

CCSS Investigator Meeting

June 14-15, 2017

Atlanta, GA

Meeting Agenda

<u>Day/Time</u>	<u>Topic</u>	<u>Presenter</u>	<u>Room</u>
Wednesday, June 14	<u>Update Reports</u>		Emory Amphitheatre
2:00 – 3:40 pm	Principal Investigator	G. Armstrong	
	Coordinating Center	T. Gibson	
	Data and Statistics Center	W. Leisenring	
	Radiation Physics Center	R. Howell	
	Biopathology Center	M. Arnold	
	Biorepository/Molecular Genetic Bank	S. Davies	
	Research and Publications Committee	D. Green	
	Education Committee	M. Hudson	
3:40 – 4:00 pm	Break		
4:00 – 4:30 pm	New CCSS mHealth Technology Center	M. Pletcher	Emory Amphitheatre
4:30 – 6:30 pm	<u>Research Presentations</u>		Emory Amphitheatre
	Temporal Trends in Medulloblastoma Outcomes	R. Salloum	
	Lack of Concern About Future Health in Survivors	T. Gibson	
	Utility-based Health-related Quality of Life	J. Yeh	
	Chronic Health Conditions and Cognitive Outcomes	Y. Cheung	
	Susceptibility Loci that Modify Radiation-Related Risk for Breast Cancer and Update on Genotyping/Sequencing	L. Morton	

Meeting Agenda

<i>Thursday, June 15</i>			
7:00 – 8:00 am	Breakfast Buffet	All Attendees	Conference Dining Room
8:00 am – 12:00 pm	Plenary Session*	All Attendees	Emory Amphitheatre
12:00 – 2:00 pm	Box Lunch Break-Out Sessions	All Attendees	See Plenary Session Agenda
2:00 pm	Adjourn		

Slide 3

AG3 revise to only include first day, new slide for day two
Armstrong, Greg, 6/5/2017

Principal Investigator Report

CCSS Investigator Meeting
June 14, 2017
Atlanta, GA

Funding Years 23-27

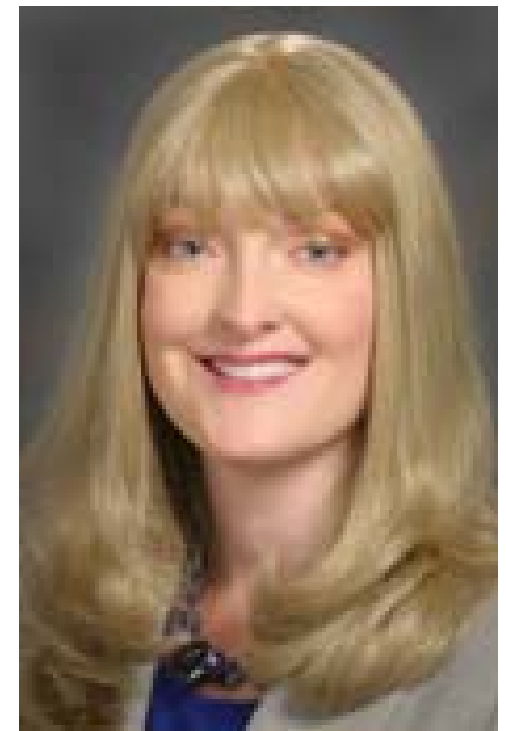
- September 2015 RFA (U24):
 - \$13.5 million (direct) over five years
- February 2016: Application submitted with budget of \$23.4 million (total)
- July 2016: Impact score of 13
- January 2017: NOA for \$19,121,066 (total)
 - 17% cut from proposed budget

Funding Years 23-27

- Enhance the Resource
 - New CCSS Support facility: CCSS mHealth Technology Center (Mark Pletcher, PI)
 - Ascertainment of 500 SMN somatic tissue specimens over five years
- 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
- One year hold:
 - CCSS Home Sample initiative
 - Career Development award

CCSS Radiation Dosimetry Center

- Marilyn Stovall, Director (1994-2016)
- New director as of 2016
 - Provide organ-specific absorbed doses from RT
 - Planning of research studies
 - Maintenance of data documenting RT for individual participants
 - Novel volume-based analyses



Rebecca Howell, PhD
Medical Physics

CCSS Biopathology Support Facility

- Sue Hammond, Director (2000-2015)
- New director as of December 2015
 - Continuing first evaluation of new SNs
 - Detailed cataloging of paraffin biospecimens
 - Reviewing and scoring histology of all previously banked and newly submitted material
 - Data and specimens now housed within Nationwide Children's Hospital Biopathology Center



Michael Arnold, M.D., Ph.D.

