

Advance Care Planning for Older Patients with Diabetes at High Risk for
Hypoglycemia Manual of Operating Procedures (MOP)

**Manual of Operations and Procedures
&
Statistical Analysis Plan**

Advance Care Planning for Older Patients with Diabetes at High Risk for Hypoglycemia
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MOP Contents and Organization

1.0 Introduction

A copy of the study protocol should be included as an appendix.

The MOP should include all of the relevant sections from this list that apply to the specific study. If a section does not apply (e.g., randomization for a study with no randomization), it is not included in the MOP. Additionally, if the study involves a drug intervention, either the Package Insert for an approved drug or the Investigator's Brochure for an investigational product must be included as an appendix.

The following documents should also be included in the MOP appendices: Study Protocol, Study Forms, Informed Consent, and HIPAA, Standard Operating Procedures, Recruitment Flyers, Letters to Participants, etc.

The population of US adults aged 75 and older is expected to nearly double from 25 million today to 46 million by 2060 and 80% of these older individuals have chronic health conditions such as type 2 diabetes (T2D). As patients age, they become more prone to adverse consequences of treatment. Among the nearly 9 million adults ≥ 75 with T2D, for example, hypoglycemia and its adverse consequences have become the leading preventable treatment complication.

Hypoglycemic episodes in older adults are associated with a 1.7-fold increased incidence of fall-related fractures, a 2-fold increase in cardiovascular events,⁵ and 2.3-fold increase in mortality. Other studies have demonstrated the association of hypoglycemic episodes with lower self-reported quality of life, greater cognitive decline, and increased risk for hospitalization. New strategies are needed to reduce this epidemic of hypoglycemia and its related complications in older adults with T2D.

Many older adults with T2D would experience better health and quality of life by reducing their T2D medication treatment intensity and risk for hypoglycemic episodes. However, the decision to reduce medication intensity ("deprescribing") by setting less stringent glucose/HbA1c treatment goals is not straightforward nor commonly implemented. Due to the lack of definitive, evidence-based treatment guidelines in older patients with T2D the decision to reduce treatment intensity must be informed by patient preferences and values. However, patient-provider conversations to address whether and how to deprescribe medicines can be challenging. New tools that educate patients and build their communication skills to voice their preferences offer a promising strategy for improving the safety of T2D care in high-risk older adults.

The goal of advance care planning (ACP) is to ensure that patients receive medical care that is aligned with their goals and preferences. Although often applied to end-of-life decisions, the ACP paradigm has recently been expanded to include preparation for communication and decisions across the illness trajectory. This expanded ACP aims to prepare patients to define their preferences and values and to participate more effectively with their clinicians in making complex medical decisions over time. By preparing and supporting patients to participate in re-assessing

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their T2D treatment, changing health, and care goals, we hypothesize that this expanded ACP strategy can be a powerful tool to support T2D treatment decisions by older adults.

The goal of this study is to apply the expanded ACP paradigm (values elicitation and skill building for communication and decision making) to the specific clinical problem of hypoglycemia-related adverse outcomes in vulnerable older patients (Prepare for Your Diabetes Care). We previously developed a patient-directed online ACP tool (PREPARE, prepareforyourcare.org) and validated its acceptability, usability, and clinical impact on engagement and documentation of patients' general ACP preferences in two randomized controlled trials. We will adapt this tool to test the hypothesis that expanded ACP can support safer long-term T2D care among older adults at high risk for treatment-related hypoglycemia. Our approach tests a new expanded ACP strategy to support value-aligned care and to address the growing clinical problem of treatment-related adverse events in older patients with T2D. This strategy represents an innovative and potentially widely applicable method to help older adults and their providers improve safety by preparing patients to make informed decisions based on their goals and preferences. If successful, this framework could be scaled and applied in a wide variety of healthcare settings and chronic conditions in which evolving risks, benefits, and consequences of treatment require re-assessment with age.

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2.0 Study Overview

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This study will test the efficacy of delivering an educational web-based program to support safer, long-term T2D care among older adults at high risk for treatment-related hypoglycemia.

The primary outcome of interest will be to compare incidence and prevalence of hypoglycemia between study arms; specifically, the differences in clinically significant hypoglycemia in KP Members who are ages 75 or older, with T2D, able to communicate in English, ≥1 year of continuous KPNC membership, and prescribed insulin and/or SU. The primary hypothesis (H1) is that the **Prepare for Your Diabetes Care** intervention will result in reduced prevalence of severe hypoglycemia.

