Childhood Cancer Survivor Study
Concept Proposal and Analytic Plan

1. **Study Title**
   Validation of the Fear of Cancer Recurrence Inventory – Short Form (FCRI-SF) in Adult Survivors of Childhood Cancer

2. **Working Group:** Psychology

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4. **Background and Rationale:**

Fear of cancer recurrence is defined as the fear, worry, or concern relating to the possibility that a primary cancer or subsequent malignancy will return or progress to other parts of the body.[1] In survivors of adult-onset cancer, it is estimated that that close to 40% of survivors experience elevated levels of fear of cancer recurrence that impact day-to-day functioning.[2] Moreover, elevated levels of fear of cancer recurrence in survivors of adult-onset cancer are associated with a host of negative outcomes, including elevated psychological distress (i.e., anxiety and depression), physical symptoms (e.g., pain and fatigue), impaired quality of life, and increased prescription of psychotropic medications and use of outpatient hospital services.[2,3]

In recent years, research has started to examine fear of cancer recurrence among *adult survivors of childhood cancer.* Preliminary investigations have found positive associations between fear of cancer recurrence and psychological distress, pain, and increased healthcare utilization in this population.[4,5] In our recent study within the Childhood Cancer Survivor Study (CCSS), one-third of survivors endorsed clinical levels of fear of cancer recurrence – that is, levels of fear of cancer recurrence that are impairing and where psychological interventions would be recommended.[6] Clinical levels of fear of cancer recurrence were also associated with psychological factors (e.g., anxiety, depression), poor self-perceived health, intolerance of uncertainty (i.e., personality-based factor involved in the development of anxiety), and chronic pain.[6]

Unfortunately, initial studies examining fear of cancer recurrence among adult survivors of childhood cancer have used either unvalidated measures of fear of cancer recurrence or

measures that have only been validated in survivors of *adult-onset cancer*.[4,5] This is problematic as these measures may fail to accurately characterize the scope and impact of fear of cancer recurrence among adult survivors of childhood cancer, which significantly limits the conclusions that can be drawn from these studies.

One of the most common measures used to screen for fear of cancer recurrence in survivors of adult-onset cancer is the Fear of Cancer Recurrence Inventory – Short Form (FCRI-SF).[7,8] The 9-item FCRI-SF represents the severity subscale of the Fear of Cancer Recurrence Inventory and was validated among survivors of adult-onset cancer treated within the past four years. The FCRI-SF has been shown to have excellent internal consistency and strong convergent validity with alternative measures of fear of cancer recurrence and psychological distress. The FCRI-SF items are rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (a great deal). Scores on the FCRI-SF range from 0 to 36, and higher scores indicate greater levels of fear of cancer recurrence. Several cut-off scores for clinically significant fear of cancer recurrence have been proposed, including ≥13, ≥16, and ≥22.[7,8]

Indeed, the FCRI-SF would seem to be an optimal measure to assess fear of cancer recurrence among adult survivors of childhood cancer. However, important differences exist between long-term survivors of childhood cancer and adult-onset cancer, which may impact the use and psychometric properties of the FCRI-SF when used among adult survivors of childhood cancer. For example, in contrast to survivors of adult-onset cancer, childhood cancer survivors are at low risk for recurrence of their primary cancer but still at elevated risk for subsequent malignant neoplasms.[9,10] However, items on the FCRI-SF generally ask if survivors are concerned about "the recurrence of cancer" and do not specify concern about the primary cancer and/or subsequent malignant neoplasms. Therefore, survivors may interpret these items as asking about concerns of recurrence of their primary cancer only, which may significantly underestimate fear.

Given these potential differences in the construct of fear of cancer recurrence between survivors of adult-onset cancer and long-term survivors of childhood cancer, studies assessing the psychometric properties of the FCRI-SF among adult survivors of childhood cancer are needed to confirm that it is a valid and reliable measure of fear of cancer recurrence in this population. Despite this, no studies have assessed whether the FCRI-SF is a valid and psychometrically sound measure of fear of cancer recurrence among adult survivors of childhood cancer.

Exploring Aspects of Survivors Pain Ancillary Study

The Exploring Aspects of Survivors Pain (EASE) is an ancillary study within CCSS. The primary aims of EASE were to examine the prevalence and risk factors of chronic pain and pain interference among adult long-term survivors of childhood cancer as well as survivors daily pain experience via ecological momentary assessment (EMA). Moreover, additional aims related to examining the prevalence and risk factors for fear of cancer and intolerance uncertainty were added to EASE in a prior CCSS concept. A random sample of survivors enrolled in CCSS (n=700) were recruited and invited to download Eureka – an mHealth app where all study activities were completed. After study eligibility was assessed and informed consent obtained, all participants completed baseline measures. A total of 38% of recruited survivors downloaded the mHealth app and 35% provided informed consent. The final study sample included 233 survivors.

We are interested in examining the psychometric properties of the FCRI-SF among adult survivors of childhood cancer via the EASE study. Apart from demographic and treatment-related data, the proposed aims and associated analyses only use data already collected as part of the EASE study. The FCRI-SF and associated measures that will be used to determine its validity in this

sample are summarized below. Alex Pizzo, MSc (PhD student in Clinical Psychology in my lab at Concordia University) will be leading this project under my supervision.

