Low-Carbohydrate Diabetes Prevention Program Among Veterans With Prediabetes (VA LC-DPP)

Prepared for ClinicalTrials Resubmission 4/20/21

IRB Application (Version 1.8)

1.0 General Information

***Please enter the full title of your protocol. Be sure to click the ? to the right to ensure the protocol is correctly named.**

A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes

***Please enter the Short Name you would like to use to reference the protocol:**

VA LC-DPP
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this study.

2.0 Add Department(s)

2.1 List departments associated with this protocol:

Primary Dept?	Department Name
◉	**VAAAHS** - CCMR

3.0 Grant research staff access to the protocol

3.1 *Click the "Add User" button to select the protocol's Principal Investigator:

Griauzde, Dina

3.2 Please add all research staff, including co-investigators, support staff, WOC employees and IPA employees:

A) Additional Investigators

Kullgren, Jeffrey T, MD
Co-Investigator

B) Research Support Staff

Hershey, Cheryl
Project Manager/Study Coordinator
Metreger, Tabitha
Research Associate

3.3 *Please add a Study Contact

Griauzde, Dina

Study contact(s) receive all important project notifications along with the Principal Investigator. The most common study contacts are project managers/study coordinators although at times the PI is the only contact.

4.0 VA Ann Arbor Healthcare System IRB Application

Preliminaries

4.1 Is this IRB Protocol Federally Funded?

○ Yes ○ No

4.2 What is the funding source for this IRB Protocol?

4.3 EXEMPTION from further IRB Review

4.4 Are you requesting EXEMPTION from further IRB review?

○ Yes ◉ No

4.18 Expedited Review

4.19 Are you requesting EXPEDITED IRB Review? (There is no need to request expedited review if you have requested an EXEMPTION from further IRB Review.) ***NOTE: Expedited IRB Review does not indicate a faster review process, it simply means that review will take place outside of the convened IRB Meeting.***

○ Yes ◉ No

5.0 Summary Protocol Description

This section consists of a number of short questions that will provide an overview to the IRB and help guide you through the rest of the application.

5.1 PROTOCOL BASICS

5.2 Please include an ABSTRACT (Less than 500 words, organized under these headings: Objectives, Research Plan, Methods, and if a basic science study, Clinical Relevance)

Background / Objectives

Individuals with prediabetes can significantly reduce their risk of developing type 2 diabetes mellitus (T2DM) by achieving at least 5% body weight loss. Behavioral weight loss programs (MOVE!, TeleMOVE) are widely available within the Veterans Health Administration (VHA), but most participants do not achieve 5% body weight loss. This may be due, in part, to the programs' dietary advice, which teach participants to follow a low-fat, calorie-restricted diet. A low-carbohydrate diet may be one promising strategy to augment weight loss among Veterans with prediabetes. Our team previously adapted the Center for Disease Control and Prevention's National Diabetes Prevention Program—a group-based lifestyle change program similar to MOVE!—to teach participants to follow a very low carbohydrate diet (VLCD), defined as 20-35 non-fiber grams of carbohydrate per day. This pilot intervention was feasible, acceptable, and demonstrated preliminary weight loss effectiveness among patients of one academic medicine primary care clinic. It is unknown whether such a program may be feasible, acceptable, or effective for weight loss among Veterans with prediabetes.

The objectives of this single-arm mixed methods pilot study are (1) to test the feasibility and acceptability of a low-carbohydrate Diabetes Prevention Program (LC-DPP) among veterans with prediabetes and (2) to estimate weight loss among LC-DPP participants.

Methods

We will recruit up to 30 patients with body mass index ≥ 25 kg/m2 and prediabetes (defined as hemoglobin A1c [A1c] 5.7-6.4%) from the Ann Arbor VA primary care clinic. Participants will be identified by chart review and invited to participate by postal letter. Individuals that do not opt-out of study contact will be screened for eligibility by telephone call. Interested and eligible participants will be invited to attend an in-person information session. During this session, they will receive information about the dietary intervention; written informed consent will be obtained at this time. Study participants will attend a total of 24 group-based classes over the course of 1-year. Body weight will be measured at each session. At baseline, 6-months, and 12-months, we will measure waist circumference and participants will be asked to complete a survey that includes measures of quality of life, mood, hunger, cravings, and self-reported physical symptoms. Primary outcomes will be feasibility (e.g., enrollment, retention) and acceptability (e.g., session attendance, qualitative feedback). Secondary outcomes will change in weight, achievement of ≥5% body weight loss, and change in A1c. During semi-structured interviewed conducted at 6-months and 12-months, we will explore participants' experiences with the program, barriers to and facilitators of adherence to a low-carbohydrate diet, and perspectives on ways to improve the intervention.

Impact/Implications

Through this study, we will demonstrate the feasibility and acceptability of a LC-DPP among Veterans with prediabetes. These data will inform a large-scale comparative effectiveness trial of LC-DPP versus VA-MOVE.

5.3 What are the research questions or hypotheses to be studied?

Hypothesis #1:
A low-carbohydrate Diabetes Prevention Program (LC-DPP) will be feasible and acceptable among Veterans with prediabetes?

Hypothesis #2:
A LC-DPP can help more Veterans with prediabetes to achieve at least 5% body weight loss compared to existing lifestyle change programs (e.g., MOVE!)

5.4 Describe the relevance to Veterans of studying the stated research questions or hypotheses and the importance of the knowledge this protocol is likely to generate:

Twenty-five percent of Veterans have type 2 diabetes and an estimated 28% have prediabetes, an asymptomatic state characterized by abnormal blood glucose levels and an elevated risk of type 2 diabetes. Modest weight loss (i.e., at least 5%) can substantially reduce the risk of progression from prediabetes to type 2 diabetes. Behavioral change programs for weight loss are available within the VA, but most participants do not achieve clinically-significant weight loss.

Novel and scalable strategies are needed to help more Veterans with prediabetes to lose weight. Through this study, we will demonstrate the feasibility and acceptability of a LC-DPP among Veterans with prediabetes. These data will inform a large-scale comparative effectiveness trial of LC-DPP versus VA-MOVE.

5.5 What is the estimated duration of the entire protocol? (From IRB approval to IRB closure)

2 years

5.6 Check one of the boxes below based on your study design:

- ☐ Prospective Study
- ☐ Retrospective Study
- ☑ Both

☐ Other

5.7 What research methods will be used in the protocol? *(Check all that apply)*

☑ Surveys/Questionnaires
☐ Behavioral Observations
☐ Focus Groups
☐ Control Group
☑ Specimen Collection
☑ Interviews
☑ Chart Reviews
☐ Randomization
☐ Placebo
☐ Deception
☑ Audio Recording
☐ Video Recording
☐ Double-Blind
☐ Withhold/Delay Treatment
☐ Other (Specify)

Other:

5.8 Indicate whether or not each of the following applies to this protocol:

Does the Protocol involve international research?
NOTE: International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA Investigator.

○ Yes ◉ No

The protocol includes interaction between research staff (or clinicians acting on behalf of the researchers) and human subjects.

◉ Yes ○ No

This protocol involves the use of retrospective data, including, but not limited to, data from CDW and CMS.

◉ Yes ○ No

This protocol includes **ONLY** retrospective data use.

○ Yes ◉ No

A data repository will be maintained, i.e. data will be retained after completion of the protocol for other uses. (see ? for more details)

○ Yes ◉ No

The **ONLY** subjects will be providers or staff.

○ Yes ◉ No

Protocol is a clinical trial. (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 the interventions on biomedical or behavioral health-related outcomes.) Please see Help (?) on the right...

The Ann Arbor IRB is ONLY responsible for providing oversight of research activities conducted either at 1) the Ann Arbor VA, 2) at a site with whom there is a contract to use space or equipment by Ann Arbor Investigators while on VA time, or 3) a site without its own IRB that has established an MOU for the Ann Arbor IRB to serve as the IRB of record. As you complete this form, CONFINE DETAILED DESCRIPTION TO THESE ACTIVITIES.

○ Yes ◉ No

This protocol involves collaborative research activities conducted at both VAAAHS and other sites, VA or non/VA.

○ Yes ◉ No

5.12 USE OF HUMAN SPECIMENS

5.13 Indicate whether or not each of the following applies to this protocol

The protocol involves the use or collection of human specimens.

◉ Yes ○ No

Involves specimens that are left over from pathological or diagnostic testing (**non-research specimens**).
(Please attach a copy of the approval from the Chief of Pathology to use these specimens.)

○ Yes ◉ No

Involves **specimens collected for research** purposes **only.**

◉ Yes ○ No

This protocol includes **specimen banking** (specimens are retained for use outside of the purposes of this protocol).

○ Yes ◉ No

5.14 DRUGS AND DEVICES

5.15 Will the protocol include the use of any drugs?

○ Yes ◉ No

5.16 Will the protocol include use of any medical devices?

○ Yes ◉ No

5.17 RISKS

5.18 Indicate whether or not each of the following applies to this protocol (see ? for a definition of minimal risk)

Protocol places subjects at **greater than minimal risk** (do not include risks that are due to standard care)

○ Yes ◉ No

Human subjects are exposed to **radioisotopes.** Do not include standard care.
*Please contact the Radiation Safety Officer x53406 as soon as possible to see if any other safety mandates must be met.

○ Yes ◉ No

Subjects have other **radiation exposure** (e.g., x-rays). Do not include standard clinical use.
*Please contact the Radiation Safety Officer x53406 as soon as possible to see if any other safety mandates must be met.

○ Yes ◉ No

5.19 MEDICAL PROCEDURES

5.20 Indicate whether or not each of the following applies to this protocol

Findings from medical procedures already being performed as part of standard medical care will be used for research data collection.

○ Yes ◉ No

Protocol involves medical interventions or clinical services that are **NOT** part of standard care.

◉ Yes ○ No

Protocol involves invasive procedures, e.g. muscle biopsy, bronchoscopy.

○ Yes ◉ No

5.21 SUBJECT EXPENSES AND COMPENSATION

5.22 Indicate whether or not each of the following applies to this protocol

There may be expense or added **costs to the subject** or the subject's insurance.

○ Yes ◉ No

Subjects will be **compensated,** either in cash or other means such as a gift certificate.

◉ Yes ○ No

5.23 OTHER RESEARCH ACTIVITIES

5.24 Indicate whether or not each of the following applies to this protocol

Involves **surveys or questionnaires** completed by subjects

◉ Yes ○ No

The protocol includes the use of interviews and/or focus groups.

◉ Yes ○ No

Involve audio recordings of subjects.

◉ Yes ○ No

Includes the use of **recruitment materials** such as flyers, advertisements, emails or letters.

◉ Yes ○ No

Involves facial **photographs** or video **recordings** of **patients.**

○ Yes ◉ No

5.25 USE OF HAZARDOUS MATERIALS

5.26 Does the protocol include the use of any of the following?

- **Human tissue, blood, other body fluids (collected and/ or tested by non-clinical staff)**

- **Ionizing Radiation**
- **Biological Agents (microbiological, viral or plant agents, pathogens, toxins, poisons, or venoms)**
- **Chemicals (toxic, flammable, explosive, corrosive, carcinogenic, neurotoxins)**
- **Recombinant DNA**
- **Non-Human Cell Lines and Tissue Culture**
- **Physical Agents (UV light, lasers, radio-frequency or microwaves, electricity, trauma)**
- **Controlled Substances**

Do NOT include any Standard of Care activities performed by Clinicians. The following boxes should only be checked if Research Personnel will be involved in the activity. **If you checked YES... Please go to your Protocol Assistant and Create a New Protocol => VA Laboratory Safety Hazard Assessment Form.** **(This New form will go through the Research Safety Committee.)**

○ Yes ◉ No

5.27 CATEGORIES OF SUBJECTS REQUIRING SPECIAL ATTENTION

5.28 For each of the special categories of subjects listed below, indicate whether or not you plan to recruit them as part of your protocol. Exclude cases of data or specimens only.

Individuals with Impaired Decision Making Capacity

○ Yes ◉ No

Economically or educationally disadvantaged

○ Yes ◉ No

Pregnant Women - Check this box if your protocol will target pregnant women for recruitment, for studies in which the risk level is greater than mininal and pregnant women are not excluded, or for any protocol in which there may be increased risk to the mother or fetus due to study interventions or procedures.

○ Yes ◉ No

Prisoners - Check this box if your protocol involves prisoners as potential participants or if you are submitting a Request for an Amendment (and revising your IRB application) if a subject becomes a prisoner during the course of the study and it has been determined it is in the best interest of the subject to continue in the study.

○ Yes ◉ No

Non-Veteran patients (Note: A justification will be required later in the application form)

○ Yes ◉ No

VA employees (or WOCs) as the subject of the protocol. This does not include patients who also happen to be employees of the VA.

○ Yes ◉ No

Other non-Veterans (e.g. patient family members)

○ Yes ◉ No

6.0 Design and Methods

6.1 MEDICAL PROCEDURES AND USE OF CLINICAL SERVICES

6.2 Describe any use of medical procedures used in the protocol that are not part of standard therapeutic care of the subject .

(Note: this differentiation should be clear in the consent form as well)

Patients will have 5 ml of blood drawn at baseline, 6, and 12 months to test HbA1c and cholesterol. Patients will also have waist circumference measured at baseline, 6, and 12 months.

6.3 Could any of the interventions interfere with other care the subjects are receiving or may receive.

○ Yes ◉ No

6.4 Describe any usual healthcare procedures already being performed for diagnostic/treatment purposes that will be used for research data collection.

not applicable

6.5 For each research laboratory test (not lab tests used as part of standard care), identify the test and indicate if the test results will or will not be used clinically for diagnosis, treatment, or prevention of disease.

HbA1c, cholesterol, and waist circumference tests will not be used clinically for purposes of this study. However, results will be provided to patients' primary care providers and we will follow up with the PACT nurse and PCP when tests indicate a concern such as results in the diabetes range. A progress note will be entered into CPRS and the PACT nurse and PCP will be added as additional signers.

6.25 HUMAN SPECIMENS

6.26 Identify biological materials that will be used, their source, and procedures for obtaining material:

5 mL of blood will be obtained from each participant via intravenous blood draw at baseline, 6 months and 12 months, which corresponds to LC-DPP sessions 16 and 24. Blood samples will be used to test hemoglobin A1c and lipid levels.

The laboratory tests will be ordered by the study PI (Dina Griauzde, MD).
Dr. Chensu has approved the use of laboratory staff to obtain and process these tests using standard laboratory resources. Study team members will not handle any of the specimens. Email correspondence with Dr. Chensu is included as an attachment.

To avoid duplicate testing, we will accept these laboratory tests if ordered by participants' PCPs 2 weeks prior to the study-specific testing window.

6.27 Describe how and where tissues will be stored:

Specimens will be handled according to routine laboratory procedures.

6.30 Does the protocol involve genetic testing?

○ Yes ◉ No

6.33 Will samples be de-identified to maintain confidentiality? *NOTE: Coded specimens are not considered de-identified.*

○ Yes ◉ No

6.35 Will participants be informed of the results of the specimen testing?

(•) Yes ( ) No

6.36 What measures will be taken to minimize the potential for physical, psychological, financial, social, or legal harm from breaches of confidentiality and privacy resulting from unauthorized access to or loss of the specimens?

Biologic specimens will be handled according to routine laboratory procedures by laboratory staff.

6.37 Will specimens be destroyed after the protocol-specific use is completed?

(•) Yes ( ) No

6.38 Describe how the destruction of samples will be substantiated:

Specimens will be destroyed according to routine laboratory procedures by laboratory staff. These processes are identical to those performed as part of routine clinical care for patients that have blood drawn at the AAVA.

6.40 SURVEYS, QUESTIONNAIRES, FOCUS GROUPS AND INTERVIEWS

6.41 Describe any externally validated survey instruments that will be used, along with reference(s) to any published material about them. Also describe other questionnaires and/or surveys that will be used. Attach copy of each instrument to the Initial Protocol Submission Form.

We will use the following validated instruments:

1. Control of Eating - Cravings subsection:
Dalton M, Finlayson G, Hill A, Blundell J. Preliminary validation and principal components analysis of the Control of Eating Questionnaire (CoEQ) for the experience of food craving. 2015.

2. Stress Eating:
- Tsenkova, V., Boylan, J. M., & Ryff, C. (2013). Stress eating and health. Findings from MIDUS, a national study of US adults. Appetite, 69, 151-155.
- Burgess, E. E., Turan, B., Lokken, K. L., Morse, A., & Boggiano, M. M. (2014). Profiling motives behind hedonic eating. Preliminary validation of the Palatable Eating Motives Scale. Appetite, 72, 66-72.

3. Health and wellbeing: PROMIS Health Organization and PROMIS Cooperative Group, 2008-2012.
https://www.iconquerms.org/sites/all/files/attachments/pdfs/PROMISGlobalHealthScaleV1.0-1.1.pdf

4. Social Support:
- Norman, G. J., Carlson, J. A., Sallis, J. F., Wagner, N., Calfas, K. J., & Patrick, K. (2010). Reliability and validity of brief psychosocial measures related to dietary behaviors. International Journal of Behavioral Nutrition and Physical Activity, 7(1), 56.

5. Locus of motivation (e.g., internal vs. external)
- Williams et al. Health-Care, Self-Determination Theory Questionnaire Packet via selfdeterminationtheory.org

6. Physical activity:
- Craig et al. International Physical Activity Questionnaire: 12-Country Reliability and Validity. 2003.

7. Fatigue and Sleep:
- Kemper-Gascon, Global Health and Well-being. The Ohio State University. (See PDF)

We will also explore energy levels between meals and experiences with the program using non-validated question items and ask patients to complete diet and exercise logs.

See attached Excel file for summary of question items.

6.42 Describe in detail the interviews and/or focus groups that will be conducted as part of this protocol. Include information about the subjects, setting and topics. Include any information regarding the likelihood of the interview/focus group causing significant anxiety in a subject. Attach a copy of the interview and/or focus group guide(s) to the Initial Protocol Submission Form.

We will conduct semi-structured interviews with patient participants. Patients (n=up to 30) will be purposively sampled based on weight loss outcomes (e.g., achievement vs. non-achievement of at least 5% body weight loss). We will explore participants' experiences with the program and barriers to and facilitators of adherence to the diet.

We plan to interview LC-DPP coaches and Primary care providers (PCPs) in the future. However, this component of the study is not yet fully developed. An amendment will be submitted and we will obtain approval for all recruitment activities and materials prior to commencement of these interviews.

6.43 PHOTOS AND/OR AUDIO/VIDEO RECORDINGS

6.44 Describe the protocol's use of audio recordings of subjects. Include details on equipment to be used and the protection of the resulting files.

Individuals specified in section 6.42 will be interviewed by telephone or in-person. Interviews will be audio-recorded using the Olympus DS-7000 after written informed consent is obtained. If an individual does not wish to be audio recorded, we will take detailed written notes instead. To protect individuals' privacy, we will not record individuals' names. Rather, each interviewee will have a unique participant ID. A crosswalk file linking participant ID to identifying information will be maintained in a HiPAA secure, password-protected file. Interviews will be professionally transcribed verbatim and the audio files will then be destroyed.

6.54 EXPENSES & COMPENSATION

6.55 Describe specifically which procedures/drugs will be billed to the participant (or the participant's insurance) and which will be provided at no cost. Include a justification for expenses to the subject. See ? for more detail.

None.

6.56 Provide all details and justifications of the compensation plan. See ? for detailed requirements.

- **What form of payment will be used, i.e., check, voucher, electronic funds transfer, gift card?**
- **What is the schedule of payments, I.e., one-time or after specific visits?**
- **Provide justification that the proposed payments are reasonalbe and commensurate with the expected contributions of the participant to the protocol.**
- **Will the payment include transportation costs? If no, will transportation costs be paid separately?**
- **Specify the source of payment - VAAAHS, UM, Other...**

Participants will receive Visa and/or Amazon gift cards ($25 each) to compensate them for their time after completing the following study activities:
- Baseline labs
- 6-month survey
- 6-month labs
- 6-month interview
- 12-month survey
- 12-month labs
- 12-month interview

6.57 Will an SSN be requested and/or used in making payment/compensation? *Note: If yes, be sure and include in the HIPAA authorization form and in the informed consent the name of the organization making payment to include any VA-affiliated Non-profit Corporation or other non-VA entity.*

○ Yes ◉ No

6.58 RETROSPECTIVE DATA USE

6.59 Describe in detail all sources of retrospective data that will be used by the protocol.

Retrospective data will be used for screening only. Data from VA medical records will be obtained via the Clinical Data Warehouse (CDW) to identify patients with prediabetes. We will look at data for patients seen at VAAAHS in the past year (May 2019- May 2020). We will not review identified data of individuals in the VA MOVE program. Rather, there have been many published reports of VA MOVE program outcomes and we will compare our data with published VA MOVE! data as well as data from similar programs (e.g., Center for Disease Control and Prevention's National Diabetes Prevention Program).

