

# CCSS Investigator Meeting

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May 27, 2022

**CCSS**  
Childhood Cancer  
Survivor Study



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An NCI-funded Resource

# Meeting Agenda Overview

CCSS

Time (Central Time)	Presentation
9:00 am – 10:00 am	Introduction to the Childhood Cancer Survivor Study, 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"><li>-Chronic Disease</li><li>-Genetics</li><li>-Epidemiology/Biostatistics</li></ul>
2:30 pm – 3:30 pm	Working Group Breakout Session #2 <ul style="list-style-type: none"><li>-Cancer Control and Intervention</li><li>-Psychology</li><li>-Second Neoplasm</li></ul>

# Introduction to the Childhood Cancer Survivor Study

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May 27, 2022

**CCSS**  
Childhood Cancer  
Survivor Study



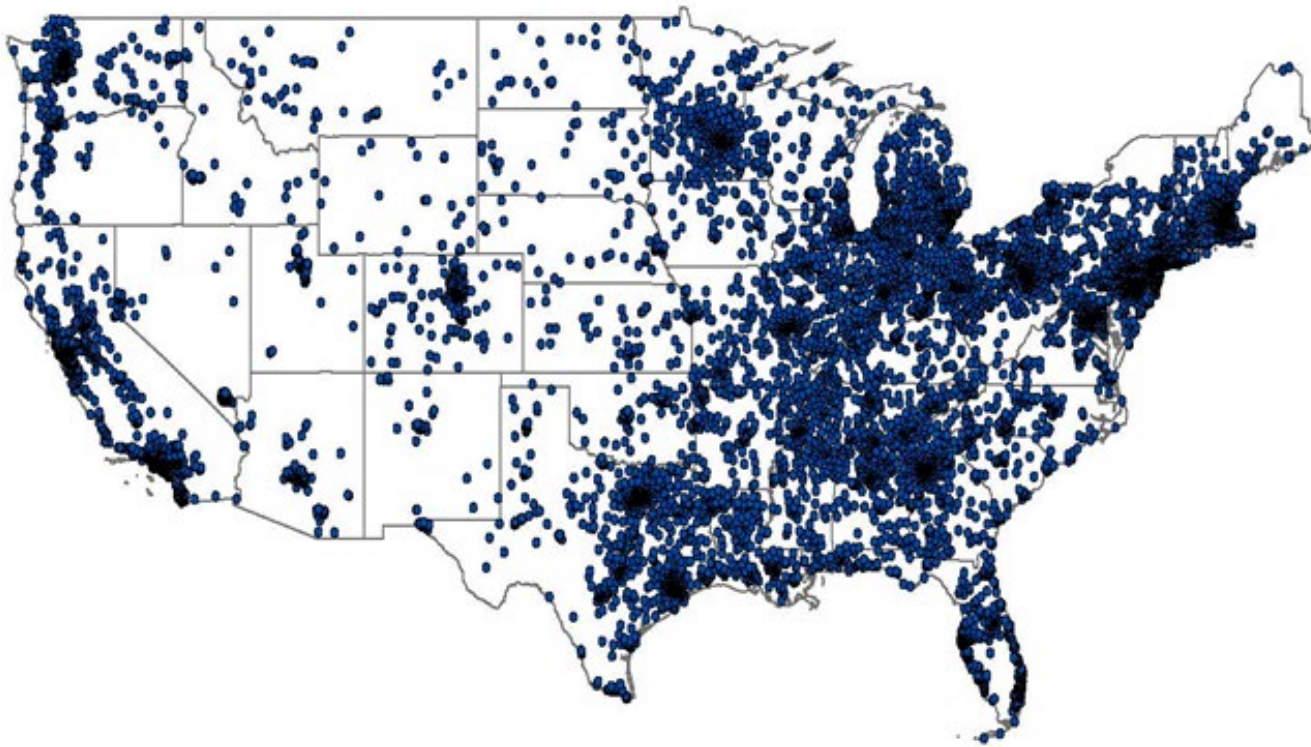
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# Childhood Cancer Survivor Study (U24 CA 55727)

## Study Participants

CCSS



### Resource for Survivorship Research

- Multi-institutional (n=31)
- 38,036 eligible survivors
- Open resource
- 384 Abstracts presented
- 411 Publications, cited >26,500 times
  - >1,225 Investigators
  - 91 Early career trainees
- 66 Investigator-initiated studies
- >\$80 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 Center  
Northwestern University  
University of Chicago

