

CCSS Investigator Meeting

June 19, 2019
Atlanta, GA

CCSS

Childhood Cancer
Survivor Study



St. Jude Children's
Research Hospital

An NCI-funded Resource

Meeting Agenda: Day 1

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Wednesday, June 19			
7:00 – 8:00 am	Breakfast Buffet	Executive Committee	Conference Dining Room
8:00 – 10:00 am	CCSS Executive Committee		Salons 3-5
10:00 am – 1:00 pm	CCSS Steering Committee and Principal Investigators	Steering and Executive Committees, Institutional PIs	Salons 3-5
1:00 – 2:00 pm	Lunch	Steering and Executive Committees, Institutional PIs	Conference Dining Room
2:00 – 6:30 pm	Plenary Session	All Attendees	Emory Amphitheatre
6:30 – 7:30 pm	Founders Reception	All Attendees	Garden Courtyard
6:30 – 9:00 pm	Dinner		Conference Dining Room

Meeting Agenda: Day 2

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<i>Thursday, June 20</i>			
7:00 – 8:00 am	Breakfast Buffet	All Attendees	Conference Dining Room
7:00 – 7:45 am	CCSS 101 (E. Chow)	Early Career/New CCSS Investigators	Maple Room
8:00 am – 10:30 am	Plenary Session	All Attendees	Emory Amphitheatre
10:30 – 12:00 pm	Break-Out Sessions	All Attendees	To Be Announced
12:00 pm	Adjourn		

CCSS Principal Investigator Report

June 19, 2019
Atlanta, GA

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Childhood Cancer
Survivor Study



St. Jude Children's
Research Hospital

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Funding Years 23-27: Work Scope

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Maintain and Promote the Resource

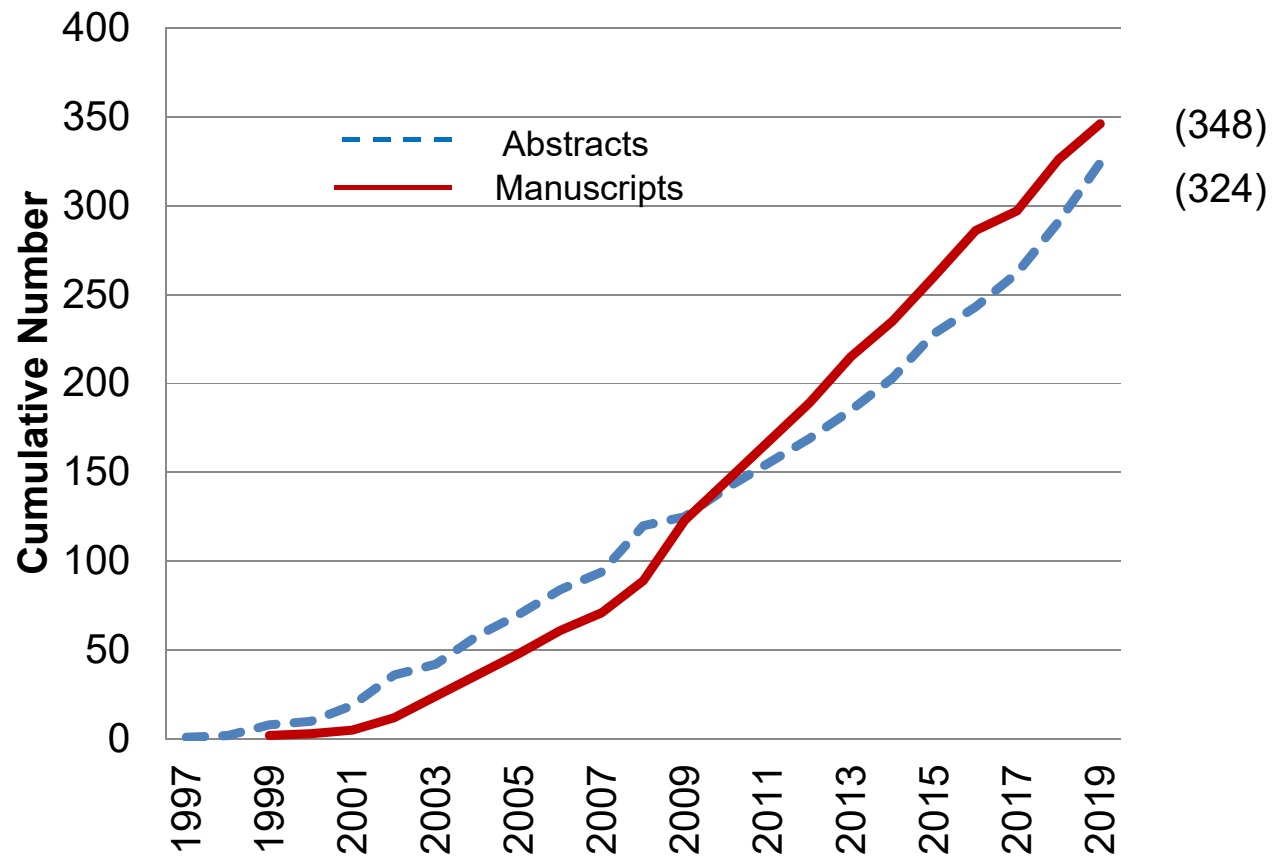
- Ongoing Follow-up of the active participants in the cohort (1970-1999)
- Support for Coordinating Center (St. Jude) and four support facilities for tracking/tracing, data cleaning/freeze, Oragene and blood/tissue collection, SMN pathology confirmation, biorepository, ongoing genotyping/sequencing efforts with NCI, and analysis/publication of results