Thus far, three manuscripts have been published using data from EASE. The first was the primary study which examined the prevalence and risk factors for chronic pain and pain interference among survivors. This paper also included the EMA portion of the study described above and which examined the daily pain and symptoms experiences of survivors with chronic pain over the course of 2 weeks (see Alberts et al., 2024; PAIN). The second study examined fear of cancer recurrence (see Pizzo et al., 2024; JAMA Open Network). A third manuscript examining intolerance of uncertainty and its associations with pain and psychological symptoms was recently published (see Alberts et al., 2025; Journal of Cancer Survivorship).

Importance of a Psychometric Analysis

Psychometric studies are critical for establishing whether a measure assesses its intended construct and functions equivalently across different populations.[11] As previously stated, although the FCRI-SF has been extensively validated among survivors of adult-onset cancer,[7,8] its psychometric performance has not been examined in adult survivors of childhood cancer. Evaluating the measure in this population is necessary to confirm that the FCRI-SF appropriately captures fear of cancer recurrence among adult survivors of childhood cancer. Accordingly, the additional analyses outlined in the aims below are essential for determining whether the FCRI-SF demonstrates psychometric properties comparable to those observed in samples of adult-onset cancer survivors. Differential psychometric performance in adult survivors of childhood cancer may indicate that the FCRI-SF is not an appropriate measure of fear of cancer recurrence in this population and should be revised.

5. Specific Aims:

Overarching Objective: Examine the psychometric properties of the FCRI-SF within a sample of adult survivors of childhood cancer (N=229).

Aim 1: Examine the internal consistency (i.e., reliability) of the FCRI-SF using Cronbach's alpha.

Hypothesis 1: The FCRI-SF will demonstrate strong internal consistency among adult survivors of childhood cancer.

Aim 2: Examine the construct validity of FCRI-SF via exploratory factor analysis.

Hypothesis 2: All items will load on one factor with loadings of all items of ≥0.35.

Aim 3: Examine the convergent and divergent validity of the FCRI-SF by assessing the associations between scores on the FCRI-SF and measures of depression, anxiety, intolerance of uncertainty, self-perceived physical health, and sleep-related problems.

Hypothesis 3: The FCRI-SF will be significantly correlated with measures of depression, anxiety, self-perceived health, intolerance of uncertainty, and sleep-related problems with effect sizes of ≥0.3.

6. Analysis Framework:

Study population: Adult survivors of childhood cancer who took part in the EASE ancillary study. The final EASE sample included 229 survivors.

Inclusion criteria

- Participant in the EASE study
- CCSS survivors ≥ 18 years of age
- Speak and read English
- Own a smartphone
- Access to data/Wi-Fi/Internet

Outcomes of interest

- **Fear of cancer recurrence** will be assessed by the Fear of Cancer Recurrence Inventory-Short Form (FCRI-SF).[7,8] As previously stated, the FCRI-SF has strong psychometric properties among survivors of adult-onset cancer and contains 9-items that assess the severity of fear of cancer recurrence. Each item is rated on a scale ranging from 0 (not at all) to 4 (a great deal). A summed score is created ranging from 0 to 36, with higher scores indicating greater fear of cancer recurrence. Several cut-off scores for clinically significant fear of cancer recurrence have been proposed, including ≥13, ≥16, and ≥22. Please see **Appendix A** for a copy of the FCRI-SF.

- **Depression** will be assessed with the Patient Health Questionnaire-8 (PHQ-8).[12] The PHQ-8 is composed of eight items rated on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The PHQ-8 assesses symptoms of depression within the last two weeks. Examples of items on the PHQ-8 include “Little interest or pleasure in doing things” and “Feeling, depressed, irritable or hopeless”. The PHQ-8 is a reliable and valid measure of depression with excellent psychometric properties. Higher scores on the PHQ-8 indicate more symptoms of depression and a total score of ≥10 represents the cut-point for moderate or clinically significant depression.

- **Anxiety** will be assessed with the Generalized Anxiety Disorder-7 (GAD-7).[13] The GAD-7 is composed of seven items rated on a 4-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). The GAD-7 assesses symptoms of anxiety within the last two weeks. Examples of items on the GAD-7 include “Feeling nervous, anxious, or on edge” and “Not able to stop or control worrying”. The GAD-7 has strong test-retest reliability, good internal consistency, and good convergent validity with alternative measures of anxiety. Higher scores on the GAD-7 represent more symptoms of anxiety and a total score of ≥10 represents the cut-point for moderate or clinically significant anxiety.

- **Intolerance of uncertainty** will be assessed with the Intolerance of Uncertainty Scale-12 (IUS-12).[14] The IUS-12 is composed of twelve items rated on a 5-point Likert scale ranging from 1 (not at all characteristic of me) to 5 (entirely characteristic of me). Examples of items on the IUS-12 include “Unforeseen events upset me greatly” and “Uncertainty keeps me from living my life”. The IUS-12 has excellent internal consistency and is strongly correlated with measures of anxiety and alternative measures of intolerance of uncertainty. Higher scores on the IUS-12 indicate higher levels of intolerance of uncertainty.

