Cover Page

Official Title of Study: A Pilot Feasibility Trial of a Tailored Intervention to Improve Adherence in Adolescents and Young Adults with Cancer

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Protocol Title: A tailored intervention to improve adherence in adolescents and young adults with cancer

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Revision History

#	Date	Summary of Changes	Consent Change?
1	December 2022	Updates to measures (resulted in updates to consent), study timeline, and patient-facing materials and clarifications to study procedures (i.e., risk protection procedures updated to be relevant to multi-site study) following the receipt of the award in December 2022.	Yes

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1.0 STUDY SUMMARY

Study Title	A tailored intervention to improve adherence in adolescents and young adults with cancer
Study Design	Randomized feasibility pilot trial
Primary Objective	To conduct a feasibility pilot RCT of a tailored adherence-promotion intervention as compared to uniform standard of care including 40 AYAs with cancer (n = 20 per arm).
Secondary Objective(s)	To explore group differences in improvements in electronically-monitored medication adherence to inform the next phases of intervention development and testing.
Research Intervention(s)/ Investigational Agent(s)	Tailored adherence-promotion intervention
IND/IDE #	Not Applicable
Study Population	Adolescents and Young Adults with Cancer
Sample Size	40
Study Duration for individual participants	Approximately 17 weeks
Study Specific Abbreviations/ Definitions	AYA (Adolescent and Young Adult)

2.0 OBJECTIVES

The purpose of this study is to conduct a pilot feasibility trial of a tailored adherence-promotion intervention as compared to uniform standard of care. This goal will be achieved via the following aims:

Aim 1: Conduct a feasibility pilot RCT of a tailored adherence-promotion intervention as compared to uniform standard of care including 40 AYAs with cancer (*n* = 20 per arm).
Hypothesis 1a: The intervention will meet enrollment, retention, fidelity, and data completion feasibility criteria.
Hypothesis 1b: AYAs will rate the intervention as easy to use and acceptable.

Exploratory Aim 2: To explore group differences in improvements in electronically-monitored medication adherence to inform the next phases of intervention development and testing.

3.0 BACKGROUND AND SIGNIFICANCE

3.1 Prior Experience and Gaps in Current Knowledge

Clinical care and treatment advances in the last 40 years have increased survival rates by more than 30% for children under 15 with cancer.[1] Progress for adolescents and young adults (AYAs) with the same diagnoses, however, has been far slower, and 5-year survival rates for 20 of the 34 most common AYA cancers have not improved since the 1990s.[2] Even in diseases where survival rates have improved (e.g., acute lymphoblastic leukemia), AYAs demonstrate particularly poor outcomes and have mortality rates well above those of children < 15 years.[3] As a result, cancer remains the leading cause of disease-related death among AYAs ages 15-24 years in high income countries[4] and accounts for 5% of the AYA lives lost in the United States each year.[5]

A likely contributor to the poor outcomes faced by AYAs with cancer is non-adherence to the oral chemotherapy and/or prophylactic (e.g., antibiotic) medications included in cancer treatment protocols. For patients with leukemia prescribed oral chemotherapy, non-adherence, or medication-taking behavior that deviates from the prescribed treatment protocol,[6] is associated with a 2.5x greater likelihood of relapse[7] and a 1.6x greater likelihood of death.[8] In addition, AYAs with cancer who are non-adherent to antibiotics are 4.6x more likely to die[9] than adherent AYAs. Our recent systematic review indicated that 21-60% of AYAs with cancer are non-adherent to protocol medications.[10] This means that thousands of AYAs with cancer are currently at risk for devastating consequences which could be prevented.[11] In response, professional organizations have endorsed adherence promotion as a standard of pediatric[12] and AYA[4,13] cancer care.

The factors that may lead AYAs to miss medication doses and thus should be targeted in adherence-promotion efforts can be conceptualized as barriers to adherence. According to the Theoretical Domains Framework, barriers are driven by an individual's capabilities, opportunities, and motivation.[14,15] Capabilities, opportunities, and motivations change throughout the lifespan and when these domains change, so do our barriers. For example, neurodevelopmental changes beginning at age 15 and stabilizing after age 24 coupled with the developmental transitions of this period (i.e., independent living) mean that AYAs ages 15-24 years display a distinct pattern of capabilities,[16-18] opportunities,[19] and motivation[16,20,21] and as a result, different barriers to adherence than younger children[22,23] or older adults.[24] Because barriers change with age, improving adherence is likely to require a developmentally-specific approach. While the National Cancer Institute defines the AYA period as 15-39 years,[25] a more conservative definition of 15-24 years represents an ideal target population due to the similarities in barriers experienced by AYAs 15-24 years.[24]

Fig 1. Theoretical Model

Data from 3 studies[26] and 1 systematic review[10] led by Dr. McGrady (PI), suggest that the capabilities, opportunities, and motivations of AYAs ages 15-24 years with cancer result in 18 primary barriers (Fig 1). One of the challenges to improving adherence is that overcoming each of these barriers requires a distinct set of strategies, or behavior change techniques (BCTs).[27,28,29] For example, improving adherence in an AYA who forgets her medication (barrier) may require prompts or cues (BCT).[30] Alternatively, an AYA who feels his regimen gets in the way of other activities (barrier) may benefit from problem-solving (BCT).[31] Guided by this theory, we propose that improving adherence requires that each AYA receives BCTs matched to their top barriers.

Ensuring AYAs with cancer receive BCTs matched to their barriers is not as simple as creating another "one-size-fits-all" intervention. This is because, in our preliminary studies, 81% of AYAs with cancer endorsed different barriers than any other AYA. The vast majority of AYAs, thus, likely need a unique set of BCTs to overcome their barriers and improve their adherence. Guided by these data and theory,[14,28,31,32] we hypothesize that we can improve on the effects of interventions to date by testing a rigorous tailored adherence-promotion intervention in which each AYA receives BCTs matched to their top barriers. The scientific premise of this approach is supported by an RCT of an adherence-promotion intervention with 4,078 adults with diabetes, hyperlipidemia, and hypertension. Adults who received BCTs tailored to their top barriers exhibited greater improvements in adherence than adults in the control group.[33] Post-hoc analyses of data from the mobile app trial suggest this approach also holds promise for AYA oncology as the 3 of 23 AYAs whose adherence *did* improve were more likely than their peers to endorse forgetting as a barrier.[24] The AYAs who improved, thus, happened to receive BCTs (reminders & tracking) targeting their specific barrier.

