility pilot study, we will not attempt the expensive and labor-intensive process of collecting and analyzing all data on cost, outcomes and efficacy associated with this trial from all possible standpoints, as would be required in a full-scale cost-effectiveness analysis. We will propose such an analysis in the full-scale R18 study.

i. Intervention evaluation

Participants randomized to the lifestyle intervention will be asked to complete a brief, anonymous evaluation at the conclusion of the 6-month close-out visit. This evaluation will capture qualitative data on the conduct of the intervention, participants' interaction with members of the study team, and each

participants' experience in the weight-loss components of the study. The data collected on this evaluation will not be linked to study-related process or outcome data as no ID number, acrostic, or other identifier will be collected. Prior to completing the survey, participants will be provided with a cover letter explaining the purpose of the evaluation and explaining that completion is voluntary. Participants will be provided the opportunity to ask questions about the evaluation and can refuse to complete it at their discretion. The data collected from this evaluation will inform intervention conduct and design in a larger trial.

VI. Analytical Plan

This feasibility study is designed to provide useful pilot information that can be used subsequently to develop a grant application to translate the HELP PD intervention into the VA healthcare system. Specifically, we will assess our ability to recruit Veterans, obtain estimates of adherence to the intervention and retention to the study, and obtain estimates of the means and standard deviations of outcome measures such as weight loss, waist circumference, BMI, self-reported levels of physical activity, and caloric intake. For recruitment, we will estimate the proportion of referred patients who are eligible for the study and the proportion of eligible patients who agree to participate. For adherence, we will estimate the proportion of intervention sessions attended. For retention, we will estimate the proportion of participants who complete the study. For the continuous outcome measures, we will estimate the means and standard deviations at each measurement time and the correlation over time. These data are necessary for developing larger scale VA translational efforts. Participants will be assigned to HELP PD Vets or EUC with equal probability using variable length permuted block randomization through a web-based data entry system. Estimates of intervention efficacy will be obtained using the 'intent to treat' approach, in which all randomized participants will be used in the analyses, regardless of protocol adherence. Data will be collected at baseline and 6-months at visits conducted by appropriate medical staff at the VA.

Missing Data

In longitudinal trials, it is likely that some data will be missing due to missed forms, missed visits, or patient drop-out. We will minimize missingness by: 1) using incentives and sending multiple reminders, 2) providing multiple methods for data collection (paper, phone), and 3) attempting to contact participants with missing items. Additionally, multiple imputation methods will be used to assess the sensitivity of our conclusions to assumptions regarding the missingness.

Descriptive statistics (means, standard deviations, frequencies, etc.) will be presented for pretreatment participant characteristics and the outcome measures mentioned above. Each of the outcomes will be analyzed and reported separately. Exact confidence intervals will be provided for the estimated proportions. Analysis of covariance will be used to obtain estimates of the intervention effect for each outcome and to obtain adjusted estimates of the variability of these outcomes. Least squares means and 95% confidence intervals will be provided for each outcome, stratified by intervention, and for the difference between the treatment arms. Subsequent models will include additional covariates such as age and gender. Regression diagnostics and residual plots will be used to find appropriate

transformations for the variables in the models to satisfy the linearity, homogeneity of variances, and normality assumptions. Limited (because of our small sample size) exploratory analyses will be done to determine if the treatment effect differs for different levels of the covariates (e.g., by including intervention by covariate interactions in the model) to see if the subsequent fully-powered trial should be conducted in particular subsets (e.g. specific age ranges) of participants. Logistic regression will be used to determine which participant characteristics are associated with the binomial outcomes such as retention and successful adherence (in the intervention arm).

Data Management and Quality Control

In HELP PD, we implemented an electronic data management system using a secure web-based data entry system for randomization, data collection and participant tracking. For this study, we will leverage the forms and processes already in existence, along with our existing web infrastructure. As in other trials coordinated by Wake Forest School of Medicine in which the VA has participated and in order to comply with IRB and institutional regulations, only de-identified data will be entered in this website. This system has substantial functionality in major areas such as security and authentication, user access management, calendar functionality, directory, document, and committee management and dynamic reporting. Electronic data being entered by staff and CHWs are immediately transmitted to a secure server at the Data Center, where data will reside throughout the study. The web-based system allows great flexibility in processing data management tasks, including the ability to register participants and verify eligibility criteria before randomization; provide the randomization assignment; allow real-time monitoring and reporting of accrual, retention, and intervention adherence; and track participant phone calls and follow-ups. If needed, data can be securely downloaded directly by study team members for use in analyses. There will also be public areas of the website for posting of non-secured information available to the general public, if needed.

