Cover Page: Study Protocol and Statistical Analysis Plan

Official Title: Dissemination of a Diabetes Prevention Program for Medicare Eligible Older Adults

ClinicalTrials.gov Identifier: NCT03192475 (first posted 6/20/17)

Document Date (approved): 5/24/12

[reviewer notes¬]

1.1 Objective: What is the overall purpose of this research study? (Limit response to 1-2 sentences.)

We propose to disseminate a novel, yet practical, diabetes prevention program among Medicare eligible adults. This study will provide baseline, 4, 12, and 24 month data to help determine whether a continued contact telephone intervention is feasible and effective (compared to a newsletter control condition) in enhancing health outcomes and physical functional ability in adults aged 65-80.

1.2 Specific Aims: List the goals of the proposed study (e.g., describe the relevant hypotheses or the specific problems or issues that will be addressed by the study).

Several dissemination studies have shown that DPP-adapted interventions (including the Group Lifestyle Balance program) are feasible in diverse community settings with initial body weight reductions of 5-7% that are accompanied by cardio-metabolic improvements. However, the goal of establishing a prevention program infrastructure in managed health care remains elusive. This application seeks to address three important dissemination challenges. First, although effective treatments are available to mitigate diabetes risk among older adults, resources have been directed much more frequently to younger, employed individuals. Second, traditional medical settings alone have not been equipped to provide the screening and behavioral support required to implement prevention programs and innovative approaches to screening and intervention delivery platforms are needed. Finally, although we know from obesity research that longer treatment duration (beyond an initial 4-6 months) appears critical to enhance weight loss and prevent weight regain, dissemination studies have not systematically examined the role of continued contacts in sustaining longer term weight loss, and improving cardio-metabolic risk factors and physical functional ability among older individuals.

The proposed project is based on the premise that the annual Medicare enrollment period in an institutional context presents an ideal opportunity to reach eligible, high-risk elders. Retired adults, considering their future health care coverage needs, may be particularly receptive to the proposed intervention and employers and insurers providing such benefits may be more likely to offer programs that have been demonstrated to be effective and sustainable. Thus, we propose to implement the GLB 12-session intervention (GLB-12) as part of the annual health benefit package offered to high-risk retirees at a large public university. Participants will be 320 non-diabetic adults, aged 65-80, with a BMI ≥ 27 and at least one additional cardio-metabolic risk factor. First, we will evaluate the feasibility of recruiting for and implementing an in-person group program (GLB-12) within this infrastructure. Next, we will conduct a randomized, controlled comparison of two follow up protocols for the remainder of one year of intervention, 8-sessions of continued small group contact by telephone (GLB+8TC; N = 160) or a 2-newsletter control condition (GLB + NC; N = 160). The primary aims are to:

Aim 1: Document that the GLB-12 intervention is feasible and effective when implemented with Medicare enrolled retirees.
Hypothesis 1 (feasibility): We will enroll 107 participants per year, they will complete 65% of sessions, return 50% of self-monitoring records and report above average program satisfaction at the month 4.
Hypothesis 2 (effectiveness): Participants will achieve 5% weight loss and 150 minutes of self reported physical activity per week, and show corresponding waist, glucose, blood pressure and lipid improvements (adjusted for medication use) at month 4.

Aim 2: Evaluate the effects of continued small group contact by telephone (GLB+8TC) compared to a newsletter control condition (GLB+NC) on anthropometric, cardio-metabolic, physical function and health related quality of life (HRQL) measures at 12- and 24-months follow up.
Hypothesis 3: GLB+8TC will be associated with more favorable weight, waist, glucose, lipid, blood pressure gait speed, grip strength, balance and HRQL at month 12 and 24 assessments.

An exploratory aim will be to evaluate direct program costs and self reported health care utilization.

1.3 Background: Briefly describe previous findings or observations that provide the background leading to this proposal.

We have assembled a team of investigators with extensive background experience in screening, assessing and delivering behavior modification interventions for obesity and the reduction of diabetes risk. Our training manuals, protocols and procedures have been used to translate evidence based intervention programs to a variety of community settings. The original individually administered DPP Lifestyle Balance© intervention (copyright 1996; 2011) was developed at the University of Pittsburgh by Dr. Venditti and colleagues for the DPP Research Group under the leadership of Dr. Rena Wing. Dr. Venditti continues as Director of the Lifestyle Resource Core for the Diabetes Prevention Program Outcomes Study (DPPOS) and oversees content development for all intervention materials as well as the training of a wide array of clinical staff for this longitudinal follow up study. Between 2004 and the present, Dr. Venditti and several original members of the DPP team in Pittsburgh established the Diabetes Prevention Support Center (DPSC) with the express purpose of conducting dissemination research. With Department of Defense funding, several primary prevention projects were delivered in underserved urban and rural areas of Western Pennsylvania and, in parallel, to the military community through the United States Air Force (USAF).

To date, we have accomplished the following: 1) updated and consolidated the individually administered 16-session DPP intervention to the Group Lifestyle BalanceTM (GLB) program with available content for 12 core treatment sessions and 10 continued contact sessions; 2) we have created a DVD version of the first 12 sessions using multi-ethnic professional actors filmed "as if" they were participating in a group using a script that mirrors the written participant materials, and; 3) we have developed a 2–day GLB training workshop for health professionals (all disciplines) that includes continuing education hours for nurses and registered dietitians. All manuals and materials have been made publicly available for downloading and adaptation, and we have established additional procedures for licensing the GLB program for research modification, education and/or commercial use nationally and internationally. Our DPSC group has offered over 25 training workshops and trained over 900 people. Thus, this application reflects the cumulative experience of Dr. Venditti and her colleagues at the University of Pittsburgh in creating, adapting and disseminating evidence-based lifestyle intervention programs to reduce obesity and diabetes risk in multiple community environments. If effective, the GLB program proposed in the current application could be available immediately for employers, managed healthcare systems and older Americans.

Although Dr. Venditti and her colleagues have demonstrated their ability to train and translate the GLB 12-session intervention in a number of community based settings it has most often been in the context of primary healthcare. They have demonstrated feasibility and effectiveness but not necessarily sustainability. Thus, the current application will focus on a novel adaptation of the Group Lifestyle Balance intervention as disseminated in an alternative institutional setting that provides health benefits to Medicare eligible retirees. Our findings will clarify the role of an additive, scalable treatment model that is directly applicable to the managed health care environment.

1.4 Significance: Why is it important that this research be conducted? What gaps in existing information or knowledge is this research intended to fill?

There is great urgency to intervene with diabetes risk factors as the population ages. The provision of lifestyle intervention to prevent or delay diabetes and associated co-morbidities in older adults has critical implications for decreasing the total burden of diabetes care in the U.S. during the next decades. Adults ≥ 65 account for approximately 12 percent of the total population and this number will approach 20% during the years 2010-2030 (http://2010.census.gov/2010census). Epidemiologic evidence has provided strong support for focusing diabetes prevention efforts on older adults. About 70% of US men and women over age 60 are overweight or obese.

Although diabetes is increasing throughout the lifespan, the US incidence remains highest among adults aged 65-79 years. In 2009, the percentage of diagnosed diabetes among people aged 65–74 (19.9%) was over 11 times that of people younger than 45 years of age (1.7%). A recent ten-year prospective study of Medicare eligible adults sought to clarify the relationship between adiposity and diabetes risk in this age group and demonstrated that those individuals whose activity, diet, smoking and alcohol habits remained in the lowest risk category had an 82% lower incidence of diabetes compared to other participants; lower BMI and central adiposity were associated with additional decreases in diabetes risk. The newly established Center for Medicare and Medicaid Innovation has mandated that community-based coordination for screening individuals at risk and providing affordable

preventive services are a top national priority.

There have been several prior demonstrations of community based diabetes prevention programs, but important translation questions remain regarding sustainable screening and enrollment strategies, intervention platform, continued contact and scalable delivery methods for older individuals in managed care. The original DPP lifestyle intervention was labor intensive and consisted, on average, of 50 individually administered, in person sessions over 2.8 years –an implementation dose that is not feasible in real world practice.

We also know that older adults are particularly responsive to structured diet and activity programs. Adults over age 60 randomized to the lifestyle intervention group sustained ≥ 5 kg of weight loss for more than 5 years and at each time point their weight losses were significantly greater than that of their younger counterparts. The data confirm that participants ≥ age 60 were more likely to attend sessions, complete self monitoring records, report a lower percentage of calories from fat and meet the 150 minute weekly exercise goal compared to younger individuals. Interventions in this high risk, but relatively healthy group clearly are worthy of translation efforts, but such opportunities have not been exploited systematically. Careful examination of the most feasible and effective continued contact methods to sustain modest weight loss and associated physiologic risk reductions or enhance physical function and quality of life in older adults is warranted.

