Support Through Remote Observation and Nutrition Guidance (STRONG), a digital health intervention to reduce malnutrition among pancreatic cancer patients: A study protocol for a pilot randomized controlled trial

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ABSTRACT

Background: Malnutrition is a common and distressing condition among pancreatic cancer patients. Fewer than a quarter of pancreatic cancer patients receive medical nutrition therapy (MNT), important for improving nutritional status, weight maintenance, quality of life and survival. System, provider, and patient level barriers limit access to MNT. We propose to examine the feasibility of a 12-week multi-level, digital health intervention designed to expand MNT access among pancreatic cancer patients.

Methods: Individuals with advanced pancreatic cancer starting chemotherapy (N = 80) will be 1:1 randomized to the intervention or usual care. The Support Through Remote Observation and Nutrition Guidance (STRONG) intervention includes system-level (e.g., routine malnutrition and screening), provider-level (e.g., dietitian training and web-based dashboard), and patient-level strategies (e.g., individualized nutrition plan, self-monitoring of dietary intake via Fitbit, ongoing goal monitoring and feedback). Individuals receiving usual care will be referred to dietitians based on their oncologists' discretion. Study assessments will be completed at baseline, 4-, 8-, 12-, and 16-weeks.

Results: Primary outcomes will be feasibility (e.g., recruitment, retention, assessment completion) and acceptability. We will collect additional implementation outcomes, such as intervention adherence, perceived usability, and feedback on intervention quality via an exit interview. We will collect preliminary data on outcomes that may be associated with the intervention including malnutrition, quality of life, treatment outcomes, and survival.

Conclusion: This study will advance our knowledge on the feasibility of a digital health intervention to reduce malnutrition among individuals with advanced pancreatic cancer. Trial registration: NCT05675059, registered on December 9, 2022.

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1. Introduction

Abbreviations

PRIME   Protocol for Remotely Improving, Monitoring, and
         Extending Patient Quality of Life
STRONG   Support Through Remote Observation and Nutrition
         Guidance

Malnutrition is a common and distressing condition among individuals with pancreatic cancer. Studies estimate that at diagnosis up to 80% of pancreatic cancer patients report significant weight loss and half of patients are identified as malnourished [1–5]. Malnutrition negatively impacts quality of life, treatment adherence, and survival among pancreatic cancer patients and results in unnecessary hospitalizations [3,4,6–13]. Despite its devastating effects, malnutrition is underdiagnosed and undertreated among pancreatic cancer patients [14–16]. Clinical guidelines recommend malnutrition screening for all cancer patients and medical nutrition therapy (MNT) for cancer patients at-risk for malnutrition [17–20]. Currently, less than a quarter of pancreatic cancer patients identified as at-risk for malnutrition receive MNT [15, 16]. Therefore, interventions are needed to increase access to malnutrition screening and MNT among pancreatic cancer patients.

Malnutrition among pancreatic cancer patients stems from several factors including a reduced appetite, impaired pancreatic digestive function, and progressive wasting of muscle mass and body fat [21–23]. As a result, pancreatic cancer patients may have additional conditions, such as exocrine pancreatic insufficiency (EPI), that interfere with nutrition [24–26]. Additionally, advanced pancreatic cancer patients often receive multi-modal chemotherapy, leading to additional symptoms that interfere with nutritional intake (e.g., nausea) [27]. Oncology dietitians play a critical role in helping pancreatic cancer patients manage their nutrition. For example, dietitians can develop individualized nutrition plans with patients, provide advice regarding nutritional supplements, pancreatic enzymes, and nutritional support (e.g., feeding tube), and recommend strategies for managing nutrition-related symptoms (e.g., separating food and beverages to reduce nausea) [14, 28,29]. Research has shown that MNT improves nutritional status, energy intake, and quality of life among cancer patients [2,13,28,30–33]. Despite these benefits, MNT for cancer patients is not routinely implemented [34,35].

There are multiple barriers at the system-, provider-, and patient-level that affect access to and effectiveness of MNT among pancreatic cancer patients. At the system level, malnutrition screening and dietitian referral are not consistently implemented in the outpatient setting [34]. Currently, patients are referred to dietitians by oncologists, resulting in variation across providers [34] At the provider level, MNT is not standardized for pancreatic cancer [34,35], resulting in variation regarding what topics are covered (e.g., EPI). This variation stems from several factors including variability in dietitian experience with cancer (e.g., oncology board certification) and pancreatic cancer specifically. There are also barriers at the patient level including adherence to dietitian visits and nutrition advice. Cancer patients often struggle to adhere to nutrition advice due to clinical factors (e.g., treatment-related symptoms) and social factors (e.g., decreased motivation) [36]. Given the complex barriers that limit access to MNT among pancreatic cancer patients, multi-level interventions are needed.

