UCSF Helen Diller Family Comprehensive Cancer Center

Addressing the Nutritional Needs of Cancer Survivors with Nutrition Insecurity

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Protocol Signature Page

I agree to follow this protocol version as approved by the Institutional Review Board (IRB).

I will conduct the study in accordance with Good Clinical Practices (ICH-GCP) and the applicable IRB, ethical, federal, state, and local regulatory requirements.

I certify that I, and the study staff, have received the required training to conduct this research protocol.

I agree to maintain adequate and accurate records in accordance with IRB policies and federal, state and local laws and regulations.

UCSF Principal Investigator

_____
Printed Name

_____ _____
Signature Date

Abstract

Title	Addressing the Nutritional Needs of Cancer Survivors with Nutrition Insecurity
Study Description	This study aims to determine the acceptability and feasibility of a 4-week household level intervention to increase nutrition security among cancer survivors who are experiencing food insecurity, have low income, or live in persistent poverty areas.
Study Intervention	4-week household level intervention using grocery deliveries via the Instacart platform, navigation, and patient education to improve nutrition security and adherence to American Cancer Society nutrition guidelines
Study Population	Up to 45 cancer survivors who are facing food insecurity, have low income or live in persistent poverty areas in the UCSF catchment.
Primary Objective	To determine the intervention's feasibility and acceptability.
Secondary Objectives	1. To estimate the effect of the intervention on adherence to American Cancer Society nutrition guidelines. 2. To estimate the effect of the intervention on self-reported food insecurity. 3. To evaluate the feasibility of patient navigation calls. 4. To evaluate the feasibility of Instacart vouchers.
Recruitment Methods	Participants will be recruited through MyChart messages and letters from the UCSF CTSI Participant Recruitment Program, as well as clinician referrals at the University of California, San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center (HDFCCC) and the Zuckerberg San Francisco General (ZSFG) hospital. Participants will also be identified through re-contact of participants from the investigator's previous studies, referrals from the community, and advertisements such as flyers.
Sample Size	Participants from this study will include up to 45 cancer survivors
Duration of Study Participation	4 weeks
Unique Aspects of this Study	This is the first study at UCSF to utilize home grocery deliveries via the Instacart platform to improve nutrition security among cancer survivors.

List of Abbreviations

ACS	American Cancer Society
AE	adverse event
CRC	Colorectal Cancer
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
CTMS	Clinical Trial Management System
DSMC	Data and Safety Monitoring Committee
DSMP	Data and Safety Monitoring Plan
GCP	Good Clinical Practice
HDFCCC	Helen Diller Family Comprehensive Cancer Center
HIPAA	Health Insurance Portability and Accountability Act
ICF	informed consent form
ICH	International Conference on Harmonization
IRB	Institutional Review Board
PRMC	Protocol Review and Monitoring Committee (UCSF)
ZSFG	Zuckerberg San Francisco General

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1 Introduction

1.1 Background on Nutrition Among Cancer Survivors

Structural barriers to appropriate cancer screening, treatment, and survivorship care contribute to socioeconomic disparities in cancer survival.[1] Nutrition security, in particular, may be part of the pathway by which structural barriers and the social and built environment impact outcomes among cancer survivorship. Indeed, the 2020 American Association for Cancer Research (AACR) Cancer Disparities Progress Report suggested that health behavior interventions may reduce cancer disparities.[2]

The American Cancer Society (ACS) recommends normal body mass index (BMI), regular physical activity, and a healthy diet for cancer survivors. In 2018, we estimated that 38% of deaths within 5 years of diagnosis could be prevented in stage III colon cancer if all patients followed the ACS guidelines[2]. Yet, few cancer patients closely follow national nutrition guidelines (based on intake of whole grains, fruits, vegetables, red meat, and processed meat).[2]

Nutrition security (defined as the consistent and equitable access to healthy, safe, and affordable foods essential to optimal health and wellbeing)[3] may play a role in the limited uptake of nutrition guidelines, particularly for individuals in the safety net setting. It is estimated that 8% to 23% of people with a history of cancer experience nutrition insecurity, often due to financial barriers.[4] Nutrition insecurity disproportionately impacts racial/ethnic minority patients and those with low income.[4] In fact, work by our group has found that 50% of participants in a study of colorectal cancer (CRC) survivors at Zuckerberg San Francisco General Hospital (ZSFG) often or sometimes worried about food running out and not having enough money to buy more; 37.5% experienced hunger and/or skipped meals because there wasn't enough money for food in the 12 months prior; and 25% reported that they had lost weight because they did not have enough money for food.[5] Furthermore, nutrition insecurity is associated with worse health outcomes among patients with cancer, including difficulty managing gastrointestinal toxicities of cancer-directed therapy, poor adherence to therapy, worse physical performance status, and worsened anxiety/depression during and after treatment.[4,6]

1.2 Background on Food Insecurity Intervention

Interventions to address food insecurity have been implemented in a variety of patient populations. Systematic reviews concluded that interventions such as referrals to food pantries, vouchers, and home delivered meals likely improve food insecurity, quality of life, and healthcare utilization.