Enhance the Resource

- New CCSS Support facility: CCSS mHealth Technology Center (Jeff Olgin, PI)
- Ascertainment of 500 SMN somatic tissue specimens over five years
- Replenish Oragene specimens

CCSS Abstracts and Publications

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2018 CCSS Abstract Highlights

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2018

29 abstracts accepted for presentation (19 as oral presentation)

- ASCO (12 submitted/5 oral presentations)
- SIOF (5 submitted, 3 oral)
- AACR (3 submitted, 2 oral)

2019

31 submitted to date

- ASCO (17 submitted: 3 oral, 2 poster discussion)
- NASLCCC (23 submitted: 13 oral presentations)

2018 CCSS Publications (n=27)

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Impact Factor >10

Lancet Oncology
J Clin Oncol (3)
JAMA Oncol (2)
JNCI (2)
Nature Communications

Impact Factor 5-10

Neuro Oncol
Cancer (6)

Impact Factor <5

BMC Genomics
CEBP
J Cancer Surv (2)
Pediatr Blood Cancer
Psychooncology (2)
Radiat Res
Scan Journal Stat
Stat Med
Stat Interfac

-33% in journals with impact factor >10

-60% moderate to high impact journals

2019 CCSS Publications (to date: n= 22)

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Impact Factor >10

Blood
JAMA Oncol
JAMA Pediatrics
J Clin Oncol (6)
JNCI
Lancet Oncology

Impact Factor <5

Addiction
Genes Chrom Cancer
Psychooncology

Impact Factor 5-10

Cancer (4)
Eur J Cancer
Int J Radiat Onc Biol Phys
J Invest Dermatol (2)