The secondary outcomes are diabetes medication de-prescribing and patient-reported outcomes.

The study is a 2-arm, parallel group, clinical trial with random allocation to intervention (Prepare for Your Diabetes Care) vs. control (usual care) at the patient level stratified by primary care practice using a concealed random number generator.

At the start of the trial, all potential participants (n=600) will be randomized and then will be contacted by mail for recruitment. They will be directed on how to opt into study procedures.

All data will be collected by Kaiser Permanente Division of Research Study Staff into REDCap, during recruitment and guidance calls. Research participants are in the study for 12 months, where they will complete a baseline survey at time of enrollment (T0), another survey 6 months (T6), and a final survey 12 months after initial enrollment (T12).

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3.0 Study Organization and Responsibilities

Richard Grant (MPI) – Oversees all aspects of research study, contributes to study design and decision making, responsible for the content of the intervention and its deployment identification, recruitment, screening, and enrollment of participants, submitting documents to regulatory bodies, compliance with and accountability of study intervention administration, ensuring compliance with human subject's regulations and policies

Rebecca Sudore (MPI) – Oversees all aspects of research study, contributes to study design and decision making, responsible for the content of the intervention and its deployment identification, recruitment, screening, and enrollment of participants, submitting documents to regulatory bodies, compliance with and accountability of study intervention administration, ensuring compliance with human subject's regulations and policies

Ilana Peterson (Coordinator) – Development and maintenance of all study materials including the protocol, MOP and study forms, obtaining informed consent from each participant, recruitment, screening, and enrollment of participants, maintenance of study binder.

Brookelle Li (Coordinator) – Development and maintenance of all study materials including the protocol, MOP and study forms, obtaining informed consent from each participant, recruitment, screening, and enrollment of participants, maintenance of study binder.

Jose Mejia (Coordinator) – Development and maintenance of all study materials including the protocol, MOP and study forms, obtaining informed consent from each participant, recruitment, screening, and enrollment of participants, maintenance of study binder.

Dilrini Ranatunga (Data Analyst) – Development of the randomization scheme and procedures, collecting study data and following participants through study completion, reporting and monitoring of Adverse Events (AEs) and Serious Adverse Events (SAEs), and developing and implementing: quality control procedure, data management procedures, reports on enrollment and participant status.

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4.0 Study Flow

An overview of the study processes, presented in a flow diagram in Figure 1, describes each of the study's major steps. It should be uniquely tailored to the study and is helpful in describing the study to new staff members.

Figure 1: Study Flow Diagram

Identify pool of potential participants
Randomize all potential participants
Pre-screening Eligibility by EHR – no = indicate reason
Screen inv Initial call cognitive– no = indicate reason
Obtain Informed consent (verbal)
Conduct baseline survey
Administer intervention or control
Survey at 6 months post-initial visit and another 12 months post-initial visit
END

5.0 Informed Consent

This is a low-risk, study involving a benign behavioral intervention that is brief (20-30 minutes), harmless (educational video), not physically invasive, and not likely to have lasting adverse impact or to be offensive or embarrassing. The consent process informs the patient about the study, indicates the participation is voluntary and they have the right to stop participation at any time. Risks are described orally during the consent process. This consent process has been modified for elderly patients considering the COVID-19 pandemic where in-person is contact is limited.

Individuals for whom we have PCP approval will be mailed a packet to their listed home address. This packet will include the following documents: 1) a letter explaining the study, 2) information on how to contact the study team (via phone or email) to express interest in participation or to opt out of study participation and further contact by the study team, 3) a hard copy of the information sheet (containing the elements of consent), and 4) a hard copy of HIPAA Privacy Rule Authorization form. After 1 week, we will begin contacting patients who have not yet responded, and using our telephone script, invite patients to participate in the study. During this call, verbal informed consent will be obtained from patients wishing to participate in the study. We have developed a modified informed consent process designed for older populations that adheres to the Agency for Healthcare Research and Quality recommendations. The process involves: using a consent form written $\leq$ 6th-grade reading level and $\geq$ 14-point font; reading the

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consent form verbatim; allowing time for questions; and verifying comprehension through repeated and targeted “teach-to-goal” education until comprehension is achieved. The process takes approximately 10 minutes.

