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SWOG CANCER RESEARCH NETWORK

A RANDOMIZED TRIAL OF THE **A**LTERING **I**NTAKE, **M**ANAGING **S**YMPTOMS INTERVENTION FOR BOWEL DYSFUNCTION IN **R**ECTAL **C**ANCER SURVIVORS COMPARED TO A HEALTHY LIVING EDUCATION CONTROL: A FEASIBILITY AND PRELIMINARY EFFICACY STUDY **(AIMS-RC)**

NCT# 04205955

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NRG/NRG Oncology
SWOG/SWOG Cancer Research Network

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PROTOCOL CONTACT INFORMATION

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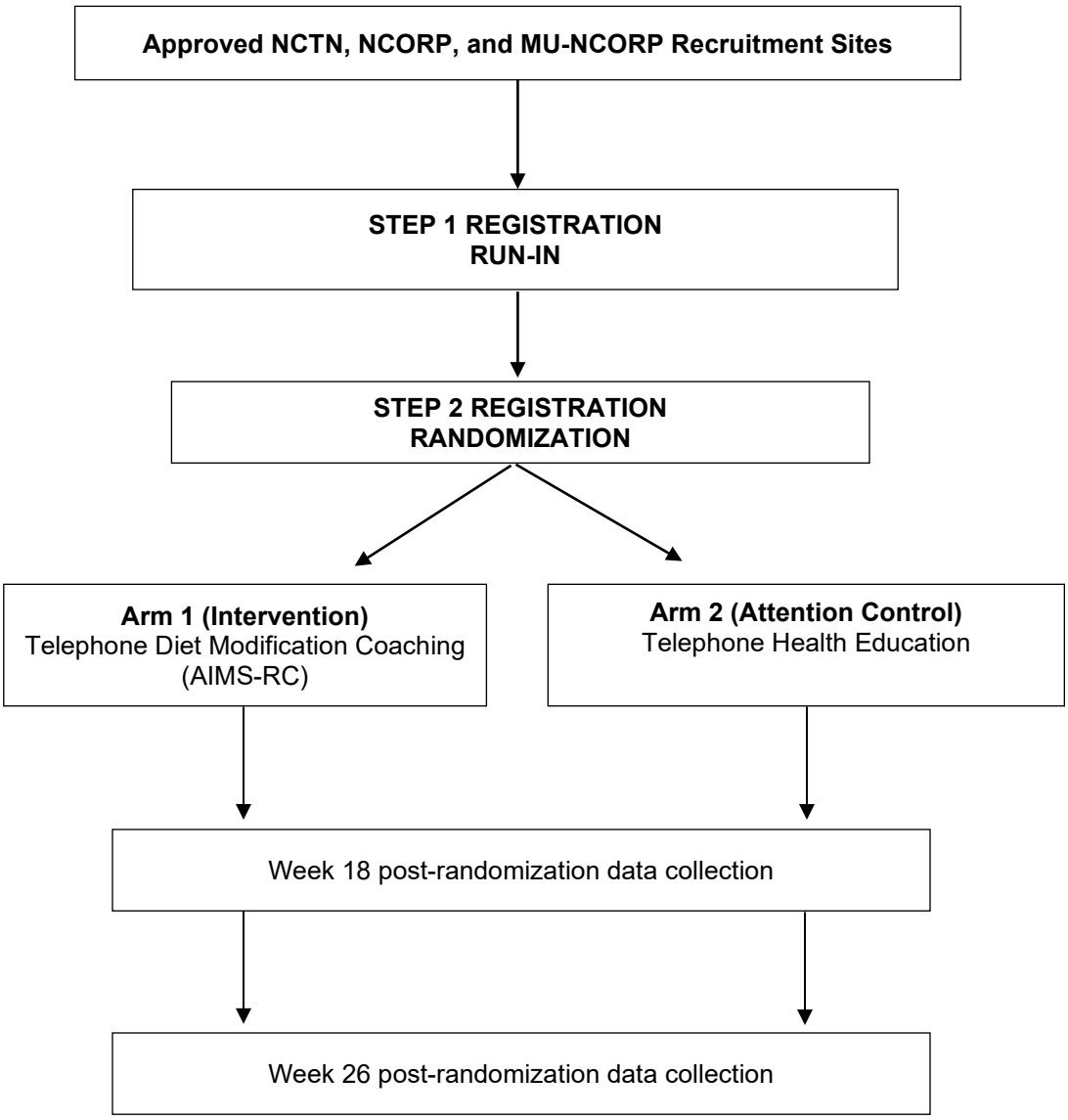
Clinical-Related Questions	Email: vsun@coh.org or call: Virginia Sun, Ph.D., R.N at: Office Phone: 626/218-3122; Cell Phone: 626-257-4717
Training-Related Questions	Email: cbrauninglis@cc.hawaii.edu Or call: Christa Braun-Inglis Office Phone: 808-440-5213
Amendments, Errors, Connectivity Issues and Technical issues with the SWOG CRA Workbench:	technicalquestion@crab.org
Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM)	To review CTEP-IAM account (new requests, reset passwords): https://ctepcore.nci.nih.gov/iam/index.jsp
Access to Medidata Rave	See Protocol Section 14.3 or contact CTSU Help Desk: Phone: 1-888-823-5923 or Email: ctsucontact@westat.com
Questions related to: Oncology Participant Enrollment Network (OPEN)	See Protocol Section 13.3 or contact CTSU Help Desk: Phone: 1-888-823-5923 or Email: ctsucontact@westat.com
Participant Transfers:	patienttransfer@crab.org

CANCER TRIALS SUPPORT UNIT (CTSU) ADDRESS AND CONTACT INFORMATION

CONTACT INFORMATION		
For regulatory requirements:	**For patient enrollments:**	**For study data submission:**
Regulatory documentation must be submitted to the CTSU via the Regulatory Submission Portal: (Sign in at www.ctsu.org, and select the Regulatory Submission sub-tab under the Regulatory tab.) Institutions with patients waiting that are unable to use the Portal should alert the CTSU Regulatory Office immediately at 866-651-2878 to receive further information and support. Contact the CTSU Regulatory Help Desk at 866-651-2878 for regulatory assistance.	Please refer to the patient enrollment section of the protocol for instructions on using the Oncology Patient Enrollment Network (OPEN) which can be accessed at https://www.ctsu.org/OPEN_SYSTEM/ or https://OPEN.ctsu.org. Contact the CTSU Help Desk with any OPEN-related questions at ctsucontact@westat.com.	Data collection for this study will be done exclusively through Medidata RAVE®. Please see the data submission section of the protocol for further instructions. Other Tools and Reports: Institutions participating through the CTSU continue to have access to other tools and reports available on the SWOG Workbench via the SWOG website (www.swog.org).
The most current version of the **study protocol and all supporting documents** must be downloaded from the protocol-specific Web page of the CTSU Member Web site located at https://www.ctsu.org. Access to the CTSU members' website is managed through the Cancer Therapy and Evaluation Program - Identity and Access Management (CTEP-IAM) registration system and requires user log on with CTEP-IAM username and password.		
For patient eligibility or data submission questions contact the SWOG Statistics and Data Management Center (SDMC) by phone or email: 206/652-2267 cancercontrolquestion@crab.org **For study-related questions**, please contact the Study Chair at 626/218-3122, 626/257-4717, vsun@coh.org		
For non-clinical questions (i.e. unrelated to patient eligibility, treatment, or clinical data submission) contact the CTSU Help Desk by phone or e-mail: CTSU General Information Line: 1-888-823-5923 ctsucontact@westat.com. All calls and correspondence will be triaged to the appropriate CTSU representative.		
The CTSU Website is located at https://www.ctsu.org.		

SCHEMA



1.0 OBJECTIVES

1.1 Primary Objective

a. To compare total bowel function score, as measured by the Memorial Sloan-Kettering Cancer Center Bowel Function Instrument (BFI), at 18 weeks post-randomization between the intervention and attention control arms.

1.2 Exploratory Objective(s)

a. To compare total bowel function score at 26 weeks post-randomization between the intervention and attention control arms.

b. To compare bowel function subscale scores (dietary, urgency, frequency), as measured by the BFI at both 18 and 26 weeks post-randomization between the intervention and attention control arms.

c. To compare lower anterior resection syndrome (LARS) scores (for anastomosis participants only), quality of life, and dietary quality at both 18 and 26 weeks post-randomization between the intervention and attention control arms.

d. To compare motivation, self-efficacy, and positive/negative affect at both 18 and 26 weeks post-randomization between the intervention and attention control arms.

e. To assess study feasibility, adherence, retention, and acceptability at both 18 and 26 weeks post-randomization.

f. To explore variation in primary and exploratory study outcomes according to sex, and to investigate whether intervention effects on the primary outcome differ across subgroups defined by sex.

2.0 BACKGROUND

Combination therapy (surgery/chemotherapy/radiation) has significantly improved long-term survival for men and women with rectal cancer.[1, 2] However, cancer survival brings common and feared treatment-related side effects such as irreversible bowel dysfunction. Bowel dysfunction is associated with frequent and erratic bowel movements, fecal incontinence, soiling, gas, bloating, and oscillations between diarrhea and constipation. Our previous observational research have found that bowel dysfunction occurs regardless of the type of surgery and ostomy status (with or without a permanent ostomy), and results in reduced social activities, poor social well-being, and decrements in quality of life (QOL).[3-7] Additionally, bowel dysfunction is a significant barrier to survivor adoption of dietary guidelines for cancer survivorship.[8,9]

One promising approach for bowel symptom control is diet modifications. In our previous research (N=1,057), diet modification was the most consistently reported self-care strategy used by long-term (>5 years) rectal cancer survivors.[3] The ability to successfully manage bowel symptoms results in improved QOL; however, the choice of diet modifications varied tremendously, and was often based on a trial-and-error approach without structured coaching that is grounded in theory-based strategies. This resulted in inconsistent efficacy, unnecessary delays in symptom improvement and, for some, avoidance of cancer preventive foods for health promotion after cancer.[3] While registered dietitian nutritionists (RDNs) provide the expertise to meet this challenge, evidence shows that even in comprehensive cancer centers RDN services are not readily available. Current patient-to-RDN ratios exceed 1000:1.[10, 11] Alternative, scalable approaches are essential to meet the growing demand.

Rectal Cancer as a Unique Cancer Diagnosis. Nearly 1.2 million individuals are living with a history of colorectal cancer in the United States; it is the third largest cancer survivorship population.[2] Approximately 68% of individuals with a history of rectal cancer are long-term (> 5 years) survivors.[2, 12] The proportion of rectal cancer diagnosed in adults ≤ 55 years doubled from 14.6% to 29.5% in the last 40 years.[13] The observed rise of rectal cancer in younger populations is likely partially fueled by lifestyle factors, including obesity and diet quality.[14] Rectal cancer has been largely ignored in terms of evaluation and symptom management, secondary to combining colon and rectal cancer statistics, despite highly different etiologies, treatments, symptoms and survival trajectories.[15]

QOL in rectal cancer survivors is influenced by treatment, which involves the sequenced combination of chemotherapy, radiotherapy, and surgery. The two most common surgical procedures include 1) abdominoperineal resection (APR), a resection of the rectum/anus with the creation of a permanent ostomy; and 2) low anterior resection (LAR) with rectal anastomosis (rejoining of healthy ends of the bowel).[16] For ease, we refer to the two techniques as “permanent ostomy” or “anastomosis, respectively. In 90% of survivors who undergo low-mid rectum resection, an anastomosis is accompanied by a temporary (“protective”) diverting ileostomy.[17]

Bowel Function as a Driver of QOL. Bowel dysfunction is one of the most common and feared long-term symptoms of rectal cancer treatment. [18-23] For anastomosis patients, the term “anterior resection syndrome” describes the constellation of postoperative bowel symptoms; these include fecal incontinence, frequency, urgency, sense of incomplete fecal evacuation, and flatulence.[24-27] Bowel dysfunction significantly affect QOL in rectal cancer survivors.[28-32] Our previous observational research suggests that bowel control varies greatly, and that 27% to 56% of survivors report moderate to severe bowel dysfunction at 1-year post-treatment.[33-38] Consequently, rectal cancer survivors must adjust psychologically and behaviorally to bowel dysfunction. Importantly, bowel symptoms are modifiable, underscoring the need to identify and test interventions that contribute to symptom relief.