To address this gap, our research team developed the Support Through Remote Observation and Nutrition Guidance (STRONG), a multi-level digital health intervention to reduce malnutrition among pancreatic cancer patients. The intervention includes system-level strategies (e.g., malnutrition screening and dietitian referral); provider-level strategies (e.g., dietitian discussion guide and web-based dashboard); and patient-level strategies (e.g., individualized nutrition plan, self-monitoring of dietary intake through Fitbit, and goal monitoring and feedback). When possible, patients' caregivers are trained on the intervention to provide additional support. The intervention is targeted towards pancreatic cancer patients with advanced disease who are undergoing chemotherapy and delivered during the first three months of chemotherapy. We targeted this population given the high burden of malnutrition and we chose the first three months of chemotherapy, a time when malnutrition often worsens [1–5]. This manuscript describes the protocol for a pilot study that will examine the feasibility of the STRONG intervention to reduce malnutrition among individuals with pancreatic cancer. The intervention will be compared with usual care, the best alternative available. This study will advance our knowledge about the feasibility of a digital health intervention to address malnutrition among pancreatic cancer patients.

2. Methods

2.1. Study design

This single-site, two-armed, pilot randomized controlled trial will include 80 individuals with metastatic or locally advanced pancreatic cancer who are starting chemotherapy at Moffitt Cancer Center (Moffitt), a National Cancer Institute (NCI)-designated Comprehensive Cancer Center. Participants will be 1:1 randomized to the 12-week STRONG intervention versus usual care. Participants will complete study assessments at baseline, 4-, 8-, 12-, and 16-weeks.

2.2. Trial registration and funding

The pilot trial is funded by the Pancreatic Cancer Action Network. The trial is approved by the Moffitt Institutional Review Board of Record, Advarra, and is registered at ClinicalTrials.gov (NCT05675059). The protocol is reported in accordance with the SPIRIT guidelines [37].

2.3. Participants

We will recruit individuals who meet the following criteria: 1) ≥18 years old; 2) newly diagnosed locally advanced (unresectable) or metastatic pancreatic adenocarcinoma; 3) planning to initiate chemotherapy; 4) able to speak and read English; and 5) able to provide informed consent. Individuals will be excluded if they meet the following criteria: 1) documented or observable psychiatric or neurological disorder that would interfere with study participation (e.g., psychosis, active substance abuse); 2) undergoing concurrent treatment for a secondary primary cancer; 3) ECOG performance status of 2 or greater; 4) receipt of chemotherapy in the past 6 months for prior pancreatic cancer; 5) use of parenteral or enteral nutrition; 6) presence of peritoneal carcinomatosis with associated malignant ascites; and 7) enrollment in a related clinical trial (e.g., other nutritional interventions).

2.4. Participant recruitment

We will recruit participants from the Gastrointestinal (GI) Oncology and the Senior Adult Oncology (e.g., patients aged 70 and older) Programs at Moffitt.

2.5. Procedures

2.5.1. Informed consent

Research staff will be trained in research ethics, the Health Insurance Portability and Accountability Act, and the study protocol prior to study enrollment. Research staff will review the informed consent sheet with

potential participants and obtain written consent prior to study enrollment. Research staff will inform participants of the voluntary nature of the study, safeguards taken to protect participant confidentiality, and that the medical care they receive will not be affected by their decision to enroll or not enroll in the study.

2.5.2. Randomization

Participants will be randomized 1:1 to the STRONG intervention or usual care. Randomization will be facilitated by an internet-based randomization table developed by the study statistician and uploaded to REDCap® (Research Electronic Data Capture) [38,39]. Individuals will be randomized in blocks of four to attain balance across study arms. To minimize risk of bias, only assessors who are unaware of randomization status will assess study outcomes. Given the nature of the intervention, it is not possible to blind dietitians or study participants to treatment allocation.

2.5.3. Intervention overview

The STRONG intervention is based on the behavioral change theory, Theoretical Domains Framework (TDF), which has been applied to multi-level interventions involving healthcare provider and patient behavior change [40]. A study conceptual model is presented in Fig. 1. The TDF maintains that individuals require opportunity, capability, and motivation to change their behavior [41,42].

