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Project Requirements and Description

Requirements to submit AOI (all answers must be "yes" to proceed)

A comprehensive review of previously published data has been completed	Yes
The specific aims are clear and focused	Yes
The investigator has appropriate experience and expertise to develop the concept proposal; if not, has identified a mentor or senior co-investigator.	Yes
The investigator agrees to develop an initial draft of the concept proposal within 6 weeks of approval of the AOI and to finalize the concept proposal within 6 months	Yes

Project Title	Post-Traumatic Growth (PTG) and Life Satisfaction (LS) as Predictors of Long-Term Functioning in Childhood Cancer Survivors

Planned research population (eligibility criteria)

Childhood Cancer Survivor Study (CCSS) survivors from the original cohort who:
•   Were ≥5 years old at cancer diagnosis to ensure autobiographical memory of their cancer experience, a prerequisite for valid measurement of post-traumatic growth.
•   Were alive and completed Baseline assessments

•   Have Modified Post-Traumatic Growth Inventory (PTGI) and/or Cantril's Ladder of Life (Cantril's Ladder) data available at FU2. These are our primary exposure/independent variables. In addition to measuring these variables globally, we will subcategorize as follows:
•   PTG subscales (as per Taku et al. Journal of Traumatic Stress, Vol. 21, No. 2, April 2008, pp. 158–164):
    o   New possibilities (items 3, 7, 11, 14, 17)
    o   Relating to others (items 6, 8, 9, 15, 16, 20, 21)
    o   Personal strength (items 4, 10, 12, 19)
    o   Spiritual change (items 5, 18)
    o   Appreciation of life (items 1, 2, 13)
•   LS subgroups (as measured in national Gallup polls)
    o   Thriving (high current/future scores)
    o   Suffering (low current/future scores
    o   Struggling (everyone else)
•   Have data available at ≥1 FU survey for our four outcome/dependent variables of interest:
•   Cognitive functioning: Measured using CCSS Neurocognitive Questionnaire (FU5 Q1-33; FU6 long

version G1-33; FU7 P1-33)
- Emotional functioning: Measured using BSI depression and anxiety symptom subscales (FU5 L1-18; FU7 L1-18)
- Social functioning: Composite variable incorporating the following measured at FU5 and FU7
    o Employment status: Full-time (working full time; student; caring for family) vs. other
    o Marriage/partnership: History (married; living as married; widowed; divorced; separated) vs. single never married
    o Independent living: Yes (live with spouse/partner, alone, with roommates) vs. No
    o Insurance coverage: Yes (yes; Canadian resident) vs. No
- Physical functioning: Measured using frailty criteria (as previously defined in CCSS by Hayek S, et al. J Clin Oncol. 2020 Jan 20;38(3):232-247.) and SF-36 physical component at FU5 and FU7

Proposed specific aims

Aim 1: Characterize survivors based on cluster profiles of post-traumatic growth (PTG) and life satisfaction (LS) at FU2 using the modified Post-Traumatic Growth Inventory (PTGI) and Cantril's Ladder of Life (Cantril's Ladder).
    Aim 1.1: Which profiles of PTG and LS are most predictive of our four long-term functioning outcomes? (see planned research population (eligibility criteria) above for definitions of PTG/LS subcategories and four functioning outcomes)
        1.1.1. Identify and characterize distinct cluster profiles of PTG and LS
    1.1.2. Evaluate predictive utility of said clusters on our four long-term functioning outcomes
    Aim 1.2: Are there host and treatment factors (e.g., demographic, cancer-related, and treatment-related variables) associated with PTG/LS profiles?
Hypothesis: Cluster profiles of PTG and LS at FU2 will more strongly predict our four long-term functioning outcomes compared to the five PTG subscales or three LS subgroups individually
- Methods: Using CCSS survivors with PTGI and Cantril's Ladder data at FU2, we will classify PTG and LS both combined/globally as well as broken down into subscales of PTG and subgroups of LS.
    o Perform cluster analysis on PTG and LS data at FU2 to identify optimal profile groupings to characterize our survivors.
    o Mixed-effects regression models will evaluate associations between different PTG/LS cluster profiles and four functional outcomes over time.
    o Examine differential host and treatment factors for each PTG/LS profile using ANOVA and chi-squared tests respectively