Study Informed Consent Process: General description of the study and participant’s responsibilities –

- Consent is obtained verbally after a study member is deemed eligible, a recruitment packet is sent, and the participant has passed the cognitive screening.
- Study Coordinator explains risks and benefits, reminding patient participation is voluntary, and may discontinue at any time (and procedure for termination).
- Coordinator provides contact information for questions about subject rights.
- Coordinator explains who has access to patient’s protected health information, and how confidentiality is maintained.
- Coordinator explains how participant may learn outcome of study, and be provided with a copy of publication of any article published

5.1 HIPAA Authorization

This study will collect the following information that could potentially identify the participant. This information will be collected and used only for research purposes and will only be made accessible to study staff.

- Name
- Date of Birth/Age
- Home Address, including Zip Code
- Phone Number(s)
- Qualifying Medical Condition for Inclusion into Research Study

Deidentified information could be used for future research studies or shared with another investigator for future research studies.

Waiver of HIPAA Privacy Rule Authorization for recruitment:

It would not be practical to contact each participant to obtain consent and authorization to review their medical records. Requiring authorization would introduce biases into the selection of patients into the cohort of potentially eligible individuals. This would have a substantial and detrimental impact on the validity and generalizability of our research findings thus, the research could not be practicably carried out without the HIPAA waiver.

Waiver of HIPAA Privacy Rule Authorization for non-responders:

We feel that a waiver of authorization for non-responders is appropriate, as:

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- Requiring a signed HIPAA Privacy Rule Authorization would affect our ability to assess the representativeness of our study population, as well our ability to assemble the concurrent usual care study cohort, which in turn will affect the validity and generalizability of our research findings.
- The recruitment materials will include an opt-out provision with instructions for how individuals can affirmatively refuse use of their data for this study.
- Any non-responder data will only be presented in aggregate.

The lack of non-responder data would have substantial and detrimental impact on the validity and generalizability of our research findings; thus, the research could not be practicably carried out without the non-responder HIPAA waiver.

Waiver of signed HIPAA Privacy Rule Authorization for RCT participants:

Requiring a signed HIPAA Privacy Rule Authorization would burden potential participants and affect the diversity of the recruited sample. Given this, we plan to send a copy of the HIPAA Authorization form advising the participants we will be accessing their medical records.

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6.0 Recruitment and Retention Plan

6.1 Participant Recruitment

We will contact PCPs by email and include a list of potentially eligible patients on their panels so that they will be given the opportunity to exclude patients not deemed appropriate to be contacted. Providers will have 10 business days to respond to our request, and we will send a reminder 1 week after the initial request. We will then send a letter to the PCP-approved patients and their caregivers inviting them to participate in the Prepare for Your Diabetes Care clinical trial (RCT). The letter will include an e-mail and phone number, any one of which can be used to decline or accept the invitation to participate. We will also call subjects who have not responded after a 3-week interval to participate in the Prepare for Your Diabetes Care clinical trial.

Please note the following KPNC IRB guidelines:

- Contact of prospective subjects will be limited to three (3) attempts in one week, for no longer than three (3) continuous weeks.
- Messages left will be limited to one (1) per week for no more than three (3) weeks.
- No more than two (2) recruitment mailings (email, flyer, brochure, etc.).
- If permission from the patient's PCP is necessary to contact the patient:
 - *If PCP does not respond to request, recruitment attempts (phone, mailings, etc.) may not begin until 2 weeks after the PCP's permission was requested.*
 - *If PCP grants permission, recruitment attempts may begin with no waiting period.*

6.2 Participant Retention

Every effort will be made by the PI and study team to ensure participants complete each study visit and the study overall. We will use the following strategies to help to maximize retention and minimize loss to follow-up:

- Following a proactive plan for retention, including calling participants when they have scheduled an appointment with their PCP and remind them to utilize the intervention their next appointment.
- Giving participants and their families the opportunity to ask questions and express concerns pertaining to their condition throughout the study.
- Enhancing participant's understanding of the study's objectives and the protocol by reminding the participant of the study aim during reinforcement and follow-up survey calls.
- Assessing each participant's drop-out potential.
- Increasing incentives should study retention be poor.

If a participant does not answer follow-up calls, the PI and/or study coordinator will make

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several contacts using all the contact information provided by the participant. This will include sending certified return receipt letters to the participant's listed address.