Empirically-based interventions to manage bowel dysfunction are lacking. The American Cancer Society Colorectal Cancer Survivorship guidelines categorized the evidence for bowel dysfunction interventions at the lowest level (case studies or reports only).[39] In the absence of evidence-based interventions, survivors use trial-and-error self-care strategies to manage bowel symptoms. Functional self-care strategies include diet modifications, medications/supplements, and protective pads/diapers.[40] Social activity alterations (e.g. scheduling social outings around bowel patterns, intentional isolation) are often used to avoid bowel accidents in public.[41]

Dietary Modification as a Scalable, Empirically-Based Approach for Bowel Symptom Management. Diet modifications are one of the most common self-care strategies to manage bowel symptoms.[42-44] Beyond symptom management, a healthy diet is associated with decreased recurrence and improved survival after rectal cancer.[45-47] Specifically, cancer survivors are advised to eat a plant-based diet, avoid red and processed meats, consume adequate fiber (25-30 grams), limit animal fat intake, and moderate or no alcohol consumption.[9] Yet, current dietary guidance for cancer survivorship may be difficult to achieve in symptomatic rectal cancer patients. Survivors often avoid foods, including vegetables, fruits and whole grains, because of a perceived risk of bowel problems.[3] Behavioral approaches in the context of cancer survivorship should consider promotion of healthy eating behaviors to enhance QOL and survivorship, while concurrently identifying and addressing barriers to adoption of such eating patterns. For rectal cancer survivors this should include the modification of food selections that impact bowel symptoms. Left on their own, survivors may select approaches that delay symptom resolution and/or reduce their diet quality.

While professional dietetic services would be one solution to support bowel symptom management, recent reports describe the dearth of available registered dietitian nutritionists (RDN) and nutrition services available to survivors, even at comprehensive cancer centers.[10] Furthermore, bowel symptom characteristics are dynamic in terms of frequency and severity, suggesting that effective interventions will need to be flexible in meeting individual needs. Clinic-based counseling that

requires on-site appointments, travel, with limited time availability, increases barriers to access for rectal cancer survivors.[11] Less burdensome approaches are needed.

Sex-Specific Differences in Telephone-Based Lifestyle Behavior Interventions. Although behavior change remains a challenge for all cancer survivors, the current literature suggest that men may respond differently to lifestyle behavior interventions compared to women.[48] Reasons for these differences include 1) misperception of the need for behavior change[49]; 2) lack of reporting of attempts to change behaviors[50]; 3) lack of interest in undertaking behavior change[51]; and 4) perception that behavior change interventions are unappealing or designed to meet the needs of women.[52] Current evidence suggesting sex-specific variance in telephonic and/or multimodal behavioral counseling in cancer survivorship is limited.

Motivational Interviewing-Based Interventions for Cancer Symptom Management and Lifestyle Behaviors. Motivational interviewing (MI) is a patient-centered approach to facilitate behavior change.[53] MI is widely used to address a variety of behavioral targets, with demonstrated success in diet, smoking cessation, exercise and other health behaviors. A recent systematic review by Spencer and Wheeler evaluated the effectiveness of MI for lifestyle behavior change in cancer patients; the review concluded that MI was successful in enhancing healthy diet behaviors, such as increasing the number of servings of fruits and vegetables, including RC survivors.[54] MI was also successful in managing cancer symptoms, such as fatigue, pain, distress, and lymphedema.[55-58]

Despite the current evidence that supports the efficacy of MI-based interventions, cancer survivors continue to struggle with healthy behaviors and symptom management. Approaches that are grounded in new and existing knowledge is needed. A novel method of combining skills training and motivational strategies is the Motivation and Problem Solving (MAPS) approach. MAPS incorporate social cognitive strategies (coping and problem-solving skills) within an overarching MI framework. Its innovation lies in a design that considers all individuals regardless of their readiness for behavior change. Instead of conceptualizing behavior change as phases and stages, MAPS is novel in conceptualizing motivation for behavior change as contextual, fluid, and dynamically fluctuating in a moment to moment basis.[59] MAPS was initially developed for substance abuse and tobacco dependence, and has been demonstrated to be effective in RCTs of smoking cessation.[59]

Rationale: Recent trends suggest that rates of rectal cancer are increasing, particularly in adults ≤55 years.[13] These trends suggest that the number of younger rectal cancer survivors living with bowel dysfunction will continue to rise in years to come. Furthermore, significant QOL issues are associated with bowel symptoms after rectal cancer treatment and there is a lack of evidence-based interventions to support symptom management concurrent with achievement of dietary survivorship guidance. Current evidence suggests that cancer survivors fall short in achieving national survivorship diet guidelines.[8] These trends will continue, unless effective interventions are developed, tested, and disseminated. There is also a lack of empirical data on sex-specific differences in behavioral intervention uptake and response. Importantly, this trial will explore efficacy by sex, affording opportunities to tailor the intervention as justified by the sex-specific data collected. Finally, there is a need to develop approaches that are scalable to a larger number of cancer survivors.

Preliminary Work: As the foundation of this trial we assessed survivors' dietary and behavioral modifications for bowel control in two cohorts of rectal cancer survivors (N=919).[3] Diet modifications were common, regardless of ostomy status (40.5% ostomy, 42.7% anastomosis). Most survivors report some reduction in symptoms over 12 months. Some never reported symptom resolution (18.9% ostomy, 11.3% anastomosis). Lack of symptom resolution was associated with lower QOL ($p<.0001$). Diet modifications and meal-related behaviors were the most common strategy for bowel control (13 focus groups, N=63). A second analysis described the specific bowel symptoms that were mitigated or exacerbated by diet modifications (N=577). Fruits and vegetables were helpful in mitigating constipation, obstruction, frequency, and improving predictability. Survivors also endorsed water, fiber-rich foods, cereal, and bread as helpful for bowel symptoms. Troublesome foods included vegetables, dairy, fruits, protein, fried foods, spices/spicy food, nuts, and sweets. These foods reportedly increased diarrhea, gas, and urgency.

A single group, pre-post intervention study was initiated to evaluate the feasibility and acceptability of AIMS-RC in 10 rectal cancer survivors.[60] A total of 20 patients were eligible and were invited to participate. Of these, 3 declined participation (no time, being overwhelmed); 16 consented (average of four per month). Of these, six were lost to follow-up after consent. A process evaluation suggested that consent by the study CRA, largely independent of clinic personnel, may have contributed to higher early loss to follow-up. Of the remaining 10 participants, eight completed the sessions. One participant completed 4 sessions and declined further participation. Another completed 5 sessions, suffering a major life event that precluded further engagement. Mean age was 57 ± 2.55 years, and the majority were female (80%). Four had anastomosis, 3 had a temporary ostomy and re-anastomosis, and 2 had a permanent ostomy. Average length of the telephone sessions was approximately 30 minutes. The majority of participants found the intervention helpful and acceptable. Safety data for a control intervention are not available as the study was a single group, pre-post intervention design with no control condition. Of note, we did not experience any safety issues or concerns from patients in the pilot study.

Inclusion of Women and Minorities and Planned Enrollment Report

This study was designed to include women and minorities. We expect adequate representation of women in the trial. The anticipated accrual in the ethnicity/race and sex categories for randomized patients is shown in the table below.

DOMESTIC PLANNED ENROLLMENT REPORT					
Racial Categories	**Ethnic Categories**				**Total**
	Not Hispanic or Latino		**Hispanic or Latino**		
	Female	**Male**	**Female**	**Male**	
American Indian/ Alaska Native	0	0	0	0	0
Asian	2	1	0	0	3
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	4	2	0	0	6
White	50	31	2	1	84
More Than One Race	0	1	0	0	1
Total	56	35	2	1	94

3.0 DRUG INFORMATION

Drug information is not applicable to this study.

4.0 STAGING CRITERIA

There are no staging criteria applicable for study enrollment. The American Joint Committee on Cancer 2010 Staging System, 8th Edition for rectal cancer is listed in Appendix 18.1 as a reference only.

5.0 ELIGIBILITY CRITERIA

Each of the criteria in the following section must be met for a patient to be considered eligible for either Step 1 or Step 2 registration in OPEN. For each criterion requiring test results and dates, please record this information on the Onstudy Form and submit via Medidata Rave® (see Section

14.3). Any potential eligibility issues should be addressed to the SWOG SDMC in Seattle at 206/652-2267 or cancercontrolquestion@crab.org prior to registration.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday 4 weeks later would be considered Day 28. This allows for efficient patient scheduling without exceeding the guidelines.

Prior to Step 1 registration, patients must meet the following criteria:

5.1 Disease Related Criteria

a. Patients must have prior history of rectosigmoid colon cancer, rectal cancer, or sigmoid colon cancer. For patients with sigmoid colon cancer, there must be documentation of either partial proctectomy and/or anastomosis to the rectum

b. Patients must have a post-surgical permanent ostomy or anastomosis.

5.2 Prior/Concurrent Therapy Criteria

a. Patient's last date of treatment for rectal cancer (any surgery, chemotherapy, radiation therapy) must be at least 6 months prior to registration and not more than 24 months prior to registration.

5.3 Clinical/Laboratory Criteria

a. Anastomosis patients must have low anterior resection syndrome (LARS) score of 21-42 (minor to major symptoms) within 7 calendar days prior to registration.

b. Patient must have completed all baseline questionnaires within 7 days prior to registration. (See Section 18.5 for COVID-19-related exception.)

c. The **S1820** Patient Contact form must be completed prior to patient registration.

d. Patients must be able to read, write and speak English. Study materials and telephone calls are only available in English.

e. Patients must be ≥ 18 years of age.

f. Patients with a prior malignancy (other than as noted in Section 5.1a) or concurrent malignancy that is currently not being treated, whose natural history or treatment (in the opinion of the treating physician) does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

g. Patients who are currently undergoing treatment for another cancer will have a different symptom profile than what this study is targeting and are not eligible.

h. Patients who have been diagnosed with inflammatory bowel disease (IBD), such as ulcerative colitis or Crohn's disease, are not eligible.

Prior to Step 2 registration, patients must meet the following criteria:

5.4 Clinical/Laboratory Criteria

a. Patient must meet all eligibility criteria for Step 1.

b. Patient must have successfully completed ("pass") the run-in period, as per email notification from the University of Arizona (see Section 7.1).

c. Patient must be registered to Step 2 no more than 40 days after Step 1 registration. If Day 40 falls on a weekend or holiday, the limit may be extended to the next working day.

5.5 Regulatory Criteria

a. Patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines. Remote consent is allowed with adequate documentation, as outlined in Section 18.6.

b. As a part of the OPEN registration process (see Section 13.3 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

6.0 STRATIFICATION FACTORS

Randomization will be dynamically balanced according to sex (female vs. male) and ostomy status (permanent ostomy vs. anastomosis).