[reviewer notes¬]

2.1 Does this research study involve the *use* or evaluation of a drug, biological, or nutritional (e.g., herbal or dietary) supplement?

* No

[reviewer notes¬]

2.2 Will this research *use* or evaluate the safety and/or effectiveness of one or more devices?

* No

[reviewer notes¬]

2.3 Summarize the general classification (e.g., descriptive, experimental) and methodological design (e.g., observational, cross-sectional, longitudinal, randomized, open-label single-blind, double-blind, placebo-controlled, active treatment controlled, parallel arm, cross-over arm) of the proposed research study, as applicable.

The current research can be classified as a feasibility/effectiveness design . First we will document the feasibility of community based implementation of an evidence-based 12-session Group Lifestyle Balance (GLB-12) intervention among retirees and/or their dependent spouses/partners who have enrolled or are about to enroll in Medicare benefits through the University of Pittsburgh. We will also recruit from other community locations. Following implementation of the non-randomized GLB-12, participants will be assigned by a stratified block randomization scheme to continued telephone contact (GLB + 8TC; N = 160) or to newsletter control (GLB + NC; N = 160) for the remainder of the one year intervention. Stratification will be based on the category of percent weight loss achieved during the first phase of intervention (<3.5 % and >3.5%). Major outcome assessments will be conducted at 0, 4, 12 and 24 months.

2.3.1 Does this research study involve a placebo-controlled arm?

* No

[reviewer notes¬]

2.4 Will any research subjects be withdrawn from known effective therapy for the purpose of participating in this research study?

* No

[reviewer notes¬]

2.5 Will screening procedures (i.e., procedures to determine research subject eligibility) be performed specifically for the purpose of this research study?

* Yes

2.5.1

List the screening procedures that will be performed for the purpose of this research study. Do NOT include the inclusion/exclusion criteria in this section as they will be addressed in section 3; questions 3.13 and 3.14.

Two staff members, using a dedicated phone line, will respond to individuals expressing interest during regular office hours and complete a participant intervention eligibility checklist (see below). An alternate scenario is that these same screening activities will be performed at Medicare benefits fairs. Screeners will complete daily logs to document their phone, or other in-person screening activities.

Potential participants with self-reported eligibility will be invited to an orientation/information session which includes a weight and a height measurement to confirm a minimum BMI of 27. They will also be asked to have a physician (or other primary health care provider) referral form completed, including approval for moderate physical activity during the GLB intervention. Because of the age of this cohort (65-80), only those individuals who can provide a medical referral form will be included. This is not anticipated to be a problem since, by definition, University of Pittsburgh retirees are provided with the Medicare benefit and any other screening activities will be for those who are signing up for Medicare benefits. However, those individuals who have not yet established a primary care provider relationship and are interest in participation will be helped to do so, if possible.

[reviewer notes¬]

2.6

Provide a detailed description of all research activities (e.g., all drugs or devices; psychosocial interventions or measures) that will be performed for the purpose of this research study.

This description of activities should be complete and of sufficient detail to permit an assessment of associated risks.

At a minimum the description should include:

- **all research activities**
- **personnel (by role) performing the procedures**
- **location of procedures**
- **duration of procedures**
- **timeline of study procedures**

Study Timeline
There will be at least three annual waves of recruitment. Baseline and annual assessments will be conducted in the period between January and March of each year; additional recruitment may occur between May and July of each year. Waves of intervention will commence within 8-12 weeks of screening and enrollment. Prior experience in our community based GLB projects indicates that these are optimal times to initiate programs. It will also allow for some groups to start in early Spring to accommodate older adults who travel during the winter months. If recruitement targets are lagging, there may be an additional wave of recruitment and intervention commencing in May/June annually---all procedures will be identical.

Training and Supervision.
The GLB-12 intervention will be administered in groups of approximately 15-20 participants

by three part-time lifestyle coaches, with Bachelor's degree training at minimum, and previous experience in health promotion, health education or lifestyle interventions. They will be trained by the Diabetes Prevention Support Center staff in a two-day workshop conducted by a nurse diabetes educator (CDE), registered dietitian, exercise specialist and a behavioral scientist. These individuals will be available for specialty consultation as needed. Each coach will conduct 3-10 groups (GLB-12) per year and be responsible for all associated follow up protocols. Drs. Venditti and Marcus will provide additional monitoring and supervision for the telephonic continued contact coaching protocol and each lifestyle coach will be required to audiotape 10% of their telephone contact sessions. Independent reviewers will complete a session content checklist of these recordings as an intervention fidelity check. If necessary, lifestyle coaches will be trained at remote campus locations to implement the GLB-12.

Description of GLB-12 session intervention.
The instructional content of the original individually administered DPP 16-session curriculum was consolidated into 12-sessions designed to be administered weekly over 3-4 months. Other modifications to this content include 1) broad behavioral focus on the principles for making healthy food choices, meal planning and the plate model as opposed to the earlier USDA food pyramid, 2) instructions to monitor calories and fat beginning in Session 1, and 3) inclusion of the pedometer to help increase self-awareness and motivation for increasing overall movement. As in the DPP, the goals of the GLB intervention are to achieve and maintain a 7% weight loss, and safely and progressively increase to 150 minutes per week of moderately intense physical activity similar to a brisk walk. Participants will receive standard tools to complete the program: 1 –GLB participant notebook for weekly session handouts; 1- Calorie King ® Calorie Counter; GLB Food Activity and Weight Diaries. Those who miss group meetings will be mailed the GLB-DVD for that session and asked to watch prior to the next meeting. There will be no additional phone support offered during the GLB-12 session program. Participants will be weighed at each in-person treatment contact (research weight measures will be conducted by independent assessors), diaries will be collected weekly and data-entered, and attendance recorded.

Randomized Intervention condition-GLB followed by Telephone Coaching (GLB + 8TC).
Following GLB-12, group telephone sessions will be the delivery format for the remaining one year of intervention. The content, structure and sequence of these sessions is similar to those conducted in person; however, a group phone coaching script and a participant handout will be developed that details norms and procedures for phone interactions. As with face-to-face intervention, the phone coaching sessions amplify core diabetes prevention and cardiovascular health messages and allow for continued weight, diet, and activity monitoring and accountability. Prior studies have shown that this method of coaching has been employed successfully both for initial standard (core) as well as maintenance interventions with older rural women (44, 45). All participants will be asked to call into a toll-free conference line, and to treat the weekly call time as a standing appointment for which they need to be in a private location free from distractions. Participants will be asked to dedicate a maximum of 45 minutes for actual phone call time, and to utilize15 minutes post-call time to review home assignments on their own. In the GLB + 8TC condition, the first of the eight continued contact sessions be delivered face to face to orient those randomized to telephone continued care to the specific protocol and procedures, provide a new participant manual and other materials necessary to complete the remainder of the program. Because problem solving strategies will be a dominant focus of these continued contact sessions, we will limit participation on each group phone call to approximately 5-7 individuals. In addition, because of the critical importance of transitioning from face-to-face weekly sessions to home-based self-monitoring during the follow up phase, all GLB +8TC participants will be provided with a digital bathroom scale and a set of post-cards with instructions to mail in (or phone in) their weekly weights and physical activity minutes for the duration of the intervention.

During these group phone consultations the participants will be encouraged to discuss their major barriers to achieving their dietary and physical activity goals and share the kinds of approaches/strategies that they have been attempting to use during the prior month, since the last contact. The specific information that is discussed/shared in these group interactions is at the discretion of each individual participant; the nature of these interactions is expected to be very similar to the types of discussions that occur in the live group interaction. Participants will not be asked to report their current weight or weekly physical activity minutes over the phone during the group interaction, although they will be asked to phone or mail this specific information in to their lifestyle coach monthly .

GLB followed by Newsletter only (GLB+ NC). Following GLB-12, four newsletter packets containing information related to general health and well being (as opposed to specific behavioral diet, weight loss and activity messages) will be mailed to participants at month 6

and month 11 from baseline. The packets will also include reminders about pending assessments, and colorful, professional quality pamphlets and brochures from the National Institute on Aging (NIA) that pertain to the self-management of sleep, stress, arthritis and osteoporosis.

2.6.1

Will blood samples be obtained as part of this research study?

* Yes

*If submitting a protocol for expedited review, it should be clear that the planned blood draws are within the parameters described here:
http://www.hhs.gov/ohrp/policy/expedited98.html (see Expedited Research Category #2)

If **Yes**, address the frequency, volume per withdrawal, the total volume per visit, and the qualifications of the individual performing the procedure:
Fasting Glucose and Lipids (total, HDL and LDL cholesterol, and triglycerides): will be collected via finger stick sampling after at least an 8 hour fast (last food/drink consumption will be documented prior to collection of sample). We will use the Cholestech LDX® System, with results available immediately, and adhere to all quality control measures published by the Cholestech Company. Each procedure requires no more than one or two drops of blood or 40 ul (microliters) or less than one teaspoon maximum. The person completing the procedure will be either a trained phlebotomist or other medical technician.

