Title: Predicting Childhood Cancer Survivors' Transition Readiness & Transfer Outcomes (SURV Transfer Outcomes)

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Predicting Childhood Cancer Survivors' Transition Readiness & Transfer Outcomes

(SURV Transfer Outcomes)

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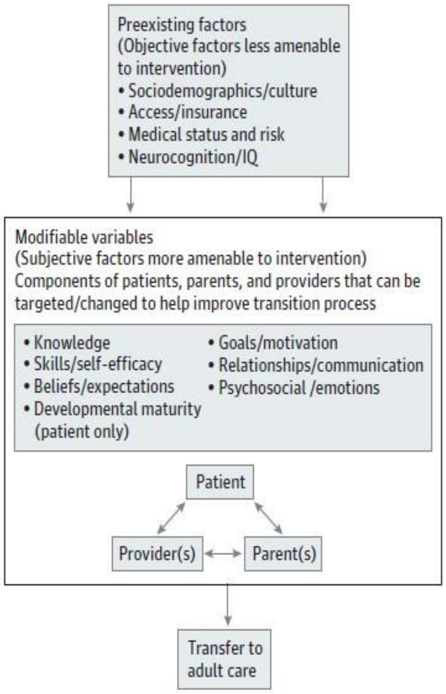
I. Background and Significance

Recent data estimate that over 80% of children and adolescents diagnosed with cancer will become long-term survivors, thereby establishing a growing patient population with increasing medical and psychosocial needs. The Children's Oncology Group (COG) recommends that survivors participate in continuous long term follow-up (LTFU) survivor care across the lifespan to monitor for late effects of treatment. Chronic health conditions and late effects of treatment impact over 60% of adult survivors of childhood cancer and over 25% of survivors have severe or life-threatening conditions. Ongoing survivor care and surveillance tests are essential for adolescents and young adult (AYA)survivors because many late effects do not emerge until years after treatment, and late effects of childhood cancer treatment place survivors at an 8.4 times higher risk for mortality as compared to age- and sex-matched U.S. population. Despite these increased risks, less than 50% of young adult survivors ages 18-24 years are adherent with cancer-related medical care and less than 20% had a survivor visit at a cancercenter in the past 2 years. Regrettably, childhood cancer morbidity and mortality risks increase over time, and thus, the majority of young adult survivors are non-adherent with their survivor care during the period in which they are becoming increasingly vulnerable to late effects. Although research into transition outcomes in survivor care has been repeatedly called for in the literature, no empirical studies characterizing successful childhood cancer survivor transition have been published to date.

Figure 1. SMART Model- Social-

Given the lack of empirical literature evaluating successful transition of pediatric cancer survivors to adult survivor care, we pulled from an empirically-based, stakeholder supported theoretical framework for childhood cancer survivor transition to guide the development of our aims. Schwartz et al. (2013) published on the validation process of the <u>SocialEcological Model of Adolescent and Young Adult Readiness to Transition (SMART)</u> (Figure 1). The SMART model synthesized the available empirical transition literature from other pediatric chronic illnesses and also analyzed the childhood cancer survivor transition review literature. The SMART model is comprised of "preexisting factors" which may impact transition readiness and transfer success but are not likely to be altered by any intervention (i.e., demographics, neurocognition, etc.), as well as "modifiable variables" which may be beneficial targets for intervention to improve transition outcomes (i.e., knowledge, self-efficacy, health beliefs, psychosocial functioning, etc). The SMART model also recognizes that transition to adult survivor care is a complicated process involving not only patient-factors, but parent and provider related factors as well.

ecological model of AYA readiness for transition, Schwartz et. al (2013)



Overall, the proposed study addresses significant questions currently unanswered in the literature and takes an empirical approach to resolve these gaps in knowledge. <u>At the end of this award, we will know which social-ecological factors to target to improve transition readiness and adherence to adult survivor health care.</u> Moving forward, these findings will inform the development of extramural grant applications to fund the implementation and evaluation of evidence-based interventions designed to facilitate successful transition to adult survivor care.

