Cancer Control and Intervention Working Group

A Report from the Childhood Cancer Survivor Study

Claire Snyder, PhD, and Paul Nathan, MD, MSc, on behalf of the Working Group

CCSS
Childhood Cancer
Survivor Study

St. Jude Children's
Research Hospital

An NCI-funded Resource

Scope of Research

Focused on reducing the long-term impact of cancer therapy on physical, psychological and social outcomes

- Health care utilization and late effects surveillance
- Health behaviors
- Health status
- Financial and social outcomes
- Interventions designed to promote early detection or reduce risk of late effects

Working Group Membership

CCSS

Member	Institution
Paul Nathan, MD, MSc (Co-Chair)	Hospital for Sick Children; University of Toronto
Claire Snyder, PhD (Co-Chair)	Johns Hopkins Schools of Medicine and Public Health
Jackie Casillas, MD, MSHS	University of California-Los Angeles
Elena Elkin, PhD, MPA	Columbia University
Jennifer Ford, PhD	Hunter College-CUNY
Tara Henderson, MD, MPH	University of Chicago-Medicine
I-Chan Huang, PhD	St. Jude Research Children's Research Hospital
Melissa Hudson, MD	St. Jude Research Children's Research Hospital
Xu Ji, PhD, MSPH	Emory University
Anne Kirchhoff, PhD, MPH	University of Utah
Wendy Leisenring, ScD	Fred Hutchinson Cancer Center
Kiri Ness, PhD	St. Jude Research Children's Research Hospital
Kevin Oeffinger, MD	Duke University
Jennifer Yeh, PhD	Dana-Farber/Harvard Cancer Center

Working Group Progress

8	Published/In Press Manuscripts (since 1/1/2020)
1	Currently Submitted Manuscripts
8	Analysis/Manuscript in Process
NA	Concepts in development
7	New AOIs (total, since 1/1/2020)

Highlights of Recently Completed Research

- Progress on financial hardship analyses
- Bhatt et al “Temporal Changes in Employment Among Survivors of Childhood Cancer”

Financial Hardship Analyses

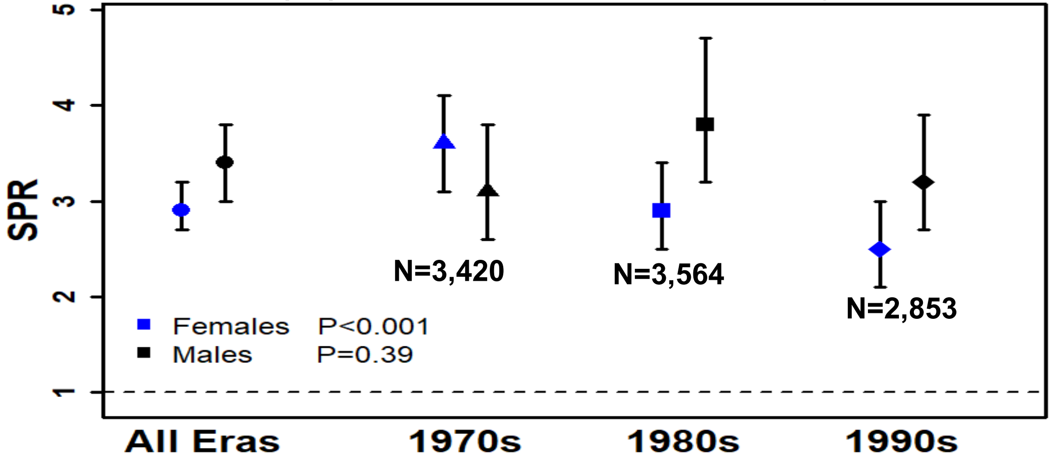
- Master paper (Nathan et al.):
  - Revision submitted to JCO
  - Compares survivors to siblings on 21 items
  - Factor analysis defined 3 domains: behavioral hardship; material hardship/financial sacrifices; psychological hardship

- Other approved concepts using data:
  - Impact of evolution of chronic conditions on financial hardship (Huang)
  - Comparison of financial hardship in siblings to general population (Ohlsen/Chow)
  - Impact of community economic characteristics on financial hardship in AYA (Fauer/Ganz)
  - Financial hardship in stem cell transplant survivors (Buchbinder)
  - Changes in insurance pre/post ACA (using data from prior insurance ancillary study; Park/Kirchhoff)