3.2 Preliminary Data Informing the Proposed Study Design

With support of her NCI K07, Dr. McGrady is conducting a longitudinal observational study to identify predictors of medication adherence among AYAs (15-24 years) with cancer. Defining adherence as ≥ 95% of prescribed doses taken, the threshold associated with a lower risk of relapse in acute lymphoblastic leukemia,[7] our preliminary data indicate that 71% of AYAs are non-adherent per electronic monitoring data. This rate of non-adherence may be due to barriers faced by AYAs. At baseline, 90% of AYAs reported ≥ 1 barrier and a greater number of barriers was associated with lower electronically monitored (r = -.49, p = .01) and self-reported (r = -.41, p = .01) adherence. These data suggest that targeting barriers has the potential to improve adherence. Doing so, however, is complicated by the individual variability inherent in barriers. Of the 54 AYAs reporting barriers, only 10 reported the same barriers. The other 81% reported a different set of barriers than any of their peers. In addition, only 26% endorsed forgetting and/or lack of knowledge, the barriers targeted by previous interventions.[24,34,35] Because most AYAs have unique barriers, it is not surprising that "one-size-fits-all" interventions targeting barriers endorsed by only some AYAs demonstrate limited efficacy.[24,34,35] Instead, our data suggest that delivering BCTs tailored to an AYA's top barriers may improve adherence.

Additionally, with support of her NCI K07, Dr. McGrady conducted qualitative interviews with 15 AYAs with cancer to understand their intervention preferences. AYAs were enthusiastic about a tailored intervention, with one noting "there are just so many different reasons that somebody might not be receiving their medication." AYAs, even those living with their parents, reported taking primary responsibility for adherence and wanted a say in if/how their parents or other support person were involved in the intervention. To align with these preferences, the intervention is patient-focused (versus family-based) and AYAs will be invited to engage a parent or other support person to implement BCTs as appropriate (e.g., asking fiancé to remind them to implement the BCT "prompts/cues"). We also matched the tailored adherence-promotion intervention with AYA preferences for "convenient" "every other week" sessions over "a few months" by designing an 8 week intervention that includes 4 bi-weekly videoconferencing sessions, with 4 text check-ins occurring on alternating weeks.

3.3 Scientific and Clinical Significance of the Proposed Study

If feasible and efficacious, this intervention has the potential to transform AYA oncology clinical care across the country. Creating an intervention with standardized modules and a standardized tailoring algorithm means that hospitals could adapt the delivery to fit their institutional resources without compromising "active" components. For example, Hospital A may decide that psychologists are best-suited to deliver all modules of BCTs while Hospital B may have psychologists deliver modules of BCTs for some barriers but engage their social work team to deliver modules of BCTs for others (e.g., cost). The flexibility inherent in this design can facilitate implementation without negatively impacting rigor and allows for adaption to other AYA populations.[36]

4.0 STUDY ENDPOINTS

4.1 Primary and Secondary Study Endpoints

Hypothesis 1A: The primary endpoint for this study is the enrollment rate. Secondary outcomes for Hypothesis 1A include retention rate, assessment completion, and intervention fidelity as detailed in Table 1.

Table 1. Hypothesis 1A Measures

Domain	Measure	Outcome	Criteria
Feasibility (Hyp 1a)	**Enrollment Rate**	Percentage of eligible approached AYAs who enroll	≥ 70%
	Retention Rate	Percentage of AYAs completing all study procedures	≥ 80%[36]
	Assessment Completion	Percentage of AYAs with complete data	≥ 80%[36]
	Intervention Fidelity: Contact[37]	Percentage of AYAs who received 4 intervention sessions (planned number of sessions)	≥ 80%[38]
	Intervention Fidelity: Length[37]	Percentage of AYAs whose average session length was between 30 and 45 minutes (planned session duration)	≥ 80%[38]
	Intervention Fidelity: Duration[37]	Percentage of AYAs who completed the intervention sessions within an 8-10 week timeframe (8 weeks = planned duration; 10 weeks = upper limit set to include a 2 week buffer to provide flexibility for patients who may be hospitalized and/or experience major complications during the intervention period)	≥ 80%[38]
	Intervention Fidelity: Content[37]	Percentage of AYAs receiving the BCTs matched to their barriers per protocol (assessed via listening to audio recordings of sessions and coding delivered BCTs using a fidelity rating checklist)	≥ 80%[38]

Hypothesis 1B: Outcomes for Hypothesis 1B include usability and acceptability as detailed in Table 2. Open-ended questions regarding usability and acceptability will also be asked to inform potential refinements.

Table 2. Hypothesis 1B Measures

Domain	Measure	Outcome	Criteria
Usability (Hyp 1b)	**System Usability Scale (SUS)**[39]	Mean score of AYAs randomized to treatment group	M ≥ 68[39]
	System Usability Scale Adjective Rating[40]	Mean score of AYAs randomized to treatment group	M ≥ 4[40]
Acceptability (Hyp 1b)	**Acceptability &Adherence Scale**[41]	Mean score of AYAs randomized to treatment group	M ≥ 28[42]
Refinements	**3 Open-Ended Questions** (1. What did you like best about the program?; 2. What could we change to make the program better?; 3. Anything else we should think about as we work to make this program better?)		N/A

Exploratory Aim 2: The outcome for Exploratory Aim 2 is electronically-monitored medication adherence.

4.2 Primary and Secondary Safety Endpoints

No safety endpoints are included.

5.0 STUDY INTERVENTION/INVESTIGATIONAL AGENT

5.1 Description

The intervention being tested is a tailored adherence-promotion intervention.

Intervention Dose and Duration: AYAs in the intervention group will participate in 4 bi-weekly intervention sessions (1 every other week over 8 weeks). These sessions are estimated to last 30-45 minutes each. On alternating weeks, AYAs will receive a text message check-in from the interventionist. An 8 week duration was selected to mirror the amount of time over which adherence naturally declines, is short enough to be completed during the prescribed oral medication regimen of most AYAs with cancer, and is consistent with the "couple of months" duration preferred by AYAs in our preliminary studies.

Intervention Session Content: During the intervention sessions, each AYA will receive modules of behavior change techniques (BCTs) tailored to their individual barriers. Intervention content (BCTs) will be tailored to each AYA's barriers via a 4-step tailoring process. First, AYAs randomized to the intervention condition will complete a barriers tool. Second, the barriers tool will generate a list of the AYA's top 3 barriers, which will be sent to the interventionist. Third, in the first session, the interventionist will review the list and engage in shared decision-making with the AYA to determine which of the 3 barriers the AYA would like to target. Fourth, following a standardized tailoring algorithm (see Fig 2), the interventionist will select and deliver the module of BCTs matched to this barrier during Sessions 1 and 2. As barriers are likely to change over time, the AYA will complete the barriers tool a second time prior to Session 3 and the AYA and interventionist will again engage in shared decision-making to choose the barrier to be targeted in Sessions 3 and 4.

Figure 2 summarizes the tailoring algorithm and content. When the barrier in column 1 is selected as the intervention target, the interventionist will deliver the BCT(s) in column 2. Each BCT represents a component of a health behavior change intervention that has been standardized via expert consensus and over 10 years of empirical research as published in the Theory and Techniques Tool (https://theoryandtechniquetool.humanbehaviourchange.org/tool). The study protocol will include the full definition of each BCT per the Theory and Techniques Tool and include examples relevant to AYA cancer to help guide the interventionist (e.g., "Prompts/cues" = "Introduce or define environmental or social stimulus with the purpose of prompting or cueing behavior. The prompt or cue would normally occur at the time or place of performance. Examples: Help the AYA to set an alarm for when their doses are due").