New Steering Committee Members

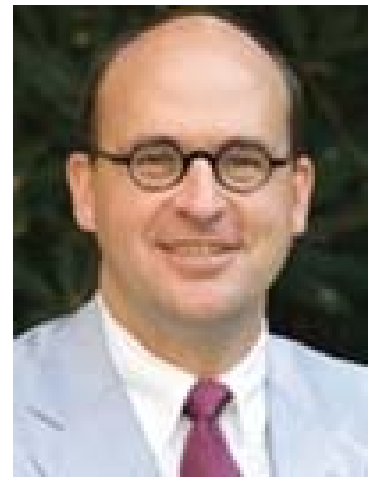


Louis S. Constine, MD

- Philip Ruben Professor of Radiation Oncology and Pediatrics
- Vice chair, Department of Radiation Oncology, Univ. of Rochester
- Director of the Judy DiMarzo Cancer Survivorship Program, Wilmot Cancer Institute
- PENTEC: Pediatric Normal Tissue Effects in Clinic

Chris Weldon, MD, PhD

- Assistant Professor of Surgery, Harvard Medical School
- Director, Surgical Critical Care, Boston Children's Hospital
- Director, Pediatric Surgery Critical Care Fellowship
- Pediatric Surgical Oncology, DFCI and BCH



New Institutional Principal Investigators

- University of Minnesota:
 - Joe Neglia (1994-present)
 - Karim Sadek, MD, MPH
- Memorial Sloan Kettering:
 - Chuck Sklar (1994-present)
 - Danielle Friedman, MD
- Stanford University:
 - Neyssa Marina (2000-present)
 - Sheri Spunt, MD