7.0 Special Human Subject Categories

8.0 Recruitment

8.1 Describe the inclusion criteria for this protocol, along with the rationale for these criteria. This includes retrospective chart reviews. *Use bullet or numbering format.

We will recruit Veterans from AAVA primary care clinics.

Inclusion criteria:
- Age >= 18 years
- Prediabetes (defined as A1c 5.7% to 6.4% drawn within 12 months of study start date)
- Lipids drawn within 12 months of study start date
- Body mass index >= 25 kg/m^2
- Willingness to participate in group-based classes
- Able to engage in at least light physical activity such as walking
- Established primary care at the AAVA (defined as at least one office visit within 12 months of the study start date). This will ensure that participants can have access to a medical provider for medication changes and side effective management, if necessary.

We plan to interview LC-DPP coaches and Primary care providers (PCPs) in the future. However, this component of the study is not yet fully developed. An amendment will be submitted and we will obtain approval for all recruitment activities and materials prior to commencement of these interviews.

8.2 Describe the exclusion criteria for this protocol (including retrospective chart reviews). Include the rationale for excluding any patients who might particularly benefit from participation. Also address whether subjects enrolled in another protocol are excluded. *Use bullet or numbering format.

Exclusion criteria are:

- History of type 1 diabetes or type 2 diabetes
- Current participation in another lifestyle or behavior change program or research study
- Vegetarian or vegan lifestyle
- History of bariatric surgery
- Inability to read, write, or speak English
- Inability to provide informed consent
- Women who are pregnant or intend to become pregnant during the intervention period
- Individuals with LDL>190
- Individuals with a history of eating disorders
- Individuals with advanced kidney disease (defined as eGFR < 45 mL/min)

8.3 Will there be more than one group/type of subject recruited for the protocol?

○ Yes ◉ No

8.4

Describe the recruitment strategy for the just, fair, and equitable recruitment and selection of subjects, and reference recruitment procedures as cited in the scientific narrative to include the following: Plans for recruitment of all subjects (or selection of subjects as in record review). This description must include:

- **How, when, and where (include the exact location) the potential subjects are approached**
- **Description of different groups/types of subjects**
- **The maximum number of each subject group planning to enroll and whether the protocol will have access to a population with this number.**
- **Recruitment procedures such as data mining, physician referral, etc.**
- **How selection is equitable.**

NOTE: VA policy prohibits "cold calls" to potential VA research participants. Initial contact must be made in person or by letter prior to making any telephone contact, unless there is written documentation that the subject is willing to be contacted by phone about the specific study or the specific kind of research. The initial telephone contact must also provide a telephone number or other means for the potential participant to use to verify the study constitutes VA research (VHA Directive 1200.05).

Eligible patients will be sent a letter inviting them to participate in the study. We estimate that 10% of eligible individuals will enroll in our study. Thus, we will send study invitation letters by postal mail to up to 220 potentially eligible individuals. The letter will explain the purpose of the study. A phone number will be provided to individuals to allow for them to opt-in to study participation or opt-out of future contact by the study team. A member of the study team will contact individuals who opt-in. The study team member will confirm individuals' study eligibility and answer any questions. If up to 30 veterans are not recruited via the opt-in approach, a member of the study team member will call those individuals that did not opt-out within 3 weeks of the letter being sent; these individuals will be invited to participate.

All interested and eligible individuals will be invited to attend the in-person recruitment session. The purpose of this session is to conduct the informed consent process. We will explain the program and dietary approach (i.e., low-carbohydrate, high-fat) in detail and obtain written informed consent. In our prior pilot work at Canton Health Center, program participants informed us during qualitative interviews that they wished for additional education about the dietary approach to alleviate concerns regarding dietary fat and cholesterol intake. Because this is information that participants should, ideally, understand as part of the informed consent process, we will deliver a brief presentation (~20-30 minutes) as part of the recruitment session. An additional 20-30 minutes will be allocated to answering individuals' questions. Afterwards, those still interested in study participation will be asked to provide written, informed consent. Once written informed consent is obtained, they will be asked to complete a baseline survey.

A progress note will be entered into CPRS with the PACT nurse and PCP added as additional signers once an individual has enrolled in the study. We will also upload the signed consent form into the medical record.

8.5 **Identify all recruitment materials (flyers, advertisements, letters, etc.) that will be used. This should include how and where (VA, non-VA) the materials will be circulated/displayed. The text of all communications with prospective participants must be reviewed and approved by the IRB before they can be used.** ***If there will be telephonic contact during the recruitment process, a script must be provided for review.*** **Please attach copies of recruitment materials to the Initial Protocol Submission Form.** ***NOTE: All recruitment materials must be reviewed and approved by the IRB prior to use as part of any recruitment activities. All recruitment materials must include a statement that the study involves VA Research and a telephone number or other means for the potential participant to use to verify that the study is VA Research.***

Recruitment will be done via a letter and telephone follow-up/outreach. These documents have been attached for the committee's review.

We plan to interview LC-DPP coaches and Primary care providers (PCPs) in the future. However, this component of the study is not yet fully developed. An amendment will be submitted and we will obtain approval for all recruitment activities and materials prior to commencement of these interviews.

9.0 Risks and Benefits

9.1 **Describe and assess any potential or known risks and discomforts, including possible loss of confidentiality, and assess their likelihood and seriousness. Also describe precautions to decrease the likelihood of harm and procedures to deal with harms if they occur.** ***NOTE: Risks or harms can be physical, financial, social, or legal. They may involve breaches of***

confidentiality and privacy. Do not include the risks of usual care unless usual care is part of the research interventions being performed.

Physical

A low carbohydrate diet may cause side effects, particularly during the first several weeks. These include:

1. Constipation: this is a common side effect, which will be managed by instructing individuals to increase their consumption of water and low-carbohydrate, fiber-rich foods such as leafy greens.

2. Headaches: this is a likely side effect, which will be managed by instructing individuals to increase their water and salt consumption.

There is also a small risk patients may experience harm or injury if they increase their physical activity as a result of taking part in this program.

Psychological - (For Example: Loss of privacy and confidentiality may cause psychological issues.)

There is a potential risk of loss of data confidentiality, which could have psychological risks. We will mitigate this risk by using a secure, HIPAA compliant, crosswalk file linking participant IDs and direct identifiers.

Participants may be concerned about their risk for developing type 2 diabetes. We will ease their anxiety by emphasizing that type 2 diabetes is a preventable condition and that this intervention is one way to help them to reduce their risk.

Social and economic - (For Example: Loss of confidentiality may cause social or economic duress though the unlikely risk is low.)

There is a potential risk of loss of data confidentiality, which could have social or economic consequences, although this risk is low.

9.2 Describe any risk of discovering abnormal findings and how you will inform the subject and/or the subject's primary care provider.

We will obtain HbA1c and lipid levels at 6 months and 12 months. If these tests are abnormal, participants' PCPs will be notified via the electronic health record. Additionally, participants will be sent a letter informing them of their test results so that they can also arrange for appropriate follow-up care. This letter will be submitted with a future amendment prior to the start of study recruitment.

9.3 Indicate the level of risk you believe this protocol has: (The IRB will make the final risk level determination.)

- (•) Minimal Risk
- ( ) Greater than Minimal Risk

9.4 Discuss benefits that may be gained by the subject as well as potential benefits to society in general. (see ? for guidance)

The risks of the intervention are minimal and side effects are completely reversible if an individual discontinues the low-carbohydrate diet. In contrast, there is a great potential benefit to this intervention, as the dietary advice may help study participants to lose weight and decrease their risk of type 2 diabetes.

9.5 Describe the availability of resources subjects may need as a consequence of their participation, including medical and mental health services (e.g. ER, hotlines, clinical staff available).

Study participants will be provided with the phone number of the PI to contact with any concerns raised

due to participation in the program.

9.6 Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.

The risks are minimal relative to the potential benefits. The probability and magnitude of risks of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. In addition, the potential benefits of preventing type 2 diabetes is significant.

9.7 Briefly describe the procedures or explain why there is no need for established procedures for the orderly withdrawal or termination of participation in the protocol by the participants:

Participants will notify the study team if they desire to withdraw from the study. Study team members will explore and document reasons for withdrawal. No data will be collected from participants after they withdraw from the study. Data collected prior to their withdrawal will be used in analyses.

The PI reserves the right to withdraw participants from the study for any of the following reasons:

•She believes that it is not in their best interest to stay in the study.
•They become ineligible to participate.
•They do not follow instructions.
•Their behavior toward the staff or other participants is disruptive or inappropriate.
•The study is suspended or canceled.

Please note that patients do not have to follow a low-carb diet to remain in the study. Weight loss is our measure of dietary adherence.

9.9 The procedures regarding reporting adverse events and protocol deviations/violations to the IRB should be described. If these are adequately described in your DSMP/DSMB, there is no need to duplicate the information here. In these cases, please attach a copy to the Initial Protocol Submission Form.

All serious adverse events, unanticipated problems, and protocol deviations will be reported to the IRB according to VAAAHS policy. Please see narrative for DSMP.

9.10 The Principal Investigator and the Study Team will report all adverse event, complaints, problems and non-complicance according to this VAAAHS policy and using the appropriate form (Adverse Event Reporting Form can be found in the upper right corner in the Help (?) Section). *Do not submit in AAROW. Please contact IRB Coordinator to discuss x53440.

◉ Agree

10.0 Informed Consent and HIPAA Authorization

10.1 Informed Consent Process and Waivers

10.2 The baseline assumption is that before ANY research procedures are conducted, all subjects will:

1. **Participate in an informed consent process;**
2. **Including all required elements ;**
3. **Using a signed consent form.**

Because many protocol designs make this difficult or impossible, VHA Directive 1200.05 - "Requirements for the Protection of Human Subjects in Research" allows two types of informed consent waivers: The first (Section 18 of 1200.05) waives the requirement to get SIGNED informed consent. This waiver does NOT waive the requirement for an informed consent PROCESS. The second type of waiver (Section 17 of 1200.05) allows a protocol to alter or omit some or all of the elements of informed consent OR to waive the requirement to obtain informed consent. HIPAA waivers and authorizations apply to all research subjects in which the Ann Arbor investigators will use or

disclose PHI. *VAAAHSis a Covered Entity and HIPAA Rule applies regardless if it is VA patients or not. It is STRONGLY suggested that you see ? for 1) policy language, 2) guidance for use of consent waivers, and 3) a list of the required elements of consent stipulated in VHA Directive 1200.05.

10.3 Will the Study Team obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the prospective subject's Legally Authorized Representative (LAR)?

(•) Yes ( ) No

If yes, check one or both of the below boxes if they apply to this study:

- [ ] Information will be obtained through oral or written communication with the prospective subject or the subject's Legally Authorized Representative (LAR)
- [x] Identifiable information or biospecimens will be obtained by accessing records or stored identifiable biospecimens

Please describe how this will be done:

If either or both of the above boxes is checked, an informed consent waiver request does not have to be submitted for this activity. However, a request for a HIPAA waiver will still need to be submitted and informed consent obtained for any research interventions after eligibility is established. ***If neither box was checked, this activity will need to be included in a request for an informed consent waiver.***

10.4 Which of the following options will be utilized to address informed consent requirements for all subjects, at all phases of the protocol? This section of the application form applies only to subjects who are participating in research that is overseen by the Ann Arbor VA IRB.

- [x] Signed VA Consent Form
- [ ] An alteration to the informed consent process. NOTE: If deception is involved, this box should be checked.
- [ ] Waiver of documentation of informed consent (using a Research Information Letter or other approved mode of communication)
- [ ] Waiver of informed consent process for the entire study
- [ ] Waiver of informed consent process for only a specific portion(s) of the study (not including recruitment)
- [ ] None of the above

What is the maximum number of subjects to be enrolled with a signed VA Consent Form?

30

10.5 USE OF VA CONSENT FORM

10.6 Consent will be obtained before any protocol procedures, including screening, are performed unless the IRB has granted a waiver of the informed consent process for either phase.

(•) Agree

10.7 Information being communicated to the participant or legally authorized representative during the consent process will not include exculpatory language through which the participant or legally authorized representative is made to waive or appear to waive any of the participant's legal rights or release or appear to release the Researcher, Sponsor, the VA or its agents from liability for negligence.

(•) Agree

10.8 **Identify the circumstances under which consent will be obtained including where the process will take place; any waiting period between describing the research and obtaining consent including sufficient time for the prospective participant to consider participation, and any steps taken to minimize the possibility of coercion or undue influence.**

We will obtain written informed consent at the recruitment session, as described in section 8.4. We will convey that all survey questions and interviews are voluntary and that participants are able to withdraw at any time for any reason without fear of repercussions. Prior to each interview, we will review each interviewee's rights as a research subject and reiterate their right to:
- Refuse to participate
- Refuse to answer any questions for any reason
- Refuse to have the interview recorded for the partial or full duration

Details on recruitment and consent for staff interviews will be submitted with a future amendment.

10.9 ***Reminder - If the research involves photos, videos, or voice recordings of a VA participant, then this information must be covered in the informed consent process and consent documents (VA Consent Form, Research Information Letter, Telephone Screen Scripts, etc...).***

10.33 **HIPAA AUTHORIZATIONS AND WAIVERS**

10.34 ***NOTE: Written HIPAA authorization signed by the individual to whom the information or record pertains is required when VA health care facilities need to utilize individually-identifiable health information for a purpose other than treatment, payment, or health care operations, e.g., research. (VHA Handbook 1605.1).***

10.35 **Does the protocol use any health information? Please note that the VA takes a broad definition of health, extending to any information that could reasonably be considered related to health.**

(•) Yes ( ) No

10.37 **Does the protocol use any health information with personal identifiers that the protocol staff has access to?**

(•) Yes ( ) No

10.38 **Is any waiver of HIPAA authorization being requested?**

(•) Yes ( ) No

10.39 **Criteria to be Eligible to Submit a Waiver Request: The Principal Investigator must check that the proposed research meets all of the following criteria in order to be eligible to submit a request (you will also need to describe how they are being met in your scientific narrative):**

- [x] The use of disclosure of protected health information involves no more than minimal risk to the privacy of the individuals.
- [x] There is an adequate plan to protect the participant identifiers from improper use and disclosure.
- [x] There is an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers, or such retention is otherwise required by law.
- [x] The research cannot be practicably conducted without the waiver.
- [x] The research cannot be practicably conducted without access to and use of the protected health information.

- [x] The protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research prototocol, or for other research for which the use or disclosure of the requested information would be permitted under the HIPAA Privacy Rule.

10.40 Check all of the following that apply if Protected Health Information (PHI) will be used:

- [x] A protocol specific HIPAA Authorization is combined with the informed consent document.
- [ ] A separate protocol specific participant HIPAA Authorization form (VA Form 10-0493) is attached. Note: This is required when enrolling individuals with impaired decision making or with longitudinal studies requiring reconsent.
- [ ] A HIPAA Waiver of Individual Authorization is being requested to cover the entire study.
- [x] A HIPAA Waiver of Individual Authorization is being requested for recruitment purposes only.
- [ ] A HIPAA Waiver of Individual Authorization is being requested to cover a portion of the study.

Specify portion of study the request for HIPAA Authorization is being reqested for:

We need to obtain PHI to determine which patients are eligible for participation. Without the waiver, we would need to send letters to thousands of patients (who might or might not be eligible) to ask their permission to access their medical record data to determine their eligibility for the study, which would be highly impractical.

10.41 Indicate the sources of the health information the protocol will be using:

- [x] Medical records
- [ ] Images or audio recordings
- [ ] Biological specimens

Provide any details necessary to fully describe the sources of PHI:

We will use medical record data (e.g. HbA1c) to screen for eligibility for study participation. We need to review HbA1c data to determine potential eligibility for the study, as individuals must have HbA1c's within the prediabetic range.

10.42 Indicate the PII to be collected, used, and/or disclosed.

- [x] Names
- [x] Any geographic area smaller than a state
- [x] Any date (except year) that is directly related to an individual and/or any age over 89
- [x] Telephone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [x] Social Security Numbers (SSNs) or scrambled SSNs
- [x] Medical record numbers
- [ ] Health plan beneficiary numbers
- [ ] Account numbers
- [ ] Certificate and/or license numbers
- [ ] Vehicle ID and serial numbers including license plate numbers
- [ ] Device identifiers and serial numbers
- [ ] Web Universal Resource Locators (URLs)
- [ ] Internet Protocol (IP) addresses
- [ ] Biometric identifiers, including finger & voice print
- [ ] Full-face photographic images and any comparable images
- [x] Any other unique identifiers (number, characteristic or code)

Please explain the other unique identifer(s).

As data will be collected from CDW, PatientICNs will also be collected.

10.43 **Will the protocol access or collect any of the following Protected Health Information that requires higher levels of confidentiality?**

- **Alcoholism or alcohol abuse information**
- **Drug abuse information**
- **Sickle cell anemia information**
- **HIV test/infection results**

○ Yes ◉ No

☐ Alcoholism or alcohol abuse information
☐ Drug abuse information
☐ Sickle cell anemia information
☐ HIV test/infection results

10.44 **Identify all Protected Health Information (PHI) that you will access or collect for use in this research protocol:**

☑ Progress notes
☐ History & physical
☐ Discharge summary
☐ Operative reports
☑ Diagnostic/Laboratory Reports
☐ Imaging (x-ray, CT, MRI, etc.)
☐ Immunizations
☑ Allergy reports
☑ Medications
☐ Consultations
☑ Clinic notes
☐ Dental notes
☐ Mental health (not psychotherapy) notes
☐ Psychologial test results
☐ Genetic testing
☐ Survey/questionnaire responses
☐ Billing records
☑ Other PHI to be used

Specify any other PHI to be collected.

Problem list diagnoses

10.45 **Provide details on the items checked above and describe any other types of PII/PHI that will be used.**

As noted above in the description of inclusion and exclusion criteria, these data will be used to determine if patients meet the following criteria: BMI >= 25 and HbA1c 5.7%-6.4% in the prior 12 months.

10.46 **Specify the date range(s) of all PII/PHI to be collected.**

April 2019 - April 2020

10.47 **The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals.**

◉ Agree

Explain why risk is no more than minimal

We have extensive experience maintaining the confidentiality of PHI for research purposes. A cross-

walked file will be maintained to link participants to unique, de-identified study IDs. The crosswalk file will be kept in a separate, secure folder. Access to this folder will be restricted to study team members. All data will
be maintained in restricted folders on the VA network.

10.48 A plan exists to move all identifiable data to a location accessible only to the Research Service Records Liaison or an honest broker at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law. These records will be disposed of when they have met their Records Control Schedule or other contractual obligation, whichever is longest.

◉ Agree

Describe the plan:

All research data will be de-identified at the termination of the study, if not sooner. Study data will be moved to the CCMR data archive and destroyed by the CCMR data manager six (6) years following the end of the Fiscal Year after completion of the research project as described in the Records Control Schedule.

10.49 The plan to protect the identifiers from improper use and disclosure is adequate.

◉ Agree

Describe the plan:

Protection of screening data: A cross-walk file will be established that includes patient names linked to study ID numbers assigned by the CDW. Unique study ID numbers are needed to link multiple records for a patient in CDW. The cross-walk file will be kept in a folder on the VA network that is restricted to access by members of the study team. The study ID number will be maintained with the health data pulled from CDW in a separate, access restricted folder on the VA network.

Protection of patients' data following screening: Once we randomly select 220 eligible patients, we will create a separate folder that includes these patients' names, addresses, and phone numbers, but no health data. These data will be maintained in an access-restricted folder on the VA network. Interview responses will not include any patient identifiers.

10.50 The research could not practicably be conducted without access to and use of the PHI.

◉ Agree

Describe how the PHI access/use under the waiver enables the conduct of the research

We need access to PHI to identify the appropriate subset of patients (who meet are eligibility criteria for pre-diabetes) to whom we can send recruitment letters.

10.51 The research could not practicably be conducted without the waiver.

◉ Agree

Describe how the waiver/alteration enables the research to be conducted:

We need access to PHI to identify the appropriate subset of patients (who meet are eligibility criteria for pre-diabetes) to whom we can send recruitment letters.

10.52 By Signing this protocol for submission, the Prinicipal Investigator acknowledges the following:

1. The information listed in this waiver application is accurate and all the research protocol staff will comply with HIPAA regulations and the criteria set forth in this request.

