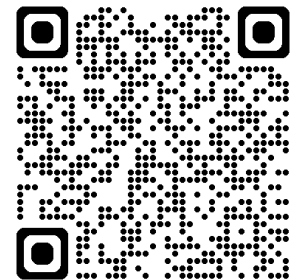


CCSS Principal Investigator Report

June 18, 2025



View agenda and
[eMeeting Book](#):

CCSS
Childhood Cancer
Survivor Study

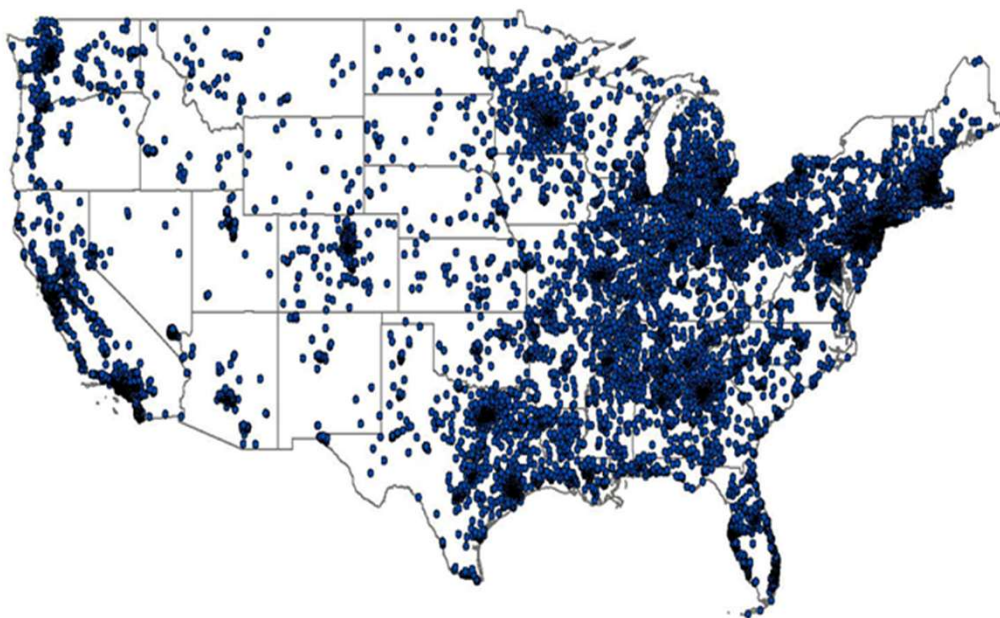


An NCI-funded Resource

Childhood Cancer Survivor Study

(U24 CA55727)

CCSS



“Our national resource for childhood cancer survivorship research.”

- Francis Collins

NCI-supported *resource* for survivorship research (Year 31)

- Multi-Institutional (n=31)
- 38,036 eligible survivors

>490 Publications, cited >30,000 times

- >1,300 Investigators
- 91 Early career trainees
- Evidence base for COG Guidelines

76 Investigator-initiated studies

- >\$84 million investigator-initiated grant support

Funding Plan Years 28-32

ccss

Renewal Submitted: November 18, 2020; Overall Impact Score 15

Funding **Year 31** (year 4 of current award): began December 1, 2024

Funding Plan:

- NOA received 3/5/2025
- 10% cut due to Congressional funding under a Continuing Resolution (CR)
 - No cut to sub-contracts