7.0 STUDY PROCEDURES

For study procedure-related questions, please contact the SWOG Statistics and Data Management Center (SDMC) in Seattle at 206/652-2267 or cancercontrolquestion@crab.org. For questions related to the study intervention, please contact the Study Chair, Virginia Sun, Ph.D., R.N. at 626/218-3122, 626/257-4717. If Dr. Sun is not available, contact the University of Arizona at aims-rc@email.arizona.edu, toll free number: 855-624-AIMS.

See Appendix 18.3 for a general overview of the study.

7.1 Communication Between Study Sites and University of Arizona:

Study site staff must be aware of and follow their institutional policies related to transmission of Protected Health Information (PHI). All study related communication between the study sites and the University of Arizona will happen through the following secure modes only:

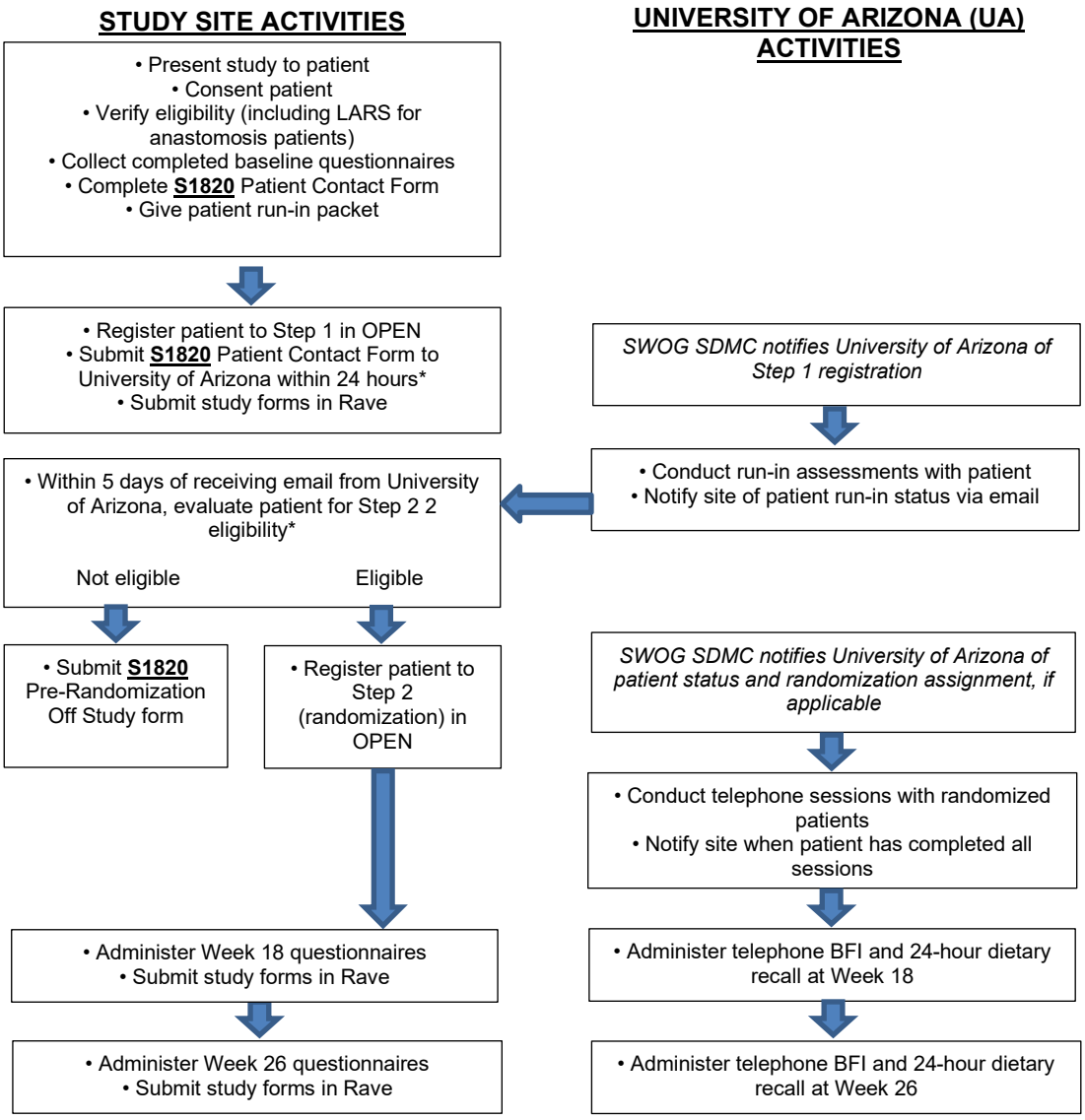
a. REDCap-generated secure form – within 24 hours of Step 1 registration, the site must complete the **S1820** Patient Contact Form to provide clinic and patient information to the University of Arizona via the following link: https://is.gd/aims_pcf. This allows the information to be sent securely and efficiently to the University of Arizona. (See Section 18.5 for COVID-19-related exception.)

b. Telephone calls using the study-specific toll-free number (855-624-AIMS) are used by the site staff to communicate questions about the coaching calls or telephone assessments to the University of Arizona.

c. Secure emails (aims-rc@email.arizona.edu) are used by the University of Arizona to communicate run-in results to site staff. It will also be used by the University of Arizona to communicate patient's refusal to continue with the coaching calls.

7.2 Study Flow Diagram

SITE AND UNIVERSITY OF ARIZONA ACTIVITIES



* (See Section 18.5 for COVID-19-related exception.)

7.3 Run-In Period

Recruitment Strategies: All eligible patients will be screened and recruited by the enrollment site staff. All patients will be inform consented by enrollment site staff. A major source of direct recruitment at enrollment sites include direct referrals from surgical, medical oncology, radiation oncology clinics. For enrollment sites with an existing survivorship clinic and/or ostomy clinics, potential patients can be recruited directly from survivorship care teams and/or ostomy nurses. Additionally, patients will be recruited through colorectal cancer advocacy groups and SWOG Cancer Research Network patient advocate efforts. Recruitment strategies will be vetted with the SWOG Cancer Research Network Recruitment and Retention Committee in accordance with established guidelines and policies.

All patients registered to Step 1 will be asked to complete the study run-in activities. The run-in period and related activities are designed to enhance patient participation in the study and enhance adherence to procedures in both randomization arms. The run-in period will range between 14-21 days after Step 1 registration.

NOTE: Sites will receive a supply of run-in packets after completing recruitment site training. If more run-in packets are needed, they can be requested by completing a form via the following link: http://j.mp/2EKjuEk. Each run-in packet includes the following:

1) BFI (versions for both anastomosis and ostomy);
2) 3-day food and symptom diary;
3) written instructions and examples for the food and symptom diary;
4) Food Amounts Booklet (FAB) for 24-hour dietary recall;
5) run-in-period calendar;
6) postage paid envelope.

Procedures for the run-in period are as follows:

1. The site must consent the patient, verify eligibility (including the LARS for anastomosis patients) and verify all baseline questionnaires are complete (see Section 9.0 and Section 15.1). Eligible patients will be registered to Step 1.

   Patients will receive a run-in packet by site staff. The sites will inform the patient to review the packet at home and to expect a telephone call from the University of Arizona for instructions on using the packet. The site will write the patient's full name on the cover page of the run-in packet, above the box for the SWOG patient ID. The University of Arizona staff member will provide the SWOG Patient ID to the patient during their first call.

2. Site register patients to Step 1. Send **S1820** Patient Contact Information form per Section 7.1a.

3. Within 48 hours of receiving the **S1820** Patient Contact Information form and receiving confirmation from the SDMC that the patient has been registered to Step 1, a trained staff member from the University of Arizona will contact the patient via telephone. The University of Arizona staff member will provide run-in instructions and support to the patient on the use of the 3-day food/symptom diary, schedule the baseline 24-hour dietary recall, and answer any additional questions the patient may have about the study or the run-in packet materials. The patient will be instructed to complete the 3-day food/symptom diary within 5 days, and mail or email (patient preference) the diary back to the University of

Arizona within 5 days of completion. The trained staff member will attempt to administer the BFI and the 24 hour dietary recall at this time or schedule a more convenient time for the patient.

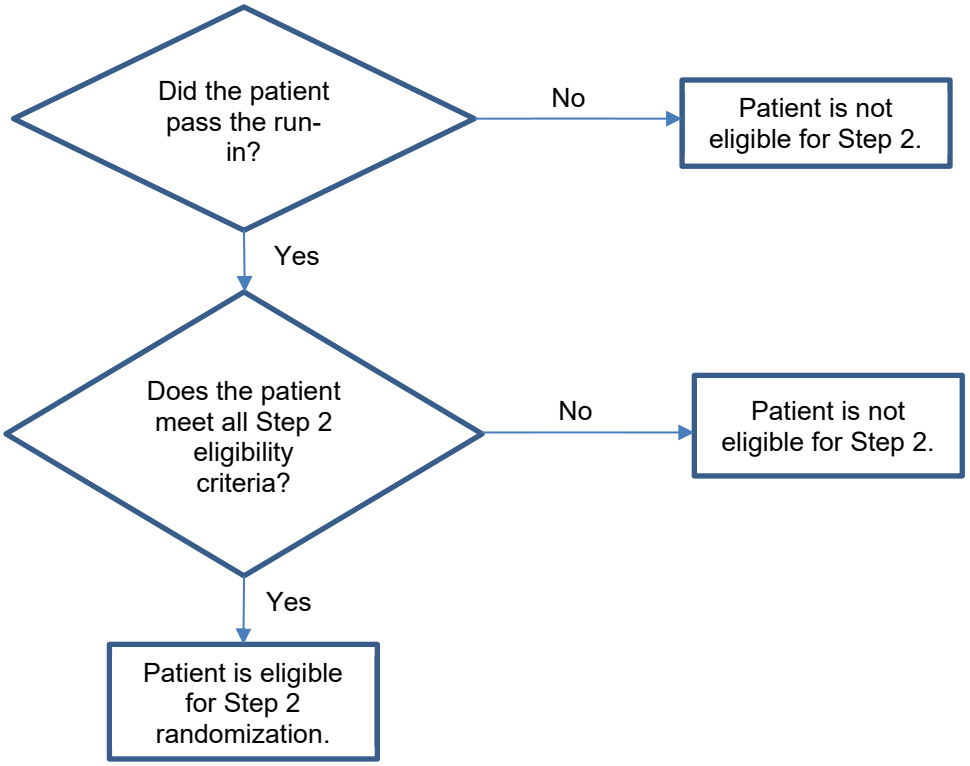
4. Trained staff at the University of Arizona will review the returned diary and evaluate successful completion according to protocol standards.

5. A trained staff member at the University of Arizona will call the patient to administer the BFI and the 24-hour dietary recall.

6. Trained staff at the University of Arizona will evaluate successful completion of the run-in period requirements ("pass" vs. "not pass") based on the criteria listed in Section 10.2.

7. The site will receive a secure email from the University of Arizona confirming the patient's run-in completion status ("pass" or "not pass"). The site assesses the patient for eligibility for Step 2 registration within 5 days after receipt of that email (Step 2 Eligibility Assessment schema). Patients eligible for Step 2 randomization must be registered within 5 days after receipt of the run-in status confirmation email. For patients who will not be registered to Step 2, the site must submit the **S1820** Pre-Randomization Off Study form per Section 14.4. (See Section 18.5 for COVID-19-related exception.)