Temporal Changes in Employment Among Survivors of Childhood Cancer

- **Aim 1:** Assess the prevalence of health-related unemployment across treatment eras (1970-79, 1980-89, 1990-99) and the impact chronic conditions compared to the general population
- Sample matched to participants in the Behavior Risk Factor Surveillance System (BRFSS) by sex, race/ethnicity, census bureau division, age, and year of survey

Standardized prevalence ratio (SPR) and 95% confidence interval (CI) for health-related unemployment



Relative standardized prevalence ratios (rSPR) of chronic conditions with health-related unemployment among survivors

Chronic conditions	Female rSPR (95% CI)	Male rSPR (95% CI)
One grade 2, no grade 3-4	1.1 (0.7-1.8)	1.2 (0.7-2.1)
Two or more grade 2, no grade 3-4	2.9 (1.8-4.5)	2.2 (1.3-3.9)
One grade 3-4	4.0 (2.8-5.7)	3.4 (2.3-5.0)
Two or more grade 3-4	10.1 (7.2-14.0)	7.6 (5.3-11.0)
No grade 2, no grade 3-4	1	1
Models adjusted for age at survey, age at diagnosis, race/ ethnicity		

Conclusions:

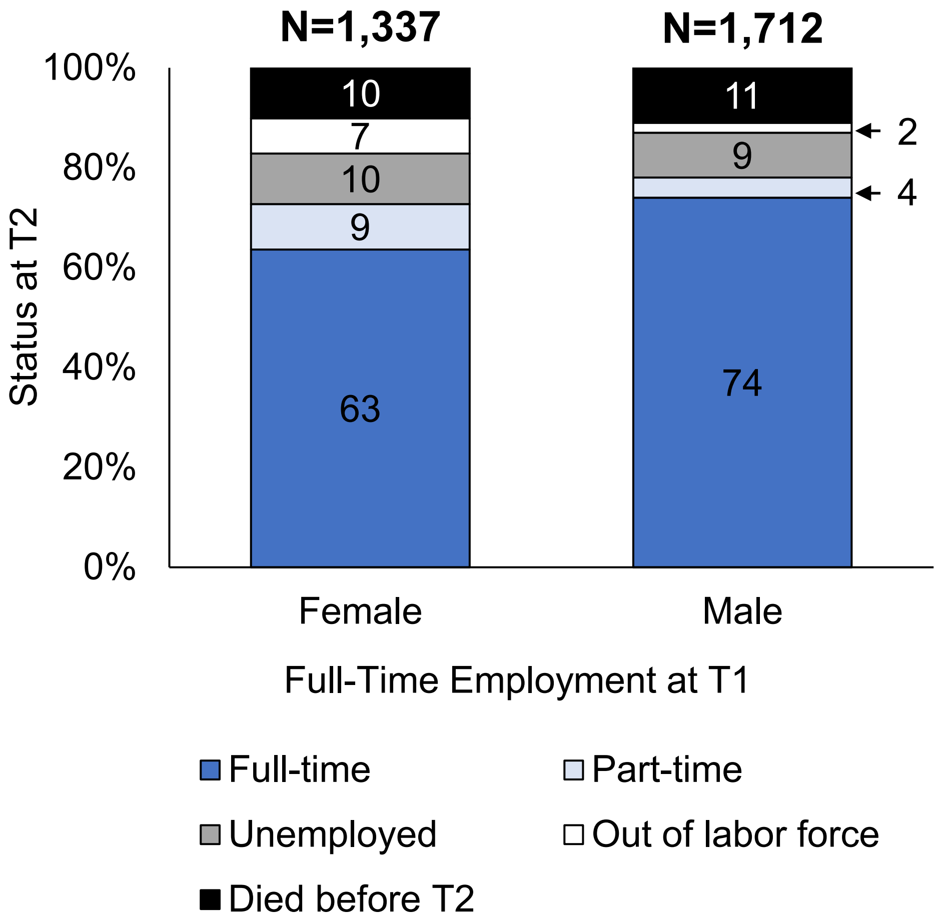
- Compared to the general population, survivors had a persistently higher prevalence of health-related unemployment across all three decades.
- Changes in treatment did not explain the decline in SPR (data not shown here)
- The number and severity of Chronic health conditions are associated with a higher prevalence of health-related unemployment

