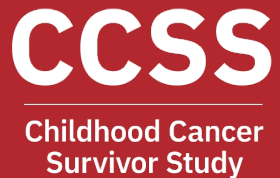


CCSS Investigator Meeting

June 14, 2021



An NCI-funded Resource

Meeting Agenda Overview

CCSS

Time (Central Time)	Presentation
9:00 am – 10:00 am	Principal Investigator Report, Support Facility Reports
10:00 am – 11:00 am	Research Presentations
11:00 am – Noon	Working Group Chair Presentations
Noon – 12:30 pm	Lunch Break
12:30 pm – 1:30 pm	Working Group Chair Presentations
1:30 pm – 2:30 pm	Working Group Breakout Session #1 <ul style="list-style-type: none">-Chronic Disease-Genetics-Epidemiology/Biostatistics
2:30 pm – 3:30 pm	Working Group Breakout Session #2 <ul style="list-style-type: none">-Cancer Control and Intervention-Psychology-Second Neoplasm

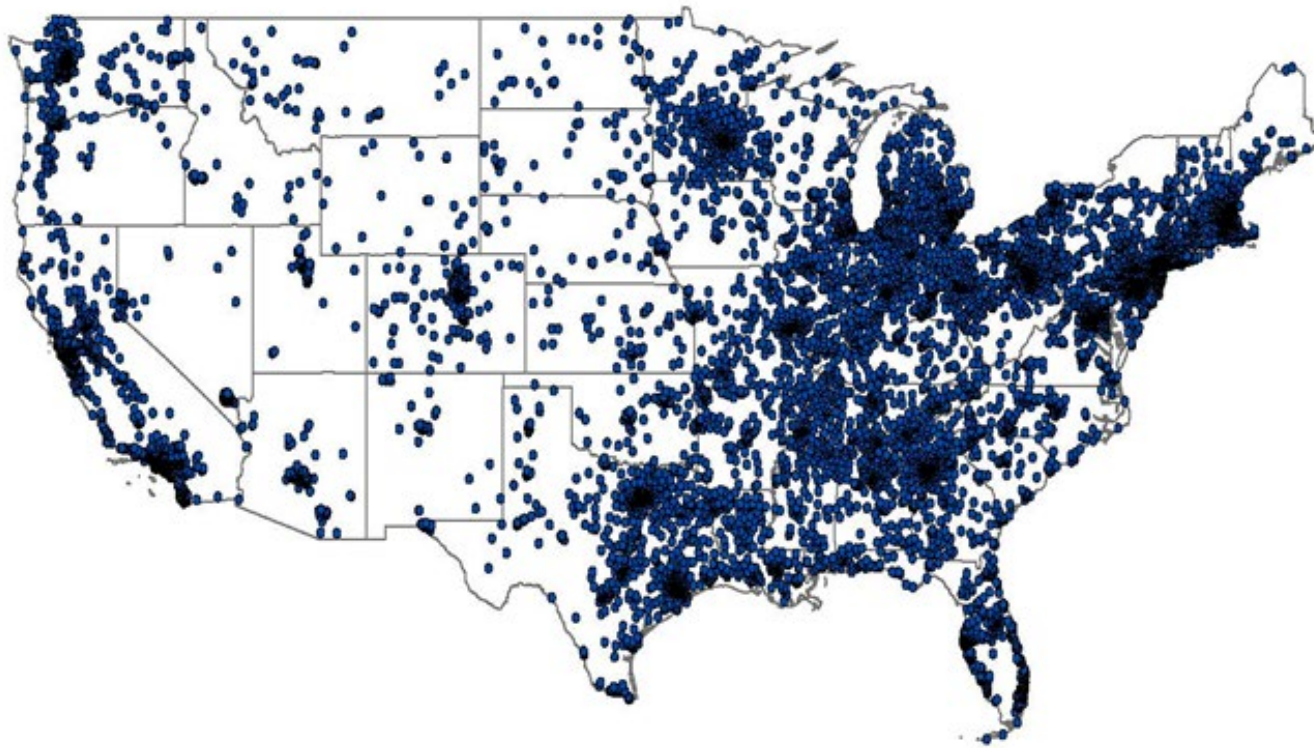
Introduction to the Childhood Cancer Survivor Study

April 19, 2021

Childhood Cancer Survivor Study (U24 CA 55727)

Study Participants

CCSS



Resource for Survivorship Research

- Multi-institutional (n=31)
- 38,036 eligible survivors
- Open resource
- 363 Abstracts presented
- 395 Publications, cited 26,500 times
 - >1,225 Investigators
 - 91 Early career trainees
- 60 Investigator-initiated studies
- \$69.2 million investigator-initiated grant support

- **Limitations of single institution studies**
 - Sample size
 - Heterogeneity of exposure
- **Lack of extended follow-up of childhood cancer survivors**
 - Incomplete and passive follow-up

Childhood Cancer Survivor Study

(U24 CA55727)

CCSS

- Funded in 1994
- Retrospective cohort, recent expansion includes survivors diagnosed 1970-1999
- 5-year survival
- Leukemia, lymphoma, CNS, bone, Wilms, NBL, soft-tissue and bone sarcoma
- Detailed treatment data
- Wide range of outcomes

38,036	Eligible
	20,687 (1970-86)
	16,906 (1987-99)*
↓	
25,665	Participants
	14,361 (1970-86)
	11,304 (1987-99)*

* indicates expansion cohort population

Childhood Cancer Survivor Study (U24 CA 55727)

Participating Centers

CCSS

St. Jude Children's Research Hospital
University of Minnesota
Children's Hospital of Pittsburgh
Stanford University
Dana-Farber Cancer Institute
Children's National Medical Center
Roswell Park Cancer Center
Memorial Sloan-Kettering Cancer Center
Texas Children's Hospital
University of California San Francisco
Seattle Children's Hospital
Toronto Hospital for Sick Children
Denver Children's Hospital
Nationwide Children's Hospital
Emory University
Cook Children's Medical Center