<u>Preliminary Data.</u> Our team has sought to assess and measure health self-management and perceptions of transition readiness by adapting the Readiness for Transition Questionnaire (RTQ) for use with AYA survivors of childhood cancers and their parents. The RTQ was originally developed by the PI for use with AYA kidney transplant recipients at Children's Healthcare of Atlanta and was tailored to assess overall transition readiness (RTQ-Overall), AYA healthcare responsibility (RTQ-AR), and parent involvement in pediatric survivor healthcare (RTQ-PI). In a recent review of transition readiness measures, the RTQ was one of only 10 measures meeting criteria for "promising" assessment as defined by the American Psychological Association Division 54 EvidenceBased Assessment Task Force. To evaluate the use of the tailored RTQ within the AYA childhood cancer survivor population, we recruited AYA survivors (N=74) ages 14 to 21 and their parents (N=68). <u>The preliminary psychometric properties of the RTQ appear to be supported within the AYA pediatric cancer survivor population,</u> including internal consistency (Cronbach's alphas=.80-.90), convergent validity, and construct validity.

To evaluate healthcare responsibility among our young adult survivor patients, we collected pilot data from N=41 childhood cancer survivors ages 18-21 years-old participating pediatric survivor care. Although these survivors will be transferring to adult care in the next 1-2 years, <u>over half of patients reported that their parents were primarily responsible for their healthcare (56.2%) and that parents were almost always involved in the scheduling of survivor medical appointments (63.4%).</u> As young adult patients transfer out of pediatric care, it will be important to clearly understand the role of parents and family in the transition process and create interventions that target all parties involved in survivors' health management.

II. Goals/Aims Overview

The objectives of this study are to clarify: what are the most salient social-ecological risk and resilience factors that should serve as targets for interventions and who are the survivors most at risk to be recruited for future interventions, how survivors want to receive educational interventions, and which educational interventions are most effective. Using a cross-sectional cohort study of 18-25 year old childhood cancer survivors and/or their parents, this study will determine predictors of transition readiness (Aim 1) and predictors of adherence to adult survivor-focused healthcare (Aim 2), as well as evaluate the quality (Aim 3) and efficacy (Aim 4) of electronic educational interventions for AYA survivors. The specific aims are to:

Aim 1: Evaluate social-ecological factors among AYA childhood cancer survivors participating in pediatric survivor care to determine factors associated with decreased transition readiness (i.e., risk factors) and increased transition readiness (i.e., resilience factors), as well as characterize patterns of co-occurring risk factors associated with transition readiness.

Aim 2: Evaluate social-ecological factors among AYA childhood cancer survivors following transfer to identify factors associated non-adherence (i.e., risk factors) and adherence (i.e., resilience factors) to adult survivor care, as well as characterize patterns of co-occurring risk factors associated with non-adherence to adult survivor care.

Aim 3: Develop and assess quality of electronic multimedia materials to educate AYA survivors about lifelong survivor care through qualitative interviews with AYAs.

Aim 4: Evaluate the impact of electronic educational materials on AYA survivors' knowledge about late effects, perceived benefits, self-efficacy, and intentions to engage in lifelong survivor care.

III. Study Design

This is a mixed methods study involving cohorts of 18-25 year old childhood cancer survivors and/or their parents to determine predictors of transition readiness among those engaged in pediatric survivor care (Aim 1), predictors of adherence to adult survivor-focused healthcare among those who have transferred out of pediatrics (Aim 2), and optimize content, format, and delivery of electronic educational media to increase knowledge about and motivation for survivor care among AYA survivors (Aims 3 & 4). Through our design and methods, we are seeking to clarify what are the most salient social-ecological risk and resilience factors that should serve as targets for interventions, as well as what patterns exist among co-occurring risk factors that maximize patients' risk for poor transition outcomes. The planned approach to accomplish our specific aims will employ both quantitative and qualitative methods to test the following hypotheses:

Aim 1 Hypotheses:

- *A1 Hypothesis 1*: AYA healthcare responsibility, survivor health beliefs, and developmental maturity will be significantly related to increased perceptions of transition readiness.

- *A1 Hypothesis 2*: AYA psychosocial distress, poorer neurocognitive functioning, and deprived neighborhoodlevel social determinants will be significantly related to decreased perceptions of transition readiness.
- *A1 Hypothesis 3*: The relationship between parental involvement in survivor healthcare and perceptions of transition readiness will be mediated by AYA healthcare responsibility.
- *A1 Hypothesis 4*: When individual transition readiness risk factors are included in principal component analyses (PCA), 2 or more components will emerge indicating subgroups at risk for poor transition outcomes.