◉ Agree

2. The protected health information described above is the minimum necessary in order to conduct the research.

◉ Agree

3. The requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would permit.

◉ Agree

11.0 Alternatives to Participation

11.1 Describe the alternatives to participation in this research protocol (see ? for guidance)

Participation in this research study is voluntary. Eligible individuals may choose to instead engage in other lifestyle change programs for weight loss (e.g., MOVE!) or to pursue other weight loss opportunities (e.g., bariatric surgery, pharmacotherapy).

12.0 Privacy and Confidentiality

12.1 What type of data will be received by the Princpal Investigator/Study Team?

Check all that apply:

- ☐ De-identified – Data does not contain any identifiers that could link the data to a specific participant. (See VHA Handbook 1605.01, Appendix B, para 2b, for a list of identifiers that must be removed before data can be considered de-identified. Data must be de-identified in accordance with HIPAA and Common Rule criteria. Scrambling of names and social security numbers is not considered de-identified information.
- ☑ Identified – Data contains direct identifiers sufficient to identify participants as indicated in VHA Handbook 1605.01, Appendix B, para 2b.
- ☑ Coded – Data linked to a specific subject by a code rather than a direct identifier. While the data may contain some protected health information only someone possessing the code can link the data to a particular participant.

If coded data is checked, specify how the link or code will be maintained, and list each person /role who will have access to the link or code (or state Not Applicable):

A cross-walk file will be established that includes patient names linked to study ID numbers assigned by the CDW. The cross-walk file will be kept in a folder on the VA network that is restricted to access by members of the study team. The study ID number will be maintained with the health data pulled from CDW in a separate, access restricted folder on the VA network.

12.3 Provide a brief description of how participant privacy will be protected in this protocol. See ? for details.

Protection of screening data: A cross-walk file will be established that includes patient names linked to study ID numbers assigned by the CDW. The cross-walk file will be kept in a folder on the VA network that is restricted to access by members of the study team. The study ID number will be maintained with the health data pulled from CDW in a separate, access restricted folder on the VA network.

Protection of patients' data following screening: Once we randomly select 220 eligible patients, we will create a separate folder that includes these patients' names, addresses, and phone numbers, but no health data. These data will be maintained in an access-restricted folder on the VA network.

To protect the privacy of interview participants, we will not audio record their names; the recording will only be linked to the individual using their study ID. The study ID will be cross-walked to the individual in a separate, secured file on the VA network that is restricted to members of the study team. The recordings will be uploaded to the secure study folder as soon as possible following each interview. Once

the recordings are saved to the study folder, they will be deleted off the DVR. The interviews will be transcribed verbatim. The de-identified transcripts will be used for analysis and no identifiable information will be provided in reports or publications.

12.4 Provide a brief description of how participant confidentiality will be protected in this protocol. See ? for details.

Locked office
Lock cabinet or storage unit
Restricted access
Access rights terminated when authorized users leave the project or unit
Individual ID plus password protection
Security software (firewall, anti-virus, anti-intrusion) is installed and regularly updated on all servers, workstations, laptops, and other devices used in the project.

12.5 Will a Certificate of Confidentiality (CoC) be obtained? (If yes, include the required information in the informed consent document.) ***NOTE: If this is a qualifying NIH Study, the CoC will be assumed. A CoC helps Investigators protect the privacy of human research participants enrolled in biomedical, behavioral, clinical, and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identigying characteristics of a research participant. Form more information on CoCs go to: http://grants.nih.gov/grants/policy/coc/.***

- ○ Yes
- ◉ No

12.6 Is SSN used for any purpose other than scanning Consent/HIPAA into the medical record? (e.g. identifiying patients in administrative data, subject payments, use of clinical record)

- ◉ Yes
- ○ No

Indicate purpose and justification:

While PatientICN should be sufficient to pull data from CDW, we are still requesting access to SSNs in cases in which we may need to consult CPRS. Our data manager does not consider last initial + last 4 to be a unique identifier in this case.

12.7 Does the informed consent and HIPAA authorization forms thoroughly describe to subjects that their data will be combined with data from other sites?

- ○ Yes
- ○ No
- ◉ N/A

12.8 Will the informed consent and HIPAA authorization forms thoroughly describe to subjects that their data will be disclosed to the Coordinating Center where it will be combined with data from other sites and analyzed.

- ○ Yes
- ○ No
- ◉ N/A

13.0 Data Security

13.1 CONFIRMATIONS

13.2 In the event of a real or suspected breach of security, the IRB, Information Security Officer, Privacy Officer, VA Police (if appropriate), and the individual's supervisor will be notified immediately.

◉ Agree

13.3 Protocol staff will be up to date on any required VHA Privacy Policy and Information Security training or they will not be allowed access to VA Sensitive Information.

◉ Agree

13.4 Access to research sensitive information, if any, will be removed when protocol personnel are no longer part of the research team.

◉ Agree

13.5 At least one copy of all protocol records (whether sensitive or non-sensitive) will be retained under VA control and only destroyed in compliance with the approved Records Control Schedule

◉ Agree

Note: Investigators are responsible for protecting at least one copy of VA data, including non-sensitive data. Should you need to change any storage location in the future, please revise this Privacy and Data Security Plan

13.6 The VA retains ownership of any data collected as part of VA research. If the PI leaves the VA, custody of the research records will be determined by the Research Service. IRB approval is required to transfer the protocol to a new PI.

◉ Agree

13.7 NON-SENSITIVE DATA

13.8 List the VA location(s) [Room and Building] where you will store both paper and electronic non-sensitive protocol records.

Non-sensitive hard copy records will be maintained in VA CCMR offices in VA leased space, Building 16, third floor, North Campus Research Complex, 2800 Plymouth Road, Ann Arbor. Electronic, non-sensitive records will be kept in a restricted folder on a secure drive on the VA computer network.

13.9 VA SENSITIVE DATA (VASI)

13.10 Please describe your use of VA Sensitive Information (VASI):

○ This protocol does not collect or use VASI
○ This protocol uses, but does not save, collect, copy, or record VASI.
◉ This protocol collects, records, or saves VASI.

In which of the following ways will VASI be accessed/collected?

☐ Computer access
☑ Medical chart review
☐ Patient treatment
☑ Personal interviews
☑ Other

Please give a brief description of the data sources mentioned above and how they will be accessed.

Medical charts will be used to identify patients who meet study eligibility criteria and also to order and record laboratory tests (i.e., HbA1c, lipid panel). Study participants will be invited to take part in optional semi-structured interviews at 6 and 12 months. Participants will complete surveys at baseline, 6 months, and 12 months; these surveys will include self-reported side effects and experiences with the intervention.

13.11 Indicate the type of PII to be accessed. If you requested a HIPAA waiver for screening only, indicate any additional PII types that will be used post-screening.

- [x] Names
- [x] Any geographic area smaller than a state
- [x] Any date (except year) that is directly related to an individual and/or ages over 89
- [x] Telephone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [x] Social Security Numbers (SSNs) or Scrambled SSNs
- [x] Medical record numbers
- [ ] Health plan beneficiary numbers
- [ ] Account numbers
- [ ] Certificate and/or license numbers
- [ ] Vehicle ID and serial numbers including license plate numbers
- [ ] Device identifiers and serial numbers
- [ ] Web Universal Resource Locators (URLs)
- [ ] Internet protocol (IP) addresses
- [x] Biometric identifiers, including finger & voice prints
- [ ] Full-face photographic images and any comparable images
- [x] Any other unique identifiers (number, characteristic, or code)
- [ ] None of the above

Please explain the other unique identifer(s).

Other identifier is CDW PatientICN. Biometric identifiers refer to voice recordings collected during interviews.

13.12 Will this protocol include the use of Protected Health Information (PHI) that requires specific consent from subjects? If you requested a HIPAA waiver for screening only, indicate any PHI types that will be used post-screening.

- [ ] Alcoholism or alcohol abuse information
- [ ] Drug abuse information
- [ ] Sickle cell anemia information
- [ ] HIV test/infection results
- [x] None of the above

13.13 Identify all Protected Health Information (PHI) that you will access for use in this research protocol. If you requested a HIPAA waiver for screening only, indicate any additional PHI types that will be used post-screening.

- [x] Progress notes
- [ ] History & physical
- [ ] Discharge summary
- [ ] Operative reports
- [x] Diagnostic/Laboratory Reports
- [ ] Imaging (x-ray, CT, MRI, etc.)
- [ ] Immunizations
- [x] Allergy reports
- [x] Medications
- [ ] Consultations
- [x] Clinic notes
- [ ] Dental notes

- [ ] Mental health (not psychotherapy) notes
- [ ] Psychologial test results
- [ ] Genetic testing
- [ ] Survey/questionnaire responses
- [ ] Billing records
- [x] Other PHI to be used

Specify any other PHI to be collected.

semi-structured interviews; surveys

13.14 Provide details on the items checked above and describe any other types of PII and/or PHI that will be used.

For screening and recruitment, we will use patients' names, laboratory test results, phone numbers and street addresses.
During the intervention period, we will obtain laboratory tests at 6 months and 12 months. We will administer surveys at 0, 6, and 12 months. We will conduct interviews (audio recorded) at 6 and 12 months.

13.15 Specify the date range(s) of all PII and/or PHI to be collected.

January 2019 to December 2021

13.17 Will the VASI be stored electronically and/or will there be paper documents?

- [x] Hardcopy, including paper, tape recordings, film, etc.
- [x] Electronic, including computer files, removable disk files, etc.

13.18 LOCAL DATA STORAGE

13.19 Storage of Hardcopy VASI

List the VA location(s) where you will store **hardcopy VA Sensitive Information** (VASI) for this protocol. Include the security measures such as in a locked cabinet inside a locked room when unattended.

Hardcopies of the surveys with study ID numbers (rather than participants' names) will be stored in a locked cabinet in the PI's office (371C, NCRC).
The tape recorder with recorded interviews will be stored in this same locked cabinet until the recordings are transcribed and uploaded, at which point the audio recordings will be destroyed.

13.20 Identify electronic VASI storage locations

Electronic VASI will be stored in the protocol folder on a secure VAAAHS server.

(•) Yes ( ) No

Provide the folder name.

v11.med.va.gov\ann\HSRDFS1\Research\VA_LCDPP

VASI is stored on a computer local hard drive (even temporarily) such as by specially obtained software.

( ) Yes (•) No

VASI is stored on VINCI.

( ) Yes (•) No

13.22 Indicate where the photos or recordings are stored

With the protocol hardcopy VASI

○ Yes ◉ No

With the protocol electronic VASI

◉ Yes ○ No

13.24 How long will the research data be stored and describe how the data will be destroyed once the maximum retention period as specified by the VHA Records Control Schedule 10-1 or the indicated retention period (if longer) is met?

Data will be stored for 6 years after the termination of the project, following records control schedule 10-1, at which time the data will be destroyed.

13.25 COLLECTION, STORAGE, TRANSPORTATION AND SHARING OF VASI OUTSIDE VAAAHS

13.26 Indicate yes or no for each off-site data category below:

Will VASI be collected outside of the VA, including by a web application or on specially obtained software?
Note: An approved Authorization to Transport may be required.

○ Yes ◉ No

Will mobile devices be used in the study, i.e., laptops, audio recorders?

◉ Yes ○ No

If yes, indicate that mobile devices will encrypted and that the encryption is FIPS 140-2 validated (or state N/A):

The audio recorders have been approved for use by the ISO.

Will any VASI, electronic or hard copy, be stored outside of the VA firewall?

○ Yes ◉ No

Will a copy of VASI be shared outside the VA for any purpose (e.g. collaborators, sponsors) by HIPAA Authorization?

○ Yes ◉ No

13.31 AGREEMENTS WITH THIRD PARTIES REGARDING DATA USE

13.32 Will a Data Use Agreement (DUA) or Memorandum of Understanding (MOU) regarding data use be required? **Please contact the Privacy Officer and Information Security Officer (immediately) to make sure you are completing the correct form.*

○ Yes ◉ No

13.33 Will this protocol require any data-related financial transactions?

○ Yes ◉ No

13.35 CODED DATA

13.36 Will coded data that excludes all HIPAA identifiers per VHA Handbook 1605.1 Appendix B (personal identifiers) be

used? (see ? for more information and definitions) *Coded data is not considered de-identified.

(●) Yes ( ) No

13.37 Where will the code key be stored?

( ) With hardcopy VASI, but separate from the coded data
(●) With electronic VASI, but separate from the coded data
( ) Both of the above

13.38 ADDITIONAL DETAILS

13.39 What is the plan for protecting protocol research data from improper use or disclosure? *NOTE: As part of the response to this question, indicate that removal of access to research study data will be accomplished for study personnel when they are no longer part of the research team. Include that the ISO and Privacy Officer will be notified within one hour of the improper use or disclosure.*

All study records will be kept in a restricted folder on a restricted server behind the VA firewall. Only study team members will have access to this folder. Access will be revoked from study personnel when they are no longer part of the research team. We will notify the ISO and Privacy Officer will within one hour of improper use or disclosure.

13.40 Add any other privacy or information security details here.

None.

14.0 Staffing

14.1 Identify ALL personnel, including the PI, who will work in this research protocol.

	Name (Last, First)	Employee is functioning within their scope of practice	Employee will be viewing identifiable data	Employee has verified VA work status and background check	Employee familiar with protocol termination procedure	Employee familiar with incident reporting procedures	Employee will be obtaining Informed Consent
	Griauzde, Dina	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No ( ) N/A	( ) Yes (●) No
	Kullgren, Jeffrey T, MD	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No ( ) N/A	( ) Yes (●) No
	Hershey, Cheryl	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No

14.2 Describe how the researchers will have adequate time to conduct and complete the protocol.

The PI has 75% protected research time. She will also have research staff to assist her in these activities. Research staff will be hired at a later date and an amendment will be submitted.

14.3 **Describe how the above list contains an adequate number of qualified staff.**

Based on our prior experiences conducting a similar study at UM's Canton Health Center, we will need one part-time research assistant. We may also hire a project manager to further assist with study-specific tasks if our budget allows.

14.4 **Conflict of Interest: Individuals directly involved in the conduct, design or reporting of research involving human subjects should not have more than a minimal personal financial interest in a company that sponsors the research or owns the technology being studied. A conflict of interest arises when a researcher is or may be in a position to put his or her own interest before the best interests of research subjects. Conflicts involving the IRB itself or conflicts involving the institution must be managed. In order to mange such conflicts, the IRB must be informed of potential conflicts of interest. Researchers submitting protocols using human subjects must disclose all interests that may be perceived as a conflict with the best interest of the subject in order for the research to be considered for approval.**

The Principal Investigator and/or Co-Investigators have the following conflicts of interest to report to the IRB (or please state No Conflicts of Interest to declare):

No Conflicts of Interest to declare.

In addition, all Principal Investigators and Co-Investigators MUST complete a Research Financial Conflict of Interest Form (annually) and Project Specific Conflict of Interest Form located on their AAROW Dashboard. Please contact the RDC Coordinator at x55602 if you have any questions.

15.0 Project Association

15.1 **The protocol must be associated with a new R&D Project. Identify the R&D Project(s) that correspond to this protocol.**

Project Status	Proposal Number	Project Title	Principal Investigator
RDC Approved - New Project	RDC-2019-1270	VA LC-DPP	Dina Griauzde
		A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes	

15.2 **As the Principal Investigator for this protocol, I certify that I have read, understand, and accept the Investigator responsibilities as outlined in VHA Directive 1200.05, paragraph 5g and that these include but are not limited to the following (please read and check all selections):**

- ☑ Giving first priority to the protection of human subjects; upholding professional and ethical standards and practices; and adhering to all applicable VA and other Federal requirements, include IRB and the local VA Facility's policies and procedures regarding the conduct of research and the protection of human subjects.
- ☑ Ensuring all investigators and other staff participating in this human subjects research are qualified; have the appropriate training, education, and experience to perform procedures assigned to them; and that they have been appropriately credentialed and privileged as applicable per VAAAHS requirements.
- ☑ Submitting all amendments to the project or changes in the informed consent to the IRB for review

and approval prior to initiation, except when necessary to eliminate immediate hazard to the participants. Any changes implemented as a result of an immediate hazard will be promptly reported to the IRB as a project deviation and an amendment submitted if determined necessary.

- [x] Obtaining and documentating legally effective informed consent of the subject or the subject's legally authorized representative (LAR), as well as a HIPAA authorization, unless the IRB approves an applicable waiver.
- [x] Reporting problems, adverse events, and apparent serious or continuing noncompliance, including local research deaths, in accordance with VHA Handbook 1058.01, local VA Facility requirements, and IRB SOPs.
- [x] Ensuring appropriate research records are maintained that includes all information made or received by a VA Investigator over the entire lifecycle of the research activity and that these records are maintained in accordance with the VA Records Control Schedule and local policies and procedures.
- [x] Providing continuing review and/or requested updates for the study as applicable in a timely manner and in accordance with the VA and IRB policies and procedures. This includes submission of a closure reports upon completion of protocol.
- [x] Ensuring research does not start until final approval has been received from the IRB, and written notification from the local Facility ACOS/R&D in accordance with local R&D Committee approval policies and procedures.

15.3 **In addition, the VA Office of Research Oversight mandates that all Human Studies Research undergo Informed Consent Audit (ICA) annually and full Regulatory Binder Audit (RBA) every three years (triennially). The Principal Investigator must assure that informed consent is appropriately obtained and documented and that a complete and up to date Regulatory Binder (hardcopy or electronic) is maintained from time of initial approval. A complete set of Regulatory Binder instructions is available here: https://www.annarbor.research.va.gov /ANNARBORRESEARCH/docs/compliance/HS_REG_BINDER_INSTRUCTIONS_122314.doc**

(•) Agree ( ) Disagree

15.4 **The Protocol Application is now complete. Next you will complete the Initial Protocol Submission Form. This form is used to collect the Application and any other needed attachments for submission to the IRB for review.**

15.5 **Press *Save and Continue***

A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes

Principal Investigator: Dina Griauzde

Funding Agency: None

VA Ann Arbor Healthcare System – (506)

Abstract

Background: Individuals with prediabetes can significantly reduce their risk of developing type 2 diabetes mellitus (T2DM) by achieving at least 5% body weight loss. Behavioral weight loss programs (MOVE!, TeleMOVE) are widely available within the Veterans Health Administration (VHA), but most participants do not achieve 5% body weight loss. This may be due, in part, to the programs' dietary advice, which teach participants to follow a low-fat, calorie-restricted diet. A low-carbohydrate diet may be one promising strategy to augment weight loss among Veterans with prediabetes. Our team previously adapted the Center for Disease Control and Prevention's National Diabetes Prevention Program—a group-based lifestyle change program similar to MOVE!—to teach participants to follow a very low carbohydrate diet (VLCD), defined as 20-35 non-fiber grams of carbohydrate per day. This pilot intervention was feasible, acceptable, and demonstrated preliminary weight loss effectiveness among patients of one academic medicine primary care clinic. It is unknown whether such a program may be feasible, acceptable, or effective for weight loss among Veterans with prediabetes.

Objective: The objectives of this single-arm mixed methods pilot study are (1) to test the feasibility and acceptability of a low-carbohydrate Diabetes Prevention Program (LC-DPP) among veterans with prediabetes and (2) to estimate weight loss among LC-DPP participants.

Methods: We will recruit up to 30 patients with body mass index $\geq$ 25 kg/m2 and prediabetes (defined as hemoglobin A1c [A1c] 5.7-6.4%) from the Ann Arbor VA primary care clinic. Participants will be identified by chart review and invited to participate by postal letter. Individuals that do not opt-out of study contact will be screened for eligibility by telephone call. Interested and eligible participants will be invited to attend an in-person information session. During this session, they will receive information about the dietary intervention; written informed consent will be obtained at this time. Study participants will attend a total of 24 group-based classes over the course of 1-year (not including initial information session). Body weight will be measured at each session. At baseline, 6-months, and 12-months, we will measure waist circumference, A1c, lipid levels, and self-reported outcomes including quality of life, mood, hunger, cravings, physical symptoms, and medication use/changes. Primary outcomes will be feasibility (e.g., enrollment, retention) and acceptability (e.g., session attendance, qualitative feedback). Secondary outcomes will change in weight, achievement of $\geq$5% body weight loss, change in A1c, and change in lipid levels. During semi-structured interviews conducted at 6-months and 12-months, we will explore participants' experiences with the program, barriers to and facilitators of adherence to a low-carbohydrate diet, and perspectives on ways to improve the intervention.

Impact/Implications: Through this study, we will demonstrate the feasibility and acceptability of a LC-DPP among Veterans with prediabetes. These data will inform a large-scale comparative effectiveness trial of LC-DPP versus VA-MOVE.

