CCSS Concept Proposal

A. Study title: Evaluating the Need for Dyadic Intervention Adaptation in the Health Insurance Navigation Tools Intervention (HINT)

B. Working group and investigators:

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C. Background and rationale:

C1. Multiple reports from the Childhood Cancer Survivor Study (CCSS) detailed that childhood cancer survivors require health insurance assistance. While more childhood cancer survivors have insurance following the implementation of the affordable care act (ACA),[1] they have a history of lacking knowledge about ACA provisions.[2] Childhood cancer survivors are more likely than siblings to be uninsured[3] and experience financial hardship across all domains (behavioral, material, and psychological).[4,5] Those who are older at diagnosis, female, and with chronic conditions are most at risk for financial hardship.[6] While having health insurance increases survivors' likelihood of receiving follow-up primary and specialty care,[7] job lock (i.e., fear of leaving a job due to losing health insurance) is a problem for one in four survivors.[8] Job lock, as well as enrollment in supplemental security income and disability insurance, is more common among childhood cancer survivors with severe chronic conditions, suggesting that certain groups of survivors experience different access to insurance.[8,9] Caregivers play a critical role in supporting the health, wellbeing, and financial outcomes of childhood cancer survivors, and are often equally impacted financially as their assets and finances are often shared with survivors. Despite decades of research, financial support remains one of the top unmet needs among cancer caregivers.[10] Improving health insurance literacy (HIL) may be one solution to this persistent gap.

C2. Promising interventions exist for improving HIL among childhood cancer survivors. The Health Insurance Navigation Tools (HINT) intervention is a virtually delivered patient navigation program that has demonstrated feasibility, acceptability, and strong preliminary efficacy for improving HIL and reducing financial toxicity in a pilot randomized controlled trial (RCT) among 82 CCSS participants.[11] HINT has five educational sessions on key health insurance topics, with

the goal of improving insurance literacy and knowledge. Following the successful pilot, the HINT efficacy trial is now enrolling survivors from CCSS to be randomized to receive a navigator delivered version of HINT (HINT-S), a video version of HINT (HINT-A), or usual care, which is a booklet on insurance. To date, n=295/520 participants have enrolled in the HINT efficacy trial. Addressing low HIL reduces financial hardship among childhood cancer survivors, but certain survivors face substantial barriers (e.g., cognitive limitations, chronic conditions), that require caregiver involvement.

C3. Caregivers of childhood cancer survivors could play an essential role in supporting survivors' insurance and cost management, but no studies to date have included them. The inclusion of caregivers, non-clinical family members or friends who support the cancer survivor, could greatly equalize the benefit of HIL for all survivors, and improve caregiver outcomes. During the pilot RCT, 39% of HINT participants endorsed the desire for a family member or friend (henceforth referred to as a “caregiver”) to be involved in the intervention. Reasons for this included that some survivors may have a spouse/partner as their insurance policy holder. Other survivors, such as those with neurocognitive limitations or other severe chronic health conditions, may require additional assistance to navigate health insurance, manage finances, and support their health care management. Thus, a dyadic version of HINT may be necessary to support all survivors equally. However, dyadic interventions that include both a survivor and a caregiver can be complex and may be more or less suited for different groups of survivors. Thus, the current HINT trial includes questions in the 12-month follow-up survey regarding survivor interest in caregiver participation.

C4. For this CCSS Career Development Grant, we propose to gather data to inform a future dyadic trial of HINT within the CCSS. In Aim 1, we will analyze the HINT 12-month follow-up survey data combined with existing CCSS data (i.e., neurocognitive impairment, chronic illness) to investigate factors associated with the extent to which participants endorse caregiver involvement in HINT (**primary outcome**). Further, in Aim 2 we will purposively interview HINT participants from each intervention arm (approximately 10 per arm), who endorsed caregiver involvement in HINT and those who did not, to identify barriers, facilitators, and necessary adaptations for a future dyadic intervention. We estimate, with our current 90% 12-month survey completion rate, that we will have approximately 240 12-month follow-up survey respondents for analysis and subsequent interview recruitment over the next year. Our specific aims are to:

D. Specific aims/objectives/research hypotheses:

Aim 1: Examine sociodemographic and clinical factors that are associated with endorsement of caregiver involvement in HINT. We will analyze 12-month follow-up surveys of current HINT participants combined with CCSS data to evaluate their responses to questions about caregiver involvement in HINT.