-50% in journals with impact factor >10
-86% moderate to high impact journals

Investigator Initiated Ancillary Studies: 2018-2019

Eight Studies, \$12.2 million in funding

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PI	Topic	Funding Source
Kevin Oeffinger (Duke)	EMPOWER II: Promoting Breast Cancer Screening in Female Survivors	NIH R01
Liang Zhu (MD Anderson)	Statistical Analysis for Mixed Outcome Measures in Recurrent Event Studies	NIH R03
Cecile Ronckers (Princess Maxima)	Risk Factors for Female Breast Cancer after Treatment: An International Collaboration	Kika Foundation
Lucie Turcotte (Univ. of Minnesota)	Breast Cancer after Treatment for Childhood Cancer: Survival, Treatment Choices and Outcomes	NIH K08
Jennifer Yeh (Harvard)	Using Anthracycline-associated Cardiomyopathy as a Model to Guide Care	NIH R01
Elyse Park (Mass General)	Developing a Health Insurance Navigation Program for Survivors	American Cancer Society
Awaiting NOA		
Tara Brinkman (SJCRH)	Impact of eHealth Intervention on Insomnia	NIH R01
I-Chan Huang (SJCRH)	Developing PRO-CTCAE for Childhood Survivors	NIH R01

Follow-Up 6 Participation Rates

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Timeline: Began August 2017, anticipated completion July 2019

	Length	Contents	Participation Rate to Date (limited to batches mailed in 2017)
FU6 Short	8 pages	SMN, Sleep Quality	75.9%
FU6 Medium	12 pages	+ Financial Toxicity	74.4%
FU6 Long	16 pages	Full Survey	70.9%

Follow-Up 7: 32 page survey, to begin August 1, 2019

Attrition

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	Baseline		Participating		Deceased		Drop Out	
	N	%	N	%	N	%	N	%
Overall	25,658	-	19,506	76%	3,897	15%	2,255	9%

Summary:

- Overall, strong continued participation
- Drop out rate is low to moderate
- Death is the more significant threat to the study

SMN Tissue Enrichment

- Goal of 500 new tissues during the funding period
- >370 samples added to Bio-Pathology Center, total of 632 samples
- Need: to promote the resource for research

Resource for Genetic Investigation

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Genome Wide Association Studies

- Genetic variants associated with therapy-related late effects
- **5,739** survivors genotyped, Original Cohort (diagnosed 1970-1986)
- Collaboration with Division of Cancer Epidemiology and Genetics (Morton/Chanock)

Next-generation Sequencing

- Whole Exome: **5,451** survivors, Original Cohort (Morton/Chanock DCEG)
- Whole Genome (30X) + Whole Exome (100X): **3,000** survivors (SJCRH), Expansion Cohort (1987-1999)
 - Publicly available, St. Jude Cloud

>8,000 survivors sequenced and available as a resource by end of 2019

Enhance the Resource: New Objective for a New Funding Period

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Direct Assessment:



New CCSS Support facility: CCSS mHealth Technology Center
(Jeff Olgin, PI)

- Resource for mHealth/technology based intervention studies
- Primary engagement: ~~App-based~~ interaction with CCSS

Benchmarks for mHealth Success

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1. mHealth-based intervention research

- Two funded intervention trials (Oeffinger, Brinkman)
- Two intervention trials submitted (UO1: Su & Ehrhardt)
- Four additional studies under development

Topic	Investigator
Colon cancer screening <u>intervention</u>	Tara Henderson
Chronic pain <u>intervention</u>	Nicole Alberts
Autonomic dysfunction assessment	Kiri Ness/John Groarke
Mobile-based symptom assessment	I-Chan Huang

mHealth Developmental “Lab”

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1. Pilot home BP monitoring (Chow)

- Will follow completion of CHIP Trial with deliver of bluetooth BP cuff
- Goal of routine BP monitoring over one week, for use in CHIP II grant
- Eureka (Olgin) working closely with CHIP team on rapid timeline



2. Spire Stone and Tag (Alberts)

- Respiratory monitor/feedback, chronic pain intervention
- Recruiting survivors who completed the EASE study and have pain
- 36 invited, 21 (58%) participating (ongoing) for one month trial (randomized)
- Excellent engagement to date
- Preliminary data for R01 submission



mHealth Developmental “Lab”

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3. SAM: Symptom Assessment and Monitoring (I-Chan Huang)