External Advisory Committee

David Hodgson

Daniel Sargent

Flora van Leeuwen

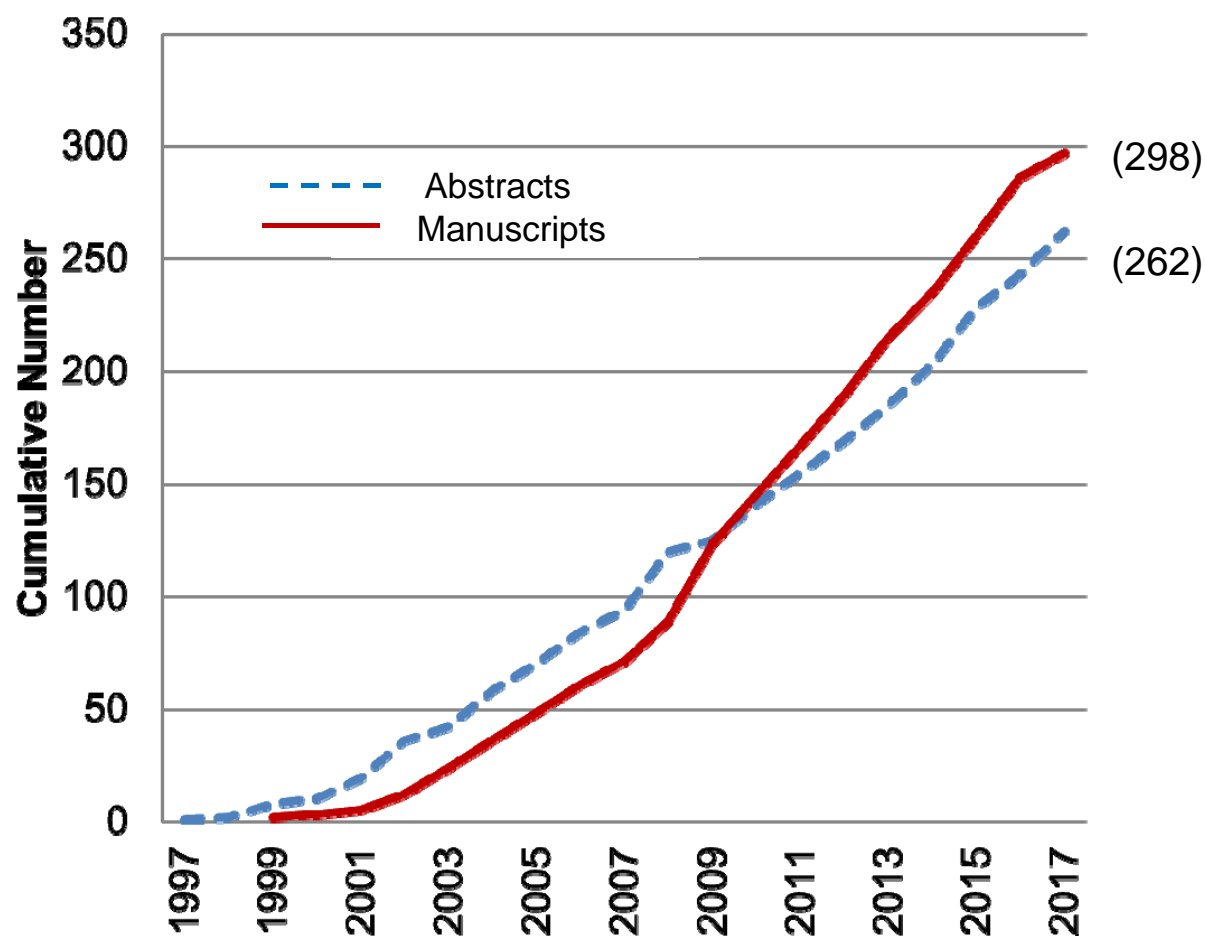
Susan Weiner

Melissa Bondy

Tim Rebbeck

Sue Cohn

CCSS Abstracts and Publications



As of June 14

2017 CCSS Abstract Highlights

- 9 submitted to ASCO
 - 4 accepted for oral presentation (J. Bates, R. Salloum, T. Gibson, J. Brooke)
- 12 submitted to Dan Green's International Meeting
 - 8 accepted for oral presentation
- 2 submitted to other conferences

2016 CCSS Publications (n=28)

Impact Factor >10

NEJM
Lancet Oncology
J Clin Oncol (4)
Ann Intern Med
JNCI

Impact Factor 5-10

Clin Cancer Res
Int J Epidemiol
Neuro Oncol
Cancer (7)

Impact Factor <5

Int J Radiat Oncol Biol Phys
J Adolesc Young Adult Oncol
J Cancer Surv (2)
J Sex Medicine
Lancet Psychiatry
Oncol Nurs Forum
Pediatr Blood Cancer
Radiat Res (2)

-30% in journals with impact factor >10,
-65% moderate to high impact journals

High Priority Expansion Analyses

- Reduction in Late Mortality
- Pregnancy/fertility after Ifosfamide, Cisplatin (Chow, EJ,)
- Social/behavioral comorbidities and profiles in adolescent survivors (Brinkman)
- Cognitive, behaviors and academic problems in AYA survivors of childhood ALL (Jacola)
- Emotional distress (D'Agostino)
- Health status (Ness)
- Temporal trends in subsequent neoplasms (Turcotte)



The NEW ENGLAND
JOURNAL of MEDICINE

THE LANCET **Oncology**



THE LANCET **Psychiatry**

Cancer

Annals of Internal Medicine

JAMA

Newly Funded Investigator Initiated Ancillary Studies: 2017

Principal Investigator: Lennie Wong (City of Hope)

Title: Cost effectiveness of breast cancer screening guidelines for female survivors of pediatric cancers

Dates of Funding: 7/17 - 6/20

Funding Source: American Cancer Society

Award: \$527,00

Newly Funded Investigator Initiated Ancillary Studies: 2017

Principal Investigator: Yutaka Yasui, Jinghui Zhang (St. Jude Children's Research Hospital)

Title: Late Effects Prediction using Clinical Phenotypes and Whole Genome Sequencing

Dates of Funding: 4/17 - 3/22

Funding Source: National Institutes of Health, RO1

Award: \$3,457,455

Study Aims:

1) Build individual risk prediction models with the SJLIFE cohort for 11 outcomes including meningioma, basal cell carcinoma, and multiple subsequent neoplasms, cardiomyopathy, obstructive/restrictive lung disease, diabetes mellitus, oligo/azoospermia, primary hypogonadism, memory deficit, executive function

2) Validate the SN risk prediction models in a larger cohort study: CCSS.

Communicating Health Information & Improving Coordination with Primary Care



Communicating
Health
Information &
Improving Coordination with
Primary Care

Principal Investigator: Eric Chow, M.D. (Fred Hutchison Cancer Institute)

Award: Scored 2nd percentile, NOA for \$3.7 million

Study Aims: Among survivors newly diagnosed, or undertreated for CVRFs (hypertension, dyslipidemia, diabetes), randomized controlled intervention to reduce undertreatment of CVRFs

Intervention: provision of lab results, survivorship care plan and remote counseling

Data Collection: 800 in-home assessments; 480 randomized to trial

International Collaborations

- Current Collaborations:
 - CHF Calculator (Chow)
 - NWTS, Emma Children's/AMC, SJLIFE
 - Anthracycline equivalence (Feijen, Chow)
 - NWTS, Emma Children's/AMC
 - Breast Cancer Prediction Model (Moskowitz, R01)
 - Validation with Dutch cohort
 - Genetic predictors of breast cancer
 - Dutch Hodgkin lymphoma cohort
 - Esophageal strictures (Asdhal)
 - ALiCCS and SJLIFE
 - Late Mortality
 - BCCSS, Miranda Fidler (CCSS Career Development Award)