List of Abbreviations

LC-DPP – low-carb Diabetes Prevention Program

A1c – hemoglobin A1c

Contents

Protocol Title: A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes

1.0 Study Personnel

- Provide name, contact information, and affiliations/employee status for the following:

  Principal Investigator/Study Chair:

  Dina Griauzde MD, MSc
  North Campus Research Center
  2800 Plymouth Road Ann Arbor, MI 48109
  734-845-5129 dhafez@med.umich.edu

  Co-Investigators:

  Jeffrey T. Kullgren MD, MPH, MSc

  Associate Professor
  Division of General Medicine
  Department of Internal Medicine
  University of Michigan
  Ann Arbor VA Health System

2.0 Introduction

The United States is currently facing an unprecedented burden of obesity and metabolic disease and prevalence of these conditions are higher among the Veteran population. Approximately 72% of Veterans using the Veteran Health Administration services are overweight or obese, compared to 57% of the general population.[1] The Veteran population faces high rates of type 2 diabetes mellitus (T2DM), with estimates surpassing 20%[2] compared to 14% among the general population.[3] Prediabetes, defined as having a HbA1c between 5.7-6.4%, is increasingly recognized as an important diagnosis for early identification of glucose intolerance with high potential for lifestyle intervention. An estimated 84.1 million Americans have prediabetes,[4] however data on prediabetes prevalence among Veterans is limited as routine screening has historically not been an established practice.[5] Data from proposed screening algorithms estimate over 25% of overweight or obese Veterans have prediabetes.[5] The relatively low estimated rate of prediabetes among Veterans may be a function of the high rate of progression to T2DM among this population.[2] Although sometimes considered a benign harbinger of T2DM, prediabetes itself is associated with microvascular and macrovascular disease.[6] Furthermore, without intervention, many patients with prediabetes will develop T2DM with time.[2]

Fortunately, T2DM can be prevented or delayed through modest lifestyle changes. The landmark Diabetes Prevention Program (DPP) Trial demonstrated a 58 percent reduction in the 3-year incidence of T2DM among individuals with prediabetes who achieved 7 percent body

weight loss and engaged in routine physical activity.[7] Accordingly, the DPP lifestyle intervention has been translated to communities across the United States [89], and mean participant weight loss is approximately 4 percent at 12 months.[10] The VA Health System offers a lifestyle program modeled after the DPP entitled VA MOVE!. Similar to the DPP, MOVE! teaches participants to follow a low-fat, calorie-restricted diet with the goal of gradual, sustained weight loss. Although VA MOVE! is widely adopted across the VA Health System, weight loss outcomes are modest with a range of 0.13-3.3kg loss over one year.[11] Additionally, only 15-18% achieved the clinically significant endpoint of 5% weight loss. When MOVE! was directly compared to the VA DPP in a clinical demonstration trial, the DPP had higher engagement and significantly higher weight loss at 6 months, however the weight loss difference at 12 months was not statistically significant.[12] Lifestyle interventions have an important role in population level prevention and VA delivered lifestyle programs could be a powerful and scalable tool, however there is clearly opportunity to improve weight loss outcomes.

One promising approach to help program participants lose more weight through group lifestyle programs may be through a low-carbohydrate (LC) dietary intervention. Consistent with United States Dietary Guidelines (USDG),[13] the original DPP Trial[7] and translational group-based curricula[14,15] including VA MOVE! recommend a low-fat (LF), calorie-restricted diet. However, there is growing controversy regarding the scientific merit of the Dietary Guidelines[13,16] as well as growing recognition that LC diets may be more effective than LF diets for short-term weight loss[17,18] and long-term weight maintenance[19,20]. Notably, weight loss occurs without calorie restriction[21] and LC diets improve blood glucose levels among individuals with T2DM and insulin resistance. [21,22,23] Thus, a LC dietary intervention for prediabetes may augment individual weight loss and reduce progression to T2DM.

3.0 Objectives

In this mixed methods pilot study, we aim to test whether a LC-DPP is feasible to deliver in the VA Health System. We hypothesize a LC-DPP will lead to greater participation and weight loss than VA MOVE! In addition to objective measures of this program's preliminary efficacy (e.g. weight, HbA1c) we will also obtain qualitative participant feedback on the intervention. Taken together, these data will be used to improve the curriculum and inform larger-scale interventions.

Aim 1: To evaluate acceptability and feasibility of delivering a Low-Carb Diabetes Prevention Program in the VA Health System

The VA Health System has an established infrastructure to deliver group-based lifestyle programs including VA MOVE! We will deliver a VA LC-DPP that was piloted at a Michigan Medicine primary care clinic in 2017. We will collect data on participant recruitment, session attendance, and intervention satisfaction to assess the acceptability of a VA LC-DPP. Qualitative feedback from VA diabetes educators, primary care providers and LC-DPP participants will be collected to better understand barriers and facilitators of a VA LC-DPP and identify challenges to scalability.

Aim 2: To estimate weight loss from a Diabetes Prevention Program that is modified to incorporate a Low Carbohydrate (LC-DPP) rather than the traditional low fat diet among veterans with prediabetes. We will conduct a single-arm mixed methods pilot study to estimate weight loss as well as the percentage of participants who achieve 5% weight loss in a 16-week LC-DPP. Weight loss from the pilot LC-DPP cohort will be compared to weight loss

outcomes from previously published VA DPP and VA MOVE! studies. We will also evaluate secondary outcomes including change in physical activity, neuropathy symptoms, hemoglobin A1c, triglycerides, cholesterol and HDL over the 12- month study period.

4.0 Resources and Personnel

The research will be conducted at the Ann Arbor VA.

A research assistant and/or project manager will be hired to assist with subject recruitment and informed consent processes. This individual/these individuals will also administer surveys, conduct semi-structured interviews, and conduct data analyses.

The group sessions will be help in one of the patient education rooms (TBD based on availability). The group sessions will be run by one of the primary care dietitians who is also a Certified Diabetes Educator (Jamie Michaels RD, CDE). In her absence, another primary care dietitian and Certified Diabetes Educator will run the group sessions.

5.0 Study Procedures

5.1 Study Design

We will conduct a single-arm mixed methods pilot study to test the preliminary efficacy on weight loss of a LC-DPP among Veterans with prediabetes (as defined by the American Diabetes Association [ADA] [24]). We hypothesize that at least 50% of LC-DPP participants will achieve at least 5% weight loss at 12 months and that the average weight loss in the LC-DPP will be greater than the average weight loss among historical controls in VA MOVE!.[11]

Our team previously adapted the Centers for Disease Control and Prevention's (CDC's) National Diabetes Prevention Program (NDPP) curriculum—a lifestyle change program similar to MOVE!—to teach participants to follow a low-carbohydrate rather than a low-fat diet. We pilot tested our low-carbohydrate Diabetes Prevention Program (LC-DPP) among adults with prediabetes at a single, academic medicine primary care clinic.

The LC-DPP curriculum was adapted from the CDC National Diabetes Prevention Program materials and consists of 16 weekly one-hour group sessions over first 6 months (i.e. core phase) and 8 one-hour group sessions once or twice a month over the next 6 months (i.e. maintenance phase). Importantly, our adapted curriculum will adhere to the CDC's Diabetes Prevention Recognition Program (DPRP) guidelines, which aim to maintain the integrity of the DPP in heterogeneous settings. The DPRP formally recognizes sites that achieve specific targets (e.g. session attendance, weight loss) through use of a CDC-approved curriculum. Therefore, our curriculum, if effective, may be eligible for CDC-approval, which would facilitate future dissemination of this intervention.

We will use a mixed-methods sequential explanatory design, which is to say that quantitative data and qualitative data will be collected in two consecutive phases within the study [25]. Specifically, in the first phase, we will collect and analyze the quantitative data (e.g. surveys, weight, A1c, lipids). In the second phase, we will collect and analyze qualitative data (e.g. semi-structured interviews). The rationale for this approach is that the quantitative data will provide a general overview of the intervention's efficacy and limitations, and the qualitative data will help to explain these findings by exploring participants' experiences and perspectives in more depth.

Intervention

We will recruit up to 30 veterans with prediabetes to participate in the LC-DPP. The intervention will be delivered in partnership with VA Certified Diabetes Educators who will serve as lifestyle coaches for the group-based intervention. The LC-DPP lifestyle coaches will deliver 16-weekly one-hour group sessions over the first 6 months and 8 maintenance sessions over the subsequent 6 months. **Table 1** shows session topics. Participants will receive a binder to hold study materials. They will be provided with printed handouts on a session-by-session basis. Individuals that are absent for a particular session will receive corresponding session materials by e-mail or postal mail.

The CDC's Diabetes Prevention Program instructs participants to adhere to a fat-restricted diet with an explicit cap of less than 33-55 grams of fat per day depending on starting body weight. In contrast, LC-DPP participants will be initially instructed to follow *ad-libitum* very low-carbohydrate diet, which restricts carbohydrate intake (not including fiber) to 20-35 grams per day with the goal of achieving nutritional ketosis. Participants will be encouraged to eat a normal amount of protein (roughly 80-120 grams per day) and to derive the remaining calories from fat. Allowable foods include: meats, fish, poultry, eggs, cheese, seeds, nuts, leafy greens, non-starchy vegetables, and some fruits.

During the LC-DPP's maintenance phase, participants will be instructed to gradually reintroduce carbohydrates (e.g., 5 non-fiber grams of carbohydrates per week) if: (1) they have met their weight loss target and (2) if they desire to liberalize their carbohydrate intake.

To minimize potential side effects (e.g. headache, constipation, muscle cramps, diarrhea, general weakness, and rash) participants will be instructed to replace one meal a week with a low-carbohydrate alternative, starting with breakfast. Participants will be counseled to drink sufficient water and to consume adequate sodium. Further, primary care providers will be notified of their patients' involvement in this study, and they will be given a handout that describes the intervention, potential side effects, and strategies to minimize side effects.

Table 1. Group session topics[1]

Session Number	Topic
Core phase	
0	Study information session (Informed consent to be obtained)
1	Welcome to the Low-Carb Diabetes Prevention Program
2	Be a Carbohydrate Detective
3	Low-Carb Meals
4	Low-Carb Cooking and Shopping
5	Move Those Muscles
6	Being Active – A Way of Life
7	Challenges and Support
8	Take Charge of What's Around You
9	Problem Solving
10	Eating Out on Your Low-Carb Meal Plan
11	Talk Back to Negative Thoughts
12	The Slippery Slope of Lifestyle Change
13	Jump Start Your Activity Plan
14	Make Social Cues Work for You
15	You Can Manage Stress
16	Ways to Stay Motivated

Maintenance phase	
17	Welcome to Post-Core
18	Handling Holidays, Vacations, and Special Events
19	Fats – Saturated, Unsaturated, and Trans Fat
20	Preventing Relapse
21	Staying on Top of Physical Activity
22	Revisiting Recipes and Cooking
23	Stress and Time Management
24	Long-Term Maintenance and Looking Forward
[1]Session order and specific topics may change. However, the general content will remain the same.	

Study Population

We will recruit individuals based on the following inclusion criteria: (1) age >= 18 years; (2) prediabetes (defined as A1c 5.7% to 6.4% drawn within 12 months of study start date); (3) body mass index >= 25 kg/m^2; (4) willingness to participate in group-based classes, and able to engage in at least light physical activity such as walking. The participants must have established primary care at the AAVA (defined as at least one office visit within 12 months of the study start date). This will ensure that participants can have access to a medical provider for medication changes and side effective management, if necessary.

We will exclude individuals based on the following criteria: (1) history of type 1 diabetes or type 2 diabetes; (2) current participation in another lifestyle or behavior change program or research study; (3) vegetarian or vegan lifestyle; (4) history of bariatric surgery; (5) inability to read, write, or speak English; (6) inability to provide informed consent; or (7) women who are pregnant or intend to become pregnant during the intervention period.

Risks and Benefits:

Risks of participation may include:

- Loss of confidentiality:
  - The study team may be required to break confidentiality if we believe there is a risk of harm to a participant. The participant's regular care providers or authorities would be informed to protect the subject and others.
- Inconvenience:
  - Participants may find it inconvenient to participate in the group sessions or to track dietary intake or physical activity minutes.
  - Participants may also find it inconvenient to complete the surveys or laboratory tests.
  - The researchers will minimize this risk by compensating participants for the time required to complete the surveys at 6 and 12 months and to complete blood draws at 0, 6, and 12 months.
- Blood draws:
  - Adverse effects of blood draw may include lightheadedness, dizziness, bruise or infection at blood draw site.
  - If participants experience any adverse effects, we will ensure that participants receive appropriate medical care

- Questionnaires:
    - Some of the questions may make participants feel uncomfortably or upset. All participants are free to decline to answer any questions they do not wish to answer and to discontinue participation at any time.
- Diet:
    - Participants may experience some side effects when first reducing the amount of carbohydrates in the diet. This may include constipation, headache, bad breath, and muscle cramps. These symptoms usually go away after the first couple weeks on the diet. Participants can speak with study staff and study physicians (Dr. Dina Griauzde). We have also shared information with participants' primary care providers regarding the benefits and potential side effects of low-carbohydrate diets.
- Increase in physical activity:
    - Participants may experience harm or injury from exercise if they increase their physical activity as a result of participation. As there is no requirement for patients to engage in physical activity as part of this study and no physical activity will be encouraged other than that ordinarily encountered in daily life, we do not consider the risk to be above minimal. Participants will be encouraged to contact the study team and/or their PCP in the event of any adverse events.

As with any research study, there may be additional risks that are unknown or unexpected. We do not know if participants will get any benefits from taking part in this research study. However, possible benefits may include weight loss, decreased risk of diabetes, reduction in hemoglobin A1c. Participation in this study may also help the study team to design and test new ways to help more people prevent type 2 diabetes.

Participants will receive results of a hemoglobin A1c and cholesterol tests at 6 and 12 months.

5.2 Recruitment Methods

Recruitment

Data from VA medical records will be obtained via the Clinical Data Warehouse (CDW) to identify patients with prediabetes. Patients seen at VAAAHS in the past year (January 2019 - December 2019) with a A1c recorded over that time period will be screened.

Eligible patients will be sent a letter inviting them to participate in the study. We estimate that 10% of eligible individuals will enroll in our study. Thus, we will send study invitation letters by postal mail to up to 220 potentially eligible individuals. The letter will explain the purpose of the study. A phone number will be provided to individuals to allow for them to opt-in to study participation or opt-out of future contact by the study team. A member of the study team will contact individuals who opt-in. The study team member will confirm individuals' study eligibility and answer any questions. If up to 30 veterans are not recruited via the opt in approach, a member of the study team member will call those individuals that did not opt-out and invite them to participate.

All interested and eligible individuals will be invited to an in-person recruitment session. The purpose of this session will be to explain the program and dietary approach (i.e., low-carbohydrate, high-fat) in detail. This session is necessary to ensure full and proper informed consent. In our prior pilot work at Canton Health Center, program participants informed us during qualitative interviews that they wished for additional education about the dietary approach to alleviate concerns regarding dietary fat and cholesterol intake. Because this is

information that participants should, ideally, understand prior to enrollment, we will deliver a brief presentation (~20-30 minutes) during this recruitment session. An additional 20-30 minutes will be allocated to answering individuals' questions. Afterwards, those interested in study participation will be asked to provide written, informed consent and to complete a baseline survey and laboratory testing.

Participants will receive a Visa or Amazon gift card to compensate you for completing each of the following study activities:

- Baseline labs ($25)

- 6-month survey ($25)

- 6-month labs ($25)

- 6-month interview ($25)

- 12-month survey ($25)

- 12-month labs ($25)

- 12-month interview ($25)

5.3 Informed Consent Procedures

Informed consent will be obtained prior to study enrollment. This will be obtained in person by study staff. Participants will have the opportunity to ask any questions prior to signing the consent. We expect that there will be no special considerations required for obtaining consent.

5.4 Inclusion/Exclusion Criteria

We will recruit individuals based on the following inclusion criteria: (1) age >= 18 years; (2) prediabetes (defined as A1c 5.7% to 6.4% drawn within 12 months of study start date); (3) body mass index >= 25 kg/m^2; (4) serum lipid levels drawn within 12 months of study start date; (4) willingness to participate in group-based classes, and able to engage in at least light physical activity such as walking. The participants must have established primary care at the AAVA (defined as at least one office visit within 12 months of the study start date). This will ensure that participants can have access to a medical provider for medication changes and side effective management, if necessary.

We will exclude individuals based on the following criteria: (1) history of type 1 diabetes or type 2 diabetes; (2) current participation in another lifestyle or behavior change program or research study; (3) vegetarian or vegan lifestyle; (4) history of bariatric surgery; (5) inability to read, write, or speak English; (6) inability to provide informed consent; or (7) women who are pregnant or intend to become pregnant during the intervention period.

5.5 Study Evaluations

Quantitative Data source

a) *Weight*

Participants will be encouraged to self-monitor weight using a home scale although this

data will not be collected by the study team. In accordance with standard DPP operating procedure, participants will be weighed in a private room prior to each session and their weight will be recorded by a member of the study team.

b) *Physical activity*

In accordance with standard DPP operating procedure, participants will be encouraged to self-monitor physical activity minutes and to report this information to the lifestyle coach at the start of each session.

c) *Laboratory metrics*

We will evaluate change in A1c and lipids over the study period. Baseline laboratory studies will be obtained once individuals have consented to participate in this study. Repeat A1c and lipid levels will be drawn at 6 and 12 months.

d) *Session attendance*

Participants will be encouraged to attend all sessions and attendance will be recorded by the lifestyle coach.

e) *Survey Data*

At baseline, 6 months, and 12 months, study participants will be invited to complete a written survey. Paper copies will be given to individuals at session 15/16. Because we aim to obtain complete follow-up data, we will make efforts to collect survey responses from participants that are not present for session 15/16. We will send surveys to non-attendees via postal mail. All individuals will be asked to return their survey to the study team via pre-paid envelope or in-person delivery. The survey will assess domains related to the following: global health and well-being; sleep; food cravings; stress eating; hunger; energy; mood; physical symptoms, neuropathic symptoms (e.g., tingling, burning in feet); side effects; and cost of food. At baseline, we will ask participants to provide sociodemographic characteristics. At 6 months and 12 months, participants will be asked to provide feedback about the study and will receive compensation for each survey.

Qualitative Data Sources

Participants will be encouraged to maintain a log of food intake and physical activity. Each week, the lifestyle coach will review the logs and provide individual feedback. We will retain copies of participants' logs from their first 2 weeks in the study and their last 2 weeks in the study. In this way, we can qualitatively assess changes in dietary habits and physical activity.

We will conduct qualitative, semi-structured interviews with a purposive sample of LC-DPP participants to solicit participant feedback on the LC-DPP curriculum and to better understand barriers to (e.g. food cravings, side effects) and facilitators of (e.g. satiety, energy) intervention adherence. The participants interviewed (n=14) will be purposively sampled based on weight loss outcomes (e.g., achievement vs. non-achievement of at least 5% body weight loss). Participants' experiences with the program and barriers to and facilitators of adherence to the diet will be explored. Participants will receive Visa and/or Amazon gift cards to compensate them for their time after completing the 6 and 12-month interview.

We will conduct interviews with VA LC-DPP coaches and VA primary care providers to evaluate perceptions about the diet and the program. We will explore coaches' experiences with leading the program and solicit feedback on challenges and opportunities for improvement.

Outcomes

Primary Measures: Feasibility and Acceptability

Primary outcome measures are feasibility (e.g., uptake and retention rates) and acceptability (e.g., session attendance, qualitative feedback). LC-DPP uptake rate will be defined as the number of participants recruited to the intervention divided by the total number of individuals invited to participate. LC-DPP retention rate will be determined by calculating the rate of completion of the 6-month and 12-month surveys. Because some individuals may remain engaged in the intervention (e.g., communicated via phone or email with the coach) despite personal barriers to in-person session attendance, we will use survey completion rate rather than a session attendance threshold (e.g., attendance at 9 core sessions) to measure study retention.

Intervention acceptability will be determined by calculating the rate of attendance at core and maintenance sessions. To further understand the program's acceptability, we will conduct semi-structured interviews at 6 and 12 months. During interviews, we will explore participants' general experiences with the intervention as well as specific facilitators of and barriers to VLCD adherence.

Secondary Measures:

Change in body weight: Body weight will be measured and recorded at each attended session. We will calculate average body weight change and percent body weight loss at the end of the program's core phase (6 months) and maintenance phase (12 months). Among session non-attendees, we will attempt to schedule 6- and 12-month weigh-ins at participants' convenience within 2 weeks of the final core and maintenance sessions. All weights will be obtained using the same calibrated scale.

Change in HbA1c: We will calculate change in HbA1c from baseline to 6 and 12 months

Change in lipids: We will calculate change in triglycerides and total cholesterol/HDL ratio from baseline to 6 months and 12 months.