Step 2 Eligibility Assessment



7.4 Bowel Symptom Management Assessment

To obtain data on additional bowel symptom management and assess site standard of care bowel symptom treatment for each participant, sites must complete two questions in the **S1820** Onstudy Form (completed before Step 1 registration), and at each follow-up timepoint (Week 18 and Week 26) using the **S1820** Follow-Up Form.

7.5 Arm 1: Intervention Arm (AIMS-RC)

AIMS-RC sessions are targeted to begin within 10 days of randomization and are delivered over approximately 17 weeks via 10 telephone sessions that last 15-60 minutes each. (See Table 7.5). University of Arizona staff mails an AIMS-RC resource manual to patients; this is used during the sessions to guide discussions between the coach and patients. Details on each of the sessions are provided in Appendix 18.2.

The Intervention Arm (AIMS-RC) is delivered in addition to standard of care for post-treatment rectal cancer survivors. All patients will continue to receive standard care per their physician and care team's direction at the enrollment sites. Our intent is not to replace or change standard care being provided.

The AIMS-RC sessions are centrally-administered via telephone by one trained health coach and one back-up coach (as needed only) from the University of Arizona. The health coach will only be working with patients randomized to the Intervention Arm. The health coach has experience with health coaching among cancer survivors and has been trained on rectal cancer-specific knowledge. The health coaches were jointly trained by Drs. Sun, Thomson, and Crane; their delivery of the intervention will be monitored by the Study Chair and Co-Chairs throughout the study.

a. Motivational Text/Email Messaging

Patients receive electronic communication messaging between scheduled telephone calls after Session 6. Patients have the option of receiving the messages via smartphone text messaging (SMS) and/or email messaging. The messages are specific to the AIMS-RC intervention to support participant-specific bowel symptom management goals. Health coaches use the messages to provide support, promote diet behavior change and bowel symptom management, and to sustain participant engagement. Patients will receive three messages per week after Session 6, when calls move to every other week. The messaging ends after Session 10 (end of intervention).

b. Newsletters

Patients will receive quarterly newsletters during the 17 weeks of telephone sessions. The newsletter is designed to sustain patient engagement throughout the 17 week intervention. The content will vary each month and will contain information to support diet modification skills. The health coaches will send newsletters to the participants.

Table 7.5 Arm 1: AIMS-RC Intervention Coaching Call Content

SESSION	SESSION CONTENT	PARTICIPANT ACTIVITIES
1 (Week 1)	Introductions, program overview Review food & symptom diary Wellness Plan/goals overview	Food and symptom diary Reflect on wellness plan
2 (Week 2)	Review food and symptom diary Introduction to food trials Introduction to SMART goals	Food and symptom diary Review pages in handbook
3 (Week 3)	Review food and symptom diary Implementation of food trial Set SMART goal	Review handbook as needed Work on SMART goal
4 (Week 4)	Review food and symptom diary Continuation of food trial Set SMART goal	Review handbook as needed Work on SMART goal
5 (Week 5)	Review food and symptom diary Continuation of food trial Other symptom management strategies Set SMART goal	Review handbook as needed Work on SMART goal
6 (Week 6)	Review food and symptom diary Continuation of food trial Other symptom management strategies Set SMART goal	Review handbook as needed Work on SMART goal
7 (Week 8)	Review food trial, problem solving Review survivorship recommendations Set SMART goal	Work on SMART goal ***Begin receiving text/email messages*
8 (Week 10)	Review food trial, problem solving Review survivorship recommendations Set SMART goal	Review handbook as needed Work on SMART goal ***Receive 3 text/email messages this week*
9 (Week 14)	Review food trial, problem solving Review survivorship recommendations Set SMART goal	Work on SMART goal ***Receive 3 text/email messages this week*
10 (Week 18)	Review Wellness Plan Final ref1ections on knowledge/skills	No further activities ***Receive 3 text/email messages this week*

7.6 Arm 2: Attention Control Arm

The Attention Control sessions begin within 10 days of randomization and are delivered over approximately 17 weeks via 10 telephone sessions that last about 15-60 minutes each (see Table 7.6). University of Arizona staff mails a Health Education resource manual to patients; this is used during the sessions to guide discussions between the coach and patients. Our choice of the attention control arm (Healthy Living Education) is based on our previous experience with the design of control conditions for behavioral interventions (i.e. GOG/NRG 225). The 10 topics are selected based on national survivorship guidelines on healthy living post-treatment for cancer survivors.

The Attention Control Arm (Healthy Living Education) is delivered in addition to standard of care for post-treatment rectal cancer survivors. All patients will continue to receive standard care per their physician and care team's direction at the enrollment sites. Our intent is not to replace or change standard care being provided.

The Attention Control sessions are centrally administered via telephone by one trained health coach and one back-up coach (as needed) from the University of Arizona. The health coach will only be working with patients randomized to the Attention Control Arm. The Attention Control Arm coaches are different from the Intervention Arm coaches. The health coach has experience with health coaching among cancer survivors and has been trained on rectal cancer-specific knowledge. They were jointly trained by Drs. Sun, Thomson, and Crane; their delivery of the Health Education program will be monitored by the Study Chair and Co-Chairs throughout the study.

a. Text/Email Messaging

Patients receive electronic communication messaging between scheduled telephone calls after Session 6. Patients have the option of receiving the messages via short smartphone text messaging (SMS) and/or email messaging. The messages are used for retention purposes only. They are standardized messages containing information on the 10 topics listed in Table 7.6. Patients receive three messages per week beginning with Session 6 when calls move to every other week. The messaging will end after Session 10.

b. Newsletters

Patients will receive quarterly newsletters during the 17 weeks of telephone sessions. The newsletters are designed to sustain patient engagement throughout the 17 week intervention. The content will vary each month and will contain information on the ten healthy living education topics designed for the attention control condition.

Table 7.6 Arm 2: Attention Control Call Content

Session	Session Content	Weekly Activities
Session 1 (within 10 days of randomization)	• Introductions • Program overview • ACS Diet and Activity	•
Sessions 2-6 (weekly calls)	• Sleep • Skin Care • Sun safety • Active wear • Bone health	• None
Sessions 7-8 (every other week calls)	• Food safety • Survivorship and Surveillance •	• Receive SMS/emails (3 per week)
Sessions 9-10 (monthly calls)	• Evaluating online resources • Clinical Trials • Program Wrap-Up	• Receive SMS/emails (3 per week)

7.7 Assessment Telephone Calls

a. The BFI is administered by telephone by University of Arizona research staff, independent of the study coordinator and study health coaches, during the run-in period, at week 18 and week 26. The questionnaire takes approximately 10 minutes to complete. Data will be collected in REDCap and transferred to RAVE® by University of Arizona staff trained in research data collection.

b. 24-hour dietary recalls will be collected during the run-in period, at week 18 and week 26 by trained dietary assessors at the University of Arizona, independent of the study coordinator and study health coaches. The data are collected via telephone and reflect patient recall of all food and beverages consumed in the prior 24-hour period. Data are collected using the University of Minnesota Nutrient Data System for Research (NDS-R); summary nutrient analyses will be derived from the NDS-R nutrient database.

7.8 Criteria for Removal from Protocol Intervention

a. Completion of all coaching calls.

b. Re-initiation of cancer treatments due to disease recurrence/progression.

c. The patient may withdraw from the study at any time for any reason.

d. Patient death.

7.9 Discontinuation of Protocol Intervention

a. All reasons for discontinuation of study intervention (coaching calls) must be documented in the **S1820** Off Treatment Notice.

b. The University of Arizona staff will notify the site via secure email when a patient completes or discontinues the intervention (coaching calls).

7.10 Follow-Up Period

Patients who are registered but ultimately not randomized will require no additional follow up.

All randomized patients will be followed for 26 weeks after randomization.

8.0 TOXICITIES TO BE MONITORED AND DOSE MODIFICATIONS

This is not a treatment study. No dose modification instructions or adverse event information will be collected. Symptoms will be assessed by the investigator at each study visit.

9.0 STUDY CALENDAR

REQUIRED STUDIES	Run-In Reg Step 1	Randomization Reg Step 2	Post-Randomization		
			Weeks 1 – 16 [7]	Week 18 (+/- 2 weeks)	Week 26 (+/- 2 weeks)
PATIENT QUESTIONNAIRES [9]					
S1820 Run-In Packet [1]	X				
LARS [8]	X			X	X
Quality of Life [2]	X			X	X
PROMIS Self-Efficacy for Managing Symptoms – Short Form 4a	X			X	X
S1820 Reasons for Managing Bowel Health	X			X	X
Positive and Negative Affect Scale (I-PANAS-SF)	X			X	X
S1820 Baseline Questionnaire [2]	X				
Acceptability of Intervention Measure				X	X
SITE COMPLETED FORMS [9]					
Registration Worksheet - Step 1 (not submitted)	X				
S1820 Patient Contact Form [4]	X				
Vital Status	X			X	X
S1820 Onstudy	X				
S1820 Investigator Symptom Assessment	X			X	X
S1820 Cover Sheet for Patient-Completed Questionnaires	X			X	X
S1820 Pre-Randomization Off Study	X [5]				
S1820 Registration Worksheet - Step 2 (not submitted)		X			
S1820 Follow Up				X	X
S1820 Off Treatment Notice [6]					
SITE COMPLETED ASSESSMENT					
Vital Signs 10	X			X	X
ARIZONA DIRECTED DATA COLLECTION AND PATIENT CONTACTS					
Run-in Telephone Calls	X [3]				
Assessment Telephone Calls			X	X [3]	X [3]
Arm 1: Intervention Telephone Calls			X		
Arm 2: Attention Control Telephone Calls			X		

Footnotes:

1 Site must give the patient the run-in packet, but it will not be collected by the site. It is to be completed at home by the patient, for use during run-in telephone calls.
2 Use anastomosis or ostomy version, as appropriate
3 Includes dietary recalls and BFI assessment (primary endpoint)
4 Submitted to Arizona via REDCap
5 Submit only if patient will not be registered to Step 2
6 Submit after patient completes intervention (coaching calls) or otherwise meets criteria in Section 7.8
7 All coaching calls are planned for completion by Week 18. Due to the patient's schedule, the calls may extend beyond 18 weeks.
8 For anastomosis patients only
9 All data collection time points (baseline, Week 18, Week 26) should be aligned with standard clinic visits for rectal cancer surveillance (every 3-6 months), per NCCN Clinical Guidelines. If a patient has a clinic visit that falls outside the window for data collection, sites are allowed to collect patient questionnaires by the telephone.
10 Vital signs: temperature, weight, heart rate, respiratory rate, and blood pressure. Sites should assess for these signs but are not required to collect the data and submit via Medidata RAVE®.

10.0 CRITERIA FOR EVALUATION AND ENDPOINT ANALYSIS

10.1 Primary Endpoint

The primary endpoint for this study is bowel function at 18 weeks after randomization, as measured by Memorial Sloan-Kettering Cancer Center Bowel Function Instrument (BFI) total score.

The BFI is a validated instrument that assesses bowel function in post-surgery rectal cancer patients. Total scores range from 18 to 90; higher scores indicate better bowel function. The responses are measured on a 5-point Likert scale, apart from the frequency of bowel movements item.[61, 62] There are separate versions for patients with ostomy (17 items) and anastomosis (20 items). The BFI total score was validated in an observational cohort of post-surgery rectal cancer patients, but only in those with anastomosis not ostomies.[61] The results of a recent confirmatory factor analysis of data from that cohort showed that an eight-item BFI total score that excludes frequency items is valid and reliable and can apply to people with ostomy or anastomosis.[92] Bowel function is assessed during the run-in (this is the baseline measure), and at Week 18 and Week 26 via telephone interview by the University of Arizona.