> *H1: Survivors who are younger, married/partnered, and who are not their own insurance policy holder, who have low HIL and high financial hardship will be more likely than older, single, policy holders, those with high HIL and low hardship to endorse caregiver involvement.*
> *H2: Survivors who report neurocognitive impairment and those with severe chronic conditions will be more likely than survivors without these conditions to endorse caregiver involvement.*
> *RQ 1: Are participants who engaged in HINT-S and HINT-A more or less likely to desire caregiver involvement than those randomized to usual care?*

Aim 2: Explore survivor preferences for caregiver involvement in future dyadic implementation of the HINT intervention. Through purposive sampling, we will interview

participants from each study arm who do and do not endorse caregiver involvement in HINT to explore qualitatively:

RQ 1. Among survivors who wanted caregiver involvement, what educational content, modes of delivery, and dyadic features are preferred by survivors for engaging in HINT with a caregiver?

RQ 2. Among survivors who did not want caregiver involvement, what do they perceive as the barriers and limitations to caregiver involvement and how might those be overcome?

Aim 3: Contextualize the survey findings through integration of the interview feedback regarding the content, modes of delivery, and dyadic features required for caregiver involvement. As part of this aim, we will generate potential solutions to barriers and limitations of a dyadic rollout of HINT.

E. Analysis framework:

Only Aim 1 of the proposed study will require CCSS data. Our proposed Aim 1 analysis will begin by estimating descriptive statistics (mean, percentage) to summarize sociodemographics and cancer factors. Then, bi-variate associations will be estimated to compare differences in the outcome, caregiver endorsement, by sociodemographics, cancer factors, HIL, and financial toxicity (*H1*). Next, we will perform multivariable logistical regression analyses, controlling for key sociodemographic and cancer factors. We will consider options for variable selection in the models, including elastic net techniques. Key predictors of interest will be maintained in the models to ensure the aims of the study are achieved (e.g., neurocognitive impairment, chronic conditions). The first regression will estimate the odds of caregiver endorsement by neurocognitive impairment and chronic conditions (*H2*). We will examine alternatives for grouping chronic conditions, but our plan is to operationalize as no conditions, mild-moderate (1-2), and severe/life-threatening/ disabling (3-4), like prior CCSS studies.[16] We will also explore the extent to which those with visual or auditory chronic conditions may be more likely to want caregiver involvement. The second regression will compare whether, when controlling for potential confounders, participants in the HINT-A or HINT-S arm are more or less likely to endorse caregiver involvement than usual care participants (*H3*).

E1. Outcome(s) of interest:

Our **primary outcome** is the extent to which survivors endorse caregiver involvement in HIT. This is derived from a question in the HINT 12-month follow-up survey asking participants if they think it would be helpful to have a caregiver (spouse/partner, family member or friend) involved in the study. Response options are recorded on a scale of 1-10 with 1=no interest to 10=high interest. Individuals rating 7-10 are considered “interested” for the purposes of this study and those with scores 1-6 are considered disinterested (binary outcome), although we will explore different ranges once the surveys are complete to better understand potential patterns of interest, including potentially operationalizing this as an ordinal variable if there are no clear patterns of high and low interest, in which case we would adjust the statistical tests accordingly.

E2. Subject population to be included and, if appropriate, cases and controls:

Our sample will include childhood cancer survivors from CCSS who enrolled in the ancillary HINT study. This is the only inclusion criteria for this secondary data analysis (Aim 1, Aim 2). We propose to link survey records from HINT participants to CCSS data for Aim 1 analyses. The

purpose of this linkage is to examine potential differences in participants' preferences for caregiver involvement in HINT (primary binary outcome) by whether the patient experiences neurocognitive difficulties (operationalized using CCSS-NCQ) and those with severe chronic illnesses (operationalized using the Chronic Conditions measure (CTCAE v3). We will require support from CCSS staff to facilitate data access to the CCSS data for inclusion of the CCSS-NCQ and CTCAE v3 measures in the statistical analysis for Aim 1. For Aim 2, we will collect primary data from interviews with purposively selected HINT respondents. Aim 2 will not require any additional CCSS data. HINT excludes individuals who have a proxy complete their surveys, thus we will likely systematically exclude survivors who have the more severe neurocognitive impairment. This is a limitation that will be acknowledged in resultant manuscripts.

E3. Exploratory variables:

The following exploratory variables are being requested from the CCSS for Aim 1 analyses. Additional variables from the HINT survey are shown in the Table below.