Funding Years 28-32: Update

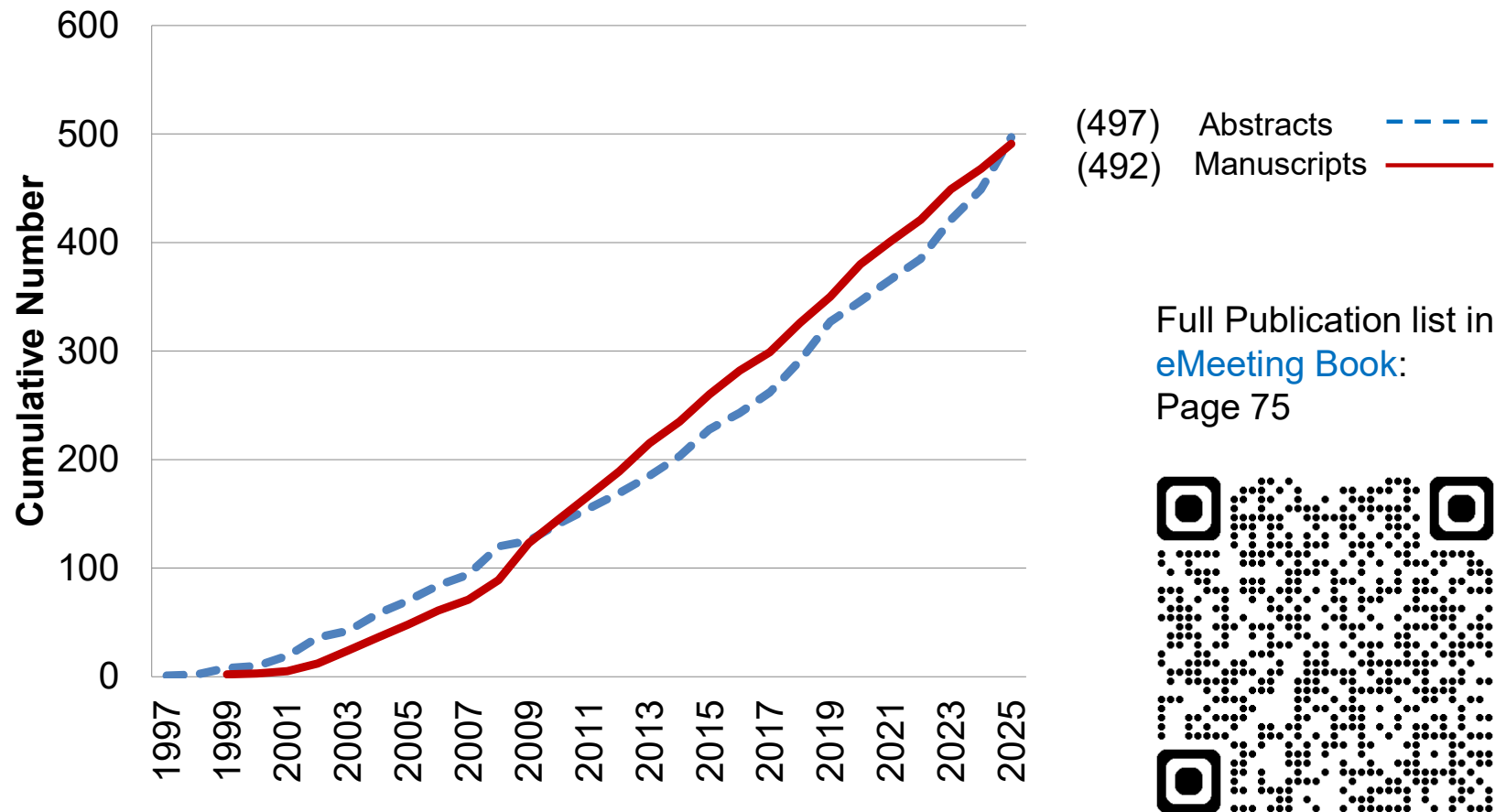
ccss

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, blood/tissue collection, SMN pathology confirmation, biorepository, and [analysis/publication of results](#)

CCSS Abstracts and Publications

ccss



2024-2025 To Date: CCSS Publications (n=42)

CCSS

Impact Factor >10 (N=18)

JACC
JACC Cardio-Oncology
J Clin Oncol
JAMA Netw Open
JAMA Oncol
JNCI
Nature Cancer
Nature Communications
Nature Medicine

- **43%** in journals with
impact factor >10

Impact Factor 5-10 (N=8)

Cancer
Circ Genom Precis Med
J Clin Epidemiology
Pain

Impact Factor <5 (N=16)

Ann Clin Transl Neurol
BMC Health Services Research
Cancer Epidemiol Biomarkers Prev
Cancer Med
J Cancer Surv
JCO Oncol Prac
JNCI Cancer Spect
Stat Med
Pediatr Blood Cancer

CCSS Abstract Highlights

ccss

2025 to date:

30 unique abstracts submitted for presentation

ASCO: 2 rapid oral, 8 poster

- Rapid Oral:

- 1) Dana Barnea, MD: Mortality after Thyroid Cancer as an SMN
- 2) Cindy Im, PhD: Social Determinants of Health and Late Mortality

ISLCCC

- 25 submissions, 11 oral presentations

CCSS Abstracts at ISLCCC

ccss

Title

First Author

Oral Presentation

Accelerated aging among long-term survivors

AnnaLynn Williams (U. Roch.)

