

Childhood Cancer Survivor Study  
**Epidemiology/Biostatistics Working Group**

# **Epidemiology/Biostatistics Working Group**

**CCSS Investigator Meeting  
June, 2013**

## **WG Committee**

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### **Priorities**

- **Opportunity to publish methodology publications**
- **Evaluate and respond to methodological issues that arise in CCSS**

### **Current membership**

- **Members from Statistical Center, Coordinating Center**
- **Others recruited at PI meetings**
- **Monthly conference calls**

## **Publications in past two years**

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- **Watt et al. Radiation-related risk of basal cell carcinoma in childhood cancer survivors. J Nat Cancer Inst, 2012.**
- **Zhu et al. Statistical analysis of mixed recurrent event data. Stat Med, 2013**
- **Steele et al. Predictors of Risk-based Medical Follow-up: A Report from the Childhood Cancer Survivor Study. J Cancer Survivor, 2013**

## **Progress on active analyses/projects**

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### **Cost Effectiveness of Cardiac Guideline for Survivors of Pediatric Cancers (Wong) – **manuscript submitted****

- **Utilizes CCSS data to estimate mortality rates used in simulations evaluating impact of screening guideline**

### **Impact of health behaviors and health perceptions on subsequent mortality (Cox/Nolan) – **Draft manuscript written****

- **Assess associations between overall and cause-specific mortality with health promotion, risk behaviors, screening, and health perceptions**

## **Progress on active analyses/projects**

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**Missing data imputation (Martin/Liu/Adewale/Yasui) – draft manuscript, under revisions**

- **Account for uncertainty in missing treatment data in analyses, due to not signing the medical record release form or incomplete abstraction**

**Use of inverse probability censored weighting to evaluate and handle impact of dropout bias in the CCSS (Di/Stratton/Leisenring) - draft manuscript, under revisions**

- **Evaluate whether subjects dropping out over time differ; Use information about missing subjects to adjust analyses**

## **Progress on active analyses/projects**

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**Estimating effects of anthracycline exposure on late cardiac outcomes (Ryerson/Mertens) - manuscript, under revisions**

- **Methods to determine what fraction of early cardiac outcomes among childhood cancer survivors treated with anthracyclines could be prevented by improving physical fitness.**

**Repeated-Event Cumulative Incidence (Dong/Yasui/Robison) - draft manuscript under review**

- **Develop method to describe the entire burden of multiple events over time in a cohort (e.g., multiple SMNs per subject in CCSS)**

## **Progress on active analyses/projects**

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**Access to Health Information Technology and Health Information Seeking in Adult Survivors (Claridy, Mertens) –  
Draft manuscript under review**

- **Determine the needs, preferences, attitudes, and behaviors towards health information seeking**

**Determining the best comparison group for a cancer survivor study (Kirchhoff) – Manuscript in preparation**

- **Evaluate and compare utility of other potential comparisons groups for CCSS survivors (NHANES, BRFSS)**

## **Recent findings - Conditional Survival in Pediatric Malignancies (Mertens, Yasui, Wasilewski)**

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**Previous studies of childhood cancer survivors have shown excesses in long-term mortality**

- **High-risk groups identified by demographic and treatment characteristics.**

**Conditional survival (CS) is the likelihood of not having an event (death) after a cohort of patients has actually survived for specific interval after diagnosis**

- **CS is more clinically relevant because the likelihood of survival changes after a patient has survived for a period of time**
- **Particularly useful for malignancies with a relatively high initial mortality or relapse rate that then tapers off**



## **Conditional Survival in Pediatric Malignancies**

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**To investigate conditional survival further we performed a comparative analysis of conditional survival in two large cohorts of survivors of childhood cancer:**

- **Childhood Cancer Survivor Study (CCSS)**
  - **Data from National Death Index**
- **Surveillance, Epidemiology and End Results (SEER)**
  - **SEER registries were limited to nine regions**

