Complete Title: A pilot randomized factorial trial to promote physical activity and healthy eating among young adult cancer survivors

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Study Principal Investigator: Erin Coffman, PhD
Faculty Advisor: Carmina Valle, PhD
CB#7440 Chapel Hill, NC 27599
919-966-7546
email: carmina.valle@unc.edu

PROTOCOL TITLE: A pilot randomized factorial trial to promote physical activity and healthy eating among young adult cancer survivors

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I confirm that I have read this protocol and understand it.

Principal Investigator Signature: 

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ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Definition
API	Application Program Interface
BCT	Behavior Change Technique
BMI	Body Mass Index
DSMB	Data Safety Monitoring Board
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders
HEI	Healthy Eating Index
IMPACT	IMproving Physical Activity after Cancer Treatment
IRB	Institutional Review Board
MOST	Multiphase Optimization Strategy
MVPA	Moderate to Vigorous Physical Activity
PA	Physical Activity
NCI	National Cancer Institute
NIH	National Institutes of Health
OCT	Office of Clinical Trials
PAR-Q	Physical Activity Readiness Questionnaire
PAQ	Paffenbarger Physical Activity Questionnaire
REDCap	Research Electronic Data Capture
RCT	Randomized Clinical Trial
SCT	Social Cognitive Theory
SDT	Self-Determination Theory
SNAP	Studies of Novel Approaches to Prevention
TraCS	North Carolina Translational and Clinical Scices
YACS	Young Adult Cancer Survivor

PROTOCOL SYNOPSIS

Study Title	A pilot randomized factorial trial to promote physical activity and healthy eating among young adult cancer survivors
Clinical Phase	NA
Study Rationale	Few studies have tested PA interventions specifically for YACS, and no studies have tested nutrition interventions among this population. To accelerate science in this area, we propose a pilot randomized factorial trial as part of the preparation phase of the Multiphase Optimization Strategy (MOST) framework to test the feasibility, acceptability, and effects of a digital PA and nutrition intervention designed specifically for YACS. Previous interventions have demonstrated the importance of self-regulation (i.e., self-monitoring of behaviors, small changes, goal setting and feedback) approaches to improve PA and nutrition behaviors among young adults and YACS. We aim to leverage our prior work to deliver a theory-based intervention using digital tools to simplify self-monitoring of PA, and dietary monitoring to provide tailored behavioral goals and messages to support increased physical activity and diet quality among YACS.
Study Objective(s)	Primary • To evaluate the feasibility of a of a theory-based, mobile PA and nutrition intervention, as characterized by the participation, accrual, and retention rates at 3-months. Secondary • To evaluate acceptability of the intervention as characterized by ratings of program acceptability and satisfaction at 3-months. • To evaluate the adherence to the intervention as measured by daily self-monitoring of activity (Fitbit) and dietary tracking (Traffic Light Approach) from baseline to 3-months based on experimental conditions. • To estimate the main effects of each of four intervention components on changes in behavioral measures (Fitbit measured MVPA and healthy eating index (HEI) using the NCI's 24-hour Recall (ASA-24)) at 3-months. • To estimate the main effects of each of four intervention components on changes in secondary outcomes including anthropometric (weight), clinical (Fried physical phenotype using the FRAIL index) and psychosocial measures (health related quality of life) at 3 months.
Test Article(s) *(If Applicable)*	All participants will receive a core 3-month physical activity and healthy eating intervention that includes evidence-based lessons, behavioral skills training, and daily self-monitoring of physical activity and diet.

Study Design	The YACS HEAL (Young Adult Cancer Survivors Healthy Eating and Active Lifestyles) trial utilizes the Multiphase Optimization Strategy (MOST) framework and a 2^4 full factorial experimental trial to test the efficacy of 4 intervention components, to determine feasibility, acceptability, and effects of intervention components on physical activity (PA) and diet quality. Participants will receive a core 3-month digital PA and nutrition intervention delivered through a mobile app, with digital tools (PA tracker) and self-monitoring of behaviors. All participants will receive evidenced based lessons and behavioral skills training focused on PA and nutrition behavioral change, skills training, goal-setting, and weekly feedback on progress. Using the highly efficient, randomized factorial experimental design, we will test 4 intervention components--each with two levels-: 1) simplified dietary tracking based on the Traffic Light Approach (TLA, daily tracking of green (low-calorie, high nutrients) vs. red (high-calorie, high-fat, low nutrients) foods), 2) dietary goals using the TLA (daily green or red food goals vs. no goals), 3) supportive text messages (yes (≤ 5 per week) vs. no), and 4) lesson delivery (all provided once vs. weekly).
Subject Population	**Inclusion Criteria** 1. Age ≥18-39 2. Diagnosed with invasive cancer malignancy between the ages of 15-39 years 3. Diagnosed with invasive malignancy in the last 10 years of diagnosis, and with no evidence of progressive disease or second primary cancers 4. Completed active cancer directed therapy (cytotoxic chemotherapy, radiation therapy and/or definitive surgical intervention), except may be receiving "maintenance" therapy to prevent recurrences 5. No pre-existing medical conditions(s) that preclude adherence to an unsupervised exercise program including cardiovascular disease, congestive heart failure, pulmonary conditions, renal disease, and severe orthopedic conditions 6. Not currently meeting guideline recommendations of 150 MVPA minutes/week (self-report) and guideline recommendations for fruit and vegetable consumption 7. Have the ability to read, write and speak English 8. Own a smartphone with a data and text messaging plan 9. Willing to be randomized to any levels of the factors **Exclusion Criteria** 1. History of heart attack or stroke within past 6 months 2. Untreated hypertension, hyperlipidemia, or diabetes, unless permission is provided by their health care provider. 3. Health problems which preclude ability to walk for PA 4. Report a heart condition, chest pain during periods of activity or rest, or loss of consciousness on the Physical Activity Readiness Questionnaire (PAR-Q; items 1-4). 5. Report a past diagnosis of or receiving treatment for a DSM-IV-TR eating disorder (anorexia nervosa or bulimia nervosa). 6. Currently pregnant, pregnant within the past 6 months, or planning to become pregnant within the next 6 months. 7. Hospitalization for depression or other psychiatric disorder within the past 12 months. History of psychotic disorder or bipolar disorder. 8. Plans for major surgery (e.g., breast reconstruction) during the study time

	frame 9. Currently participating in a weight loss, nutrition or physical activity study or program or other study that would interfere with this study. 10. Currently using prescription weight loss medications
Number Of Subjects	72
Study Duration	Each subject's participation will last 4 months.
Study Phases **Screening** **Study Treatment** **Follow-Up**	(1) Screening: screening for eligibility and obtaining consent and (2) Baseline assessment (3) Intervention: study intervention/experimental treatment. (4) Follow-up assessment will occur at 6 weeks and 3 months
Efficacy Evaluations	NA
Pharmacokinetic Evaluations	NA
Safety Evaluations	All medical events and safety data will be assessed at assessment points or when interim events are reported by participants using a standard form used in our ongoing NIH funded trials.
Statistical And Analytic Plan	The primary objective is to evaluate the feasibility and acceptability of a digital intervention components to increase PA and improve nutrition behaviors among YACS (n=80) at 3 months. Our primary feasibility measures are participation, accrual, and retention rates. The secondary outcome analysis will use mixed effects models to test for differences in MVPA and HEI by intervention components across time (baseline, 6 weeks, and 3 months).[24] Effects will be modeled as component x time interactions with the 3-month outcome as the primary endpoint.
DATA AND SAFETY MONITORING PLAN	Data safety management in this trial is intended to achieve 4 objectives: 1) to minimize the occurrence of adverse effects, especially those related to intervention; 2) to effectively manage adverse events as they relate to the study; 3) to identify when the interventions should be suspended because of concerns for participant safety; and 4) to determine when interventions may be resumed after having been suspended. The Principal Investigator (Coffman) will have primary responsibility for the safety of participants as it relates to the study protocol, which must be approved by the UNC IRB prior to study initiation. In addition, the North Carolina Translational and Clinical Sciences (TraCS) Institute Data Safety Monitoring Board (DSMB) is responsible for reviewing data from clinical trials approved by the UNC Biomedical IRB. Because the risks to subjects participating in this phase of this study are expected to be low, we do not anticipate the need for a formal Data Safety Monitoring Board. The research team will provide continuous monitoring of participant safety and periodic reporting to the IRB as required, including any Unanticipated Problems/Severe Adverse Events that may have occurred during the study. If risk or complexity is significant, the UNC Office of Human Research Ethics may require

Additional reporting or alternative data and safety monitoring. Data safety and monitoring activities continue until all participants have completed treatment and until all participants have been followed to the point at which study related adverse events would likely no longer be encountered.