7 Ongoing Intervention Trials (Ancillary Studies)

CCSS



Communicating
Health
Information
with

Recruitment & Follow-up
Complete

ASPIRES



health
insurance
navigation
tools

EMPOWER

Recruitment & Follow-up
Complete



ENGAGE



salsa

Study of Active
LifeStyle Activation



Recruitment & Follow-up
Complete

SLEEPWELL

Detailed updates in [eMeeting Book](#): Page 113

NEW Randomized Trials

CCSS



Decreasing Cardiometabolic Risk in Survivors of Childhood Cancer: Survivors Engaged in [Time-Restricted Eating](#) after Therapy (STRENGTH study)

- Danielle Freidman MD, [Memorial Sloan Kettering Cancer Center](#)







ECHOS II

- Evaluation of Cardiovascular Health Outcomes Among Survivors II (ECHOS II)
 - Matt Ehrhardt MD, [SJCRH](#)
 - 4th percentile score, awaiting NOA

**Detailed Presentations This Afternoon at the
Plenary Session!**

NEW Ancillary Studies Leveraging the Genetic Resource

CCSS

- Origins and Vulnerabilities of Pediatric, Treatment-induced Gliomas (R01)
 - Adam Green MD, [Univ. of Colorado](#)
- Developing Race-specific Risk Prediction Models in African-American Survivors (R01)
 - Yadav Sapkota PhD, [SJCRH](#)
 - Cindy Im PhD, [Univ. of Minnesota](#)
- Genetic Pleiotropy Across Pediatric Cancer Outcomes (R01)
 - Zhaoming Wang, [SJCRH](#)
 - Cindy Im PhD, [Univ. of Minnesota](#)
- Genomics-based Mechanistic Investigation of Treatment-related Cardiotoxicity (R01)
 - Zhaoming Wang PhD, [SJCRH](#)

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	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

Funding Years 28-32: Update

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, 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
- } Follow-up 8 & 9 Surveys



**St. Jude Survivorship
Portal: Full Presentation
at Plenary Session**

Current Funding Period: 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.

1. PRO-based data collection, focused on functional outcomes

Follow-up 8: New Measures for Aging

ccss

- 20 pages in length, Development Team: Ness, Krull, Snyder, Nathan, Leisenring, Alston, McDonald
- 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
PHYSICAL PERFORMANCE ASSESSMENT	
Katz Activities of Daily Living	Self-reported functional status including bathing, transferring, dressing, self-care tasks for independent living.
Lawton Instrumental Activities of Daily Living	Self-reported functional status including using the telephone, transportation, housekeeping, ability to manage finances and prepare meals and other tasks required to live independently.
Fried Frailty Criteria (Self-reported)	Identifies survivors with physiologic frailty
Cumulative Illness Rating Scale	Summarizes disease burden across 14 organ-systems, with items scored 0-4 (none to extremely severe problem).
NEUROCOGNITIVE ASSESSMENT	
CCSS Neurocognitive Questionnaire (NCQ)	Task efficiency (attention + processing speed), memory, executive function.
PROMIS Cognitive Function SF	General cognitive function.
PROMIS Social Roles and Activities SF	Social roles and community activities.
Alzheimer's Disease Caregiver Questionnaire	Caregiver Proxy Identified for Future Survey on: Memory, language, executive function, behavior.

Ongoing Participation of the Cohort

ccss

Follow-Up Survey Participation (Survivors)

Questionnaire	Number of Pages	Presumed Eligible	Participation Rate	Non-Response	Refused Questionnaire	Dropout of Study	Lost to Follow-Up
Follow-Up 1	16	n = 12,884	81%	6%	2%	4%	7%
Follow-Up 2	24	n = 11,859	78%	8%	3%	5%	6%
Follow-Up 3	4	n = 11,393	78%	5%	1%	3%	13%
Follow-Up 4	28	n = 10,143	82%	9%	2%	1%	5%
Follow-Up 5	36	n = 18,041	66%	20%	2%	1%	11%
Follow-Up 6	8 – 16 ¹	n = 17,297	77%	13%	.2%	1%	9%
Follow-Up 7	32	N = 17,557	67%	22%	.5%	1%	9%

¹ The three versions of the FU6 survey were 8, 12, and 16 pages. The return rates for each version were:

- 8 pages: 78% (n = 10,245)
- 12 pages: 77% (n = 5,426)
- 16 pages: 74% (n = 1,626)

Follow-Up 8 Survey Complete

ccss

Status:

- 65% overall response rate after:
 - One initial electronic only push
 - Two paper mail outs (with ongoing electronic reminders)
 - Third paper mail out with two major changes
 - Divided 20-page survey into three, 8-page surveys, randomly distributed (based on experience that shorter survey increases participation)
 - \$10 bill on cover (paper only)

Follow-Up 8 Data Freeze

ccss

Goal: Summer 2025

What should you do in the meantime?