Aim 2 Hypotheses:

- *A2 Hypothesis 1*: Survivor health beliefs, developmental maturity, and healthcare responsibility will predict adherence to adult survivor care.
- *A2 Hypothesis 2*: Parental involvement in survivor healthcare will predict adherence to survivor care; this relationship will be stronger for survivors with higher psychosocial distress, as well as lower levels of developmental maturity and neurocognitive functioning.
- *A2 Hypothesis 3*: Access to care problems (e.g., geographical distance, insurance) and lower patient satisfaction will negatively predict adherence to initial survivor care.
- *A2 Hypothesis 4*: When individual risk factors for non-adherence are included in principal component analyses (PCA), 2 or more components will emerge indicating subgroups at risk for poor transition outcomes.

Aim 3 Hypothesis:

- *A3 Hypothesis:* Stakeholder input and review of electronic media developed in this study using qualitative methods will increase acceptability and value to AYA survivors of childhood cancer

Aim 4 Hypotheses:

- *A4 Hypothesis 1:* Exposure to multimedia educational materials will significantly increase AYA survivors' knowledge about late effects and surveillance.

- *A4 Hypothesis 2:* Exposure to multimedia educational materials will significantly increase AYA survivors' perceived benefits of, self-efficacy to, and intentions to engage in survivor care across the lifespan.

A. Outcomes

For Aim 1, our metrics of "transition readiness" will be determined by patient- and parent-reported scores from the Readiness for Transition Questionnaire (RTQ-Overall). The RTQ-Overall assesses perceived preparedness to transfer both healthcare responsibility (from parent to teen) and services (from pediatric to adult care), with higher scores indicating increased transition readiness. For Aim 2, we will operationalize "adherence to adult survivor-focused healthcare" as the attendance of at least one healthcare visit with an adult provider focused on survivorship within 18 months following transfer from pediatric care. This operationalization of adherence was chosen based on recommendation by COG that survivors of childhood cancer should be evaluated annually and has been previously utilized to classify survivor clinic attendance. For participants who report attending an adult survivor care appointment, we will obtain a medical record release to verify date and attendance at an appointment with the adult survivor care provider. For Aim 3, we will elicit stakeholder feedback on the content, clarity, style, and interest-level of the electronic educational materials. For Aim 4, AYA health beliefs, knowledge about survivor care and late-effects, patient activation, and self-efficacy and intentions to engage in lifelong survivor care will be evaluated using patient reported outcome (PRO) measures. In addition, a 15-item multiple choice quiz will be utilized to assess participants' knowledge of the content covered in the electronic educational materials.

B. Setting & Participants

The clinical research aspects of this project will occur through Children's Healthcare of Atlanta's Aflac Cancer Survivor Program (CSP). Eligible participants will be patients of the Aflac Cancer Survivor Program and identified for recruitment using Aflac CSP clinical databases. Participants' CHOA electronic medical records will also be reviewed. The staff from the Aflac Cancer Center's Clinical Research Office has extensive experience in coordinating and managing clinical research projects with childhood cancer survivors. The Aflac CSP was established in 2001 and currently follows over 850 pediatric cancer survivors each year. This program consists of a multidisciplinary team (oncology, endocrinology, and pediatric psychology) who see patients for annual longterm follow-up survivor care beginning when the survivor is two years off therapy. Per CHOA policy, the Aflac CSP must transition patients to adult providers prior to age 22; however, patients are provided with the option to transition between the ages of 19 and 21 years.

For this study, we will be recruiting all eligible young adult survivor patients and/or one of their parents/caregivers. Participant inclusion criteria are as follows, patients must be 18-25 years of age, diagnosed with cancer at ≤ 18 years of age, ≥ 2 years since the last cancer treatment, and seen at least once in the Aflac CSP in the past 2 years (Aims 1, 3, & 4) or transitioned out of the Aflac CSP to adult survivor care since 2013 (Aims 2, 3, & 4). Although our goal is to enroll patient-parent dyads for Aims 1 & 2, patients and/or parents will be recruited individually and either may choose to participate or not to participate. Patient ineligibility will not impact parent eligibility and vice versa. Patients and/or parents will be excluded from participation in the study if the participant is non-English speaking. Young adult survivors who are cognitively impaired and unable to complete the questionnaires will be excluded. Any eligible subjects for Aims 3 & 4 will be excluded if they do not consent to the recording of their interviews.