Aim 2: Determine whether neighborhood-level socioeconomic factors modify associations between PTG/LS cluster profiles and our four long-term functioning outcomes.
- Neighborhood socioeconomic status will be measured using the Area Deprivation Index (ADI) derived from residential zip code at FU5.
Hypothesis: Neighborhood-level resources will significantly moderate associations between PTG/LS profiles and long-term functioning outcomes
- Methods: Effect modification will be evaluated by including interaction terms between PTG/LS and SES measures in longitudinal models our four functioning outcomes

Aim 3: Evaluate potentially modifiable factors (e.g., smoking, alcohol consumption and physical activity) as moderators of the relationship between PTG/LS cluster profiles and long-term functioning outcomes.
- Lifestyle and health behavior measures will include:
    o Healthcare engagement (primary care access, screening adherence; FU4–FU8)
    o Physical activity (CDC-recommended ≥150 minutes/week MVPA; FU5, FU8)
    o Sleep quality (Pittsburgh Sleep Quality Index; FU6)
    o Substance use (smoking and alcohol use; FU4, FU5, FU7, FU8)
Hypothesis: Healthy behaviors—including greater healthcare engagement, regular physical activity, adequate sleep, and abstinence from substance use—will amplify the positive associations between PTG/LS cluster profiles and our four long-term functional outcomes.
- Methods: Moderation analyses will assess whether these behaviors strengthen or attenuate associations between PTG/LS profiles and each of the four functioning outcomes using interaction terms in longitudinal regression models.

Will the project require non-CCSS funding to complete?　No

If yes, what would be the anticipated source(s) and timeline(s) for securing funding?

Does this project require contact of CCSS study subjects for:

Additional self-reported information	No
Biological samples	No
Medical record data	No

If yes to any of the above, please briefly describe.
N/A

What CCSS Working Group(s) would likely be involved? (Select all that apply)

	Primary	Secondary
Second Malignancy		
Chronic Disease		✓
Psychology/Neuropsychology	✓	
Genetics		
Cancer Control		✓
Epidemiology/Biostatistics		

Outcomes or Correlative Factors

	Primary	Secondary	Correlative Factors
Late Mortality			
Second Malignancy			

Health Behaviors

	Primary	Secondary	Correlative Factors
Tobacco			✓
Alcohol			✓
Physical Activity			✓
Medical Screening			✓
Other			

If other, please specify

Psychosocial

	Primary	Secondary	Correlative Factors
Insurance	✓		
Marriage	✓		
Education	✓		
Employment	✓		
Other	✓		

If other, please specify

Independent living: Yes (live with spouse/partner, alone, with roommates) vs. No

Medical Conditions

	Primary	Secondary	Correlative Factors
Hearing/Vision/Speech			
Hormonal Systems			
Heart and Vascular			
Respiratory			
Digestive			

	Primary	Secondary	Correlative Factors
Surgical Procedures			
Brain and Nervous System			
Other			✓

If other, please specify

CTCAEv3 correlative factors - see below, Frailty as previously defined in CCSS by Hayek S, et al. J Clin Oncol. 2020 Jan 20;38(3):232-247.

Medications

Describe medications

Psychologic/Quality of Life

	Primary	Secondary	Correlative Factors
BSI-18	✓		
SF-36	✓		
CCSS-NCQ	✓		
PTS			
PTG	✓		
Other			

If other, please specify

Other

	Primary	Secondary	Correlative Factors
Pregnancy and Offspring			
Family History			
Chronic Conditions (CTCAE v3)			✓
Health Status			✓

Demographic

	Primary	Secondary	Correlative Factors
Age			✓
Race			✓
Sex			✓
Other			✓

If other, please specify

Cancer Treatment

	Correlative Factors
Chemotherapy	✓
Radiation Therapy	✓
Surgery	✓

Anticipated Sources of Statistical Support

CCSS Statistical Center	Yes
Local Institutional Statistician	No

If local, please provide the name(s) and contact information of the statistician(s) to be involved.

Will this project utilize CCSS biologic samples? No

If yes, which of the following?

If other, please explain

Other General Comments

This AOI has been discussed and aims approved for submission by the leads of the Psychology working group (Drs. Tara Brinkman and Ellen van der Plas). Dr. Tricia King provided substantial contributions to the development of the study aims and methods as a co-investigator. Additional proposed study members include Dr. AnnaLynn Williams.