BACKGROUND AND RATIONALE

1.1 Introduction

Adolescent and young adult cancer survivors are a historically understudied population that require interventions designed to address their unique care needs.[1,2] Cancer treatment effects can lead to prolonged periods of sedentary behaviors, lack of PA, and poor nutrition, resulting in loss of lean muscle mass, and increases in fat mass, putting YACS at elevated risk for chronic diseases and premature frailty and mortality.[3,4]

1.2 Name and Description of Investigational Intervention

The YACS HEAL (Young Adult Cancer Survivors Healthy Eating and Active Lifestyle) trial is a 2^4 full factorial experimental trial testing the efficacy of 4 intervention components (factors), each with two levels, to identify component levels that contribute to greater change in MVPA and diet quality among YACS. To do so, we will randomize 80 YAs with overweight or obesity to receive one level of each of the 4 intervention components, in addition to a core mobile-delivered behavioral physical activity and nutrition program.

1.3 Relevant Literature and Data

Young adult cancer survivors (YACS) have historically been under-represented in research studies and clinical trials, and lack treatments and survivorship programs that address their specific needs.[4] In comparison to children and older adults, adolescents and young adults have not experienced the same improvements in diagnosis, treatment and long-term survival rates, health disparities recognized by the National Cancer Institute (NCI).[4,5] By 10 years post treatment, over 40% of YACS have $\geq$ 2 comorbidities compared to 20% for age-matched peers without a history of cancer.[8] Obesity, number of comorbidities (i.e., high cholesterol, hypertension, arthritis, diabetes), and anxiety or depression are all positively associated with increased frailty risk.[9] Frailty is traditionally associated with age-related functional decline and has not been studied extensively in the YACS population, but recent research suggest that YACS have similar incidences of prefrailty and frailly similar to those of adults over the age of 60 without a history of cancer.[10–13] Among adult cancer survivors PA has been shown to improve BMI, weight, muscle strength, peak oxygen consumption, gait speed, fatigue, depression, quality of life,[14] and reduced cancer-specific and all-cause mortality.[15] Dietary interventions among adult cancer survivors have led to significant improvements in dietary quality, reduction in dietary fat, and increased fruit and vegetable consumption.[16] RCTs testing combined diet and exercise interventions have resulted in improved diet quality, increases in physical activity, physical function, health-related quality of life, and decreased obesity.[17] Thus, there is a need to prospectively measure frailty and develop interventions to improve health outcomes in younger populations.

To our knowledge, no interventions that concurrently promoted physical activity and nutrition have been developed specifically for YACS. Current international and US consensus guidelines for cancer survivors are based on the current evidence relating to diet, PA, and energy balance for cancer prevention and survival.[18] Adherence to guideline recommendations among cancer survivors has repeatedly been demonstrated to be associated with reduced risk of overall cancer incidence, all-cause mortality, non-cancer related mortality, and metabolic syndrome in large cohort studies, which have consisted primarily of white survivors and survivors of breast and prostate cancers.[19–23] Despite the benefits of a healthy lifestyle, previous studies have found that majority of cancer survivors do not adhere to consensus guidelines. Less than half of YACS meet recommendations for vegetable consumption, two-thirds meet the recommendations for fruit consumption, and less than half meet recommendations for aerobic or resistance physical activity.[24] Survivors ages 20-44 have poorer diet quality compared to older populations,[25] and adherence to health behaviors decreases with

survivorship duration.[26] To date there have been few randomized controlled trials to promote PA among YACS, and none have addressed nutrition related behaviors or a combination of PA and nutrition related outcomes. Thus, there is a need for rigorous and systematically designed interventions targeting PA and dietary behaviors among YACS.

Previous studies have shown that YACS have a desire to engage in healthy behaviors, and 92% use the internet to search for information relating to healthy eating and exercise.[27] A large proportion report information needs related to PA, diet, and rehabilitation.[28] However, they reported that there was too much information available, that the information was not specific to their needs as YACS, and that the information may not be trustworthy.[27] Additional barriers to healthy diet and exercise among YACS include lack of resources (i.e. financial and professional services), negative thoughts and feelings (e.g., feeling embarrassed, frustrated, fatigue), and negative environmental and social influences (e.g., unhealthy snacks at work, lack of support from family and friends).[27] Facilitators for YACS to engage in healthier lifestyles include cognitive motivators (e.g., health beliefs, fatigue, fear of recurrence, goals), "tools" to engage in health behaviors (e.g., access to farmer's markets, gyms, wellness programs, skills-building), and positive environmental and social influences.[29]

Digital behavior change interventions are an opportunity to deliver evidence-based tailored interventions that incorporate self-regulation via self-monitoring of PA, diet, and weight.30 The majority (78%) of YACS want support for PA and have a desire to increase their PA levels (70%), and prefer interventions that are individually tailored, home-based, consisting of a variety of modalities.[31] Self-monitoring devices like PA trackers and digital scales to provide data-driven adaptive goal-setting and personalized feedback to promote self-efficacy and self-regulation.[32] Self-regulation of behaviors include self-monitoring of behaviors, evaluation of current behavior compared to goals, and reinforcement or self-correction of behaviors. The phases of self-regulation include goal selection/setting, active goal pursuit, and goal attainment/maintenance.[33]

Our team has demonstrated the importance of self-weighing to promote self-regulation and weight management in young adults[34–36] and cancer survivors.[37,38] Additionally, small, discrete changes to dietary behaviors, promote the shaping and mastery of behaviors, and has been shown to be effect for weight gain prevention in young adults.[39,40] Our previous interventions using a simplified dietary monitoring approach based on the Traffic Light approach (TLA) that categorizes foods as green (low-calorie, high nutrients), yellow (moderate calories, high nutrients), and red (high-calorie, high-fat, low nutrients) have shown promise for promoting adherence to dietary goals and weight loss in young adults.[41,42] A simplified approach to dietary monitoring may improve adherence to dietary self-monitoring and lead to improvements in diet quality among YACS. Nutritional goals are an important for self-regulation, and self-efficacy beliefs directly shape goals, outcome expectations, and perceived barriers and facilitators of behavior change. Among YACS, higher self-efficacy beliefs were associated with engaging in self-regulation behaviors and meeting ACS guideline recommendations for fruit and vegetable consumption and PA.[26] Text message reminders serve as a powerful aid to promote self-monitoring and intervention engagement and may increase self-efficacy and feelings of social support and relatedness.[43]

1. STUDY OBJECTIVES

Few studies have tested PA interventions specifically for YACS, and no studies have tested nutrition interventions among this population. To accelerate science in this area, we propose a pilot randomized factorial trial to test the feasibility, acceptability, and effects of a digital PA and nutrition intervention designed specifically for young adult cancer survivors. Previous interventions have demonstrated the importance of self-regulation (i.e., self-monitoring of behaviors, small changes, goal setting and feedback) approaches to improve PA and nutrition behaviors among young adults and YACS. We aim to leverage our prior work to deliver a theory-based intervention using digital tools to simplify self-monitoring of PA, dietary monitoring, and self-weighing to provide tailored behavioral goals and messages to support increased physical activity and diet quality among YACS.

Using a factorial experiment, we will test main effects of each of 4 candidate intervention components and interactions between the components, making efficient use of a smaller sample size than a typical RCT would require. We propose to conduct a 3-month, 2^4 full factorial trial testing the effects of four intervention components--each with two levels— including (Table 1):
1) simplified dietary tracking based on TLA (daily tracking of green (low-calorie, high nutrients) vs. red (high-calorie, high-fat, low nutrients) foods),
2) dietary goals using TLA (daily goals vs. no goals),
3) supportive text messages (yes vs. no),
4) lesson delivery (all provided once vs. weekly).

Proposed intervention strategies and components are based on previous nutrition and PA interventions that have been conducted in cancer survivors targeting these health behaviors. The conceptual model guiding intervention development includes theoretical constructs from social cognitive theory (SCT) and self-determination theory (SDT); intervention strategies will incorporate behavior change techniques (BCTs) that have demonstrated efficacy in previous behavioral interventions in cancer survivors. Intervention components will target the SDT and SCT constructs associated with improved dietary and PA behaviors: perceived autonomy (self-efficacy and self-regulation through goal setting and self-monitoring of behaviors), perceived competence (behavioral capability, perceived barriers, and outcome expectations targeted with behavioral lessons and feedback), and perceived relatedness (social support from text message and tailored feedback on goals and progress).

The primary outcomes of interest are feasibility and acceptability. Secondary outcomes include change in minutes/week of MVPA and HEI dietary quality index score.

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The primary outcomes of interest are feasibility and acceptability. Secondary outcomes include change in minutes/week of MVPA and HEI dietary quality index score.