# Population Characteristics

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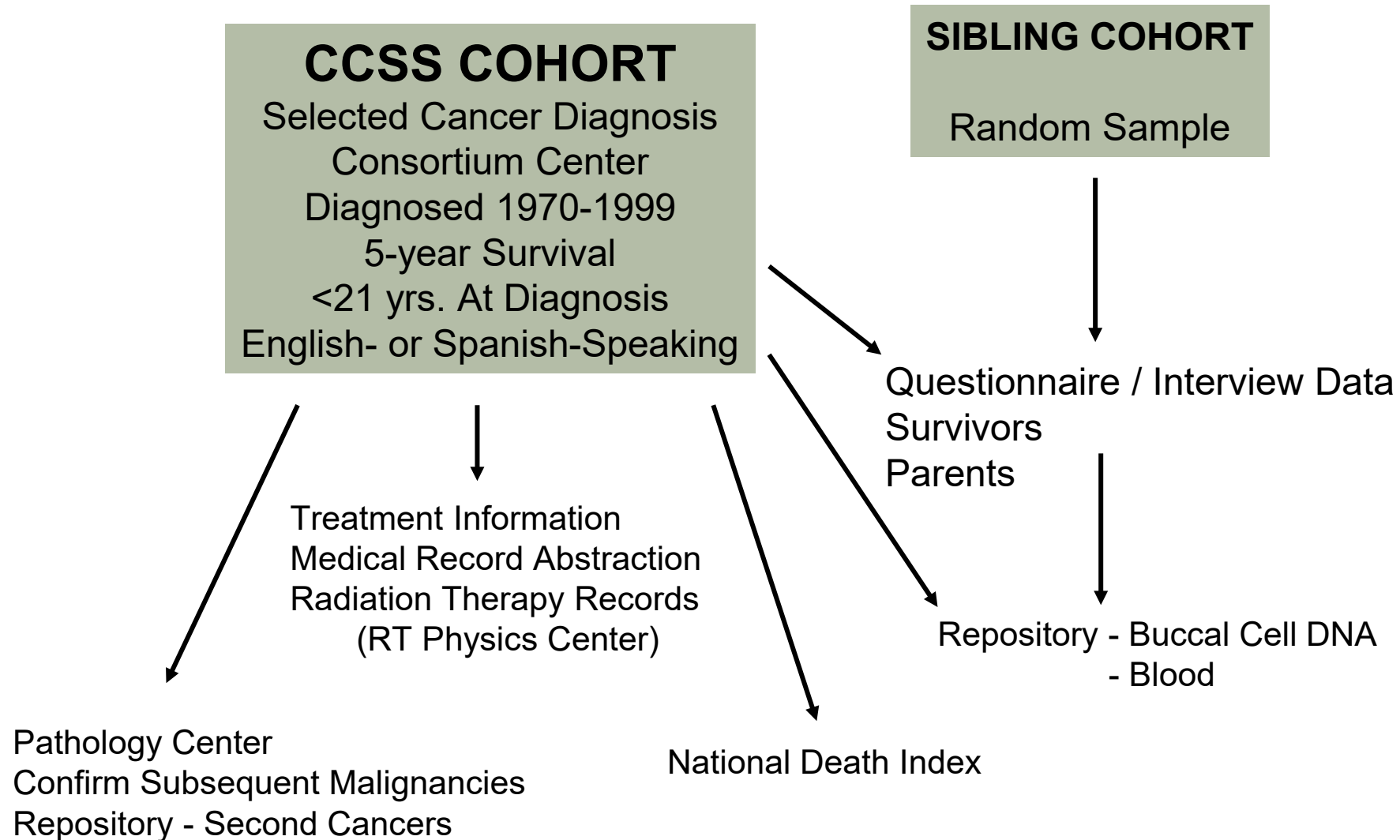
Characteristic	Participating	% of Cohort
<b>Primary Cancer Diagnosis</b>		
Leukemia	7,872	40.0%
CNS tumors	4,489	15.2%
Hodgkin lymphoma	3,107	10.5%
Non-Hodgkin lymphoma	2,116	7.1%
Wilms tumor	2,276	7.7%
Neuroblastoma	1,948	6.6%
Soft tissue sarcoma	1,756	5.9%
Bone tumors	2,100	7.0%
<b>Race/Ethnicity</b>		
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)