Change in survey measures: We will calculate change in self-reported survey measures from baseline to 6 months and 12 months.

Fidelity: We will measure intervention fidelity (i.e., extent to which components of an intervention are delivered as intended) using quantitative measures adapted from the literature[26] as well as qualitative interview feedback from participants and dietitians.

5.6 Data Analysis

Quantitative analysis

Descriptive statistics will be used for baseline survey response data including demographic and socioeconomic characteristics. For all continuous outcomes, we will calculate mean change and standard deviation from baseline to 6 months and 12 months and compare outcomes from baseline to 6 months and 12 months using paired *t*-tests. For all categorical outcomes, we will

use chi-square or Fisher's exact tests to examine changes from baseline to 6 and 12 months. All analyses will be conducted using Stata 14.

Qualitative analysis:

Semi-structured interviews will be recorded and transcribed verbatim. Interviews will then be imported into qualitative analysis software. Two investigators will independently read and code transcribed interviews. Interviews will then be coded jointly using consensus conferences. Interviews will be analyzed using directed content analysis [27], which is to say that codes will be created to reflect the main topics in the interview guide and to characterize the patterns and themes that emerged from the data.[28]

5.7 Withdrawal of Subjects

Participants will be free to leave the study at any time. If any participants leave the study before it is finished, there will be no penalty. Participants will not lose any benefits to which they may otherwise be entitled. If the participant chooses to tell the researchers why they are leaving the study, the reasons for leaving may be kept as part of the study record. The study team may continue to review the data collected prior to study withdrawal but cannot collect further information. If participants decide to leave the study before it is finished, they will notify the study primary contact.

Subjects may be withdrawn from the study for the following reasons: (1) the study team believes that it is not in the subject's best interest to stay in the study; (2) a subject displays disruptive behavior towards group members or staff; (3) a subject become ineligible to participate; (4) a subject's condition changes and they need treatment that is not allowed while you are taking part in the study; (5) subjects do not follow instructions from the researchers; (6) the study is suspended or canceled.

6.0 Reporting/Data Safety Monitoring Plan

We will report any unanticipated problems, serious adverse events, and protocol deviations to the AAVA IRB within 24 hours of their occurrence and we will follow standard operating procedures to ensure appropriate follow-up and resolution.

We will monitor A1c and lipid levels at 0, 6 months, and 12 months. Participants and their PCPs will be notified of laboratory test results. In the event that a participant's A1c is in the type 2 diabetes range, we will ensure that they have timely PCP follow-up to discuss management. Participants will be encouraged to inform the study team of any adverse events due to increased physical activity throughout the study period.

When following a low-carbohydrate diet, some individuals can experience an elevation in their LDL cholesterol levels. The cause for this elevation is not completely known. These results will also be communicated to PCPs. Depending on the degree of elevation, participants may be advised to start a cholesterol-lowering medication or to increase the dose if they are already taking a cholesterol medication. Participants may also be advised to modify their diet by increasing their intake of carbohydrates.

All paper data will be stored in locked cabinets accessible only to research staff in VA-rented space on the third floor of Building 16, North Campus Research Center. All electronic data will be stored in access-restricted study folders behind the VA firewall.

7.0 Privacy and Confidentiality

We will keep all subjects' records confidential to the extent provided by federal, state, and local law. All records will be kept in a secure area with restricted access available only to the research staff from the VA. Paper files will be stored in a locked filing cabinet and electronic files will be stored on a secure server. All surveys or paper documentation will be identified with a unique study ID number and will not include personal information.

If the results of this study are reported in any way, subjects will not be identified by name, photograph or any other means without consent. No information that identifies subjects will be released unless required by law. In our analysis of the data, we may have to share data with a third-party analysis company. In this event we will strip the data of any information that can identify subjects as individuals.

8.0 Communication Plan

This is a single-site study. It will be conducted at the Ann Arbor VA. We have full support for this pilot study from Dr. Adam Tremblay, Associate Chief of Staff/Ambulatory Care and Director of Primary Care/Associate Chief of Medicine at the AAVA (see attached letter).

We will obtain approval for any changes in the protocol, informed consent, and HIPAA authorization from the AAVA IRB prior to initiating the proposed change(s).

We will notify the AAVA IRB of any Serious Adverse Events, Unanticipated Problems, or interim results that may impact conduct of the study.

9.0 References

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IRB Application (Version 1.8)

1.0 General Information

***Please enter the full title of your protocol. Be sure to click the ? to the right to ensure the protocol is correctly named.**

A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes

***Please enter the Short Name you would like to use to reference the protocol:**

VA LC-DPP
* This field allows you to enter an abbreviated version of the Protocol Title to quickly identify this study.

2.0 Add Department(s)

2.1 List departments associated with this protocol:

Primary Dept?	Department Name
◯	**VAAAHS** - CCMR

3.0 Grant research staff access to the protocol

3.1 *Click the "Add User" button to select the protocol's Principal Investigator:

Griauzde, Dina

3.2 Please add all research staff, including co-investigators, support staff, WOC employees and IPA employees:

A) Additional Investigators

Kullgren, Jeffrey T, MD
Co-Investigator

B) Research Support Staff

Hershey, Cheryl
Project Manager/Study Coordinator
Metreger, Tabitha
Research Associate

3.3 *Please add a Study Contact

Griauzde, Dina

Study contact(s) receive all important project notifications along with the Principal Investigator. The most common study contacts are project managers/study coordinators although at times the PI is the only contact.

4.0 VA Ann Arbor Healthcare System IRB Application

Preliminaries

4.1 Is this IRB Protocol Federally Funded?

○ Yes ○ No

4.2 What is the funding source for this IRB Protocol?

4.3 EXEMPTION from further IRB Review

4.4 Are you requesting EXEMPTION from further IRB review?

○ Yes ◉ No

4.18 Expedited Review

4.19 Are you requesting EXPEDITED IRB Review? (There is no need to request expedited review if you have requested an EXEMPTION from further IRB Review.) ***NOTE: Expedited IRB Review does not indicate a faster review process, it simply means that review will take place outside of the convened IRB Meeting.***

○ Yes ◉ No

5.0 Summary Protocol Description

This section consists of a number of short questions that will provide an overview to the IRB and help guide you through the rest of the application.

5.1 PROTOCOL BASICS

5.2 Please include an ABSTRACT (Less than 500 words, organized under these headings: Objectives, Research Plan, Methods, and if a basic science study, Clinical Relevance)

Background / Objectives

Individuals with prediabetes can significantly reduce their risk of developing type 2 diabetes mellitus (T2DM) by achieving at least 5% body weight loss. Behavioral weight loss programs (MOVE!, TeleMOVE) are widely available within the Veterans Health Administration (VHA), but most participants do not achieve 5% body weight loss. This may be due, in part, to the programs' dietary advice, which teach participants to follow a low-fat, calorie-restricted diet. A low-carbohydrate diet may be one promising strategy to augment weight loss among Veterans with prediabetes. Our team previously adapted the Center for Disease Control and Prevention's National Diabetes Prevention Program—a group-based lifestyle change program similar to MOVE!—to teach participants to follow a very low carbohydrate diet (VLCD), defined as 20-35 non-fiber grams of carbohydrate per day. This pilot intervention was feasible, acceptable, and demonstrated preliminary weight loss effectiveness among patients of one academic medicine primary care clinic. It is unknown whether such a program may be feasible, acceptable, or effective for weight loss among Veterans with prediabetes.

The objectives of this single-arm mixed methods pilot study are (1) to test the feasibility and acceptability of a low-carbohydrate Diabetes Prevention Program (LC-DPP) among veterans with prediabetes and (2) to estimate weight loss among LC-DPP participants.

Methods

We will recruit up to 30 patients with body mass index ≥ 25 kg/m2 and prediabetes (defined as hemoglobin A1c [A1c] 5.7-6.4%) from the Ann Arbor VA primary care clinic. Participants will be identified by chart review and invited to participate by postal letter. Individuals that do not opt-out of study contact will be screened for eligibility by telephone call. Interested and eligible participants will be invited to attend an in-person information session. During this session, they will receive information about the dietary intervention; written informed consent will be obtained at this time. Study participants will attend a total of 24 group-based classes over the course of 1-year. Body weight will be measured at each session. At baseline, 6-months, and 12-months, we will measure waist circumference and participants will be asked to complete a survey that includes measures of quality of life, mood, hunger, cravings, and self-reported physical symptoms. Primary outcomes will be feasibility (e.g., enrollment, retention) and acceptability (e.g., session attendance, qualitative feedback). Secondary outcomes will change in weight, achievement of ≥5% body weight loss, and change in A1c. During semi-structured interviewed conducted at 6-months and 12-months, we will explore participants' experiences with the program, barriers to and facilitators of adherence to a low-carbohydrate diet, and perspectives on ways to improve the intervention.

Impact/Implications

Through this study, we will demonstrate the feasibility and acceptability of a LC-DPP among Veterans with prediabetes. These data will inform a large-scale comparative effectiveness trial of LC-DPP versus VA-MOVE.

5.3 What are the research questions or hypotheses to be studied?

Hypothesis #1:
A low-carbohydrate Diabetes Prevention Program (LC-DPP) will be feasible and acceptable among Veterans with prediabetes?

Hypothesis #2:
A LC-DPP can help more Veterans with prediabetes to achieve at least 5% body weight loss compared to existing lifestyle change programs (e.g., MOVE!)

5.4 Describe the relevance to Veterans of studying the stated research questions or hypotheses and the importance of the knowledge this protocol is likely to generate:

Twenty-five percent of Veterans have type 2 diabetes and an estimated 28% have prediabetes, an asymptomatic state characterized by abnormal blood glucose levels and an elevated risk of type 2 diabetes. Modest weight loss (i.e., at least 5%) can substantially reduce the risk of progression from prediabetes to type 2 diabetes. Behavioral change programs for weight loss are available within the VA, but most participants do not achieve clinically-significant weight loss.

Novel and scalable strategies are needed to help more Veterans with prediabetes to lose weight. Through this study, we will demonstrate the feasibility and acceptability of a LC-DPP among Veterans with prediabetes. These data will inform a large-scale comparative effectiveness trial of LC-DPP versus VA-MOVE.

5.5 What is the estimated duration of the entire protocol? (From IRB approval to IRB closure)

2 years

5.6 Check one of the boxes below based on your study design:

- ☐ Prospective Study
- ☐ Retrospective Study
- ☑ Both

☐ Other

5.7 What research methods will be used in the protocol? *(Check all that apply)*

☑ Surveys/Questionnaires
☐ Behavioral Observations
☐ Focus Groups
☐ Control Group
☑ Specimen Collection
☑ Interviews
☑ Chart Reviews
☐ Randomization
☐ Placebo
☐ Deception
☑ Audio Recording
☐ Video Recording
☐ Double-Blind
☐ Withhold/Delay Treatment
☐ Other (Specify)

Other:

5.8 Indicate whether or not each of the following applies to this protocol:

Does the Protocol involve international research?
NOTE: International research does not include studies in which VA is only one of multiple participating sites where the overall study-wide PI is not a VA Investigator.

○ Yes ◉ No

The protocol includes interaction between research staff (or clinicians acting on behalf of the researchers) and human subjects.

◉ Yes ○ No

This protocol involves the use of retrospective data, including, but not limited to, data from CDW and CMS.

◉ Yes ○ No

This protocol includes **ONLY** retrospective data use.

○ Yes ◉ No

A data repository will be maintained, i.e. data will be retained after completion of the protocol for other uses. (see ? for more details)

○ Yes ◉ No

The **ONLY** subjects will be providers or staff.

○ Yes ◉ No

Protocol is a clinical trial. (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 the interventions on biomedical or behavioral health-related outcomes.) Please see Help (?) on the right...

The Ann Arbor IRB is ONLY responsible for providing oversight of research activities conducted either at 1) the Ann Arbor VA, 2) at a site with whom there is a contract to use space or equipment by Ann Arbor Investigators while on VA time, or 3) a site without its own IRB that has established an MOU for the Ann Arbor IRB to serve as the IRB of record. As you complete this form, CONFINE DETAILED DESCRIPTION TO THESE ACTIVITIES.

○ Yes ◉ No

This protocol involves collaborative research activities conducted at both VAAAHS and other sites, VA or non/VA.

○ Yes ◉ No

5.12 USE OF HUMAN SPECIMENS

5.13 Indicate whether or not each of the following applies to this protocol

The protocol involves the use or collection of human specimens.

◉ Yes ○ No

Involves specimens that are left over from pathological or diagnostic testing (**non-research specimens**).
(Please attach a copy of the approval from the Chief of Pathology to use these specimens.)

○ Yes ◉ No

Involves **specimens collected for research** purposes **only.**

◉ Yes ○ No

This protocol includes **specimen banking** (specimens are retained for use outside of the purposes of this protocol).

○ Yes ◉ No

5.14 DRUGS AND DEVICES

5.15 Will the protocol include the use of any drugs?

○ Yes ◉ No

5.16 Will the protocol include use of any medical devices?

○ Yes ◉ No

5.17 RISKS

5.18 Indicate whether or not each of the following applies to this protocol (see ? for a definition of minimal risk)

Protocol places subjects at **greater than minimal risk** (do not include risks that are due to standard care)

○ Yes ◉ No

Human subjects are exposed to **radioisotopes.** Do not include standard care.
*Please contact the Radiation Safety Officer x53406 as soon as possible to see if any other safety mandates must be met.

○ Yes ◉ No

Subjects have other **radiation exposure** (e.g., x-rays). Do not include standard clinical use.
*Please contact the Radiation Safety Officer x53406 as soon as possible to see if any other safety mandates must be met.

○ Yes ◉ No

5.19 MEDICAL PROCEDURES

5.20 Indicate whether or not each of the following applies to this protocol

Findings from medical procedures already being performed as part of standard medical care will be used for research data collection.

○ Yes ◉ No

Protocol involves medical interventions or clinical services that are **NOT** part of standard care.

◉ Yes ○ No

Protocol involves invasive procedures, e.g. muscle biopsy, bronchoscopy.

○ Yes ◉ No

5.21 SUBJECT EXPENSES AND COMPENSATION

5.22 Indicate whether or not each of the following applies to this protocol

There may be expense or added **costs to the subject** or the subject's insurance.

○ Yes ◉ No

Subjects will be **compensated,** either in cash or other means such as a gift certificate.

◉ Yes ○ No

5.23 OTHER RESEARCH ACTIVITIES

5.24 Indicate whether or not each of the following applies to this protocol

Involves **surveys or questionnaires** completed by subjects

◉ Yes ○ No

The protocol includes the use of interviews and/or focus groups.

◉ Yes ○ No

Involve audio recordings of subjects.

◉ Yes ○ No

Includes the use of **recruitment materials** such as flyers, advertisements, emails or letters.

◉ Yes ○ No

Involves facial **photographs** or video **recordings** of **patients.**

○ Yes ◉ No

5.25 USE OF HAZARDOUS MATERIALS

5.26 Does the protocol include the use of any of the following?

- **Human tissue, blood, other body fluids (collected and/ or tested by non-clinical staff)**

- **Ionizing Radiation**
- **Biological Agents (microbiological, viral or plant agents, pathogens, toxins, poisons, or venoms)**
- **Chemicals (toxic, flammable, explosive, corrosive, carcinogenic, neurotoxins)**
- **Recombinant DNA**
- **Non-Human Cell Lines and Tissue Culture**
- **Physical Agents (UV light, lasers, radio-frequency or microwaves, electricity, trauma)**
- **Controlled Substances**

Do NOT include any Standard of Care activities performed by Clinicians. The following boxes should only be checked if Research Personnel will be involved in the activity. **If you checked YES... Please go to your Protocol Assistant and Create a New Protocol => VA Laboratory Safety Hazard Assessment Form.** **(This New form will go through the Research Safety Committee.)**

○ Yes ◉ No

5.27 CATEGORIES OF SUBJECTS REQUIRING SPECIAL ATTENTION

5.28 For each of the special categories of subjects listed below, indicate whether or not you plan to recruit them as part of your protocol. Exclude cases of data or specimens only.

Individuals with Impaired Decision Making Capacity

○ Yes ◉ No

Economically or educationally disadvantaged

○ Yes ◉ No

Pregnant Women - Check this box if your protocol will target pregnant women for recruitment, for studies in which the risk level is greater than mininal and pregnant women are not excluded, or for any protocol in which there may be increased risk to the mother or fetus due to study interventions or procedures.

○ Yes ◉ No

Prisoners - Check this box if your protocol involves prisoners as potential participants or if you are submitting a Request for an Amendment (and revising your IRB application) if a subject becomes a prisoner during the course of the study and it has been determined it is in the best interest of the subject to continue in the study.

○ Yes ◉ No

Non-Veteran patients (Note: A justification will be required later in the application form)

○ Yes ◉ No

VA employees (or WOCs) as the subject of the protocol. This does not include patients who also happen to be employees of the VA.

○ Yes ◉ No

Other non-Veterans (e.g. patient family members)

○ Yes ◉ No

6.0 Design and Methods

6.1 MEDICAL PROCEDURES AND USE OF CLINICAL SERVICES

6.2 Describe any use of medical procedures used in the protocol that are not part of standard therapeutic care of the subject .

(Note: this differentiation should be clear in the consent form as well)

Patients will have 5 ml of blood drawn at baseline, 6, and 12 months to test HbA1c and cholesterol. Patients will also have waist circumference measured at baseline, 6, and 12 months.

6.3 Could any of the interventions interfere with other care the subjects are receiving or may receive.

○ Yes ◉ No

6.4 Describe any usual healthcare procedures already being performed for diagnostic/treatment purposes that will be used for research data collection.

not applicable

6.5 For each research laboratory test (not lab tests used as part of standard care), identify the test and indicate if the test results will or will not be used clinically for diagnosis, treatment, or prevention of disease.

HbA1c, cholesterol, and waist circumference tests will not be used clinically for purposes of this study. However, results will be provided to patients' primary care providers and we will follow up with the PACT nurse and PCP when tests indicate a concern such as results in the diabetes range. A progress note will be entered into CPRS and the PACT nurse and PCP will be added as additional signers.

6.25 HUMAN SPECIMENS

6.26 Identify biological materials that will be used, their source, and procedures for obtaining material:

5 mL of blood will be obtained from each participant via intravenous blood draw at baseline, 6 months and 12 months, which corresponds to LC-DPP sessions 16 and 24. Blood samples will be used to test hemoglobin A1c and lipid levels.

The laboratory tests will be ordered by the study PI (Dina Griauzde, MD).
Dr. Chensu has approved the use of laboratory staff to obtain and process these tests using standard laboratory resources. Study team members will not handle any of the specimens. Email correspondence with Dr. Chensu is included as an attachment.

To avoid duplicate testing, we will accept these laboratory tests if ordered by participants' PCPs 2 weeks prior to the study-specific testing window.

6.27 Describe how and where tissues will be stored:

Specimens will be handled according to routine laboratory procedures.

6.30 Does the protocol involve genetic testing?

○ Yes ◉ No

6.33 Will samples be de-identified to maintain confidentiality? *NOTE: Coded specimens are not considered de-identified.*

○ Yes ◉ No

6.35 Will participants be informed of the results of the specimen testing?

(•) Yes ( ) No

6.36 What measures will be taken to minimize the potential for physical, psychological, financial, social, or legal harm from breaches of confidentiality and privacy resulting from unauthorized access to or loss of the specimens?

Biologic specimens will be handled according to routine laboratory procedures by laboratory staff.

6.37 Will specimens be destroyed after the protocol-specific use is completed?

(•) Yes ( ) No

6.38 Describe how the destruction of samples will be substantiated:

Specimens will be destroyed according to routine laboratory procedures by laboratory staff. These processes are identical to those performed as part of routine clinical care for patients that have blood drawn at the AAVA.

6.40 SURVEYS, QUESTIONNAIRES, FOCUS GROUPS AND INTERVIEWS

6.41 Describe any externally validated survey instruments that will be used, along with reference(s) to any published material about them. Also describe other questionnaires and/or surveys that will be used. Attach copy of each instrument to the Initial Protocol Submission Form.

We will use the following validated instruments:

1. Control of Eating - Cravings subsection:
Dalton M, Finlayson G, Hill A, Blundell J. Preliminary validation and principal components analysis of the Control of Eating Questionnaire (CoEQ) for the experience of food craving. 2015.

2. Stress Eating:
- Tsenkova, V., Boylan, J. M., & Ryff, C. (2013). Stress eating and health. Findings from MIDUS, a national study of US adults. Appetite, 69, 151-155.
- Burgess, E. E., Turan, B., Lokken, K. L., Morse, A., & Boggiano, M. M. (2014). Profiling motives behind hedonic eating. Preliminary validation of the Palatable Eating Motives Scale. Appetite, 72, 66-72.