Assessments of outcomes will be conducted at baseline, 6 weeks, and 3 months (post-intervention. We hypothesize that it will be feasible to recruit and retain post-treatment YACS for this intervention. We also hypothesize that the intervention will be acceptable to YACS participants. We will examine recruitment potential, retention, pilot intervention procedures, satisfaction, and adherence to the intervention.

This proposed study presents an opportunity to deliver an evidence-based, theory-driven digital behavior intervention to YACS with the goal of improving nutrition and PA behaviors and subsequently reducing risk for adverse health outcomes. If the proposed aims are achieved, we will expand our understanding of ways to improve health outcomes among YACS, an underserved population of cancer survivors with unique needs. This study utilizes innovative intervention design frameworks to test multiple novel components that have not previously been tested in this population and will provide preliminary evidence for future optimization trials. Findings will enhance our understanding of promising intervention approaches to improve lifestyle behaviors in cancer survivors.

2. INVESTIGATIONAL PLAN

Study Design

The intervention approach is based on previous PA and nutrition interventions that have been conducted in cancer survivors and targeting these health behaviors and outcomes including frailty. The present intervention incorporates theoretical constructs from multiple behavior change theories including the social cognitive theory (SCT), self-determination theory (SDT) and will incorporate behavior change techniques (BCTs) that have been demonstrated efficacy in previous behavioral interventions. Primary goals of the intervention are to improve PA and diet quality through self-regulation of PA and diet behaviors using evidence-based strategies that have been previously developed and tested by our study team. These self-regulation strategies include developing knowledge and skills through behavioral lessons, promoting daily self-weighing, self-monitoring of PA and small progressive increases in PA, and simplified dietary monitoring using the Traffic Light Approach. This intervention

will target self-regulation via 1) self-monitoring of target behaviors (e.g., self-weighing, PA, green/red foods); 2) weekly self-evaluation of goal progress (e.g., weight change, weekly PA goal, daily green/red goal); and 3) self-reinforcement if goal was met, or additional behavior change if goal was not.

Elements Common to All Experimental Conditions

Core Intervention (n=80) all participants will receive a core intervention that includes PA and nutrition education modified from concepts of the Diabetes Prevention Program [51], our prior studies[37,42,52–55], and based around the consensus guideline recommendations for cancer survivors[49]. Participants will be given digital tools to facilitate self-monitoring – a PA tracker and simplified diet tracking tool to support self-regulation of behaviors. The intervention will be delivered a mobile app integrated with Fitbit. Participants will receive an activity tracker (Fitbit) in the mail, followed by an introductory videochat session with an interventionist. In this session they will receive information relevant to their participation in the program, including an overview of how to use the study app (for both iOS and Android); Fitbit; the Traffic Light Log; how to self-monitor to achieve their daily goals (eating, activity, and self-weighing), and other information relevant to the conditions to which they have been randomized. Activity and dietary data are synced to study servers and activity is available in the app on pages that display participants' daily and overall progress towards their goals. The study app also includes 12 behavioral lessons that are delivered based on randomization. These include behavioral strategies with specific instruction on core cognitive and behavioral skills (i.e., goal setting, self-monitoring, problem solving, overcoming barriers, reaching out for social support, and cognitive restructuring).

Participants will receive qualitative feedback on self-monitoring behaviors and goal progress specific to MVPA and diet tracking (and goals). Feedback will include positive reinforcement and encouragement, strategies for barrier identification and overcoming barriers, and strategies for improving dietary and PA behaviors. Participants will receive tailored feedback summaries weekly. Participants will receive an email directing them to their feedback page. The feedback message will include feedback based on participants' number of days tracking diet and PA, and progress toward goals.

Physical activity recommendation. The ultimate goal for the study will be to progress the participant to at least 150 minutes of moderate to vigorous physical activity. The initial session and behavioral lesson materials will highlight both that the current physical activity guideline for cancer survivors is at least 150 minutes per week of moderate-to-vigorous PA (MVPA) minutes/week (i.e., 3-5 metabolic equivalents (METs) and the benefits of light PA (e.g., every 60-minute increase in light PA is associated with a 16% reduction in mortality). An initial goal will be based on baseline levels of activity as established during the baseline assessment for the study. Progression will occur each week based standard gradual physical activity plans we have previously used in distance-based intervention for YACS (LCCC1323, LCCC1709), and will be based on baseline PA activity levels and individual progress each week.

Dietary recommendations. The specific recommendations for diet composition are consistent with American Cancer Society and American Institute for Cancer Research nutrition guidelines for cancer survivors[49,58] and the Traffic Light Approach (TLA) concept we have used in previous interventions.[41,42] This intervention component will test a simplified dietary monitory approach that emphasizes ACS[49] recommended dietary approaches: eating foods that help achieve and maintain a healthy body weight such as a variety of whole fruit and vegetables in a variety of colors, fiber-rich legumes, and whole grains, and limiting or excluding red and processed meats, sugar-sweetened beverages, highly processed foods and refined grain products, and alcohol.

Traffic Light Approach. To encourage long-term adherence to dietary monitoring, this study will use a simplified form of tracking based on the Traffic Light system. Rather than tracking calories as in traditional behavioral interventions, TLA is a simplified approach to dietary monitoring that categorizes food into colors of the stoplight based on their nutrient and calorie content.[60,60] In the Traffic Light Approach, foods are categorized into green, yellow and red categories. Users are encouraged to increase green foods, moderate yellow foods, and limit red

foods. Foods in the green category include fruits, vegetables, and certain very lean proteins, are low in calories, fat, and sugar and rich in nutrients. The high volume, water content and fiber in fruits and vegetables and the protein from the lean meats and egg whites in this category help promote satiety while consuming fewer calories. The yellow category includes moderately lean proteins, legumes, low fat dairy, whole grains, starchy vegetables, and low-fat dressings. These foods are higher in calories than green food but are still a good source of nutrients. Red foods are high in calories, fat, and/or sugar and are not a good source of nutrients. The goal in the Traffic Light Approach is to increase green foods and to limit red foods.

Description of Intervention Components (Factors)

In addition to the core intervention, participants will receive one level of each of four candidate intervention components to be evaluated: 1) simplified dietary tracking based on the Traffic Light Approach (daily tracking of green (low-calorie, high nutrients) vs. red (high-calorie, high-fat, low nutrients) foods), 2) dietary goals using Traffic Light Approach (daily green or red food goals vs. no goals), 3) supportive text messages (yes (≤ 5 per week) vs. no), and 4) lesson delivery (all provided once vs. weekly).

Candidate intervention components and their levels are described in detail below:

Simplified Dietary Tracking (green foods vs. red foods*).* Self-monitoring has repeatedly been shown as an essential self-regulation strategy for physical activity and dietary behavior change success. However, traditional dietary self-monitoring is challenging and time-consuming and adherence to self-monitoring typically declines over time.[61,62] The TLA might be more feasible and sustainable since participants only monitor a subset of foods reducing participant burden to engaging with self-monitoring behaviors.[42,63–65]

Simplified dietary tracking using the TLA targets self-regulation through specific cognitive behavioral strategies including—reducing intake of certain foods (red foods), increasing intake of healthier choices (green foods), planning meals in advance, regular mealtimes, self-monitoring of foods, etc. Dietary approaches that promote increased fruit and vegetable intake can lead to improved diet quality and displacement of calorie-dense foods.[66] Our previous interventions that used a simplified dietary monitoring approach based on the TLA have shown promise for promoting adherence to dietary goals and weight loss in young adults.[41,42] However, no interventions have compared the effects of maximizing green food consumption or minimizing red food consumption on diet quality in young adults.

Participants will be randomized to use the TLA to either self-monitor their consumption of GREEN foods OR RED foods.

Nutrition Goals (yes/no). Weekly goals will target self-efficacy by improving dietary behaviors gradually starting at baseline values, emphasizing self-monitoring of behaviors, and graded tasks by increasing with goal attainment. This intervention component will facilitate the evaluation of the main and interaction effects between dietary monitoring and goal setting for healthy eating. Provision of weekly goals by the study team may facilitate self-monitoring of behaviors, however, goal setting (by individual) may lead to greater feelings of autonomy, self-efficacy, and facilitate greater self-regulation.

Participants will be randomized (yes/no) to receive weekly goals for their TLA assigned food group (e.g., increase green foods, decrease red foods) based on baseline intakes. If randomized to nutrition goals: participants in the RED food condition will be given a daily limit of 2-6 red foods based on their baseline intake of foods that are recommended to be avoided or limited by the American Cancer Society guidelines (e.g., processed foods, alcohol, etc.). Participants in the GREEN food condition will be given a daily goal of 6-12 green foods based their baseline intake of foods recommended by the ACS guidelines (e.g., fruits and vegetables, fiber).