U.T. - M.D. Anderson Cancer Center
Mayo Clinic
Children's Hospitals of Minnesota
Children's Hospital of Philadelphia
St. Louis Children's Hospital
Children's Hospital of Los Angeles
UCLA Medical Center/Miller Children's
Children's Hospital of Orange County
Riley Hospital for Children – Indiana Univ.
UAB/Children's Hospital of Alabama
University of Michigan – Mott Children's
Children's Medical Center of Dallas
Fred Hutchinson Cancer Research Center
Northwestern University
University of Chicago

Population Characteristics

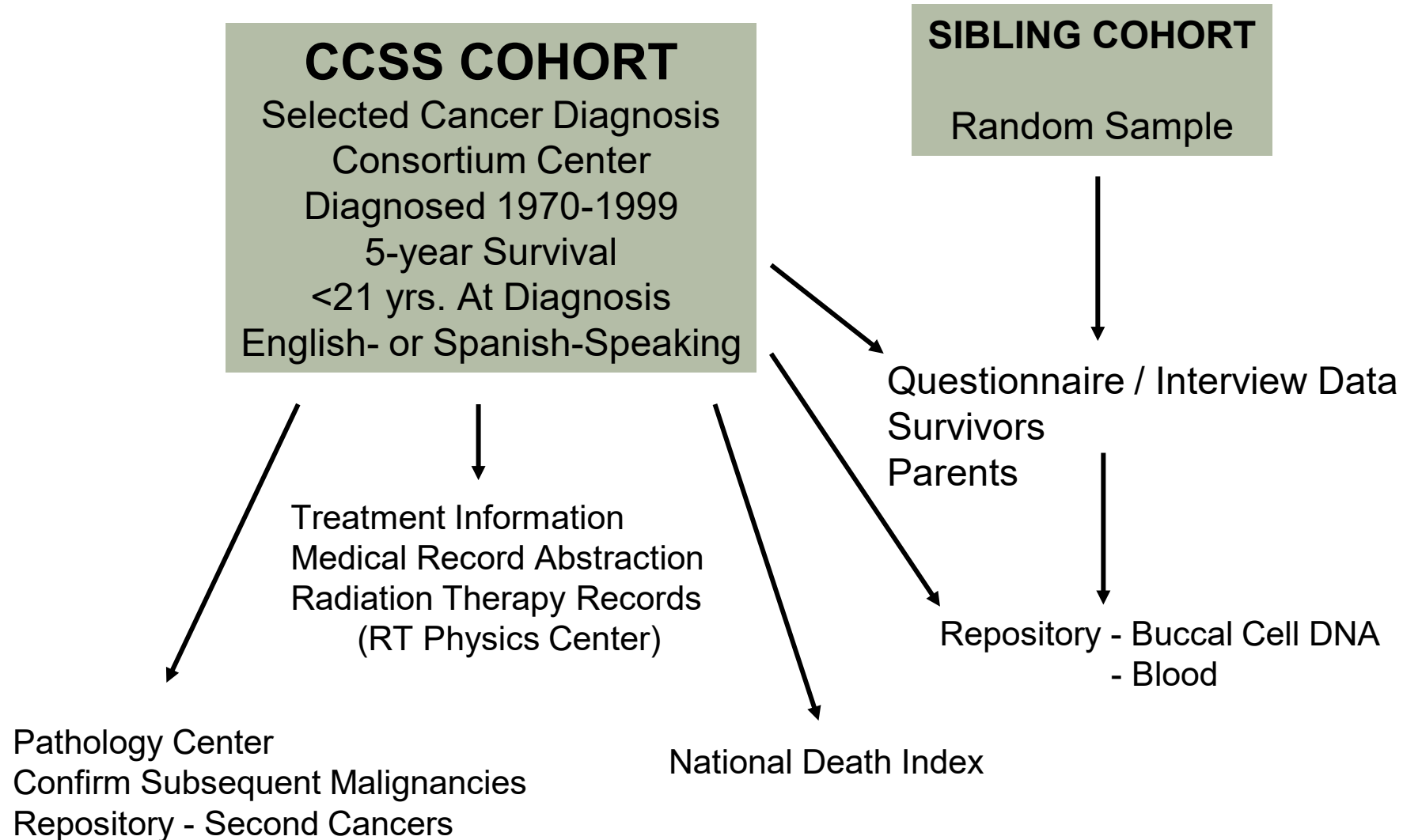
CCSS

Characteristic	Participating	% of Cohort
Primary Cancer Diagnosis		
Leukemia	7,872	40.0%
CNS tumors	4,489	15.2%
Hodgkin lymphoma	3,107	10.5%
Non-Hodgkin lymphoma	2,116	7.1%
Wilms tumor	2,276	7.7%
Neuroblastoma	1,948	6.6%
Soft tissue sarcoma	1,756	5.9%
Bone tumors	2,100	7.0%
Race/Ethnicity		
Hispanic	2,045	8.8%
Non-Hispanic Black	1,704	6.7%
Non-Hispanic, Mixed Race	1,030	4.7%

Childhood Cancer Survivor Study (U24 CA 55727)

