Opportunities to Advance Knowledge and Care of Survivors of Childhood Cancer

The Childhood Cancer Survivor Study

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An NCI-funded Resource
Cancer Survival, 0-14 Years of Age

Survivorship Statistics

- >83% of children with a malignancy will achieve five-year survival
- In 2013, estimated 420,000 survivors of childhood cancer in the U.S.
- By 2020, estimated 500,000 survivors
- 1 in 750 in US is a childhood cancer survivor

Childhood Cancer Survivor Study (U24 CA55727)

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

35,649 Eligible
20,687 (1970-86)
14,962 (1987-99)*

24,363 Participants
14,361 (1970-86)
10,002 (1987-99)*

13,062 Stored DNA

* indicates expansion cohort population
Childhood Cancer Survivor Study (U24 CA 55727)
Study Participants

Resource for Survivorship Research

- Multi-disciplinary, multi-institutional (n=31) resource
- 291 Abstracts presented
- 330 Publications
  - >700 Investigators
  - 80 Trainees
- 54 Investigator-initiated ancillary studies
- $53.1 million investigator-initiated grant support
Late Mortality Among 5-Year Survivors

- Magnitude of excess cause-specific late mortality
  J Clin Oncol, 2001; JNCI, 2008

- Health-related mortality (SMN/cardiac/pulmonary etc.) exceeded recurrence
  J Clin Oncol, 2009

- Reduction in health-related mortality in more recent eras attributable to reductions in treatment intensity
  NEJM, 2016
Chronic Health Conditions

- First to document the magnitude and severity of chronic health conditions in the first three decades following treatment
  NEJM, 2006

- 54% of survivors experienced a CTCAE grades 3-5 condition by age 50
  J Clin Oncol, 2014

- Reduction in chronic health conditions in more recent eras, attributable to reductions in treatment exposure for HD, NHL, STS, Astrocytoma, Osteosarcoma
  Lancet Oncol, 2018
Subsequent Neoplasms

- Cumulative incidence SN (30%) and SMN (11%) at 30 years from diagnosis
  (JNCI, 2001; JNCI, 2010)

- First breast cancer dose-risk models and documented breast screening practices of this high-risk population
  (J Clin Oncol, 2011; JAMA, 2009)

- Breast cancer risk at 50 years (35%) identified to be similar to women with BRCA1 (31%)
  (J Clin Oncol, 2014)

- Breast cancer risk associated with anthracycline & alkylators
  (J Clin Oncol, 2015)

- Radiation dose-risk for subsequent neoplasms
  (Lancet, 2005; JNCI, 2006; JNCI, 2012)
Psychosocial & Cognitive Outcomes

- Financial Toxicity: Survivors more likely to have out of pocket costs >10% of income, which is associated with deferred care, skipping treatment follow-up
  J Clin Oncol, 2017

- Increased risk for underinsurance and “job-lock”
  JAMA Intern Med, 2017; JAMA Onc, 2018

- First comprehensive assessment of QOL and psychosocial outcomes two- to three-decades following childhood cancer
  Cancer Epi Bio Prev, 2008

- Neurocognitive impairment in survivors of CNS and certain non-CNS tumors
  JNCI, 2010; Neuropsych, 2009

- ALL Survivors without CNS RT remain at risk for cognitive dysfunction
  Lancet Psych, 2016
CANCER SURVIVORS

Cancer Diagnosis and Treatment

“Primary” Prevention

Implementation

Clinical Trials of Efficacy

Development of Intervention Strategies

High-risk Groups

Evidence-based Clinical Care Guidelines

Health-related and QOL Outcomes

“Secondary” Prevention

Model for Late Effect Research

Robison & Bhatia, Cancer Epi Bio Prev 2008
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Resource for Evidence-based Guidelines

- 50% (36 of 72) of COG Long-Term Follow-up Guidelines after chemotherapy and RT exposure informed by CCSS publications

- 82 CCSS publications referenced

- CCSS provides current status of cancer surveillance practices

Robison & Bhatia, Cancer Epi Bio Prev 2008
Model for Late Effect Research

CANCER SURVIVORS

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Randomized Controlled Intervention Trials

**ECHOS**
- Doubled rate of echocardiography screening with risk-based counsel

**EMPOWER**
- Improved rate of mammography through brief motivational interview

**ASK about skin cancer**
- Doubled skin cancer screening (physician and self-exam)

**EQUAL**
- Remote delivery of diet and physical activity for obesity

**EMPOWER**
- Smartphone-based activation to improve breast MRI screening

- Improve diagnosis and treatment of traditional CVRFs
Intervention Trials in Development

- Fatigue/sleep and neurocognitive function
- Improving delivery of remote genetic services
- Fertility concerns of female cancer survivors
- Surveillance of cardiac function using mobile health
- Colorectal cancer screening
- Chronic pain
- Patient reported outcomes for early identification of health conditions
Genome Wide Association Studies

• Genetic variants associated with therapy-related late effects
• 5,739 survivors genotyped
• Collaboration with Division of Cancer Epidemiology and Genetics (Morton/Chanock)

Next-generation Sequencing

• Whole Exome: 5,451 survivors (Morton/Chanock DCEG)
  Priority: genes associated with radiation sensitivity and cancer predisposition
• Whole Genome (30X) + Whole Exome (100X): 2,900 survivors (SJCRH)
  Publicly available, April 2019

>8,000 survivors sequenced and available as a resource by end of 2019
Enhancing the CCSS Resource

Direct Assessment: mobile health technology

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

- Primary engagement: App based interaction for CCSS participants: Eureka Platform

- Establish a “connected” sub-cohort of 12,000, sensor-based outcomes

- Resource for mHealth/technology based intervention studies
Future Priorities

- Aging-related risks and biologic mechanisms
- Precision prevention: clinical risk prediction tools
- Expanded portfolio of intervention-based research
- Genetic contributions
- Health-services needs and barriers
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