Text Messages (yes/no). The efficacy of text messages for behavior change are inconsistent due to heterogeneity of study designs the use of additional intervention components in complex multicomponent behavior change interventions.[67] The factorial design allows for the examination of the independent effect of text messages in a multicomponent intervention. Text messages serve as a reminder for self-monitoring and engagement in health behaviors but may also increase participant burden and decrease intervention efficacy. Additionally YACS prefer interventions that provide social support, and text-messages may be an efficient and economical method to provide study-related content.[31]

Text messages will include a variety of content including reminders of goals, self-monitoring behaviors, personal assessment of fatigue, energy levels and mood, PA nutrition tips, and positive reinforcement. Text messages will target perceived relatedness by providing social support, prompts and cues, and verbal persuasion about capabilities.

Participants will be randomized (yes/no) to receive up to 5 weekly text messages pertaining to their personal goals and reminders to self-monitor based on intervention components.

Behavioral Lessons (once/weekly). Due to heterogeneity of methods and lack of clarity in reporting, the efficacy of timing and delivery of behavioral lessons in mhealth interventions is unclear. Behavioral interventions typically provide content on a weekly basis. Providing lessons all at once gives YACS the autonomy to select content in the order and time of their choosing, increasing their self-efficacy and self-regulation of behavior change.

Behavioral lessons will be delivered through using the mobile app. Lesson content will focus on behavioral strategies: self-monitoring, goal setting, barrier identification, problem solving and action planning to overcome barriers. Behavioral lessons are based on standard behavioral and weight management content and adapted from previous PA and weight management trials with YACS.[37,42,51–53,68,69]

Participants will be randomized to receive all 12 lessons in week 1 or receive one lesson each Monday over 12 weeks.

Study Population

Individuals will be eligible if they meet the following criteria: age ≥18-39 years at the time of consent, diagnosed with invasive cancer malignancy between the ages of 15-39 years, diagnosed with invasive malignancy in the last 10 years, with no evidence of progressive disease or second primary cancers, completed active cancer directed therapy (cytotoxic chemotherapy, radiation therapy and/or definitive surgical intervention), except may be receiving "maintenance" therapy to prevent recurrences, have no pre-existing medical conditions(s) that preclude adherence to an unsupervised exercise program including cardiovascular disease, congestive heart failure, pulmonary conditions, renal disease, and severe orthopedic conditions, not currently meeting guideline recommendations of 150 MVPA minutes/week (self-report) and guideline recommendations for fruit and vegetable consumption, have the ability to read, write and speak English, have access to the Internet on at least a weekly basis, posess and usage of an Internet e-mail address or willingness to sign up for a free email account (e.g., Gmail), have smartphone with internet access and text messaging plan and be willing to be randomized to any condition.

Exclusion criteria include a history of heart attack or stroke within past 6 months; untreated hypertension, hyperlipidemia, or diabetes, unless permission is provided by their health care provider; health problems which preclude ability to walk for PA; a heart condition, chest pain, or other health problems that influence the ability to follow physical activity recommendations; plans for major surgery (e.g., breast reconstruction) during the study time frame; currently using prescription weight loss medications; currently pregnant, pregnant within the past 6 months, or planning to become pregnant within the next 6 months; report a past diagnosis of or receiving treatment for an eating disorder; hospitalization for depression or another psychiatric disorder in the past 12 months or history of bipolar or other psychotic disorder; currently participating in another weight loss, nutrition, or physical activity study or program; already adherent to the American Cancer Society's recommendation of exercising > 150 minutes/week of moderate-to-vigorous intensity PA and the American Cancer Society's recommendation of consuming > 5 servings of fruits and vegetables/day.

Individuals that reported joint problems, some prescription medications, or current treatment for hypertension or hyperlipidemia will be required to obtain written physician consent to participate (Appendix).

The trial is registered on clinicaltrials.gov (NCT05887401) and was approved by the Institutional Review Board at the University of North Carolina at Chapel Hill on August 18, 2022.

3. STUDY PROCEDURES

Data Collection

All study participants will complete objective weight measurements, two dietary recalls, and self-administered online surveys at baseline and 3 months (post-intervention). At 6 weeks, only psychosocial measures and medical events will be collected via online survey and telephone. Participants will receive $25 for completing the 3-month assessments. Online surveys will include measures of theoretical mediators, other psychosocial constructs, and process measures. We will send emails and texts prompting participants to complete assessments, with follow-up emails and phone calls to non-respondents, as necessary. Measures and timing are described below.

Measures

Behavioral Measures (collected at baseline and 3 months)

Device-measured physical activity will be assessed at baseline and 3 months using the study provided activity tracker. Participants will be instructed to wear the device at all times for a full week; monitoring for at least 600 min/day for at least 4 days in the week (including at least one weekday and one weekend day) is considered adequate for analysis. Data are transmitted to Fitbit each time the participant syncs their tracker with the Fitbit app on their phone. Weekly minutes of moderate-to-vigorous activity (termed "active minutes" in Fitbit) and steps per day will be computed from the participant's Fitbit data and averaged over a minimum of 4 out of a 7-day period.

Self-reported physical activity will be assessed using the Paffenbarger Activity Scale (PAQ)[76], which assesses leisure-time activity. The PAQ provides an estimate of minutes per week of moderate-to-vigorous intensity, and calories/week of light (5 kcal/min), medium (7.5 kcal/min), and high (10 kcal/min) intensity activities. PAQ changes have been predictive of weight change.

Dietary Intake: Changes in dietary intake will be assessed using the NCIs 24-hour Recall (ASA-24)[46] by trained administrators. Participants will complete two self- reported recalls; one weekday and one weekend day. The 24 recall is a validated method of measuring diet. Using two recalls permits adjustment of estimates for intraindividual variation and is superior to administering one recall. We will examine change in overall energy intake and saturated fat intake, as well as change in fruit and vegetable consumption, fiber consumption, and change in the Healthy Eating Index score.[77]

Healthy Eating Index: The HEI-2020[78] consists of 13 component scores, including: total fruit, whole fruit, total protein foods, total vegetables, greens and beans, whole grains, dairy, seafood and plant proteins, fatty acids, sodium, refined grains, added sugars, and saturated fats. The summation of the 13 component scores ranges from 0 to 100, with higher scores indicating closer compliance with the 2020 DGA.

Anthropometric and clinical measures (collected at baseline and 3 months unless otherwise noted)

Weight: will be objectively measured at the participant's home. We will instruct participants to weigh themselves in light clothing, without shoes, on the cellular-enabled scales at each assessment time point.

Height (baseline only): Participants will provide self-reported height using a single item from Behavioral Risk Factor Surveillance System and adapted for use in the NCI's Health Information and National Trends Survey.

Body Mass Index (BMI). Height and weight will be used to calculate BMI (kg/m2).

Fried Frail Index.[75] Frailty will be assessed among all participants with a Frailty Index (all participants) previously used by Co-I Dr. Smitherman among AYA survivors. The FRAIL Questionnaire includes five components that reliably predict declining health function and mortality without requiring a face-to-face evaluation. The items assess: 1) self-reported fatigue (PROMIS Fatigue Short form), 2) weight loss, 3) comorbidities (11 items from UNC Health Registry Comorbidity Assessment), 4) difficulty with ambulation (1 item from PROMIS Physical Function Short Form), and 5) ability to overcome resistance (1 item from PROMIS Physical Function)). The number of positive responses for these components is summed to create the FRAIL index (range 0–5) and characterized as 0-1: robust, 2: prefrail, and 3+: frail. Changes in individual components and overall frailty scores will be assessed.

Psychosocial mediators and consequences (collected at baseline and 3 months).

Health-related Quality of Life: will be assessed using the AYA PROMIS PRO Core battery,[79] which has recently been recommended by the National Cancer Institute's Clinical Trials Network AYA PRO Task Force. These measures assess relevant HRQoL domains for AYA cancer survivors that are most likely to be impacted during and after cancer treatment. The AYA PRO Core battery includes the following PROMIS short forms: depression, anxiety, fatigue,

physical function, pain interference, emotional support, cognitive function, pain intensity. Each question has five responses ranging in value from 1 to 5, which are summed to find the total raw score. Total raw scores are translated to a T-score, standardized with a population mean of 50 and a standard deviation of 10. A higher PROMIS T-score represents more of the concept being measured.

Depressive Symptoms: Depressive symptoms have been associated with changes in weight, diet, and PA and will be assessed with the PROMIS v1.0-Depression Short Form 4a.