Study Flow Chart:

Name	Modified Date

[reviewer notes¬]

2.7 Will follow-up procedures be performed specifically for research purposes? Follow-up procedures may include phone calls, interviews, biomedical tests or other monitoring procedures.

* Yes

Detailed procedures listed in the textbox below:

Randomized Intervention condition-GLB followed by Telephone Coaching (GLB + 8TC). Following GLB-12, group telephone sessions will be the delivery format for the remaining one year of intervention. The content, structure and sequence of these sessions is similar to those conducted in person; however, a group phone coaching script and a participant handout will be developed that details norms and procedures for phone interactions. As with face-to-face intervention, the phone coaching sessions amplify core diabetes prevention and cardiovascular health messages and allow for continued weight, diet, and activity monitoring and accountability. Prior studies have shown that this method of coaching has been employed successfully both for initial standard (core) as well as maintenance interventions with older rural women (44, 45). All participants will be asked to call into a toll-free conference line, and to treat the weekly call time as a standing appointment for which they need to be in a private location free from distractions. Participants will be asked to dedicate a maximum of 45 minutes for actual phone call time, and to utilize15 minutes post-call time to review home assignments on their own. In the GLB + 8TC condition, the first of the eight continued contact sessions be delivered face to face to orient those randomized to telephone continued care to the specific protocol and procedures, provide a new participant manual and other materials necessary to complete the remainder of the program. Because problem solving strategies will be a dominant focus of these continued contact sessions, we will limit participation on each group phone call to approximately 5-7 individuals. In addition, because of the critical importance of transitioning from face-to-face weekly sessions to home-based self-monitoring during the follow up phase, all GLB +8TC participants will be provided with a digital bathroom scale and a set of post-cards with instructions to mail in (or phone in) their weekly weights and physical activity minutes for the duration of the intervention. Session content for the telephonic continued contact phase is described in Appendix B.

GLB followed by Newsletter only (GLB+ NC).
Following GLB-12, four newsletter packets containing information related to general health and well being (as opposed to specific behavioral diet, weight loss and activity messages) will be mailed to participants at month 6 and month 11 from baseline. The packets will also include reminders about pending assessments, and colorful, professional quality pamphlets and brochures from the National Institute on Aging (NIA) that pertain to the self-management of sleep, stress, arthritis and osteoporosis.

[reviewer notes¬]

2.8 Does this research study involve the use of any questionnaires, interview or survey instruments?

* Yes

Upload a copy of all materials except for the SCID or KSADS which are on file at the IRB. The use of all instruments must be addressed in question 2.6 and/or question 2.7 (except for an exempt submission where they should be addressed on the appropriate uploaded exempt form).

Name	Modified Date
Well Being (CES-D).docx	1/18/2013 11:07 AM
Falls History Screening - PRS Form A70.docx	1/18/2013 11:08 AM
Past Month Activity Questions	1/9/2014 6:24 PM
Clinical Data Collection Form - PRS A50.docx	1/18/2013 11:08 AM
Weight and Activity Questions	1/9/2014 6:25 PM
Demographic, Family & Personal History Data Input Form - PRS Form A20.docx	1/18/2013 11:06 AM
SF-12v2.pdf	1/18/2013 11:13 AM
Short Physical Performance Battery - PRS Form A60.docx	1/18/2013 11:07 AM
GLB Satisfaction Survey - 4mos	1/9/2014 6:22 PM
Use of Medical Services Data Input Form - PRS Form A15.docx	1/18/2013 11:05 AM
Emergency and Physician Contact List - PRS Form A30.docx	1/18/2013 11:04 AM
Medication List - PRS Form A25.docx	1/18/2013 11:05 AM
Food Frequency Questions	1/9/2014 6:21 PM
CHAMPS Activity Questionnaire for Older Adults	1/18/2013 11:02 AM
Social Problem Solving Inventory-Revised (Instructions)	1/9/2014 6:25 PM
GLB Postcore Phone and Newsletter Satisfaction	1/9/2014 6:23 PM
Screening Data Input Form - PRS Form S02.docx	1/18/2013 11:03 AM
Duke Index - A40.doc	1/18/2013 11:06 AM
Mediterranean Diet Questions	1/9/2014 6:20 PM

Previously the name and publisher for commercially available materials were listed in the textbox below but effective 9/1/2015, all materials (except for the SCID and KSADS) must be uploaded using the Add button above.

[reviewer notes¬]

2.9 **If subjects are also patients, will any clinical procedures that are being used for their conventional medical care also be used for research purposes?**

* yes

If **Yes,** describe the clinical procedures (and, if applicable, their frequency) that will be used for research purposes:
Only for purposes of physician documentation of additional risk factors for diabetes based on the physician referral. No new tests or procedures will be requested from the medical provider for research purposes.

2.10 The blood sample question was moved to 2.6.1.

[reviewer notes¬]

2.11 **What is the total duration of the subject's participation in this research study across all visits, including follow-up surveillance?**

* 24 months

[reviewer notes¬]

2.12 **Does this research study involve any type of planned deception?**
If Yes, you are required to request an alteration of the informed consent process (question 4.7)

* No

[reviewer notes¬]

2.13 **Does this research study involve the use of UPMC/Pitt protected health information that will be de-identified by an IRB approved "honest broker" system?**

* No

[reviewer notes¬]

2.14 **Will protected health information from a UPMC/Pitt HIPAA covered entity be accessed for research purposes or will research data be placed in the UPMC/Pitt medical record?**

* No

2.14.1 **Will protected health information from a non-UPMC/Pitt HIPAA covered entity be obtained for research purposes or will research data be placed in the non-UPMC/Pitt medical record?**

* No

[reviewer notes¬]

2.15 Does this research study involve the long-term storage (banking) of biological specimens?

* No

[reviewer notes¬]

2.16 Will research participants be asked to provide information about their family members or acquaintances?

* Yes

2.16.1

Describe what information about the third party will be obtained from the participant:

Only whether there is a family history of type 2 diabetes or other cardiovascular disease in a first degree relative

2.16.2

If the information about the third party is of a private nature, can the identity of the third party be readily ascertained or associated with this information?

*
No

Describe the **private information** that will be collected and recorded about the third party:
Only whether there is a family history of type 2 diabetes or other cardiovascular disease in a first degree relative

[reviewer notes¬]

2.17 What are the main outcome variables that will be evaluated in this study?

Measurement Description

Demographic Questionnaire: will be used to collect data on sex, age, race, ethnicity, education, income and family contact information.

Weight and Height: will be taken twice using a standardized protocol. Weight will be measured to the nearest 0.1 kg at all screening/ assessment points using a digital scale (SECA 880) placed on a hard, flat surface. Height will be measured at screening events and the baseline visit only in street clothes, without shoes, using a portable stadiometer (Shorr productions) and rounded to the nearest 0.1 cm.
BMI: will be calculated as average weight divided by average height squared (kg/m2).

Waist Circumference: will be measured as an index of truncal fat using a standardized protocol. A Gulick tape will be placed around the bare abdomen horizontally at the midpoint between the highest point of the iliac crest and the lowest part of the costral margin in the mid-axillary line. Measurements are taken three times and averaged.

Fasting Glucose and Lipids (total, HDL and LDL cholesterol, and triglycerides): will be collected via finger stick after at least an 8 hour fast (last food/drink consumption will be documented prior to collection of sample). We will use the Cholestech LDX® System, with results available immediately, and adhere to all quality control measures published by the Cholestech Company.

Blood Pressure: will be measured using an automatic inflatable digital blood pressure monitor (OMRON HEM90HXC®) with appropriate cuff size according to a standardized protocol.

Nutrition/Nutrition Related Behavior: We will administer 2 questions from the CDC NHANES

Food Frequency Quesitonnaire and 14 items from the Mediterranean Diet Assessment Tool.

Physical Activity Behavior: We will administer, by interview, the Champs Physical Activity Questionnaire for Older Adults (46). This survey consists of 41 items that have been shown to be a highly reliable and valid measure of the weekly frequency and duration of various physical activities typically undertaken by older adults. It has been shown to be sensitive to changes following activity interventions in persons aged 65-90. We will also ask some questions by interview about past month activity level.

Other behavioral, psychosocial functioning and mood questionnaires and surveys are as follows:

SF-12v2 Health Survey: Quality Metric's SF-12v2® is a shorter version of the SF-36v2® (47). We will use this extensively norm-referenced measure of functional health and well-being, which captures the same eight health domains and produces a physical component (PCS) and mental component (MCS) summary score that may be compared to the longer version.