	Barriers	BCTs
Capabilities	Knowledge of how/when to take it	Instruction on how to perform behavior
	Forget to take it	Prompts/cues; Problem-solving; Associative learning (e.g., pairing w activity)
	Don't realize when I run out	Problem-solving; Prompts/cues; Conserving mental resources (e.g. auto refills)
	Hard to time with meals	Instruction on how to perform behavior; Problem-solving
	Too many pills to take	Problem-solving
	Not home when doses due	Problem-solving; Restructure environment; Prompts/cues
Opportunities	Don't like taking in front of others	Restructure social environment; Info about others' approval
	Don't like the taste	Adding objects to environment (e.g., gel capsule, food to mask taste)
	Hard to swallow	Graded tasks; Behavioral practice/rehearsal; Verbal persuasion
	Don't like the side effects	Instruction on how to perform behavior (discuss with team)
	Hard to get refills	Prompts/cues; Practical social support; Restructure environment
	Can't afford it	Practical social support (e.g., consult with social worker)
	Don't get enough help	Practical social support; Social reward
Motivation	Tired of taking medication	Pros and cons; Goal setting; Incentives/rewards
	Don't feel like taking it	Pros and cons; Goal setting; Incentives/rewards
	It's inconvenient	Focus on past successes; Problem-solving
	Gets in the way of activities	Focus on past successes; Problem-solving
	Doesn't matter if I take it	Information about consequences; Pros and cons; Incentives/rewards

Fig 2. Barriers and Behavior Change Techniques (BCTs)

Text Check-Ins: On alternating weeks, the interventionist will check-in with the AYA via a text message including the AYA's target barrier, BCTs, and adherence calendar. The AYA may respond to obtain additional support on how to implement the BCTs if desired.

6.0 PROCEDURES INVOLVED

6.1 Study Design

This is a multisite feasibility pilot RCT that includes 4 sets of study procedures: 1) electronic monitoring of medication adherence; 2) intervention or control group participation; 3) self-report measure completion; and 4) an electronic medical record review (Fig. 3). Reminders (and thank you messages) for completing study procedures may be provided via text, email, and/or phone as preferred by the AYA.

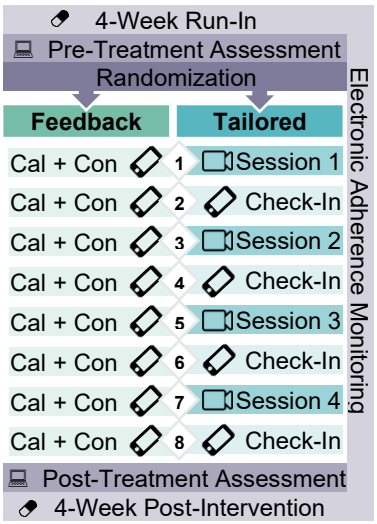

Fig 3. RCT Procedures
Cal + Con = Adherence calendar + contact information for medical team

6.2 Study Procedures

6.2.a. Electronic Monitoring of Medication Adherence. In this study, medication adherence will be monitored using an electronic pill bottle. The electronic pill bottle includes a computer chip in the cap that records a date- and time-stamp of each time the bottle is opened, our proxy for medication-taking behavior.

To be eligible for the study, AYAs must demonstrate < 95% adherence and use the electronic monitor without difficulty. A 4-week run-in period is included to assess these eligibility criteria. After an AYA is enrolled, they will receive an electronic monitoring device and be asked to store their eligible oral medication in this device for the duration of their participation in the study. AYAs who demonstrate ≥ 95% adherence during the 4-week run-in period and/or who have difficulty using the electronic monitoring device will be informed that they do not meet the eligibility criteria and their study participation will be ended at that point. AYAs with < 95% run-in adherence will continue with study procedures per Fig. 3 and be asked to continue to use the electronic adherence monitoring device until the end of the 4-week post-intervention period (for 17 total weeks).

Electronic Monitoring Device Distribution: AYAs will either be provided an electronic monitoring device at their recruitment visit or mailed an electronic monitoring device and provided instructions by a member of the CCHMC research team.

For participants currently enrolled in an ongoing clinical initiative including electronic adherence monitoring, adherence data will be downloaded from the clinic-provided device. Doing so will ensure that participants are only provided with one electronic monitor.

Electronic Monitoring Device Return: Participants will be asked to return their adherence electronic monitoring device at the conclusion of their participation in the study. In instances where participants are unable to bring their adherence electronic monitoring device to a study visit, a pre-paid addressed envelope will be provided so participants can mail their devices to the study team.

Cellular Phones: AYAs will be asked to download a mobile application to their personal cellular phone that they will use to upload data from their electronic monitoring device to a secure Cloud-based application (CertiScan® Cloud). If AYAs would not be able to participate in the study because they do not have access to an appropriate mobile phone (phone with NFC capabilities) and/or a data package, they will be given a CCHMC-provided cellular phone to use for the duration of the study.

6.2.b. Intervention or Control Group Participation. AYAs randomized to the intervention group (tailored adherence-promotion intervention, termed “Tailored Program”) will participate in 4 bi-weekly sessions with an interventionist and receive text check-ins on alternating weeks (see Section 5). AYAs randomized to the control group (uniform standard of care condition, termed “Feedback Program”) will receive a weekly text message

from the interventionist including a calendar depicting their adherence and a medical team contact should they desire support (Fig 3).

Intervention sessions will be delivered via a HIPAA-compliant videoconferencing system (Zoom for Healthcare) or phone should technical difficulties arise with Zoom. All intervention sessions will be recorded.

6.2.c. Self-Report Measure Completion. AYAs will complete pre- and post-treatment assessments remotely via REDCap, a secure, HIPAA-compliant web-based platform. Prior to use, the PI will test the online measures. The consent forms signed by all participants will detail the use of online measures. The self-report measures are summarized in Table 3. Published and validated versions of all measures will be used unless noted in Table 3.

Table 3. Self-Report Measures

Domain	Measures Completed by AYAs, Psychometrics	Pre-	Post-
Usability	**System Usability Scale (SUS)**[39] 10-item rating of usability, α=.91[39]		X
	System Usability Scale Adjective Rating[40] 1-item rating of user-friendliness, r=.82 w SUS[40]		X
Acceptability	**Acceptability &Adherence Scale**[41] 7-item rating of psychological treatment acceptability (adapted from the Treatment Acceptability & Adherence Scale,α=.88[41,42])		X
Refinements	**3 Open-Ended Questions regarding potential refinements** (see Table 2)		X
	Consultation and Relational Empathy (CARE) Measure 10-item rating of rapport and empathy, α=.93[50]		X
Preliminary Efficacy	**Barriers Measure** 18-item measure of barriers to adherence	X	X
	Medical Adherence Measure[43] 2-item report of N missed and late doses, r=.4 with monitor[44]	X	X
Control Covariates	**Demographics** – Self-reported Demographics	X	
	Parental Involvement – Allocation of Treatment Responsibility, α=.85[45]	X	
	Emotional Distress – Pediatric (ages 15-17) or Adult (ages 18-24) PROMIS Depression and PROMIS Anxiety Short Forms, α=.84-86.[46,47]	X	

6.2.d. Chart Review. Medical diagnoses, date of cancer diagnosis, current medical regimen, cancer status (e.g., relapse), cancer-related complications, and health care utilization will be obtained via medical chart review. Trained study staff will conduct chart reviews.