Patients will be excluded from participation in the study if patient is non-English speaking (as survey battery is available in English only). No patients will be excluded because of gender. We anticipate that at least 50% of our population will be women. Within the oncology division of the Aflac Cancer Center where our research will be conducted, the reported ethnic/racial distribution of patients is: White (62%), Black or African American (26%), Asian (4%), Other (7%); 13% are persons of Hispanic or Latino origin. No patients will be excluded because of race or ethnicity. Adolescent and young adult survivors of childhood cancer who are 18-25 years of age during the study enrollment periods will be eligible to participate, along with their parents. No minors who are under the age of 18 years will be included in this study.

C. Procedures & Recruitment

Each family that has been identified from our institutional survivor database and screened for eligibility will be contacted via phone, email, or in survivor clinic by research staff to be recruited for the study using information from the medical record. Patient names, post mailing addresses, phone numbers, and emails will be collected from EPIC and program databases.

Aims 1 & 2. All eligible participants will be emailed by research staff and/or receive a printed recruitment letter in the postal mail before being contacted by phone. The initial recruitment email will be sent to eligible participants containing an email link to a secure electronic consent and survey battery via CHOA's secure, webbased Research Electronic Data Capture (REDCap) platform. The printed recruitment letter will also contain information on how to access the secure electronic consent and survey battery via the Research Electronic Data Capture (REDCap) platform. Two additional follow-up recruitment emails will be sent at two week intervals. After three unsuccessful email attempts to recruit participants, email recruitment will be discontinued. One week following email and mail recruitment, research staff will initiate phone recruitment. After three unsuccessful phone attempts to recruit participants, phone recruitment will be discontinued. Phone script, letter text, and email text are attached with this protocol.

The consent process will be completed online prior to completing any study questionnaires. The initial page of the REDCAP survey will contain a brief written consent outlining the purpose of the study, its voluntary nature, time commitment, incentive information, release of PHI, and contact information of PI and Emory IRB should a participant have questions. To record participants' consent to participate, we will have them click a radio button labeled "Yes, I agree to take part" or "No, I do not want to take part". We will also have participants insert the current date. Participants who select "Yes, I agree to take part" will be routed to the study survey battery following their typed signature. Participants who select "No, I do not want to take part" will exit the REDCap system and route to a screen that thanks them for their consideration. Copies of the electronic consent from REDCap are attached with this protocol.

There will be instances where only one email address or phone number is available in our records (e.g., patient or parent). Once a participant consents and begins the survey, we will ask: 1.) patients for parents' contact information in the survey and 2.) parents for patients' contact information. Participants may elect not to share this additional contact information.

Aims 3 & 4. We will utilize a mixed methods design to gather data to consider and revise our AYA electronic educational tools as outlined in Table 1.

Table 1. **Overview of Specific Aims and Approach**	
Aim 3. *Develop & demonstrate quality of electronic multimedia materials to educate AYA survivors about LTFU care*	
	INITIAL DEVELOPMENT: Create infographics and videos ↓
Stakeholder Input & Review (N=20)	Semi-structured interviews with AYA stakeholders via teleconference
	REVISION #1: Revise material based on stakeholder review ↓
Aim 4. *Evaluate the impact of electronic educational materials on AYA survivors' knowledge about late effects, perceived benefits, and self-efficacy and intentions to engage in LTFU care.*	
AYA Pre-test & Post-test (N=58)	Pre-test assessment of survivor health beliefs & knowledge via REDCap → 1 week → AYAs review electronic educational material → 2 weeks → Post-test assessment of survivor health beliefs & knowledge via REDCap ↓
AYA Exit Interview (up to N=25)	Exit interviews via teleconference to assess impact on survivor health beliefs

REVISION #2: Revise material based on AYA performance & review
↓

DISSEMINATION: Share AYA educational material via implementation toolkits (R01 CA218389-01) & Post material on www.cancersurvivorlink.org educational platform & share with registrants via email

For Aim 3, eligible stakeholders will be recruited (N=20 AYA survivors) via phone or in clinic by a member of the Aflac Cancer Survivor Research team, and survivors interested in participating will be verbally consented via WebEx. Example questions are outlined in Table 3. These stakeholder reviews will be used to inform revisions to the infographics and videos, which will be made prior to engaging in Aim 4.

For Aim 3 and 4, all interviews will be recorded for transcription/qualitative data analysis.

The consent and interview processes in Aim 3 will be completed sequentially during the subject's webex interview; therefore, this consent discussion will be recorded. All Aim 3 subjects must verbally consent to this recording prior to the recorded consent process. Once the subject has consented to recording, the recording will begin. The study staff will follow Aim 3 telephone scripts for the entire consenting process. Telephone scripts for Aim 3 are included in this protocol.