Center for Epidemiological Studies-Depression Scale (CES-D): This 20-item instrument is used to measure clinical depression and has well-established psychometric properties including reference norms for the elderly (48, 49).

Participant Satisfaction Survey: We will adapt a standard one-page post-intervention program satisfaction survey that has been used previously by the Group Lifestyle Balance Program and utilizes 5-point Likert scale ratings and other open ended questions. There will be one version for the GLB 12 and another for the newsletter or phone followup phase.

Physical Function Tests: Evaluation of physical functional ability will be based on a short-physical performance battery (SPPB adapted from epidemiologic/longitudinal studies on aging. We will include:
Grip Strength Test using a Jamar dynamometer (51) from the Cardiovascular Health Study (Johns Hopkins)

Balance, Gait Speed and Chair Stand Tests from the National Institute of Aging
These measures are been demonstrated to be sensitive to functional decline and frailty and have associated with adverse health outcomes

Self-Reported Health Care Utilization: We will administer, by interview, 4 questions from the Stanford Chronic Disease Self Management Program evaluation protocol. This protocol measures the number of times, in the previous six months, an individual has visited a physician/health care provider (outpatient), a hospital emergency room, the total number of separate hospital admissions, and the total number of nights spent in the hospital. It has been utilized as an outcome measure for several disease self-management programs and specifically diabetes.

Social Problem Solving Inventory-Revised: Participants will answer a 25-item survey about some ways they may think, feel or act when faced with important problems in everday life situations. The psychometric properties of this instrument are well established in all age groups.

2.18 Describe the statistical approaches that will be used to analyze the study data.

* Addressed below:

All analyses will be conducted in consultation with Dr. Arena, the study biostatistician. Descriptive analyses and graphic displays will be used to identify outliers, missing data and patterns of attrition that will guide decisions about the use of transformations and appropriate tests. Demographic variables and baseline measures will be compared between the GLB+10TC and GLB+NC conditions. In all outcome analyses we will use an intent-to-treat (ITT) approach in which participants remain in the study arm to which they are randomized regardless of attrition. The primary analytic strategy will be a mixed models approach in which treatment group, time, and time by group interaction are treated as fixed effects, and subject and percent weight loss during the first phase of intervention (<3.5% and >3.5%) are treated as a random effects to account for individual subject variability. Hypothesis tests will be two-sided and significance will be set at the 0.05 level. Analytical tools will include SAS (SAS Institute, Inc., Cary NC), Stata (StatCorp LP, College Station, TX) and StatXact (Cytel, Inc. Cambridge, MA).
Mixed models are applicable to longitudinal datasets that contain missing observations, with

the assumption that the data are considered to be missing at random (MAR) or ignorable missing. Although we will be proactive in maximizing subject retention, we anticipate 75% adherence over the 12-month intervention period. Those who drop out or are lost to follow-up will be compared to those who have completed intervention sessions and research assessments using standard parametric and non-parametric methods, as appropriate. We will examine the patterns of missingness and, if necessary, account for missingness in outcome analysis (e.g.,the covariate approach). Finally, regression modeling will be conducted to adjust for covariates, including demographic variables such as age, race, sex, number of sessions completed, as well as any other variables that have been found to differ across treatment conditions at baseline.

Research Questions
Hypothesis 1 (feasibility): On average, we will enroll ≥107 participants per year for each of three years to GLB-12; they will complete > 65% of sessions, return ≥ 50% of self-monitoring records and report above average program satisfaction at the 4-month assessment.
Analysis Plan: The overall approach will be to report descriptive statistics, including the total number of participants enrolled, the distribution of the number of GLB-12 sessions completed, the percentage of participants completing 8 (65%) or more sessions (the definition for acceptable attendance), the percentage of participants who return six (50%) or more of the self monitoring records (the definition for acceptable behavioral adherence) and the distribution of program satisfaction ratings. Summary descriptive statistics will include mean, median, standard deviation and confidence intervals for continuous variables and proportions, ranges and percentiles for categorical variables.

Hypothesis 2 (effectiveness): On average, participants will achieve ≥ 5% weight loss (the definition of acceptable weight outcome in prevention programs) and ≥ 150 minutes of self reported moderately vigorous physical activity minutes per week (the recommended level in prevention programs), and show corresponding waist, glucose, blood pressure and lipid improvements (adjusted for medication use).
Analysis Plan: For the weight measure, we will examine both absolute weight change (kg) and percent weight change pre to post-intervention (0-4 months). Student t-test and Chi-Square statistics will be used to assess the absolute and percent weight change outcomes, respectively. We will also use descriptive statistics to identify the proportion of total participants achieving ≥ 5% weight loss and the proportion achieving ≥ 150 minutes Similarly, Student t-tests will also be used to assess pre to post intervention changes in waist, glucose, lipid, and blood pressure measures. Because we know that medications will effect these outcomes we will conduct separate sub-group analyses for lipid endpoints to control for statin use, and for blood pressure endpoints to control for blood pressure medication use.

Power and Sample Size Considerations: The primary endpoint of this investigation is defined as the proportion of participants, in each intervention arm, who maintain the designated target weight loss of ≥ 5% at 12 months from baseline. Additional power calculations were derived for the changes in absolute weight loss from 0-12 months and in fasting glucose levels from 0-12 months. For our primary endpoint of ≥ 5% weight loss at 12 months, with N = 160 in each arm and assuming no more than 25% attrition, we have 80% power to detect differences of 19% between the two intervention conditions in the proportion of subjects achieving this weight loss target. There is 90% power to detect differences of 21% between the two groups. This translates to roughly half or more of the participants in the telephonic continued contact group maintaining ≥ 5% weight loss compared to only about one-third of those in the newsletter control condition. These estimates are based on a Fisher's Exact test conducted at alpha = 0.05 two sided with N = 120 in each arm. In addition, we also calculated power estimates for various differences in absolute weight loss (lbs) between GLB + 10TC and GLB + NC based on previous GLB outcomes presented in Table 2 (23). Assuming a two sample t-test conducted at alpha = 0.05 two-sided with a standard deviation of 10.5 we find that there is 80% power to detect group differences of 3.8 lbs or 90% power to detect group differences of 4.4 lbs between the two arms at 12 months. Finally, for the secondary endpoint analysis of differences between GLB + 10TC and GLB + NC in fasting plasma glucose changes from 0-12 months and assuming a two sample t-test conducted at alpha = 0.05 two-sided with a standard deviation of 11.9 based on data presented in Table 2 (23), we project that there will be 80% power to detect a difference of ≥ 4.3 mg/dl decrease or 90% power to detect a difference of ≥ 5.0 mg/dl decrease between the two intervention arms.

Hypothesis 3: GLB+10TC will be associated with more favorable weight, waist, glucose, lipid, blood pressure gait speed, grip strength, balance and HRQL (based on the physical component summary and the mental component summary scores from the SF-12v2®) compared to the GLB + NC group at 12- and 24-month follow up assessments.

Analysis Plan: We will compare GLB + 10TC and GLB + NC on changes in absolute and percent weight loss and each of the other outcome measures with a repeated measures mixed model. To test the treatment effect we will evaluate the coefficients associated with group and the group by time interaction. Planned contrasts will be constructed from the mixed model to evaluate differential changes in percent weight loss between the two conditions from baseline to post-treatment at 12 and 24 months. This procedure will be utilized for each of the other secondary measures.

An exploratory aim will be to evaluate direct program costs and self reported health care utilization.
Analysis Plan: The overall approach will be to report descriptive statistics, including the following: overall and component specific program costs, including allocation of time expenditures by screening staff and GLB interventionists, and the direct cost of all materials provided. For health care utilization we will summarize the self-reported number of times an individual has visited a physician/health care provider (outpatient), a hospital emergency room, the total number of separate hospital admissions, and the total number of nights spent in the hospital in the previous six months. Comparisons will be made between the two groups (GLB + 10TC and GLB + NC). Summary descriptive statistics will include mean, median, standard deviation and confidence intervals for continuous variables and proportions, ranges and percentiles for categorical variables.

[reviewer notes¬]

2.19

Will this research be conducted in (a) a foreign country and/or (b) at a site (e.g., Navajo Nation) where the cultural background of the subject population differs substantially from that of Pittsburgh and its surrounding communities?

* No

Note that copies of training records, licenses, certificates should be maintained in the study regulatory binder and are subject to audit by the Research Conduct and Compliance Office (RCCO).

In addition, individuals planning to conduct human subject research outside the United States must complete an optional module on the CITI training website: International Studies. Click here to access the instruction sheet for accessing optional CITI modules.

[reviewer notes¬]

2.21

Will this research study be conducted within a nursing home located in Pennsylvania?