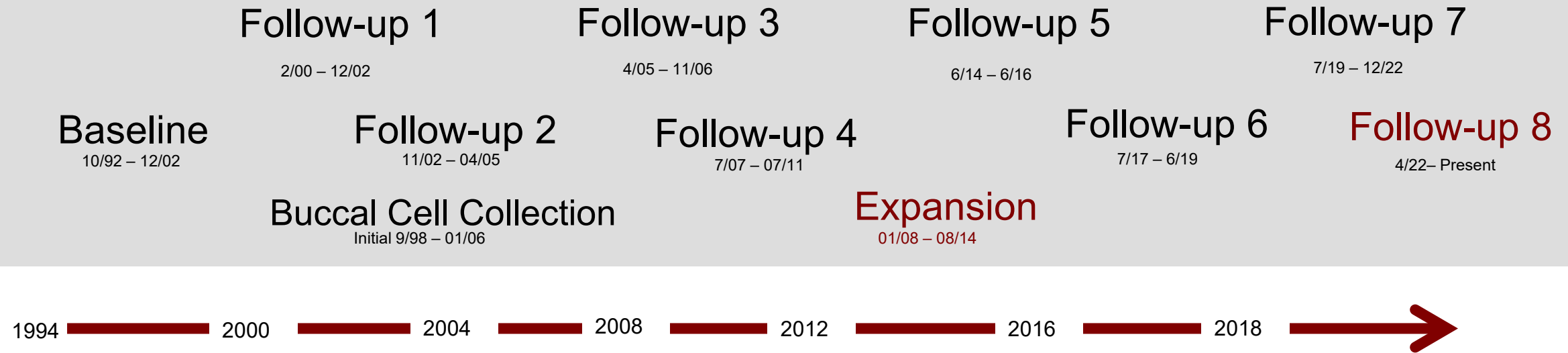
## Study Overview

CCSS



# Childhood Cancer Survivor Study (U24 CA 55727) Cohort History

CCSS



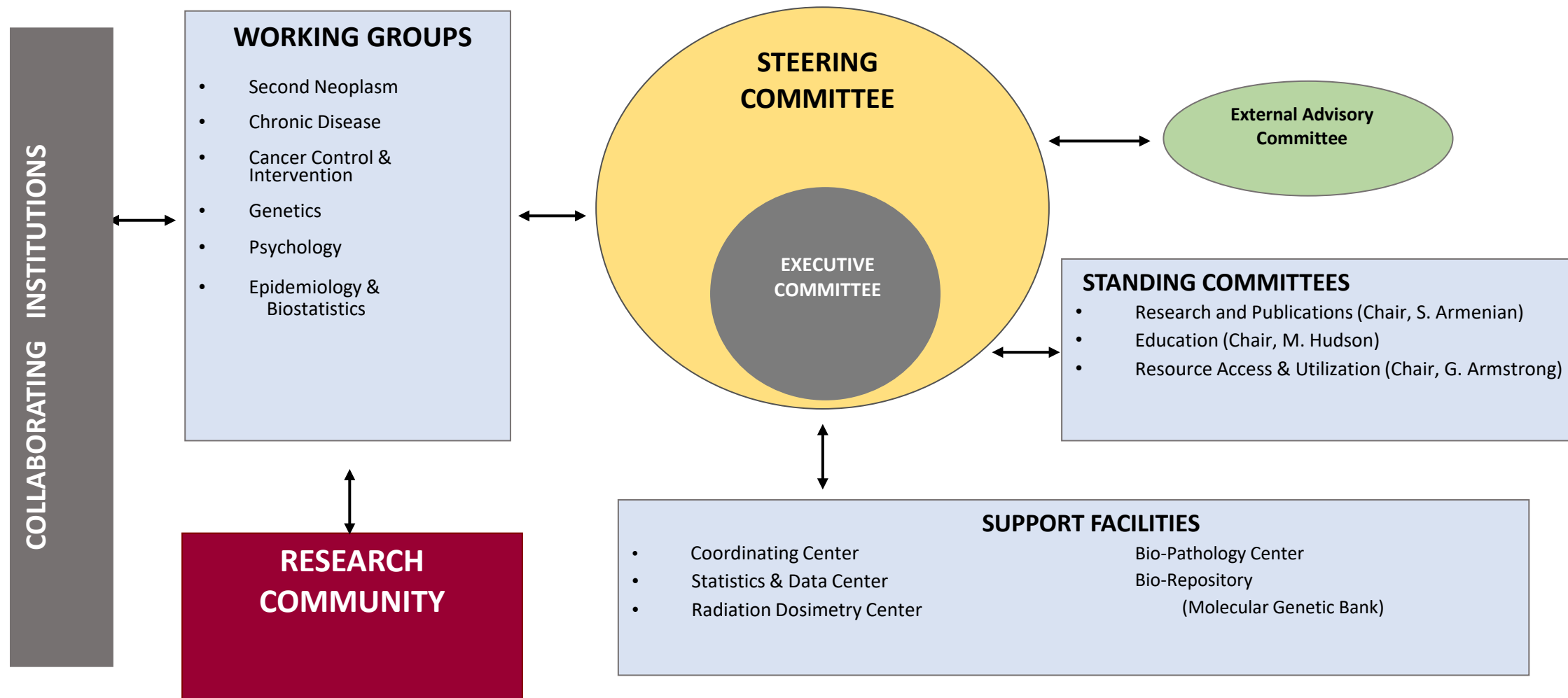
U01  
Cooperative  
Agreement

**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

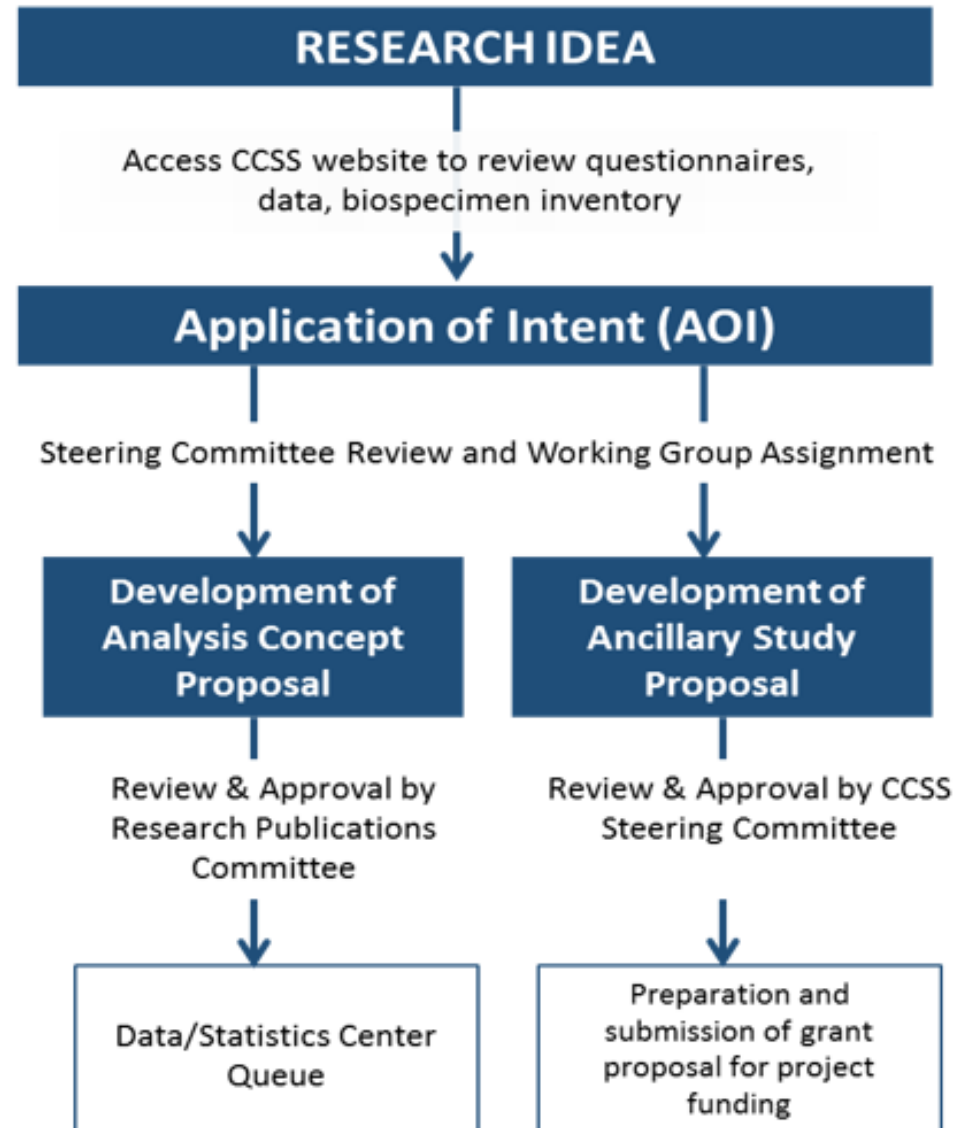