Once the interview recording begins, study staff will ask if the subject has provided recording consent (for documentation purposes). Next, all subjects will have to confirm their identity (for security and data validity purposes) by providing their name and date of birth. The information provided by the subject must match the information gathered in Epic for the main study consenting to begin. Subjects will then go over the main study and verbally consent for their participation in it.

For Aim 4, we will recruit a total of N=58 AYA survivors to evaluate our revised electronic educational materials (eligibility requirements described above). Recruitment procedures will be the same as in Aim 3 except that in Aim 4, subjects will review and complete consent online as in Aims 1 & 2. The initial page of the REDCap survey will contain a brief online consent outlining the purpose of the study, its voluntary nature, time commitment, incentive information, release of PHI, and contact information of PI and Emory IRB should a participant have questions. To record participants' consent to participate, we will have them click a radio button labeled "Yes, I agree to take part" or "No, I do not want to take part". We will also have participants insert the current date. Participants who select "Yes, I agree to take part" will be routed to the study survey battery following their typed signature. Participants who select "No, I do not want to take part" will exit the REDCap system and route to a screen that thanks them for their consideration. Copies of the online consent from REDCap are attached with this protocol.

After consenting to Aim 4, participants will be asked to complete an online pre-test survey via REDCap. The pre-test will be the first step in a survey queue from REDCap. After subjects complete the pretest, the queue will allow them to review the materials that were created for Aim 4 within the REDCap platform. If the survey queue is started but not finished, study staff may contact the consented subjects via phone call, text or email in order to remind them to finish. Study staff will confirm receipt and review of material and schedule a post-test survey to be completed in REDCap two weeks after material is reviewed (the date when initial survey queue is completed).

These pre- and post-tests will be designed to assess AYA health beliefs, knowledge about survivor care and lateeffects, and self-efficacy and intentions to engage in lifelong survivor care. We have selected scales to assess participants' health beliefs and intentions (Table 3, and will generate a 15-item multiple-choice quiz to assess participants' knowledge of the content covered in the electronic educational materials). The pre- and post-test should take approximately 20-25 minutes each to complete. Up to five reminders will be sent to ensure survey completion.

At the time of initial consent for Aim 4, subjects will have the option to participate in telephone exit interviews via Zoom (N=25), lasting 30 minutes. All Aim 4 exit interviews will be recorded for transcription purposes and conducted 2-3 weeks following completion of the post-test. Example questions are outlined in Table 3. Following the completion of the AYA testing and interviewing, the electronic educational materials will be revised again using the quantitative and qualitative data collected as a guide to inform the revisions prior to dissemination.

D. Measures

Aims 1 & 2: Table 2 outlines the pre-existing factors and modifiable variables that we will assess and instruments we will use to measure these variables. After patients and parents have affirmed their willingness to participate via the electronic consent, they will be asked to complete a battery of self-report measures. The questionnaires will also be administered electronically using the REDCap platform. The surveys will take about 20-35 minutes to complete. Copies of the survey batteries from REDCap for Aims 1 & 2 are attached with this protocol. The following are links to the REDCap Consent and Survey: https://redcap.choa.org/redcap/surveys/?s=KNRMDF7WYX (Aim 1) https://redcap.choa.org/redcap/surveys/?s=TPJY93F7TJ (Aim 2)

Table 2. Methods and Measures (Aims 1 & 2)	
<u>Constructs</u>	**<u>Method/Instrument</u>**
Patient Factors	