Submit your Application of Intent (AOI, found on the CCSS Website) and then complete a Concept for Analysis for approval by the CCSS Publications Committee!

Total Call, Email, and Text Communication Efforts

ccss

Total Participant Communication Efforts Recorded after Invite: 342,782

Total FU8 Calls 50,427

Total Emails 244,845

Total Text Messages 47,510

Average Calls, Email, Texts to Eligible Participants: 17,621

Average FU8 Call Per Participant 3

Average FU8 Emails Per Participant 14

Average FU8 Text Messages Per Participant 3

Call Center Activity following FU8 Survey Mailing

ccss

10,869 (84%) non-participants were placed in follow-up call rotation

- 10,528 (97%) were called one or more times.
 - 38,640 total calls
 - 3,863 (36%) were reached during the call
 - 9,122 non-responders were left 24,745 messages
 - 292 participants activated their myLTFU Portal Account during a call
 - 483 participants completed their Follow-Up 8 survey during a call

Follow-up 9 Plan

CCSS

Two major decisions were TBD at our last meeting regarding the plan for the Follow-Up 9 Survey distribution:

- **Survey Length:** 3 short surveys
 - Randomly distributed electronically, include \$10 gift card.
 - At completion of first survey, the second survey will be offered immediately for those who “want it now”
 - If they don’t complete immediately, at 4 months from completion of first survey second survey will be distributed, with goal of completing 3 short surveys in two year (full content of 20-page version)
 - Limitations:
 - Number who will complete all three short surveys is unknown
 - Higher cost for incentives
- **Survey Mode:** Full electronic (no paper version, but use of a postcard reminder)
 - Strength: can “pre-fill” chronic health conditions
 - Limitation: Impact on participation rate is not known
 - Alternative Strategy: We will have a paper version ready


Current Funding Period: 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.

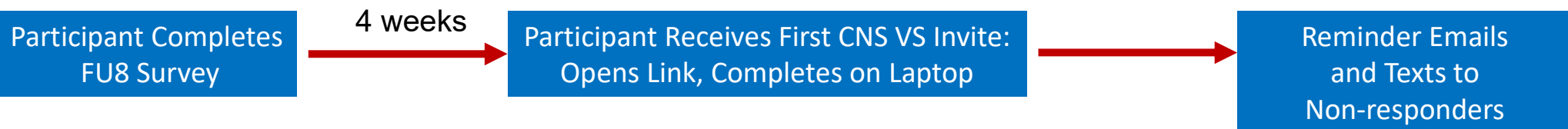
1. PRO-based data collection, focused on functional outcomes
2. Web-based neurocognitive assessment (CNS Vital Signs)

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

CNS Vital Signs

CCSS

Procedure:



Pilot (2019):

- 70/90 (77.8%) invited participants completed CNS VS within 4 weeks
- Data received was sufficient quality for analysis
- Moderate/severe neurocognitive impairment performed worse on all domains

CNS VS Results:

Survivors	N	%	Siblings	N	%
Invited to CNS VS	10,462		Invited to CNS VS	1,830	
Assessment Completed	5,441	52.0%	Assessment Completed	1,011	55.2%
Pending	4,332	41.4%	Pending	729	39.8%
In Tracing	139	1.9%	In Tracing	27	2.0%
Refused CNS VS	394	5.4%	Refused CNS VS	49	3.6%


Detailed updates in [eMeeting Book](#): Page 22

Current Funding Period: 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.

1. PRO-based data collection, focused on functional outcomes
 2. Web-based neurocognitive assessment (CNS Vital Signs)
 3. Develop a population [resource for intervention trials](#) through in-home functional/lab assessment of 1000 sub-cohort of survivors (frail, pre-frail, not frail)
- 
- A blue callout box with a white arrow pointing left towards the first two items of the list. The box contains the following text:
1. Entire CCSS population
 2. Twice in funding period