- Marriage, education, employment
- CCSS-NCQ
- Chronic conditions (CTCAE v3)
- Cancer factors

Independent variables and data sources		
Variables	*Examples*	*Source*
Sociodemographics	Current age, sex, race/ethnicity, insurance status,	HINT
Cancer factors	Diagnosis type, time since diagnosis, age at diagnosis	CCSS
Health insurance literacy (HIL)	Health insurance literacy measure, 9 -items[12]	HINT
Financial hardship	Material, behavioral, and psychological domains	HINT
Intervention arm	HINT-A, HINT-S, usual care	HINT
Neurocognitive impairment (Revised CCSS-NCQ)	Domains include: emotional regulation, organization, task efficiency, memory, impaired status $\geq 90^{th}$ percentile[13]	CCSS
Chronic conditions (CTCAE v3)	Severity: no condition, mild (Grade 1), moderate (Grade 2), severe (Grade 3), life threatening/disabling (Grade 4)[14,15]	CCSS

Continued below.

E4. Draft tables/figures

Table 1. Preferences for caregiver involvement in HINT by sociodemographic and cancer factors (N=xx)

Characteristic[1]	Desired caregiver involvement		No caregiver involvement desired		p-value[2]
	N	%	N	%	
Sex assigned at birth					
Female					
Male					
Current age, years					
26-39					
40-54					
55-66					
Race/Ethnicity					
Asian/Pacific Islander					
Black					
Hispanic					
Non-Hispanic White					
Age at diagnosis, years					
0-4					
5-9					
10-14					
15-20					
Original cancer diagnosis					
Leukemia					
Non-Hodgkin lymphoma					
Hodgkin lymphoma					
Wilms tumor					
Soft tissue sarcoma					
Bone cancer					
Central nervous system tumor					
Neuroblastoma					
Marital status					
Married					
Never married					
Divorced/separated					
Education					
High school diploma/GED or less					
Some college/technical school					
College graduate or higher					
Health and cancer treatment information					
History of subsequent malignant neoplasm					
Yes					
No					
Recurrence of primary cancer					
Yes					
No					
Radiation therapy for treatment of primary cancer					

Yes					
No					
Chemotherapy for primary cancer treatment					
Yes					
No					
Surgery for primary cancer treatment					
Yes					
No					
Anthracycline treatment					
Yes					
No					
Alkylating agent treatment					
Yes					
No					
Unknown					
Cranial radiation treatment					
Yes					
No					

[1] Variables missing for xxxx

[2]Chi-square or Fisher exact tests (applied for cells with sample size less than n=5).

Table 2. Preferences for caregiver involvement in HINT by financial toxicity, chronic conditions, and neurocognitive impairment (N=xx)

	Desired caregiver involvement		No caregiver involvement desired			Odds of endorsing caregiver involvement		
	N	%	N	%	p-value[1]	aOR[3]	95% CI	p-value
Health insurance literacy								
High literacy						Ref.		
Low literacy								
Financial toxicity								
<16								
≥16						Ref.		
Chronic conditions								
No conditions						Ref.		
Mild-moderate (Grade 1-2)								
Severe/Life-threatening/Debilitating (Grade 3-4)								
Visual conditions[2]								
Yes								
No						Ref.		
Auditory conditions[2]								
Yes								
No						Ref.		
Neurocognitive impairment								
No impairment						Ref.		
Memory								
Task efficiency								
Organization								
Emotional regulation								

[1]Chi-square or Fisher exact tests (applied for cells with sample size less than n=5).
[2]Among those with any conditions
[3]Adjusted for age, sex assigned at birth, insurance status

Table 3. Preferences for caregiver involvement in HINT by intervention arm (N=xx)

	Odds of endorsing caregiver involvement[1]			Adjusted odds of endorsing caregiver involvement[1]		
Intervention arm	OR	95% CI	p-value	aOR	95% CI	p-value
Usual care HINT-S HINT-A	Ref.			Ref.		

[1]Adjusted for potential confounders, including age, sex assigned at birth, insurance status

F. Special consideration: Provide any additional information that you consider important in considering the proposed analysis.

This explanatory sequential mixed methods study will occur cross-sectionally, with a secondary data analysis of HINT 12 month survey responses and iterative semi-structured interviews with HINT participants. The HINT study excludes individuals who require a proxy to participate in research, so those with the most severe neurocognitive impairment may be systematically excluded, and this will be reported as a limitation. The only additional CCSS data required are: CCSS NCQ and CTCAE for the participants enrolled in the HINT trial. All other required data are collected as part of the HINT ancillary study.