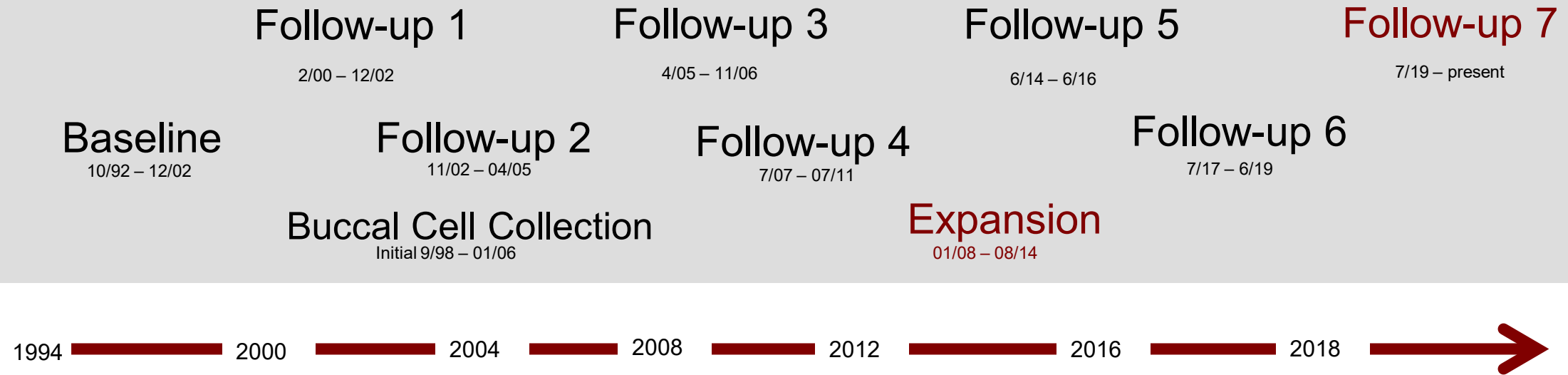
Study Overview

CCSS



Childhood Cancer Survivor Study (U24 CA 55727) Cohort History

CCSS



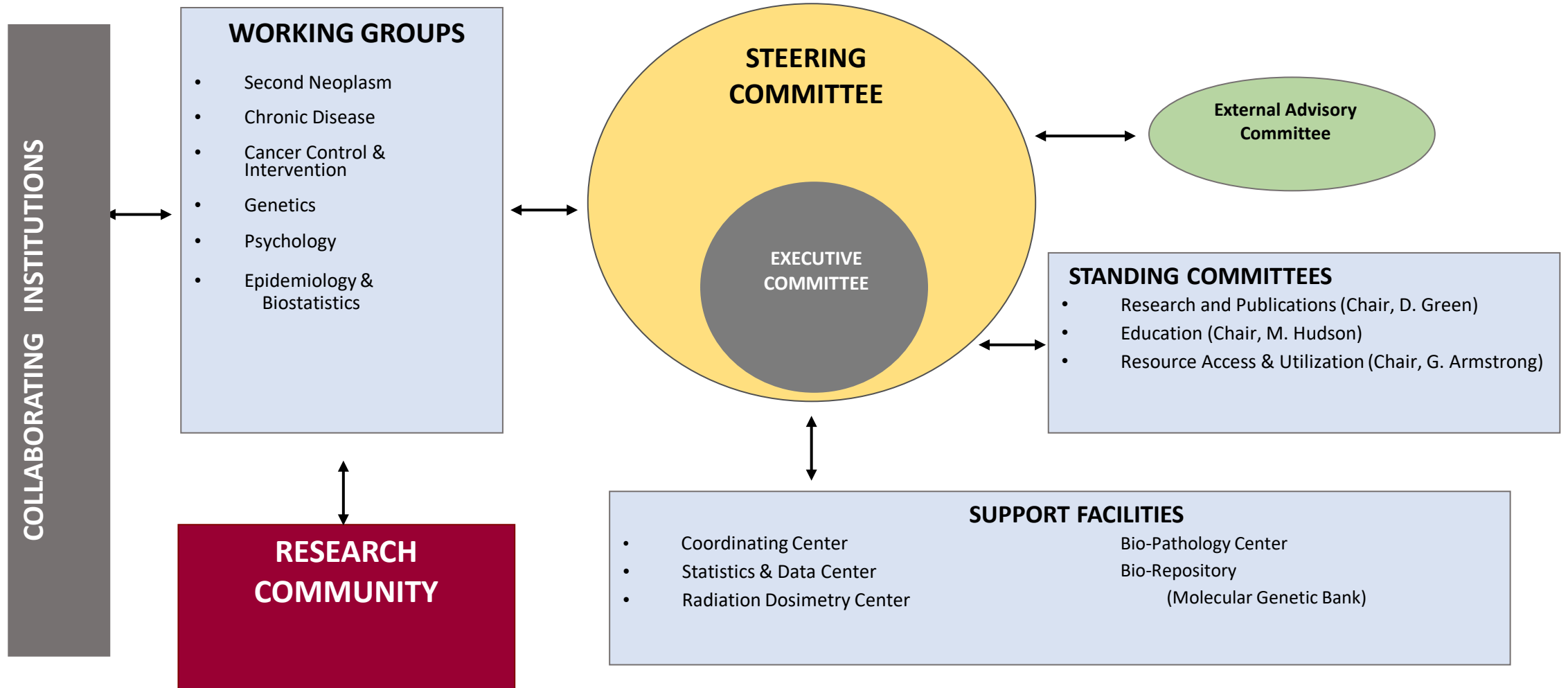
U01
Cooperative
Agreement

U24
Resource
Grant

- CCSS is an NCI-funded Resource
- Available to Researchers
- Analysis and Publication of Existing Data
- Use of Biological Samples
- Interventional Research
- Investigator Initiated Research - Grants