## **Conditional Survival in Pediatric Malignancies**

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### **Inclusion criteria:**

- **Original cancer diagnosis between 1975-1986**
- **Survived at least 5 years post-diagnosis**
- **Eight major diagnoses eligible for CCSS**

**Cause of death information using ICD-9**

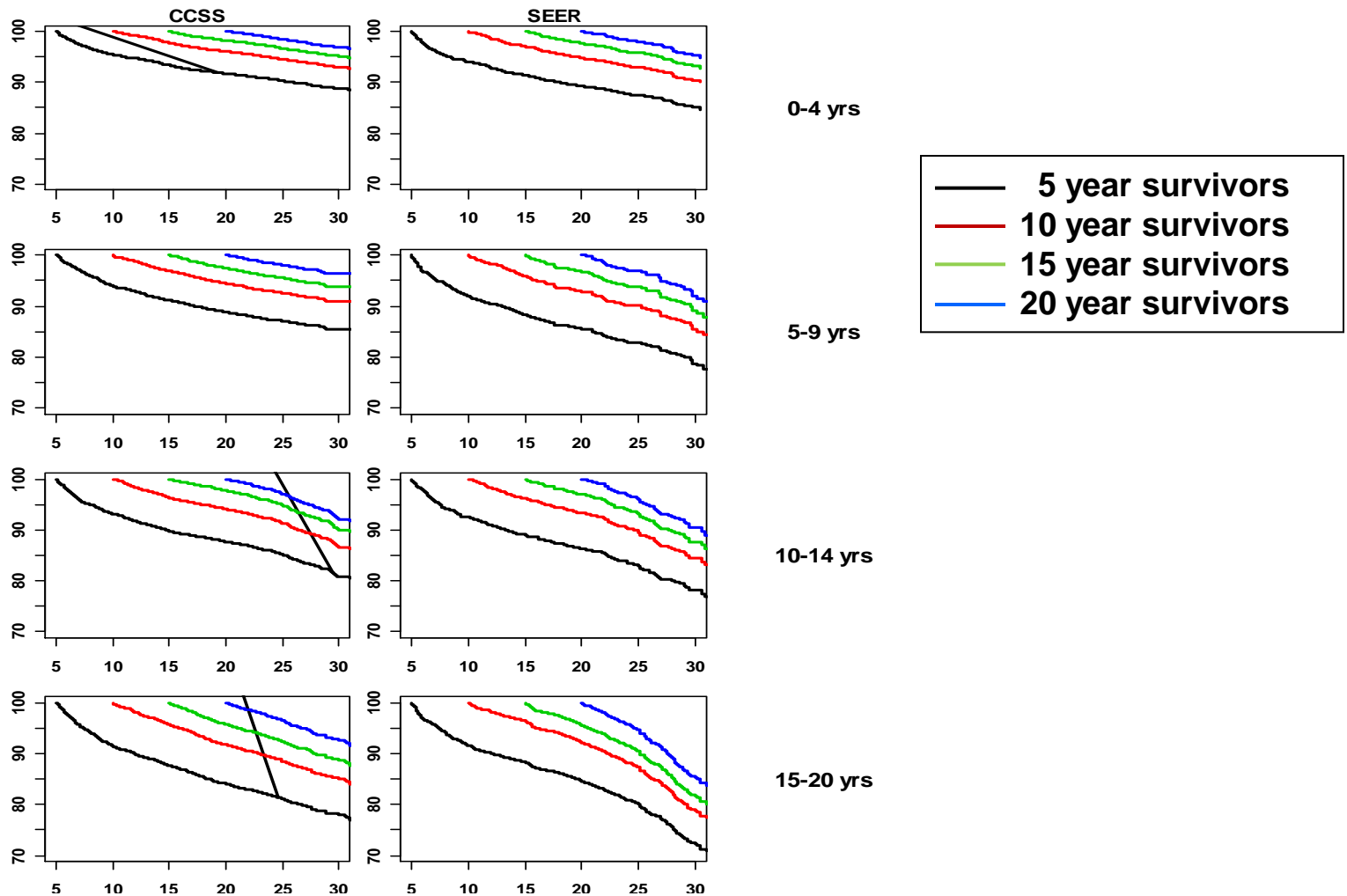
## Characteristics of pediatric cancer patients who survived 5+ years post diagnosis