6.3 Blinding. Participants will be blinded to the study hypotheses in that they will not be told that we expect the "Tailored Program" (intervention condition) to result in greater improvements in adherence (Exploratory Aim 2) than the "Feedback Program" (control condition). Dr. McGrady (PI) will not be blinded as she will be providing clinical supervision to the study interventionist.

6.4 Procedures Conducted by Collaborating Site Staff. Study staff at collaborating sites will have 3 main responsibilities: 1) recruiting patients per the procedures described in Section 13; 2) conducting weekly medical record reviews to provide updates to the patient's medical regimen (to allow for adherence data to be adjusted according to medication holds, etc.); and 3) assisting with a medical record review at the end of the study to obtain the information detailed in 6.2.d. Once a participant is recruited, their information will be securely transferred to CCHMC (as per 13.1) and CCHMC staff will oversee all other procedures as detailed in 6.5.

6.5 Procedures Conducted by CCHMC Staff. CCHMC staff will be responsible for enrolling CCHMC patients. CCHMC staff will also be responsible for: 1) assigning participants to the intervention or control condition; 2) delivering the intervention or control condition (i.e., distributing electronic adherence monitoring devices and cellular phones as necessary); 3) providing supervision to the coach delivering the intervention or control condition; 4) tracking participants' progress; 5) overseeing adherence data collection and synthesis with data from weekly electronic medical record reviews; 6) administering and overseeing pre- and post-treatment

assessment visits; 7) managing all study data; 8) managing participant compensation; and 9) conducting data analyses. Each of these tasks will be detailed in our Standard Operating Procedures.

7.0 DATA AND SPECIMEN BANKING

7.1 Location of Data Storage. Data will be retained from this pilot feasibility study to inform the development and refinement of future versions of the adherence intervention. The Excel database containing identifiable information, connecting participants to their study ID number (see Section 17.3), will be deleted at the closure of the study. Databases including de-identified adherence (from CertiScan® cloud) and questionnaire (from REDCap) data will be stored in a password-protected electronic file on the CCHMC hard drive for 10 years after the study has been closed. Data from this study will be used to inform an R01 or U-series multi-site trial of an adherence promotion intervention. A 10 year period was selected to ensure that data informing the larger study (data from this study) are available to inform modifications throughout the potential R01 or U-award period. After the study has been closed, only the PI will have access to the data.

7.2 Procedures to Release Data.
De-identified data may be shared with other individuals according to procedures outlined in the Data Sharing Agreement linked to this protocol.

8.0 SHARING OF RESULTS WITH SUBJECTS

AYAs will receive feedback on their adherence as part of this study. If a provider suspects non-adherence and believes that reviewing adherence data in our study could help to inform their clinical care, we will share the relevant data with the participant's provider. Participants will consent to this data sharing during the consent process. The AYA may also share these data with their care providers if they choose. No other individual subject results will be shared with participants or others not involved in the conduct of this study.

A summary of study results will be provided to study participants via a newsletter.

9.0 STUDY TIMELINE

9.1 Subject Participation Duration
Adolescents and young adults enrolled in this study will participate in a 4-week run-in period, 1 week pre-treatment assessment, 8-week intervention or control group, and 4 week post-treatment period. In all, the estimated duration of subject participation is 17 weeks.

Given the demanding nature of cancer treatment, all study procedures can be completed +/- 2 weeks of the planned completion date and still be considered completed "on time."

9.2 Enrollment Duration
Based on the number of eligible AYAs receiving care at the 3 participating institutions, it is estimated that participant enrollment will be completed in 12 months.

9.3 Study Timeline
The Notice of Award was issued on December 12, 2022. The proposed study timeline is detailed in Table 4.

Table 4. Study Timeline

Dates	Tasks
December 2022 to February 2023	Prepare study materials and train study staff
February 2023 to November 2024	Participant enrollment
January 2023 to March 2025	Data collection
July 2023 to December 2026	Data analysis, cleaning, and publication

10.0 INCLUSION AND EXCLUSION CRITERIA

10.1 Eligibility Screening and Criteria

This study includes a 4 week run-in period during which eligibility will be determined. First, AYAs deemed eligible per inclusion and exclusion criteria 1-7 (Table 5) will be identified by a member of the study team via electronic medical record review. A waiver of HIPAA authorization is requested for preparatory research to identify potential participants based on inclusion/exclusion criteria. AYAs deemed eligible per criteria 1-7 and interested in participating will then complete the consent process as per Sections 13 and 22.

Table 5. Inclusion and Exclusion Criteria and Rationale
Inclusion Criteria (Rationale)
1. Patient between 15 and 24 years of age at consent visit (unique biological characteristics and behavioral transitions)
2. Patient diagnosis of cancer (intervention designed to address medical components of oncology treatment)
3. Patient prescribed oral prophylaxis or chemotherapy (non-adherence to these medications is linked to relapse & death)
Exclusion Criteria (Rationale)
4. Patient is not fluent in English (piloting an intervention to be delivered in multiple languages is beyond the scope of this study)
5. Patient evidences significant cognitive deficits per medical team (may interfere with intervention comprehension and/or participation)
6. Patient's medical status/condition precludes participation per medical team, patient, or caregiver (ensuring ethical recruitment)
7. Patient enrolled on a medical trial requiring medication storage in a trial-provided container (adherence measured via electronic monitor)
*8. Patient demonstrates ≥ 95% adherence[9] during run-in (maximize accuracy of evaluation of preliminary efficacy)**
*9. Patient declines to use or has difficulty using the electronic monitoring device (minimize missing data)**
**determined during run-in period*

Prescribed Oral Medication Regimen Eligibility Criteria: An AYA's oral medication regimen can be modified based on their treatment response and thus it is possible that some enrolled AYAs will discontinue their medication prior to the end of the 17 week study. To minimize the likelihood of enrolling these patients, we will consult with an oncologist prior to enrolling each patient and only enroll patients who the medical team believes (at the time of enrollment) will be prescribed an oral prophylactic or chemotherapy medication for the 17 week study duration.

Run-In Period to Confirm Eligibility: After an AYA is enrolled, they will receive an electronic monitoring device and be asked to store their eligible oral medication in this device for the duration of their participation in the study. These criteria will be confirmed during the 4-week run-in period as detailed in Section 6.2.a.

10.2 Inclusion of Vulnerable Populations

Teenagers ages 15-17 years of age are eligible to participate in this study.