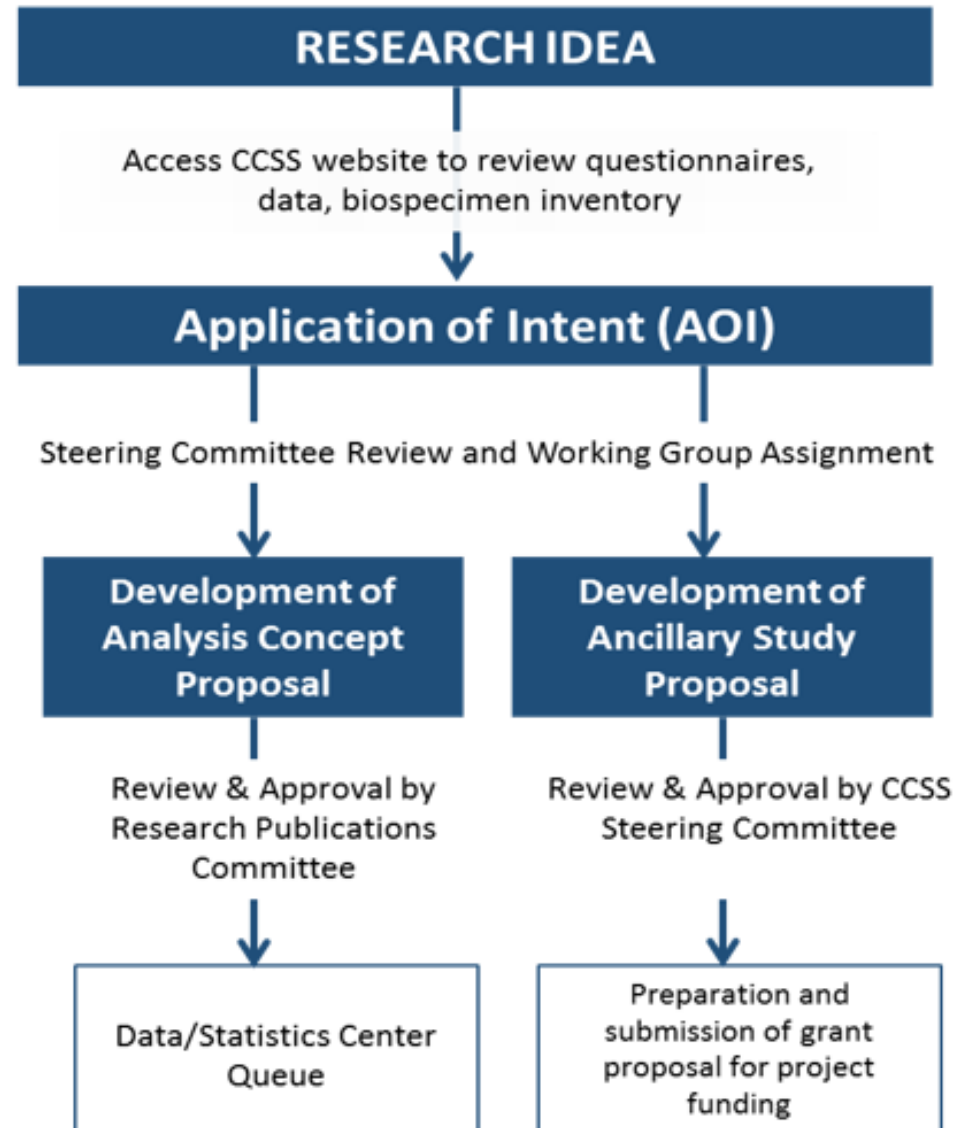
Organizational Structure

CCSS



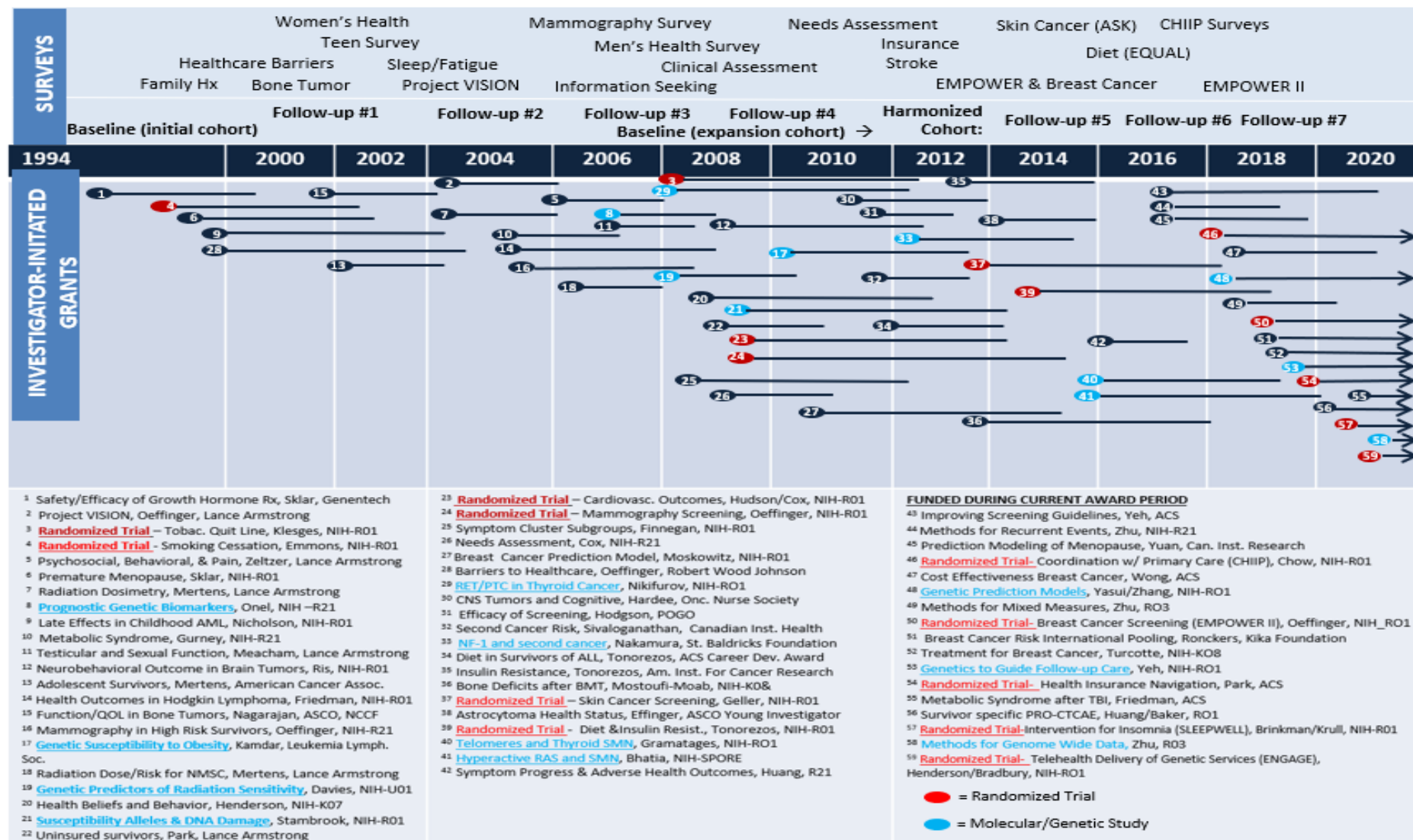
Procedure for Review and Approval of Proposals

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CCSS Ancillary Studies

CCSS



myLTFU Platform:

CCSS

10:50 sj-ltfu.datstat.com

myLTFU

Email Address *

Password *

☐ Login on this browser using a PIN from now on

Login

[Forgot Password](#)

Disclaimer/Privacy Notice: The myLTFU Portal is designed for educational purposes only and is not engaged in rendering medical advice or professional services. The information provided through this site should not be used for diagnosing or treating a health problem or a disease. is not a substitute for professional care. If you have or suspect you may have a health

10:52 sj-ltfu.datstat.com

Follow-Up Survey

Not Started

COVID-19 Resources

The COVID-19 pandemic has presented new challenges and worries for all of us. Although we do not yet know how cancer survivors may be affected by this virus in comparison with the general population, please know that we are working to provide you with up-to-date resources to help you stay informed. To this end, we have created the [COVID-19 Resources](#) tab.