Website activity will be monitored and audited for security purposes. Restricted areas of the website will be protected by user login. Prior to gaining access to the restricted area, the user will be required to enter a username and password that will be checked against a database. If the combination is correct, a "flag" will be set to allow the user to enter certain areas of the website. This system allows precise assignments for access based on the person's role in the study. Once a user has successfully logged into the system, inactivity for a period of 30 minutes will automatically force the user to re-authenticate prior to using the system again.

Users may view detailed tracking and management information for each participant and/or by intervention session or follow-up visit. When study team members access the website, a list of upcoming participant assessments is presented for them to view so that participant management is easily accessible: they may run reports, enter data into forms, review and edit data, and access trial-specific documents. As data are entered, validation rules are applied before data are saved. Inconsistencies are noted for staff to resolve. To integrate database content within the website we use a secure Windows server running Internet Information Server, with a middleware product (ColdFusion). Data will be stored in a secure SQL server relational database. With this web infrastructure, data entered

into the system are immediately available for review and reporting. All systems are backed up nightly to disk or tape and tapes are rotated off-site several times a month.

In addition to our electronic quality control procedures, data quality will be assured through standardized procedures and forms, training and supervision of data collection personnel, and attention to detail in data entry, management and analysis. We will monitor data quality throughout the study. A random sample of the data will be double-entered and compared using SAS PROC COMPARE. Discrepancies between databases will be resolved by reviewing the original paper form, correcting them in the original database. If deemed necessary, all data will be double-entered.

All original data and study documents will be maintained within the VAMC system. Only fully de-identified data will be transcribed from the existing electronic medical record system maintained by the VA or collected on case report forms. Only de-identified data will be entered into the web-based data management system developed and maintained by WFUHS. Access to the data management system will require password authentication and WFUHS will take full measures to minimize the risk of breaching the confidentiality of data including electronic firewalls, audit trails, and systems certification. WFUHS has coordinated a number of trials previously in which the VA participated including ACCORD, SPRINT, and ACCORDION and established systems to ensure that all data is managed to be compliant with VA policy and to meet the requirements for approval from the VA's Institutional Review Board. The WFUHS research team will complete research training and complete the verification and credentialing processes required of "Without Compensation" (WOC) employees through the VAMC system. Risks related to inadvertent release of confidential information will be minimized through adherence to best practices for data collection and management. All research staff will be trained in methods for assuring participant confidentiality and safety. The information we are collecting is not of a particularly sensitive nature and we will follow exacting procedures to maintain confidentiality of the participant level data. Identifying information will be kept separate from research data and will be linked only by a participant ID, generated so as to be independent of any identifying information. All original records will be maintained within the VAMC system. Only de-identified data will be released outside of the VAMC. No identifying information will be released in any published reports. Research study materials and documents will be maintained at the end of the study as required by VAMC directives under double lock.

VII. Human Subjects Protection

Approval to proceed with this project will be sought from the Institutional Review Boards (IRBs) of the Department of Veterans Affairs, Salisbury VAMC Medical Center and Wake Forest University Health Sciences and the Research and Development Committee of Salisbury VAMC. We will submit an informed consent document, including HIPAA authorization, to both IRBs as part of our application for approval. In dealing with human subjects, Both IRBs comply with all rules and regulations of the Department of Health and Human Services (DHHS) regarding the protection of human subjects (Title 45 CFR Part 46). The principal investigator and research team routinely complete formal education on the protection of human research participants and all new staff, including those participants in research-activities at the Kernersville Health Care Center, will be required to do so as well. The principal investigators and research team will complete and maintain all required VAMC research training and

NIH Information Security and Privacy Awareness Training. Investigators will participate in additional formal and informal training in research ethics and scientific integrity throughout the study provided from time to time by ethics educators affiliated with Wake Forest School of Medicine. A Manual of Procedures (MOP) will be developed for all aspects of the study, and the procedures will be strictly followed. All study personnel will receive formalized training that will cover all recruitment, informed consent, measurements, specimen handling, participant follow-up, adverse events, side effects, and reporting issues. Adherence to the procedures in the MOP will be assured by periodic assessment and retraining.

a. Subject Recruitment Methods

We plan to identify patients seen at the Kernersville Health Care Center who are at high risk for developing T2DM by engaging primary care providers in identifying potential participants and referring them to the program for participation. In this pilot study, we plan to identify opportunities to integrate the recruitment process into the existing healthcare delivery system by educating providers at all levels about the study, providing materials that they can share with patients at risk for developing diabetes, and developing support from clinic leadership to support our recruitment efforts. We hope to use the strategies identified in this pilot study to inform our recruitment efforts in a larger trial testing implementation in the VA system.