Demographics: Gender; Ethnicity; Age; Education; Employment	Demographics Questionnaire
Medical status & risk: Diagnosis; Treatment history & intensity; Late-effects risks, Global Health	Medical record review Intensity of Treatment Rating Scale (ITR-3) PROMIS v.1.1 – Global Health
Neurocognition: Executive Functioning; Perceived Cognitive Competence	Neurocognitive Questionnaire (CCSS-NCQ-R) Health Competence Beliefs Inventory (HCBI)
Developmental Maturity: AYA Autonomy; AYA Self-Efficacy	Health Competence Beliefs Inventory (HCBI) PROMIS SF v1.0 – Self-Efficacy Manage Emotions 4a PROMIS SF v1.0 – Self-Efficacy Manage Soc Inter 8a
Health Knowledge & Beliefs: Health Perceptions; Perceived Benefit of Survivor care; Perceived Vulnerability to Late-effects	Health Competence Beliefs Inventory (HCBI) Benefits Scale for Survivor Screening Absolute Perceived Vulnerability Survivor Knowledge Questionnaire (SKQ)
Psychosocial functioning: Anxiety, Depression, Social Isolation, Anger, & Post-Traumatic Stress Symptoms, Self-Esteem, Social functioning	PROMIS v1.0 Anxiety 8a & Depression 8a PROMIS v1.1 Anger 5a PROMIS v.2.0 – Social Isolation Impact of Events Scale–Revised (IES-R) Posttraumatic Growth Inventory (PTGI) Rosenberg Self-Esteem Scale PROMIS Pediatric Peer Relationships
AYA Healthcare Responsibility	Readiness for Transition Questionnaire (RTQ)- Adolescent Responsibility
Parent & Family Factors	
Parent Psychosocial functioning: Anxiety, Depression, Post-Traumatic Stress Symptoms, Self-Esteem, Social functioning	PROMIS Anxiety/Depression Impact of Events Scale–Revised (IES-R) Posttraumatic Growth Inventory (PTGI) Rosenberg Self-Esteem Scale NIH Friendship - Fixed Form
Parent Health Beliefs: Perceived Benefit of Survivor care; Perceived Vulnerability to Late-effects	Benefits Scale for Survivor Screening Absolute Perceived Vulnerability
Family Functioning: Parental Involvement in Healthcare; General family functioning	RTQ-Parent Involvement Family Assessment Device (FAD)
Family SES: Income; AYA Financial Support Parent education	Demographics Questionnaire
Provider & System Factors	
Patient Satisfaction: Accessibility & Convenience; Communication; Autonomy Support	Patient Satisfaction Questionnaire (PSQ) Health Care Climate Questionnaire (HCCQ)
Access to care issues: Insurance status; Geographic distance, neighborhood-level social determinants	Demographics Questionnaire

Aims 3 & 4: We will accomplish aims 3 and 4 by conducting a comprehensive formative evaluation of interactive infographics and videos designed to educate young adult survivors about the impact of childhood cancer treatment on future health and subsequent need for survivor care across the lifespan. As part of our formative evaluation process, we will seek feedback and revisions from stakeholders (Aim 3), test the effectiveness of these materials with regard to improving knowledge, perceived benefits, self-efficacy, and intentions with AYA survivors through a pretest posttest design (Aim 4), and solicit AYA feedback for additional improvements through exit interviews (Aim 4).

Table 3 outlines the modifiable variables we will measure along with the methods and instruments we will use to measure these variables. After patients have consented and before they review the learning materials, they will complete a pre-test online. Later, after viewing the materials, they will take a post-test online. The questionnaires will be administered electronically using the REDCap platform. The surveys will take about 20-35 minutes to complete. Copies of the pre and post-test surveys from REDCap for Aims 3 & 4 are attached with this protocol.

Table 3. Methods and Measures (Aims 3 & 4)

Quantitative Measures		
Outcome	**Instrument**	**No. of Items**
Aim 4. Change in Knowledge: Pre-test & post-test		
Survivor Care Knowledge	Knowledge questions based on material developed in Aim 1 (Example Questions) - What are late effects of treatment? What determines risk for late effects? - How do survivors' risks for recurrence/chronic diseases/second cancers change over time? - How many survivors experience late effects/chronic diseases during middle age? - What is the point of long-term survivor care? How long do I need to go for survivor care? - What is a Survivor Care Plan? Where do I get a Survivor Care Plan?	15
Aim 4. Changes in Health Belief Model and Patient Activation Constructs: Pre-test & post-test		
Benefit of survivor care	Adapted Champion Benefits Scale for Mammography Screening	5
Barriers to survivor care	Adapted Champion Barriers Scale for Mammography Screening	11
Susceptibility of late effects	Adapted Champion Susceptibility Scale for Mammography Screening	3
Intentions for survivor care	Adapted from Ajzen's Theory of Planned Behavior	2
Self-efficacy	Perceived Health Competence Scale (PHCS)	8
Qualitative Methods		
Aim 3. Stakeholder Review (Example questions)		
Stakeholder semi-structured interview	- What was the main idea the materials were trying to get across? - Is the content complete? What is missing? Is the content current? What should be updated? - Will this appeal to survivors? How can we increase appeal? Is it acceptable and appropriate? - What information do survivors need to manage LTFU care? How can education help? - What should be changed to increase impact on survivors' health beliefs? - If you could change one thing, what would it be?	
Aim 4. AYA Exit Interviews (Example questions)		

AYA Exit Interviews	- What did the materials say/show? Is the information clear? What was confusing? - How would you explain the need for LTFU care to a fellow survivor? - Is the style of the material current? What should be updated? - What do you like about this material? What is off-putting? How can we increase appeal? - Did the material influence your opinions about LTFU care? If, so how? - What did you learn by reviewing this material? - If you could change one thing, what would it be?