In Home Assessment of 1000 Survivors: Sub-cohort for Intervention Trials

CCSS

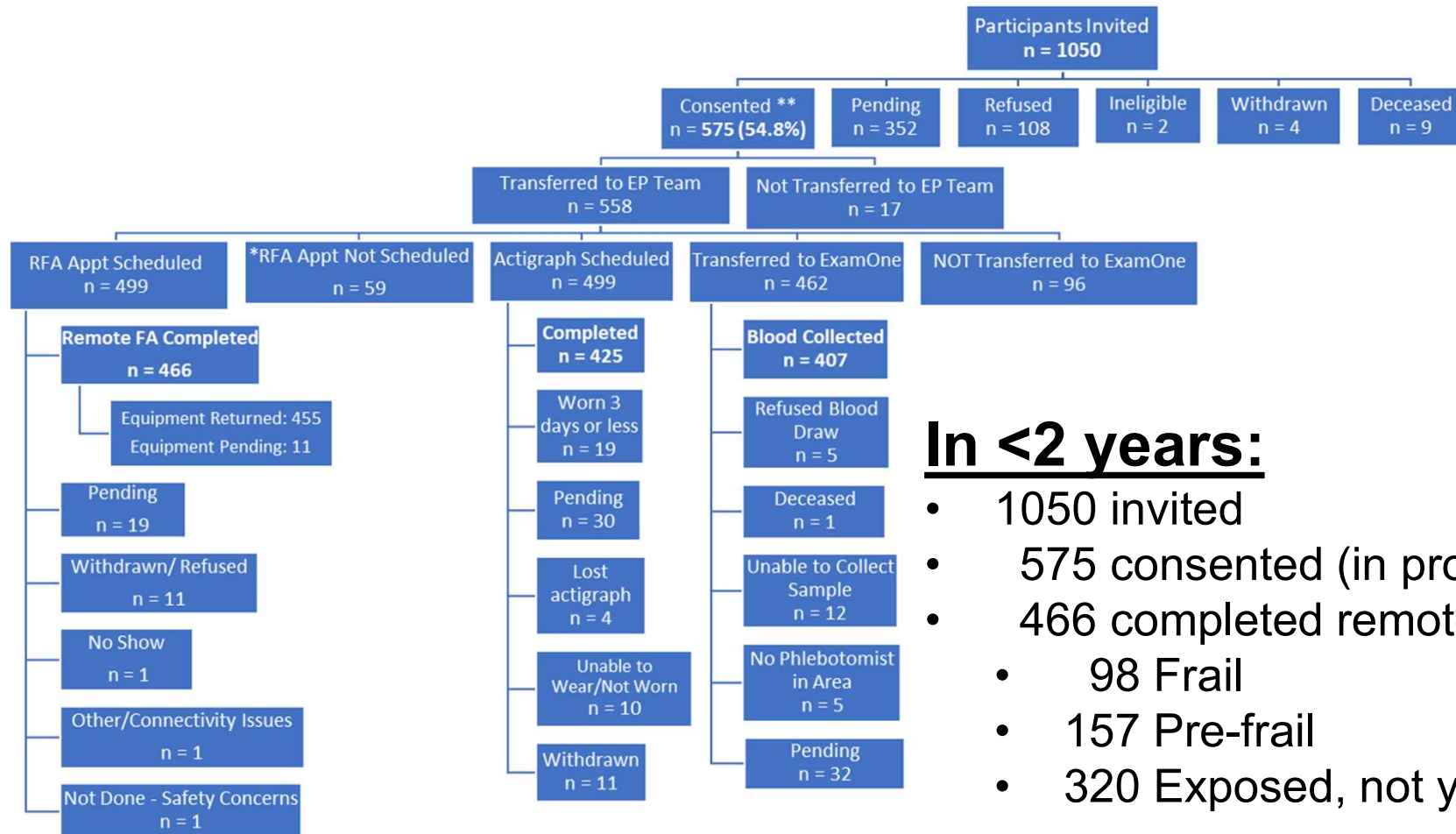
Year 29 (12/1/22)

- 01/26/23: Phlebotek (vendor) announces ***IMMEDIATE SHUT DOWN!***
- Decision to abandon vendor-based in home assessment
 - Leverage telehealth remote assessment to complete evaluation
- 6/12/23: Sub-cohort evaluation began



In Home Assessment (as of 4/3/24)

ccss



In <2 years:

- 1050 invited
- 575 consented (in process)
- 466 completed remote assessment
 - 98 Frail
 - 157 Pre-frail
 - 320 Exposed, not yet frail

Current Funding Period: 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.