Anxiety. Anxiety will be assessed using the PROMIS v1.0-Emotional Distress Anxiety Short Short Form 4a.

Fatigue. Fatigue will be assessed using the PROMIS v1.0-Fatigue Short form 4a.

Physical Function. Physical function will be assessed using the PROMIS v2.0 Physical function Short Form 4a.

Pain Interference. Pain interference will be assessed using the PROMIS Short form v1.1 Pain Interference Short Form 4a.

Emotional Support. Emotional support will be assessed using the PROMIS v2.0 Emotional Support Short form 4a.

Cognitive Function. Cognitive function will be assessed using the PROMIS v2.0 Cognitive function short form 4a.

Pain Intensity. Pain intensity will be assessed with the 1-tiem PROMIS v1.0 pain intensity 1a, "In the past 7 days, how would you rate your pain on average?" Scored 0-10 from no pain to worst imaginable pain.

Competence for Exercise and Nutrition. The Perceived Competence Scale[80] includes 4 items that measure perceived competence for nutrition and 4 items for physical activity. Ratings are on a 7-point Likert scale with higher scores indicating greater perceived competence for the behavior.

Self-efficacy for Exercise and Nutrition: Nutrition and exercise self-efficacy will be measured using the Nutrition and Physical Activity Self-Efficacy Scale, a 10-item scale that assesses an individual's confidence in their ability to eat healthy foods and exercise in the presence of barriers. Ratings are on a 4-point Likert scale with higher scores indicating greater self-efficacy for exercise and nutrition.[81]

Self-Regulation for Exercise and Nutrition. The Treatment Self-Regulation Questionnaire (TSRQ)[82] will be used to assess autonomous and controlled motivation for making changes in diet (15 items) and PA (15 items). Ratings are on a 7-point Likert scale indicating agreement with statements regarding motivation for behavior change such as, "I try to exercise on a regular basis: because I enjoy exercising." This questionnaire contains four subscales: external regulation, introjected regulation, identified regulation, and intrinsic motivation which are determined by averaging the responses to each of the subscale's items.

Autonomy Support and Relatedness: The Virtual Care Climate Questionnaire (VCCQ)[83] a 15-item measure of perceived support for autonomy provided by the study team in a virtual care setting. Ratings are on a 7-point Likert scale with higher scores indicating a higher level of perceived autonomy support.

Other Supporting Measures (collected at baseline and 3 months unless otherwise indicated)
Medical events. Will be collected at 3 months. Any responses will be reviewed by the study team to determine if a Serious Adverse Events report is required.

Process and Adherence Measures (collected over 6 months)

Dietary Monitoring. Engagement will be assessed via frequency of dietary monitoring. Each food entry will be time-stamped and automatically captured by the study website interface. Frequency of dietary monitoring will be defined as the total number of days during the 3-month intervention that participants tracked breakfast or lunch AND dinner, which will be considered a full (versus partial) day of tracking.

PA monitoring. Objective self-monitoring of PA will be assessed via the Fitbit tracker data for all groups. Data will be collected using the Fitbit application program interface (API). We will collect data on frequency and number of days that activity was tracked using the Fitbit (steps>500/day). These data will be tabulated to derive a measure of percent of days in which activity was tracked, and average activity tracking days per week. We will also ask participants how often they viewed the Fitbit website/mobile app to access graphs of their physical activity trends.

Adherence to Dietary Goals. Adherence will be measured as the total number of full days of tracking (i.e., breakfast or lunch AND dinner) during which participants met their dietary goal. Non-adherence will be assumed for partial days of tracking, or days where participants did not track.

Engagement measures: Using REDcap and study specific TLA website analytics we will examine website logins, goal setting, viewing feedback, lesson views, calculated as average logins and component views per week.

*Program Acceptability and Satisfaction***.** Participants will be asked to complete a post-treatment program evaluation. Measures will be adapted from previous studies and assess intervention exposure and attention, perceived personal relevance, and satisfaction with intervention components.

Other Measures (collected at baseline, 6 weeks, and 3 months, unless otherwise indicated)

Medical events and symptoms will be collected at 6 weeks and 3 months in a self-report questionnaire. Responses will be reviewed to determine if follow up is necessary with a scheduled telephone call, and if a Serious Adverse Events form is required.

Demographics. At baseline, standard demographic information will be collected

Medical history, Medication use. Self-report of both prescription and non-prescription medications.

Smoking, alcohol use. Smoking and alcohol use will be assessed at each time point.

4. STATISTICAL CONSIDERATIONS

Sample Size and Power

The sample size is based on feasibility. Our primary feasibility measures are participation, accrual, and retention rates. Anticipated participation and retention rates are based on pilot feasibility studies among YACS and our previous work with this population. With an estimated participation rate of 85% (consistent with CO-I's experience, LCCC 1707), we anticipate it will be feasible to recruit 80 YACS within 6 months. We will test the null hypothesis that the proportion recruited is 50% or lower versus the alternative that it is 65% or greater using a one-tailed test at an alpha level of 0.05 with 95% power, which would support that the study is feasible.

We plan to accrue no more than 100 participants looking to have at least 80 evaluable participants, for 5 participants in each of the 16 groups. We expect accrual to take a total of 10 months at a rate of approximately 10 participants per month. We anticipate accruing 80 participants within 10 months, or 12-15 participants per month. A sample size of 80 achieves 99% power to detect a difference between a null hypothesis mean accrual rate of 12 participants/month and an alternative hypothesis mean of 15 participants/month with a significance level of 0.05 using a one-sided one-sample Poisson test.

For retention, we will test the null hypothesis that the retention is 70% or below versus the alternative that the retention is 90% or greater using a one-tailed test at a 0.05 alpha level. With 80 participants we would reject the null hypothesis that the retention is 70% if at least 62 participants are retained with 90% power, which would support that the study is feasible. With 80 participants we would reject the null hypothesis that the retention is 70% if at least 66 participants are retained with 97% power, which would support that the study is feasible.

All three endpoints must meet the proscribed criteria in order for the study to have successfully demonstrated feasibility.

Statistical Analysis

Primary Endpoint Analysis. *Accrual rate* will be defined as the number of YACS who agreed to participate divided by the number of weeks of recruitment. *Participation rate* will be defined as the percent of eligible participants who agreed to participate. *Retention rate* will be defined as the number of participants who completed 3-month measures divided by the number who consented to participate. Means and 95% confidence intervals will be computed for all rates. The proportion of patients who complete the 3-month assessment will be reported along with an exact 95% confidence interval. This percentage will also be reported for experimental condition individually. We will test the hypothesis that the recruitment rate is ≤50% vs. ≥65% using a one-sample test of proportions with a one-sided alpha level of 0.05. We will test the hypothesis that the retention rate is ≤70% vs. ≥90% using a one-sample test of proportions with a one-sided alpha level of 0.05. We will use a one-sample Poisson test to compare the average number of participants accrued per month with a null hypothesis of 12 participants per month and a one-sided alternative of 14 participants per month at an alpha level of 0.05.

Secondary Endpoint Analysis. Ratings of program acceptability and satisfaction will be summarized using descriptive statistics (mean, standard deviations, frequencies) of the post-treatment evaluation (Objective 2.1.3). Descriptive statistics (percentages, medians, interquartile ranges) will be used to estimate adherence to daily self-monitoring (Objective 2.1.4), and study measures relating to demographics, anthropometric, clinical, behavioral, and psychosocial measurements (Objectives 2.1.5-2.1.7.). These study measures will be reported at baseline and 3 months. We will also estimate changes in weight, anthropometric, clinical, behavioral, and psychosocial measures from baseline to 3 months, and within each experimental condition, the change scores

will be tested to see if they are significantly different from 0 using Wilcoxon Signed Rank tests.

Using maximum likelihood methods, we will use mixed model analyses with repeated measures to estimate changes in MVPA and HEI (and other secondary measures; Objectives 2.1.5-2.1.7) at 3 months and to test for statistical differences across conditions in changes over time, adjusting for age, cancer type, and time since diagnosis. Models will include random intercept, time, component, and component*time variables. A proper error covariance structure will be chosen based on model fit indicated by model likelihood, Akaike Information Criterion and Bayesian information Criterion.

Handling Missing Data

While every effort will be made to avoid missing data, we expect some attrition. If the combined missingness on predictor variables is <5%, missing data will not be replaced. If levels of missing data are higher, we will examine the nature of the missing data and extent of bias it may introduce. We will compare respondents to non-respondents to see if they differ on non-response systematically and assess if missing data are missing completely at random (MCAR), missing at random (MAR), or missing not at random (MNAR). Assuming the data are (MCAR/MAR), multiple imputation methods will be used.

Strengths and Limitations.