- Symptom assessment via smartphone
- Multiple assessments over 3 months to assess change over time
- Rapid identification of symptoms for early intervention
- 30 recruited to date, 15 (50%) participating (recruitment ongoing)
- 100% completion of daily symptom tracker by all participants

4. Autonomic dysfunction (Ness/Groarke)

- WHOOP device: measures HR, HR variability, recovery
- Validation in Ness lab (SJLIFE)
- Preliminary data for R01 submission (Fall 2019):
 - Prevalence and predictors of autonomic dysfunction



Benchmarks for mHealth Success

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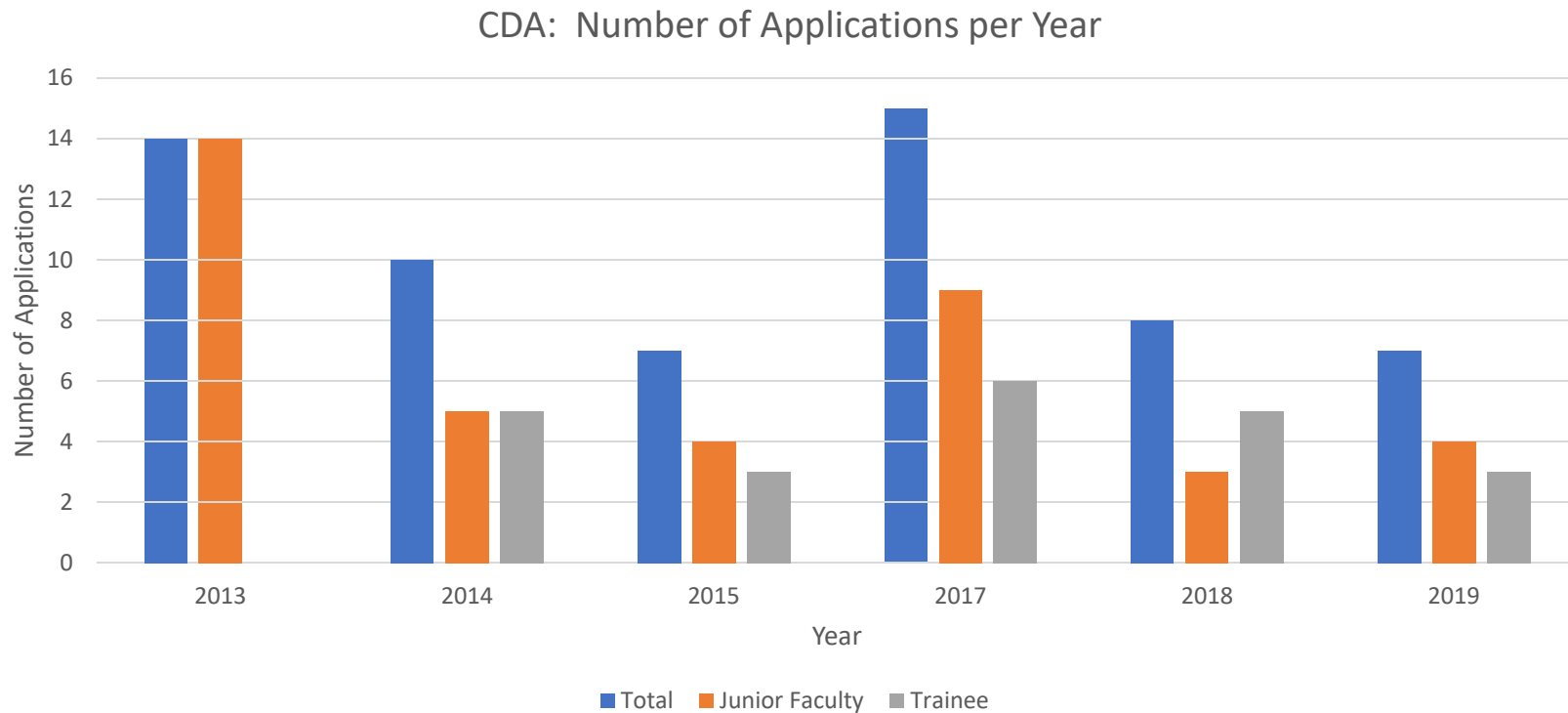
2. Develop a pool of 10,000-12,000 survivors on an mHealth platform available for intervention trials