However, limited data exists among patients with cancer. The Food to Overcome Outcomes Disparities (FOOD) program at Memorial Sloan Kettering Cancer Center is a novel network of medically tailored food pantries combined with comprehensive cancer nutrition education embedded into 15 safety net and comprehensive cancer center clinics in the New York City area. Two interventions utilizing the FOOD program among patients with a variety of cancers found that food security scores improved significantly in all arms. The voucher plus pantry treatment arm in this program also had the highest rate of completion of cancer treatment[7,8]. Other studies have shown that interventions addressing food insecurity may improve cancer related outcomes such as mortality[9]

Furthermore, there is no data on the use of medically tailored grocery deliveries to address food insecurity among cancer survivors residing in a larger geographic area. To our knowledge, our study will be the first to specifically partner with Instacart to improve nutrition security among cancer survivors who have low income or are living in persistent poverty areas.

We have partnered with Instacart as a component of our intervention because of its national presence as a well-recognized food delivery platform, with many available options for grocery stores from which to order food. Instacart allows the intervention to be scaled for a future, federally funded, national randomized controlled trial. Our pilot provides an opportunity to refine and test its feasibility in a smaller cohort.

1.3 Study Rationale

Addressing nutrition security is an essential component of an overall goal to improve cancer survivorship. Little data exists regarding the optimal interventions for food insecurity in this population. As such, our study seeks to improve nutrition security and adherence to ACS guidelines among cancer survivors who are experiencing food insecurity, have low income, or live in persistent poverty areas using a combined intervention that includes Instacart vouchers for grocery delivery, nutrition navigation, and patient education materials.

1.4 Risk/Benefit Assessment

Potential Risks

The risks involved in this study are few. There is a risk of loss of confidentiality, either through the breach of data collected via the Internet or text messaging or through the breach of secure study databases, physical files, etc.

Dietary modifications may result in changes in bowel function, including but not limited to diarrhea, constipation, increased urgency, flatulence, and/or bloating. These changes are not expected to be clinically significant but could impact quality of life if they occur.

Potential Benefit of the Proposed Research to Participants and Others

The benefits of healthy diet are well established. Intervention participants may experience decreases in symptom burden and improved physical functioning and quality of life. This study will produce societal benefit regarding knowledge about how to optimize an intervention to improve food security among cancer survivors. Given the minimal risk of study participation and potential benefits, the risks to participants are reasonable in relation to the anticipated benefits to society.

Procedures used to minimize risk

- Numerous studies have demonstrated that healthy diet is safe, feasible, and beneficial for cancer patients and survivors.
- Participants will be asked to contact the study team at any time if they have questions or concerns about the study.
- All study files, folders, and records will be kept in locked file cabinets that can be accessed only by study personnel.
- All data will be exchanged over an SSL-protected connection, and all data will be encrypted.
- The study database and all survey data will be collected and stored in REDCap, secure Box folders, and UCSF's Research Analysis Environment (RAE), which have protections needed for storage of PHI. Interviews will be conducted and recorded over Zoom.

Limited private identifiable information necessary for the conduct of the study will be collected in the proposed research project. For example: names, phone numbers, mailing addresses, and email addresses.

Importance of Knowledge to be Gained

Promotion of a healthy diet and reducing food insecurity is an important aspect of cancer survivorship care. This research aims to create an intervention that can be remotely delivered and is appropriate for implementation on a large scale. We believe that the minimal risk involved with study participation are reasonable in relation to the knowledge that is expected to result.

2 Objectives

2.1 Primary Objective

Primary Objective	Endpoint(s)	Time Frame
1. To determine the intervention's feasibility and acceptability.	• Feasibility of Intervention Measure (FIM) score at 4 weeks. • Acceptability of Intervention Measure (AIM) score at 4 weeks. • The Appropriateness of the Intervention (IAM) score at 4 weeks. FIM, AIM, and IAM are surveys that will be given to participants at the end of the study (after 4 weeks). Acceptability and feasibility of the intervention are considered as continuous endpoints and will be described using medians (IQR) of the AIM, IAM and FIM scores. See Section 9.2.1.	For each participant, about 4 weeks. For the study, about 19 months.