IV. Risks, Benefits, & Incentives

This research will inform the development of behavioral interventions designed to help future young adult survivors remain adherence with survivor healthcare. Potential risk is minimal, and relates to data privacy where the study subject's identity and/or medical information may become known by individuals not directly involved in the research. Participants may choose not to answer a question for any reason.

Gift card incentives will be given to participants upon completion survey batteries for Aim 1 ($20) and Aim 2 ($20). An additional $20 gift card incentive will be given to Aim 2 participants who return a signed medical record release to authorize us to review their medical records of the adult providers they transitioned their survivor care.

Stakeholders who complete a 1-hour, semi-structured interview will be provided with a $50 incentive (Aim3). Each participant in Aim 4 will receive a $25 gift card when they complete the pre-test and post-test surveys (total=$50), as well as a $25 gift card for completing an exit interview (total=$75).

If participants would prefer to donate their incentives, we will provide them the option to donate it toward meal tickets for Aflac patient families in need.

V. Data Management & Confidentiality

Participant identifying information will be recorded in a secure Access database for the purposes of recruitment. Participants in Aim 1, Aim 2, and Aim 4 will complete all survey measures in Children's Healthcare of Atlanta's REDCap (http://project-redcap.org/), which is a secure, web-based application for building and managing online surveys and databases. REDCap is HIPAA compliant and designed to support data capture for research studies, providing an intuitive interface for validated data entry; audit trails for tracking data manipulation and export procedures; automated export procedures for seamless data downloads to statistical software packages; and procedures for importing data from external sources. Unique participant identification numbers will be assigned and maintained throughout the database management system to ensure accuracy and protect confidentiality. Outside of the secure REDCap platform & Access database, files will be linked by subject number only. To calculate neighborhood-level social determinants, mailing addresses from the Access database will be linked to 9-digit zip codes using the ArcGIS software program on Woodruff Health Science library computers. On the basis of the 9-digit zip codes, the Area Deprivation Index (ADI) rank will be assigned based on residential Census block group and the Environmental Justice Index (EJI) rank will be assigned based on residential Census tract using the ArcGIS program. All databases will be HIPAA-compliant and password protected. All statistical analyses for Aims 1 and 2 will be conducted using SAS, SPSS® Statistics, or R.

Study data for Aims 3 and 4 will be collected and managed using WebEx and Zoom (AYA interviews) electronic tools hosted at Children's Healthcare of Atlanta and Emory University. AYA survivors' qualitative responses to the teleconference interview questions will be audio-recorded using the secure and HIPAA compliant WebEx (or Zoom) platform and then transcribed. All subjects will confirm their identity prior to the consenting process. Unique participant identification numbers will be assigned to ensure accuracy and protect confidentiality. All databases will be HIPAA-compliant and password protected. All statistical analyses for Aims 3 and 4 will be conducted using SAS, SPSS® Statistics, or NVivo.

No biological specimens will be collected as part of this research. Participants' electronic medical records will be reviewed to abstract treatment data. Confidentiality within this study will be rigidly maintained. Computer files will use study identification numbers only and are password protected. Only necessary personnel will have access to any of these files. Based on existing best practices for security and privacy in health information technology, we will identify the technologies and features to be employed to ensure privacy and security of personal information. This will address identity and access management, secure storage, secure messaging, encryption, and other security technologies and approaches.