- Will push FU7 to 25,000 participants via mHealth platform as the primary mode for survey completion
- To achieve this we will deliver the new *myLTFU* web-app to all participants
 - Multi-channel: web-app, pc-based, tablet-based completion
 - *myLTFU*: new home for “all things LTFU” including newsletters, resources
- Plan: Full court press of *myLTFU* deployment and app-based survey completion August 1- January 1, 2020 to maximize web-based and app-based completion

Career Development Award

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2018: 7 applications (4 Junior faculty, 3 trainee)



Career Development Award

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Among 17 awardees:

- 5 Published/In Press Manuscripts (JCO x2, Psychooncology, J Cancer Surv., Genes Chrom Cancer)
 - 6 abstracts submitted
- 1 Currently Submitted Manuscripts (JNCI)
- 4 Manuscript Drafted
- 7 Analysis Underway

Career Development Award

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St. Jude Children's
Research Hospital
ALSAC • Danny Thomas, Founder

The Childhood Cancer Survivor Study



CCSS
Childhood Cancer Survivor Study

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Announcing the 2020 CCSS Career Development Award
Application due date: October 1, 2019

[Call for Applications](#)

CCSS Newsletter

Sign up for the CCSS Newsletter to receive notifications, new publications and new abstracts that have been added to the site.

Name *

New Executive Committee Member

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Saro Armenian, DO, MPH

- Associate Professor, Depts. Of Pediatrics and Population Sciences, City of Hope
- Director, Division of Outcomes Research
- Director, Childhood Cancer Survivorship Clinic

New Institutional Principal Investigator

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Katharine Rae Lange, MD

- Assistant Professor, Pediatric Hematology/Oncology
Children's Hospitals and Clinics of Minnesota
- Completed Fellowship at Memorial Sloan Kettering Cancer Center
- Succeeding Joanna Perkins as Institutional PI

Founders Reception

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You are formally invited to attend the
CCSS Founders Reception

6:30 - 7:30 pm
Garden Courtyard

Steering Committee: Initial Members

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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

Initial Institutional Principal Investigators

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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

Thank you, Chuck!

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Charles A. Sklar, MD

- Professor, Pediatric Endocrinology, Memorial Sloan Kettering Cancer Center
- Director, Long-Term Follow-Up Program
- Original Working Group Chair: Chronic Conditions Working Group
- Founding PI: MSKCC
- Founding Steering Committee Member
- Retiring from MSKCC this year

Questions?

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Four New CCSS Institutions: Enrollment and Data Freeze Complete!

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	White		Black		Asian/Pacific Islander		Other		Hispanic	
	N	%	N	%	N	%	N	%	N	%
TOTAL ELIGIBLE	1461	-	166	-	58	-	260	-	361	-
TOTAL PARTICIPATING	851	58%	83	50%	35	60%	125	48%	195	54%

Other Opportunities

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Administrative supplement

- NCI supplement for grant and cooperative agreement awards to support pediatric cancer control research across the lifespan (NOT-CA-18-088)
- Total Award: \$120,439 to support NDI linkage