* No

[reviewer notes¬]

Section 3 - Human Subjects

3.1 What is the age range of the subject population?

64-82

3.2 What is their gender?

* Both males and females

Provide a justification if single gender selected:

3.3 Will any racial or ethnic subgroups be explicitly excluded from participation?

* No

If **Yes**, identify subgroups and provide a justification:

3.4 For studies conducted in the U.S., do you expect that all subjects will be able to comprehend English?

* Yes

[reviewer notes¬]

3.5 Participation of Children: Will children less than 18 years of age be studied?

* No

If **No**, provide a justification for excluding children:
This is a study of Medicare eligible retirees

[reviewer notes¬]

3.6 Does this research study involve prisoners, or is it anticipated that the research study may involve prisoners?

* No

[reviewer notes¬]

3.7 Will pregnant women be knowingly and purposely included in this research study?

* No

[reviewer notes¬]

3.8 Does this research study involve neonates of uncertain viability or nonviable neonates?

* No

[reviewer notes¬]

3.9 **Fetal Tissues: Does this research involve the use of fetal tissues or organs?**

* No

[reviewer notes¬]
--->

3.10

What is the total number of subjects to be studied at this site, including subjects to be screened for eligibility?

Note: The number below is calculated by summing the data entered in question 3.11. Any additions or changes to the values entered in 3.11 will be reflected in 3.10.

* 1500

3.11

Identify each of the disease or condition specific subgroups (include healthy volunteers, if applicable) that will be studied.

Click on the "Add" button and specify for each subgroup:

1) how many subjects will undergo research related procedures at this site; and

2) if applicable, how many subjects will be required to undergo screening procedures (e.g., blood work, EKG, x-rays, etc.) to establish eligibility. Do Not include subjects who will undergo preliminary telephone screening.

*

	Subgroup	Number to undergo research procedures	Number to undergo screening procedures
View	Enrolled in GLB 12 session	320	1500

3.12 **Provide a statistical justification for the total number of subjects to be enrolled into this research study at the multicenter sites or this site.**

* If applicable, refer to the statistical section in the protocol or grant. Specify the page numbers in the textbox.

Power and Sample Size Considerations: The primary endpoint of this investigation is defined as the proportion of participants, in each intervention arm, who maintain the designated target weight loss of ≥ 5% at 12 months from baseline. Additional power calculations were derived for the changes in absolute weight loss from 0-12 months and in fasting glucose levels from 0-12 months. For our primary endpoint of ≥ 5% weight loss at 12 months, with N = 160 in each arm and assuming no more than 25% attrition, we have 80% power to detect differences of 19% between the two intervention conditions in the proportion of subjects achieving this weight loss target. There is 90% power to detect differences of 21% between the two groups. This translates to roughly half or more of the participants in the telephonic continued contact group maintaining ≥ 5% weight loss compared to only about one-third of those in the newsletter control condition. These estimates are based on a Fisher's Exact test conducted at alpha = 0.05 two sided with N = 120 in each arm.

[reviewer notes¬]

3.13 **Inclusion Criteria: List the specific criteria for inclusion of potential subjects.**

Study Inclusion Criteria.
Non-diabetic, Medicare eligible men and women, ages 65-80 (by 1/1/13), with a BMI ≥ 27 and at least one of the following additional risk factors will be included. Eligible participants

must reside in the Western PA or Tri-State region at least half the year and be available to attend the 12 in-person sessions at a location closest to their residence. In addition, eligible participants must meet the following criteria:
EITHER a score of 15 or greater on the ADA risk test,
OR one of the following:
1) Large waist circumference (> 40 inches men, >35 inches women);
2) hypertension or taking hypertension mediciation;
3) physician confirmed low HDL level (<40 mg/dL men, < 50 mg/dL women);
4) physician confirmed elevated triglyceride level ≥ 150 mg/dL;
5) physician confirmed fasting glucose ≥ 100 mg/dL and < 126 mg/DL

The eligibility criterion of BMI ≥ 27 has been selected (as opposed to BMI ≥ 25, a standard overweight cut point) in order to insure that the selected participants are indeed at higher risk for diabetes (1) and to insure that elderly women at a BMI of 25 will not be at increased risk for bone loss and/or muscle loss with weight reduction.

Finally, study participants must have access to a telephone (including appropriate assistive devices if they have hearing impairments), and be able to read at the 6th grade level.

Eligible individuals are those who meet the following criteria:
1. Overweight or obese (BMI of ≥27 kg/m2)
2. Do not currently have a diagnosis of diabetes
3. Are between the ages of 65-80 as of January 1, 2013
4. Documented evidence of at least one additional health risk factor for diabetes including EITHER
a) a score of 15 on the ADA risk screening test, OR
b) one of the following: history of hypertension or currently taking hypertensive medications; large waist circumference (> 40 inches men, > 35 inches women); physician confirmed low HDL level (<40 mg/dL men, <50 mg/dL women); physician confirmed high fasting glucose level (≥ 100 mg/DL and < 126 mg/DL); physician confirmed high triglyceride level (≥ 150 mg/DL)

Individuals who meet the above criteria will be invited to complete the informed consent procedure and will be scheduled for a baseline assessment (it is anticipated that it will take approximately 1-3 months to complete these procedures prior to the baseline assessment and the first GLB session).

3.14 Exclusion Criteria: List the specific criteria for <u>exclusion</u> of potential subjects from participation.

Study Exclusion Criteria.
1) prior diagnosis of diabetes or currently using medicines used to treat diabetes;
2) unable to provide physician (or other health care provider) referral/ clearance for exercise participation;
3) a weight loss of 4.5 kgs or more in the past six months (to rule out unintentional weight loss that may be an indicator of current or incipient physical illness);
4) current use of weight loss medications;
5) unable to attend at least 75% of the GLB 12-session program
6) unwilling to self-monitor food, activity and weight as prescribed
7) participants who have had bariatric surgery will be excluded if at the time of study enrollment they are less than 2 years status/post surgery (this is the period in which individuals are likely to have had the maximum amount of weight loss and some will begin to experience weight regain). Individuals who are greater than 2 years status/post bariatric surgery may be considered for inclusion as long as they have not had a weight loss of greater than 4.5kgs in the past six months.

Excluded individuals will be referred to other resources as appropriate.

3.15 Will HIV serostatus be evaluated specifically for the purpose of participation in this research study?

* No

	Section: Section 4 - Recruitment and Informed Consent Procedures

[reviewer notes¬]

4.1 Select all recruitment methods to be used to identify potential subjects:
Advertisements
Recruitment Letters and/or Scripts
Research Registry
Pitt + Me
Other Strategies: Described below

Advertisements

Upload the advertisements for review:

Name	Modified Date
10-4-12 Kozar Letter and Eligibility Checklist-revised.docx	10/4/2012 8:13 PM
10-1-12 Kozar Letter and Eligibility Checklist.docx	10/4/2012 8:00 PM
PowerPoint for In Person Screening Events	11/12/2012 9:37 PM
Letter to participants-outline of next steps-PRS- describe locations.docx	1/18/2013 11:18 AM

Recruitment Letters and Scripts

Upload recruitment letters/scripts/text:

Name	Modified Date
GLB Written Screening Consent	5/14/2012 7:52 PM
ADA Risk Screening Test	5/14/2012 7:55 PM

Research Registry

List the IRB approval number and title for each registry source:
http://www.pepper.pitt.edu/
The Pittsburgh Claude D. Pepper Older Americans Independence Center
(Dr. Steven Albert) The Center for Research on Health and Care, Graduate School of Public Health, University of Pittsburgh). The IRB approval number for this registry is IRB0503150.

Dr. Susan Greenspan, a Co-Investigator with the Pitt Retiree Study, introduced us to Dr. Albert and we made a formal application to use the Registry. We were approved by the Executive Committee and have received permission to access the database/mailing list. Letters were generated and sent to registry participants in the same way as was done with the University of Pittsburgh retiree database (based on age and zipcode).

4.2

Provide a detailed description of your recruitment methods, including identifying and initiating contact with participants:

As a community translational research study targeting individuals who had been previously employed at either the main campus or the four branch campuses of the University of Pittsburgh, all procedures will be coordinated through the University Human Resources (HR)

benefits department utilizing 2 (FTE) project assistants under the supervision of the PI and the Program Coordinator. All screening and recruitment procedures are being designed to meet with the approval of Mr. John Kozar, Director of Benefits. Mr. Kozar (and the HR database) indicate that many of these individuals remain in the Western PA region.

Annual preparations for screening and recruitment for the GLB-12 session intervention will commence in September 2012 for years 1, 2, and 3 of the study prior to the benefits elections deadline in early December. We will target these retirees through mass mailings, benefits counseling sessions, and/or Medicare benefits screening fairs that are held for this group. The screening and recruitment activities will take place either by phone (in association with the mass mailings) or in person (using existing benefits events).