	CCSS		SEER	
	N	%	N	%
<b>Total patients</b>	<b>16602</b>		<b>6576</b>	
<b>Death status</b>				
<b>Alive</b>	<b>14315</b>	<b>86.2</b>	<b>5389</b>	<b>82.0</b>
<b>Dead</b>	<b>2287</b>	<b>13.8</b>	<b>1187</b>	<b>18.1</b>
<b>Gender</b>				
<b>Female</b>	<b>7411</b>	<b>44.6</b>	<b>3056</b>	<b>46.5</b>
<b>Male</b>	<b>9191</b>	<b>55.4</b>	<b>3520</b>	<b>53.5</b>
<b>Race</b>				
<b>missing</b>	<b>4859</b>	<b>29.3</b>	<b>37</b>	<b>0.6</b>
<b>White, NH</b>	<b>10094</b>	<b>60.8</b>	<b>5610</b>	<b>85.3</b>
<b>Black, NH</b>	<b>591</b>	<b>3.6</b>	<b>553</b>	<b>8.4</b>
<b>Other</b>	<b>1058</b>	<b>6.4</b>	<b>376</b>	<b>5.7</b>

## Cancer characteristics of pediatric cancer patients

	CCSS		SEER	
	N	%	N	%
<b>Diagnosis Group</b>				
Leukemia	5609	33.8	1559	23.7
CNS tumor	2343	14.1	1532	23.3
Hodgkins disease	1999	12.0	1244	18.9
Non Hodgkin lymphoma	1273	7.7	475	7.2
Kidney tumors	1413	8.5	408	6.2
Neuroblastoma	1101	6.6	345	5.3
Soft tissue sarcoma	1399	8.4	649	9.9
Bone tumor	1465	8.8	364	5.5
<b>Age at diagnosis</b>				
0-4	6714	40.4	1902	28.9
5-9	3715	22.4	1189	18.1
10-14	3318	20.0	1157	17.6
15-20	2855	17.2	2328	35.4

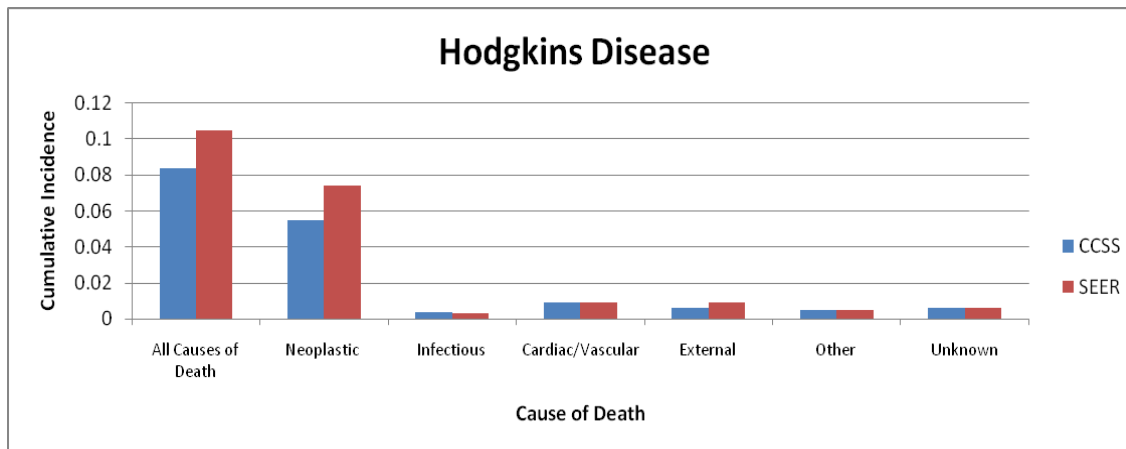
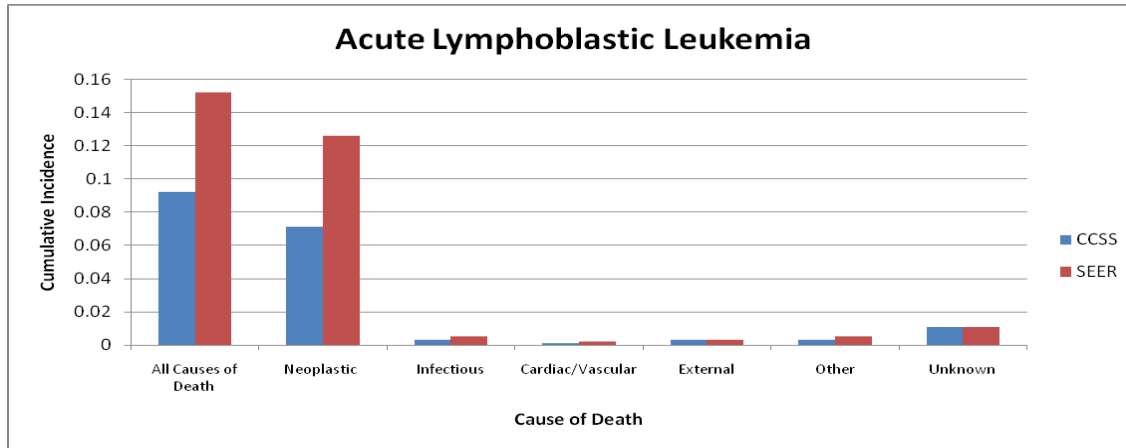
## Conditional survival by age at diagnosis