# Organizational Structure

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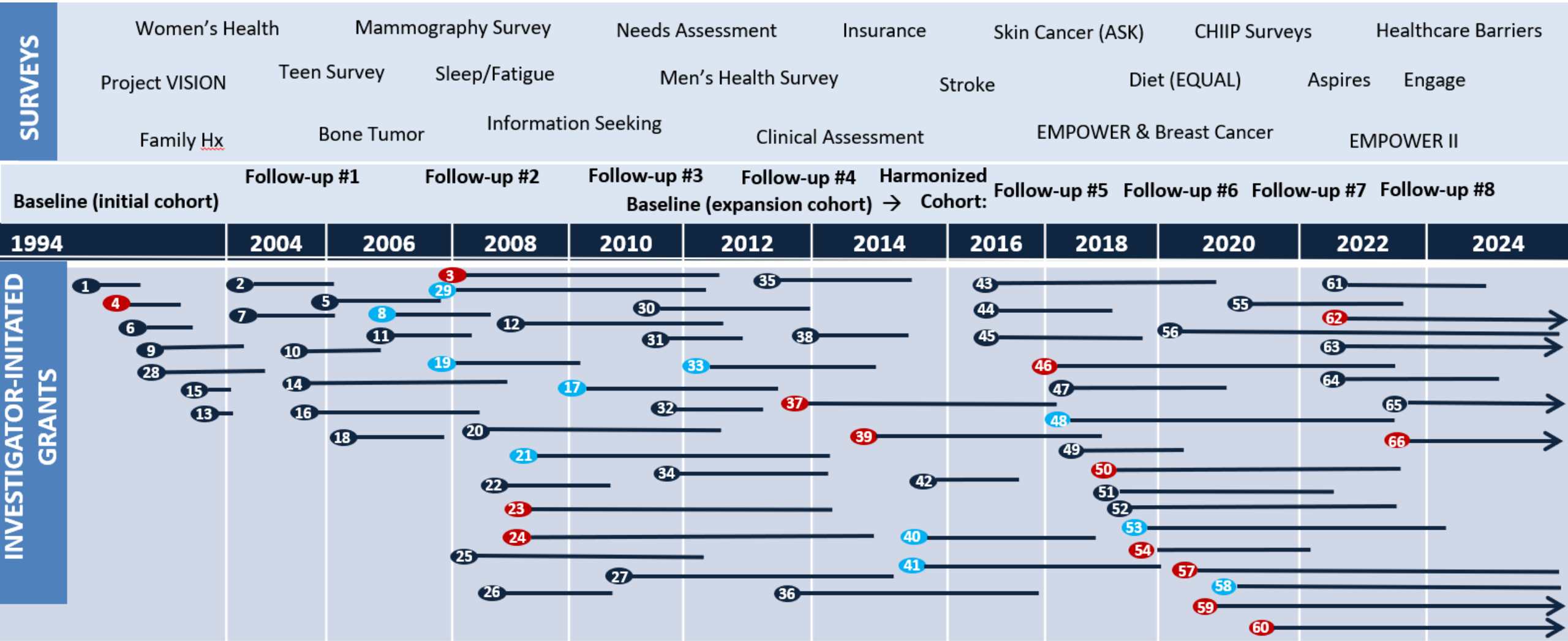
# Procedure for Review and Approval of Proposals

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# CCSS Ancillary Studies

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# 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. It 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