A letter and/or flyer describing the Group Lifestyle Balance (GLB) program along with the 7-question American Diabetes Association risk screening test (a form commonly used at community health screenings to raise awareness, see uploaded attachments) will be utilized. Once subjects are screened and eligible they will be invited to complete the informed consent procedures and schedule baseline assessments

In addition we have added community based screening methods to meet recruitment targets:
1. Claude Pepper Registry (as above)
2. Outreach to other community facilities where there may be networks of 65-80 year olds interested in participation (e.g., church based programs, senior centers, recreational facilities, municipal and borough facilities associated with programs for older adults).

Note: Questions jump from 4.2 to 4.6 as questions 4.3-4.5 have been removed and the information is now captured in 4.1

[reviewer notes¬]

4.6 **Are you requesting a waiver to document informed consent for any or all participants, for any or all procedures? (e.g., a verbal or computerized consent script will be used, but the subjects will not be required to sign a written informed consent document.** ***This is not a waiver to obtain consent.***

* Yes

4.6.1

Identify the specific research procedures and/or the specific subject populations for which you are requesting a waiver of the requirement to obtain a signed consent form.

Addressed below:

If not all, identify the specific procedures and/or subject populations for which you are requesting a waiver:
In some, but not all, cases screening will occur completely by phone and the participants will be determined to be eligible (with the exception of the height and weight confirmation, in person, to determine BMI status). In those cases where subjects appear to meet all of the eligibility criteria they may be invited directly to sign informed consent and proceed with baseline research assessments at the first and only in person contact prior to the start of intervention.

4.6.2

Indicate which of the following regulatory criteria is applicable to your request for a waiver of the requirement to obtain a signed consent form.

45 CFR 46.117(c)(2)

45 CFR 46.117(c)(1) That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or

45 CFR 46.117(c)(2) That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

4.6.2.1

Address why the specific research procedures for which you are requesting a waiver of the requirement to obtain a signed consent form present no more than minimal risk of harm to the research subjects:

These are procedures that are typically done at health screens and benefits fairs that present only minimal risk to subjects

4.6.2.2

Justify why the research listed in 4.6.1 involves no procedures for which written informed consent is normally required outside of the research context:

These are procedures that are typically done at health screens and benefits fairs that present only minimal risk to subjects

4.6.3

Address the procedures that will be used and the information that will be provided (i.e., script) in obtaining and documenting the subjects' verbal informed consent for study participation:

See the Script and Screening Interview attached

Upload Scripts:

Name	Modified Date
ADA Risk Screen	5/14/2012 8:33 PM
Script for Screening Interview and Verbal Consent	5/14/2012 8:33 PM

[reviewer notes¬]

4.7 **Are you requesting a waiver to obtain informed consent or an alteration of the informed consent process for any of the following?**

* No

4.7.1 **If Yes, select the reason(s) for your request:**

There are no items to display

General Requirements: The Federal Policy **[45 CFR 46.116 (d)]** specifies in order for a waiver of consent to be approved, the request must meet four criteria. For each request, you will be asked to provide a justification addressing how each of these criterion is met.

[reviewer notes¬]

4.8 **Are you requesting an exception to the requirement to obtain informed consent for research involving the evaluation of an 'emergency' procedure?**

Note: This exception allows research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent.

* No

[reviewer notes¬]

4.9

Upload all consent documents for watermarking:

Draft Consent Forms for editing:

Name	Modified Date
Final Revised Consent for Participation in a Research Study-May 22.docx	1/16/2014 9:24 AM

Approved Consent Form(s):
Name Modified Date

[reviewer notes¬]

4.10 **Will all potential adult subjects be capable of providing direct consent for study participation?**

*
Yes

[reviewer notes¬]

4.11

At what point will you obtain the informed consent of potential research subjects or their authorized representative?

Prior to performing any of the research interventions/interactions

4.11.2

Taking into account the nature of the study and subject population, indicate how the research team will ensure that subjects have sufficient time to decide whether to participate in this study. In addition, describe the steps that will be taken to minimize the possibility of coercion or undue influence.

We will be marketing obesity management/diabetes prevention programs to retirees during the Medicare open enrollment benefits selection period. Essential operational procedures are already in place (marketing materials, mass mailing schedules, "Welcome to Medicare" benefits fairs and health screening events) and this is a naturally occurring annual cycle. Thus, what we will be offering (GLB intervention) may be viewed as complimentary to what these individuals are already seeking (health care) and participation is completely voluntary.

Using this natural infrastructure as a platform for health dissemination efforts will enhance sustainability and magnify public health impact. However, we will make it clear to individuals that there is no obligation to participate in the GLB program and choosing not to do so will in no way affect their other retirement or medical benefits choices.

[reviewer notes¬]

4.12 **Describe the process that you will employ to ensure the subjects are fully informed about this research study.**

* Addressed below:
This description must include the following elements:

- who from the research team will be involved in the consent process (both the discussion and documentation);

- person who will provide consent or permission;
- information communicated; and
- any waiting period between informing the prospective participant about the study and obtaining consent

In addition, address the following if applicable based on your subject population:

- process for child assent and parental permission
  - continued participation if a child subject turns 18 during participation
- process for obtaining proxy consent and assent for decisionally impaired subjects
  - continued participation if subject regains capacity to consent

All members of the research team have potential to be involved in some aspect of the consent process including the PI (Elizabeth M. Venditti, PhD) and/or other Co-Investigators (Marsha Marcus, PhD; Vincent Arena, PhD; Susan Greenspan, MD). In addition research staff members including the Program Coordinator, Elizabeth Cwenar and other staff (listed below) may be involved in consenting and documentation. All persons included on the consent document are listed here:
Marsha Marcus, PhD (412) 246-6372 marcusmd@upmc.edu
Vincent Arena, PhD (412) 624-3023 arena@pitt.edu
Rachel Miller, MS (412) 383-2328 millerr@edc.pitt.edu
Susan Greenspan, MD (412) 692-2476 greenspn@pitt.edu
Elizabeth Cwenar, BS, BA (412) 647-1845 cwenare@upmc.edu
Mary Racek, BSN, MEd (412) 647-1845 racekm@upmc.edu
Kristin Schroeder, MEd (412) 647-1845 schroederk@upmc.edu
Bonnie Gillis, RD, MS, LDN (412) 647-1845 gillisbp@upmc.edu

Non-diabetic, obese retirees aged 65-80, who report at least one additional risk factor for diabetes will be invited to provide informed consent (approximately 320 persons). During an approximate one to three month waiting period in which a single wave of the study is being advertised, individual pre-screening will occur by telephone, at health and benefits fairs as part of the regular Medicare enrollment events, and/or orientation sessions arranged by the investigators and research staff.

The purpose of the pre-screening is to obtain self-reported data from interested subjects regarding their potential eligibility. The pre-screening check-list and/or phone script assesses the following: 1) date of birth, 2) sex, 3) ethnic or racial group 4) retirement status, 5) self-reported weight and height, 6) personal health history and medication use, 7) family health history, and 8) the 7-question diabetes risk test.

We will invite to orientation/informed consent sessions those individuals who self-report a BMI greater than or equal to 27 and at least one additional risk factor including the following: 1) hypertension or taking hypertensive medications, 2) a physician referral form indicating either a large waist circumference (greater than 40 inches men, greater than 35 inches women), low HDL level (less than 40 mg/dL men, less than 50 mg/dL women), high triglyceride level (greater than or equal to 150 mg/dL) and/or fasting glucose greater than or equal to 100 mg dL but less than 126 mg/DL.

Alternatively those individuals with a self-reported BMI greater than or equal to 27 and a score of 15 on the 7-question diabetes risk test will also be invited to come to an orientation/consent session. It will be communicated to all individuals who come to the orientation and consent sessions that a confirmation height and weight (in order to confirm a BMI of greater than or equal to 27) will be collected. Individuals who do not meet that criterion will be referred to other programs available through their Medicare plan or elsewhere in their community

4.13

Are you requesting an exception to either IRB policy related to the informed consent process?

- For studies involving a drug, device or surgical procedures, a *licensed physician who is a listed investigator* is required to obtain the written informed consent unless an exception to this policy has been approved by the IRB
- For all other studies, a *listed* investigator is required to obtain consent (Note: In order to request an exception to this policy, the study must be minimal risk)

* No

If **Yes**, provide a justification and describe the qualifications of the individual who will obtain consent:

4.14 Will you inform research subjects about the outcome of this research study following its completion?

* Yes

If **Yes**, describe the process to inform subjects of the results:
Participants will be mailed a letter from the PI describing the results of the study

[reviewer notes¬]

5.1

Describe potential risks (physical, psychological, social, legal, economic or other) associated with screening procedures, research interventions/interactions, and follow-up/monitoring procedures performed specifically for this study:

*

View

Research Activity:	Assessment Activities
Common Risks:	Fingerstick blood draw -- temporary discomfort with the finger stick Surveys and questionnaires -- minor discomfort answering questions that are personal in nature.
Infrequent Risks:	Fingerstick blood draw -- possible bruising or redness of the skin, lightheadedness, and on very rare occasion infection. Physical function tests -- some lightheadedness or imbalance with gait and balance tests, muscle strain or soreness with the grip strength test, or a rare risk of injury or joint discomfort with any the physical function tests.
Other Risks:	There is a rare risk that a breach of confidentiality could occur; however, every effort is made to prevent this from happening.