- *Opportunity* is defined as factors external to the individual that may affect behavior change, such as lack of standardized malnutrition screening and dietitian referral [34]. To address this barrier, the intervention includes routine malnutrition screening and dietitian referral. Another external barrier to MNT is insurance coverage. Certain plans, such as Medicare Part B, only cover MNT for certain conditions (e.g., renal disease) and not cancer [35]. To address this barrier, individuals who cannot afford MNT will be referred to Moffitt's financial counselors who routinely provide patients with financial assistance.
- *Capability* is defined as an individual's capacity to engage in behavior change. On the provider side, MNT can be difficult to deliver due to

dietitian lack of knowledge regarding pancreatic cancer and limited access to data on malnutrition risk [34,35]. The current intervention will address these provider-level barriers by providing dietitians with a guide on MNT for pancreatic cancer patients and a web-based dashboard that collects and displays data on malnutrition risk, dietary intake, and nutrition-related symptoms. The guide was developed based on input from registered dietitian nutritionists (RDNs) who have extensive experience working with pancreatic cancer patients. On the patient side, barriers to participation may be related to the mode of delivery (e.g., transportation issues with in-person only delivery) [43,44], lack of tools for self-monitoring [36], and competing clinical factors, such as nutrition-related symptoms [36]. To address these barriers, participants will be provided with a Fitbit app for food logging, offered the option to participate in virtual dietitian visits, and will receive ongoing follow-up with a dietitian to address competing clinical factors.
- *Motivation,* or an individual's willingness to change, can affect cancer patients' adherence to MNT [36]. The intervention will address this by using a motivational interviewing approach to MNT, establishing individualized goals for nutrition intake, and providing ongoing feedback on progress towards goals. Each intervention component is described in greater detail below.

2.5.4. Malnutrition screening and dietitian referral

Given the high risk of malnutrition among advanced pancreatic cancer patients [1–5], all participants in the intervention group will be referred to a registered dietitian for an initial malnutrition screening using the Patient-Generated Subjective Global Assessment (PG-SGA) short form. While the majority of the dietitians that serve this patient population at Moffitt have experience in pancreatic cancer, patients are sometimes referred to a new dietitian or a dietitian that does not specialize in pancreatic cancer. All RDs supporting the intervention will receive training including the dietitian guide to ensure consistent intervention delivery. The PG-SGA short form has been validated in cancer patients receiving outpatient care and includes weight history, food intake, nutrition-related symptoms, activity, and function. [[45, 46].
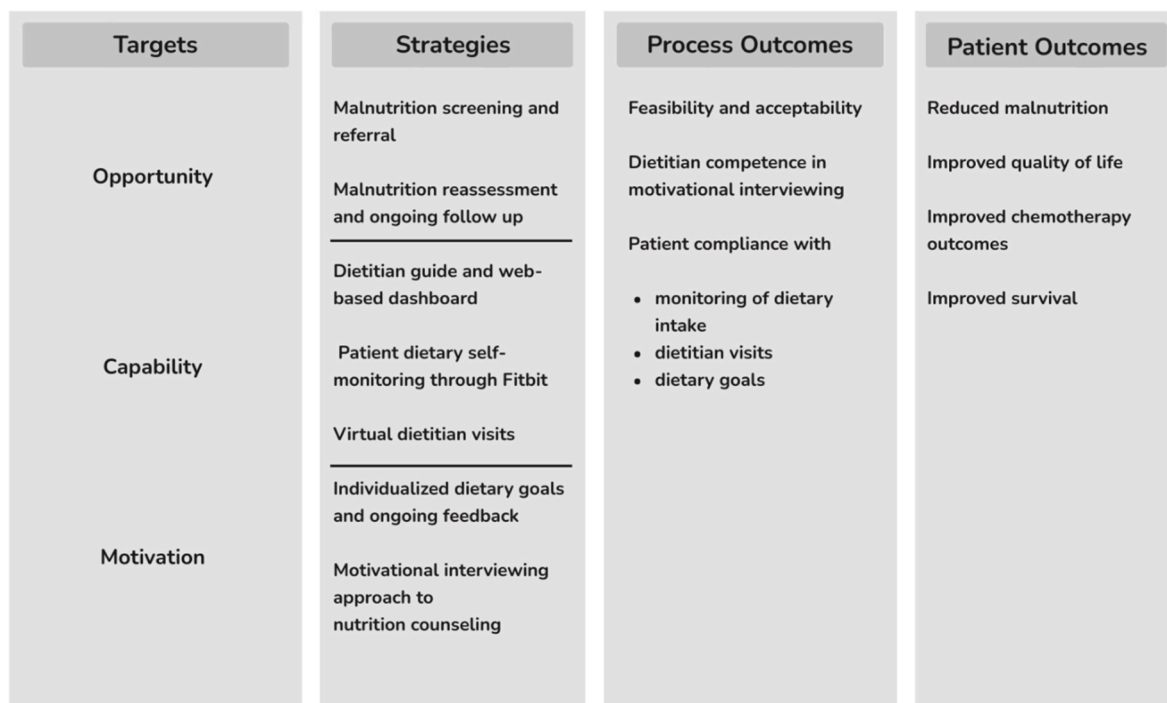