2.2 Secondary Objectives

Secondary Objective	Endpoint(s)	Time Frame
To estimate the effect of the intervention on adherence to American Cancer society nutrition guidelines.	• Change from baseline in intake of fruit and vegetables, whole grains, sugar-sweetened beverages, red meat, and processed meat.	For each participant, about 4 weeks. For the study, about 19 months.
To estimate the effect of the intervention on self-reported food insecurity.	• Change in participant reported USDA Food Insecurity score at baseline and after intervention.	For each participant, about 4 weeks. For the study, about 19 months.
To evaluate the feasibility of patient navigation calls.	• Completion of patient navigation calls (# completed / # expected)	For each participant, about 4 weeks. For the study, about 19 months.
To evaluate the feasibility of Instacart vouchers.	• Use of Instacart vouchers ($ spent / $ provided)	For each participant, about 4 weeks. For the study, about 19 months.

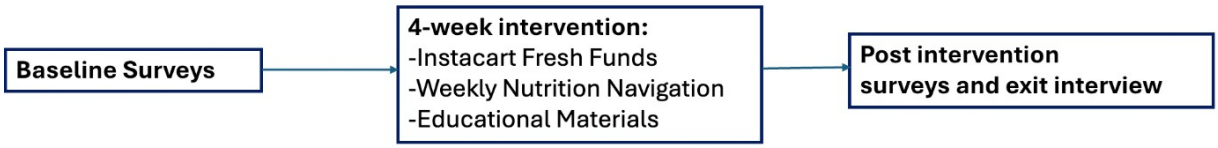
2.3 Exploratory Objectives

Exploratory Objective	Endpoint(s)	Time Frame
To evaluate the feasibility of the intervention through an end-of-study semi-structured interview.	• Semi-structured interviews at end of the study that are audio/visual recorded via Zoom. Thematic content analysis to understand barriers and facilitators to the intervention and inform future intervention development.	For each participant, about 4 weeks. For the study, about 19 months.

3 Study Design

3.1 Characteristics

This is a single-arm proof-of-concept feasibility study to determine the acceptability and feasibility of a 4-week household-level intervention to increase nutrition security among cancer survivors who are facing food insecurity, have low income, or live in persistent poverty areas. Our intervention will include healthy food delivered to participants' households via Instacart vouchers, a nutrition navigator, and education materials.



3.2 Sample Size

We will accrue up to 45 cancer survivors. Participants who withdraw or are otherwise not evaluable will not be replaced.

3.3 Primary Completion

The expected primary completion date is 19 months after the study opens to accrual.

3.4 Study Completion

The expected study completion date is 19 months after the study opens to accrual.

4 Selection and Enrollment of Participants

4.1 Eligibility Criteria

4.1.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria, as self-reported by the participant:

1. Age >18 years
2. Diagnosis of a malignant cancer (except non-melanoma skin cancer)
3. Not on active treatment at the time of screening and not expected to receive active anti-cancer therapy (e.g., surgery, radiation, chemotherapy, immunotherapy, targeted therapies) during the study period. Hormonal therapies are allowed for patients with breast or prostate cancer
4. At least 6 weeks since a major surgery and fully recovered.
5. Have access to the internet and able to send and receive text messages.
6. Able to speak/read English.
7. Based on the USDA U.S. Household Food Security Survey, identify as experiencing food insecurity[10] and/or belong to a population that the NIH has identified as being at risk for health disparities:
    a. Identify as a racial or ethnic minoritized group, as defined by the NIH (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Pacific Islander, Latino or Hispanic)
    b. Identify with a sexual or gender minoritized group.
    c. Annual household income < 200% of the federal poverty definition and/or education <bachelor's degree.

d. Live in a rural and/or a persistent poverty area (based on zip code).

4.1.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study (this information can be self-reported by the participant):

1. Contraindication to any study-related procedure or assessment.
2. Planned major surgery or cancer-directed therapy during the study period.
3. Living outside of the US or Canada during screening and/or the study period (outside the geographic areas that Instacart covers).

4.2 Recruitment Methods

The recruitment and screening procedures outlined below present no more than minimal risk to the privacy of the patients who are screened, and a screening log containing minimal patient health information (Protected Health Information (PHI)) will be maintained. For these reasons, we seek a waiver for the purposes of 1) reviewing medical records to identify potential research participants and obtain information relevant to the enrollment process; 2) conversing with patients regarding possible enrollment, 3) handling of PHI contained within those records and provided by the potential participants; and 4) maintaining information in a screening log of patients approached.

Participants will be recruited through MyChart messages and letters from the UCSF CTSI Participant Recruitment Program, as well as clinician referrals at the University of California, San Francisco (UCSF) Helen Diller Family Comprehensive Cancer Center (HDFCCC) and the Zuckerberg San Francisco General (ZSFG) hospital.