Slide courtesy of Neel Bhatt

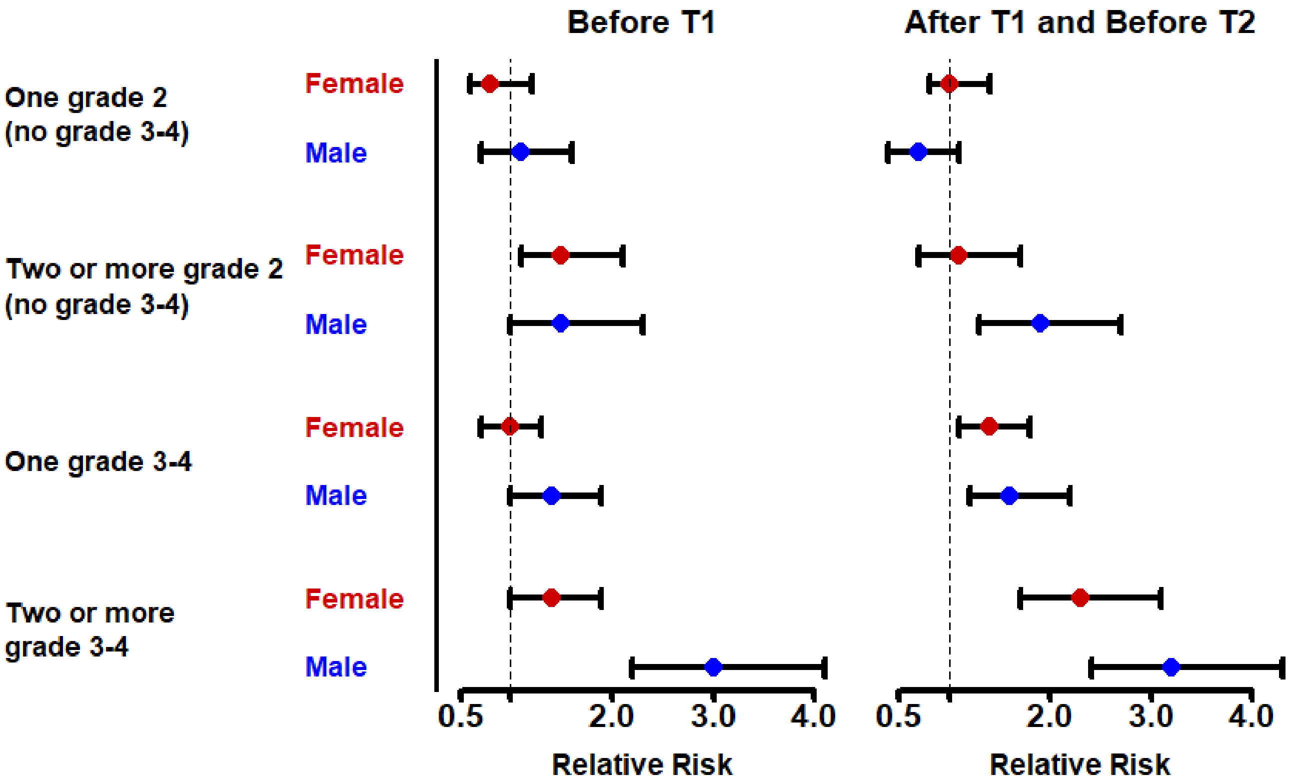
Temporal Changes in Employment Among Survivors of Childhood Cancer

- **Aim 2:** Study the impact of chronic health conditions on negative employment transitions (full-time to part-time or unemployed) between 2002-04 (T1) and 2014-16 (T2)

Status at T2 of survivors reporting full-time employment at T1



Associations between the number, timing, and severity chronic health conditions and negative employment transitions



Conclusion: A substantial portion of adult survivors of childhood cancer with chronic health conditions of varying number, onset, and severity are at risk for losing full-time employment