10.2 Exploratory Endpoints

a. Bowel function: Dietary, Urgency, Frequency

The BFI has three subscales: a four-item Dietary subscale (score range of 4–20), a four-item Urgency subscale (4–20), and a 6-item Frequency subscale (6–30); higher scores indicate better bowel function. The responses are measured on a 5-point Likert scale, apart from the frequency of bowel movements item.[61, 62]

b. Low Anterior Resection Syndrome (LARS)

Lower anterior resection syndrome is measured using the LARS Score, a validated 5-item instrument that evaluates severe long-term bowel dysfunction in post-surgery rectal cancer patients. [33] Scores range from 0 to 42 points. Scores are categorized into three groups: no LARS (0-20), minor LARS (21-29), and major LARS (30-42).[63-65] This instrument will only be used with anastomosis patients. LARS is assessed prior to Step 1 registration (baseline), Week 18 and Week 26.

c. Quality of Life

The City of Hope-Quality of Life-Colorectal Cancer (COH-QOL-CRC) is a validated instrument that assesses overall quality of life in post-surgery colorectal cancer patients. It evaluates overall QOL and four QOL dimensions: physical, psychological, social, and spiritual well-being. The overall score is calculated using all subscales, with a range of 0 to 10; higher scores indicate higher quality of life. Subscales scores are also scaled from 0 to 10, with higher scores indicating higher quality of life in that domain.[66] There are separate versions for patients with ostomy (43 items) and anastomosis (35 items). Quality of life is assessed prior to Step 1 registration (baseline), Week 18 and Week 26.

d. Dietary Quality

Dietary quality is based on the Healthy Eating Index 2015 (HEI-2015), which reflects the American Cancer Society dietary guidance for prevention and

survivorship (greater fruit, vegetable and grain intake, lower animal fat intake, greater fiber intake, and lower empty calorie intake that contributes to undesirable weight status). Dietary quality scores are calculated from the dietary recall data according to the HEI-2015 [67-72] and adapted for restriction in alcohol intake. Scores range from 0 to 100, with higher scores indicating higher diet quality. Dietary quality is measured during the run-in period (baseline), Week 18 and Week 26.

e. Motivation

Motivation is measured using a 10-item scale assessing motivation to change dietary behaviors in rectal cancer survivors from the **S1820** Reasons for Managing Bowel Health form. It was developed internally, based on the Reasons for Quitting (Intrinsic and Extrinsic Motivation) scale.[73] Items are scored on a 5-point Likert scale, from 0 ("Not true at all") to 4 ("Extremely true"). The score is calculated by summing all responses; higher scores indicate higher motivation. Motivation is assessed prior to Step 1 registration (baseline), and at Week 18 and Week 26.

f. Self-Efficacy

Self-efficacy is measured using the Patient-Reported Outcomes Measurement Information System (PROMIS) Self-Efficacy for Managing Symptoms – Short Form 4a, a validated instrument that measures confidence in one's ability to successfully perform specific tasks or behaviors related to self-efficacy for managing symptoms. The four items are scored on a 5-point Likert scale, from 1 ("I am not at all confident") to 5 ("I am very confident"). The overall score is calculated by summing all responses and converting to a PROMIS T-score; higher scores indicate greater self-efficacy.[74] Self-efficacy is assessed prior to Step 1 registration (baseline), Week 18 and Week 26.

g. Positive and Negative Affect

Affect is measured using the 10-item International Positive and Negative Affect Schedule Short Form (I-PANAS-SF), a validated instrument comprised of two mood scales: Positive Affect (PA) and Negative Affect (NA).[75, 76] The scores are calculated by summing the responses for positive and negative affect items separately. Scores range from 5 to 25, with higher scores on these scales indicate greater positive affect or negative affect, respectively. Affect is assessed prior to Step 1 registration (baseline), Week 18 and Week 26.

h. Feasibility, adherence, retention, and acceptability

Feasibility, adherence, retention, and acceptability are descriptive measures that will be used to characterize the successfulness of the intervention in this pilot trial and guide the study team in preparing for the Phase III trial. These measures are evaluated based on data obtained throughout the study period.

Feasibility is measured by the percentage of patients who successfully complete ("pass") the run-in period and are randomized. Successful completion is defined as meeting all five of the following measures:

1. Patient answers the telephone calls from trained staff at the University of Arizona.

2. Patient completes 24-hour dietary recall with trained staff from University of Arizona.

3. Patient completes the food and symptom diary with least 3 entries of any kind (food OR symptom) for 3 days (consecutive or not).

4. Patient returns their food and symptom diary, by mail or email, to the University of Arizona within 14 days of completion.

5. Patient completes the BFI with trained staff from University of Arizona.

Adherence measures successful completion of intervention or attention control coaching calls. Adherence is defined as completing all five of Sessions #1-5 and at least three of Sessions #6-10 within 18 weeks after randomization; patients who do not meet this criterion are classified as non-adherent.

Retention is defined by completion of follow-up assessments in Step 2, including those administered at follow-up site visits and the dietary recalls.

Acceptability is measured for all participants using the Acceptability of Intervention measure (AIM)[77]. It is scored on a 5-point Likert scale from 1 ("completely disagree") to 5 ("completely agree"). Acceptability is assessed at Week 18 and Week 26.

11.0 STATISTICAL CONSIDERATIONS

11.1 Primary Endpoint and Sample Size

The primary endpoint for this study is bowel function total score at 18 weeks after randomization, as measured by the BFI. Thirty-seven patients per arm (74 total) will provide 80% power to detect an effect size of 0.5, based on a two-sample t-test with a 1-sided alpha=0.1. The effect size is justified by data from a study of post-surgery rectal cancer patients with anastomosis, which gave a BFI SD estimate of 9.3 points[61, 62, 78], and a clinically meaningful study arm difference of approximately 4.6 points as defined by the Sloan empirical rule effect size (defined as a mean difference of approximately 8% of BFI range).[79] We assume that the 0.5 SD effect size is similarly meaningful for the validated eight-item BFI total score. [92] We will accrue additional patients to account for 7% ineligibility and 15% attrition at 6 months, for a total accrual goal of 94 randomized patients.

11.2 Primary Endpoint Analyses

The analysis of the primary endpoint will be conducted in all eligible patients randomized to the study with 18-week BFI data regardless of adherence to the coaching calls, according to a modified intention-to-treat principle. Study arm differences in BFI at 18 weeks will be assessed by a linear regression model as a function of randomization assignment, BFI baseline value, and stratification factors. Due to the low safety risks of this study, we will not perform an interim futility analysis.

11.3 Other Analyses

Given the modest size of this trial, the exploratory endpoint analyses are considered hypothesis-generating. Study arm differences in BFI at 26 weeks will be assessed by a linear regression model as a function of randomization assignment, BFI baseline value, and stratification factors. Other continuous exploratory outcomes at both 18 and 26 weeks (BFI subscales, LARS, quality of life, dietary quality, motivation, self-efficacy, and positive/negative affect) will be assessed by a repeated measures linear regression model as a function of

randomization assignment, baseline value of the outcome, stratification factors, and visit. Robust standard errors will be estimated via generalized estimating equations to adjust for correlation between repeated outcome measures. The dependent variables will be transformed to approximate normality as appropriate.

Accrual rates and feasibility will be summarized. Study arm differences in adherence and retention will be assessed by chi square tests. Study program acceptability will be compared across arms via t-test.

Although the sample size provides limited statistical power for subgroup analyses, we will explore the impact of sex by reanalyzing all outcomes according to sex as feasible. The potential for differential intervention effects according to sex on the primary endpoint will also be considered.

To assess the sensitivity of intervention effects to the potential confounding factor of site-based symptom management, additional exploratory BFI models will adjust for such treatments used by participants at baseline and during the intervention.

11.4 Accrual

Based on a survey of sites represented at the SWOG Survivorship Committee, we estimate availability of at least 600 potentially eligible patients each year. If 75% of eligible patients registered to Step 1 will be randomized to Step 2, we anticipate registering 126 patients to Step 1. Thus, we have set a target of registering 5-6 patients per month to Step 1 to allow for complete enrollment to Step 2 (randomization) in approximately 2 years.

11.5 Data and Safety Monitoring

A Data and Safety Monitoring Committee will oversee the conduct of the study. The Committee consists of four members from outside of SWOG, 3 SWOG members, 3 non-voting representatives from the National Cancer Institute (NCI), and the Group Statistician (non-voting). The members of this Committee will receive confidential reports every 6 months from the SWOG Statistics and Data Management Center, including CTCAE-graded symptom data, and will meet at the Group's bi-annual meetings as necessary. The Committee will be responsible for decisions regarding possible termination and/or early reporting of the study, based on accrual and feasibility.

12.0 DISCIPLINE REVIEW

There is no discipline review for this study.

13.0 REGISTRATION GUIDELINES

13.1 Registration Timing

For Step 1 registration: Patients must be registered within 7 days after consent and completion of baseline questionnaires. This will allow for timely completion of the run-in period at a maximum of 40 days. (See Section 18.5 for COVID-19-related exception.)

For Step 2 registration (randomization): Patients must be registered within 5 days after notification of run-in completion from the University of Arizona. (See Section 18.5 for COVID-19-related exception.)

13.2 CTEP Investigator Registration Procedures

Food and Drug Administration (FDA) regulations and National Cancer Institute (NCI) policy require all individuals contributing to NCI-sponsored trials to register and to renew their registration annually. To register, all individuals must obtain a Cancer Therapy Evaluation Program (CTEP) Identity and Access Management (IAM) account at https://ctepcore.nci.nih.gov/iam. In addition, persons with a registration type of Investigator (IVR), Non-Physician Investigator (NPIVR), or Associate Plus (AP) (i.e., clinical site staff requiring write access to OPEN, Rave, or acting as a primary site contact) must complete their annual registration using CTEP's web-based Registration and Credential Repository (RCR) at https://ctepcore.nci.nih.gov/rcr.

RCR utilizes five person registration types.

- IVR — MD, DO, or international equivalent;
- NPIVR — advanced practice providers (e.g., NP or PA) or graduate level researchers (e.g., PhD);
- AP — clinical site staff (e.g., RN or CRA) with data entry access to CTSU applications (e.g., Roster Update Management System (RUMS), OPEN, Rave,);
- Associate (A) — other clinical site staff involved in the conduct of NCI-sponsored trials; and
- Associate Basic (AB) — individuals (e.g., pharmaceutical company employees) with limited access to NCI-supported systems.

RCR requires the following registration documents:

Documentation Required	IVR	NPIVR	AP	A	AB
FDA Form 1572					

https://ctep.cancer.gov/investigatorResources/default.htm. For questions, please contact the **RCR Help Desk** by email at RCRHelpDesk@nih.gov.

a. CTSU Registration Procedures

This study is supported by the NCI Cancer Trials Support Unit (CTSU).