We will also advertise the study to participants from the investigators' prior studies and by posting flyers.

4.2.1 Recruitment of UCSF Patients

Potentially eligible patients may be identified through searches of the UCSF Cancer Registry, APeX, review of clinic schedules, and people who have participated in past studies. The study team will review medical records of identified patients to assess initial eligibility. Potential participants may be contacted in clinic and/or e-mailed information about the study. We may call patients to tell them about the study and ask if they are interested in participating. If they are interested, they will be asked to complete a brief screening survey either by phone or online using REDCap.

4.2.2 MyChart Recruitment at UCSF

We will also work with the UCSF CTSI's Participant Recruitment Program to use MyChart for recruitment along with cohort identification and direct mail for recruitment of patients who are not enrolled in MyChart. MyChart (Apex) conducts a search for patients based on the study's inclusion and exclusion criteria. This is a computer-aided search, meaning the computer — and not a person — searches patient charts. When a patient is identified as potentially eligible, they receive an email from MyChart that says to log in to MyChart to read about a study that they might be interested in. The email is short and is the same for every recipient—there is no

patient-specific, study-specific or disease information in it. When the patient logs into MyChart, there is a new "Research" page with template information about participating in research and how to opt out of receiving recruitment messages. Then, the patient can click through to learn about a specific study that they may be eligible for. The study-specific language is attached to this submission.

The patient has the option of clicking a link/button to let the study team know that they are interested in learning more about the study. Only if the patient takes this action will the study team receive information about the patient. If the patient clicks "No thanks", they will not be contacted by the study team, they will not receive any follow-up emails from MyChart about this study, and their information will not be shared with the study team. The messaging in all recruitment materials—email, MyChart research page, and study description—have been written to clearly state that the patient is being contacted about research, not clinical care. We are also collaborating with the CTSI Participant Recruitment Program (PRP), which will provide cohort identification and direct mail for recruitment of patients who are not enrolled in MyChart to address disparities that exist in MyChart enrollment.

4.2.3 Recruitment of ZSFG Patients

At ZSFG, providers will ask potentially eligible patients for permission to be contacted by the research coordinator about a research opportunity. If they say yes, the coordinator will contact the patient either in person in the clinic or by phone or email. In addition, people who have participated in past studies may be contacted about this study and flyers will be posted in clinic waiting areas and clinic rooms.

4.2.4 Compensation

Participants will be provided a [redacted] gift card for completion of surveys at the end of the study. They will receive an additional [redacted] for completion of the semi-structured exit interview. As part of the intervention, participants will receive 1 voucher to purchase groceries using the Instacart app. The voucher value will be [redacted] per household member. For example, a participant who lives with a spouse will receive [redacted] voucher.

4.3 Inclusion of Women and Minorities

4.3.1 Eligibility of Women and Minorities

Individuals of any sex, gender, race, or ethnicity may participate. Inclusion Across the Lifespan

4.3.2 Age Range of Participants

Individuals ages 18 and over are eligible for this study. Children are excluded from the study because Instacart's use is restricted for minors.

4.3.3 Study Design/Recruitment Considerations Related to Age Groups

The study design and recruitment strategy aim to achieve representation of age groups that reflect the demographics of the affected population. Individuals ages 18 and over are eligible for this study.

4.4 Participant Registration

Following verification of eligibility based on the screening survey and before any on-study assessments are initiated, a written, signed, informed consent form (ICF) must be obtained.

Consent may be obtained via paper (mail or in-person) or DocuSign. A copy of the signed ICF will be given to the subject. The original will be kept on file with the study records.

All participants consented to the study will be registered in OnCore®, the UCSF Helen Diller Family Comprehensive Cancer Center Clinical Trial Management System (CTMS). The system is password protected and meets HIPAA requirements.

5 Study Intervention

5.1 Delivery of Study Intervention

We will use REDCap to track participant enrollment and follow-up. REDCap is a secure study management and database platform with mature features for online surveys and forms for data entry.

We will include the following intervention components in our 4-week pilot feasibility study. We chose 4-weeks for this single-arm proof-of-concept study because that duration is long enough for participants to assess the acceptability, appropriateness, and feasibility of the intervention and feasible in a 1-year grant period.

1) **Instacart Vouchers (Fresh Funds) and Care Carts:** Instacart has two features that we plan to use for our pilot study. "Fresh Funds" are vouchers that limit the type of items that may be purchased, such as fresh produce and whole grains. "Lists for Nutrition" is a tool that patients can access in the upper right-hand corner of the app. The lists provide tailored recommendations on foods, recipes, and other health tips (developed by our team). We will work with Instacart before study implementation to curate the "Lists for Nutrition" and to limit voucher use to only foods that are compliant with ACS recommendations (fruits, vegetables, whole grains, legumes, nuts, seeds, lean proteins, low-fat dairy, olive oil, etc.).