3. Health and wellbeing: PROMIS Health Organization and PROMIS Cooperative Group, 2008-2012.
https://www.iconquerms.org/sites/all/files/attachments/pdfs/PROMISGlobalHealthScaleV1.0-1.1.pdf

4. Social Support:
- Norman, G. J., Carlson, J. A., Sallis, J. F., Wagner, N., Calfas, K. J., & Patrick, K. (2010). Reliability and validity of brief psychosocial measures related to dietary behaviors. International Journal of Behavioral Nutrition and Physical Activity, 7(1), 56.

5. Locus of motivation (e.g., internal vs. external)
- Williams et al. Health-Care, Self-Determination Theory Questionnaire Packet via selfdeterminationtheory.org

6. Physical activity:
- Craig et al. International Physical Activity Questionnaire: 12-Country Reliability and Validity. 2003.

7. Fatigue and Sleep:
- Kemper-Gascon, Global Health and Well-being. The Ohio State University. (See PDF)

We will also explore energy levels between meals and experiences with the program using non-validated question items and ask patients to complete diet and exercise logs.

See attached Excel file for summary of question items.

6.42 Describe in detail the interviews and/or focus groups that will be conducted as part of this protocol. Include information about the subjects, setting and topics. Include any information regarding the likelihood of the interview/focus group causing significant anxiety in a subject. Attach a copy of the interview and/or focus group guide(s) to the Initial Protocol Submission Form.

We will conduct semi-structured interviews with patient participants. Patients (n=up to 30) will be purposively sampled based on weight loss outcomes (e.g., achievement vs. non-achievement of at least 5% body weight loss). We will explore participants' experiences with the program and barriers to and facilitators of adherence to the diet.

We plan to interview LC-DPP coaches and Primary care providers (PCPs) in the future. However, this component of the study is not yet fully developed. An amendment will be submitted and we will obtain approval for all recruitment activities and materials prior to commencement of these interviews.

6.43 PHOTOS AND/OR AUDIO/VIDEO RECORDINGS

6.44 Describe the protocol's use of audio recordings of subjects. Include details on equipment to be used and the protection of the resulting files.

Individuals specified in section 6.42 will be interviewed by telephone or in-person. Interviews will be audio-recorded using the Olympus DS-7000 after written informed consent is obtained. If an individual does not wish to be audio recorded, we will take detailed written notes instead. To protect individuals' privacy, we will not record individuals' names. Rather, each interviewee will have a unique participant ID. A crosswalk file linking participant ID to identifying information will be maintained in a HiPAA secure, password-protected file. Interviews will be professionally transcribed verbatim and the audio files will then be destroyed.

6.54 EXPENSES & COMPENSATION

6.55 Describe specifically which procedures/drugs will be billed to the participant (or the participant's insurance) and which will be provided at no cost. Include a justification for expenses to the subject. See ? for more detail.

None.

6.56 Provide all details and justifications of the compensation plan. See ? for detailed requirements.

- **What form of payment will be used, i.e., check, voucher, electronic funds transfer, gift card?**
- **What is the schedule of payments, I.e., one-time or after specific visits?**
- **Provide justification that the proposed payments are reasonalbe and commensurate with the expected contributions of the participant to the protocol.**
- **Will the payment include transportation costs? If no, will transportation costs be paid separately?**
- **Specify the source of payment - VAAAHS, UM, Other...**

Participants will receive Visa and/or Amazon gift cards ($25 each) to compensate them for their time after completing the following study activities:
- Baseline labs
- 6-month survey
- 6-month labs
- 6-month interview
- 12-month survey
- 12-month labs
- 12-month interview

6.57 Will an SSN be requested and/or used in making payment/compensation? *Note: If yes, be sure and include in the HIPAA authorization form and in the informed consent the name of the organization making payment to include any VA-affiliated Non-profit Corporation or other non-VA entity.*

○ Yes ◉ No

6.58 RETROSPECTIVE DATA USE

6.59 Describe in detail all sources of retrospective data that will be used by the protocol.

Retrospective data will be used for screening only. Data from VA medical records will be obtained via the Clinical Data Warehouse (CDW) to identify patients with prediabetes. We will look at data for patients seen at VAAAHS in the past year (May 2019- May 2020). We will not review identified data of individuals in the VA MOVE program. Rather, there have been many published reports of VA MOVE program outcomes and we will compare our data with published VA MOVE! data as well as data from similar programs (e.g., Center for Disease Control and Prevention's National Diabetes Prevention Program).

7.0 Special Human Subject Categories

8.0 Recruitment

8.1 Describe the inclusion criteria for this protocol, along with the rationale for these criteria. This includes retrospective chart reviews. *Use bullet or numbering format.

We will recruit Veterans from AAVA primary care clinics.

Inclusion criteria:
- Age >= 18 years
- Prediabetes (defined as A1c 5.7% to 6.4% drawn within 12 months of study start date)
- Lipids drawn within 12 months of study start date
- Body mass index >= 25 kg/m^2
- Willingness to participate in group-based classes
- Able to engage in at least light physical activity such as walking
- Established primary care at the AAVA (defined as at least one office visit within 12 months of the study start date). This will ensure that participants can have access to a medical provider for medication changes and side effective management, if necessary.

We plan to interview LC-DPP coaches and Primary care providers (PCPs) in the future. However, this component of the study is not yet fully developed. An amendment will be submitted and we will obtain approval for all recruitment activities and materials prior to commencement of these interviews.

8.2 Describe the exclusion criteria for this protocol (including retrospective chart reviews). Include the rationale for excluding any patients who might particularly benefit from participation. Also address whether subjects enrolled in another protocol are excluded. *Use bullet or numbering format.

Exclusion criteria are:

- History of type 1 diabetes or type 2 diabetes
- Current participation in another lifestyle or behavior change program or research study
- Vegetarian or vegan lifestyle
- History of bariatric surgery
- Inability to read, write, or speak English
- Inability to provide informed consent
- Women who are pregnant or intend to become pregnant during the intervention period
- Individuals with LDL>190
- Individuals with a history of eating disorders
- Individuals with advanced kidney disease (defined as eGFR < 45 mL/min)

8.3 Will there be more than one group/type of subject recruited for the protocol?

○ Yes ◉ No

8.4

Describe the recruitment strategy for the just, fair, and equitable recruitment and selection of subjects, and reference recruitment procedures as cited in the scientific narrative to include the following: Plans for recruitment of all subjects (or selection of subjects as in record review). This description must include:

- **How, when, and where (include the exact location) the potential subjects are approached**
- **Description of different groups/types of subjects**
- **The maximum number of each subject group planning to enroll and whether the protocol will have access to a population with this number.**
- **Recruitment procedures such as data mining, physician referral, etc.**
- **How selection is equitable.**

NOTE: VA policy prohibits "cold calls" to potential VA research participants. Initial contact must be made in person or by letter prior to making any telephone contact, unless there is written documentation that the subject is willing to be contacted by phone about the specific study or the specific kind of research. The initial telephone contact must also provide a telephone number or other means for the potential participant to use to verify the study constitutes VA research (VHA Directive 1200.05).

Eligible patients will be sent a letter inviting them to participate in the study. We estimate that 10% of eligible individuals will enroll in our study. Thus, we will send study invitation letters by postal mail to up to 220 potentially eligible individuals. The letter will explain the purpose of the study. A phone number will be provided to individuals to allow for them to opt-in to study participation or opt-out of future contact by the study team. A member of the study team will contact individuals who opt-in. The study team member will confirm individuals' study eligibility and answer any questions. If up to 30 veterans are not recruited via the opt-in approach, a member of the study team member will call those individuals that did not opt-out within 3 weeks of the letter being sent; these individuals will be invited to participate.

All interested and eligible individuals will be invited to attend the in-person recruitment session. The purpose of this session is to conduct the informed consent process. We will explain the program and dietary approach (i.e., low-carbohydrate, high-fat) in detail and obtain written informed consent. In our prior pilot work at Canton Health Center, program participants informed us during qualitative interviews that they wished for additional education about the dietary approach to alleviate concerns regarding dietary fat and cholesterol intake. Because this is information that participants should, ideally, understand as part of the informed consent process, we will deliver a brief presentation (~20-30 minutes) as part of the recruitment session. An additional 20-30 minutes will be allocated to answering individuals' questions. Afterwards, those still interested in study participation will be asked to provide written, informed consent. Once written informed consent is obtained, they will be asked to complete a baseline survey.

A progress note will be entered into CPRS with the PACT nurse and PCP added as additional signers once an individual has enrolled in the study. We will also upload the signed consent form into the medical record.

8.5 **Identify all recruitment materials (flyers, advertisements, letters, etc.) that will be used. This should include how and where (VA, non-VA) the materials will be circulated/displayed. The text of all communications with prospective participants must be reviewed and approved by the IRB before they can be used.** ***If there will be telephonic contact during the recruitment process, a script must be provided for review.*** **Please attach copies of recruitment materials to the Initial Protocol Submission Form.** ***NOTE: All recruitment materials must be reviewed and approved by the IRB prior to use as part of any recruitment activities. All recruitment materials must include a statement that the study involves VA Research and a telephone number or other means for the potential participant to use to verify that the study is VA Research.***

Recruitment will be done via a letter and telephone follow-up/outreach. These documents have been attached for the committee's review.

We plan to interview LC-DPP coaches and Primary care providers (PCPs) in the future. However, this component of the study is not yet fully developed. An amendment will be submitted and we will obtain approval for all recruitment activities and materials prior to commencement of these interviews.

9.0 Risks and Benefits

9.1 **Describe and assess any potential or known risks and discomforts, including possible loss of confidentiality, and assess their likelihood and seriousness. Also describe precautions to decrease the likelihood of harm and procedures to deal with harms if they occur.** ***NOTE: Risks or harms can be physical, financial, social, or legal. They may involve breaches of***

confidentiality and privacy. Do not include the risks of usual care unless usual care is part of the research interventions being performed.

Physical

A low carbohydrate diet may cause side effects, particularly during the first several weeks. These include:

1. Constipation: this is a common side effect, which will be managed by instructing individuals to increase their consumption of water and low-carbohydrate, fiber-rich foods such as leafy greens.

2. Headaches: this is a likely side effect, which will be managed by instructing individuals to increase their water and salt consumption.

There is also a small risk patients may experience harm or injury if they increase their physical activity as a result of taking part in this program.

Psychological - (For Example: Loss of privacy and confidentiality may cause psychological issues.)

There is a potential risk of loss of data confidentiality, which could have psychological risks. We will mitigate this risk by using a secure, HIPAA compliant, crosswalk file linking participant IDs and direct identifiers.

Participants may be concerned about their risk for developing type 2 diabetes. We will ease their anxiety by emphasizing that type 2 diabetes is a preventable condition and that this intervention is one way to help them to reduce their risk.

Social and economic - (For Example: Loss of confidentiality may cause social or economic duress though the unlikely risk is low.)

There is a potential risk of loss of data confidentiality, which could have social or economic consequences, although this risk is low.

9.2 Describe any risk of discovering abnormal findings and how you will inform the subject and/or the subject's primary care provider.

We will obtain HbA1c and lipid levels at 6 months and 12 months. If these tests are abnormal, participants' PCPs will be notified via the electronic health record. Additionally, participants will be sent a letter informing them of their test results so that they can also arrange for appropriate follow-up care. This letter will be submitted with a future amendment prior to the start of study recruitment.

9.3 Indicate the level of risk you believe this protocol has: (The IRB will make the final risk level determination.)

- (•) Minimal Risk
- ( ) Greater than Minimal Risk

9.4 Discuss benefits that may be gained by the subject as well as potential benefits to society in general. (see ? for guidance)

The risks of the intervention are minimal and side effects are completely reversible if an individual discontinues the low-carbohydrate diet. In contrast, there is a great potential benefit to this intervention, as the dietary advice may help study participants to lose weight and decrease their risk of type 2 diabetes.

9.5 Describe the availability of resources subjects may need as a consequence of their participation, including medical and mental health services (e.g. ER, hotlines, clinical staff available).

Study participants will be provided with the phone number of the PI to contact with any concerns raised

due to participation in the program.

9.6 Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and in relation to the importance of the knowledge that may reasonably be expected to result.

The risks are minimal relative to the potential benefits. The probability and magnitude of risks of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. In addition, the potential benefits of preventing type 2 diabetes is significant.

9.7 Briefly describe the procedures or explain why there is no need for established procedures for the orderly withdrawal or termination of participation in the protocol by the participants:

Participants will notify the study team if they desire to withdraw from the study. Study team members will explore and document reasons for withdrawal. No data will be collected from participants after they withdraw from the study. Data collected prior to their withdrawal will be used in analyses.

The PI reserves the right to withdraw participants from the study for any of the following reasons:

•She believes that it is not in their best interest to stay in the study.
•They become ineligible to participate.
•They do not follow instructions.
•Their behavior toward the staff or other participants is disruptive or inappropriate.
•The study is suspended or canceled.

Please note that patients do not have to follow a low-carb diet to remain in the study. Weight loss is our measure of dietary adherence.

9.9 The procedures regarding reporting adverse events and protocol deviations/violations to the IRB should be described. If these are adequately described in your DSMP/DSMB, there is no need to duplicate the information here. In these cases, please attach a copy to the Initial Protocol Submission Form.

All serious adverse events, unanticipated problems, and protocol deviations will be reported to the IRB according to VAAAHS policy. Please see narrative for DSMP.

9.10 The Principal Investigator and the Study Team will report all adverse event, complaints, problems and non-complicance according to this VAAAHS policy and using the appropriate form (Adverse Event Reporting Form can be found in the upper right corner in the Help (?) Section). *Do not submit in AAROW. Please contact IRB Coordinator to discuss x53440.

◉ Agree

10.0 Informed Consent and HIPAA Authorization

10.1 Informed Consent Process and Waivers

10.2 The baseline assumption is that before ANY research procedures are conducted, all subjects will:

1. **Participate in an informed consent process;**
2. **Including all required elements ;**
3. **Using a signed consent form.**

Because many protocol designs make this difficult or impossible, VHA Directive 1200.05 - "Requirements for the Protection of Human Subjects in Research" allows two types of informed consent waivers: The first (Section 18 of 1200.05) waives the requirement to get SIGNED informed consent. This waiver does NOT waive the requirement for an informed consent PROCESS. The second type of waiver (Section 17 of 1200.05) allows a protocol to alter or omit some or all of the elements of informed consent OR to waive the requirement to obtain informed consent. HIPAA waivers and authorizations apply to all research subjects in which the Ann Arbor investigators will use or

disclose PHI. *VAAAHSis a Covered Entity and HIPAA Rule applies regardless if it is VA patients or not. It is STRONGLY suggested that you see ? for 1) policy language, 2) guidance for use of consent waivers, and 3) a list of the required elements of consent stipulated in VHA Directive 1200.05.

10.3 Will the Study Team obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the prospective subject's Legally Authorized Representative (LAR)?

(•) Yes ( ) No

If yes, check one or both of the below boxes if they apply to this study:

- [ ] Information will be obtained through oral or written communication with the prospective subject or the subject's Legally Authorized Representative (LAR)
- [x] Identifiable information or biospecimens will be obtained by accessing records or stored identifiable biospecimens

Please describe how this will be done:

If either or both of the above boxes is checked, an informed consent waiver request does not have to be submitted for this activity. However, a request for a HIPAA waiver will still need to be submitted and informed consent obtained for any research interventions after eligibility is established. ***If neither box was checked, this activity will need to be included in a request for an informed consent waiver.***

10.4 Which of the following options will be utilized to address informed consent requirements for all subjects, at all phases of the protocol? This section of the application form applies only to subjects who are participating in research that is overseen by the Ann Arbor VA IRB.

- [x] Signed VA Consent Form
- [ ] An alteration to the informed consent process. NOTE: If deception is involved, this box should be checked.
- [ ] Waiver of documentation of informed consent (using a Research Information Letter or other approved mode of communication)
- [ ] Waiver of informed consent process for the entire study
- [ ] Waiver of informed consent process for only a specific portion(s) of the study (not including recruitment)
- [ ] None of the above

What is the maximum number of subjects to be enrolled with a signed VA Consent Form?

30

10.5 USE OF VA CONSENT FORM

10.6 Consent will be obtained before any protocol procedures, including screening, are performed unless the IRB has granted a waiver of the informed consent process for either phase.

(•) Agree

10.7 Information being communicated to the participant or legally authorized representative during the consent process will not include exculpatory language through which the participant or legally authorized representative is made to waive or appear to waive any of the participant's legal rights or release or appear to release the Researcher, Sponsor, the VA or its agents from liability for negligence.

(•) Agree

10.8 **Identify the circumstances under which consent will be obtained including where the process will take place; any waiting period between describing the research and obtaining consent including sufficient time for the prospective participant to consider participation, and any steps taken to minimize the possibility of coercion or undue influence.**

We will obtain written informed consent at the recruitment session, as described in section 8.4. We will convey that all survey questions and interviews are voluntary and that participants are able to withdraw at any time for any reason without fear of repercussions. Prior to each interview, we will review each interviewee's rights as a research subject and reiterate their right to:
- Refuse to participate
- Refuse to answer any questions for any reason
- Refuse to have the interview recorded for the partial or full duration

Details on recruitment and consent for staff interviews will be submitted with a future amendment.

10.9 ***Reminder - If the research involves photos, videos, or voice recordings of a VA participant, then this information must be covered in the informed consent process and consent documents (VA Consent Form, Research Information Letter, Telephone Screen Scripts, etc...).***

10.33 **HIPAA AUTHORIZATIONS AND WAIVERS**

10.34 ***NOTE: Written HIPAA authorization signed by the individual to whom the information or record pertains is required when VA health care facilities need to utilize individually-identifiable health information for a purpose other than treatment, payment, or health care operations, e.g., research. (VHA Handbook 1605.1).***

10.35 **Does the protocol use any health information? Please note that the VA takes a broad definition of health, extending to any information that could reasonably be considered related to health.**

(•) Yes ( ) No

10.37 **Does the protocol use any health information with personal identifiers that the protocol staff has access to?**

(•) Yes ( ) No

10.38 **Is any waiver of HIPAA authorization being requested?**

(•) Yes ( ) No

10.39 **Criteria to be Eligible to Submit a Waiver Request: The Principal Investigator must check that the proposed research meets all of the following criteria in order to be eligible to submit a request (you will also need to describe how they are being met in your scientific narrative):**

- [x] The use of disclosure of protected health information involves no more than minimal risk to the privacy of the individuals.
- [x] There is an adequate plan to protect the participant identifiers from improper use and disclosure.
- [x] There is an adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research, unless there is a health or research justification for retaining the identifiers, or such retention is otherwise required by law.
- [x] The research cannot be practicably conducted without the waiver.
- [x] The research cannot be practicably conducted without access to and use of the protected health information.

- [x] The protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research prototocol, or for other research for which the use or disclosure of the requested information would be permitted under the HIPAA Privacy Rule.

10.40 Check all of the following that apply if Protected Health Information (PHI) will be used:

- [x] A protocol specific HIPAA Authorization is combined with the informed consent document.
- [ ] A separate protocol specific participant HIPAA Authorization form (VA Form 10-0493) is attached. Note: This is required when enrolling individuals with impaired decision making or with longitudinal studies requiring reconsent.
- [ ] A HIPAA Waiver of Individual Authorization is being requested to cover the entire study.
- [x] A HIPAA Waiver of Individual Authorization is being requested for recruitment purposes only.
- [ ] A HIPAA Waiver of Individual Authorization is being requested to cover a portion of the study.

Specify portion of study the request for HIPAA Authorization is being reqested for:

We need to obtain PHI to determine which patients are eligible for participation. Without the waiver, we would need to send letters to thousands of patients (who might or might not be eligible) to ask their permission to access their medical record data to determine their eligibility for the study, which would be highly impractical.

10.41 Indicate the sources of the health information the protocol will be using:

- [x] Medical records
- [ ] Images or audio recordings
- [ ] Biological specimens

Provide any details necessary to fully describe the sources of PHI:

We will use medical record data (e.g. HbA1c) to screen for eligibility for study participation. We need to review HbA1c data to determine potential eligibility for the study, as individuals must have HbA1c's within the prediabetic range.

10.42 Indicate the PII to be collected, used, and/or disclosed.

- [x] Names
- [x] Any geographic area smaller than a state
- [x] Any date (except year) that is directly related to an individual and/or any age over 89
- [x] Telephone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [x] Social Security Numbers (SSNs) or scrambled SSNs
- [x] Medical record numbers
- [ ] Health plan beneficiary numbers
- [ ] Account numbers
- [ ] Certificate and/or license numbers
- [ ] Vehicle ID and serial numbers including license plate numbers
- [ ] Device identifiers and serial numbers
- [ ] Web Universal Resource Locators (URLs)
- [ ] Internet Protocol (IP) addresses
- [ ] Biometric identifiers, including finger & voice print
- [ ] Full-face photographic images and any comparable images
- [x] Any other unique identifiers (number, characteristic or code)

Please explain the other unique identifer(s).