1. **IRB Approval:**

For CTEP and Division of Cancer Prevention (DCP) studies open to the National Clinical Trials Network (NCTN) and NCI Community Oncology Research Program (NCORP) Research Bases after March 1, 2019, all U.S.-based sites must be members of the NCI Central Institutional Review Board (NCI CIRB). In addition, U.S.-based sites must accept the NCI CIRB review to activate new studies at the site after March 1, 2019. Local IRB review will continue to be accepted for studies that are not reviewed by the CIRB, or if the study was previously open at the site under the local IRB. International sites should continue to submit Research Ethics Board (REB) approval to the CTSU Regulatory Office following country-specific regulations.

Sites participating with the NCI CIRB must submit the Study Specific Worksheet for Local Context (SSW) to the CIRB using IRBManager to indicate their intent to open the study locally. The NCI CIRB's approval of the SSW is automatically communicated to the CTSU Regulatory Office, but sites are required to contact the CTSU Regulatory Office at CTSURegPref@ctsu.coccg.org to establish site preferences for applying NCI CIRB approvals across their Signatory Network. Site preferences can be set at the network or protocol level. Questions about establishing site preferences can be addressed to the CTSU Regulatory Office by emailing the email address above or calling 1-888-651-CTSU (2878).

2. **Downloading Site Registration Documents:**

Download the site registration forms from the protocol-specific page located on the CTSU members' website. Permission to view and download this protocol and its supporting documents is restricted based on person and site roster assignment. To participate, the institution and its associated investigators and staff must be associated with the LPO or a PO on the protocol.

- Log on to the CTSU members' website (https://www.ctsu.org) using your CTEP-IAM username and password;
- Click on *Protocols* in the upper left of your screen
  - Enter the protocol number in the search field at the top of the protocol tree, or
  - Click on the By Lead Organization folder to expand, then select *[Corresponding Organization]*, and protocol number *[NCI Protocol #]*;
- Click on *Documents*, select *Site Registration*, and download and complete the forms provided. (Note: For sites under the CIRB initiative, IRB data will load automatically to the CTSU as described above.)

3. **Requirements for S1820 Site Registration:**

- IRB approval (For sites not participating via the NCI CIRB; local IRB documentation, an IRB-signed CTSU IRB Certification Form, Protocol of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption Form, or combination is accepted).
- **Study Site Staff Training Requirement:** Sites interested in participating in **S1820** will need to have at least one designated staff member complete a training session. Training must be completed

prior to enrollment of any patients. Training requirements and content for can be obtained in the following methods:

- A 2-hour training session will be held at select semi-annual meetings (April and October).
- Web-based training will be available and will require online access and speakers. To enroll in the training, sites must register for the training at https://www.swog.org/required-s1820-training .
- . A list of study staff training including name, site, contact information and date of training completion will be maintained by the Study Chair. The designated trained staff at each SWOG site will also be invited to participate in monthly study telephone conference calls, which may include training updates.
- If the designated trained staff leaves the SWOG institution, sites will need to provide access and completion of training for all new personnel participating in this protocol prior to any new enrollment of patients.

4. **Submitting Regulatory Documents:**

Submit required forms and documents to the CTSU Regulatory Office via the Regulatory Submission Portal on the CTSU website.

To access the Regulatory Submission Portal log on to the CTSU members' website → Regulatory → Regulatory Submission.

Institutions with patients waiting that are unable to use the Regulatory Submission Portal should alert the CTSU Regulatory Office immediately at 1-866-651-2878 in order to receive further instruction and support.

13.3 OPEN Registration Requirements

The Oncology Patient Enrollment Network (OPEN) is a web-based registration system available on a 24/7 basis. OPEN is integrated with CTSU regulatory and roster data and with the Lead Protocol Organization (LPOs) registration/randomization systems or Theradex Interactive Web Response System (IWRS) for retrieval of patient registration/randomization assignment. OPEN will populate the patient enrollment data in NCI's clinical data management system, Medidata Rave.

Requirements for OPEN access:

- A valid CTEP-IAM account;
- To perform enrollments or request slot reservations: Be on a LPO roster, ETCTN Corresponding roster, or PO roster with the role of Registrar. Registrars must hold a minimum of an AP registration type;
- If a Delegation of Tasks Log (DTL) is required for the study, the registrar(s) must hold the OPEN Registrar task on the DTL for the site; and
- Have an approved site registration for a protocol prior to patient enrollment.

To assign an Investigator (IVR) or Non-Physician Investigator (NPIVR) as the treating, crediting, consenting, drug shipment (IVR only), or receiving investigator for a patient transfer in OPEN, the IVR or NPIVR must list the IRB number used on the site's IRB approval on their Form FDA 1572 in RCR. If a DTL is required for the study, the IVR or NPIVR must be assigned the appropriate OPEN-related tasks on the DTL.

Prior to accessing OPEN, site staff should verify the following:

- Patient has met all eligibility criteria within the protocol stated timeframes; and
- All patients have signed an appropriate consent form and HIPAA authorization form (if applicable).

Note: The OPEN system will provide the site with a printable confirmation of registration and treatment information. Please print this confirmation for your records.

Access OPEN at https://open.ctsu.org or from the OPEN link on the CTSU members' website. Further instructional information is in the OPEN section of the CTSU website at https://www.ctsu.org or https://open.ctsu.org. For any additional questions, contact the CTSU Help Desk at 1-888-823-5923 or ctsucontact@westat.com.

13.4 Registration Procedures

a. All site staff will use OPEN to enroll patients to this study. OPEN is integrated with the CTSU Enterprise System for regulatory and roster data and, upon enrollment, initializes the patient in the Rave® database. OPEN can be accessed at https://open.ctsu.org, from the OPEN tab on the CTSU members' side of the website at https://www.ctsu.org, or from the OPEN Patient Registration link on the SWOG CRA Workbench.

b. Prior to accessing OPEN site staff should verify the following:

- All eligibility criteria have been met within the protocol stated timeframes and the affirmation of eligibility on the Registration Worksheet has been signed by the registering investigator or another investigator designate. Site staff should refer to Section 5.0 to verify eligibility.

- All patients have signed an appropriate consent form and HIPAA authorization form (if applicable).

c. The OPEN system will provide the site with a printable confirmation of registration and intervention information. Please print this confirmation for your records.

d. Further instructional information is provided on the OPEN tab on the CTSU members' side of the website at https://www.ctsu.org or at https://open.ctsu.org. For any additional questions contact the CTSU Help Desk at 888/823-5923 or ctsucontact@westat.com.

13.5 Exceptions to SWOG registration policies will not be permitted.

a. Patients must meet all eligibility requirements.

b. Institutions must be identified as approved for registration.

c. Registrations may not be cancelled.

14.0 DATA SUBMISSION SCHEDULE

14.1 Data Submission Requirement

Data must be submitted according to the protocol requirements for **ALL** patients registered, whether assigned intervention has been initiated, including patients deemed to be

ineligible. Patients for whom documentation is inadequate to determine eligibility will generally be deemed ineligible.

14.2 Master Forms

Master forms can be found on the protocol abstract page on the SWOG website (www.swog.org). The sample consent form, and the Registration Worksheet, and the **S1820** Patient Contact Form must be submitted on-line via the Web; see below for details.

14.3 Data Submission Procedures

- Data collection for this study will be done exclusively through the Medidata Rave® clinical data management system. Access to the trial in Rave® is granted through the Medidata application to all persons with the appropriate roles assigned in Regulatory Support System (RSS). To access Rave® via Medidata, you must have an active CTEP-IAM account (check at https://ctepcore.nci.nih.gov/iam) and the appropriate Rave® role (Rave® CRA, Read-Only, CRA Lab Admin, SLA, or Site Investigator) on either the LPO or participating organization roster at the enrolling site. To hold the Rave® CRA role or CRA Lab Admin role, the user must hold a minimum of an AP registration type. To hold the Rave® Site Investigator role, the individual must be registered as an NPIVR or IVR. Associates can hold read-only roles in Rave®. If the study has a DTL, individuals requiring write access to Rave® must also be assigned the appropriate Rave® tasks on the DTL.

  Upon initial site registration approval for the study in RSS, all persons with Rave® roles assigned on the appropriate roster will be sent a study invitation e-mail from Medidata. To accept the invitation, site users must log into the Select Login (https://login.Medidata.com/selectlogin) using their CTEP-IAM user name and password and click on the "accept" link in the upper right-corner of the Medidata page. Please note, site users will not be able to access the study in Rave® until all required Medidata and study specific trainings are completed. Trainings will be in the form of electronic learning (eLearning), and can be accessed by clicking on the link in the upper right pane of the Medidata screen.

  Users that have not previously activated their Medidata/Rave® account at the time of initial registration approval for the study in RSS will also receive a separate invitation from Medidata to activate their account. Account activation instructions are located on the CTSU website, Rave® tab under the Rave® resource materials (Medidata Account Activation and Study Invitation Acceptance). Additional information on Medidata/Rave® is available on the CTSU members' website under the Rave® tab at www.ctsu.org/RAVE® / or by contacting the CTSU help Desk at 888/823-5923 or by e-mail at ctsucontact@westat.com.

- You may also access Rave® via the SWOG CRA Workbench via the SWOG website (www.swog.org).

  For difficulties with the CRA Workbench, please email technicalquestion@crab.org.

- Institutions participating through the Cancer Trials Support Unit (CTSU), please refer to the CTSU Participation Table.

14.4 Data Submission Overview and Timepoints

a. WITHIN 24 HOURS AFTER STEP 1 REGISTRATION:

Submit the following:

S1820 Patient Contact Form (submit to University of Arizona via REDCap; see Section 7.1)

b. WITHIN 15 DAYS AFTER STEP 1 REGISTRATION:

Submit the following:

Vital Status Form

S1820 Onstudy Form

S1820 Investigator Symptom Assessment

Operative report used to document surgery*

Pathology report documenting initial diagnosis*

Discharge summary documenting post-operative complications*

S1820 Cover Sheet for Patient-Completed Questionnaires

LARS (anastomosis patients only)

Quality of Life (anastomosis or ostomy version)

PROMIS Self-Efficacy for Managing Symptoms – Short Form 4a

S1820 Reasons for Managing Bowel Health

Positive and Negative Affect Scale (I-PANAS-SF)

S1820 Baseline Questionnaire (anastomosis or ostomy version)

*NOTE: Upload reports via the Source Documentation: Baseline Form in Rave®

c. WITHIN 15 DAYS OF NOTIFICATION OF PATIENT RUN-IN STATUS:

Submit the following:

S1820 Pre-Randomization Off Study (if patient will not be registered to Step 2)

d. WITHIN 15 DAYS OF WEEK 18 ASSESSMENT (STEP 2):

Submit the following:

Vital Status

S1820 Follow-Up Form

S1820 Investigator Symptom Assessment

S1820 Cover Sheet for Patient-Completed Questionnaires

LARS (anastomosis patients only)

Quality of Life (anastomosis or ostomy version)

PROMIS Self-Efficacy for Managing Symptoms – Short Form 4a

S1820 Reasons for Managing Bowel Health

Positive and Negative Affect Scale (I-PANAS-SF)

Acceptability of Intervention Measure

A +/- 14-day window around the target date is permitted for administration of patient questionnaires (see Section 15.1)

NOTE: The BFI (anastomosis or ostomy version) and a telephone 24-hour dietary recall will be administered by trained University of Arizona staff at Week 18.

e. WITHIN 15 DAYS OF WEEK 26 ASSESSMENT (STEP 2):

Submit the following:

Vital Status

S1820 Follow-Up Form

S1820 Investigator Symptom Assessment

S1820 Cover Sheet for Patient-Completed Questionnaires

LARS (anastomosis patients only)

Quality of Life (anastomosis or ostomy version)