7.0 Screening and Eligibility Criteria

7.1 Screening

The Study Coordinator will use the following steps to screen participants for the study:

- I. Pre-Screening Phase
 - a. Study team will create a patient eligibility pool by primary care provider (PCP), as outlined in Section 7.3.
 - i. We will enroll eligible participants from Kaiser Permanente Northern California.
 - b. Study coordinator will pre-screen all eligible participants before recruitment attempts by examining their electronic health record and confirming their eligibility as outlined in Section 7.3.
- II. Screening Phase
 - a. Study coordinator will call the potential participant to explain the study.
 - i. Study coordinator will begin the process of ensuring that participant meets eligibility criteria as outlined in Section 7.3, such as screening cognitive ability using the Short Portable Mental Status Questionnaire (SPMSQ) and Mini-Cog.
 - b. If the participant leaves a message expressing interest, study staff will return their call and explain the study. If participant is interested and meets eligibility criteria as outlined in Section 7.3, study staff will screen the patient's cognitive ability using the SPMHQ and Mini-Cog.
 - c. Study coordinator will proceed with enrollment and informed consent process described in Section 5.0.
 - d. Study coordinator will obtain verbal informed consent and will verify contact information, such as phone number, address for material to be sent, and email.

7.2 Screening Log

This study will use REDCAP, a secure web application for building and managing online surveys and databases, for Screening Logs. Screening Logs are saved within REDCAP Data Analyst, Dilrini Ranatunga, is responsible for updating and editing screening logs. Study Coordinators are responsible for data entry into the secure REDCap database.

Sample Screening Log:

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Screening ID	Screened By	Age	Gender	Race / Ethnicity	Screen Date	Eligibility Status
T0001	JD	71	F	C	21/DEC/2015	Eligible; Declined
T0002	JD	66	M	C	28/DEC/2015	Eligible; Enrolled 28/DEC/2015
T0003	MO	70	F	AA	04/JAN/2016	Ineligible; Unable to Make Own Medical Decisions
T0004	JD	78	F	C	09/JAN/2016	Eligible; Declined due to Moving Away

Screening Log Checklist:

- Screening/Identification ID
- Screening Member of Study Team
- Date Screened
- Identifying Characteristics (Demographics)
- Eligibility Status

7.3 Eligibility Criteria

Study eligibility is determined by inclusion/exclusion criteria:

KPNC members with T2D, ≥ 75 years old, prescribed insulin or SU, with last measured HbA1c $< 8\%$. We will exclude participants who do not speak English, who screen positive for moderate-to-severe cognitive impairment as determined by a score of < 3 on the Mini-Cog or who self-report being deaf or blind.

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8.0 Study Intervention

The study intervention for Advance Care Planning for Older Patients with Diabetes at High Risk for Hypoglycemia is an educational, web-based program, Prepare for Your Diabetes Care to support safer long-term T2D care among older adults at high risk for treatment-related hypoglycemia. This educational study consists of the participant reviewing 4 5-minute video modules as well as an “Action Plan” Handout before their next appointment with their primary care provider (PCP), who handles their diabetes care at Kaiser Permanente.

1. The study coordinator will review the Prepare for Your Diabetes Care tool with the study participant and walk through how to navigate and utilize the tool.
2. The study coordinator will answer any questions that the participant has about the tool and encourage the participant to utilize the Action Plan.
3. If relevant, study coordinators will encourage participants to discuss their Action Plan with their and family and their primary care provider during the participant’s next scheduled appointment.
4. Study coordinators will call the participant during subsequent appointment bookings to encourage participants to utilize the Prepare tool before their visit and offer to assist participant access the tool if needed.

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9.0 Randomization

The Data Analyst will be responsible for generating randomization codes.

Method:

1. The Data Analyst will be notified of new eligible participants by the Study Coordinator/Principal Investigator.
2. The Data Analyst will use the assigned and blinded randomization code in an automated, computerized log that is separate from the study data.
3. The Data Analyst will program the randomization assignments into the REDCap database, which will apply to the screening log, and notify the Study Coordinator that the randomized assignment is available.

The Data Analyst will maintain the master randomization list, assign randomization codes, notify appropriate study staff regarding randomization, and securely store randomization files. The Study Coordinator will initiate randomization procedure and must know who to contact once a participant is deemed eligible for the study, including which forms to complete prior to randomization.

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11.0 Study Measurements and Procedures

Participants will complete three surveys throughout a 12-month period by telephone.