Virtual Pooled Registry

- CCSS invited to participate in pilot

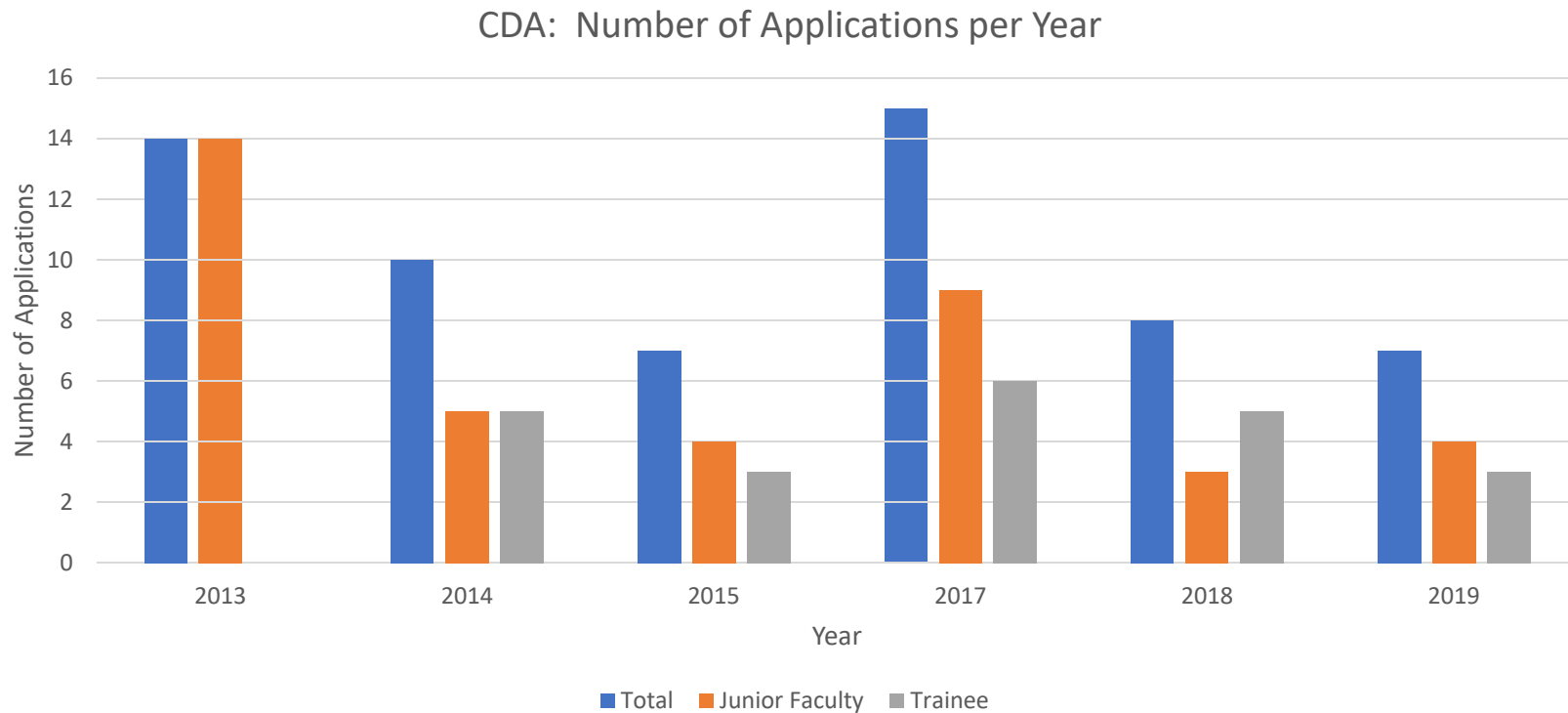
BIG TEAM

LITTLE ME

Career Development Award (page 133)

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2018: 7 applications (4 Junior faculty, 3 trainee)



Career Development Award (page 133)

CCSS

Among 15 awardees:

- 4 Published/In Press Manuscripts (JCO, Psychooncology, J Cancer Surv.,
Genes Chrom Cancer)
 - 6 abstracts submitted
- 1 Currently Submitted Manuscripts (JCO)
- 5 Manuscript Drafted
- 2 Analysis Underway
- 3 Concepts Approved (all from 2018 awardees)

LTFU Long-Term Follow-Up Study Update Spring 2017

A NOTE FROM US

On behalf of our entire study team, thank you for your dedication to the Long-Term Follow-Up Study (LTFU). You are a vital partner in this research.