VI. Statistical Analysis Plan

Aims 1 & 2: In 2015, the Aflac Cancer Survivor Program (Aflac CSP) saw over 200 AYA survivors aged 18-22 years (Aim 1). Additionally, the Aflac CSP has transitioned approximately N=165 survivor patients since 2013 (Aim 2). Based on our previous research with survivor patients > 18 years of age, we estimate that less than 2% of AYAs will be non-English speakers. During the year-long study period, we anticipate that there will be at least N=200 AYA patients who are eligible for participation in Aim 1 and at least N=160 AYA patients who are eligible for participation in Aim 2. Previous studies with our AYA population have yielded initial recruitment rates and retention rates above 80%. Of the eligible AYA patients, we estimate that 75% [Aim 1: N=220 patient-parent dyads (440 participants), Aim 2: N=120 patient-parent dyads (240 participants), Aim 3: N= 20 patients, Aim 4: N=58] will participate in each aim of the study. In our univariate analysis, these sample sizes provide us with at least 80% or greater power to detect correlations of magnitude ≥ 0.25 and odds ratios of at least 2.5, depending on the prevalence of the risk factor, assuming that approximately 20-30% of patients meet our definition of successful transition. Power analyses were conducted using PASS v. 11 (Kaysville, UT) using a two-sided test for a single correlation and a two sample Z-test for proportions. Given these anticipated numbers, we can assess at most 15 possible predictors for aim 1 and 12 predictors for aim 2 to ensure that we have at least 10 observations per predictor in our principal component analysis.

The primary goals of this study are to determine characteristics that influence or predict transition readiness and transition to adult survivor care. Because there are many candidate predictors and overlap between variables with respective substantive meaning, predictors are likely to be highly correlated (i.e., neurocognition and developmental maturity). Therefore, we propose a three-step modeling process to identify general groups or constructs associated with the outcomes of interest. First, in a univariate analysis setting, we will investigate the relationship between each potential predictor and the continuous outcome transition readiness using simple linear regression and correlation analysis. Similarly, we will use Chi-square tests and/or logistic regression to identify factors associated with the binary outcome successful transition (yes/no). Due to the high correlation/overlap with some of the potential predictors, principal component analysis (PCA) will be performed using those variables significant at the 0.1 level from step 1. The number of components retained in the model with will determined by eigenvalues and percent-variance explained. Finally, based on the results of the PCA, composite variables (which will contain multiple predictors) will be created by standardizing (convert to a z-score) each predictor variable and taking the mean value of the standardized predictor variables that uniquely load on a given component. We will examine the effect of each composite variable on the outcome transition readiness using linear regression and the outcome successful transition using logistic regression. All statistical analyses will be performed using SAS.

Aims 3 & 4: Qualitative data analysis should be conducted until data “saturation”, or the point at which no new information is likely to be garnered from additional interviews/focus groups Given that previous research has indicated that over 85% of analytic themes are identified within the first 12 interviews, we are confident that we will reach saturation of new information with N=20 stakeholder interviews with AYA survivors in Aim 3, as well as N=25 AYA post-test interviews in Aim 4 In order to analyze our qualitative data, separate codebooks for analyzing data will be developed at each stage of the formative evaluation using thematic analyses based on guide questions and evaluation attributes. Following development of the codebooks, each response will be coded by two independent raters. Open coding methods will be used to analytically evaluate the data and comparisons will be made for data similarities and differences A qualitative analysis software package, NVivo, will be used to assist in the identification of patterns and relationships between concepts (i.e., acceptability, appropriateness). Frequencies of all codes will be tabulated and used to inform the revision of the electronic educational materials by types. Differences in the frequency of codes will be examined among subgroups of AYA small group participants (i.e., age, years post diagnosis, gender) using Chi-square and ANOVA analyses. Our team and the Winship Cancer Institute’s Intervention Development, Dissemination and Implementation (IDDI) core has vast experience with qualitative and mixed methods analyses.

In Aim 4, paired t-tests or Wilcoxon signed-rank tests will be used to compare AYA HBM constructs and knowledge about survivor care and late-effects before and after reviewing the electronic educational material. Given 58 AYA survivors, we will have greater than 80% power to detect an average of a 1.5 point increase (or an effect size of 0.40) in AYA average knowledge score after reviewing the electronic educational materials.

After data are exported from REDCap, we will perform data cleaning and run descriptives on all variables. We will analyze pre and posttest differences on knowledge, HBM constructs, self-efficacy and intentions using paired t-tests. Reliability analyses will be run for scales. Differences in HBM constructs, knowledge, PAM activation, and self-efficacy to manage cancer care and demographic or cancer history will be assessed by ANOVAs or independent t-tests to test moderator effects. Power was calculated using a paired t-test with an assumed standard deviation of paired difference of 4.0 points using a 0.05 level of significance and a medium correlation between pre- and post-test.

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