11.1 Timeline and visit schedule

Assessment	Screening: (Day -14 to Day -1)	Recruitment, Enrollment, Baseline: (Day 0)	6-month survey Day 180 (±10 Days)	12-month survey Day 365 (±10 Days)
Informed Consent Form	X	X		
Demographics	X	X		
Medical History	X	X		
Current Medications	X	X		
Inclusion/Exclusion Criteria	X	X	X	X
Randomization	X			
Treatment		X	X	X

11.2 Visit Procedures

During a recruitment and enrollment call, following the recruitment procedure and obtaining informed consent per Section 5.0, the Study Coordinator will administer the baseline survey. After the participant completes the baseline survey, the Study Coordinator will reveal their treatment status. The Study Coordinator will set-up a time to review the Prepare tool before their next appointment with their primary care provider (PCP).

Study Coordinator will call the study participant and walkthrough the Prepare tool with the participant. This will include navigating the 4 5-minute video modules and answering any questions that the participant might have. After reviewing the video modules, the Study Coordinator will guide the participant to access the “Action Plan” from the Prepare tool. The Study Coordinator will ask the participant to review the “Action Plan” with their family and/or PCP.

The Study Coordinator will call the study participant when the participant books subsequent appointments and encourage him/her to use the Prepare For Your Diabetes Care tool and “Action Plan” during their next visit with their PCP.

11.3 Follow-up

The Study Coordinator will call the participant in 6 and 12 months to administer the follow-up surveys. The Study Coordinator will remind the participant about the study timeline and purpose of the study and encourage the use of the treatment (Prepare tool and “Action Plan”).

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12.0 Concomitant Medications

Not applicable: there are no exclusions of any concomitant medications for this study.

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13.0 Safety Reporting

Many of the outcomes that might reasonably be classified as adverse events (AE) and serious adverse events (SAE) are unlikely for this low-risk educational study designed to help patients communicate with their providers. We do not expect any SAEs in this educational study designed to help patients communicate with their providers.

A serious adverse event (SAE) is defined as psychological distress requiring medical help. We will not attribute our educational intervention to SAEs such as (1) death; (2) hospitalization; and/or (3) persistent or significant disability or incapacity. Patient-level medical events that are usually considered SAEs in RCTs of non-educational interventions (e.g. hyperglycemic symptoms, etc.) are NOT considered study-related in this trial of an educational intervention and are therefore NOT considered an SAE.

An adverse event (AE) is defined as stress related to answering survey questions or engaging with the web-site educational module. Expected AEs could include reports from participants that they are experiencing stress related to the study questions and the research study. There is a very low risk of AEs such as anxiety or other emotional responses manifesting in somatic ways, such as headaches.

Assessment of the SAE or AE:

We will assess a serious adverse event or adverse event using the following classifications:

- **Severity:** (1) Mild: Awareness of signs or symptoms, but easily tolerated and are of a minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient. (2) Moderate: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning. (3) Severe: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating
- **Expectedness:** (1) Unexpected: Nature or severity of the event is not consistent with information about the condition under study or intervention in the protocol, consent form, product brochure, or investigator brochure (e.g., any physical AE or SAE). (2) Expected: Event is known to be associated with the intervention or condition under study. None are expected in this study except perhaps feelings stressed or uncomfortable answering some of the focus group or interview questions.
- **Relatedness:** (1) Definitely Related: The event is clearly related to the investigational

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agent/procedure. That is, an event that follows a reasonable temporal sequence from administration of the study intervention; follows a known or expected response pattern to the suspected intervention; is confirmed by improvement on stopping and reappearance of the event on repeated exposure; and that could not be reasonably explained by the known characteristics of the subject's clinical state. (2) Possibly Related: An event that follows a reasonable temporal sequence from administration of the study intervention and follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors. (3) Not Related: The event is clearly not related to the investigational agent/procedure. That is, another cause of the event is most plausible and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

AE/SAE Reporting

We will follow the NIA Clinical Research Investigator's Toolbox [process](#) and forms for reporting AEs and SAEs. All unexpected SAEs will be reported to the NIA Program Officer and KPNC's IRB within 48 hours of the study's knowledge of SAE. The Project Manager will complete the SAE form within 3 days. After evaluation of a reported SAE, the MPIs will convene a conference call with the PO to discuss the SAE and to determine whether or not any aspect of the study needs to be modified; this will occur within 4 weeks of the SAE. A summary of all other (i.e., those that are not unexpected) SAEs will be reported to the NIA Program Officer and the institutional IRB quarterly, unless otherwise requested.