Fig. 1. Strong intervention conceptual model.

Patients will complete the PG-SGA short form prior to their dietitian visit via REDCap® and the oncology dietitian will review the collected information during the visit. The dietitian will establish an individualized nutrition plan and set goals for daily calorie and protein consumption based on the European Society for Clinical Nutrition and Metabolism guidelines of 25–30 kcal/kg/day and 1.2–1.5 g/kg/day of protein [49]. The dietitian may adjust these goals based on clinical judgement as needed.

2.5.5. MNT

Given that malnutrition often worsens during chemotherapy [27], all intervention group participants will complete bi-weekly dietitian follow-up visits via Zoom (Zoom Video Communications Inc., San Jose, CA) that are approximately 30 min. Participants will receive assistance with Zoom from the research team and be provided with Moffitt's Zoom help line. Participants unwilling or unable to participate in Zoom visits will be offered alternatives (e.g., in-person visit). Prior to the visit, the patient will complete the PG-SGA short form so that the dietitian can reassess malnutrition risk. During follow-up visits, the dietitian will review the patient's dietary intake and progress toward nutrition goals, readjust goals as needed, and provide advice for managing nutrition.

2.5.6. Dietitian discussion guide

Dietitians will receive a discussion guide that includes recommended topics for MNT for pancreatic cancer patients and tips for integrating motivational interviewing into MNT. Motivational interviewing approaches have been applied in prior MNT interventions and have demonstrated success in increasing patient compliance with nutrition recommendations [47,48]. Dietitians will receive training on motivational interviewing and the guide prior to participant enrollment. The discussion guide will include information on nutrition topics relevant to pancreatic cancer including 1) questions to help identify patients with EPI; 2) tips for how and when to take pancreatic enzyme replacement therapy (PERT) and nutrition supplements; 3) advice for managing diabetes and pancreatic cancer; and 4) expected nutrition-related symptoms and nutrition strategies for symptom management. These topics were selected based on qualitative feedback gathered from our dietitians, clinicians, patients, and caregivers. The guide also includes recommended principles of behavior change (e.g., individuals are more likely to change their behavior when the behavior is monitored), a brief overview of motivational interviewing, and tips for integrating motivational interviewing into MNT (e.g., list of open-ended questions to gather information on what motivates the participant to improve their nutrition) [49,50].

2.5.7. Patient self-monitoring of food intake through fitbit

Participants and their informal caregivers (when available) will meet with research staff and receive a Fitbit device and training on how to download and use the Fitbit app for food logging and how to charge and sync the Fitbit device. Participants will receive advice on time-saving strategies for food logging, such as scanning product barcodes and saving favorite meals, and behavior change strategies (e.g., saving calorie goals in the app and setting app reminders for food logging). Participants will also receive training on how to estimate serving sizes. Participants can choose to download the app on a personal device or receive a loaned tablet with cellular service. This strategy will allow participants who are unwilling or unable to use a personal device to participate in the study. Participants who opt to use a loaned tablet will receive training on how to use the device.

2.5.8. Dietitian web-based dashboard

Dietary intake data from the Fitbit app will be uploaded into a web-based dashboard called the Protocol for Remotely Improving, Monitoring, and Extending Patient Quality of Life (PRIME) platform. The PRIME platform was developed by Moffitt's Biostatistics and Bioinformatics Shared Resource and can collect and visualize patient-reported

data, such as the PG-SGA (e.g., malnutrition risk) and nutrition-related symptoms (outlined below). The dietitians can access the dashboard to guide MNT (e.g., review patients' symptoms, dietary intake) and study staff can access the dashboard to monitor intervention adherence (e.g., review number of days patient logged dietary intake in prior week).