## Multivariable analysis of death rate adjusting for age at and years since diagnosis

	Hazard Ratio (95% CI)	P-value
<b>Total patients</b>		
<b>Male vs. Female</b>	1.22 (1.14 - 1.31)	<.001
<b>yeardx 1975-1980 vs. 1981-1986</b>	1.17 (1.08 - 1.24)	<.001
<b>yeardx 1975-1980 and SEER interaction</b>	1.02 (0.88 - 1.16)	0.83
<b>SEER 5-10 yrs vs. CCSS</b>	1.15 (1.01 - 1.31)	0.04
<b>SEER 10-15 yrs vs. CCSS</b>	1.07 (0.89 - 1.29)	0.44
<b>SEER 15-20 yrs vs. CCSS</b>	1.18 (0.97 - 1.43)	0.10
<b>SEER 20+ yrs vs. CCSS</b>	1.63 (1.36 - 1.96)	<.001

## Conditional probability of death within 15 years since diagnosis, conditioned on 5-year survival by cause of death and cancer type.





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## **Progress - Conditional Survival in Pediatric Malignancies**

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**Analysis complete**

**First draft of manuscript underway**



## **Progress on ancillary studies**

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**Prediction modeling for late effects in individual cancer survivors (grant funded by Canadian Institutes for Health Research) (Yasui/Chen/McBride/Greenberg/Nathan)**

- **Methodology under development**

**Feasibility of recruiting CCSS participants to participate in clinical evaluation (Mertens/Green)**

- **Draft manuscript under revisions**
- **For use as preliminary data in future ancillary grant applications**

## **Current approved AOI**

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- **Prediction of risk of serious health conditions (Salz)**
- **Predictors of healthy aging in the CCSS cohort (Ness)**
- **Estimation of risk ratios in the presence of statistical interactions (Satagopan)**
- **Cumulative incidence as a function of age (Huiru) – pending approval**

## High Priority Projects

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- **Differences in participant characteristics between the original and expanded studies (Mertens/Leisenring)**
- **Changes in treatment characteristics from the original to the expanded studies (Leisenring/Mertens)**
- **Does reduction of intensity of therapy for low/standard risk groups also reduce mortality due to non-recurrence, non-external cause late-mortality (Armstrong)**