In order to reduce the need to collect additional information, screening and eligibility data will be collected from the existing medical record.

b. Informed Consent

Any patients interested and eligible for the study will be referred by clinic providers or staff to the nurse or diabetes educator affiliated with the project for eligibility verification and administration of informed consent. At that time, the nurse or diabetes educator will inform potential participants of the study design and interventions, the risks and benefits of participation, their rights and responsibilities as research participants, and alternatives to participation. Participants will also be informed that participation is voluntary and that they can withdraw from the study if their initial or on-going experience makes it oppressive, burdensome, or otherwise uncomfortable. All participants will be required to sign informed consent and HIPAA documents prior to randomization. The informed consent and HIPAA documents will include a required text as defined by the Salisbury VAMC IRB.

c. 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. As stated previously, original data and study documents will be maintained within the VAMC system. Only fully de-identified data will be transcribed from the existing electronic medical record system maintained by the VA or collected on case report forms. Only de-identified data will be entered into the web-based data management system developed and maintained by WFUHS. 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. 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.

d. Data and Safety Monitoring

Personally identifiable information (name, address, date of birth, etc.) will be stored in an electronic database, on a local hard drive physically separate from the database storing research data, on a password protected computer within the VAMC system following all stipulations as required by VAMC Directives. This information will be kept completely separate from de-identified study data entered into the web-based data management system. Permission to view subject information will be available only to the Principal Investigator at the Salisbury VAMC or designee, as regulated by password authentication. Data obtained from this study are strictly for research purposes and will be stored in a de-identified manner in a web-based data management system maintained by WFUHS, as described above. During the sessions, each participant will report any discomfort and difficulties with the study protocol to the research staff as they occur. The PI on an individual basis will carefully and immediately review these reports. Furthermore, a monthly meeting of the research team will review the safety data and modify or stop the study protocol if necessary. No adverse effects are expected. In the event of an adverse event, a VAMC Adverse Event Report form will be completed and returned to the IRBs at both facilities within 5 working days.

As this pilot study is considered only a minor increase over minimal risk, we will utilize a Safety Officer, Alain Bertoni, MD, MPH, to monitor participant safety and any reported events. Working with Dr. Bertoni, we will also develop interim boundaries for monitoring the effect of the intervention on the primary outcome over time. All data reported to Dr. Bertoni will be fully de-identified.

Table 3. Blood Pressure Alert Values

Measure	Alert Value	Notify Participant	Notify PCP/Safety Officer
Blood Pressure (Avg.)	Level 1 SBP ≥180 mm/Hg OR DBP ≥110 mm/Hg	In clinic. Advise to follow-up with PCP within 1 week.	Within 1 week. IF symptomatic (e.g. chest pain, headache, short of breath), notify safety officer and/or PCP immediately.
	Level 2 SBP ≥160 mm/Hg OR DBP ≥100 mm/Hg (and not Level 1 BP)	In clinic. Advise to follow-up with PCP within 1 month.	Within 1 week. IF symptomatic (e.g. chest pain, headache, short of breath), notify safety officer and/or PCP immediately.
	Level 3 SBP ≥140 mm/Hg OR DBP ≥90 mm/Hg (and not Levels 1 or 2)	In clinic. Advise to follow-up with PCP within 2 months.	Per routine reporting. IF symptomatic (e.g. chest pain, headache, short of breath), notify safety officer and/or PCP immediately.
	SBP ≤90 mm/Hg OR DBP ≤50 mm/Hg	In clinic. Advise to follow-up with PCP within 1 week.	Within 1 week. IF symptomatic (lightheaded, feels faint), notify safety officer and/or PCP immediately.

e. Medical Alerts

All laboratory values used as outcome measures in this study are being collected from the existing medical record of each participant- no additional laboratory tests are being performed which could result in the need for alert values. Abnormal blood pressure measurements during the baseline and follow-up visits will be provided to the participant and his or her primary care provider (PCP) as described in Table 3 below. Dr. Bertoni, the Safety Officer, and Dr. Vitolins, the Principal Investigator will review medical eligibility criteria as needed, as well as measures collected during baseline and follow-up visits. These individuals also will serve as the primary contacts for staff, participants, and their PCPs regarding medical issues. Dr. Bertoni will review summaries of blood pressure alert values on a periodic basis along with any safety events.

f. 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 if appropriate. During participant group meetings, each participant will report any discomfort and difficulties with the study protocol to the research staff as they occur. The PI on an individual basis will carefully and immediately review these reports. Furthermore, a monthly meeting of the research team will review the safety data and modify or stop the study protocol if necessary. No adverse effects are expected. In the event of an adverse event, a VAMC Adverse Event Report form will be completed and returned to the IRBs at both facilities within 5 working days.

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