2.5.9. Individualized nutrition goals and ongoing feedback

Patients will receive individualized goals for nutrition including a daily goal for calorie intake and protein intake that will be adjusted as needed by the dietitian. At each visit, dietitians and patients will review the goals, patients' progress on the goals (e.g., Fitbit food log data), and discuss any discrepancies between patients' progress and their goals for participating in the intervention (e.g., improving quality of life).

2.5.10. Usual care

Participants randomized to usual care will be referred to dietitians based on the treating care teams' discretion (e.g., medical oncologist, nurse). Participants in this condition will be asked to wear a Fitbit for 12 weeks to passively collect data on activity level and will complete all study assessments (e.g., PG-SGA short form); however, participants will not be asked to log food intake.

2.5.11. Participant retention

We will use several strategies to retain participants including 1) loaning participants a connected device when needed; 2) reminding intervention group participants to log food if data is not received for a period greater than 3 days; 3) allowing participants to complete study assessments via multiple modalities (e.g., paper, electronic, on a tablet during a clinic visit); 4) involving informal caregivers in intervention delivery when possible; and 5) incentivizing assessment completion. Participants will be compensated with a $25 gift card for completing each of the five study assessments. Participants who complete all five study assessments will receive an additional $25 gift card (up to $150 in gift cards per participant). Patients, caregivers, and providers can also participate in a one-time exit interview; patients and caregivers will receive a $50 gift card for completion. Providers will not receive a gift card; in our experience, monetary incentives are not a motivator for provider participation in research studies.

2.6. Study measures

2.6.1. Study assessment schedule

Data collection will include a patient survey at baseline, 4, 8, 12, and 16 weeks, collection of electronic health record and cancer registry data, a one-time patient and provider survey about implementation, and a one-time exit interview with patients, caregivers, and providers about implementation (Fig. 2). Surveys will be administered via REDCap®; patients will be offered alternative methods of completion (e.g., paper) when necessary. Interviews will be approximately 30 min, conducted by phone, audio-recorded, and professionally transcribed. The interviews will be led by a qualitative research specialist from Moffitt's Participant Research, Interventions, and Measurement Core using a semi-structured interview guide. Measures are described below.

2.6.2. Primary outcomes

The primary outcomes of this pilot study are feasibility and acceptability, and we will collect additional implementation data. Measures and expected outcomes are presented in Table 1 and were selected based on pilot study design recommendations [51,52] and our team's prior experience working with advanced cancer patients. For feasibility, we will measure recruitment, retention, assessment completion, and provider perceptions about ease-of-implementation using a validated, four-item scale, the Feasibility of Intervention Measure (FIM) (score range 0–20 with higher scores indicating greater ease-of-implementation) [53]. We have set 12 as the cutoff, indicating a moderate level of feasibility. We will obtain IRB approval to record

	STUDY PERIOD						
	Enrolment	Allocation	Post-allocation				Close-out
TIMEPOINT	*-t₁*	*0*	*Baseline*	*4 weeks*	*8 weeks*	*12 weeks*	*16 weeks*
ENROLLMENT:							
Eligibility screen	X						
Informed consent	X						
Allocation		X					
INTERVENTIONS:							
Dietitian training			X				
Dietitian dashboard set-up			X				
Patient referral and screening			◆━━━━━━━━━━━━━━━━━━━━━━━◆				
Fitbit monitoring of dietary intake			◆━━━━━━━━━━━━━━━━━━━━━━━◆				
Dietitian visits and goal feedback			◆━━━━━━━━━━━━━━━━━━━━━━━◆				
Usual care group			◆━━━━━━━━━━━━━━━━━━━━━━━◆				
ASSESSMENTS:							
Sociodemographic and clinical characteristics			X				
Feasibility and implementation						X	
Malnutrition [a]			◆━━━━━━━━━━━━━━━━━━━━━━━◆				
Inflammation			◆━━━━━━━━━━━━━━━━━━━━━━━◆				
Quality of life			◆━━━━━━━━━━━━━━━━━━━━━━━◆				
Treatment outcomes			X				X
Survival			X				X

Fig. 2. Enrollment, intervention, and assessment schedule
a. All malnutrition-related measures (nutritional status, weight, body mass index, dietary intake) will be assessed at all time points. Skeletal muscle mass will only be assessed at baseline, 8 and 16 weeks due to timing of patients' CT scans.

reasons for non-participation and collect basic demographics from individuals who decline to participate to compare participants and non-participants (e.g., sex, race/ethnicity). We will attempt to contact participants who dropped out of the study early to record reasons for withdrawal and overall reaction to the study protocol. We will record how many participants required a loaned tablet to participate in the study.