Slide courtesy of Neel Bhatt

Approved Concept Proposals

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- List proposals approved by the Publications Committee but not yet published (stratified by progress)
  - Concept Progressing as Planned – Analysis/Manuscript in Process
    1. Ohlsen et al. Medical financial hardship among long-term survivors of childhood cancer and their siblings in the Childhood Cancer Survivor Study (CCSS) in comparison to the general population (03/22)
    2. Fauer et al. Impact of Community Economic Characteristics on Financial Hardship among Adolescent and Young Adult Cancer Survivors (11/21)
    3. Buchbinder et al. Financial Hardship Among Adult Survivors of Pediatric Hematopoietic Stem Cell Transplantation (08/21)
    4. Shoag et al. Disparities in Adherence to Screening Guidelines in Hodgkin's Lymphoma Survivors (07/21)
    5. Ji et al. Understanding Health Service Utilization and Cost in Childhood Cancer Survivors Within the Medicaid System (03/20)
    6. Huang et al. Progression of Late Medical Effects and Impact on Financial Hardship Among Adult Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (10/20)
    7. Tonorezos et al. Use and Correlates of Carotid Ultrasound in Survivors of Childhood Cancer (02/20)
    8. Bhatt et al. Temporal Changes in Employment Outcomes of Survivors of Childhood Cancer: A Report from the Childhood Cancer Survivor Study (CCSS) (06/19)
  - Concepts Not Progressing as Planned
    - NA

Ancillary Studies

- EMPOWER-II (Oeffinger)
- Activating cancer Survivors and their Primary care providers to Increase coloREctal cancer Screening (ASPIRES) Study (Henderson, Kim)
- Improving delivery of genetic services to high-risk CCS (Henderson)
- CHIIP (Chow)
- Health Insurance Navigator Program (Park)
- Impact of eHealth intervention for insomnia on late effects of childhood cancer (SLEEPWELL Intervention Trial) (Brinkman)

EMPOWER-II & ASPIRES

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- EMPOWER-II
  - Eligible women treated for a childhood cancer with chest radiotherapy randomly assigned to: control, patient activation using a smartphone-based intervention, or patient activation + primary care provider activation which will include physician materials about breast cancer risk in this population along with guidelines for breast cancer surveillance.
  - The primary outcome is a medical record confirmed breast MRI and mammogram with the goal of increasing the rate of women completing the national guideline-based recommended combination of breast MRI and mammogram.
  - ➢ *Participants are progressing through the study. All participants will be finished with the study by this summer.*
- ASPIRES
  - Colonoscopy is recommended by the Children's Oncology Group, starting at age 35 years in survivors exposed to any radiotherapy to the abdomen or pelvis
  - But over 90% of survivors at high risk for CRC are not adherent to screening colonoscopy in accordance with guidelines.
  - Primary aim: To determine the efficacy of a mobile intervention aimed at: 1) patient activation and; 2) PCP plus patient activation, as compared to control participants receiving targeted mailed education materials on completing a screening colonoscopy.
  - ➢ *In early enrollment phase (began February 2022).*

Improving Delivery of Genetic Services

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- To address the gap in access to genetic services, this study will evaluate the effectiveness of an adapted model of remote delivery of genetic services to increase the uptake of recommended genetic assessment and testing in childhood cancer survivors.
- Aims are as follows:
  - To evaluate the effectiveness of in-home, collaborative PCP model of remote telegenetic services to increase uptake of genetic testing
  - To evaluate the effectiveness of remote videoconferencing to provide greater increase in knowledge and decrease in distress and depression as compared to remote phone services, to examine the moderators of patient outcomes with remote telegenetic services, and to estimate intervention costs and incremental cost-effectiveness of the three study arms.
  - To conduct a multi-stakeholder, mixed-methods process evaluation to understand patient, provider and system factors associated with uptake of counseling and testing in our adapted in-home, collaborative PCP model and facilitators and barriers to uptake to provide recommendations for future implementation.

➢ *Recruitment continues (began August 2021). Some participants now reaching 6-month survey.*