- FU8 Survey will 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
 - Program Director, Building Lifestyle, Outcomes, and Care Services Research in Cancer (BLOCS), Johns Hopkins



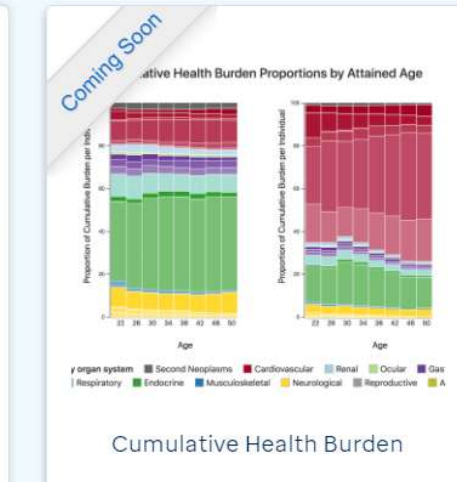
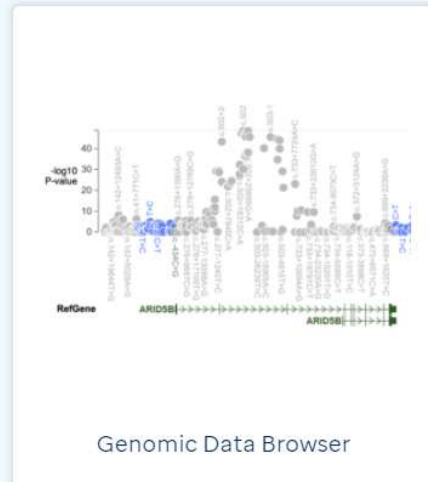
Current Funding Period: Major Objectives

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



Status:

- All 25,735 **CCSS** participants
- All 5,053 **SJLIFE** Participants
- Genotype imputation on the existing SNP array data for harmonization with the WGS samples for integrative analysis

Additional Details during the Plenary Session!



Updates on STAR ACT 2022: Supplemental Funding to Further Expand the Genomic and Biospecimen Resource

CCSS

1. Additional support to increase (maximize) **blood banking** participation

- Results: 41% consented, 34% provided blood specimen
- 2,107 new specimens
- Totals:
 - **5,029** with blood specimen available
 - **11,351** with blood OR Oragene available

Detailed updates in [eMeeting Book](#): Page 20

2. **Additional WGS/WES** of CCSS participants

- 1,750 survivors have provided a new, first-time specimen
- WGS/WES Sequencing by Hudson Alpha **ongoing**
- **Goal:** 1,500 additional survivors with WGS/WES



Childhood Cancer
STAR ACT
Survivorship Treatment Access and Research
H.R. 820 - 5292

Three New STAR ACT Supplements Awarded in 2023 & 2024

CCSS

#1: Feasibility of RT Treatment and Dose Evaluation 2000-2022

Objective: To develop and test a standardized data collection and processing methodology for use in a future CCSS expansion

- Collect 140 DICOM files from five CCSS sites
- Centralize to Dosimetry Center at MD Anderson, dosimetry estimates
- Feasibility of using IROC (Imaging and Radiation Oncology Core)



#2: Feasibility of EHR-based MRAF data abstraction to reduce (but not eliminate) need for manual abstraction in a Millennium Expansion:

- Cumulative dose chemotherapy?
- Other MRAF data: surgeries, protocols, etc.?
- Tool: ExtractEHR (Richard Aplenc, Tamara Miller)



#3: Leverage the newly banked blood specimens to perform methylation profiling on 2,500 survivors with blood specimens



#4: Leverage the newly banked blood specimens to sequence for CHIP on 2,285 survivors with blood specimens



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	WGS Available in the St. Jude Cloud

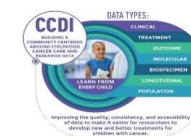
1,500 new
WGS/WES!

2,500 new
Methylation
arrays!

2,285 new
CHIP!