As our population includes women of child-bearing age, pregnant women may be eligible to participate.

Adults unable to consent and prisoners are not eligible to participate.

11.0 VULNERABLE POPULATIONS

The cohort will consist of patients between the ages of 15 and 24 years at baseline. This is a minimal risk study, including risks no greater than those encountered in routine behavioral assessment and clinical care. The steps taken to minimize coercion or undue influence during the process of obtaining informed consent will be followed in accordance with all applicable regulatory requirements. A patient and their family will not be approached if they 1) do not meet the proposed study criteria; and/or 2) are under distress. Additional procedures for obtaining consent are listed below.

This is a minimal risk study with no risk to the fetus.

12.0 LOCAL NUMBER OF SUBJECTS

12.1 Total Number of Subjects to be Accrued Locally

Recruitment will be ended when 40 AYAs are randomized. It is estimated that approximately 15 AYAs will be recruited locally with the remainder recruited at collaborating sites.

12.2 Total Numbers Completing Each Phase of Study

There are likely to be AYAs who are deemed eligible per inclusion and exclusion criteria 1-7 but are deemed ineligible due to criteria 8-9 following the 4 week run-in period. It is also possible that some participants will not complete initial study procedures (i.e., no-show for pre-treatment assessment visit). As a result, additional AYAs (estimated *n* = 10-20 AYAs) will be enrolled until a total of 40 AYAs are randomized.

13.0 RECRUITMENT METHODS

Participants will be recruited from the Cancer and Blood Diseases Institute (CBDI) at CCHMC and collaborating sites (see title page). Participants deemed eligible per inclusion and exclusion criteria 1-7 will be identified via electronic medical record review. A member of the study team will review the electronic medical records of these patients and to determine AYA eligibility.

Eligible participants can be recruited either in-person or remotely.

13.1 In-Person Recruitment Procedures

Eligible participants may be approached by study personnel during a clinic appointment or inpatient admission to extend an invitation to participate in the study and verify inclusion/exclusion criteria. A recruitment script will be followed. A study flyer may be provided to interested participants.

Primary Site (CCHMC) Procedures. If the AYA is willing to participate, the study staff will obtain appropriate informed consent/assent and a signed HIPAA authorization form. No further attempts will be made to contact disinterested AYAs. This recruitment strategy has been successful for the PI's previous studies (79-94% enrollment).

Collaborating Site Procedures. For AYAs receiving care at collaborating sites, study staff at the collaborating site will be responsible for screening and approaching eligible patients. If the patient is interested in participating in the study, study staff at that site will obtain informed consent/assent, signed HIPAA authorization form, and contact information. This information will be securely emailed to CCHMC via a password-protected Excel sheet. The password-protected Excel sheet will be saved on a secure drive on CCHMC's network. Only study staff will have access to the Excel sheet. Of note, all staff at these sites will be trained in informed consent procedures by CCHMC study staff. No further attempts will be made to contact disinterested AYAs. This recruitment strategy has been successful for the PI's previous multi-site studies (91-95% enrollment).

13.2 Remote Recruitment Procedures

Patients may also be recruited remotely. Specifically, eligible participants may be mailed a letter and flyer describing the study procedures. The letter will include instructions regarding opt-out procedures (participants call or email a designated phone number/email address). Eligible participants who do not opt-out will be contacted by a member of the study team within approximately two weeks and consent procedures will be completed. This recruitment strategy has been previously used by the PI on multi-site studies of young adult cancer survivors (IRB # 2018-1885) and AYAs with cancer (IRB # 2019-0623).

13.3 Participant Payment

Participants will be compensated for the time required for assessment completion. Compensation for survey completion (est. completion time: 30-45 minutes) was set at $20. Participants will be compensated an additional $5 weekly, for 17 weeks, for using and downloading data from their electronic adherence monitoring device. If a participant completes all Feedback Group or Tailored Group procedures, they will be compensated a $15 bonus. Participants will also be compensated an additional $10 upon return of the study-provided electronic adherence monitoring device at the conclusion of the study (either at study completion or at drop-out – whenever the electronic monitoring device is returned).

Table 6. Incentive Schedule

Task	Amount
Pre-Treatment Assessment	$20
Weekly eCAP downloads (4 week run-in + 1 week for pre-treatment assessment + 8 weeks of intervention + 4 weeks post-intervention = 17 weeks)	$5/week (total up to $85)
Group completion bonus	$15
Post-Treatment Assessment	$20
eCAP return	$10
	Max Total = $150

In the event that a study phone is not returned, we will attempt to reach the family via phone and email and set up a way to retrieve the phone. Given the high costs of the phones, if, after several months it is still not returned, we will offer an incentive of $50 for the safe return of the working mobile device, no questions asked. Other BMCP faculty have had success in using this procedure to increase mobile device return rates.

All compensation will be managed by the study team at CCHMC and provided via ClinCards.

14.0 WITHDRAWAL OF SUBJECTS

There are no anticipated circumstances under which subjects will be withdrawn from the research without their consent.

If participants wish to withdraw from the study, they are asked to contact the study team in writing. Following withdrawal, no additional attempts will be made to contact participants and no new data will be collected. Data collected prior to withdrawal, however, will still be analyzed. These procedures are detailed in the consent document.

15.0 RISKS TO SUBJECTS

This is a minimal risk study, including risks no greater than those encountered in routine behavioral assessment and clinical care. There are no medical risks. Participation in all study procedures is voluntary and participants can withdraw at any time.

Risk of Discomfort: Prior to study participation, AYAs will be reminded that they may decline to answer any question that makes them feel uncomfortable. In the unlikely event that the content of a study visit or intervention session causes emotional or psychological distress, the Principal Investigator, Meghan E. McGrady, PhD, a licensed clinical psychologist at CCHMC (or the licensed clinical psychologist providing back-up coverage) will be contacted immediately to assess the situation. The licensed clinical psychologist will follow-up with patient's medical team as necessary. These procedures will also be followed should concerns regarding abuse, self-harm, homicidal/suicidal thoughts or behaviors arise. Patients and caregivers will be made aware that any information obtained during their participation that suggests the potential for harm to self or others will be disclosed to their medical team in order to protect the patient. As study procedures are conducted virtually, patients and families will be instructed to go to the local ED or call 911 if there is an immediate safety concern.

Risk of Loss of Privacy of Data: There is also the risk of possible loss of privacy of data or loss of confidentiality. These risks are inherent in all research studies. While HIPAA-compliant health technology services will be used to remotely access medication adherence data (CertiScan® cloud) and deliver

assessments and intervention sessions (Zoom for Healthcare), there is a risk of loss of privacy of data and a risk of loss of confidentiality associated with health technology use. A statement to this effect will be included in the consent documents. Every effort will be made to ensure that all participant information will be kept confidential and secure (as detailed in Section 17).

Unanticipated problems related to the research will be reported to the IRB within 24 hours of Dr. McGrady (PI) becoming aware of the problem. Unanticipated problems will also be regularly reported to Dr. Sarah Beal, the Independent Data Safety Monitor for this study.