One of the biggest limitations of this study is the sample size. The use of a factorial design makes efficient use of the sample, but effect sizes may not provide conclusive evidence for efficacy to make determinations about component inclusion in future trials. However, it makes efficient use of resources and will provide valuable information about feasibility, acceptability, and implementation of intervention components, regardless of effect size. Another limitation that since the PA intervention is being included as a core component, it will not be possible to disentangle the main effects for this component alone. This randomized factorial pilot trial is testing an innovative theory and evidence-based approach to promoting guideline concordant PA and nutrition in AYAs followed by 3 months of behavioral maintenance. A strength of the intervention is utilizing an existing intervention framework that has been shown to improve PA in this population. The factorial design allows for the simultaneous testing of multiple novel intervention components to examine their feasibility and acceptability while conserving resources. Intervention components will be developed around ACS guidelines for cancer prevention and cancer survivors, which has not been examined in this population. The goal of the intervention is to improve PA and nutrition behaviors among AYAs, which will be beneficial to all survivors, but may provide additional benefits for those that are least compliant and at highest risk for future morbidity and mortality. This is the first intervention design for AYAs to target determinants for frailty and could provide important information for future optimization trials and fully powered RCTs. Information from this pilot will be inform future trials to optimize timing, delivery, and dose of promising intervention components. This study will add to the field of cancer prevention and control by testing interventions targeting PA and nutrition behaviors with the goal of meeting guideline recommendations among AYAs improve survivorship outcomes and reduce health disparities.

5. SAFETY MANAGEMENT

Data safety management in this trial is intended to achieve 4 objectives: 1) to minimize the occurrence of adverse effects, especially those related to the intervention; 2) to effectively manage adverse events as they relate to the study; 3) to identify when the interventions should be suspended because of concerns for participant safety; and 4) to determine when interventions may be resumed after having been suspended. The Principal Investigator (Coffman) will have primary responsibility for the safety of participants as it relates to the study protocol, which must be approved by the UNC IRB prior to study initiation. In addition, the North Carolina Translational and Clinical Sciences (TraCS) Institute Data Safety Monitoring Board (DSMB) is responsible for reviewing data from clinical trials approved by the UNC Biomedical IRB. Because the risks to subjects participating in this phase of this study are expected to be low, we do not anticipate the need for a formal Data Safety Monitoring Board. The research team will provide continuous monitoring of participant safety and periodic reporting to the IRB as required, including any Unanticipated Problems/Severe Adverse Events that may have occurred during the study. If risk or complexity is significant, the UNC Office of Human Research Ethics may require additional reporting or alternative data and safety monitoring. Data safety and monitoring activities continue until all participants have completed treatment and until all participants have been followed to the point at which study related adverse events would likely no longer be encountered.

Participant Safety

The risks to human subjects in this study, including psychological and physical risks, are judged to be minimal. The anticipated benefits are great, insofar as the results will be used to determine if mobile-delivered behavior change strategies are effective for obesity risk reduction in a sample of young adults.

Psychological Risks: We expect risk of harm, including psychosocial and emotional distress or breach of confidentiality, as a result of this study to be rare or infrequent. Most communication during the intervention period will take place via telephone, videochat, website, direct emails, or text messages—to deliver intervention components, conduct assessments, or remind participants to complete questionnaires. Mailing of materials to participants will be done with plain packaging. We do not anticipate any risks of harm as a result of these communications. As part of the intervention, participants may be asked about personal factors related to their PA, dietary behaviors, and weight. Participants are not required to share this information and can elect not to share sensitive and confidential information with the study. Intervention content teaches participants about the benefits of daily self-weighing for weight management, addressing certain myths regarding daily self-weighing, and emphasizing the use of the smart scale as a tool or indicator of progress with diet and PA behaviors. Participants will be encouraged to contact the Principal Investigator if they feel they have incurred any emotional distress as a result of study participation. As this is a voluntary study, a participant is free to exit at any point if discomfort should occur.

Participants with emotional concerns will be referred to survivor-specific support resources, including referral to: the UNC Comprehensive Cancer Support Program for psychological counseling; LIVE**STRONG** Navigation, which offers free, confidential, cancer navigation services to support individuals' cancer journey; and CancerCare Counseling, through which oncology social workers offer telephone counseling to help cancer survivors cope with emotional and practical challenges of cancer.

We will collect information at each assessment timepoint on hospitalizations for any psychiatric problem, including depression and eating disorders and make referrals as needed or suspend intervention if symptoms emerge that are study related or if the severity of the psychological symptoms warrant suspension or withdrawal.

Physical Risks: There are no major physical risks associated with the PA or healthy eating interventions or data collection. There may be some risk to increasing physical activity, including, but not limited to, injuries to the muscles, ligaments, tendons, and joints of the body. Other risks include abnormal blood pressure, fainting, dizziness, disorders of heart rhythm, exacerbation of exercise-induced asthma symptoms, and very rare instances of heart attack, stroke, or even death. A consensus statement from the American College of Sports Medicine Roundtable on Exercise Guidelines for Cancer Survivors concluded that exercise training is safe after cancer treatments. Although increasing PA can have great benefits, participants may also experience some general fatigue and sore muscles or joints from exercising. Because several studies indicate that walking is the preferred exercise type for an estimated 55%-81% of survivors of varying cancer types,[31,71] the study focuses on encouraging moderate-intensity walking. To help ensure safety, the study will follow guidelines and safety recommendations for PA set forth by the American College of Sports Medicine. PhD trained staff interventionists will oversee safety of exercise progression and suitability. Materials provided during the course of the intervention will educate participants on exercise safety and inform them of precautions to take when starting an exercise program and how to manage increasing amounts of exercise. Messages will encourage participants to start at a reasonable frequency and intensity of exercise based on their current level and to increase their exercise gradually. The informed consent will also clearly communicate the potential physical risks related to starting an exercise program and increasing PA. Participation is fully voluntary, and we will ask participants to report any problems to the study researchers.

Unsafe Rate of Weight Loss: Participants will not receive an intervention designed to produce weight loss, however, making dietary changes and increasing PA can produce a gradual, modest rate of weight loss. The intervention focuses on making small daily changes to their eating in service of shaping dietary quality over

time. Thus, although unlikely, it is still possible that some participants could experience excessive weight loss at a rate that is unsafe. We will carefully monitor rate of weight loss over the course of the study, and take appropriate action as detailed below to ensure participant safety.

Risk of wearable devices. There is also the possibility of minor skin irritation associated with wearable activity tracker devices.

Risk to privacy and/or confidentiality. We expect a breach of confidentiality to be rare or infrequent. Most communication during the study period will take place via telephone, direct emails, text messages, or through the smartphone app—either to deliver questions, conduct assessments, or remind participants to complete questionnaires. We do not anticipate any risks of harm as a result of these communications; however, there is always a possibility that their scale data, tracker data, or activity in the app will be intercepted.

Adequacy of Protection Against Risks

a. Informed Consent and Assent

Recruitment and Informed Consent: Several different efforts will be used to recruit potential participants and obtain informed consent from those eligible participants. The research team is responsible for assuring that the UNC IRB has approved the study protocol and has reviewed and approved the informed consent document. Written approval must be obtained from the IRB before the study can begin. Once an individual has been deemed potentially eligible to participate through online and telephone screening, study staff will provide more study details and describe the concept of random assignment, the 36 study conditions, and assessment procedures over the telephone. Individuals who remain interested will receive an email directing them to a unique and secure REDCap link to an online informed consent. After clicking on the link, they will be directed through a series of screens that present the informed consent document. The online informed consent records will be retained, and recruitment of participants will be done by adhering to HIPAA regulations. Accrual reports will list enrolled participants and excluded participants throughout the stages of the research. This routine monitoring allows for early identification and resolution of potential problems during the recruitment phase. The anticipated recruitment duration is 30 months. All key personnel have attended the required courses on human subject protection and HIPAA regulations, and certificates of IRB training completion are on file with the University of North Carolina.

b. Protections Against Risk

Protections against Psychological Risks: As noted above, participants are not required to share this information and can elect not to share sensitive and confidential information with the study. Participants will be encouraged to contact the Principal Investigator if they feel they have incurred any emotional distress as a result of study participation. As this is a voluntary study, a participant is free to exit at any point if discomfort should occur.