Data Freeze

- October 2016:
 - Siblings from the expansion cohort (n=1,029)
 - National Death Index, mortality data through 2013
 - CTCAE graded health conditions for expansion survivors and siblings
- June 2017
 - Follow-up 5, 36 pages fully harmonizing the expansion and original cohorts
 - Subsequent Neoplasms to follow (summer 2017)

Follow Up 5

Follow-Up Survey Participation (Survivors)

Questionnaire	Number of Pages	Presumed Eligible	Participation Rate	Passive Non-Response	Actively 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	79%	12%	2.4%	1.6%	5.1%
Follow-Up 5	36	n = 18,041	63%	23%	1.7%	1.2%	14.1%

Follow-Up 6

- Goal: Re-engage the cohort; Establish solid participation early in the next funding cycle
- Strategy:
 - Dramatically shorter survey (8-12 pages)
 - Improved communication materials and strategy – partnership with Harvard
 - Pre-mail notification
 - Incentive (\$10, up front)
 - Online survey optimized for mobile devices
 - Text messaging
- Timeline: Initiate July 2017

Harvard Health Communications Core

- Previous work with:
 - ASK Ancillary Study (Geller PI)
 - Nurses Health Study
 - Growing Up Today Study (GUTS)
- Scope of services:
 - Communication strategy
 - Participant interviews
 - Brand refinement
 - FU6: pre-mailing, survey & mailer
 - Website harmonization



Recontact Card



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 

262 Danny Thomas Place MS 735 Memphis, TN 38105-3678

Follow-up 6 Survey Preamail Notification



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**

Email us: LTFU@stjude.org

Online: ltfu.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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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.

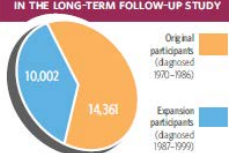
Thank you for participating!

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

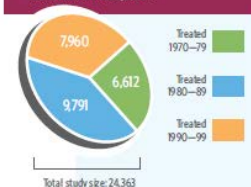
Treatments for childhood cancer have changed over time, in part because of what has been learned from the Long-Term Follow-Up Study. When the study began in 1994, we enrolled participants who were diagnosed between 1970 and 1986. More recently, we have added a new "generation" of participants diagnosed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

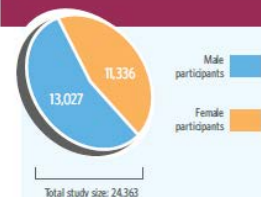
advances in treatment have improved the lives of survivors. They can also identify areas where more progress is needed to help kids diagnosed with cancer in the future.

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

Significant and Lasting Influence on the Field in the next Five Years

- Full exploitation of **expansion** analyses (1970-99)
 - Identify how risk stratification of therapy has changed patterns of late effects
 - Low risk patients, reduced therapeutic expose, fewer late effects
 - High risk patients, intensified therapy, changing pattern of late effects
- GWAS resource for **genetic investigation** (n=5,739)
 - Identify genetic variants that modify the effect of RT and chemotherapy on risk of subsequent neoplasms, and of risk independent of treatment exposure
 - Collaboration with Division of Cancer Epidemiology and Genetics
 - RFP: unparalleled resource for investigation of other chronic health conditions

CCSS GWAS Request for Proposals

- To investigate the role of genetic susceptibility in the development of non-malignant, treatment-related outcomes
- Proposals due June, October and February 1st
 - June 1, 2017: 6 applications, 5 approved
- Separate approval process for replication
 - 3 approvals to date

Whole Exome Sequencing: Original Cohort (1970-1986)

- Sequencing: 5,591 attempted (2% failure rate)
- Final quality control complete
- 5,451 in analytic build

Biospecimens : Expansion Cohort (1987-1999)

- Collection and DNA extraction on 4,646 CCSS participants
 - 3,962 (85%) oragene
 - 137 (3%) blood
 - 547 (12%) both
- SJCRH has committed to whole genome sequencing (30x) and whole exome sequencing (100x coverage)

Expansion Biospecimens

- Collaboration with St. Jude lifetime cohort (N=3000) to create the largest data set of children with cancer to date
- Will extend the work of the NIH RO1 (Yasui/Zhang)
- Data will be publicly available via the European Genomics Archive (EGA) and the St. Jude Cloud with completion of first publication
- Available through collaboration with CCSS/SJLIFE for non-overlapping aims