16.0 POTENTIAL BENEFIT TO SUBJECTS

AYAs randomized to either the treatment (Tailored Program) or control (Feedback Program) arm may benefit from improved medication adherence, which has the potential to improve health outcomes. The information gained will improve our understanding of how best to help AYAs with cancer adhere to their medication regimens. The minimal risks associated with study participation are deemed reasonable in relation to the aforementioned anticipated benefits to participants and others.

17.0 DATA MANAGEMENT AND CONFIDENTIALITY

17.1 Sample Size Justification

A medical record review was conducted to determine the number of eligible AYAs across each site. In 2019, an estimated 97 AYAs ages 15-24 years of age with a diagnosis of cancer prescribed an oral prophylactic or chemotherapy medication (anticipated duration > 17 weeks) received care at one of the three participating sites: Cincinnati Children's Hospital Medical Center (CCHMC), Seattle Children's Hospital, and St. Jude Children's Research Hospital. Of these 97 AYAs, based on enrollment data from our preliminary studies, it is estimated that 5% (n = 5) will be excluded due to lack of English fluency, presence of significant cognitive deficits, poor medical status, and/or participation in a medical clinical trial. In our preliminary studies, 29% of AYAs took ≥ 95% of doses and 3% declined to use an electronic monitoring device (total = 32%). Based on these data, we conservatively estimate that an additional 35% will not meet the adherence-related criteria (< 95% adherence during run-in; AYA uses electronic monitoring device without difficulty) and be excluded. Thus, in all, we estimate that 39 of the 97 AYAs will not meet inclusion criteria (97*[.05+.35] = 39), resulting in an estimated eligible sample of 58 AYAs (97 - 39 = 58).

We have set our recruitment rate goal of 70%, well below our previous enrollment rates of 79-92% into multi-site observational psychosocial studies including AYAs with cancer. Based on an enrollment rate of 70%, it is estimated that we will enroll 3-4 AYAs per month and meet our recruitment goal of N = 40 (58*.70 = 40) in 12 months.

As it is estimated that approximately 58 AYAs with cancer meeting the inclusion criteria will receive care at one of the 3 participating sites during the 12 month recruitment period, a target N of 40 (randomized) was set to test our ability to achieve a 70% recruitment rate (58*.70 = 40). Assuming 20% attrition, our estimated final N will be 32, a number that exceeds the recommended sample size (n = 20) for a pilot 2-arm RCT with the goal of informing an efficacy trial with 80% power to detect a medium effect.[36]

17.2 Data Analysis Plan

Hypothesis 1a: The intervention will meet enrollment, retention, fidelity, and data completion feasibility criteria.

Hypothesis 1a will be supported if descriptive statistics indicate the feasibility criteria in Table 7 are met. The percent of eligible approached AYAs who enroll will be calculated to explore the hypothesis that the intervention will meet the enrollment rate goal of 70%. The percentage of AYAs completing all study procedures and with complete data will be calculated to evaluate the hypothesis that the retention and

assessment completion rates will be "acceptable"[37] as defined as 80% or higher. In addition, the percentage of AYAs who received the intervention length, contact, content, and duration as specified in the treatment protocol will be calculated to evaluate the hypothesis that intervention fidelity will be "high"[39] as defined as 80% or higher.

Table 7. Hypothesis 1A Measures

Domain	Measure	Outcome	Criteria
Feasibility (Hyp 1a)	**Enrollment Rate**	Percentage of eligible approached AYAs who enroll	≥ 70%
	Retention Rate	Percentage of AYAs completing all study procedures	≥ 80%[37]
	Assessment Completion	Percentage of AYAs with complete data	≥ 80%[37]
	Intervention Fidelity[38]	Percentage of AYAs receiving the intervention length, contact, content, and duration as specified in the protocol	≥ 80%[39]

Hypothesis 1b: AYAs will rate the intervention as easy to use and acceptable.

Participants in both the treatment and control arms will complete usability and acceptability measures (see Table 8) in an effort to promote blinding. Data from the treatment group will be analyzed separately to explore Hypothesis 1b. Mean System Usability Scale, System Usability Scale Adjective Rating, and Acceptability &Adherence Scale scores will be calculated for AYAs randomized to the treatment group. It is hypothesized that AYAs participating in the treatment group will rate the intervention as easy to use as defined by a mean System Usability Scale score of 68 or greater[39] and a mean System Usability Scale Adjective Rating of 4 or higher.[41] It is also hypothesized that AYAs participating in the treatment group will rate the intervention as acceptable as defined by a mean Acceptability &Adherence Scale score of 28 or higher.[42]

Table 8. Hypothesis 1B Measures

Domain	Measure	Outcome	Criteria
Usability (Hyp 1b)	**System Usability Scale (SUS)**[40]	Mean score of AYAs randomized to treatment group	M ≥ 68[40]
	System Usability Scale Adjective Rating[41]	Mean score of AYAs randomized to treatment group	M ≥ 4[41]
Acceptability (Hyp 1b)	**Acceptability &Adherence Scale**[42]	Mean score of AYAs randomized to treatment group	M ≥ 28[43]

Data from the open-ended refinement questions (see Table 2) will be coded in NVivo by two independent raters using theoretical thematic analysis, a method selected as it codes for themes related to specific research questions such as those posed in this grant (i.e., "What could we change about the intervention to make it more acceptable to AYAs?").

Exploratory Aim 2: To explore group differences in improvements in electronically-monitored medication adherence to inform the next phases of intervention development and testing.

To explore group differences in improvements in electronically-monitored medication adherence to inform the next phases of intervention development and testing (Exploratory Aim 2), we will conduct longitudinal mixed effects models using Stata version 16.[49] Longitudinal trajectories of adherence will be estimated and tested for treatment group differences.

While this study is not designed to test for treatment-related differences in adherence by demographic or clinical variables, demographic (age, sex, race), clinical (side effects, diagnosis, additional adherence interventions), and psychosocial variables (parental involvement, emotional distress) previously associated with adherence[10] (see Table 3) will be explored as potential covariates. Exploring the role of these variables as covariates will enhance the precision of our efficacy estimate. Data will also be disaggregated by sex in all publications to facilitate efforts to consider sex in the interpretation and generalization of findings.

17.3 Data Security and Storage

All data will be de-identified with the use of unique assigned study identifier codes. Study identifier codes will be used on study measures for data entry and analysis. No other identifying data such as date of birth, address, phone numbers, social security number, or zip code will be entered on measures. A password-

protected Excel database will be maintained to link study identifiers to participants. This database will be housed on CCHMC's network and backed up as per below. Only trained study staff involved in the research and under the direct supervision of Dr. McGrady (PI) will have access to this database.