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

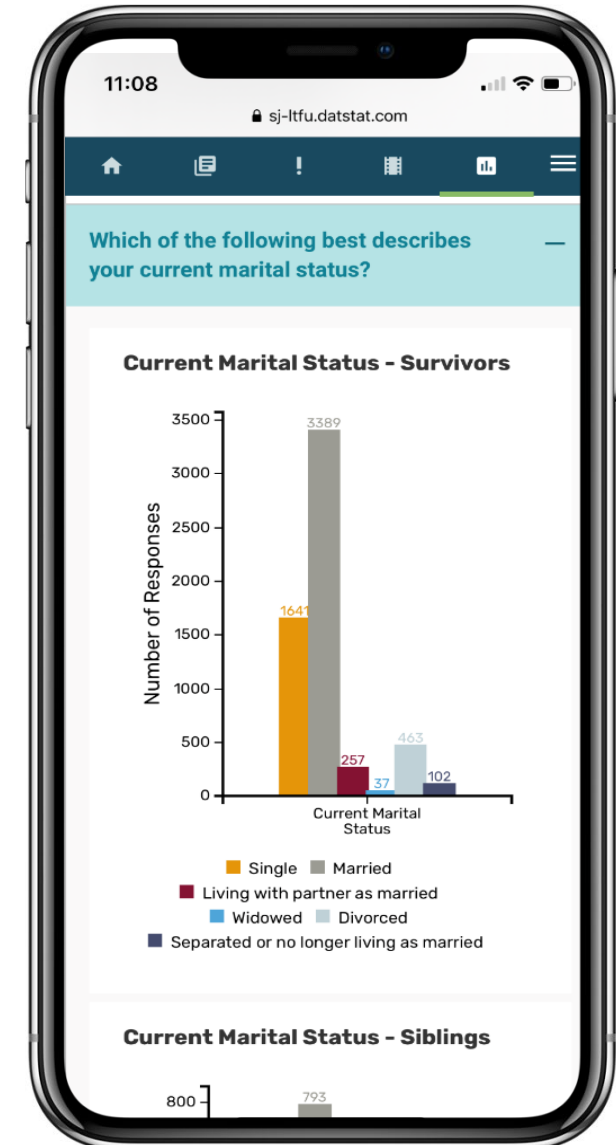
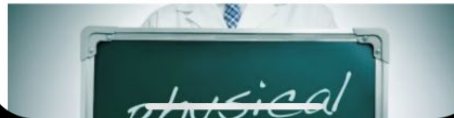
#### Important News from the Long-Term Follow-Up Study

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

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May 27, 2022

**CCSS**  
Childhood Cancer  
Survivor Study



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An NCI-funded Resource

# Funding Years 28-32: Update

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## 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, blood/tissue collection, SMN pathology confirmation, biorepository, and analysis/publication of results

## Enhance the Resource

Major New Objectives:

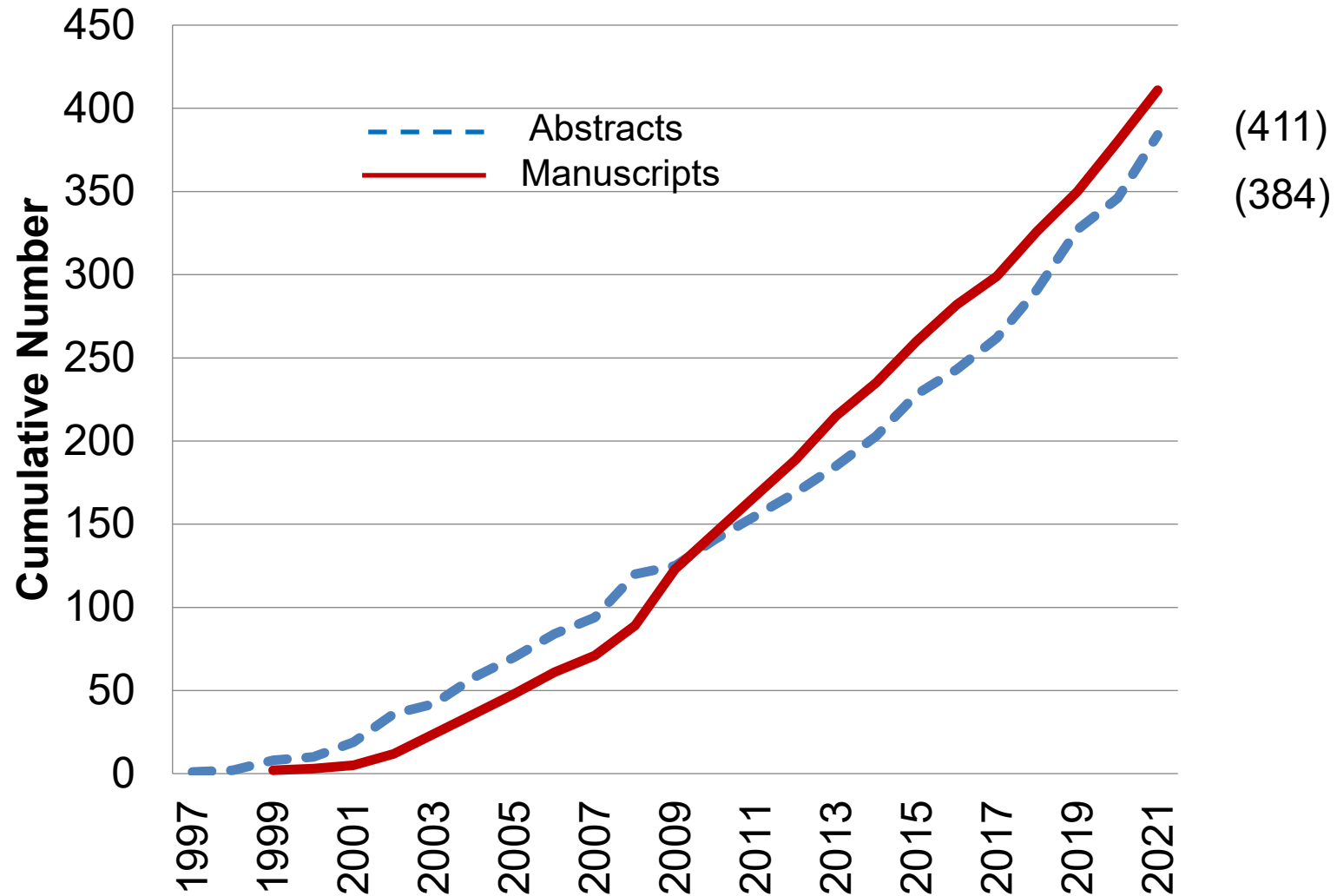
1. Aging and Accelerated Aging
2. Health Services Research
3. Cloud-based Data Sharing / Data Analysis Ecosystem
4. Strategic Plan for Future Cohort Expansion