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 - RFP: unparalleled resource for investigation of other chronic health conditions
- Ongoing **intervention** and prediction studies

An NCI-Funded
Resource

Active Intervention Studies



EQ̄UAL

The CHIIP Study

Ancillary Studies: Proposed Intervention Trials

Principal Investigator: Kevin Oeffinger (Memorial Sloan Kettering)

Title: EMPOWER II

Proposed Funding Source: National Institutes of Health RO1

Status: Submitted March 2016, 23rd percentile, planned resubmission July 2017

Principal Investigator: Alan Geller (Harvard School of Public Health)

Title: Advancing Skin Cancer Screening Practices among Survivors of Childhood Cancer and Skin Cancer (ASK2)

Proposed Funding Source: National Institutes of Health, RO1

Status: Submitted June 2016, unscored; resubmitted February 2017

Principal Investigator: Kathy Ruble (John Hopkins University)

Title: eHealth Insomnia Intervention in Childhood Cancer Survivors: Impact on Long-Term Complications

Proposed Funding Source: NIH RO1

Status: Submitted October 2016, unscored; planned resubmission July 2017

CCSS Intervention Task Force

- **Purpose:**
 - To critically assess our present position, past and current productivity, and future potential for intervention research and to develop a strategic plan for intervention research in the cohort.
- Paul Nathan (Cancer Control and Intervention WG Chair)
 - Catherine Alfano, VP for cancer survivorship, ACS
 - Saro Armenian, Director, Division for Outcomes Research, City of Hope
- Report to be presented during the plenary session Thursday

NCI's Vision for 21st Century Technology Driven Epidemiology:



1. Include **intervention**, implementation, and outcomes
2. Share more and share everything
3. Expand cohorts **across the lifespan**
4. Use **novel technologies** to measure exposures better
5. Manage **large**, complex **data sets**
6. Expand knowledge integration
7. Train for interdisciplinary and translational research
8. Design **cost-effective** resources and infrastructure

Enhance the Resource: New Objective for a New Funding Period

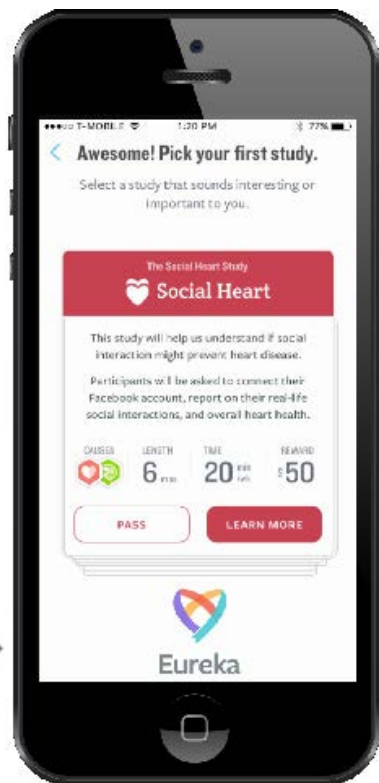
Direct Assessment:



New CCSS Support facility: CCSS mHealth Technology Center
(Mark Pletcher & Jeff Olgin, PIs)

- Resource for mHealth/technology based intervention studies
- Primary engagement: App-based interaction with CCSS, Eureka Platform
- Establish a “connected” sub-cohort of 12,000, sensor-based outcomes

Eureka Platform for CCSS Research



- Roll out Fall 2017
- Plan for three mHealth based studies
 - Activity (Ness) AG9
 - Cognitive function (Krull)
 - Chronic pain (Alberts)

Slide 38

AG9

talk with these guys

Armstrong, Greg, 6/5/2017

*An NCI-Funded
Resource*

BIG TEAM

LITTLE ME

CCSS Founders Reception

You are formally invited to attend the
CCSS Founders Reception

6:30 - 7:30 pm
Garden Courtyard

Steering Committee – Initial Members

Leslie L. Robison

John D. Boice

Norman E. Breslow

Sarah S. Donaldson

Daniel M. Green

Frederic P. Li

Anna T. Meadows

Ann C. Mertens

John J. Mulvihill

Joseph P. 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

Arthur Ablin
Roger Berkow
George Buchanan
Zoann Dreyer
Daniel Green
Mark Greenberg
Holcombe Grier
Melissa Hudson
Raymond Hutchinson
Michael Link
Anna Meadows
Joseph 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

Underline indicates presence at meeting or continuing in role as Institutional PI

CCSS Founders Reception

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6:30 - 7:30 pm
Garden Courtyard