Protections against Physical Risks: To ensure medical readiness to begin physical activity, participants will complete a physical activity readiness questionnaire (PAR-Q). The PAR-Q assesses for the following medical conditions: heart problems, chest pains, faintness or dizzy spells, high blood pressure, bone or joint problems such as arthritis that has been or could be aggravated by exercise, prescription medication use, and other medical reasons why exercise would not be advisable. Participants endorsing yes to any items 1-4 on the PAR-Q (experience of heart problems, frequent chest pains, faintness or dizziness, bone or joint problems) will be excluded from the study. We also will monitor any major musculoskeletal problems that develop during the intervention (e.g. broken bones) using a medical events questionnaire at 6 weeks and 3 months and will determine whether these appear related to our study. Participants who develop musculoskeletal problems or other health problems that may affect safe participation will be instructed to stop exercising until the problem resolves and their physician approves resumption of physical activity.

All participants will be advised about safe weight loss practices including dietary change and increasing physical activity at their initial study visit. Participants will be advised to gradually increase their physical activity and to

use walking as a primary form of activity and will be taught that the appropriate rate of weight loss is 1 to 2 pounds per week. In addition, we will carefully monitor changes in weight during our trial. We will collect information at each assessment timepoint on hospitalizations for any psychiatric problem, including depression and eating disorders.

Protections to Ensure Confidentiality of Participants: All identifying information collected from participants, including names, email addresses, Internet protocol address numbers, and zip code, will not be directly linked with research data. Instead, each study participant will be assigned a unique ID number. Identifying information will only be collected in order to contact participants. To ensure confidentiality of participants, all surveys and records related to a participant's involvement in this research study will be stored in a locked file cabinet and/or in encrypted files on servers that adhere to the University policy on storage and transmission of sensitive data. Participant identity on these records will be indicated by an ID number, and the information linking these numbers with participant identity will be kept separate from the research records. In addition, all research databases will have password-controlled access, and this will be controlled by critical staff.

During online data collection, questionnaire data will be temporarily stored on the REDCap data server. The REDCap database system provides for secure web-based data entry with the data stored on servers that are maintained by NC TraCS. The data is encrypted during transmission. The servers are located in a secure campus area with all appropriate physical security measures in place. The web and database servers are monitored by the TraCS IT staff, patched frequently, and scanned by a third -party vendor to ensure that they are protected against known vulnerabilities. The scanning application is the standard service for the entire campus. Access is by individual user id and is restricted to the forms and/or functions that the user needs to have. Data will be erased from the REDCap data server after online data collection is completed and the data is transferred to the study database in a secure password protected area.

CareEvolution's MyDataHelps™ mobile app data is securely stored in the HIPAA compliant, Meaningful Use Certified EDC HIEBus™ platform. CareEvolution® platforms comply with the security and privacy controls defined by NIST 800-53 Rev. 4 at the FISMA Moderate baseline. They regularly undergo external formal assessments by a FedRAMP-accredited Third Party Assessment Organization (3PAO). The platform has been granted an Authorization to Operate (ATO) by the National Institutes of Health (NIH) and is FDA Part 11 Compliant (info@careevolution.com). MyDataHelps integrates Fitbit using the Fitbit API.

Fitbit data will be collected using the Fitbit API (Application Programming Interface), which maintains data security by requiring an Access Token when the Fitbit user authorizes our study to access their data. During the consent process, participants will consent for the data from their specific device IDs (Fitbits) to be accessed by our study in order to drive tailored messages. Access to any individual's Fitbit account is protected by user login and password authentication. The risk of breach of confidentiality over the Fitbit website will be partly subject to each individual's comfort in sharing information in their individual profile. To further minimize the risk of breach of confidentiality, all participant activities on the Fitbit website will be voluntary. Consent forms will also clearly communicate the risk of this type of disclosure to participants.

If members of the research team wish to work with the data, they will only receive non-identifiable data. Although unanticipated, if study data need to be transmitted between study staff, encrypted files will be sent. Files will be password protected prior to sending or uploading. Only study staff will have knowledge of file passwords.

Removal of Patients from Protocol**.** Participants will be removed from the protocol should they experience greater than minimal risk as detailed above. Participants will be reminded that their participation is voluntary and that they may withdraw from the study at any time without consequence by contacting the Principal Investigator. In addition, we expect that pregnancies will occur. We will stop all intervention activities for anyone who becomes pregnant.

Potential Benefits of the Proposed Research to Research Participants and Others

Intervention participants are expected to improve dietary behaviors, physical activity, ultimately reducing their risk of secondary cancers or cancer recurrence, developing type 2 diabetes, cardiovascular disease, and other chronic diseases. In addition, the results of this study could be used to develop an optimized behavioral intervention to be tested in a similar population and, if effective, could be generalizable to a larger population of young adult cancer survivors. If successful, an automated program that uses a smartphone and other relatively low-cost digital technologies that is optimized for effective treatment components could be disseminated in a larger-scale program, thus benefiting a greater number of young adults cancer survivors.

Importance of the Knowledge to be Gained

There are currently few trials that have used a strictly mobile weight loss intervention that have resulted in clinically significant weight loss in young adults. Should this trial prove effective, it will have great public health relevance, as young adulthood is a critical period for excessive weight gain that is associated with future

This will be one of the first entirely remotely delivered interventions using digital tools to improve physical activity and diet behaviors simultaneously among YACS. This study addresses unmet needs of YACS and their demand for healthy lifestyle programs, uses the ubiquity of smartphones and technology, and employs their preference for remotely delivered health interventions. Further, the study design and digital intervention will enable nationwide recruitment and enhance external validity. This technology-based approach has the potential to deliver a novel intervention with high-reach, at low cost, with the potential for scaling the intervention for future efforts. This approach holds promise at improving body composition, physical function, and quality of life for YACS and thus has the potential for strong public health impact.

6. DATA COLLECTION AND MANAGEMENT

7.

The rigorous system used for participant tracking, data collection, management, and quality control procedures for our previous projects (SNAP: U01HL090864; IMPACT: R01CA204965) will be modified for this study. All data will be entered using the REDCap computer-assisted program that has built-in validation checks for range, data type, and completeness. All measurements will undergo consistency and outlier checks, compared with raw data, and edited as required. REDCap includes detailed audit logs that document any database changes, and we will document protocols for cleaning data.

Participants will provide physical data (objective weight and self-reported height), self-reported questionnaire data online, and self-reported physical activity data over the telephone specifically for research purposes. All self-report online data will be collected using secure REDCap surveys. Food log data will be collected using CareEvolution's MyDataHelps™ mobile app. Data is securely stored in the HIPAA compliant, Meaningful Use Certified EDC HIEBus™ platform. CareEvolution® platforms comply with the security and privacy controls defined by NIST 800-53 Rev. 4 at the FISMA Moderate baseline. They regularly undergo external formal assessments by a FedRAMP-accredited Third Party Assessment Organization (3PAO). The platform has been granted an Authorization to Operate (ATO) by the National Institutes of Health (NIH) and is FDA Part 11 Compliant (info@careevolution.com). MyDataHelps integrates Fitbit using the Fitbit API.

Identifiable information collected in online surveys will include the participant's name, address, phone numbers, and date of birth.

Risk to privacy and/or confidentiality

We expect a breach of confidentiality to be rare or infrequent. Most communication during the study period will take place via telephone, direct emails, text messages, or through the smartphone app—either to deliver questions, conduct assessments, or remind participants to complete questionnaires. We do not anticipate any risks of harm as a result of these communications; however, there is always a possibility that their scale data, tracker data, or activity in the app will be intercepted.

8. RECRUITMENT, CONSENT, AND RETENTION STRATEGY

Recruitment

Based on previous trials among young adult cancer survivors (YACS), successful recruitment and timely enrollment of 62 YACS for the THRIVE trial (LCCC1709) and 280 YACS for IMPACT trial (LCCC1707, R01CA204965) our team has demonstrated the ability to recruit this population. Based on our previous experiences and estimates of YACS served by UNC, participants will be recruited on a rolling basis and randomized to 1 of 16 intervention conditions. We will use a multi-method recruitment strategy that demonstrated previous success to reach individuals across the United States, and include the following strategies:

A) Direct mailings to individuals identified through the local UNC tumor registry. Used by Dr. Valle to recruit young adult cancer survivors (LCCC 1707, LCCC1709) and African American breast cancer survivors (LCCC1323), we will obtain a list of potentially eligible participants from the Carolina Data Warehouse for Health (CDW-H), which accesses UNC tumor registry data (i.e., participants from the UNC tumor registry are provided in a list from CDW-H). Potentially eligible survivors will be sent a letter of approach from the study PI, inviting them to participate and a study brochure describing the study and what it means to participate. The letters will invite interested individuals to visit a study

recruitment website or call research study staff to be screened by phone. We may follow up with up to two additional mailings if necessary.