14.0 Study Compliance

The study will adhere to IRB policies for reporting protocol deviations/violations. In addition, the reporting of deviations/violations should be discussed with the NIA and the safety oversight entity prior to study start and be clearly outlined in the safety monitoring plan. All events will be reported at the time of the biannual DSMB meeting or submission of the safety report.

Protocol deviations/violations, include, but are not limited to, the following:

- Enrollment or randomization of an ineligible participant
- Failure to obtain Informed Consent
- Visits or procedures conducted outside of the protocol specified window
- Failure to keep IRB approval up-to-date
- Wrong treatment administered to participant
- Follow-up visit at a time point different from that specified in the protocol

Our Study Team will maintain a log of all protocol deviations/violations and will report them as specified in the DSMP to the safety monitoring entity.

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15.0 Data Collection and Study Forms

All study data will be collected through the KP DOR (Kaiser Permanente Division of Research) REDCap database. There will be no analog data or documentation.

15.1 Data Flow

All study data will be collected through the KP DOR (Kaiser Permanente Division of Research) REDCap database. There will be no analog data or documentation.

15.2 Administrative Forms

N/A

15.3 Retention of Study Documentation

We will retain all study documents (e.g., data sets created, translation table linking SIN to patient name and medical record number) for separate analysis and they will be destroyed 3 years following study completion (i.e., the submission of the final IRB progress report). If the funding agency or other institutions require retention of study data beyond this date, then a study modification request to authorize this retention will be submitted to the IRB.

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16.0 Data Management

All study data will be collected through the KP DOR (Kaiser Permanente Division of Research) REDCap database. There will be no analog data or documentation.

16.1 External Data

EPIC Health Record data will be securely transferred to the DOR REDCap Database

16.2 Quality Control Procedures

All study data are collected through software interfaces to limit sources of error.

17.0 Data and Safety Monitoring Activities

17.1 Reports

Once a study begins, routine reports will be prepared by the study statistician on a weekly basis. Monthly reports will describe target and actual enrollment, individuals screened with reasons for screen failure, and participant disposition (enrolled, active, completed, discontinued treatment, and lost to follow-up).

17.2 Study Completion and Close-Out Procedures

17.2.1 Participant Notification

Participants will be informed during their final follow-up survey (12 months after initial visit), of the end of the study, thanking them for their participation.

17.2.2 Confidentiality Procedures

The use of PHI for this study presents no more than minimal risk to the privacy and confidentiality of the individuals whose PHI will be accessed. KPNC DOR researchers are accustomed to maintaining processes to ensure confidentiality. The risk to participants will be minimized by strict adherence to the standard protocols in place at DOR that all study staff will follow. Names and other identifying information on study subjects will be retrieved from the KPNC automated databases. We will have the link between MRN and original study ID number, and at the end of the study, this link will be destroyed. Only KPNC workforce staff directly involved in the study and current in HIPAA and IRB training will have access to data identifying subjects (PI, co-investigators, project manager, programmer, research assistants). No individuals will be identified in any reports or publications generated from this study, as all data will be presented in aggregate (i.e., no identifiers will be shown). Physical data (e.g., papers) with any identifying information will be kept in locked files, and digital data (computer files) will be stored in secure password-protected or encrypted files on protected KPNC servers within KP

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networks secured by firewalls. Furthermore, access to computerized information on the KPNC network requires simultaneous knowledge of the databases, programming language, file names, and multiple passwords. Therefore, we can ensure data security.

PHI will be stored in password protected or encrypted electronic files and stored on protected KP NCAL servers within KP network secured by firewalls. Passwords will not be disclosed to any party not involved in the study. Patient identifiers will not appear in any part of the publications. When it is necessary to share PHI information among study parties within KP NCAL, we will transmit the files (password-protected/encrypted) through encrypted KP NCAL email or secure file transfer. The information will be stored for the length of the project and destroyed after the final manuscripts are published.

Alongside these precautions, the Study Team will ensure confidentiality by:

1. Securing storage of physical data (e.g., papers) in locked files, and securing storage of digital data (computer files, digital audio) in password-protected files on password protected computers.
2. Making data that may contain identifying features accessible only to members of the research team working under the direction of the investigators during the duration of the project.
3. Ensuring that any data that participants do not want to be preserved are not collected by the investigator or study staff.
4. Ensuring no participant can be identified in any presentations or publications resulting from this study.
5. Ensuring all study staff are current in HIPAA and IRB training.
6. Ensuring that email messages with PHI sent to providers are encrypted

17.2.3 Publications

All identifiable information will be removed prior to publication. Results will be reported in aggregate.