As data will be collected from CDW, PatientICNs will also be collected.

10.43 **Will the protocol access or collect any of the following Protected Health Information that requires higher levels of confidentiality?**

- **Alcoholism or alcohol abuse information**
- **Drug abuse information**
- **Sickle cell anemia information**
- **HIV test/infection results**

○ Yes ◉ No

☐ Alcoholism or alcohol abuse information
☐ Drug abuse information
☐ Sickle cell anemia information
☐ HIV test/infection results

10.44 **Identify all Protected Health Information (PHI) that you will access or collect for use in this research protocol:**

☑ Progress notes
☐ History & physical
☐ Discharge summary
☐ Operative reports
☑ Diagnostic/Laboratory Reports
☐ Imaging (x-ray, CT, MRI, etc.)
☐ Immunizations
☑ Allergy reports
☑ Medications
☐ Consultations
☑ Clinic notes
☐ Dental notes
☐ Mental health (not psychotherapy) notes
☐ Psychologial test results
☐ Genetic testing
☐ Survey/questionnaire responses
☐ Billing records
☑ Other PHI to be used

Specify any other PHI to be collected.

Problem list diagnoses

10.45 **Provide details on the items checked above and describe any other types of PII/PHI that will be used.**

As noted above in the description of inclusion and exclusion criteria, these data will be used to determine if patients meet the following criteria: BMI >= 25 and HbA1c 5.7%-6.4% in the prior 12 months.

10.46 **Specify the date range(s) of all PII/PHI to be collected.**

April 2019 - April 2020

10.47 **The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals.**

◉ Agree

Explain why risk is no more than minimal

We have extensive experience maintaining the confidentiality of PHI for research purposes. A cross-

walked file will be maintained to link participants to unique, de-identified study IDs. The crosswalk file will be kept in a separate, secure folder. Access to this folder will be restricted to study team members. All data will
be maintained in restricted folders on the VA network.

10.48 A plan exists to move all identifiable data to a location accessible only to the Research Service Records Liaison or an honest broker at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law. These records will be disposed of when they have met their Records Control Schedule or other contractual obligation, whichever is longest.

◉ Agree

Describe the plan:

All research data will be de-identified at the termination of the study, if not sooner. Study data will be moved to the CCMR data archive and destroyed by the CCMR data manager six (6) years following the end of the Fiscal Year after completion of the research project as described in the Records Control Schedule.

10.49 The plan to protect the identifiers from improper use and disclosure is adequate.

◉ Agree

Describe the plan:

Protection of screening data: A cross-walk file will be established that includes patient names linked to study ID numbers assigned by the CDW. Unique study ID numbers are needed to link multiple records for a patient in CDW. The cross-walk file will be kept in a folder on the VA network that is restricted to access by members of the study team. The study ID number will be maintained with the health data pulled from CDW in a separate, access restricted folder on the VA network.

Protection of patients' data following screening: Once we randomly select 220 eligible patients, we will create a separate folder that includes these patients' names, addresses, and phone numbers, but no health data. These data will be maintained in an access-restricted folder on the VA network. Interview responses will not include any patient identifiers.

10.50 The research could not practicably be conducted without access to and use of the PHI.

◉ Agree

Describe how the PHI access/use under the waiver enables the conduct of the research

We need access to PHI to identify the appropriate subset of patients (who meet are eligibility criteria for pre-diabetes) to whom we can send recruitment letters.

10.51 The research could not practicably be conducted without the waiver.

◉ Agree

Describe how the waiver/alteration enables the research to be conducted:

We need access to PHI to identify the appropriate subset of patients (who meet are eligibility criteria for pre-diabetes) to whom we can send recruitment letters.

10.52 By Signing this protocol for submission, the Prinicipal Investigator acknowledges the following:

1. The information listed in this waiver application is accurate and all the research protocol staff will comply with HIPAA regulations and the criteria set forth in this request.

◉ Agree

2. The protected health information described above is the minimum necessary in order to conduct the research.

◉ Agree

3. The requested information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the requested information would permit.

◉ Agree

11.0 Alternatives to Participation

11.1 Describe the alternatives to participation in this research protocol (see ? for guidance)

Participation in this research study is voluntary. Eligible individuals may choose to instead engage in other lifestyle change programs for weight loss (e.g., MOVE!) or to pursue other weight loss opportunities (e.g., bariatric surgery, pharmacotherapy).

12.0 Privacy and Confidentiality

12.1 What type of data will be received by the Princpal Investigator/Study Team?

Check all that apply:

- ☐ De-identified – Data does not contain any identifiers that could link the data to a specific participant. (See VHA Handbook 1605.01, Appendix B, para 2b, for a list of identifiers that must be removed before data can be considered de-identified. Data must be de-identified in accordance with HIPAA and Common Rule criteria. Scrambling of names and social security numbers is not considered de-identified information.
- ☑ Identified – Data contains direct identifiers sufficient to identify participants as indicated in VHA Handbook 1605.01, Appendix B, para 2b.
- ☑ Coded – Data linked to a specific subject by a code rather than a direct identifier. While the data may contain some protected health information only someone possessing the code can link the data to a particular participant.

If coded data is checked, specify how the link or code will be maintained, and list each person /role who will have access to the link or code (or state Not Applicable):

A cross-walk file will be established that includes patient names linked to study ID numbers assigned by the CDW. The cross-walk file will be kept in a folder on the VA network that is restricted to access by members of the study team. The study ID number will be maintained with the health data pulled from CDW in a separate, access restricted folder on the VA network.

12.3 Provide a brief description of how participant privacy will be protected in this protocol. See ? for details.

Protection of screening data: A cross-walk file will be established that includes patient names linked to study ID numbers assigned by the CDW. The cross-walk file will be kept in a folder on the VA network that is restricted to access by members of the study team. The study ID number will be maintained with the health data pulled from CDW in a separate, access restricted folder on the VA network.

Protection of patients' data following screening: Once we randomly select 220 eligible patients, we will create a separate folder that includes these patients' names, addresses, and phone numbers, but no health data. These data will be maintained in an access-restricted folder on the VA network.

To protect the privacy of interview participants, we will not audio record their names; the recording will only be linked to the individual using their study ID. The study ID will be cross-walked to the individual in a separate, secured file on the VA network that is restricted to members of the study team. The recordings will be uploaded to the secure study folder as soon as possible following each interview. Once

the recordings are saved to the study folder, they will be deleted off the DVR. The interviews will be transcribed verbatim. The de-identified transcripts will be used for analysis and no identifiable information will be provided in reports or publications.

12.4 Provide a brief description of how participant confidentiality will be protected in this protocol. See ? for details.

Locked office
Lock cabinet or storage unit
Restricted access
Access rights terminated when authorized users leave the project or unit
Individual ID plus password protection
Security software (firewall, anti-virus, anti-intrusion) is installed and regularly updated on all servers, workstations, laptops, and other devices used in the project.

12.5 Will a Certificate of Confidentiality (CoC) be obtained? (If yes, include the required information in the informed consent document.) ***NOTE: If this is a qualifying NIH Study, the CoC will be assumed. A CoC helps Investigators protect the privacy of human research participants enrolled in biomedical, behavioral, clinical, and other forms of sensitive research. Certificates protect against compulsory legal demands, such as court orders and subpoenas, for identifying information or identigying characteristics of a research participant. Form more information on CoCs go to: http://grants.nih.gov/grants/policy/coc/.***

○ Yes ◉ No

12.6 Is SSN used for any purpose other than scanning Consent/HIPAA into the medical record? (e.g. identifiying patients in administrative data, subject payments, use of clinical record)

◉ Yes ○ No

Indicate purpose and justification:

While PatientICN should be sufficient to pull data from CDW, we are still requesting access to SSNs in cases in which we may need to consult CPRS. Our data manager does not consider last initial + last 4 to be a unique identifier in this case.

12.7 Does the informed consent and HIPAA authorization forms thoroughly describe to subjects that their data will be combined with data from other sites?

○ Yes
○ No
◉ N/A

12.8 Will the informed consent and HIPAA authorization forms thoroughly describe to subjects that their data will be disclosed to the Coordinating Center where it will be combined with data from other sites and analyzed.

○ Yes
○ No
◉ N/A

13.0 Data Security

13.1 CONFIRMATIONS

13.2 In the event of a real or suspected breach of security, the IRB, Information Security Officer, Privacy Officer, VA Police (if appropriate), and the individual's supervisor will be notified immediately.

◉ Agree

13.3 Protocol staff will be up to date on any required VHA Privacy Policy and Information Security training or they will not be allowed access to VA Sensitive Information.

◉ Agree

13.4 Access to research sensitive information, if any, will be removed when protocol personnel are no longer part of the research team.

◉ Agree

13.5 At least one copy of all protocol records (whether sensitive or non-sensitive) will be retained under VA control and only destroyed in compliance with the approved Records Control Schedule

◉ Agree

Note: Investigators are responsible for protecting at least one copy of VA data, including non-sensitive data. Should you need to change any storage location in the future, please revise this Privacy and Data Security Plan

13.6 The VA retains ownership of any data collected as part of VA research. If the PI leaves the VA, custody of the research records will be determined by the Research Service. IRB approval is required to transfer the protocol to a new PI.

◉ Agree

13.7 NON-SENSITIVE DATA

13.8 List the VA location(s) [Room and Building] where you will store both paper and electronic non-sensitive protocol records.

Non-sensitive hard copy records will be maintained in VA CCMR offices in VA leased space, Building 16, third floor, North Campus Research Complex, 2800 Plymouth Road, Ann Arbor. Electronic, non-sensitive records will be kept in a restricted folder on a secure drive on the VA computer network.

13.9 VA SENSITIVE DATA (VASI)

13.10 Please describe your use of VA Sensitive Information (VASI):

○ This protocol does not collect or use VASI
○ This protocol uses, but does not save, collect, copy, or record VASI.
◉ This protocol collects, records, or saves VASI.

In which of the following ways will VASI be accessed/collected?

☐ Computer access
☑ Medical chart review
☐ Patient treatment
☑ Personal interviews
☑ Other

Please give a brief description of the data sources mentioned above and how they will be accessed.

Medical charts will be used to identify patients who meet study eligibility criteria and also to order and record laboratory tests (i.e., HbA1c, lipid panel). Study participants will be invited to take part in optional semi-structured interviews at 6 and 12 months. Participants will complete surveys at baseline, 6 months, and 12 months; these surveys will include self-reported side effects and experiences with the intervention.

13.11 Indicate the type of PII to be accessed. If you requested a HIPAA waiver for screening only, indicate any additional PII types that will be used post-screening.

- [x] Names
- [x] Any geographic area smaller than a state
- [x] Any date (except year) that is directly related to an individual and/or ages over 89
- [x] Telephone numbers
- [ ] Fax numbers
- [ ] Email addresses
- [x] Social Security Numbers (SSNs) or Scrambled SSNs
- [x] Medical record numbers
- [ ] Health plan beneficiary numbers
- [ ] Account numbers
- [ ] Certificate and/or license numbers
- [ ] Vehicle ID and serial numbers including license plate numbers
- [ ] Device identifiers and serial numbers
- [ ] Web Universal Resource Locators (URLs)
- [ ] Internet protocol (IP) addresses
- [x] Biometric identifiers, including finger & voice prints
- [ ] Full-face photographic images and any comparable images
- [x] Any other unique identifiers (number, characteristic, or code)
- [ ] None of the above

Please explain the other unique identifer(s).

Other identifier is CDW PatientICN. Biometric identifiers refer to voice recordings collected during interviews.

13.12 Will this protocol include the use of Protected Health Information (PHI) that requires specific consent from subjects? If you requested a HIPAA waiver for screening only, indicate any PHI types that will be used post-screening.

- [ ] Alcoholism or alcohol abuse information
- [ ] Drug abuse information
- [ ] Sickle cell anemia information
- [ ] HIV test/infection results
- [x] None of the above

13.13 Identify all Protected Health Information (PHI) that you will access for use in this research protocol. If you requested a HIPAA waiver for screening only, indicate any additional PHI types that will be used post-screening.

- [x] Progress notes
- [ ] History & physical
- [ ] Discharge summary
- [ ] Operative reports
- [x] Diagnostic/Laboratory Reports
- [ ] Imaging (x-ray, CT, MRI, etc.)
- [ ] Immunizations
- [x] Allergy reports
- [x] Medications
- [ ] Consultations
- [x] Clinic notes
- [ ] Dental notes

- [ ] Mental health (not psychotherapy) notes
- [ ] Psychologial test results
- [ ] Genetic testing
- [ ] Survey/questionnaire responses
- [ ] Billing records
- [x] Other PHI to be used

Specify any other PHI to be collected.

semi-structured interviews; surveys

13.14 Provide details on the items checked above and describe any other types of PII and/or PHI that will be used.

For screening and recruitment, we will use patients' names, laboratory test results, phone numbers and street addresses.
During the intervention period, we will obtain laboratory tests at 6 months and 12 months. We will administer surveys at 0, 6, and 12 months. We will conduct interviews (audio recorded) at 6 and 12 months.

13.15 Specify the date range(s) of all PII and/or PHI to be collected.

January 2019 to December 2021

13.17 Will the VASI be stored electronically and/or will there be paper documents?

- [x] Hardcopy, including paper, tape recordings, film, etc.
- [x] Electronic, including computer files, removable disk files, etc.

13.18 LOCAL DATA STORAGE

13.19 Storage of Hardcopy VASI

List the VA location(s) where you will store **hardcopy VA Sensitive Information** (VASI) for this protocol. Include the security measures such as in a locked cabinet inside a locked room when unattended.

Hardcopies of the surveys with study ID numbers (rather than participants' names) will be stored in a locked cabinet in the PI's office (371C, NCRC).
The tape recorder with recorded interviews will be stored in this same locked cabinet until the recordings are transcribed and uploaded, at which point the audio recordings will be destroyed.

13.20 Identify electronic VASI storage locations

Electronic VASI will be stored in the protocol folder on a secure VAAAHS server.

(•) Yes ( ) No

Provide the folder name.

v11.med.va.gov\ann\HSRDFS1\Research\VA_LCDPP

VASI is stored on a computer local hard drive (even temporarily) such as by specially obtained software.

( ) Yes (•) No

VASI is stored on VINCI.

( ) Yes (•) No

13.22 Indicate where the photos or recordings are stored

With the protocol hardcopy VASI

○ Yes ◉ No

With the protocol electronic VASI

◉ Yes ○ No

13.24 How long will the research data be stored and describe how the data will be destroyed once the maximum retention period as specified by the VHA Records Control Schedule 10-1 or the indicated retention period (if longer) is met?

Data will be stored for 6 years after the termination of the project, following records control schedule 10-1, at which time the data will be destroyed.

13.25 COLLECTION, STORAGE, TRANSPORTATION AND SHARING OF VASI OUTSIDE VAAAHS

13.26 Indicate yes or no for each off-site data category below:

Will VASI be collected outside of the VA, including by a web application or on specially obtained software?
Note: An approved Authorization to Transport may be required.

○ Yes ◉ No

Will mobile devices be used in the study, i.e., laptops, audio recorders?

◉ Yes ○ No

If yes, indicate that mobile devices will encrypted and that the encryption is FIPS 140-2 validated (or state N/A):

The audio recorders have been approved for use by the ISO.

Will any VASI, electronic or hard copy, be stored outside of the VA firewall?

○ Yes ◉ No

Will a copy of VASI be shared outside the VA for any purpose (e.g. collaborators, sponsors) by HIPAA Authorization?

○ Yes ◉ No

13.31 AGREEMENTS WITH THIRD PARTIES REGARDING DATA USE

13.32 Will a Data Use Agreement (DUA) or Memorandum of Understanding (MOU) regarding data use be required? **Please contact the Privacy Officer and Information Security Officer (immediately) to make sure you are completing the correct form.*

○ Yes ◉ No

13.33 Will this protocol require any data-related financial transactions?

○ Yes ◉ No

13.35 CODED DATA

13.36 Will coded data that excludes all HIPAA identifiers per VHA Handbook 1605.1 Appendix B (personal identifiers) be

used? (see ? for more information and definitions) *Coded data is not considered de-identified.

(●) Yes ( ) No

13.37 Where will the code key be stored?

( ) With hardcopy VASI, but separate from the coded data
(●) With electronic VASI, but separate from the coded data
( ) Both of the above

13.38 ADDITIONAL DETAILS

13.39 What is the plan for protecting protocol research data from improper use or disclosure? *NOTE: As part of the response to this question, indicate that removal of access to research study data will be accomplished for study personnel when they are no longer part of the research team. Include that the ISO and Privacy Officer will be notified within one hour of the improper use or disclosure.*

All study records will be kept in a restricted folder on a restricted server behind the VA firewall. Only study team members will have access to this folder. Access will be revoked from study personnel when they are no longer part of the research team. We will notify the ISO and Privacy Officer will within one hour of improper use or disclosure.

13.40 Add any other privacy or information security details here.

None.

14.0 Staffing

14.1 Identify ALL personnel, including the PI, who will work in this research protocol.

	Name (Last, First)	Employee is functioning within their scope of practice	Employee will be viewing identifiable data	Employee has verified VA work status and background check	Employee familiar with protocol termination procedure	Employee familiar with incident reporting procedures	Employee will be obtaining Informed Consent
	Griauzde, Dina	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No ( ) N/A	( ) Yes (●) No
	Kullgren, Jeffrey T, MD	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No ( ) N/A	( ) Yes (●) No
	Hershey, Cheryl	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No ( ) N/A	(●) Yes ( ) No

14.2 Describe how the researchers will have adequate time to conduct and complete the protocol.

The PI has 75% protected research time. She will also have research staff to assist her in these activities. Research staff will be hired at a later date and an amendment will be submitted.

14.3 Describe how the above list contains an adequate number of qualified staff.

Based on our prior experiences conducting a similar study at UM's Canton Health Center, we will need one part-time research assistant. We may also hire a project manager to further assist with study-specific tasks if our budget allows.

14.4 Conflict of Interest: Individuals directly involved in the conduct, design or reporting of research involving human subjects should not have more than a minimal personal financial interest in a company that sponsors the research or owns the technology being studied. A conflict of interest arises when a researcher is or may be in a position to put his or her own interest before the best interests of research subjects. Conflicts involving the IRB itself or conflicts involving the institution must be managed. In order to mange such conflicts, the IRB must be informed of potential conflicts of interest. Researchers submitting protocols using human subjects must disclose all interests that may be perceived as a conflict with the best interest of the subject in order for the research to be considered for approval.

The Principal Investigator and/or Co-Investigators have the following conflicts of interest to report to the IRB (or please state No Conflicts of Interest to declare):

No Conflicts of Interest to declare.

In addition, all Principal Investigators and Co-Investigators MUST complete a Research Financial Conflict of Interest Form (annually) and Project Specific Conflict of Interest Form located on their AAROW Dashboard. Please contact the RDC Coordinator at x55602 if you have any questions.

15.0 Project Association

15.1 The protocol must be associated with a new R&D Project. Identify the R&D Project(s) that correspond to this protocol.

Project Status	Proposal Number	Project Title	Principal Investigator
RDC Approved - New Project	RDC-2019-1270	VA LC-DPP	Dina Griauzde
		A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes	

15.2 As the Principal Investigator for this protocol, I certify that I have read, understand, and accept the Investigator responsibilities as outlined in VHA Directive 1200.05, paragraph 5g and that these include but are not limited to the following (please read and check all selections):

- ☑ Giving first priority to the protection of human subjects; upholding professional and ethical standards and practices; and adhering to all applicable VA and other Federal requirements, include IRB and the local VA Facility's policies and procedures regarding the conduct of research and the protection of human subjects.
- ☑ Ensuring all investigators and other staff participating in this human subjects research are qualified; have the appropriate training, education, and experience to perform procedures assigned to them; and that they have been appropriately credentialed and privileged as applicable per VAAAHS requirements.
- ☑ Submitting all amendments to the project or changes in the informed consent to the IRB for review

and approval prior to initiation, except when necessary to eliminate immediate hazard to the participants. Any changes implemented as a result of an immediate hazard will be promptly reported to the IRB as a project deviation and an amendment submitted if determined necessary.