Five Year Plan: Progress Update

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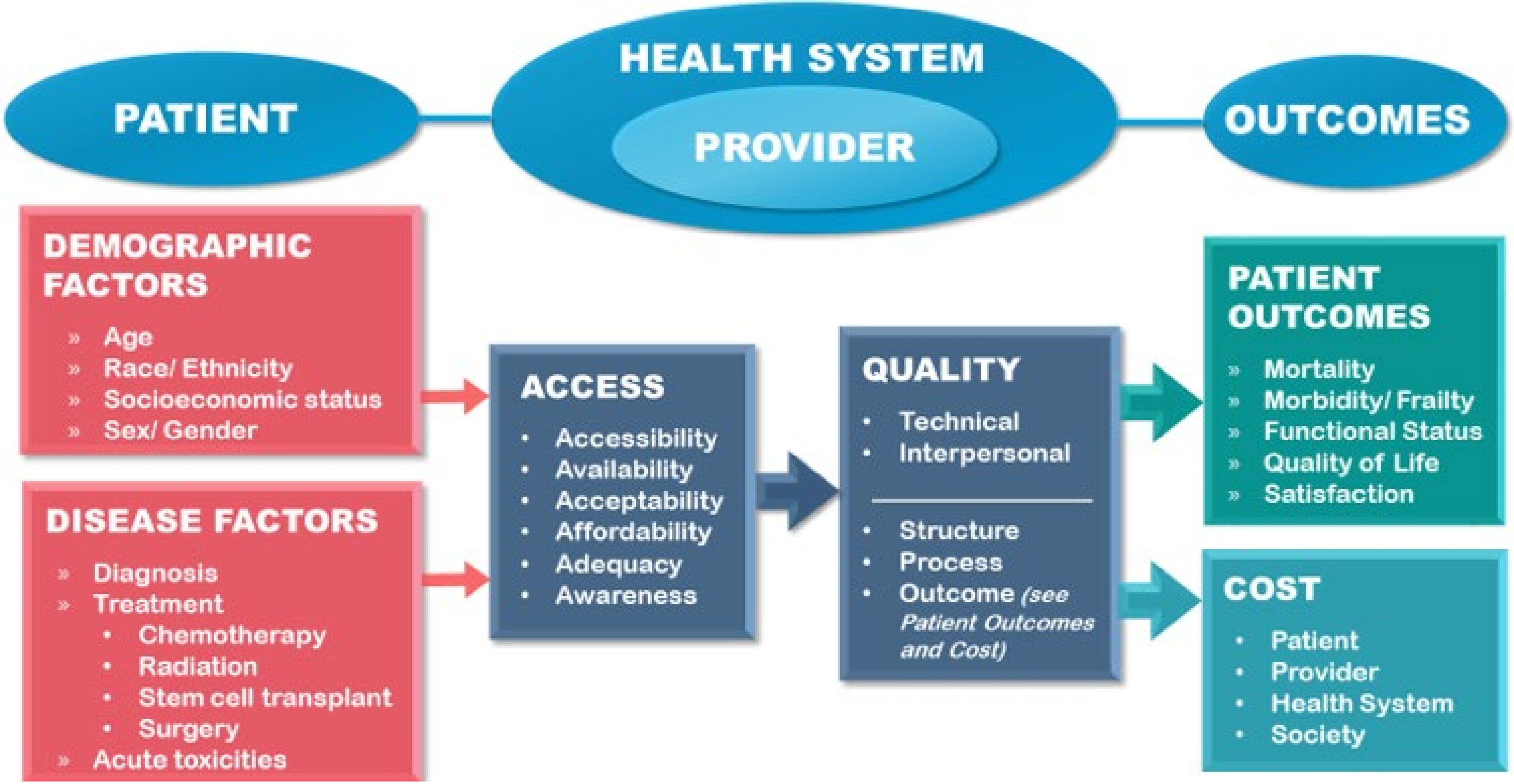
- Translate previous findings into interventions aimed at reducing risk and increasing compliance with guideline-based surveillance and care
  - Studies ongoing looking at screening in colorectal and breast
- Use of mHealth technology … will determine whether behavior change is associated with improvements in objective measures of health outcomes
  - Some ongoing work using the patient portal; SLEEPWELL using activity monitor; others applying for funding
- Explore whether survivors treated in more recent eras adhere more closely to recommended risk-based medical care and surveillance
  - Yan et al. Adherence to surveillance for second malignant neoplasms and cardiac dysfunction in childhood cancer survivors: a Childhood Cancer Survivor Study. JCO 2020
- Study whether survivors treated on contemporary protocols in more recent eras are less likely to experience adverse health status and social outcomes than those treated in prior eras
  - Ness et al. Effects of Temporal Changes in Therapeutic Exposure on Self-reported Health Status in Childhood Cancer Survivors. Annals of Internal Medicine 2017
- Develop and validate other risk prediction models…focusing on pulmonary dysfunction, premature menopause, and neurocognitive dysfunction
  - Clark et al. Predicting acute ovarian failure in female survivors of childhood cancer: a cohort study in the Childhood Cancer Survivor Study (CCSS) and the St. Jude Lifetime Cohort (SJLIFE). Lancet Oncology 2020
  - Yuan et al. *completing work on premature menopause*