View

Research Activity:	Intervention procedures
Common Risks:	It is common for participants to experience hunger, lightheadedness, and/or constipation when reducing their calorie intake.
Infrequent Risks:	The risks associated with exercise occur occasionally (1-10% or 1-10 people in 100) and include fatigue, muscle soreness, and injury such as sprained ankles or pulled muscles. There may be additional risk of heart problems for those who have a chronic disease or experience symptoms with exercise, although this risk is extremely minimal given the intensity of the recommended exercise, i.e., walking. The level of activity that we will recommend for you is thought to be more helpful than harmful, but there is a very small risk of heart attack or sudden death during exercise. Heart attack has been estimated to occur less than once out of 500,000 hours of exercise in people without know heart disease. The risk is greater in people with heart disease. It is important that you contact your physician or HCP before increasing the intensity of your physical activity program or if you develop diabetes, heart disease or other related health problems during this study.
Other Risks:	*No Value Entered*

5.1.1 **Describe the steps that will be taken to prevent or to minimize the severity of the potential risks:**

Although the overall risk to subjects participating in this protocol is minimal we will nonetheless protect subjects from all potential risks in the following manner:

Blood Samples. All study staff will be trained on standard protocols including sterile procedures.

Physical Measurements. Privacy screens (or private areas) will be used during the collection of height, weight and waist data to minimize the possibility that others will be aware of a subject's measurements. In addition all study staff will be trained about the need for sensitivity regarding the stigma of overweight/obesity and how to conduct these measurements in a professional and respectful manner.

Questionnaires, Surveys, and Interviews: Staff will be trained to be sensitive to the risk of participant embarrassment or other psychological discomfort when administering surveys. They will speak with subjects quietly and work to ensure confidentiality of the information in a community setting. In addition, subjects may refuse to answer questions that are

distressing or anxiety provoking and will be provided the opportunity to discuss any question with the Primary Investigator and study staff under her supervision.

Weight Loss and Physical Activity Lifestyle Intervention:

Behavioral intervention involves diet, physical activity, and behavior modification techniques. All participants will be required to receive written medical clearance from their primary care doctor (or other HCP) to participate. The potential benefits of healthy eating and activity are believed to far outweigh the risks. This program recommends a healthy balanced diet, rich in plant based foods, and a regular pattern of meals and snacks (consistent with USDA recommendations), which reduces the risk of lightheadedness or constipation that may occur with calorie restriction. In addition, the potential risks during intervention are minimized by including in the study only those individuals who are of a sufficiently high BMI level (≥ 27) and in sufficient physical condition (confirmed by having physician consent) to participate in the intervention. Risks are reduced by proper warm-up and cool-down periods. All physical assessment staff and lifestyle intervention coaches will be certified annually in CPR and First Aid training. Any injury or complication will be immediately reported and all appropriate emergency procedures will be followed. The PI, the Program Coordinator and Susan Greenspan, MD (a physician co-investigator with areas of expertise in the areas of lipidology, endocrinology, and geriatrics) will be available to help staff make decisions regarding the need for emergent medical care.
In addition, per the Data Safety and Monitoring Plan (DSMP) all adverse events reported during enrollment in the study will be recorded. Each event will be rated for severity (1=mild; 2=moderate; 3=severe; 4=life threatening) and degree of association with study participation (0=definitely unrelated; 1=unlikely, 2=possibly related; 3=probably related; 4=definitely related). The action taken and outcome will also be recorded. Quarterly reports will include frequency of study withdrawals and complete information on all adverse events. Information provided in the quarterly reports will include participant identification numbers, but will not include identifying information such as name. The DSMP quarterly report will be reviewed by Dr. Melissa Kalarchian the designated DSMP officer.

Protection against risk and confidentiality. Subjects will be informed that they are under no obligation to participate in the study and that participation (or non-participation) will in no way influence the terms of their Medicare benefits. They will be informed that they may withdraw at any time. To maintain the confidentiality of participants' responses, all data gathered, questionnaires, screening information and data forms will be coded with a subject identification number only. A separate file with participants' personal information (e.g., name and phone numbers) will be maintained. All participant information will be stored in a locked file cabinet in the research offices of Western Psychiatric Institute and Clinic. Only the Principal Investigator or a staff member supervised by her will have access to participant files. Participants will be reminded of the possibility that, in addition to access given to Dr. Venditti and her research staff, individuals from the agencies funding the research or other appropriate government agencies may be given access to research records. At all times, participant information will be handled in a confidential manner consistent with other research records, and individual names or results will not be specifically identified in any research publication.

5.2

What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the study?

* **Addressed below:**

We will address all emergent medical situations with the study co-investigators or the study clinical pychologist/behavioral scientist as appropriate. The data and safety monitoring plan (DSMP) for this trial focuses on close monitoring by the PI (Elizabeth Venditti, PhD) and Program Coordinator (TBD), in conjunction with an external data safety and monitoring officer (Melissa Kalarchian, PhD). Safety reports will be generated by the PI in conjunction with the statistician and adverse events will be reported promptly to the NIH and the University of Pittsburgh IRB. The Project Coordinator will coordinate this effort and assure that all co-investigators, the safety officer and NIDDK obtain copies of the reports. In addition, Dr. Susan Greenspan, MD, has been added as a co-investigator and member of the research team specifically because of her combined expertise in general internal medicine, endocrinology, and her substantial expertise in monitoring older adults living in the community for osteoporosis and risk of falls (serious and non-serious). She will be consulted by phone as needed with routine data monitoring questions that arise during the recruitment, assessment or intervention phases of the study and immediately in all

emergency situations, including unexpected disease conditions. Participants will be notified as will their primary Health Care Provider (HCP) if they give permission to do so.

5.3 All the risk questions (screening, intervention/interaction, follow-up) have been merged into one question (5.1).

[reviewer notes¬]

5.4 **Do any of the research procedures pose a physical or clinically significant psychological risk to women who are or may be pregnant or to a fetus?**

* No

[reviewer notes¬]

5.5 **Do any of the research procedures pose a potential risk of causing genetic mutations that could lead to birth defects?**

* No

[reviewer notes¬]

5.6

Are there any alternative procedures or courses of treatment which may be of benefit to the subject if they choose not to participate in this study?

* Yes - Describe below:

If **Yes**, describe in detail:
Presently there are not many programs of this kind targeted specifically to Medicare beneficiaries. However, participants may avail themselves of general weight loss and physical activity opportunities in the community at large. Most are oriented toward the general obese population and not diabetes risk reduction per se.

[reviewer notes¬]

5.7

Describe the specific endpoints (e.g., adverse reactions/events, failure to demonstrate effectiveness, disease progression) or other circumstances (e.g., subject's failure to follow study procedures) that will result in discontinuing a subject's participation?

* Not applicable - There are no anticipated circumstances that would lead to discontinuing a subject's participation in this research study.

There are no anticipated circumstances that would lead to stopping this trial

[reviewer notes¬]

5.8

Will any individuals other than the investigators/research staff involved in the conduct of this research study and authorized representatives of the University Research Conduct and Compliance Office (RCCO) be permitted access to research data/documents (including medical record information) associated with the conduct of this research study?

* No

5.9

Has or will a Federal Certificate of Confidentiality be obtained for this research study?

* No

5.10

Question has been moved to 5.17

5.11

Question has been moved to 5.16

[reviewer notes¬]

5.12 **Does participation in this research study offer the potential for direct benefit to the research subjects?**

No - Describe the general benefits to society (e.g., increased knowledge; improved safety; better health; technological advancement) that may result from the conduct of this research study.

Describe the benefit:
There will be general benefit to society in determing feasible, sustainable and effective ways to disseminate evidence based treatments to hi-risk older adults receiving Medicare coverage. Better health and quality of life may result from the conduct of this study.