Communication


The myLTFU system will send emails and texts

11:00 sj-ltfu.datstat.com

Important News

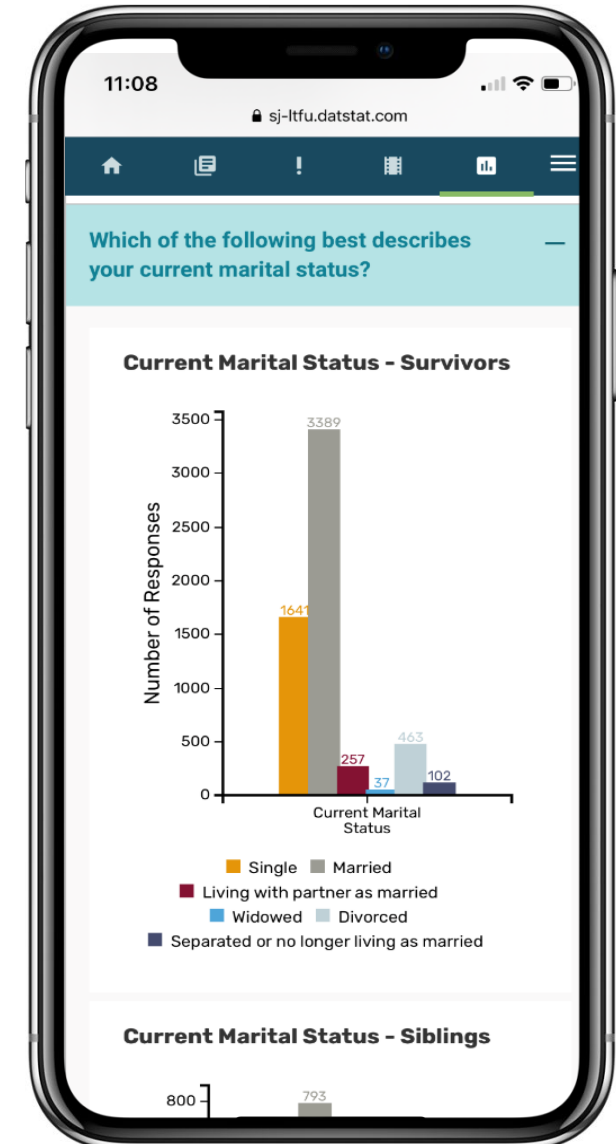
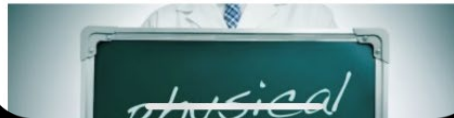
Important News from the Long-Term Follow-Up Study

The Long-Term Follow-Up Study has published more than 300 [publications](#) in scientific journals since it was launched in 1994. Some of these articles, on a wide range of topics, are summarized here.



Regular screenings can help protect your heart

Regular heart screenings can catch early signs of disease or damage for childhood cancer survivors.



CCSS Principal Investigator Report

April 19, 2021

Funding Years 23-27: Work Scope

CCSS

Maintain and Promote the Resource

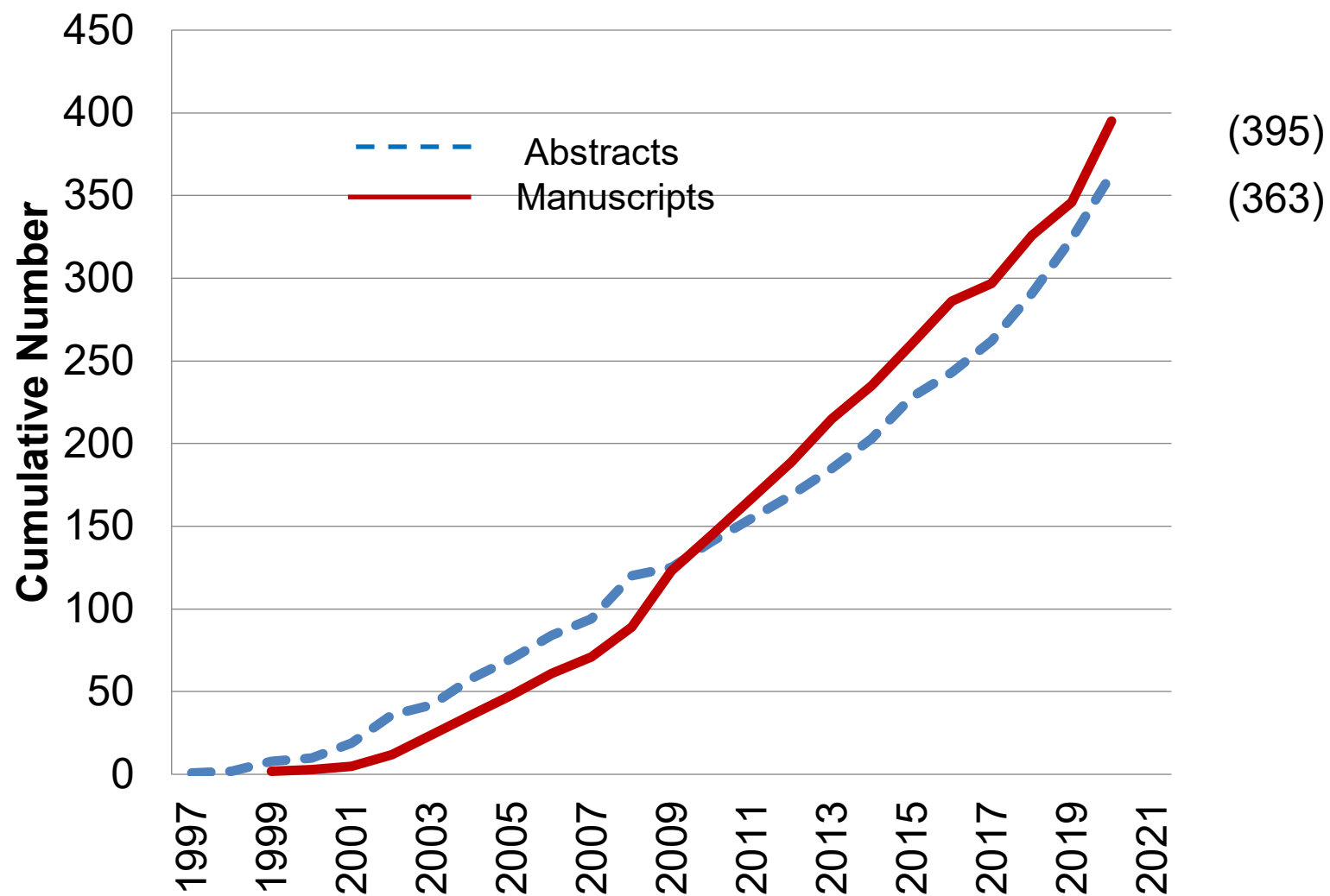
- Ongoing follow-up of the active participants in the cohort (1970-1999)
- Support for Coordinating Center (St. Jude) and four support facilities for tracking/tracing, data cleaning/freeze, Oragene and blood/tissue collection, SMN pathology confirmation, biorepository, ongoing genotyping/sequencing efforts with NCI, and analysis/publication of results
- Replenish Oragene specimens
 - Successfully obtained DNA on survivors with depleted/reduced specimens (68% participation rate)

