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Project Requirements and Description

Requirements to submit AOI

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 Impact of Methods for Incorporating Registry-based Cancer Incidence Data to Study Subsequent Neoplasms in Survivors of Childhood Cancer

Planned research population (eligibility criteria)

Eligible participants include all CCSS survivors who completed a baseline questionnaire and survived to the start of the registry coverage time period (to be determined). As appropriate, some analyses will consider the “all eligible” 5-year survivor population (vs. CCSS participants).

Proposed specific aims

The current subsequent neoplasm (SN) adjudication process in CCSS, where questionnaire-reported SNs are verified by pathologist/oncologist review of pathology/medical records or death certificates, is labor intensive and may result in an under-ascertainment of SNs due its reliance on initial self/proxy reports (e.g., more false negatives due to questionnaire non-response, i.e., loss to follow-up). We propose to formally evaluate various approaches to supplement or replace aspects of current CCSS procedures to ascertain SNs by integrating data from the Virtual Pooled Registry-Cancer Linkage System (VPR-CLS), which facilitates linkages between cohort studies and US population-based state and regional cancer registries. As of 2022, VPR-CLS includes 45 registries covering 95% of the US state populations and Puerto Rico, with most registries initiating data collection after 1995 (PMID: 39102879). Analyses for the aims below will be designed acknowledging the limitations posed by incomplete VPR-CLS US state coverage, the lack of VPR-CLS data for recent time periods, and the impracticality of matching CCSS participants’ residential information during

follow up with specific registries.

Specific Aims:

Aim 1: Compared with the current CCSS procedure for SN ascertainment, assess the overlap in SNs and changes in SN descriptive epidemiologic measures (incidence, and using SEER registry data, standardized incidence ratio and absolute excess risk) using different approaches for SN ascertainment that integrate VPR-CLS cancer incidence data with CCSS data. SNs overall (excluding neoplasms not collected in VPR-CLS) and specific SNs will be evaluated.

SN ascertainment approaches:

(a) Validated self-report only + NDI (National Death Index): This is current approach (benchmark).

Examples of the other SN ascertainment approaches that integrate VPR-CLS cancer data that may be investigated:

(b) CCSS SNs, VPR-CLS-supplemented: The limited subset of CCSS-adjudicated SNs that were self-reported but not confirmed by medical record or pathology review (e.g., death certificate-based or SNs based only on self-report) will be supplemented by VPR-CLS data, clarifying age of onset and site information.

(c) CCSS SNs, VPR-CLS-enhanced: Same as (b), but enhance SN data with any registry-based SNs not captured by the CCSS adjudication process (i.e., through last follow-up survey) and all additional registry-based SNs that are reported as of the VPR-CLS coverage end date.

(d) VPR-CLS-only + NDI: Only use SNs reported to VPR-CLS as well as any SNs identified via death certificates that are not reported to VPR-CLS.

(e) VPR-CLS-only + NDI + self-report: Same as (d), but use VPR-CLS and NDI data first for SN ascertainment and supplement with any self-reported SNs from CCSS surveys that are not captured in registry data.

(f) VPR-CLS-only + NDI + validated self-report: Same as (e), but selectively apply current CCSS adjudication procedures for the self-reported SNs not captured via VPR-CLS or NDI.

Aim 2: Evaluate whether the distribution of SN types or survivor characteristics (e.g., demographics, childhood cancer diagnosis, treatment) differs across SN ascertainment approaches.

Aim 3: Quantify the differences in time/effort and if feasible, financial cost between the SN ascertainment approaches.

- Aim 3a: Enumerate the steps of the existing CCSS SN ascertainment procedures that affect time/effort and other costs and identify components that could be more efficient.

Aim 4: Considering the current CCSS SN ascertainment approach as the benchmark, quantify differences in bias and precision for measures of association for previously reported treatment-/cancer-related risk factors for SNs overall and specific SNs for each evaluated VPR-CLS-integrated SN ascertainment approach.

- Aim 4a: Conduct similar analyses in the all-eligible population (millennium CCSS cohort) to assess associations between SN incidence and treatment-/cancer-related risk factors, adjusting for demographic characteristics.

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.

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

Medical Conditions

	Primary	Secondary	Correlative Factors
Hearing/Vision/Speech			
Hormonal Systems			
Heart and Vascular			
Respiratory			
Digestive			
Surgical Procedures			
Brain and Nervous System			
Other			

If other, please specify

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	Yes

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

Wendy Leisenring, Cindy Im

Will this project utilize CCSS biologic samples? No

If yes, which of the following?

If other, please explain

Other General Comments

Senior investigators are Lucie Turcotte, Wendy Leisenring, and Greg Armstrong.

Agree I agree to share this information with St. Jude

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