5.13 **Describe the data and safety monitoring plan associated with this study. If the research study involves multiple sites, the plan must address both a local and central review process.**

DATA SAFETY AND MONITORING PLAN (DSMP)

Introduction

This study evaluates the dissemination of an evidence-based lifestyle intervention program for diabetes risk reduction among Medicare eligible adults, aged 65-80, as well as the utility of a phone compared to newsletter follow-up protocol on observed health outcomes. Subjects are recruited primarily from the retiree pool of a large public university and potentially through other primary care venues serving Medicare participants. The data collected at 0, 4, 12, and 24 months will help evaluate the feasibility and effectiveness of these procedures as they are implemented in the community. The intervention and measurement protocols pose minimal risk to participants. Because of this low risk status, the data and safety monitoring plan (DSMP) for this trial focuses on close monitoring by the PI (Elizabeth Venditti, PhD) and Program Coordinator (TBD), in conjunction with an external data safety and monitoring officer (Melissa Kalarchian, PhD). Dr Kalarchian was chosen because of her experience in behavioral weight management in long term clinical trials with severely obese individuals. Safety reports will be generated by the PI in conjunction with the statistician and adverse events will be reported promptly to the NIH and the University of Pittsburgh IRB. The Project Coordinator will coordinate this effort and assure that all co-investigators, the safety officer and NIDDK obtain copies of the reports. In addition, Dr. Susan Greenspan, MD, has been added as a co-investigator and member of the research team specifically because of her combined expertise in general internal medicine, endocrinology, and her substantial expertise in monitoring older adults living in the community for osteoporosis and risk of falls (serious and non-serious). She will be

consulted by phone as needed with routine data monitoring questions that arise during the recruitment, assessment or intervention phases of the study and immediately in all emergency situations.

Safety Review Plan

Weekly or biweekly research team meetings led by the PI, in conjunction with the PC and research assessment staff will address safety questions and concerns on a case by case basis. Additional case conferences with the study interventionists will also be convened, at a minimum of monthly, to address safety questions or concerns that may arise during the course of the behavior change intervention.

Study data and safety will be reviewed quarterly (and more frequently if needed), as shown in the table below. Progress reports including 1. Adverse events; 2. Safety; 3. Performance measures (recruitment, retention and quality of data); and 4. Intervention (compliance and adherence) will be provided to the Safety Officer following each of the quarterly reviews. An annual report will be compiled and will include a summary of these areas. In addition, the annual report will address the areas detailed in the Safety Officer checklist, including conditions whereby the study might be terminated prematurely. The annual report will be signed by the Safety Officer and will be forwarded to the IRB and NIDDK and other applicable recipients who will review progress of this study on an annual basis.

Reported Information
1. Adverse events will be reported within 24 hours
2. Safety (rate and severity of adverse events) reports wil be produced quarterly
3. Performance (recruitment, retention and quality of data) reports will be produced quarterly
4. Treatment (compliance and adherence) reports will be produced quarterly
5. Stopping rules will be evaluated yearly

[reviewer notes¬]

Section 5 - Potential Risks and Benefits of Study Participation

5.14

What precautions will be used to ensure subject privacy is respected? (e.g. the research intervention will be conducted in a private room; the collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected, drapes or other barriers will be used for subjects who are required to disrobe)

Physical Measurements. Privacy screens (or private areas) will be used during the collection of height, weight and waist data to minimize the possibility that others will be aware of a subject's measurements. In addition all study staff will be trained about the need for sensitivity regarding the stigma of overweight/obesity and how to conduct these measurements in a professional and respectful manner.

5.15

What precautions will be used to maintain the confidentiality of identifiable information? (e.g., paper-based records will be kept in a secure location and only be accessible to personnel involved in the study, computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords, prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information, whenever feasible, identifiers will be removed from study-related information, precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys, audio and/or video recordings of subjects will be transcribed and then destroyed to eliminate audible identification of subjects)

Protection against risk and confidentiality. Subjects will be informed that they are under no obligation to participate in the study and that participation (or non-participation) will in no way influence the terms of their Medicare benefits. They will be informed that they may withdraw at any time even after signing the consent form. To maintain the confidentiality of participants' responses, all data gathered, questionnaires, screening information and data forms will be coded with a subject identification number only. A separate file with participants' personal information (e.g., name and phone numbers) will be maintained. All participant information will be stored in a locked file cabinet in the research offices of

Western Psychiatric Institute and Clinic. Only the Principal Investigator or a staff member supervised by her will have access to participant files. Participants will be reminded of the possibility that, in addition to access given to Dr. Venditti and her research staff, individuals from the agencies funding the research or other appropriate government agencies may be given access to research records. At all times, participant information will be handled in a confidential manner consistent with other research records, and individual names or results will not be specifically identified in any research publication.

5.16

If the subject withdraws from the study, describe what, if anything, will happen to the subject's research data or biological specimens.

If a subject wthdraws from the study we will continue to use the research data that has already been collected.

5.17

Following the required data retention period, describe the procedures utilized to protect subject confidentiality. (e.g., destruction of research records; removal of identifiers; destruction of linkage code information; secured long-term retention)

Investigators may continue to use and disclose identifiable information (which may include identifiable medical information) related to a subjects participation in this research study for a minimum of five years after final reporting or publication of the project. After this point, all subject research records will be completely de-identified (no-link will exist between the partiicpant's name and the assigned research code). Coded data will continue to exist and research reports may continue to be written but all original research records will be destroyed.

[reviewer notes¬]

6.1

Will research subjects or their insurance providers be charged for any of the procedures (e.g., screening procedures, research procedures, follow-up procedures) performed for the purpose of this research study?

*

No

[reviewer notes¬]

6.2 **Will subjects be compensated in any way for their participation in this research study?**

* Yes

6.2.1

Describe the amount of payment or other remuneration offered for complete participation in this research study.

Participants will receive payment for research assessments to help defray costs associated with study participation and to enhance compliance with the assessment schedule ($25 for study months 0 and 4, $50 for month 12, and $75 for month 24). Total costs are not to exceed $175 per individual.

6.2.2 **Describe the amount and term of payment or other remuneration that will be provided for partial completion of this research study.**

as above

[reviewer notes¬]

Supporting Documentation Section

References and Other Attachments

Additional documents:

Name	Modified Date	Version
American Diabetes Association Risk Screen	5/12/2012 1:17 PM	0.01
DOCUMENTATION OF APPROVAL-Crossroads Presbyterian Church Monroeville.pdf	1/18/2013 5:34 PM	0.01
DSMP and quarterly report template	5/16/2012 1:53 AM	0.01
GLB Leaders Guide & All Participant Handouts	5/12/2012 1:28 PM	0.01
GLB Misc Program Handouts	5/12/2012 1:28 PM	0.01
Physician Clearance	5/17/2012 4:45 PM	0.01

Please use the Add button to the left to upload additional documents if needed.

[reviewer notes¬]

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

"Applicable clinical trials" are required **by federal law** to be registered in ClinicalTrials.gov.

Applicable Clinical Trials (ACTs) are studies that meet the following criteria:

- The study is an interventional study AND
- The study intervention is a drug, biologic, medical device, radiation or genetic AND
- The Study is not Phase 0 or 1 AND
- The study has at least one site in the United States or is conducted under an investigational new drug application or investigational device exemption

NIH Policy

Effective January 18, 2017, revised NIH Policy requires that all clinical trials funded in whole or in part by the NIH be registered and results information posted on ClinicalTrials.gov.

As defined by the NIH, a clinical trial is:

> *A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.*

The NIH Policy extends beyond the Food and Drug Administration Amendment Act (FDAAA 801) requirements in that it requires registration and results reporting of:

- clinical trials of behavioral, surgical and other types of health and medical interventions
- phase 1 studies of drugs and biological products
- small feasibility studies of device products

Failure to submit all required registration and results information requested on ClinicalTrials.gov can jeopardize University grant funding, the future funding of the grantee and subject the University of Pittsburgh to future monetary penalties.

In addition, to promote transparency of the clinical trials process, the International Committee of Medical Journal Editors (ICMJE) has established a policy requiring the entry of clinical trials in a public registry, such as ClinicalTrials.gov, prior to subject enrollment as a condition of consideration for publication of the trial results.

* **Based on the above information, will this study be registered in ClinicalTrials.gov?**
Yes

Who will serve as the Responsible Party? UPMC/Pitt Investigator or IND/IDE Pitt Sponsor

Why are you registering your study? (Check all that apply)

It is strongly encouraged by the NIH

It is required for publication by the **International Committee of Medical Journal Editors** (*Registration is required in a publically available, searchable database system prior to informed consent being obtained from the first study participant*)

If you are not yet registered and need to establish an account for the PI or other research staff that may need to access the record, please send an email to the University of Pittsburgh PRS administrator at ctgov@pitt.edu with the following information for each individual:

- Full name
- Telephone number
- Pitt or UPMC email address

If you have any questions or concerns, please email us at ctgov@pitt.edu.

To find out additional information about how to register your study go to:
https://www.clinicaltrials.gov/ct2/manage-recs/how-register