Enhance the Resource

- Addition of mHealth and web-based infrastructure
 - Developed and deployed the myLTFU portal / mobile platform now with 12,097 survivors and siblings
- Ascertainment of 500 SMN somatic tissue specimens over five years
 - Collected 579 cases in the funding period; 734 cases total

CCSS Abstracts and Publications

CCSS



2020 CCSS Publications (n=37)

CCSS

Impact Factor >10

Ann Inter Med
British Medical Journal
Lancet Oncology (2)
J Clin Oncol (5)
JAMA Oncol (3)
JAMA Pediatrics
JNCI (5)

Impact Factor 5-10

Bone Mine Res.
Cancer (5)
Eur. J. Cancer
Genet Med

Impact Factor <5, or No Impact Factor

J Cancer Surv (2)
JCO Clin Cancer Inform (2)
JCO Precis Oncol
JNCI Cancer Spectr
Lifetime Data Anal
PLOS One (2)
Psychooncology Radiat Res
Radiother Oncol

-49% in journals with impact factor >10
-70% in journals with impact factor >5

2020

20 abstracts accepted for presentation

- ASCO (8 submitted, 1 oral, 1 poster discussion, 6 poster)
- SIOP (3 submitted: 2 oral, 1 poster)
- ASHG (3 submitted: 2 oral, 1 poster)
- ASH (1 submitted, 1 oral presentation)

2021

17 submitted to date (16 to ASCO)

- 4 oral presentation, 4 poster discussion, 8 poster, 1 on line only

CCSS Abstract Highlights

CCSS

Title	First Author
Oral Presentation	
Mortality Among 5-Year Survivors	Stephanie Dixon (SJCRH)
Disparities in Cardiovascular Risk by Race and Ethnicity	David Noyd (Duke)
Genetic and Treatment Risks for Diabetes Mellitus	Melissa Richard (Baylor)
The EQUAL Study: Exercise and Quality of Life after Leukemia, an Intervention Trial	Emily Tonorezos (MSKCC)
Poster Discussion	
Low Dose Radiation to Cardiac Substructures and Risk for Late Onset Cardiac Disease	James Bates (Emory)
Financial Hardship in Adult Survivors of Childhood Cancer	Paul Nathan (Sick Kids)
Neurocognitive Outcomes in Survivors of Early Adolescent and Young Adult (eAYA)	Amy Wang (U. of Chicago)
Hematologic Malignancies	
Efficacy of Clinical Breast Examination (CBE) in Chest-irradiated Female Survivors of Hodgkin Lymphoma	Lennie Wong (City of Hope)

Active Intervention Trials

CCSS



Communicating
Health
Information &
Improving Coordination with
Primary Care

ASPIRES



health
insurance
navigation
tools

EMPOWER



SLEEPWELL



ENGAGE

Proposed Ancillary Studies Submitted

CCSS

PI	Topic	Intervention (yes/no)	Funding Source	Status
Im (U. of Alberta)	Survivor Polygenic Risk Scores	No	NIH R21*	Score: 19
Chow (U. of Wash.)	SALSA: Study of Active Lifestyle Activation	Yes	NIH R01*	Score: 23
Nghiem (U. of Alabama)	Cost Effectiveness of Colo- rectal Cancer Screening	No	NIH R21*	Score: 32
Snyder (Johns Hopkins)	Managing Comorbid Conditions (The 7c's Study)	No	NIH R01*	Score: 33
Yeh (Dana Farber)	Estimating Cost- effectiveness of Preventative Approaches to SMN/CVD	No	NIH R01	Score: 38
Su (UC San Diego)	SMART approach to reproductive health	Yes	NIH R01*	Score: 47

10 Additional Ancillary Studies Unscored for RFA CA-20-027 or Submitted for Other Funding Opportunities

*Submitted in response to RFA CA-20-027, Research to Reduce Morbidity and Improve Care for Pediatric, AYA Survivors