May 10<sup>th</sup>, 2022: Notification of Award to  
fully fund Year 28



# CCSS Abstracts and Publications

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# 2021-2022 CCSS Publications (n=35)

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## Impact Factor >10

Blood  
J Clin Oncol (2)  
JNCI (5)  
Nature Communications  
Nature Medicine

## Impact Factor 5-10

Cancer (4)  
Eur J Cancer  
JACC CardioOncol  
J Am Heart Assoc  
J Bone Mine Res  
Radiother Oncol

## Impact Factor <5

Biomed Phys Eng Express  
BMC Health Services Research  
Cancer Epidemiol Biomarkers Prev (7)  
Clin Orthop Relat Res  
J Cancer Surv (2)  
JNCI Cancer Spectr  
Pediatr Blood Cancer (2)  
Psychooncology

-29% in journals with impact factor >10  
-54% in journals with impact factor >5

2022 to date:

24 abstracts submitted for presentation

- ASCO (10 submitted: 3 oral, 2 poster discussion, 3 poster, 2 online only)
- ISPNO (2 submitted)
- ISLCCC (5 submitted)
- Other meetings (7 submitted, each to a different meeting)

# CCSS Abstract Highlights

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## Title

## First Author

### Oral Presentation

Health Navigation Intervention Tool (HINT) Randomized Trial  
Joint Effects of PRS Score and RT Treatment on SN Risk  
Late Mortality and Morbidity in Survivors of Childhood Glioma

Elyse Park (Harvard)  
Todd Gibson (NCI)  
Pete DeBlank (Nationwide)

### Poster Discussion

Modifiable Risk Factors for Late Mortality  
Benefits, Harms, and Burden of CRC Screening

Stephanie Dixon (St. Jude)  
Jennifer Yeh (Harvard)

### Poster

Chronic Health Conditions and Employment Transitions  
Treatment Exposure-Based Risk Stratification  
Improvements in Life-Expectancy

Neil Bhatt (Fred Hutch)  
Michaela Dinan (Yale)  
Jennifer Yeh (Harvard)

# 7 New Ancillary Studies!

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PI	Topic	Intervention (yes/no)	Funding Source	Status
Im (U. of Alberta)	Survivor Polygenic Risk Scores	No	NIH R21	Year 1 Analysis Ongoing
<b>Chow</b> (U. of Wash.)	SALSA: Study of Active Lifestyle Activation	Yes	NIH R01	Year 1 Enrolling
<b>Moskowitz</b> (MSK) <b>Henderson</b> (U of C)	International Study of CRC (I-SCRY)	No	NIH R01	Year 1
<b>Xu Ji</b> (Emory)	Impact of the ACA on Healthcare Coverage, Utilization and Outcomes	No	NIH R03	Year 1
<b>Howell</b> (MDA) <b>Mulrooney</b> (SJ) <b>Yasui</b> (SJ)	Risk Prediction for Cardiac Disease w/ RT Substructure	No	NIH R01	NOA Pending
<b>Park</b> (Harvard) <b>Kirchhoff</b> (Utah)	HINT 2	Yes	NIH R01	NOA Pending
<b>Yeh</b> (Dana Farber)	Cost-effectiveness of Prevention of SMN/CVD	No	NIH R01	NOA Pending

# 7 Ongoing Intervention Trials

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Communicating  
*H*ealth  
*I*nformation &  
*I*mproving Coordination with  
*P*rimary Care