B) Local and national community-based programs. We will work with our AYA Oncology Program members, local programs and national community-based organizations dedicated to YACS with whom we have established relationship (e.g., Teen Cancer America, Ulman Foundation, Cervivor, Stupid Cancer, A Ballsy Sense of Tumor) to share and post recruitment information on various communication channels (e.g., Facebook, Instagram, Twitter, listservs, email). Unpaid Facebook posts by cancer organizations or friends was the primary approach used in our IMPACT study (LCCC 1707) to recruit 280 participants in 14 months.

C) Advertisements. We will place sponsored posts on social media, ads on relevant internet sites, and use email listservs. We will produce flyers, posters, brochures, and presentations to advertise the study at community events and cancer conferences dedicated to young adults (e.g., CancerCon, AYA Global Congress). We will work with the UNC AYA Oncology clinical staff with whom we have established relationships (i.e., Co-Investigator Dr. Smitherman, Medical Director, UNC AYA Oncology; Lauren Lux) to advertise the study and recruit potentially interested individuals.

All recruitment efforts will direct participants to a study website with a more detailed description of the research study and FAQs about participating in research. Interested individuals will click through to a REDCap web screening survey to determine initial eligibility. Those who are preliminarily eligible will be contacted by trained study staff and will undergo additional phone screening. Following an approach we have used in the past, eligible and interested individuals will receive an email directing them to a unique REDCap link to an online informed consent. After providing consent, participants will be instructed on procedures for 1) completing one weekday and one weekend self-reported 24-hour dietary recall, 2) completing baseline online questionnaires, and 3) completing their baseline weight measurement. The Fitbit activity tracker will be mailed to the participant. After completion of baseline assessments, the participant will be randomized to one level of each of the 4 factors, or one of the 16 conditions (Table 1). The participant will be scheduled for a one-on-one telephone/videochat session during which they will be informed of condition assignments, assisted with downloading of the study smartphone app, and questions about getting started will be answered.

Inclusion of Women and Minorities

All individuals will be eligible for enrollment independent of sex/gender and race/ethnicity.

Retention

Participant retention strategies have been used effectively in our other studies. A systematic protocol will be followed to minimize dropouts. Top priority will be for assessment visits. At baseline, names and addresses of several friends and family members who can be contacted are obtained for use if we lose touch with the participant. Participants will be paid a $25 honorarium for completing assessments at 3 months. For each assessment visit, we will send participants an email that will include a link to online questionnaires with an expected completion date. Missed questionnaires will be immediately followed up by phone and rescheduled.

In addition to our assessment retention protocol, participants who complete all three assessments will be able to keep their Fitbit and scale at the end of the study, which we will believe will also encourage retention to assessment measures.

9. PLANS FOR PUBLICATION

As Principal Investigator of this grant application and clinical trial, Dr. Coffman will comply with the clinical trial information dissemination expectations of the NIH policy to register and submit summary results at ClinicalTrials.gov. Consistent with the terms and conditions of NIH funding, we will ensure the submission and updating of registration and results information for this clinical trial in the timeframes established by the Final Rule. Registration and results reporting in ClinicalTrials.gov will be completed within the following timeframes:

- Registration of the trial at ClinicalTrials.gov no later than 21 days after enrolling the first participant
- All submitted information will be updated at least once a year.
- Any apparent errors, deficiencies, and/or inconsistencies identified by NIH as part of the quality control review process and any other errors identified will be addressed by the responsible party.
- Corrections to submitted information will be made within 15 days for registration information and 25 days for results information.
- Trial results will be submitted no later than one year after the primary completion date.

Informed Consent Documents for the clinical trial will include a specific statement relating to posting of clinical trial information at ClinicalTrials.gov. The UNC IRB has template language explaining that the study will be posted on ClinicalTrials.gov that investigators are required to include in the consent document for the trial.

As PI, Dr. Coffman will work closely with the UNC-CH Office of Clinical Trials (OCT), which serves as the university's internal PRS. The OCT has responsibility for ensuring that clinical trial registration and reporting occurs in compliance with NIH policies. The OCT has support staff to facilitate the process of registration and results reporting to ClinicalTrials.gov, and our team will work closely with them to register this trial and to submit summary results to the website in a timely manner, in keeping within the required timeframes. Once data collection is complete, our research team will work to prepare and submit trial results no later than one year after the primary completion date.

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APPENDIX

Table 1. Experimental conditions in the 2^4 factorial trial

Core Intervention Components (ALL)	Experimental Condition	Nutrition Tracking (Green/Red Foods)	Nutrition Goals (Yes/No)	Text Messages (Yes/No)	Lessons (Once/Weekly)
Activity Tracker Traffic Light Log Weekly MVPA Goals Weekly Feedback	1	Green	Yes	Yes	Once
	2	Green	Yes	Yes	Weekly
	3	Green	Yes	No	Once
	4	Green	Yes	No	Weekly
	5	Green	No	Yes	Once
	6	Green	No	Yes	Weekly
	7	Green	No	No	Once
	8	Green	No	No	Weekly
	9	Red	Yes	Yes	Once
	10	Red	Yes	Yes	Weekly
	11	Red	Yes	No	Once
	12	Red	Yes	No	Weekly
	13	Red	No	Yes	Once
	14	Red	No	Yes	Weekly
	15	Red	No	No	Once
	16	Red	No	No	Weekly

Deborah Tate, PhD
Principal Investigator

PHYSICIAN CONSENT TO PARTICIPATE IN A DIET AND EXERCISE PROGRAM AT UNC-CHAPEL HILL

TO:

Physician's Name

Address

City **State** **Zip**

( )

Telephone Number

RETURN TO:

Karen Hatley, MPH, RD
UNC Weight Research Program
Lineberger Comprehensive Cancer Center
1700 Martin Luther King Jr. Blvd., CB 7294
Chapel Hill, NC 27514

Telephone: (919) 966-5853
FAX: (919) 843-6663
Email: agilestudy@unc.edu

Your patient _____ has asked to participate in a lifestyle program at the University of North Carolina at Chapel Hill specifically designed for young adult cancer survivors to help them adopt healthier eating and activity habits.

The 3-month program is delivered using a study smartphone app and digital health tools. All participants will receive a standard program using the study smartphone app, which will have weekly lessons and feedback on progress. Each participant will receive a combination of tools to help them keep track of their diet and meet healthy eating and physical activity goals. The combination of tools will vary the method of dietary monitoring, physical activity goals, and personalization of study messages in the app for each study participant.

All participants groups will receive the following intervention:

1. A lifestyle program that focuses on physical activity and nutrition behavioral change, skills training, goal setting, and weekly feedback.
2. The physical activity program that will be primarily home-based. The exercise will gradually be progressed to 150 minutes per week with activities akin to brisk walking.
3. Behavioral modification techniques for changing eating and exercise behaviors.
4. Digital tools including a smartphone app and Fitbit activity tracker.

Please indicate below if this program seems appropriate for your patient or if you see any contraindications for his/her participation (*please check the appropriate box below)*.

☐ I know of no contraindications to this patient participating in any of the above components of the program.

☐ I feel that this program would not be appropriate for this patient for the following reason(s):

_____

_____

_____
Signature of Physician

Inclusion Criteria:

1. Age 18-39
2. Diagnosed with invasive cancer malignancy between the ages of 15-39 years
3. Diagnosed with invasive malignancy in the last 10 years, with no evidence of progressive disease or second primary cancers
4. Completed active cancer-directed therapy (cytotoxic chemotherapy, radiation therapy and/or definitive surgical intervention), except may be receiving "maintenance" therapy to prevent recurrences
5. No pre-existing medical conditions(s) that preclude adherence to an unsupervised exercise program including cardiovascular disease, congestive heart failure, pulmonary conditions, renal disease, and severe orthopedic conditions
6. English-speaking and writing
7. Own a smartphone with a data and texting plan
8. Achieve less than 150 minutes/week of moderate-to-vigorous intensity activity and/or consume less than 5 servings of fruits and vegetables per day
9. Willing to be randomized to any levels of the factors

Exclusion Criteria:

1. History of heart attack or stroke within past 6 months
2. Untreated hypertension, hyperlipidemia, or diabetes, unless permission is provided by their health care provider.
3. Health problems which preclude ability to walk for physical activity.
4. Report a diagnosis of psychiatric diseases (schizophrenia, bipolar disorder, depression leading to hospitalization in the past year), drug or alcohol dependency. These conditions may potentially limit intervention adherence.
5. Report a past diagnosis of or treatment for a DSM-IV-TR eating disorder (anorexia nervosa or bulimia nervosa).
6. Plans for major surgery (e.g., breast reconstruction) during the study time frame.
7. Current participation in another PA or weight control program
8. Currently using prescription weight loss medications
9. Currently pregnant, pregnant within the past 6 months, or planning to become pregnant within the next 6 months.

No exclusion criteria shall be based on race, ethnicity, or gender.