- [x] Obtaining and documentating legally effective informed consent of the subject or the subject's legally authorized representative (LAR), as well as a HIPAA authorization, unless the IRB approves an applicable waiver.
- [x] Reporting problems, adverse events, and apparent serious or continuing noncompliance, including local research deaths, in accordance with VHA Handbook 1058.01, local VA Facility requirements, and IRB SOPs.
- [x] Ensuring appropriate research records are maintained that includes all information made or received by a VA Investigator over the entire lifecycle of the research activity and that these records are maintained in accordance with the VA Records Control Schedule and local policies and procedures.
- [x] Providing continuing review and/or requested updates for the study as applicable in a timely manner and in accordance with the VA and IRB policies and procedures. This includes submission of a closure reports upon completion of protocol.
- [x] Ensuring research does not start until final approval has been received from the IRB, and written notification from the local Facility ACOS/R&D in accordance with local R&D Committee approval policies and procedures.

15.3 **In addition, the VA Office of Research Oversight mandates that all Human Studies Research undergo Informed Consent Audit (ICA) annually and full Regulatory Binder Audit (RBA) every three years (triennially). The Principal Investigator must assure that informed consent is appropriately obtained and documented and that a complete and up to date Regulatory Binder (hardcopy or electronic) is maintained from time of initial approval. A complete set of Regulatory Binder instructions is available here: https://www.annarbor.research.va.gov /ANNARBORRESEARCH/docs/compliance/HS_REG_BINDER_INSTRUCTIONS_122314.doc**

(•) Agree ( ) Disagree

15.4 **The Protocol Application is now complete. Next you will complete the Initial Protocol Submission Form. This form is used to collect the Application and any other needed attachments for submission to the IRB for review.**

15.5 **Press *Save and Continue***

VA INFORMED CONSENT CHECKLIST

Complete this checklist for each consent obtained and file with the original informed consent document

RESEARCH STUDY IDENTIFICATION (Required information)
STUDY TITLE: _____
PI: _____
NAME OF STUDY TEAM MEMBER OBTAINING CONSENT:_____
ROLE OF STUDY TEAM MEMBER OBTAINING CONSENT: _____

RESEARCH SUBJECT IDENTIFICATION: (Required information)

Last Name	First Name	Mid. Init.	Last-4 SSN	Todays Date (mm/dd/yy)
			| | | |	/ /

A.	Date ALL required SIGNATURES (Subject, Witness (If required by IRB) and Person Obtaining Consent), their PRINTED NAMES and the DATES they signed the informed consent document (ICD) have been Checked and Verified Accurate and appear in the proper location
B.	DATE AND TIME (ICD) WAS REVIEWED AND DEEMED COMPLETE AND VALID **Must be prior to date/time of Subject's First Study Activity**
C.	DATE AND TIME OF THE SUBJECT'S FIRST STUDY ACTIVITY OR INVOLVEMENT
	Verify and Initial each requirement below.
1.	Informed consent and HIPAA Authorization, if required by VA-IRB was obtained from this subject prior to study participation.
2.	A VA Scope of Practice Form has been signed by the PI and approved by the VA IRB which designates me as an authorized agent of the PI and qualified to obtain consent for this study.
3.	This prospective subject was given adequate time necessary to carefully and fully read the Informed consent document (ICD) and all questions were answered to his/her satisfaction.
4.	All aspects of this subject's study involvement, including the purpose of the study, known and potential risks, possible benefits and alternatives to study participation were explained and discussed prior to subject signing the ICD.
5.	If required, a scanned image of the Research Enrollment Note, Consent Form and/or HIPAA Authorization will be entered into the subject's electronic medical record (CPRS).
6.	*Subject has been consented using the most recently approved, VA date-stamped version of the consent form (VA Form 10-1086) and HIPAA Authorization Form (VA Form 10-0493).*
7.	A copy of the completed and signed, original informed consent document has been issued to this subject and the subject was instructed to retain that copy for reference and to ask any and all questions that might arise throughout their study involvement.
8.	The subject has been shown where in the ICD to locate study team phone number(s) and the phone number of the VAAAHS IRB Coordinator. The subject has been reminded to call with any questions or concerns. Cathy Kaczmarek @ 734.845.3439
9.	The subject has been informed that participation is entirely voluntary and that they may withdraw their participation at any time and for any reason.
10.	Original ICDs and all copies are printed and issued as single-sided documents and that the original signed ICD must be kept in the investigator's project files on VA property.
11.	Upon completion of the Informed Consent Process, this subject's name was added to the Master List of All Subjects. [Per revised VHA Handbook 1200.05 (11/12/14) a MLS is no longer required, but a list of all enrolled participants is considered good research practice.]
12.	I know I can contact the VAAAHS IRB Coordinator at 734.845.3439 or the Research Compliance Officer at 734.845.4013 if I have questions or concerns regarding the consent of this or any individual considering study participation.

Department of Veterans Affairs Research Consent Form

Title of Study:	**A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes**	
Principal Investigator:	**Dina Griauzde**	VAMC: **VA Ann Arbor Healthcare System**

Key Information

WHAT IS THE STUDY ABOUT AND WHY ARE WE DOING IT?

People with prediabetes can avoid getting type 2 diabetes by losing a modest amount of weight. This study is about a lifestyle change program that teaches people to follow a low-carbohydrate eating plan and to take part in other healthy behaviors (such as increasing physical activity and managing stress). By doing this study, we hope to learn whether this program is practical and acceptable to Veterans. The goal is to help more Veterans with prediabetes lose weight and avoid type 2 diabetes. This work is unfunded.

WHAT DOES THE STUDY INVOLVE AND HOW LONG WILL IT LAST?

Your participation in this research will last about 1 year.

As part of this study, you will attend a lifestyle change program. The program consists of:

- 16 weekly one-hour group sessions led by a lifestyle coach.
- 8 additional one-hour sessions once or twice a month.
- Learning how to follow a low-carbohydrate diet.
- Keeping a food and exercise log.
- Completing surveys and laboratory tests at study start, 6, and 12 months.
- You may be asked to take part in an optional interview about the program at 6 and 12 months.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

Participating in this study will provide instruction and support for following a low-carbohydrate eating plan and increasing your physical activity. Following this program may help you to lose weight and may help you avoid getting type 2 diabetes, but there are no guarantees.

For a complete description of benefits, refer to the Detailed Information section of this consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

Taking part in this study will involve attending group sessions, tracking food, and completing surveys which may be inconvenient. There is also a small risk you may experience any of the following:

- Side effects from starting a low-carbohydrate eating plan.
- Discomfort from the blood tests.
- Harm or injury if you exercise more as a result of taking part in this program.
- Some of the survey questions may bother you.
- Someone outside the study team may see the information we collect from you.

For a complete description of alternate treatment/procedures, refer to the Detailed Consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

RESEARCH SUBJECT IDENTIFICATION: (Required information)

Last Name	First Name	Mid. Init.	Last-4 SSN	Todays Date (mm/dd/yy)
			| | | |	/ /

Department of Veterans Affairs Research Consent Form

Title of Study:	**A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes**	
Principal Investigator:	**Dina Griauzde**	VAMC: **VA Ann Arbor Healthcare System**

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Dr. Dina Griauzde of the VA Ann Arbor Healthcare System. If you have questions, suggestions, or concerns about this study or you want to withdraw from the study, her contact information is: 734-845-5129.

RESEARCH DETAILS

INTRODUCTION

We are inviting you to take part in a research study. The purpose of this consent form is to give you information to help you decide if you want to be in the study. Please read this form carefully and ask study staff to explain anything you do not understand. You will have a chance to ask questions before you make your decision. This process is called 'informed consent.'

WHAT IS THE PURPOSE OF THIS STUDY?

With this research we hope to learn if a group-based lifestyle program teaching a low-carbohydrate eating plan will be successful in helping Veterans with prediabetes lose weight and prevent type 2 diabetes. We hope to gain a better understanding of the strengths and challenges of this program for Veterans. This will help us design lifestyle programs at the VA that are more useful for patients.

HOW LONG WILL I BE IN THE STUDY?

This research study is expected to last about 2 years. Your personal participation in the project will take about one year. This study will include up to 30 Veteran patients from the Ann Arbor VA.

WHAT WILL HAPPEN AND WHAT CAN I EXPECT IF I TAKE PART IN THIS STUDY?

If you choose to take part in this study, you will be asked to complete a survey (about 30 minutes), have 5 mL (about 1 teaspoonful) of blood drawn to check HbA1c (diabetes screening test) and cholesterol levels, and have your waist measured when you join the study. You will be free to skip any survey questions you prefer not to answer. After you complete the survey and blood tests, you will be enrolled in the VA Low-Carbohydrate-Diabetes Prevention Program (LC-DPP).

The VA LC-DPP will be led by a dietitian (lifestyle coach) from the VA Health System who is trained to teach people how to follow a low-carbohydrate eating plan. This group-based program consists of 16 weekly sessions followed by 8 sessions once or twice a month. The sessions will be held at the Ann Arbor VA Hospital. Each session will last one hour.

You will be asked to attend this program one day a week for 16 weeks. Because sessions may be cancelled during holiday weeks or due to weather conditions, these 16 sessions will take place over 6 months. After that, you will be asked to attend the program once or twice a month for the next 6 months.

During the program, you will be encouraged to follow a low carbohydrate diet and monitor your weight at home. You will be asked to keep a log of the foods that you eat. You will also be asked to write down the minutes of physical activity that you perform daily. The lifestyle coach will review these materials each week and she will provide you with written feedback. She will also get your weight using a scale in a private room before the start of each session.

You will be taught to follow a low-carbohydrate eating plan. The sessions are designed to teach you how to make specific changes to your meals and snacks so that they meet the low-carbohydrate recommendations. In general, you will be advised to eat foods such as leafy greens, non-starchy vegetables, meat, eggs, cheese, berries, nuts and seeds. You will be advised to avoid foods such as bread, pasta, potatoes, flour, and beans. You will not need to count calories. Rather,

you will be advised to eat when you are hungry and stop when you are full. The lifestyle coach and study team will be available to answer specific questions and address any concerns.

You will be asked to complete surveys, blood tests, and waist measurements again at 6 and 12 months. You will be free to skip any survey questions you prefer not to answer.

You may be invited to take part in a phone interview at 6 or 12 months to answer questions and share thoughts about the program. These interviews will be audio-recorded and the recordings will be typed into transcripts. If you would like to take part in an interview but don't wish to be recorded, we will take detailed notes instead. The transcripts and notes of the interviews will be analyzed to assess the program. They will not be given to anyone outside the VA. You may decline to take part in the interview and still take part in the study.

We will let your primary health care provider know that you are taking part in this study. We will let you and your provider know the results of the blood tests. In the event that we detect a concerning test result (e.g., hemoglobin A1c in the diabetes range), we will ensure that you have timely follow-up with your provider to discuss treatment options. We will also keep your provider informed of your progress in the program and ask that he/she adjust your medications, if necessary. For example, some people need a decrease in blood pressure medications when following a low-carbohydrate diet.

To summarize, your participation in this study will involve:

AT STUDY START	AT 6 MONTHS	AT 12 MONTHS	THROUGHOUT STUDY
• Survey with questions about your health (about 30 minutes) • HbA1c and cholesterol blood tests • Waist measurement • Be enrolled in the VA Low-Carbohydrate-Diabetes Prevention Program (LC-DPP)	• Survey with questions about your health (about 30 minutes) • HbA1c and cholesterol blood tests • Waist measurement • May be invited to take part in a phone interview	• Survey with questions about your health (about 30 minutes) • HbA1c and cholesterol blood tests • Waist measurement • May be invited to take part in a phone interview	• 16 weekly one-hour group sessions over first 6 months • 8 one-hour group sessions once or twice a month over the next 6 months • Follow a low-carbohydrate eating plan • Keep food and physical activity logs • Receive written feedback from lifestyle coach

If you take part in this study, you will be expected to:

- Keep your study appointments. Please contact the investigator or research staff to reschedule as soon as you know you will miss an appointment.
- Complete the study surveys.
- Have your blood drawn.
- Participate in the VA Low-Carbohydrate-Diabetes Prevention Program (LC-DPP).
- Fill out your food and physical activity logs as instructed.
- Ask questions as you think of them.
- While participating in this research study, do not take part in any other research project without approval from the investigators. This is to protect you from possible injury from things such as extra blood draws. Taking part

in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

Any procedure has possible risks and discomforts. The researchers have taken careful steps to minimize the risks of this study. The procedures in this study may cause all, some, or none of the risks or side effects listed.

- Inconvenience:
  - You may find it time-consuming and inconvenient to participate in the group sessions or to track your food or physical activity minutes.
  - You may find it inconvenient to travel to the VA for the group sessions and study visits. You will not be eligible for VA travel pay for these visits.
  - You may also find it inconvenient to complete the surveys or blood tests.
  - The researchers will minimize this risk by compensating you for the time required to complete the blood tests at study start, 6 and 12 months and the surveys at 6 and 12 months.
  - You may find that following a low-carbohydrate diet adds to your monthly grocery bills.
- Blood draws:
  - There may be some discomfort, bruising, or bleeding at the site where the blood is drawn. Rarely, fainting occurs because of drawing blood.
  - Only VA employees with experience drawing blood will collect your blood samples for the study.
- Surveys and sessions with the lifestyle coach:
  - Some people become uncomfortable at being asked questions about their health. You may choose to skip any questions you don't wish to answer. You may also end the session at any time.
- Diet:
  - You may experience some side effects when you first reduce the amount of sugars and starches in your diet, such as constipation, headache, bad breath, and muscle cramps. These symptoms usually go away after the first couple weeks on the diet. If this happens, you can talk to the study staff. If your concerns or side effects are severe, you can speak to the study physician (Dr. Dina Griauzde). We have also shared information with your primary health care provider regarding the benefits and potential side effects of low-carbohydrate diets, and he/she should also be able to help you manage your symptoms. If you take medications for high blood pressure, the doses of these medications may need to be reduced if you experience lightheadedness or dizziness.
  - Elevated LDL cholesterol levels: some people may experience increases in their LDL cholesterol level when following a low-carbohydrate diet. The reason for this elevation is not known. In the event that your LDL cholesterol level is increased, we will notify your health care provider. Depending on the degree of increase, you may be advised to start a cholesterol-lowering medication. If you are already taking a cholesterol medication, you may be advised to increase the dose. You may also be advised to change your diet by increasing your intake of carbohydrates.
  - Some people have developed kidney stones while following a low-carbohydrate diet. People who have had prior kidney stones may be more likely to develop stones. During the program, you will learn about steps that you can take to help decrease the chance of developing kidney stones. These include (1) drinking plenty of water; (2) eating foods high in calcium (e.g., dairy, salmon); (3) limiting intake of certain foods that are high in oxalate (e.g., celery, Brussel sprouts, certain nuts); (4) avoiding Vitamin C supplementation; and (5) eating a moderate (not high) amount of protein.
- Loss of confidentiality:
  - We will not share your answers to survey questions with your doctor or anyone else without your permission. However, if we think you are in danger of harming yourself, we are required to get help for you.
  - It is possible that someone outside the study team could get access to your study data, although we will work hard to prevent this from happening

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks of the usual care you receive are not risks of this study. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

We do not know if you will get any benefits from taking part in this research study. However, possible benefits may include weight loss, decreased risk of diabetes, and reduction in hemoglobin A1c. Also, while some people may experience an increase in LDL cholesterol levels, others may see an improvement in cholesterol levels. Your participation in this study may also help the researchers to design and test new ways to help more people prevent type 2 diabetes.

You will receive results of your hemoglobin A1c and cholesterol tests at study start, 6 and 12 months.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

You are not required to participate in this study, and you may drop out of this study at any time without penalty. If you decide not to participate or choose to withdraw, you will not lose any benefits that you are entitled to. You will not lose any services, benefits, or rights you would normally have if you choose not to volunteer.

If you choose not to participate in this study, there are other options for preventing the development of type 2 diabetes. These include VA MOVE!, traditional Diabetes Prevention Programs and other lifestyle change programs that help you to lose weight and exercise more. You may discuss these options with your doctor.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Taking part in this study will involve collecting private information about you. This information will be protected in the following ways:

- Paper study records will be kept in a locked filing cabinet in a locked VA office.
- Electronic study records will be stored in secure study folders on VA servers.
- Only approved research staff will have access to the information.
- If the results of this study are reported in medical journals or at meetings, you will not be identified by name or by any other means.

Your information collected as part of the research, even if information that identifies you is removed, will not be used or distributed for future research studies. By law, study records must be kept in a secure location for about six years after the study has ended, at which time they will be destroyed.

While this study is being conducted, you will not have access to your research related health records. This will not affect your VA healthcare including your doctor's ability to see your records as part of your normal care and will not affect your right to have access to the research records after the study is completed.

Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal and state laws and the federal medical law, known as the HIPAA Privacy Rule, also protect your privacy. By signing this form, you provide your permission called your 'authorization,' for the use and disclosure of information protected by the HIPAA Privacy Rule.

Title of Study:	**A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes**	
Principal Investigator:	**Dina Griauzde**	VAMC: **VA Ann Arbor Healthcare System**

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records such as medical history, allergies, and lab results.

The research team may also need to disclose your health information and the information it collects to others as part of the study progress. Others may include the Institutional Review Board, Food and Drug Administration (FDA), Office of Human Research Protections (OHRP), the VA Office of Research Oversight (ORO), and the Government Accountability (GAO).

Your health information disclosed pursuant to this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Principal Investigator at:

Dina Griauzde
2800 Plymouth Road
NCRC Bldg 16; Room 16-371C
Ann Arbor, MI 48109

Or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Study Team receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization, Dina Griauzde and her research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

WHAT ARE THE COST TO ME IF I TAKE PART IN THIS STUDY?

You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

Reimbursement for participation:

You will receive a Visa or Amazon gift card to compensate you for completing each of the following study activities:

- Baseline labs ($25)
- 6-month survey ($25)
- 6-month labs ($25)
- 12-month survey ($25)
- 12-month labs ($25)

Those who are invited to take part in an interview at 6 and 12 months will also receive a $25 gift card after completing the interview.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

Department of Veterans Affairs Research Consent Form

Title of Study:	**A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes**	
Principal Investigator:	**Dina Griauzde**	VAMC: **VA Ann Arbor Healthcare System**

If you are injured from taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury occurs because you fail to follow study procedures.

If you should have a medical concern or get hurt or sick from taking part in this study, call:

Dr. Dina Griauzde (Principal Investigator) at 734-845-5129.

Emergency and ongoing medical treatment will be provided as needed.

It is important for you to understand that the Ann Arbor VA does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the Ann Arbor VA will not pay for any wages you may lose if you are harmed by this study.

You do not give up your legal rights by signing this form.

DO I HAVE TO TAKE PART IN THE STUDY?

It is up to you whether to take part in this study. You may decide not to be in the study at any time. If you choose not to take part or choose to stop taking part at any time, you will still receive the same health care and benefits from the VA you currently receive. Your decision will not change that in any way.

If you choose to take part in the study but then change your mind, Dr. Dina Griauzde and her research team can continue to use the information collected from you up to that point. The research team will not collect information about you after you let them know you no longer wish to take part in the study, though they may still collect information about you that is available from public records. The blood samples you provide to the study team cannot be withdrawn.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

The Principal Investigator may withdraw you from the study without your consent for one or more of the following reasons:

- She believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- You do not follow instructions from the researchers.
- Your behavior toward the staff or other participants is disruptive or inappropriate.
- The study is suspended or canceled.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

If you have any questions, complaints, or concerns about this study, please contact Dr. Dina Griauzde at 734-845-5129. If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the IRB Coordinators at (734) 845-3440 if you have questions, complaints or concerns about the study or if you would like to obtain information or offer input.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

The researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

Department of Veterans Affairs Research Consent Form

Title of Study:	**A Mixed Methods Pilot Study of a Low-Carbohydrate Diabetes Prevention Program Among Veterans with Prediabetes**	
Principal Investigator:	**Dina Griauzde**	VAMC: **VA Ann Arbor Healthcare System**

WHO COULD PROFIT FROM THE STUDY RESULTS?

The information and samples that you provide will no longer belong to you. The research may lead to new medical knowledge, treatments, or products. These products could have some financial value. There are no plans to provide financial payment to you or your relatives should this occur.

FUTURE USE OF DATA AND RE-CONTACT

Your data will not be used in future research and you will not be re-contacted about participating in future research.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

The research coordinator has explained the research study to me. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me. I have been given the chance to ask questions and obtain answers.

By signing this document below, I voluntarily consent to participate in this study and authorize the use and disclosure of my health information for this study. I also confirm that I have read this consent, or it has been read to me. I will receive a copy of this consent after I sign it.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name (Print)	_____ Participant's Signature	_____ Today's Date

Person Obtaining Informed Consent		
_____ Name (Print)	_____ Signature	_____ Today's Date