The LTFU Study is the world's longest-running study of survivors of childhood cancer. Together we're helping to improve the health of survivors everywhere and for generations to come.

Our goal is to keep you engaged and informed. That's why we're launching a redesigned newsletter that we think is as exciting and future-oriented as the LTFU Study itself. In addition to the articles you've enjoyed in the past, you'll read about what's been happening, what's upcoming, and how your participation is making a difference.

The National Cancer Institute (NCI) recently renewed its support for the study through 2022. In announcing the award, NCI described the Long-Term Follow-Up Study as "One of the most powerful NCI-supported research efforts for tracking the needs and health of survivors."

NCI's ongoing support affirms the importance of the advances we are making, thanks to your dedication. We are proud to have their support and grateful to our 24,363 participants.

We are always glad to hear from you. We welcome your suggestions and feedback and invite you to call us toll-free at 800-775-2167 or email LTFU@stjude.org.

With thanks,

Gregory Armstrong, MD
Principal investigator



Shorter survey coming

We are in the process of finalizing our next survey, Follow-Up 2017. New questions in this survey will help us learn more about the important financial

issues that survivors may face as a result of their childhood illness.

Much shorter! Follow-Up 2017 will be short. The last survey was 36 pages, and some of you reported that it was a challenge to find the time to complete it. We value your time and recognize that you have busy lives, so we designed a much shorter survey this time.

When to expect it? We plan to start sending out Follow-Up 2017 this summer. It takes several months to actually process and send more than 20,000 surveys.

For this reason, some participants will receive their surveys in 2017, others will receive them in 2018.

We will send you an announcement a few weeks in advance so you can be on the lookout for your survey in the mail.

We need your response! When your survey arrives, please take a few minutes to fill it out. We need everyone's responses to ensure the accuracy of our results. As always, we welcome your feedback or questions on any aspect of the new survey.

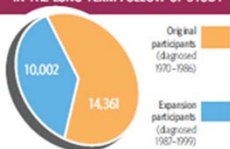
Thank you for participating!

Thank you to everyone who completed the study's most recent follow-up survey. A majority of participants completed it, and their commitment is helping to improve treatments for children newly diagnosed with cancer, and to identify ways of protecting people's health for years beyond their cancer.

The data is currently being prepared for analysis and will allow researchers to study the impact of childhood cancer in new ways, including:

- What survivors experience as they get older
- How the effects of treatment might influence the aging process

24,363 PEOPLE CURRENTLY PARTICIPATE IN THE LONG-TERM FOLLOW-UP STUDY



The LTFU Study community

Study size

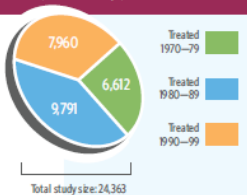
Treatments for childhood cancer have changed over time, in part because of what has been learned from the Long-Term Follow-Up Study. When the study began in 1994, we enrolled participants who were diagnosed between 1970 and 1986. More recently, we have added a new "generation" of participants diagnosed between 1987 and 1999.

Three decades of data

Now the study includes participants who were diagnosed and treated over the span of 30 years! This allows researchers to show how

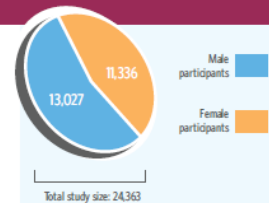
advances in treatment have improved the lives of survivors. They can also identify areas where more progress is needed to help kids diagnosed with cancer in the future.

NUMBER OF PARTICIPANTS BY TREATMENT DECADE



Gender balance

Because men and women may experience some different issues related to their childhood cancer, it is important to have good representation of both males and females.



Founder receives ACS medal of honor

Dr. Leslie L. Robison, who founded the LTFU Study in 1994, was recently awarded the American Cancer Society (ACS) Medal of Honor Award "in recognition of his lifetime contributions and dedication to research on the long-term outcomes of pediatric cancer survivors."