PROMIS Self-Efficacy for Managing Symptoms – Short Form 4a

S1820 Reasons for Managing Bowel Health

Positive and Negative Affect Scale (I-PANAS-SF)

Acceptability of Intervention Measure

A +/- 14-day window around the target date is permitted for administration of patient questionnaires (see Section 15.1)

NOTE: The BFI (Version A or Version O) and a telephone 24-hour dietary recall will be administered by trained University of Arizona staff at Week 26.

f. WITHIN 15 DAYS OF DISCONTINUATION OF PROTOCOL INTERVENTION (COUNSELING TELEPHONE CALLS):

Submit the following:

Vital Status and **S1820** Off Treatment Notice

g. WITHIN 30 DAYS OF KNOWLEDGE OF DEATH:

Submit the following:

Vital Status, Notice of Death, **S1820** Off Treatment Notice (if not already submitted), final **S1820** Follow-Up form, and final **S1820** Cover Sheet for Patient-Completed Questionnaires

15.0 SPECIAL INSTRUCTIONS

15.1 Administration of Questionnaires to Patients

The primary outcome of this study is a PRO and all patient evaluations are based on PROs.

a. Administration Timepoints

1. The following data will be self-reported by the patient within 7 days prior to Step 1 registration. The data will be collected by enrollment site staff:

- LARS (anastomosis patients only) – administered orally by site staff
- Quality of Life (anastomosis or ostomy version)
- PROMIS Self-Efficacy for Managing Symptoms – Short Form 4a
- **S1820** Reasons for Managing Bowel Health
- Positive and Negative Affect Scale (I-PANAS-SF)
- **S1820** Baseline Questionnaire (anastomosis or ostomy version)

Patient baseline questionnaires should be administered the same day the patient consents. Patients must be registered (Step 1) within 7 days after consent and completion of baseline questionnaires. *

* See Section 18.5 for COVID-19-related exception.

2. The following data will be self-reported by the patient at Week 18 and Week 26 (Step 2). The data will be collected by enrollment site staff:

- LARS (anastomosis patients only)
- Quality of Life (anastomosis or ostomy version)
- PROMIS Self-Efficacy for Managing Symptoms – Short Form 4a
- **S1820** Reasons for Managing Bowel Health
- Positive and Negative Affect Scale (I-PANAS-SF)
- Acceptability of Intervention Measure

The **S1820** Cover Sheet for Patient-Completed Questionnaires must be submitted for each time point.

Also see Section 14.0 for a list of questionnaires and submission times.

Note that the BFI and dietary recalls are conducted by the University of Arizona research staff; these do not require clinic engagement and are not listed here.

b. Administration Instructions

1. All questionnaires except the LARS will be self-administered; the LARS is administered orally by site staff. Questionnaires are anticipated to require 45 minutes to complete at baseline and 35 minutes at each follow-up time point. When a patient is randomized (registered to Step 2) to **S1820**, a calendar may be made by the local site with dates of upcoming patient-completed questionnaires noted and provided to the patient at their next visit. A copy of the planned questionnaire administration time points should be kept in the patient's research record.

2. Target follow-up assessment dates should be based on the date of Step 2 randomization. A window of ± 14 days is allowed for each assessment to provide more flexibility in scheduling. If the patient visit and form

completion are not within the target window, all attempts should be made to complete the next assessment within the target follow-up assessment schedule per Section 15.1b and Section 14.0.

3. In order to minimize patient burden and streamline patient visits, it is preferable for questionnaires to be given to the patient at the clinical visit immediately prior to the study time point and to have the patient complete it at home and returned at the routine clinical visit coinciding with the study time point; however, the study staff should accommodate the patient's preferences for filling out the questionnaires as described below. At time of consent, the patient should be provided with a copy of the forms for reference. If the participant chooses to complete questionnaire at home, research staff should provide a reminder (i.e., via phone call, text or email based on preference) to decrease the likelihood that the patient forgets to fill out the questionnaires.

4. The research site should provide the patient with options for completing the questionnaires after the patient has reviewed them. The patient's review may help them decide if they need information, they do not have with them at their visit or they may need assistance from a family member or caregiver. The patient may also be more comfortable completing the questionnaire(s) at home. The options for the patient are as follows:

Complete questionnaires at home. Provide the patient with questionnaires in advance and instructions to return them to the site at the clinical visit corresponding to the study time point (e.g., give patient questionnaires 2 weeks in advance at a routine clinical visit). Review the returned questionnaires for completeness at the clinical visit and clarify answers while the patient is at the clinic. If the patient does not return the completed questionnaires as scheduled, the patient should complete the questionnaires at the clinical visit or schedule a phone contact.

Partially complete the questionnaires in the clinic or practice. If due to illness, time or any reason the patient begins completing the questionnaires in the clinic or practice but then decides he/she cannot finish one or more questionnaire, make a photocopy of the incomplete questionnaire(s), give the patient the copy and keep the original in the patient's research chart. Give the patient a pre-addressed stamped envelope to return the questionnaire(s) by mail to the clinic or practice, but also schedule a phone call with the patient 1 week later. If questionnaire(s) are returned (by mail or in person) within 1 week, use the scheduled phone call to clarify any missing or unclear responses (if applicable). If questionnaire(s) are not returned, use the scheduled phone call to complete the questionnaire(s) by phone interview.

Complete questionnaires by phone interview. If the patient is unable to come in for their clinical visits or questionnaires were not completed before or at the clinical visit, questionnaires may be completed by phone interview. Phone interviews should be scheduled within 1 week of the clinical visit corresponding to the study time point. The patient should be given a copy of blank forms (or partially completed, if applicable) so that the patient may look at a copy of the questionnaires while the staff conducts the interview. The date of the telephone interview is to be noted on the **S1820** Cover Sheet for Patient-Completed Questionnaires. If the phone interview is to complete data on a partially completed, form, review all the questions with the patient, even those previously completed, in case the patient needs to change a previously answered question. If the phone interview is not completed as scheduled, reschedule to remain within the ± 14-day window for the study time point.

5. As a general reminder, review all completed questionnaires to be sure all of the questions have been answered and, when the patient is directed to mark only one response, that only one answer is marked. If the patient has marked more than one answer per question, ask which answer reflects how the patient is feeling. If the patient has skipped a question, tell the patient that a question was not answered and ask if the patient would like to answer the question. If the patient is unable to answer the question at the time of the visit, site staff are encouraged to retain the questionnaire and contact the patient by phone to obtain outstanding information. If patient does not want to answer a particular question, the study staff will enter "Not answered by the patient" in Medidata RAVE®.

6. Caregivers may assist patients with their questionnaires by administering the questionnaire orally to the patient, helping the patient find information and/or recording the patient's answers. Caregivers cannot answer for the patient. For patients who are too sick to complete the questionnaire (even with assistance from the caregiver) or who are not able to come to a clinical visit (e.g. enrolled in hospice care), the study staff will record on the **S1820** Cover Sheet for Patient-Completed Questionnaires that the patient was too sick to complete the questionnaire.

7. Patients will not receive incentives (e.g. gift cards, monetary compensation) for participation in this study.

8. **S1820** Cover Sheet for Patient-Completed Questionnaires. For each time point, the study staff completes the **S1820** Cover Sheet for Patient-Completed Questionnaires. The Cover Sheet is submitted with the set of patient completed forms at each scheduled assessment. The Cover Sheet is very important for tracking how and when the patient forms were completed. When a patient-completed form is not administered at a scheduled time point, it is important to know why the assessment did not occur; the form includes potential reasons for a patient not completing a form. All issues of noncompliance are noted on the **S1820** Cover Sheet for Patient-Completed Questionnaires.

15.2 Additional Quality Control Procedures

a. Anyone involved in the collection of quality of life data in SWOG trials should review the training program available on the SWOG website under the Members Resources/CRA Workbench tab. After logging on with CTEP-IAM credentials, click on the Training link for access to the Patient Reported Outcome Questionnaires Training Module. The training program is a narrated set of slides designed to standardize the way quality of life data is collected from patients. Questions regarding the quality of life assessments can be addressed to the SWOG Statistics and Data Management Center (206-652-2267).

b. Required Destruction of Source Documents: In accordance with SWOG Policy all source documents may be destroyed three-years post completion of the study. **Due to a specific contract with a PRO vendor for this study, destruction of the I-PANAS-SF at the three-year mark will be required.** Destruction of source documents related to this instrument is to include all patient completed source documents as well as any unused questionnaires. All such materials are to be destroyed on-site in accordance with institutional policy. Sites will be notified by memo from the SWOG Operations office of the destruction date. Destruction of source documents other than the I-PANAS-SF is at the discretion of the institution.

16.0 ETHICAL AND REGULATORY CONSIDERATIONS

The following must be observed to comply with Food and Drug Administration regulations for the conduct and monitoring of clinical investigations; they also represent sound research practice:

Informed Consent

The principles of informed consent are described by Federal Regulatory Guidelines (Federal Register Vol. 46, No. 17, January 27, 1981, part 50) and the Office for Protection from Research Risks Reports: Protection of Human Subjects (Code of Federal Regulations 45 CFR 46). They must be followed to comply with FDA regulations for the conduct and monitoring of clinical investigations.

Institutional Review

This study must be approved by an appropriate institutional review committee as defined by Federal Regulatory Guidelines (Ref. Federal Register Vol. 46, No. 17, January 27, 1981, part 56) and the Office for Protection from Research Risks Reports: Protection of Human Subjects (Code of Federal Regulations 45 CFR 46).

Monitoring

This study will be monitored by the Clinical Data Update System (CDUS) Version 3.0. Cumulative CDUS data will be submitted quarterly to CTEP by electronic means. Reports are due January 31, April 30, July 31 and October 31.

Adverse Experiences

There is no SAE Reporting for this study.

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18.0 APPENDIX

18.1 American Joint Committee on Cancer 2010 Staging System, 8th Edition

18.2 AIMS-RC Intervention Sessions

18.3 General Study Description – Overview

18.4 University of Arizona-Directed Data Collection

18.5 Allowances during COVID-19 pandemic

18.6 Procedures for Remote Consent

18.1 American Joint Committee on Cancer 2010 Staging System, 8th Edition

Primary tumor (pT)

- **TX:** primary tumor cannot be assessed
- **T0:** no evidence of primary tumor
- **Tis:** carcinoma in situ, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae)
- **T1:** tumor invades submucosa (through the muscularis mucosa but not into the muscularis propria)
- **T2:** tumor invades muscularis propria
- **T3:** tumor invades through the muscularis propria into the pericolorectal tissues
- **T4:**
  - **T4a:** tumor invades through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum)
  - **T4b:** tumor directly invades or adheres to other adjacent organs or structures

Regional lymph nodes (pN)

- **NX:** regional lymph nodes cannot be assessed
- **N0:** no regional lymph node metastasis
- **N1:** metastasis in 1 - 3 regional lymph nodes
  - **N1a:** metastasis in 1 regional lymph node
  - **N1b:** metastasis in 2 - 3 regional lymph nodes
  - **N1c:** no regional lymph nodes are positive but there are tumor deposits in the subserosa, mesentery or nonperitonealized pericolic or perirectal / mesorectal tissues
- **N2:** metastasis in 4 or more regional lymph nodes
  - **N2a:** metastasis in 4 - 6 regional lymph nodes
  - **N2b:** metastasis in 7 or more regional lymph nodes

Distant metastasis (pM)