Acceptability is defined as providers' and patients' satisfaction with the intervention, which will be assessed using a validated, four-item scale, the Acceptability of the Intervention Measure (AIM) (score range 0–20 with higher scores indicating greater acceptability) [53]. We have set 12 as the cutoff, indicating a moderate level of acceptability.

Additionally, we will assess patients' interest in continuing the dietitian visits after the study ends and interest in continuing to log food intake through a survey item developed for the study.

Implementation will be assessed by measuring intervention adherence, usability, fidelity, adaptation, contamination, cointervention, and intervention quality. Intervention adherence will be assessed by tracking compliance with dietitian visits, Fitbit food logging, and dietary goals (e. g., percent of daily calorie and protein goal attained). Usability is defined as the extent to which participants can use the Fitbit app to log their food intake with efficiency and satisfaction and will be measured using a validated, 10-item scale, the Intervention Usability Scale (IUS) (score range 0–100 with higher scores indicating greater usability) [54].

Table 1
Feasibility, Acceptability, and additional Implementation Measures.

Area of Interest	Outcome	Measure and/or Expected Outcome
Feasibility	Screening/eligibility for study	• Record contact attempts per participant and reasons for ineligibility
	Recruitment	• Recruit 40% of eligible patients • Record reasons for non-participation • Compare characteristics of participants and non-participants (e.g., sex, race/ethnicity, age)
	Retention	• Retain 70% of participants at the end of intervention (12 weeks) • Record reasons for withdrawal (e.g., hospice enrollment) • Compare characteristics of retained participants and participants who withdrew from the study (e.g., sex, race/ethnicity, age)
	Assessment completion rate	• At least 70% of participants will complete the baseline assessment • At least 50% of participants will complete all five assessments
	Provider rating of feasibility	• At least 70% of providers will rate the intervention as easy-to-implement (FIM score $\geq$ 12)
Acceptability	Provider and patient satisfaction with the intervention	• At least 70% of providers and 70% of patients will rate the intervention as satisfactory (AIM score $\geq$ 12) • Patient questionnaire developed for this study assessing satisfaction with the dietitian
	Intention to continue using the skills and resources provided by the intervention	• Patient questionnaire developed for this study assessing interest in continuing dietitian services and food logging
Implementation/ Practicality	Patient compliance with dietitian visits	• At least 70% of participants will attend 4 out of 6 dietitian visits
	Patient compliance with food logging	• At least 70% of participants will log food intake for at least 5 days for 8 out of 12 weeks
	Patient compliance with dietary goal	• At least 60% of participants will achieve their daily calorie goal and daily protein goal for at least 5 days for 8 out of 12 weeks
	Usability	• At least 60% of patients will rate the Fitbit app as easy-to-use for logging dietary intake (IUS score $\geq$ 60)
	Fidelity	• 100% of audited dietitian visits will have documentation of individualized nutrition plan • Intervention dietitians will achieve a score of at least 3 on the BECCI indicating mastery of motivational interviewing during study training

Table 1 (*continued*)

Area of Interest	Outcome	Measure and/or Expected Outcome
	Adaptations	• Record intervention adaptations using the FRAME reporting tool
	Contamination and co-intervention	• Record number of dietitian visits per control group participant • Patient questionnaire developed for this study to assess food logging by any method (e.g., paper record) in control group participants • Document any related interventions that occur during study period (e.g., nutrition initiative in GI or Senior Adult clinics)
	Intervention quality	• Patients, caregivers, and providers will participate in a brief exit interview to provide feedback about intervention quality and implementation barriers and facilitators