Dr. Robison (far right) was one of three individuals receiving the ACS award (he's photographed here with the two other recipients, Joan Brugge, PhD, left, and Charles Sawyers, MD, middle). Past recipients of the Society's Medal of Honor include former US President George H.W. Bush and former First Lady Barbara Bush, and former US Surgeon General C. Everett Koop, MD.

Good Morning America gives "Surprise Salute"

Dr. Gregory Armstrong, the LTFU Study's principal investigator, got a "surprise salute" from Good Morning America's hosts on September 9, 2016. You can watch the video here: <http://abcn.ws/2IQ3IE6>



2016 achievements

You can be proud of what you helped achieve in the past year:

- 22 publications in scientific journals
- 15 presentations at major conferences
- 9 open ancillary studies
- Funding support renewed through 2022 by the National Cancer Institute

Data Freeze

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- June 2018:
 - Subsequent Neoplasms, Follow-up 5 (page 16)
- Anticipated, December 2018
 - Four new institutions for expansion cohort
 - CTCAE graded Chronic Conditions, Follow-up 5

Follow-Up 6

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Goal: Re-engage the cohort; Establish solid participation early in the next funding cycle

Strategy:

- Shorter survey (8-12 pages)
- Improved communication materials and strategy – partnership with Harvard
 - Recontact Card, Pre-mail notification

Recontact Card

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People
move.

Email addresses
change.

Cell phones
replace landlines.

But we can't
replace **you!**

Please take a minute
to confirm your contact information.

 **LTFU**
Long-Term Follow-Up Study

It's been awhile
since we've heard from you.
Your participation in LTFU is important.

NONPROFIT ORG.
US POSTAGE PAID
MEMPHIS TN
PERMIT #186

How you benefit

- Knowing that you're making a difference in people's lives, now and for generations to come
- Informative newsletters
- Follow-up surveys every 2-5 years (online and mobile options available)
- Additional study opportunities

How to confirm or change your contact information

- Call toll free: **1-800-775-2167**
- Email us: **LTFU@stjude.org**
- Online: **ltfu.stjude.org**

You're more important than ever
as we continue to move forward.

LTFU Long-Term Follow-Up Study 

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Follow-up 6 Survey Premail Notification

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Your next survey, Follow-Up 2017, will be arriving in the mail soon.

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What to expect

- A shorter survey
- A \$10 gift to thank you for your time
- New questions to help us learn about financial issues that study participants and their families may face

What works best for you

Choose the option you prefer.

[Print](#) ■ [Web](#) ■ [Phone](#)

Mobile New! Now formatted for smartphones and tablets

Confirm your contact info

Please take a minute to check that we're sending your survey to the correct address.

Call toll free: [1-800-775-2167](tel:1-800-775-2167)

Email us: LTFU@stjude.org

Online: lfu.stjude.org

Thank you for making a difference in people's lives, now and for generations to come.

LTFU Long-Term Follow-Up Study

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Whole Exome Sequencing: Return of Results

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- 2015: CCSS Executive Committee with unanimous support for return of results for 59 gene (ACMG)
- 2017: Determination that research results will not be returned
 - St. Jude institutional policy
 - Need licensure for genetic counselors in 50 states
 - Cannot support cost of CLIA-certified testing
 - Need for local (not central) ordering physician
 - Consistent with consent that stated results will not be returned

Whole Exome Sequencing: Original Cohort

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- 5451 from CCSS original cohort in analytic build
- Quality control finalized in September, ensuring high quality variant calling
 - Importance of relying on multiple variant callers to improve variant quality
 - Consideration of complex variants (e.g., two variants very near one another)
 - More conservative filtering for variants in certain whole genome-amplified samples
 - More conservative filtering for variants in certain saliva samples with evidence of contamination (e.g., pig, cow DNA)
- Subsequent neoplasm analyses initiated
 - Highest priority: focus on variants in genes associated with radiation sensitivity and cancer predisposition