   We will provide 1 Fresh Fund voucher [redacted] per household member to use on Instacart to purchase and deliver foods during the study [redacted]. This value of the Instacart voucher aligns with benefits received through SNAP (https://www.cbpp.org/research/food-assistance/a-quick-guide-to-snap-eligibility-and-benefits).[11] Based on our on-going work among cancer survivors in the UCSF/ZSFGH catchment area, we expect a median of 2 members per household (including the study participant) with an anticipated range of 1-4. Before implementation, participants will be trained by the study team to use the Instacart app either in person or via Zoom.
   For those who are not able to create an Instacart account or order groceries via Instacart (for example, because they do not have Internet access or a credit card), a research coordinator will order food and set up delivery using Instacart Care Carts. Care carts are a food box delivery, where the foods are selected by the research team. The value of the care cart deliveries will be matched to the amount provided in the Fresh Funds vouchers. The content of the care carts will be selected by a study team member in consultation with the UCSF HDFCCC dietitian. Participants will also have an opportunity to note (via a Care Carts survey) any dietary restrictions or allergies before a Care Cart is ordered on their behalf. **Nutrition Navigation:** Participants will receive weekly check-ins (via telephone or Zoom, per participant preference), a study team memberto assist in ordering foods on Instacart and to answer study-related questions. We will consult with a

registered dietician at the UCSF Helen Diller Family Comprehensive Cancer Center (Greta Macaire, RD) to provide accurate nutrition guidance for specific nutrition-related questions, as we are currently doing in our other active studies (clinicaltrials.gov NCT05746195, NCT05056077). Nutrition Navigators will be clinical research coordinators or other UCSF study team members (e.g., medical trainees and patient navigators) who have undergone specific training from the study PIs and a consulting dietitian regarding nutrition guidelines in cancer survivorship.

2) **Educational material:** At enrollment, all participants will receive a booklet on nutrition and physical activity for cancer survivors.

5.2 Interventionist Training and Tracking

Consistent implementation of the study protocol, measurements, and interventions is essential. Training manuals will be created. Data will be collected in REDCap through online surveys and via Zoom for exit interviews. We will monitor recruitment and study progress using a flow sheet template consistent with the CONSORT guidelines for reporting of feasibility trials to ensure we are meeting recruitment and retention goals. Members of the study team will meet weekly, or as needed, throughout the study.

5.3 Adherence Assessment

5.3.1 Intervention Adherence

Adherence to the intervention will be measured by tracking the number of times Instacart was used to purchase and deliver groceries; the amount of money spent vs the amount provided; and the completion of weekly nutrition navigation telephone calls.

5.3.2 Proposed Engagement Strategies for Retention

To prevent attrition, our study staff will develop good rapport and open, responsive communication with participants. Participants will be provided with a phone number and email address to contact if they encounter issues with any aspect of the study. Staff will convey reminders of study tasks by phone, email, and/or text messages (based on patient preference). If a participant does not respond to a study-related request, up to five automated reminders will be sent and the study staff will reach out to the participant via phone and/or e-mail. If we are unable to reach a participant after at least three more attempts, we will determine a participant lost to follow-up.

5.4 Participant Discontinuation/Withdrawal from the Study

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue a participant from the study for the following reasons:

- Unacceptable adverse events
- Significant study intervention non-compliance, unless varying compliance is an aspect of the study objectives (participants who do not use the Instacart food vouchers will not be considered non-compliant).
- Lost-to-follow up; unable to contact participant (see Section 5 - Lost to Follow-Up)

- Any event or medical condition or situation occurs such that continued collection of follow-up study data would not be in the best interest of the participant or might require an additional treatment that would confound the interpretation of the study

5.5 Lost to Follow-up

A participant will be considered lost to follow-up if he or she fails to reply to a study-related request after the study staff have sent the following attempts to contact:

- up to five automated email reminders
- study staff will reach out to the participant via phone, text message, and/or e-mail at least three more times

These contact attempts will be documented in the participant's study file. Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

6 Study Procedures and Assessments

6.1 Schedule of Activities

Period/Procedure	Screening/Baseline	Study Intervention Period	End of Study
	Visit -1 (D-28 to D1)	**Weeks 1-4 (D1 to D28)**	**Study Week 4 (+28 days)**
Administrative Procedures			
Screening Survey	X[a]		
Inclusion/Exclusion Criteria	X		
Consent	X		
Other Study Assessments			
Sociodemographic survey	X		
Diet Screener[12]	X		X
Food Security Survey[10]	X[b]		X[b]
Pre-existing and on-study adverse events (Recent Health Survey)[c]	X		X
Care Carts Survey	X		
Instacart grocery voucher provided[d]		D1[e]	
Care Carts		Throughout[e]	