- **Self-perceived physical health** will be assessed using one item from the 36-item Short Form Health Survey.[15] Participants are asked to rate their health on a 5-point Likert scale: 1 (poor), 2 (fair), 3 (good), 4 (very) to 5 (excellent).

- **Sleep-related problems** will be assessed using the National Institute of Health Patient Reported Outcomes Measurement Information System – Sleep Disturbance (PROMIS-SD) – Short Form 8a.[16] The PROMIS-SD Short Form 8a comprises eight items rated on a 5-point Likert Scale. Examples of items include "I was satisfied with my sleep" and "My sleep was restless". The PROMIS-SD Short Form 8a is a reliable and valid measure of sleep difficulties. Higher scores on the PROMIS-SD Short Form 8a indicate more difficulties with sleep.

Covariates

- **Demographic (from FU5 or most recent survey):** age at evaluation, sex, race/ethnicity, household income, education, employment, marital status, assistance with routine needs.

- **Treatment-related (from MRAF frozen data):** age at diagnosis, primary diagnosis, radiation (cranial and non-cranial), chemotherapy, major treatment-related surgery, amputation, relapse/subsequent neoplasm.

7. Statistical Analyses

Aim 1: Examine the internal consistency (i.e., reliability) of the FCRI-SF using Cronbach's alpha.

For aim 1, Cronbach's alpha will be calculated using data from all participants who completed the FCRI-SF. The following criteria will be used to interpret Cronbach's alpha: $\alpha>0.70$ = acceptable, $\alpha>0.80$ = good, $\alpha>0.90$ = excellent.

Aim 2: Examine the construct validity of the FCRI-SF via exploratory factor analysis.

For aim 2, we will conduct an exploratory factor analysis using an oblique rotation and maximum likelihood estimator. Criteria we will use to a select a factor structure include eigenvalues >1, factor loadings, and overall variance accounted for by the model.

Aim 3: Examine the convergent and divergent validity of the FCRI-SF by assessing the associations between total scores on the FCRI-SF and total scores on measures of depression, anxiety, intolerance of uncertainty, self-perceived physical health, and sleep-related problems.

For aim 3, we will calculate Pearson's correlations to assess the relationship between the FCRI-SF and depression, anxiety, intolerance of uncertainty, self-perceived physical health, and sleep-related problems. Pearson's correlations are the gold standard for the assessment of convergent and divergent validity.[11] We will adjust for age at EASE survey completion and sex. Effect sizes will be defined as <0.3 = weak, 0.3 to 0.5 = moderate, and >0.5 = strong. In our prior study (Pizzo et al., 2024; JAMA Open Network), we examined the associations between elevated levels of FCR (i.e., score of ≥22 on FCRI-SF) and elevated levels of depression (i.e., score of ≥10 on PHQ-8) and anxiety (i.e., score of ≥10 on GAD-7), intolerance of uncertainty, and sleep disturbances using modified Poisson regression models. Pearson correlations and continuous scores were not used for these analyses.

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Table 1. Demographic and clinical characteristics of the study population (N=233)

	M (SD)	N (%)
Age at evaluation, years		
Age at diagnosis, years		
Time since diagnosis, years		
Sex		
Male		
Female		
Race/Ethnicity		
White, non-Hispanic		
Black		
Other		
Diagnosis		
Leukemia		
CNS tumor		
Hodgkin lymphoma		
Non-Hodgkin lymphoma		
Osteo/Ewing sarcoma		
Soft tissue sarcoma		
Other non-CNS solid tumor		
Other		
Radiation		
Cranial radiation		
≥20Gy		
<20Gy		
None		
Non-cranial radiation		
None		
Chemotherapy		
Antimetabolites		
Corticosteroids		
Anthracyclines		
Alkylating agents		
Other/none		
Surgery		
Amputation		
Limb sparing		
Other major therapeutic surgery		
None		
Prior Relapse/SMN		
Yes		
No		

Table 2. Factor Loadings for Fear of Cancer Recurrence Inventory – Short Form

Item	Factor Loading
Item 1 FCRI-SF	--
Item 2 FCRI-SF	--
Item 3 FCRI-SF	--
Item 4 FCRI-SF	--
Item 5 FCRI-SF	--
Item 6 FCRI-SF	--
Item 7 FCRI-SF	--
Item 8 FCRI-SF	--
Item 9 FCRI-SF	--

Table 3. Pearson's Correlations

	1	2	3	4	5	6	7	8
1. FCRI-SF	--							
2. Age		--						
3. Sex			--					
4. PHQ-8				--				
5. GAD-7					--			
6. IUS-12						--		
7. Self-Perceived Physical Health							--	
8. Sleep-Related Problems								--

Note. FCRI-SF = Fear of Cancer Recurrence – Short Form; Age = Age at EASE survey completion; PHQ-8 = Patient Health Questionnaire – 8; GAD-7 = Generalized Anxiety Disorder – 7; IUS-12 = Intolerance of Uncertainty Scale – 12.