ASPIRES



health  
insurance  
navigation  
tools

EMPOWER



SLEEPWELL



ENGAGE



salsa

Study of Active  
LifeStyle Activation

# Resource for Genetic Investigation

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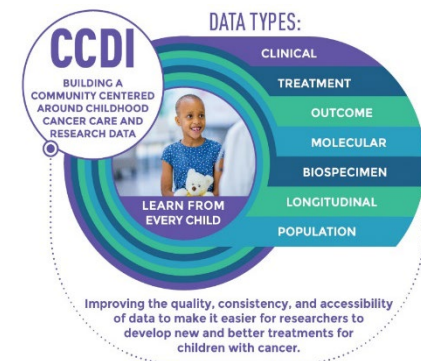
Characteristic	Genotype Data Diagnosed 1970-1986 (N=5739)	Whole Exome Diagnosed 1970-1986 (N=5451)	WGS and WES Data Diagnosed 1987-1999 (N=2641)
<b>Sex</b>	N	N	N
Male	2781	2630	1240
Female	2958	2821	1401
<b>Ancestry (based on genotype)</b>			
European	5324	5105	2114
Non-European	415	346	527
<b>Data Access</b>	Available in dbGap	Available in dbGap (Early 2021)	WGS Available in the St. Jude Cloud

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

dbGaP Study Accession: phs001327.v2.p1

# Expanding the Genomic and Biospecimen Resource: Supplemental Funding

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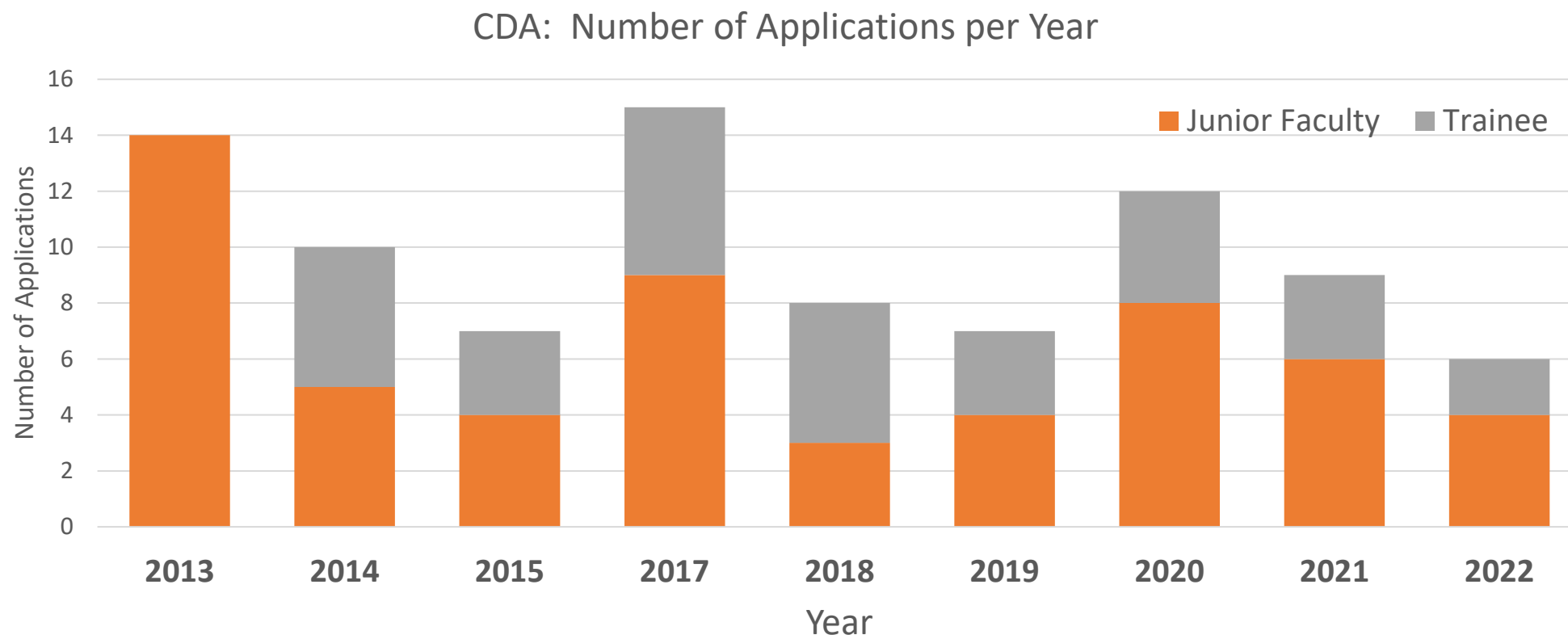
- **SMN somatic tissues with matched germline specimens**
  - 218 breast cancer, 116 thyroid, 111 meningioma
  - WGS, WES (Hudson Alpha), and RNAseq (St. Jude)
  - Approved concept to examine the effects of prior therapy on the genomic landscape, timing of mutation acquisition and immune infiltration signatures (Zhang)
- 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



# 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 2022: 6 applications (4 Junior faculty, 2 trainee)**



# Career Development Awards 2022

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Category	Awardee	Application Title	CCSS Working Group	Primary Mentor	Status
2022					
Junior Faculty	Rusha Bhandari, MD, MS City of Hope	Health Outcomes in Older Survivors of Childhood Cancer	Chronic Disease	Kiri Ness	—
Junior Faculty	Gordon Watt, PhD Memorial Sloan Kettering	Genetic modification of chemotherapy- associated subsequent malignant neoplasms	Genetics	Jonine Bernstein	—
Trainee	Tim Ohlsen, MD Seattle Children's Hospital	Financial hardship among long-term survivors of childhood cancer	Cancer Control and Intervention	Eric Chow, Arti Desai	—