Period/Procedure	Screening/Baseline	Study Intervention Period	End of Study
	Visit -1 (D-28 to D1)	**Weeks 1-4 (D1 to D28)**	**Study Week 4 (+28 days)**
Nutrition Navigation		Weekly	
Acceptability of Intervention Measure (AIM)[13]			X
Intervention Appropriateness Measure (IAM)[13]			X
Feasibility of Intervention Measure (FIM)[13]			X
End of Study Semi-structured Interview			X

[a]Participants will self-report their clinical information. Medical records will not be collected after patients are enrolled.
[b] During Screening/Baseline: Stage 1 of the Food Security Survey is asked as part of the Screening Survey. Stage 2 and Stage 3 of the Food Security Survey are asked after study consent, if Stage 2 and 3 are indicated based on their Stage 1 responses. At the end of the study, the Food Security Survey will be modified slightly to ask about food security during the study period (instead of the prior 12 months.)
[c]Pre-existing expected adverse events (e.g., diarrhea, constipation, etc.) will be assessed at enrollment via a Recent Health Survey containing questions from PRO-CTCAE v 5, and emergent events will be assessed at 4 weeks. Navigators will also ask about any health events in the past week. Adverse events from dietary changes may include diarrhea, constipation, flatulence, and bloating changes.
[d]The study team will receive data from Instacart on the use of Fresh Funds, including all items purchased using the Fresh Fund (voucher) code.
[e] Those who are not able to create an Instacart account or order groceries via Instacart (for example, because they do not have Internet access or a credit card) will receive grocery deliveries via Care Carts instead.

6.2 Study Procedures and Assessments

6.2.1 Screening Period / Visit -1 (Day -28 to Day 1)

Participants will complete the screening survey online or by phone. Interested and eligible participants will then complete consent online via DocuSign or a paper copy of the consent will be mailed to them with an addressed, prepaid return envelope. The study team will contact the patient via phone to ask if the patient has any questions about the study and confirm study procedures. The consent documents will also include contact information for the study team, in case the potential participants have any other questions.

The following enrollment surveys will be performed after consent:

- Sociodemographic survey
- Dietary Screener
- Food Security module from the National Health Interview Survey
    - Questions from Stages 2 and 3, if applicable based on the participant's responses to the Stage 1 questions asked in the Screening Survey
- Care Cart Survey

6.2.2 Study Intervention Period (Day 1-28)

- D1: Delivery of Instacart Voucher
    - For those who are not able to create an Instacart account or order groceries via Instacart, grocery deliveries will be coordinated by the study team via Care Carts instead
- D1: Delivery of patient education materials
- Weekly nutrition navigation

6.2.3 End of Study Intervention (Study Week 4 + 28 days)

- Diet Screener
- Food security module from the National Health Interview Survey
    - Modified to ask about the study period (4 weeks) instead of the last 12 months
- Adverse events in past 4 weeks assessed by a Recent Health Survey, using questions from the NCI's Patient Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE v 5).
- Acceptability of Intervention Measure (AIM)
- Intervention Appropriateness Measure (IAM)

- Feasibility of Intervention Measure (FIM)
- Exit interview

7 Reporting and Documentation of Results

7.1 Measures and Instruments

Diet Assessment

At enrollment and post-intervention, participants will complete the Dietary Screener Questionnaire (DSQ)[12] from the National Health and Nutrition Examination Survey (NHANES) to assess dietary habits. This brief screener asks participants to report on their diet in the past month. Dietary factors assessed include fruit and vegetables, fiber, whole grains, added sugars, dairy, calcium, red meat, and processed meat. The survey will be administered using REDCap. A paper survey will be made available for participants who are not able to complete the survey online.

Other Survey Data

Participants will be asked to complete additional surveys using REDCap at 0 and 4 weeks. Paper copies will be made available for participants who are not able to complete the surveys online.

Sociodemographic and clinical factors will be assessed at baseline.

At 0 and 4 weeks, we will use a validated survey to measure food insecurity: Food Security module from the National Health Interview Survey (NHIS).

At 4-weeks, we will assess feasibility and acceptability of the intervention via the Acceptability of Intervention Measure (AIM)[13], Intervention Appropriateness Measure (IAM)[13], and the Feasibility of Intervention Measure[13]. The acceptability of each intervention component (Instacart fresh funds or care carts; patient navigation; educational material) will be evaluated separately.

We will also include an 15-30 minute end of study semi-structured interview to obtain open-ended, qualitative feedback. This interview will be over Zoom, and audio and video recorded.