Resource for Genetic Investigation

CCSS

Characteristic	Genotype Data Diagnosed 1970-1986 (N=5739)	Whole Exome Diagnosed 1970-1986 (N=5451)	WGS and WES Data Diagnosed 1987-1999 (N=2641)
Sex	N	N	N
Male	2781	2630	1240
Female	2958	2821	1401
Ancestry (based on genotype)			
European	5324	5105	2114
Non-European	415	346	527
Data Access	Available in dbGap	Available in dbGap	Available in the St. Jude Cloud

Available in dbGaP: Phenotype data on all 25,665 CCSS participants, including diagnosis, treatment and long-term outcome data

dbGaP Study Accession: phs001327.v2.p1

Expanding the Genomic and Biospecimen Resource: Supplemental Funding

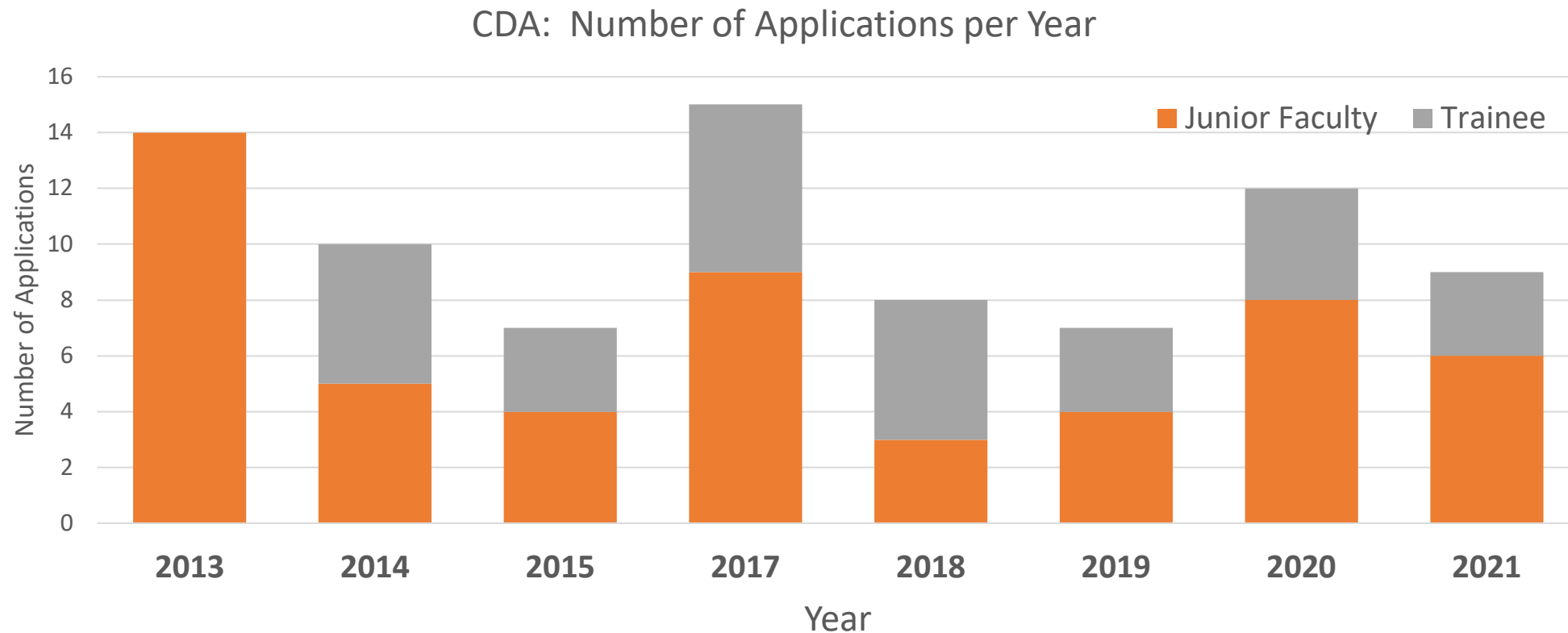
CCSS

- 645 **SMN somatic tissues** with **matched germline specimens**
 - 218 breast cancer, 116 thyroid, 111 meningioma
 - WGS** (Hudson Alpha), **WES** and **RNAseq** (St. Jude)
 - Supplement supported by the NCI, sequencing ongoing
 - Unique opportunity to examine somatic mutations and SMN etiology
- 1,350 Survivors with **CTCAE grade 3 and 4** chronic health conditions
 - At high risk for mortality
 - Banking 40ml specimen** as a resource for investigators
 - Enhance the resource to understand the molecular basis of disease
 - >400 collected to date

Career Development Award

CCSS

Designed to create an opportunity for early career investigators and trainees with an interest and aptitude in childhood cancer survivorship research to develop and complete an initial research study within the CCSS. This will serve as a foundation for the development of a career path that includes survivorship research. In 2021: 9 applications (6 Junior faculty, 3 trainee)



Career Development Award

CCSS

CCSS Career Development Award Winners						
Category	Awardee	Application Title	Direct Costs Awarded	CCSS Working Group	Primary Mentor	Status
2020						
Junior Faculty	Catherine Goudie, MD McGill University Health Center	Long-term cost-effectiveness of cancer predisposition syndrome identification strategies in survivors of pediatric leukemia, brain tumors or bone/soft tissue sarcomas	\$20,000	Genetics	Paul Nathan	Analysis Underway
Trainee	Natalie Wu, MD Fred Hutchinson Cancer Research Center	Development and validation of a prediction model for end-stage renal disease in childhood cancer survivors	\$3,000	Chronic Disease	Eric Chow	Abstract Presented, Manuscript Drafted
2021						
Junior Faculty	Kelly Rentscher, PhD University of California Los Angeles	Psychological distress, social functioning, and phenotypic aging in adult survivors of childhood cancer	\$20,000	Psychology	Kiri Ness	Concept Pending Approval
Trainee	Christina Sharkey, PhD Children's National Hospital	The impact of physical activity and psychological distress on neurocognitive functioning over time	\$3,000	Psychology	Kristina Hardy	Concept Pending Approval

Career Development Award

CCSS

Among 19 awardees:

- **11** Published/In Press Manuscripts (JCO x2, JNCI x2, Cancer, J Bone Miner Res, Psychooncology, J Cancer Surv., Genes Chrom Cancer, JCO Clin Can Inform, Radiother Oncol)
- **4** Manuscript Drafted
- **4** Analysis Underway

Competitive Renewal: Update

CCSS

Submitted: November 18, 2020

Scored: Overall Impact Score 15

Major New Objectives:

1. Aging and Accelerated Aging
2. Health Services Research
3. Cloud-based Data Sharing / Data Analysis Ecosystem
4. Strategic Plan for Future Cohort Expansion

Funding Plan:

- Presentation to NCI Senior Program Leadership, 7/2021
- Dates for new award: 12/1/2021 to 11/30/2026


Competitive Renewal: Major Objectives

CCSS

Aging and Accelerated Aging

We will expand the collection of data to evaluate physiologic and neurocognitive function with aging, characterize accelerated aging, and investigate the underlying physiology of aging as survivors enter their 4th - 6th decades of life.