Medication Adherence Data: Medication adherence data will be transmitted from the AYA's electronic adherence monitoring device to the CCHMC study team via the CertiScan® cloud, a HIPAA 21CFR Pt11 compliant cloud. Specifically, after the study team has helped the AYA to download the CertiScan mobile application, AYAs will "tap" their electronic adherence monitoring device to their study-provided near field communication (NFC)-enabled smartphone. A participant's data will then be securely transmitted to the CertiScan® cloud. Of note, all participant data stored in the cloud is identified with a study identifier only (and no identifying data such as name or date of birth). Only trained members of the CCHMC study team will have access to CertiScan® cloud.

The adherence electronic monitoring devices are not marked with any patient identifying information. The adherence electronic monitoring device is assigned to a patient using a Study ID encrypted into the device. Accessing the data from the adherence electronic monitoring device (including the Study ID used to link the patient to the device) is possible only with access to the secure online portal available only to the study team. Thus, even in the unlikely case that the envelope is lost in transit, it would not be possible for participant data to be identified.

REDCap Data: Data from pre-treatment and post-treatment assessments and clinical data obtained from the electronic medical record will be entered and stored in REDCap, a secure and HIPAA-compliant web application for building and managing online surveys and databases. The barriers tool used to tailor BCTs for AYAs assigned to the treatment condition will be completed via Sawtooth Software hosted by CCHMC. Security for these web-based applications is provided through a Secured Socket Layer certificate allowing for 128-bit encryption between client and server transactions as well as the secured demilitarized zone (DZD) network. Participant responses will be stored on the secured SQL server database. All data will be stored and accessed in accordance with the HCFA's Internet Security Policy and HIPAA.

Audio or Video Files: Audio or video files from intervention sessions (collected to rate intervention fidelity) will be stored in a password-protected folder on the secure CCHMC hard drive. Intervention fidelity will be rated on a form including the participant's Study ID and not including any identifying information. Following fidelity rating, all audio files will be deleted.

Exported Data: Exports of adherence (from CertiScan® cloud) and questionnaire (from REDCap) data will be completed by the PI or another trained member of the CCHMC study team. All exported data will be stored in password-protected electronic files on the CCHMC hard drive. Passwords will only be known to study staff directly involved in the administration and oversight of data collection. All information collected as part of this study will be accessible only to study staff who will complete human subjects training to ensure familiarity with rights of research participants and protection of confidentiality.

Electronic data stored on CCHMC's network is backed up incrementally each night, fully each week, and monthly in offsite vaults. The server is maintained and all backups are conducted by the Division of Biomedical Informatics. Access to data will be limited to study team members.

Intervention Sessions: Intervention sessions will be delivered via Zoom for Healthcare, a HIPAA-compliant videoconferencing software. It is possible that privacy can be lost when using technology. Participants will be advised about this potential loss of privacy and it will be detailed in the consent document.

Consent Forms: AYAs may complete informed consent forms electronically or on paper. Electronic informed consent documents will be maintained in REDCap and a password-protected electronic database on CCHMC hard drives. Dr. McGrady's (PI's) team has used electronic consent signing procedures (via REDCap) for multiple studies with AYAs with cancer with approval from the CCHMC IRB (sIRB of record for the proposed research). Paper informed consent documents will be maintained in locked storage cabinets. Consent forms will be maintained in separate databases from participant data.

SSN: Finally, because this research study involves payment for participation, we are required by Internal Revenue Service (IRS) rules to collect and use the AYA's social security number (SSN) or taxpayer identification number (TIN) for compensation tracking purposes. We will only use the AYA's SSN or TIN to track compensation. SSNs and/or TINs will not be used for any other purposes.

17.4 Data Quality

Self-report questionnaires will be completed via REDCap, a secure web-based application for measure administration. To maximize data integrity and minimize the likelihood of missing data, the REDCap data collection system only accepts values within allowable ranges and has been programmed to prompt participants to complete items accidentally skipped.

All data entered by a member of the study team (i.e., chart review data) will be checked by a second member of the study team for accuracy, with discrepancies resolved via consultation with the original data source.

17.5 Concerns About Access to Adult Websites and Apps on Cell Phones

Participants may be provided with a cellular phone for use for the duration of the study. During the consent process, participants will be asked to use the cell phone "as they normally would use any smartphone that has internet access." We have gone to great lengths to make the cell phone provided easy to use and compelling in terms of incentives and features so that participants will use the cell phone provided as opposed to other cell phones they likely have. However, for this endeavor to be successful, participants must feel confident that their phone activity--how they normally use the phone--will not be met with repercussion or reprimand.

We considered only installing the CertiScan® and Zoom apps and severely restricting the accessible internet websites on the study cell phones. However, this would create an "unnatural" cell phone use environment for those participants that had not previously been exposed to filtering and would cause them to not use the study cell phone as their main device they carry with them. Because this would minimize the likelihood that the participant would have the phone available for use when they needed to upload their adherence data or contact their coach, we have consulted closely with study teams who have had success providing cell phones to participants to design the following procedures for informing participants of their options while not compromising the integrity of the study. Cell phones will be loaded with the CCHMC-recommended security software program. We will explain this to the parents/guardians and AYAs. After being informed, participants will be provided with cell phone contracts to review and sign. These contracts will cover basic internet and phone safety measures and include study contact information in case the participant experiences any technical issues or has concerns. The study team will be able to erase all content in the event of a lost/stolen device. Internet access on the phone is being restricted with Safari for the web browsers. These content filters do their best to block websites with inappropriate content. The Internet content filter can identify, with a high degree of accuracy, whether a Web page is safe or not by examining various properties of the website including text and structure. The content filters are being managed by the security software and cannot be removed.

18.0 PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS

Not Applicable. This is a minimal risk pilot feasibility study of an adherence-promotion intervention as compared to uniform standard of care among AYAs with cancer.

19.0 PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

19.1 Procedures to Protect Privacy Interests

All study contacts (i.e., consent visit, intervention sessions) will be conducted in a private room or via videoconferencing (Zoom for Healthcare) or phone. At the beginning of study participation, study staff will work with the participant to come up with a plan for when/where they will complete study procedures to ensure they can be completed in a manner that aligns with their privacy interests (e.g., completing sessions in a private room so that their parents cannot hear conversations).

19.2 Procedures to Make Subjects Feel at Ease

Participants may decline answering questions that cause them to feel uncomfortable and will be reminded of this prior to each study contact. Participants may also withdraw from the study at any time and will be informed of this right during the consent process. In the unlikely event that the content of study visit causes emotional or psychological distress, the Principal Investigator, Meghan McGrady, PhD, a licensed clinical psychologist at CCHMC (or the licensed clinical psychologist providing back-up coverage) will be contacted immediately to assess the situation. The psychologist triaging any concerns will provide appropriate referrals and/or treatment.

19.3 Access to Participant Information

Individual data will not be available to anyone not directly associated with the study. All study personnel have been trained in data safety and monitoring, privacy and confidentiality, minimizing risks related to loss of privacy, and confidentiality. We will closely monitor performance of our research personnel to ensure the strictest standards.

20.0 COMPENSATION FOR RESEARCH-RELATED INJURY

Not Applicable. This research involves no more than minimal risk.