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18.0 MOP Maintenance

This plan will be maintained by the Study Coordinator

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Appendix A - Sample Schedule of Events

Assessment	Screening: (Day -14 to Day -1)	Recruitment, Enrollment, Baseline: (Day 0)	6-month survey Day 180 (±10 Days)	12-month survey Day 365 (±10 Days)
Informed Consent Form	X	X		
Demographics	X	X		
Medical History	X	X		
Current Medications	X	X		
Inclusion/Exclusion Criteria	X	X	X	X
Randomization	X			
Treatment		X	X	X

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Appendix B - Sample Protocol Deviation/Violation Log

Protocol Title: _____

Protocol Number: _____ Site: _____ Principal Investigator: _____

Protocol Deviation/ Violation Code:	Participant Initials	Participant ID#	Date Deviation / Violation Occurred: mm/dd/yyyy	Date Protocol Deviation / Violation Form Completed:	Contact Person (if applicable)

SAMPLE PROTOCOL DEVIATION / VIOLATION CODES

Randomization:

1. Ineligible participant enrolled and/or randomized
2. Participant is randomized prior to determining whether eligible for study
3. Occurs outside protocol window

IRB:

4. Approvals not kept up to date

5. Enrollment and/or treatment occurs prior to IRB approval or during period when “on hold”

Participant:

6. Receives wrong treatment

Study Data and/or Forms:

7. Missing data and/or forms

Appendix E - NIA Single-Site Clinical Trial Sample Closeout Procedures

I. INTRODUCTION

Purpose

The purpose of this document is to describe an orderly approach to the separation of participants from a clinical trial and the administrative procedures associated with the trial's completion.

Types of Closeout

- A. *Scheduled - upon completion of the trial.***
- B. *Unscheduled - as a result of failure to obtain continuation funding, negative or positive findings, findings in other studies that impact on the clinical trial, or other unforeseen events.***

II. SITE CLOSEOUT

The study site is responsible for ensuring the following activities are completed prior to study closeout along with the Participant Closeout Procedures described in Section III below.

A. *Study Forms*

- All outstanding Case Report Forms (CRFs) should be collected, organized, and corrections made, where necessary.
- All data queries should be corrected and resolved.

B. *Safety Reporting*

- All adverse events (both serious and non-serious) should be recorded and followed up to resolution in accordance with procedures detailed in the protocol.
- All serious adverse events (SAEs) should have been reported to the Data and Safety Monitoring Board (DSMB) or Safety Officer, Institute, Institutional Review Board (IRB), and other organizations, as specified in the protocol and Data and Safety Monitoring Plan (DSMP).
- All adverse events should have been reported as specified in the protocol.

C. *Study Files*

- The investigator's study files will be complete and up to date with electronic stored versions of the following:
 - Investigator(s) Curriculum Vitae(s) (CVs)
 - IRB approval letters for the protocol, all amendments, Informed Consents, annual reviews and advertisements (including updated approvals)
 - Copy of randomization code for randomization, if applicable

Study Closeout Checklist

- ☐ All appropriate documents are electronically stored.
- ☐ The final study close-out report has been submitted to the IRB.
- ☐ Final report has been submitted to the NIA.

III. PARTICIPANT RIGHTS AND NOTIFICATION – n/a

IV. INSTITUTE RESPONSIBILITIES – n/a

Statistical Analysis Plan

We will examine differences in deprescribing, hypoglycemia-related ED/IP utilization, and self-reported outcomes among participants who complete the 6- and 12-month follow-up assessments and are not censored due to death, disenrollment, or withdrawal. Continuous and binary outcomes will be evaluated using baseline-adjusted linear and logistic regression models and adjusted risk differences with 95% confidence intervals will be estimated using average marginal effects.

All analyses will be conducted in R version 4.3.2 (R Foundation for Statistical Computing). We will also examine heterogeneity of treatment effect based on demographic characteristics, baseline clinical factors, and health literacy using stratified analyses and treatment-by-subgroup interactions. Exploratory on-treatment analyses will examine outcomes among intervention participants who access the intervention website and video within 7 or 14 days before their PCP appointment.