New Priorities in 5-year Plan

- Enhance the CCSS resource *by facilitating the conduct of health services research* through collection of data to evaluate patient, provider, and health care system factors and their associations with access, quality, and cost of care

- Provide the research community with a resource that will identify *how survivors' health care influences their outcomes* in order to inform strategies to provide life-long, risk-adapted care to this vulnerable population



PATIENT

HEALTH SYSTEM

PROVIDER

OUTCOMES

DEMOGRAPHIC FACTORS

- Age
- Race/ Ethnicity
- Socioeconomic status
- Sex/ Gender

DISEASE FACTORS

- Diagnosis
- Treatment
  - Chemotherapy
  - Radiation
  - Stem cell transplant
  - Surgery
- Acute toxicities

ACCESS

- Accessibility
- Availability
- Acceptability
- Affordability
- Adequacy
- Awareness

QUALITY

- Technical
- Interpersonal

- Structure
- Process
- Outcome *(see Patient Outcomes and Cost)*

PATIENT OUTCOMES

- Mortality
- Morbidity/ Frailty
- Functional Status
- Quality of Life
- Satisfaction

COST

- Patient
- Provider
- Health System
- Society

Augment CCSS Questionnaires

- Add assessment of survivors' perspectives of their unmet needs in next survey
  - Build on *CCSS Needs Assessment Questionnaire* (Cox et al)
  - 135-item instrument comprising 9 unidimensional domains
- 58 items addressing:
  - Access (e.g., ability to see specialists)
  - Quality (e.g., knowing surveillance recommendations)
  - Costs (e.g., affordability of medical treatments)
- Plus questions regarding health care utilization previously featured in CCSS surveys
- To enable exploration of the associations between unmet needs and poor outcomes (e.g., hospitalizations), as well as health care disparities related to race/ethnicity
- Gaps in care identified by these surveys will inform subsequent research, including intervention studies

Ancillary studies

ANCILLARY STUDY	BACKGROUND & RATIONALE	SIGNIFICANCE
Leveraging the CCSS myLTFU patient portal and mobile app to collect real time data about health care use	• Limited detail regarding health service use can be collected based on retrospective questions asked every 2-3 years • Innovation: real-time reporting of health service use through the portal	• Allows for a deeper, broader and more accurate understanding of health care use in real time • Platform can be leveraged for future intervention studies
Linkage to administrative claims datasets (e.g. Medicaid, private insurance databases, etc.).	• Another approach to obtaining more detailed health service use data is to link with administrative claims databases • A current pilot is linking CCSS participants with Medicaid claims	• Captures granular information about health care use that cannot be obtained by patient report • Allows for more precise assessment of quality of care • Gives critical insight into disparities in care between different provider models
Use of geocoding to assess structural measures of health care quality by linking to area resource files	• Another approach to enhance the health service research opportunities in the CCSS is to obtain data on available resources (e.g., cancer centers, physicians) in geographic areas	• Identifies structural targets for interventions that can enhance survivor care
Obtain perspectives of primary care and specialist physicians regarding care of childhood cancer survivors	• Only limited information on primary care providers' perspectives regarding the care of childhood cancer survivors is available • Because of the many comorbidities experienced by survivors, the perspectives of specialist physicians are also highly relevant	• Will inform development of interventions to improve survivor care that target providers
Estimate the costs of caring for survivors, with an aim towards estimating the cost-effectiveness of different models of survivorship care	• There are many models of childhood cancer survivorship care • Robust data regarding the costs and resource requirements associated with these care models are needed to enable cost-effectiveness analyses	• Will inform decisions around the "best" models of survivor care
Intervention studies	• Possible interventions for exploration include patient navigators, web-based resources, and remote counseling	• Completes the translation of CCSS findings from discovery to having a direct impact on survivor outcomes • Goal is for these to be scalable to the broader population of childhood cancer survivors across North America

Discussion: Challenges & Opportunities

- Measurement of health services use using survey data – a good first step
  - Structure-Process-Outcomes
  - Access-Quality-Cost
- Transitioning from multiple, specific interventions (e.g., breast cancer screening, colorectal cancer screening, genetic testing) to global interventions that address multiple components
- Promoting implementability/disseminability of interventions
- Engagement with childhood cancer survivors and other stakeholders