- **M0:** no distant metastasis by imaging; no evidence of tumor in other sites or organs (this category is NOT assigned by pathologists)
- **M1:** distant metastasis
  - **M1a:** metastasis confined to 1 organ or site without peritoneal metastasis
  - **M1b:** metastasis to 2 or more sites or organs is identified without peritoneal metastasis
  - **M1c:** metastasis to the peritoneal surface is identified alone or with other site or organ metastases

18.2 AIMS-RC Intervention Sessions

AIMS-RC is based on the Motivation and Problem-Solving (MAPS) approach. The overarching theoretical rationale for MAPS is the social cognitive theory of behavior change.[80] The theory suggests that even with adequate self-efficacy, an individual may fail without motivation for change.[81] Similarly, Miller and colleagues[82] suggests that an internal motivational shift prompts an individual to decide and commit to long-term behavior change. In using the MAPS approach, skills training (coping, problem-solving) is systematically added with motivational interviewing (MI) and adjusted based on the individual's level of motivation. Three constructs are postulated to serve as potential mediators to behavior change. Motivation predicts both the decision to change, and the likelihood of long-term change. Motivation is dynamic, characterized by frequent fluctuations, and can change rapidly based on context.[76-79] The MAPS approach places specific emphasis on motivation and on appropriate therapeutic responses to common rapid fluctuations in motivation that occur throughout the change process. Agency/Self-efficacy reflects the ability to intentionally affect one's behavior.[83] Self-efficacy is a form of agency that is context and behavior-dependent; it can successfully predict behavior change. MAPS is thought to influence agency through the removal of barriers to change, problem-solving and coping skills training, and increased motivation.[84-86]

Positive/Negative Affect are two broad mood factors that are dominant in self-reported mood.[87] Positive affect (PA) reflects one's level of pleasurable experience with the environment; in contract, negative affect (NA) is a general factor of subjective distress.[87] Life stressors, such as those experienced by RC survivors, may suppress motivation, decrease self-efficacy, and adversely impact long-term behavior change.[88-91] Social cognitive theory posits that ambivalence and a weak commitment to change can increase NA, particularly during high-risk situations (such as those frequently encountered by RC survivors).[91] Reductions in NA are thought to increase motivation and agency.

The AIMS-RC intervention is also based on the Chronic Care Self-Management Model (CCM).[24-27] It provides one-on-one health coaching to support diet modifications for bowel health and healthy survivorship diet. The coaching incorporates cognitive behavioral therapy that is operationalized through motivational interviewing techniques to deliver behavior-based, dietary interventions for symptom management. The intervention supports behavior change with structured feedback, re-assessments, and goal setting.

Detailed content for each session is as follows:

a. Session 1

This first coaching call is targeted within 10 days after Step 2 randomization. The health coach will provide an introduction of the overall program, with support and coaching on use of the food and symptom diary. The health coach will provide an overview of the AIMS-RC resource manual with support reference materials and intervention content.

b. Session 2

This coaching call is targeted to be a week after Session 1. The health coach begins by introducing the structure of each telephone session. The resource manual provided in Session 1 is introduced and reviewed. Using the food and symptom diary, participants are coached to accurately document their food intake and note any symptoms associated with the foods. SMART (Specific, Measurable, Attainable, Relevant, Timely) goals for diet behavior change in relation to symptom management are identified by the patient, with support from the health coaches.

c. Sessions 3-6

Phone calls once per week: During these calls, the health coach reviews the food/symptom diary and SMART goals with the patient. The diary information is used to steer discussion on the elimination/substitution process of possible troublesome foods for bowel symptoms. The health coach and patient will review the food/symptom diary, as well as problem-solve to integrate other symptom management strategies beyond diet modifications (e.g., sitz baths, fiber supplements).

d. Sessions 7-8

Phone calls once every other week: Here, the health coach focuses on reintroducing, on a 3-day schedule, patient-identified foods. The elimination/re-introduction diet process helps participants identify the main food “culprits” that cause bowel symptoms, but also provides the skills needed to re-introduce other foods that are tolerable and beneficial. Participants are coached to use problem-solving skills for overcoming diet behavior change challenges. Evidence-based diet recommendations for cancer survivorship are also introduced.

e. Sessions 9-10

Phone calls once per month. Here, the health coach reviews progress that the participants made and the skills they have gained to re-enforce self-efficacy for long-term application of the intervention. The health coach also revisits the resource manual and reviews using SMART goals for appropriate diet behavior change.

18.3 General Study Description – Overview

See the study flow diagram in Section 7.2.

The patient will complete informed consent and baseline questionnaires during the initial study visit. After completion of baseline questionnaires, study site staff will provide patients with a Run-In Packet. The site will register eligible patients to Step 1 within 7 days after consent and completion of baseline questionnaires. The site will submit the **S1820** Patient Contact Form within 24 hours of Step 1 registration. (See Section 18.5 for COVID-19-related exceptions.)

All run-in activities will be performed by the University of Arizona. After a patient has completed the run-in period, the University of Arizona will notify the site via email whether the patient successfully completed the run-in requirements ("pass" or "not pass"). Within 5 days after receipt of that email, the site will evaluate Step 2 eligibility and either register the eligible patient to Step 2 or submit the **S1820** Pre-Randomization Off Study form for the ineligible patient. There is no additional patient consent required for Step 2 registration. (See Section 18.5 for COVID-19-related exceptions.)

The SWOG SDMC will notify the University of Arizona as to which arm the patient has been randomized or if they will not be randomized. For randomized patients, the University of Arizona will administer the appropriate telephone coaching sessions. The site will administer patient questionnaires and submit follow-up data at 18 and 26 weeks after Step 2 registration. Patient follow-up is complete after 26 weeks.

18.4 University of Arizona-Directed Data Collection

BFI Data Collection
In addition to their experience in administering instruments via telephone, another advantage of having University of Arizona administer the BFI is that the assessor will be blinded to study arm. The consistent telephone administration, with blinding of the assessor, will reduce potential confounding bias for the BFI, which is the primary endpoint of the trial.

24-Hour Dietary Recall Methodology
The 24-hour dietary recalls consist of three randomly assigned days per participant at each measurement time point including. Interviewers record all food and beverage consumption over a 24-hour period using the USDA multi-pass method with the University of Minnesota Nutrition Data System-Research Version (NDS-R). The University of Minnesota Nutrition Data System-Research Version (NDS-R) is a microcomputer-based system for collection and analysis of dietary data that prompts the user to describe food intake at the level of detail such as food source, processing method, fat and salt used in preparation, and ingredients that contribute to fat and sodium intake. The nutrient database contains over 18,000 foods, 8,000 brand-name products, and many ethnic foods. Values are available for 165 nutrients and nutrient ratios. The database is derived from USDA, food manufacturers, foreign food composition tables, and scientific literature. The recall documents type of food/beverages, recipes and preparation, and estimated portion sizes. The recall procedures include reviewing data entry for duplicate foods as well as single food items that exceed specified calorie, fat or weight amounts.

Other Data Collection
Data collection for certain exploratory endpoints is performed by University of Arizona staff during the run-in period and in conjunction with the coaching calls. The items used to assess successful completion of the run-in activities are collected by the University of Arizona and sent to the study sites and the SDMC (see Section 7.3). The coaching call completion rate (adherence) and dietary recall completion (retention) are collected by the University of Arizona and sent to the SDMC.

18.5 Allowances during COVID-19 pandemic

In order to provide participating sites flexibility during the COVID-19 pandemic, some of the timeframes for study procedures are extended. Use of an extended window does NOT need to be reported as a deviation. However, the rationale for utilization of the extended window must be carefully documented in the patient chart as resulting from the COVID-19 pandemic.

Step 1 Registration:

- The allowable window between consent/completion of baseline QOL forms and Step 1 registration is extended to 15 days.
- The allowable window between Step 1 registration and submission of the **S1820** Patient Contact Form to the University of Arizona is extended to 72 hours.

Step 2 Registration:

- The allowable window between receipt of notification of run-in completion from the University of Arizona and Step 2 Registration is extended to 10 days.

Note: The window between Step 1 Registration and Step 2 Registration remains at 40 days.

18.6 Procedures for Remote Consent

Remote informed consent by telephone is allowed to reduce burden. As is preferred by each individual institution, participants may be contacted and recruited in a combination of ways. These include in-person clinic visits or remote recruitment via telephone by the study coordinator to discuss the study, email and/or mailed letters, using clinically available contact information. Sites should follow the NCI's CIRB Remote Consenting Procedures outlined in Section 18.6 to implement a remote consenting process. If a participant is consented remotely, study coordinators must wait to receive the participant's signed consent form (*e.g.*, via mail, fax or email) prior to conducting any research activities, including questionnaire administration and step 1 registration.

1. The participant receives a copy of the informed consent document (*e.g.,* via mail, fax, or email) in advance of discussion regarding participation in **S1820**. If mailed, two copies must be mailed so the participant is able to retain a copy for reference when their signed document is returned to the site and they are waiting to receive the final copy with all necessary signatures back from the site. If postal mail is used, a pre-paid, self-addressed envelope must also be provided to the participant to mail the signed consent form back to the investigator.

2. The Responsible Investigator/designee discusses **S1820** with the potential participant either via telephone or video conferencing. The Responsible Investigator must have the same consent discussion via telephone/video conferencing that would occur with the participant during an in-person meeting.

3. The Responsible Investigator/ designee must also implement a method to ensure the identity of the participant, by verification of state identification or other identifying documents or use of personal questions or visual methods.

4. A witness must be present during the telephone/videoconferencing consent process. There are no restrictions on who can serve as a witness and the witness does not need to be impartial. The witness must be able to hear both sides of the conversation (*e.g.,* speaker phone, conference line). Requirements for social distancing due to Covid-19 or other extenuating circumstances, may dictate that the witness may be in a different location than the potential participant and/or the Responsible Investigator/designee obtaining consent. Any arrangement is acceptable provided that the witness can listen to both parties in the informed consent discussion.

5. If the potential participant agrees to participation, they sign the consent form and return it to the investigator via mail, fax, or email.

6. Once the research team receives the signed informed consent document(s) from the participant, the Responsible Investigator who conducted the consent process must also sign and date the document using the current date.

7. Under the signature line, the Responsible Investigator or designee must document whether consent was obtained over the telephone or video conferencing, the date of the telephone/video conference, and the date the signed consent was received. For example, "Discussed with [participant] via [telephone or videoconferencing] on [insert date] and received signed consent form on [insert date]." Include a brief reason for performing the informed consent discussion over the telephone/videoconferencing.

8. If the site has an informed consent policy that requires the witness to sign the consent document, the witness signs the informed consent. If the site does not have an informed consent policy that requires the signature of the witness on the consent document, then the name of the witness along with the date of the original

consenting phone call is recorded in the research records to document the participation of the witness.

9. The date the Responsible Investigator or designee signs the informed consent document, not the date the consent discussion with the participant took place, is the official date of informed consent for the participant on the trial.

10. The final informed consent document must be filed in the designated investigator/site regulatory file location. A copy of the final informed consent document, signed by the participant, the investigator, and the witness (if applicable), must be sent back to the participant via email/scan, fax, or postal mail.

11. No research activities related to the study can begin until all steps of the informed consent process are complete.

For sites using remote consent that allow the use of electronic signature (eSignature), submit the information on the Study Specific Worksheet (SSW) or the Signatory Institution Worksheet (SIW) using IRBManager before collecting the eSignature. See Section 13.3a.

Whether consent is obtained in-person or via remote consent, the Responsible Investigator or designee will make clear during the consent process that participation is voluntary and will not adversely affect the participant's medical care.