8 Adverse Events and Serious Adverse Events

8.1 Definition of Adverse Event

An adverse event (AE) is defined as any untoward medical occurrence associated with the use of an intervention in humans, whether considered intervention related.

Adverse event assessment:

A Recent Health Survey with modified questions from the NCI Patient Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE v 5) Measurement System will be used to collect AEs by self-report in study participants. The survey measures participant-reported frequency, severity, and interference of expected symptoms and also allows the participant to report the severity of unexpected symptoms. Most symptoms are graded on a 5 point Likert scale ranging from 0 to 4. Frequency responses are assessed by the question “How often do you have [symptom]?” and include: Never, Rarely, Occasionally, Frequently, and Almost constantly. Severity responses are assessed by the question “What was the severity of your [symptom] at its worst?” and include: None, Mild, Moderate, Severe, Very

Severe. Interference responses are assessed by “How much did [the symptom] interfere with your usual or daily activities?” and include: Not at all, A little bit, Somewhat, Quite a bit, and Very much. For this study, assessments of frequency, severity, and interference are based on a 4-week recall period.

Nutrition navigators will also ask participants if they have experienced any health events during the weekly check ins.

8.2 Definition of Serious Adverse Event

An AE that results in any of the following outcomes is defined as a Serious Adverse Event:

- Death,
- Life-threatening adverse experience*,
- Inpatient hospitalization or prolongation of existing hospitalization,
- Persistent or significant disability/incapacity,
- Congenital anomaly/birth defect, or cancer, or
- Any other experience that suggests a significant hazard, contraindication, side effect or precaution that may require medical or surgical intervention to prevent one of the outcomes listed above,
- Event that changes the risk/benefit ratio of the study.

*A life-threatening adverse experience is any AE that places the patient or subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred, i.e., it does not include a reaction that, had it occurred in a more severe form, might have caused death.

8.3 Classification of Adverse Events

8.3.1 Severity

Adverse events are graded according to the Common Terminology Criteria for Adverse Events (CTCAE v 5) as developed and revised by the Common Therapy Evaluation Program (CTEP) of the National Cancer Institute.

8.3.2 Attribution

Adverse events are further given an assignment of attribution or relationship to study intervention or procedure. Attribution categories are:

- **Definite** – The adverse event is clearly related to the study intervention or procedure.
- **Probable** – The adverse event is likely related to the study intervention or procedure.
- **Possible** – The adverse event may be related to the study intervention or procedure.
- **Unrelated** – the adverse event is clearly not related to the study intervention or procedure.

8.3.3 Expectedness

An adverse event is considered unexpected if it is not listed in the investigator brochure or package insert(s), or is not listed at the specificity or severity that has been observed, or, if an investigator brochure is not required or available, the event is not consistent with the risk information described in the general investigational plan or elsewhere in the current application.

8.4 Adverse Events Monitoring

This study is a minimal risk level study that does not require monitoring by the HDFCCC Data and Safety Monitoring Committee (DSMC) as per the National Cancer Institute-approved Data and Safety Monitoring Plan. Ultimately, the PI is responsible for the safety and conduct of this study.

8.5 Follow up of Adverse Events

All participants who experience adverse events will be followed with appropriate medical management until resolved or stabilized, as determined by the investigator.

8.6 Documenting and Reporting of Adverse Events

Adverse Events will be documented in the study Case Report Forms (CRFs) and reported to the IRB, HDFCCC DSMC, and collaborators in accordance with all applicable institutional and regulatory requirements.

9 Statistical Considerations

9.1 Sample Size Considerations

9.1.1 Sample Size and Power Estimate

Sample size: up to 45

- Our sample sizes for the feasibility study are based on past work and standards in intervention design. These numbers will guide the definition and refinement of the intervention, as appropriate for phase I studies in the ORBIT model. Small sample sizes are recommended in intervention design to efficiently assemble the intervention and assess acceptability without “wasting the resources needed for the more ambitious randomized design.[14-16]

9.1.2 Accrual Estimates

- **Zuckerberg San Francisco General (ZSFG)** is a public safety net hospital that sees 40-50 stage II-III CRC patients/year; 80-90% of whom identify with a racial/ethnic minority group. We estimate 70% will be eligible for the proposed study (~30 over 18 months). We aim to enroll 10 participants from ZSFG.

- **UCSF HDFCCC GI Oncology Clinic** sees ~150 cases of stage I-III CRC each year; 40% of whom identify with a racial/ethnic minority group. Based on prior work, ~70% of these patients will be eligible for the proposed study (~105 over 18 months). We have also identified over 3,000 people who meet our clinical eligibility criteria using the CTSI Participant Recruitment Program services. We aim to enroll 20 participants from UCSF.