# Career Development Award

CCSS

Among 21 awardees:

- **12** 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)
- **5** Manuscript Drafted/Submitted
- **4** Analysis Underway

# Follow-Up 7 Survey

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Goal: Comprehensive Outcome Assessment of the Cohort (32 pages)

Strategy:

- Initial deployment ONLY via my LTFU (8/2019)
- Initial paper survey mailout (1/2020...**COVID!**)
- Second paper survey + \$10 bill (10/2020)

Status: Complete! **67%** response rate (survivors), 59% for siblings

Plan:


- Currently cleaning, data freeze to be completed **Summer 2022**
- SMN data freeze targeting **December 2022**
- Need for **CTCAE grading** of CHCs this summer upon completion of data freeze

# Follow-Up 8: Major Objectives

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## 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 4<sup>th</sup> - 6<sup>th</sup> decades of life.

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

# Follow-up 8: New Measures for Aging

CCSS

- 20 pages in length, Development Team: Ness, Krull, Snyder, Nathan, Leisenring, Alston, McDonald
- Field tested with minor concerns addressed
- Includes all new scales as we proposed in the competitive renewal

Attachment 4, Table 2: Proposed Patient Reported Outcomes for Assessment of Aging and Accelerated Aging in the Next Funding Period	
Name of Scale	Main Constructs Included
<b><u>PHYISCAL PERFORMANCE ASSESSMENT</u></b>	
<b>Katz Activities of Daily Living</b>	Self-reported functional status including bathing, transferring, dressing, self-care tasks for independent living.
<b>Lawton Instrumental Activities of Daily Living</b>	Self-reported functional status including using the telephone, transportation, housekeeping, ability to manage finances and prepare meals and other tasks required to live independently.
<b>Fried Frailty Criteria (Self-reported)</b>	Identifies survivors with physiologic frailty
<b>Cumulative Illness Rating Scale</b>	Summarizes disease burden across 14 organ-systems, with items scored 0-4 (none to extremely severe problem).
<b><u>NEUROCOGNITIVE ASSESSMENT</u></b>	
<b>CCSS Neurocognitive Questionnaire (NCQ)</b>	Task efficiency (attention + processing speed), memory, executive function.
<b>PROMIS Cognitive Function SF</b>	General cognitive function.
<b>PROMIS Social Roles and Activities SF</b>	Social roles and community activities.
<b>Alzheimer's Disease Caregiver Questionnaire</b>	Memory, language, executive function, behavior.

# 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.

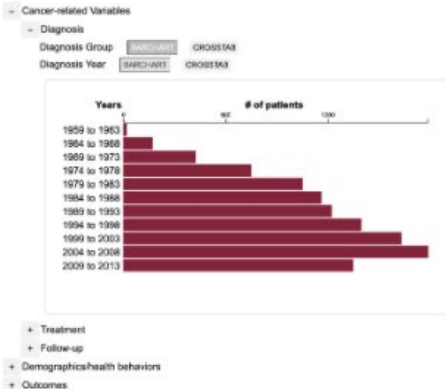
- Augment the next CCSS survey to assess survivors' perspectives of their **unmet needs** (**CCSS Needs Assessment Questionnaire & Health Care Needs Study**)
- Expand expertise: Claire Snyder, Ph.D.
  - Co-Chair, Cancer Control and Intervention Working Group with Paul Nathan
  - Solicit proposals for Ancillary studies

## CCSS

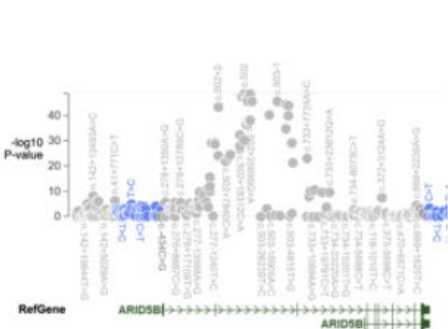
## Enhance Data Sharing

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/>)

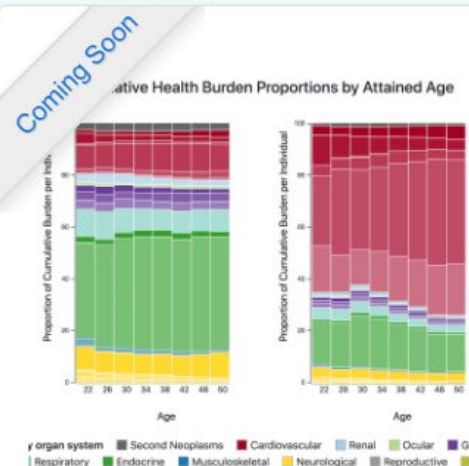
## Projects



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

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- 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

<https://islccc.prinsesmaximacentrum-events.nl>



**ISLCCC**

INTERNATIONAL SYMPOSIUM  
ON LATE COMPLICATIONS  
AFTER CHILDHOOD CANCER

**2022**

8-9 JULY 2022, UTRECHT



# 2023 CCSS Investigator Meeting

CCSS



Hold the date:

- CCSS Investigator Meeting **May 30-31, 2023**

Emory Hotel & Conference Center,  
**Atlanta, GA**

To precede the International  
Symposium on Long-term  
Complications after Childhood Cancer  
**June 1-3, 2023**



# 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](http://www.stjude.org/ccss)