21.0 ECONOMIC BURDEN TO SUBJECTS

No payment from participants will be required to participate in this study. All study components (i.e., electronic monitoring device, cellular phone and data plan) will be supplied to participants at no cost. Participants will be responsible for the usual costs of medical care. If a referral for psychosocial services is made as a result of this study, the participant is responsible for the costs of those services.

22.0 CONSENT PROCESS

Informed consent will be obtained in accordance with SOP: Informed Consent Process for Research (HRP-090). Informed consent will be obtained by trained research staff and may be obtained in-person or remotely. During the consent process, all pertinent aspects of consent/assent will be covered including study purpose, risks/benefits, confidentiality, and right to withdraw. Patients will be informed that their care will not be affected by whether they choose to participate in the study.

22.1 Consent Document Format

Consent forms may be signed electronically using REDCap, a secure web-based interface supported by the CCHMC Division of Biomedical Informatics in compliance with HIPAA and designed to protect PHI in the electronic transfer and storage of the consent form. Should technical issues arise with the REDCap interface, hard copies of consent forms may also be used. If the patient/parent agrees to participate and is signing an electronic consent form via REDCap, they will have an opportunity to check a box stating that they agree to provide their consent. There will also be fields for their typed name, date, and electronic signature to document the informed consent process. Once the electronic form has been submitted, patients (and parents as appropriate) will receive a copy of the electronically signed and dated consent form via email.

22.2 Consent Location

Participants recruited in-person will complete the informed consent/parental permission document in-person (either via REDCap or paper forms). For participants being recruited remotely, a member of the study team will schedule a phone or video call and provide a link to access the consent form in REDCap via email. A hard copy of the consent/permission form may also be mailed if necessary. During the consent phone or video call, research staff will ensure all patient (and parent) questions are answered. In compliance with CCHMC SOP Number 41-1.6, study staff will sign and date accordingly on the signature page of each form corresponding to the date the forms were received, not necessarily reviewed with the family. The method used to obtain participant consent will also be written on the Informed Consent Process Note.

22.3 Subjects Who Are Not Yet Adults

For participants who are under the age of 18, parental permission will be obtained from at least one parent. Permission will not be obtained from individuals other than parents. Assent will be obtained from all participants under 18 years of age and documented on the consent form.

23.0 PROCESS TO DOCUMENT CONSENT IN WRITING

Informed Consent/Parental Permission documents will be completed via REDCap or in-person. CCHMC SOP: Written Documentation of Consent (HRP-091) will be followed. A consent/permission document is included in this IRB submission.

24.0 SETTING

Participants will be recruited from Cincinnati Children's Hospital Medical Center, Seattle Children's Hospital, and St. Jude Children's Hospital. Seattle Children's Hospital and St. Jude Children's Hospital are referred to as a "Collaborating Site" throughout the document. Our study team includes a Patient Partner serves as a Consultant.

25.0 RESOURCES AVAILABLE

25.1 Access to Patient Population

A medical record review was conducted to determine the number of eligible AYAs across each site. In 2019, an estimated 97 AYAs ages 15-24 years of age with a diagnosis of cancer prescribed an oral prophylactic or chemotherapy medication received care at one of the three participating sites: Cincinnati Children's Hospital Medical Center (CCHMC), Seattle Children's Hospital, and St. Jude Children's Research Hospital. As detailed in Section 17, it is anticipated that this sample size is sufficient to enable us to achieve our recruitment goal of 40 randomized AYAs.

25.2 Time Commitment

This research is associated with an NIH R21 application which supports 25% of Dr. McGrady's (PI's) effort.

25.3 Facilities and Resources

Dr. McGrady (PI) has access to all of the necessary resources to conduct the proposed research through a combination of CCHMC resources (e.g., REDCap access), Divisional support, and grant-provided resources (e.g., CRC support).

25.4 Communication

A Communication Plan will be finalized prior to study initiation, but will include at a minimum, the methods proposed in Table 9. Dr. McGrady (PI) will be directly responsible for overseeing all communication efforts.

Table 9. Communication Plan			
Meeting	**Frequency**	**Attendees**	**Topics**
Standard Operating Procedure Development	Bi-Weekly (Study Start-Up)	• PI (McGrady) • Behavioral RCT Co-I (Pai) • mHealth Co-I (Hommel) • Oncology Co-I (Norris) • CCHMC Research Coordinator (Breen) • Patient Partner (Burke)	• Standard operating procedure development • Recruitment and retention procedure development • Functionality testing
Study Team Training	Single Session (Study Start-Up)	• PI (McGrady) • Site Co-Is (Tillery, Ketterl) • CCHMC, Seattle, & St. Jude Research Coordinators • Interventionist (Psychology Trainee)	• Standard operating procedure training • Research ethics training • Intervention content training
McGrady Lab	Weekly (Ongoing)	• PI (McGrady) • CCHMC Research Coordinator (Breen) • Patient Partner (Burke, ~bi-monthly)	• IRB Updates • Questions or concerns regarding study procedures
Multi-Site Zoom	Bi-Weekly (Ongoing)	• PI and Site Co-Is (McGrady, Tillery, Ketterl) • CCHMC, Seattle, & St. Jude Research Coordinators • Behavioral RCT, mHealth, Oncology Co-Is as necessary • Patient Partner (Burke, ~bi-monthly)	• Recruitment • Retention • IRB Updates • Questions or concerns regarding study procedures
Supervision	Weekly (Intervention Delivery)	• PI (McGrady) • Interventionist (Psychology Trainee)	• Clinical supervision • Review of fidelity ratings • Ethical/safety issues as necessary

25.5 Psychological Resources

In the unlikely event that the content of study visit causes emotional or psychological distress, the Principal Investigator, Meghan McGrady, PhD, a licensed clinical psychologist at CCHMC (or the licensed clinical psychologist providing back-up coverage) will be contacted immediately to assess the situation. The psychologist triaging any concerns will provide appropriate referrals and/or treatment. All AYAs enrolled in the proposed research will be currently receiving care at CCHMC or one of the collaborating sites and thus have access to psychological services through their home institution.

26.0 MULTI-SITE RESEARCH

26.1 Study-Wide Number of Subjects

Up to 40 AYAs will be randomized to the intervention or control condition.

26.2 Study-Wide Recruitment

Recruitment methods are described in Section 13. Consent methods are described in Section 22. Bi-weekly phone calls will be scheduled including the PI, Lead CRC, and Collaborating Site study staff. During these phone calls, Collaborating Site study staff will provide updates on recruitment.

26.3 Study-Wide Communication

Following the approval of the protocol and the subsequent approvals of any modifications, all updated protocols, consent documents, and HIPAA authorization will be distributed to collaborating sites by the CCHMC Lead Clinical Research Coordinator. The CCHMC Lead Clinical Research Coordinator, under the supervision of Dr. McGrady, will ensure all required approvals have been obtained at each site prior to the initiation of any study procedures.

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