- Web-based neurocognitive assessment (CNS Vital Signs)
- PRO-based data collection, focused on functional outcomes


- 
1. Entire CCSS population
 2. Twice in funding period

Competitive Renewal: Major Objectives

CCSS

Aging and Accelerated Aging

We will expand the collection of data to evaluate physiologic and neurocognitive function with aging, characterize **accelerated aging**, and investigate the underlying physiology of aging as survivors enter their 4th - 6th decades of life.

- Web-based neurocognitive assessment (CNS Vital Signs)
 - PRO-based data collection, focused on functional outcomes
 - Develop a population resource for intervention trials through in-home functional/lab assessment of 1000 sub-cohort of survivors (frail, pre-frail, not frail)
- 
1. Entire CCSS population
 2. Twice in funding period

Competitive Renewal: Major Objectives

ccss

Health Services Research

Given the unique healthcare needs of survivors we will enhance the resource to facilitate 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. Ultimately, we aim to provide a resource to identify how survivors' healthcare influences outcomes.

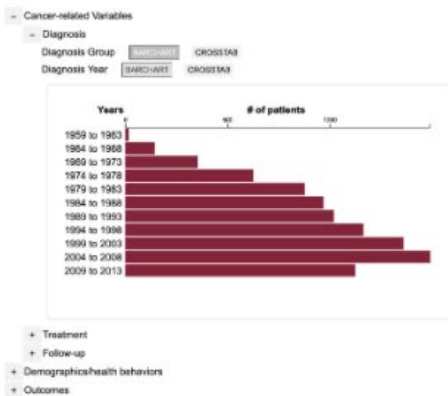
- Augment the next CCSS survey to assess survivors' perspectives of their unmet needs (CCSS Needs Assessment Questionnaire & Health Care Needs Study)
- Expand expertise: Claire Snyder, Ph.D., Professor and Director, Johns Hopkins Program for Building Lifestyles, Outcomes and Care Services Research in Cancer (BLOCS)
 - Co-Chair, Cancer Control and Intervention Working Group with Paul Nathan
 - Solicit proposals for Ancillary studies

CCSS

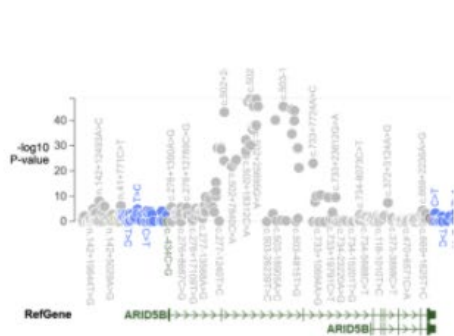
Enhance Data Sharing

To maximize access to the CCSS resource we will leverage a cloud-based sharing platform (**SJ Cloud Survivorship Portal**) to develop a data analysis ecosystem with tools for data access, visualization and analysis of genetic, treatment exposure and outcome data. (<http://survivorship.stjude.cloud/>)

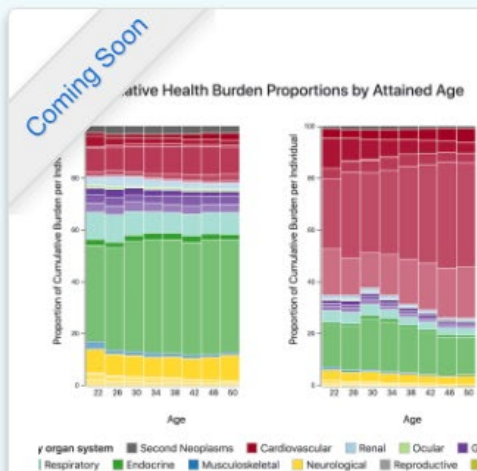
Projects



Clinical Data Browser



Genomic Data Browser



Cumulative Health Burden

Competitive Renewal: Major Objectives

ccss

Strategic Plan for Future Cohort Expansion

In the future, assessment of late outcomes of novel therapies (immunotherapy, targeted/biologic, proton beam) will be essential. Thus, with NCI oversight, CCSS will formulate a strategic plan for cohort expansion.

- Begin in Funding Year 29 (Year 2 of the next award).
 - Establish leadership / governance
 - Convene stakeholders
 - Enumerate objectives and priorities of an expansion
 - Establish expertise
 - Determine feasibility: define eligible population, recruitment, MRAF, identify and collect preliminary data
 - Summarize assessment: infrastructure needs, feasibility, timeline, cost
 - Delivery of final strategic plan report to NCI (Year 4)

Competitive Renewal: Additional Work Scope

ccss

- Follow-Up 8 and Follow-Up 9 surveys
- National Death Index linkage
- SN adjudication
- SMN tissue collection
- Peripheral blood for cases with SMN
- Newsletters, 3x per year
- CCSS Investigator Meetings
- Investigator initiated Ancillary Studies
- Serve as a resource to address questions on underserved and understudied populations
- Analysis of temporal changes and risk stratification
- Support publications, abstracts, grant submissions

Childhood Cancer Survivor Study

A RESOURCE FOR RESEARCH

CCSS

- The Childhood Cancer Survivor Study is an NCI-funded resource to promote and facilitate research among long-term survivors of cancer diagnosed during childhood and adolescence.
- Investigators interested in potential uses of this resource are encouraged to visit:

www.stjude.org/ccss