We have set 60 as the cutoff, indicating a moderate level of usability. Fidelity or the extent to which the intervention was delivered as planned will be assessed in two ways. First, we will randomly select 20% of the dietitian visits (n = 77) for audit and record whether an individualized nutrition plan was documented. Second, we will record training sessions with the study dietitians and assess their competency with motivational interviewing using the Behavior Change Counseling Index (BECCI) [55]. A score of 3 or higher will be used as a cutoff, indicating mastery of motivational interviewing. We chose to record training sessions as opposed to dietitian visits due to institutional privacy rules regarding the recording of patient visits. We will document any adaptations to the intervention using the FRAME recording tool (e.g., adaptation type, scope, and rationale) [56]. We will assess for contamination by calculating the number of dietitian visits received and the use of food logging by any method (e.g., paper record) among control group participants. While we exclude participants currently enrolled in a related clinical trial, there remains the possibility of co-intervention. We will document any nutrition related interventions that may occur after participants have enrolled in the study (e.g., nutrition initiative implemented in GI or Senior Adult Oncology clinics). We will document resource use (e.g., time dietitians spend meeting with patients).

At the end of the intervention, we will conduct exit interviews with participants, informal caregivers who participated in the intervention, and providers who helped deliver the intervention (e.g., dietitians, oncologists, advanced practice providers). The exit interviews will collect information on intervention quality and implementation barriers and facilitators (e.g., difficulty with adhering to additional interventions such as PERT).

2.6.3. Secondary outcomes

We will pilot data collection of patient outcomes that may be associated with the STRONG intervention to support a future efficacy trial. First, we will assess malnutrition using five measures: 1) nutritional status; 2) weight loss; 3) body mass index (BMI); 4) muscle mass and 5) energy intake. These measures were selected based on recent guidelines for diagnosing adult malnutrition [57]. All measures will be assessed at each time point (baseline, 4, 8, 12, and 16 weeks) except for muscle mass, which will be assessed at baseline, 8 and 16 weeks due to the timing of patient's CT scans. Nutritional status will be measured using the PG-SGA short-form (score range: 0–35) and categorized based on a prior validation study (0–1 well nourished, 2–8 at-risk, $\geq$ 9 severely

malnourished) [58]. We will use data collected during chemotherapy visits to measure weight loss and low BMI, defined as <20 kg/m^2 for adults <70 years old and <22 kg/m^2 for adults ≥ 70 years old. Muscle mass will be estimated by calculating skeletal muscle index (SMI) from routinely collected CT scans. Low muscle mass will be defined as SMI ≤ 38.9 cm^2/m^2 for females and SMI ≤ 55.4 cm^2/m^2 for males [59]. We will blind CT assessors to participants' study group. Energy intake will be measured as mean and median daily calorie and protein intake and obtained from self-reported Fitbit food log data. Additionally, we will collect activity level data (e.g., step count) from the Fitbit app as an exploratory measure.

Quality of life will be measured using three measures: 1) the Functional Assessment of Cancer Therapy General (FACT-G) scale [60]; 2) the Functional Assessment of Anorexia/Cachexia Therapy (FAACT) subscale [61]; and 3) the FACT – hepatobiliary cancer (FACT-Hep) subscale [62]. Change in FACT-G score will be measured using an established minimally important difference (MID) for pancreatic cancer patients (6 points for total score; 2 points for subscale scores) [63,64]. A prior study has established a FAACT subscale score ≤ 37 as an optimal cutoff for establishing anorexia, which will be applied in the current study [65]. Change in FACT-Hep subscale score will be measured using a previously established MID among pancreatic cancer patients (5 points) [64].

Inflammation will be measured by the Glasgow Prognostic Score, which will be scored by assigning a point for c-reactive protein (CRP) >10 and a point for Albumin <3.5 [66,67]. We will also collect additional inflammatory biomarkers associated with weight loss and malnutrition in cancer patients including CRP-albumin ratio, neutrophil-lymphocyte ratio [68,69], and pro-inflammatory cytokines (e.g., interleukin-1 beta, 6, and 8 and tumor necrosis factor α) [70]. Serum will be collected during routine blood draws at clinic visits and processed by Moffitt's Tissue Core.

Treatment-related outcomes will be measured by assessing relative dose of chemotherapy delivered, unplanned healthcare utilization, and survival. For each drug in the chemotherapy regimen, the sum of delivered doses will be divided by the sum of expected doses. Expected dose will be based on patient's starting chemotherapy dose. The percent dose delivered will be averaged for all drugs in the regimen to calculate an overall relative dose delivered. Unplanned healthcare utilization will include number of urgent care and emergency department visits. Additionally, we will measure progression-free survival and overall survival. We will also capture information about nutrition-related conditions and subsequent interventions including the diagnosis of EPI, prescription of PERT, and any adjustments made to PERT prescription.