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



Current Funding Period: Major Objectives

ccss

Strategic Plan for Future Millennium 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 current 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)

Expansion Specific Steering Committee San Diego: January 2024

CCSS



Greg Armstrong, MD, MSCE
St. Jude Children's Research Hospital



Tara O. Henderson, MD, MPH
The University of Chicago Medicine



Aaron McDonald, PhD
St. Jude Children's Research Hospital



Eric Chow, MD, MPH
Fred Hutchinson Cancer Center



Wendy Leisenring, ScD
Fred Hutchinson Cancer Center



Saro H. Armenian, D.O., M.P.H.
City of Hope



Rebecca M. Howell, PhD
MD Anderson Cancer Center



Louis (Sandy) Constine, MD
University of Rochester Medical Center St. Jude Children's Research Hospital



Shari Capers
St. Jude Children's Research Hospital



Diana Merino, PhD, M.S.c.
AstraZeneca



Vikki Nolan, DSc, MPH
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Michael Scheurer, PhD, MPH, FACE
Baylor College of Medicine



Nita L. Seibel, MD
National Cancer Institute



Logan Spector, PhD
University of Minnesota Medical School



Samuel L. Volchenboum, MD, PhD, MS
The University of Chicago Medicine



Karriem S. Watson, DHSc, MPH
National Institute of Health



Christopher B. Weldon, MD, PhD
Dana-Farber Cancer Institute



AnnaLynn M. Williams, PhD
University of Rochester Medical Center



Torunn I. Yock, MD
Mass General Research Institute

Objectives of a CCSS Expansion

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Objective: To identify the prevalence and risk factors for long-term outcomes of cancer and **contemporary cancer therapy** for children diagnosed and treated **2000-2023** compared to survivors from previous eras.

- To identify how changes in **radiation** therapy **dose, volumes**, and **treatment modality** have altered the nature and risk of late effects
- To establish a resource for identification of **early signals** of late effects from novel therapies (e.g., targeted therapy, immunotherapy, cellular therapies)

Objective: Leverage the large eligible population to develop a resource for late outcomes among populations traditionally underrepresented in research

Objective: Create a resource for **genetic, genomic** and **biomarker** research

Objective: Develop a population resource for development of evidence-based guidelines, interventions, policy and advocacy for contemporary survivors

Uncertainty
+ Chaos

Be Prepared!