9.2 Statistical Analysis Plans

9.2.1 Primary Analysis

Descriptive Analyses: We will use descriptive statistics [means (standard deviation, SD) and median (interquartile range, IQR) for continuous variables and proportions and the corresponding 95% confidence intervals for categorical variables] to summarize participant characteristics, baseline variables from the survey data, attrition and intervention adherence outcomes.

We will quantify the completeness of follow-up using counts and proportions. Acceptability and feasibility of the intervention are considered as continuous endpoints and will be described using medians (IQR) of the AIM, IAM and FIM scores. A priori, we will determine the intervention to be acceptable and feasible if the median scores on the AIM, IAM, and FIM are >=4 (out of 5).

We will describe intake of fruit and vegetables, fiber, whole grains, added sugars, dairy, calcium, red meat, and processed meat from the dietary screeners at enrollment and end of study, as well as change in intake between time points, using medians (IQR).

9.2.2 Secondary Analysis

Descriptive Analyses: We will use descriptive statistics [means (standard deviation, SD) and median (interquartile range, IQR) for continuous variables and proportions and the corresponding 95% confidence intervals for categorical variables] to summarize participant characteristics, baseline variables from the survey data, attrition and intervention adherence outcomes.

We will examine changes in dietary intakes and adherence to the ACS nutrition guidelines pre- to post-intervention using paired t-tests. For example, for intake of fruits and vegetables (servings/d), our null hypothesis is that there is no difference in fruit and vegetable intake, on average, between 0 and 4 weeks. Our alternative hypothesis is that fruit and vegetable intake is higher at 4 weeks, on average, compared to 0 weeks. We will use mean (95% CI) and median (IQR) to describe intakes at each time point and change over time. We will perform the same analysis for the change in participant reported USDA Food Insecurity score at baseline and after intervention endpoints.

Furthermore, we will treat the completion of patient navigation calls and the use of Instacart vouchers as continuous endpoints and perform descriptive analysis as described above.

9.2.3 Exploratory Analysis

We will perform qualitative analysis on the exploratory endpoint. Audio recordings of interviews will be transcribed by Transcription Wing, and imported into Dedoose software for structural coding and thematic content analyses.

10 Study Management

10.1 Pre-study Documentation

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki as stated in 21 CFR §312.120(c)(4); consistent with GCP and all applicable regulatory requirements.

Before initiating this trial, the PI will have written and dated approval from the Institutional Review Board for the protocol, informed consent form, subject recruitment materials, and any other written information to be provided to participants before any protocol related procedures are performed on any participants.

The PI must comply with GCP/ICH guidelines and all applicable regulatory requirements.

10.2 Institutional Review Board Approval

The protocol, the proposed informed consent form, and all forms of participant-facing materials related to the study (e.g., advertisements used to recruit participants, educational materials) will be reviewed and approved by the IRB. The initial protocol and all protocol amendments must be approved by the IRB prior to implementation.

10.3 Informed Consent

All participants must be provided a consent form describing the study with sufficient information for each participant to make an informed decision regarding their participation. Participants must sign the IRB-approved informed consent form prior to participation in any study specific procedure. The participant must receive a copy of the signed and dated consent document. The original signed copy of the consent document must be retained in the medical record or research file.

10.4 Changes in the Protocol

Once the protocol has been approved by the IRB, any changes to the protocol must be documented in the form of an amendment. The amendment must be signed by the PI and approved by the IRB prior to implementation.

If it becomes necessary to alter the protocol to eliminate an immediate hazard to participants, an amendment may be implemented prior to IRB approval. In this circumstance, however, the PI must then notify the IRB according to institutional requirements.

10.5 Case Report Forms (CRFs)

The PI and/or designee will prepare and maintain adequate and accurate participant case histories with observations and data pertinent to the study. Study specific Case Report Forms (CRFs) will document study data for safety monitoring and data analysis. All study data will be entered into OnCore® or other CTMS used for the study via standardized CRFs in accordance with the CTMS study calendar, using single data entry with a secure access account. Study personnel will complete the CRFs; the PI will review and approve the completed CRFs.

10.6 Record Retention

The PI is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each study participant. Study documentation includes all CRFs, data correction forms or queries, source documents, Sponsor-Investigator correspondence, monitoring logs/letters, and regulatory documents (e.g., protocol and amendments, IRB correspondence and approval, signed participant consent forms). Source documents include all recordings of observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical research study. The PI shall retain records for a period of 2 years following the conclusion of the study.

10.7 Publications

The preparation and submittal for publication of manuscripts containing the study results shall be in accordance with a process determined by mutual written agreement among the Sponsor-Investigator and collaborators.

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