2.6.4. Participant characteristics

We will collect sociodemographic information including sex, race/ethnicity, age, insurance type, language preference, education, income, presence of caregiver, rural residence, and neighborhood-level deprivation (measured at the census block level). We will collect clinical characteristics including weight, height, cancer type and stage, date of cancer diagnosis, performance status, chemotherapy regimen, comorbidities, vital status, number of metastatic sites involved, presence of a biliary stent, and pancreatic tumor location.

2.7. Data analyses

2.7.1. Power analysis

A formal power calculation was not conducted since the study's primary purpose is to examine the feasibility of the STRONG intervention [52]. We will oversample and recruit 80 participants assuming 20% will be lost due to attrition (a rate selected based on prior studies in this patient population). This will leave a proposed final sample of 64, which is adequate for estimating feasibility and acceptability for a future efficacy trial [71,72].

2.7.2. Analytic plan

We will use an intent-to-treat analytical approach and present results based on the Consolidated Standards of Reporting Trials (CONSORT) statement for randomized pilot and feasibility trials [73,74]. Participant characteristics and outcome variable differences between groups will be analyzed through Chi-squared, and *t*-tests; analyses will be adjusted if the data are not normally distributed or small cell sizes are present. We will explore within- and between-group differences in changes over time using mixed linear models. We will compare intervention and control group characteristics to determine if there are any factors that are not balanced across groups by randomization. If randomization does not produce balanced groups, we will adjust analyses accordingly. We will also compare characteristics of study participants and non-participants (e.g., selection bias) and individuals who completed the study with those who did not complete the study (e.g., attrition bias). A more detailed analytic plan is provided in a Supplemental File.

3. Discussion

This study will examine the feasibility of the STRONG intervention among individuals with advanced pancreatic cancer. Although individuals with pancreatic cancer disproportionately suffer from malnutrition compared with other cancer patients [75], MNT remains limited among these patients [15,16]. There are numerous barriers that limit counseling access, such as lack of routine malnutrition screening and dietitian referral, dietitians' limited access to data on malnutrition risk and nutrition-related symptoms, and patients' capability and motivation to change their nutrition behavior [34–36]. The STRONG intervention attempts to overcome these barriers by targeting systems change through routine malnutrition screening and dietitian referral, provider change through enhanced data access and training, and patient change through strategies to improve patient adherence to nutrition interventions. Positive findings from this feasibility study will be used to support a future efficacy trial to test the impact of the STRONG intervention on patient outcomes, such as malnutrition, quality of life, chemotherapy adherence, unplanned healthcare utilization, and survival.

CRediT authorship contribution statement

Kea Turner: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Writing – original draft, Writing – review & editing. **Dae Won Kim:** Conceptualization, Resources, Writing – review & editing. **Brian D. Gonzalez:** Methodology, Writing – review & editing. **Laurence R. Gore:** Methodology, Writing – review & editing. **Erin Gurd:** Project administration, Resources, Writing – review & editing. **Jeanine Milano:** Project administration, Resources, Writing – review & editing. **Diane Riccardi:** Project administration, Resources, Writing – review & editing. **Margaret Byrne:** Methodology, Writing – review & editing. **Mohammed Al-Jumayli:** Project administration, Resources, Writing – review & editing. **Tiago Biachi de Castria:** Project administration, Writing – review & editing. **Damian A. Laber:** Project administration, Writing – review & editing. **Sarah Hoffe:** Project administration, Writing – review & editing. **James Costello:** Project administration, Writing – review & editing. **Edmondo Robinson:** Project administration, Writing – review & editing. **Juskaran S. Chadha:** Project administration, Writing – review & editing. **Sahana Rajasekhara:** Project administration, Writing – review & editing. **Emma Hume:** Project administration, Writing – review & editing. **Ryan Hagen:** Project administration, W. **Oliver T. Nguyen:** Project administration, Writing – review & editing. **Nicole Nardella:**

Project administration, Writing – review & editing. **Nathan Parker:** Methodology, Writing – review & editing. **Tiffany L. Carson:** Methodology, Writing – review & editing. **Amir Alishahi Tabriz:** Methodology, Writing – review & editing. **Pamela Hodul:** Conceptualization, Funding acquisition, Methodology, Project administration, Resources, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.conctc.2024.101271.

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