Funding Plan for a Millennium Expansion

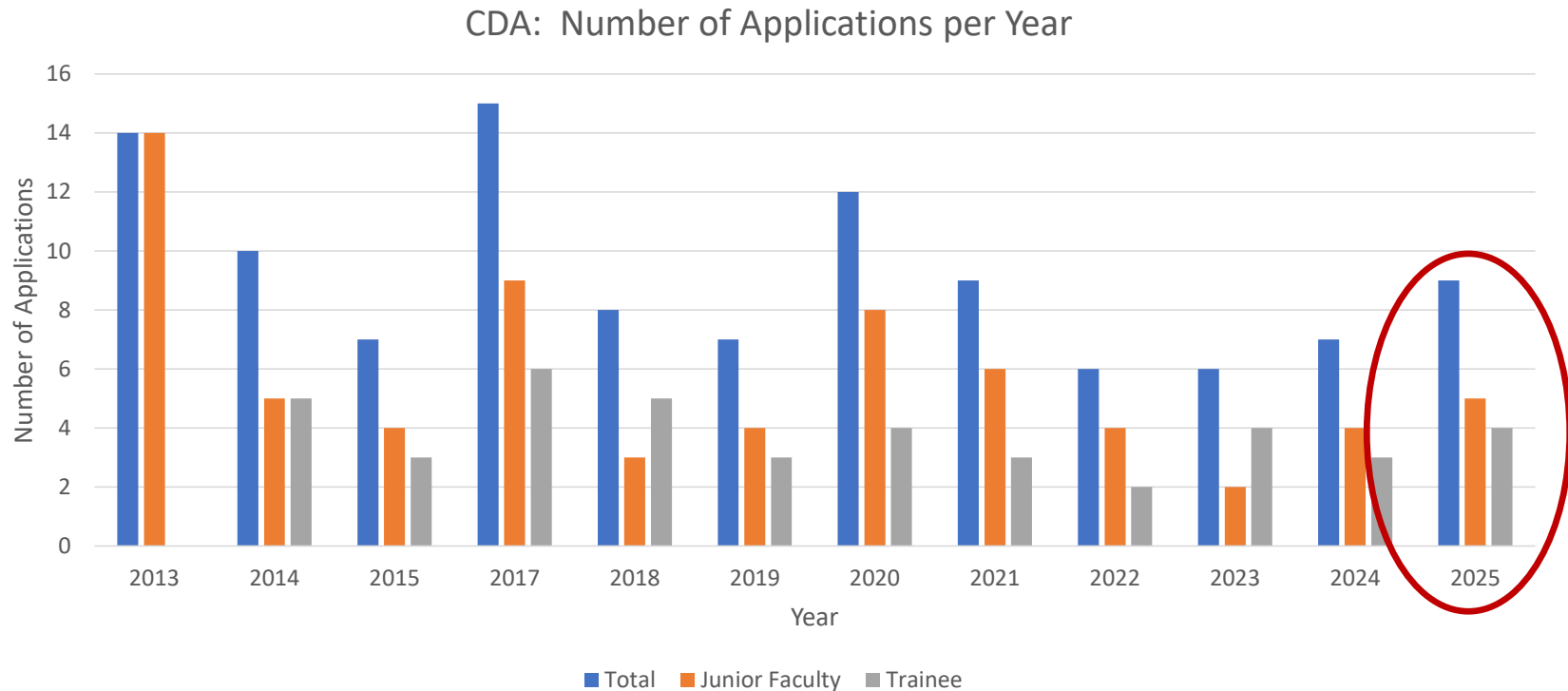
CCSS

- CCSS Expansion
 - April: approved by NCI Senior Program Leadership (SPL; Doug Lowey, Acting NCI Director)
 - Plan:
 - Present to ~~BSA~~ (NCI's Board of Scientific Advisors) this summer
 - RFA July 2025
 - Submission due December 15th, 2025
 - Late April: BSA Dissolved
 - Now: await review by the NIH, timing unknown

Career Development Award

ccss

2025: 9 applications (5 junior faculty, 4 trainee)



Career Development Award 2024

ccss

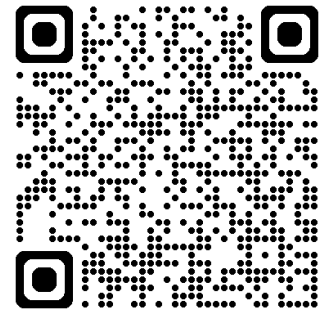
CCSS Career Development Award Winners

Category	Awardee	Application Title	CCSS Working Group	Primary Mentor	Status
2025					
Junior Faculty	Echo Warner, PhD College of Nursing, University of Utah	Evaluating the Need for Dyadic Intervention Adaptation in the Health Insurance Navigation Tools (HINT) Intervention	Cancer Control/ Psychology	Anne Kirchhoff	Analysis Underway
Trainee	Amy Berkman, MD, St. Jude Children's Research Hospital	Accelerated Aging and Risk of Subsequent Neoplasms in Survivors of Childhood Cancer	Second Malignancy/ Epidemiology and Biostatistics	Melissa Hudson	Analysis Underway
Trainee	Han-Wei Wu, MD, Memorial Sloan Kettering Cancer Center	Genetic Variants, Treatment Exposures and their Associations with the Development of Colorectal Cancer as a Subsequent Malignant Neoplasm in Long-term Survivors of Childhood Cancer	Genetics/ Second Malignancy/ Epidemiology and Biostatistics	Chaya Moskowitz	Concept Pending

Career Development Award

ccss

Announcing the 2026 CCSS Career Development Award
Application due date: October 1, 2025



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.

*Thank you to Saro who leads this effort



CCSS 101 is back!

An introduction to CCSS including how to use the resource to advance
your research

Thursday, June 19, 7:00- 7:45 AM

Location: Cove Meeting Room

Eric Chow, MD & Cindy Im, PhD

Founders Reception

ccss

You are formally invited to attend the
CCSS Founders Reception

Tonight!

6:30 - 7:30 pm

Rooftop Plaza

Dinner to Follow: [Harbor Ballroom](#) 6:30 – 9:00 pm

Steering Committee: Founding Members

ccss

Les Robison
John D. Boice
Norman E. Breslow
Sarah S. Donaldson
Dan Green
Frederic P. Li
Anna T. Meadows
Ann Mertens
John Mulvihill
Joe Neglia



Mark E. Nesbit
Roger J. Packer
John D. Potter
Charles A. Sklar
Malcolm A. Smith
Marilyn Stovall
Louise C. Strong
Yutaka Yasui
Lonnie K. Zeltzer

Founding Institutional Principal Investigators

ccss

Arthur Ablin

Roger Berkow

George Buchanan

Zoann Dreyer

Daniel Green

Mark Greenberg

Holcombe Grier

Melissa Hudson

Raymond Hutchinson

Michael Link

Anna Meadows

Joe Neglia

Lorie Odom

Maura O'Leary

Thomas Pendergrass

Gregory Reaman

Kim Ritchey

Kathy Ruccione

Frederick Ruymann

Charles Sklar

Anthony Smithson

Louise Strong

Robert Weetman

Teresa Vietti

Lonnie Zeltzer