CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

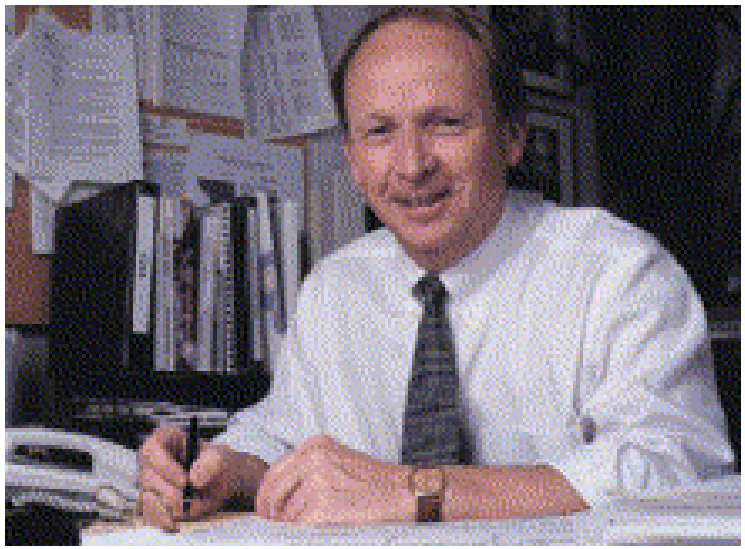
**Epidemiology/Biostatistics Working Group**

# Epidemiology/Biostatistics Working Group Report

## CCSS Investigators Meeting
## June, 2015

# 1995

- **CCSS had 0 publication**
- **Dial-up access to Internet**
- **Amazon.com sold its 1st book online**
- **I was a new PhD who got the great opportunity to work with CCSS founders**



# 2001

- **CCSS had published 5 papers**
- **Amazon.com turned its first profit**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

1. **Recent publications**
2. **Ongoing work**
3. **Future focus**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

1. **Recent publications**
2. **Ongoing work**
3. **Future focus**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# Publications 228

THE LANCET Oncology

## Risk of late effects of treatment in children newly diagnosed with standard-risk acute lymphoblastic leukaemia: a report from the Childhood Cancer Survivor Study cohort

Stefan Essig, Qiaozhi Li, Yan Chen, Johann Hitzler, Wendy Leisenring, Mark Greenberg, Charles Sklar, Melissa M Hudson, Gregory T Armstrong, Kevin R Krull, Joseph P Neglia, Kevin C Oeffinger, Leslie L Robison, Claudia E Kuehni, Yutaka Yasui, Paul C Nathan

| | Contemporary protocols for ALL therapy | | | | | | Eligible dose range |
|---|---|---|---|---|---|---|---|
| | COG-AALL0932 average risk group A | | SJCRH Total Therapy XV study low risk | | DFCI protocol (2012) | AIEOP-BFM ALL (2009) | CCSS |
| | Female | Male | Female | Male | | | |
| Dexamethasone (mg/m²) | 908 | 1298 | 1160 | 1160 | 1020 | 210 (plus tapering) | Any |
| Prednisone (mg/m²) | | | | | | ng) | Any |
| Asparaginase (IU/m²) | | | | | | | Any |
| Doxorubicin (mg/m²) | | | | | | | Cumulative anthracycline 0–120 |
| Daunorubicin (mg/m²) | | | | | | | Cumulative anthracycline 0–120 |
| Cyclophosphamide (mg/ | | | | | | | 0–1000 |
| Cytarabine (mg/m²) | | | | | | | Any |
| High-dose methotrexate | | | | | | | Any |
| Methotrexate iv (mg/m² | | | | | | | Any |
| Methotrexate oral (mg/ | | | | | | | Any |
| Mercaptopurine (mg/m² | | | | | | | Any |
| Thioguanine (mg/m²) | | | | | | | Any |
| Vincristine (mg/m²) | | | | | | | Any |
| Intrathecal chemotherap (number of doses) | | | | | | positive; 13 | Any |
| Radiation (Gy) | 0 | 0 | 0 | 0 | 0 | 0 (18 Gy for CNS positive) | 0 |

- **Anthracycline 0-120 mg/m²**
- **Cyclophosphamide 0-1000 mg/m²**
- **No radiation**

COG=Children's Oncology Group. ALL=acute lymphoblastic leukaemia. SJCRH=St Jude Children's Research Hospital. DFCI=Dana-Farber Cancer Institute. AIEOP-BFM=Associazione Italiana Ematologia Oncologia Pediatrica-Berlin-Frankfurt-Münster. CCSS=Childhood Cancer Survivor Study. iv=intravenous. im=intramuscular. PEG=polyethylene glycol. IT=intrathecal. CNS2/TLP+=CNS status ≤5 white blood cells per µL cerebrospinal fluid with blasts/traumatic lumbar puncture positive.

*Table 1:* **Cumulative doses of chemotherapy and radiation in present protocols for treatment of standard-risk ALL and definition of dose ranges for inclusion for CCSS subcohort of ALL survivors**

| | Deaths | Rate* | SMR (95% CI) |
|---|---|---|---|
| All deaths | 28 | 2·5 | 3·5 (2·3–5·0) |
| Sex | | | |
| Female | 11 (39%) | 1·8 | 4·2 (2·1–7·5) |
| Male | 17 (61%) | 3·4 | 3·1 (1·8–5·0) |
| Time after diagnosis (years) | | | |
| 5–9 | 7 (25%) | 2·5 | 8·1 (3·2–16·7) |
| 10–14 | 10 (36%) | 3·7 | 5·6 (2·7–10·3) |
| 15–19 | 7 (25%) | 2·6 | 3·0 (1·2–6·2) |
| ≥20 | 4 (14%) | 1·4 | 1·3 (0·4–3·3) |

Data are N or n (%), unless otherwise indicated. SMR=standardised mortality ratio. *Deaths per 1000 person-years.

*Table 3:* Late mortality in survivors

| | Survivors (n=556) | Siblings (n=2232) | RR or OR (95% CI)* | p value | Number needed to harm (95% CI)† |
|---|---|---|---|---|---|
| **Overall chronic health disorders‡§** | | | | | |
| Any disorder, grade 1–5 | 192 (48%) | 1058 (51%) | 1·3 (1·1 to 1·6) | 0·0005 | 107 (81 to 193) |
| Any disorder, grade 3–5 | 51 (10%) | 157 (7%) | 2·0 (1·4 to 2·8) | <0·0001 | 415 (376 to 939) |
| More than one disorder, grade 1–5 | 156 (32%) | 598 (27%) | 1·6 (1·4 to 2·0) | <0·0001 | 136 (126 to 236) |
| Multiple disorder, grade 3–5 | 6 (1%) | 18 (1%) | 1·8 (0·7 to 4·8) | 0·21 | .. |

## Publications 228 Essig *et al.*

- **In every 415 survivors, there will be one excess of Grade 3-5 chronic conditions annually**
- **In every 107 survivors, there will be one excess of chronic conditions (Grade 1-5) annually**

# Publications 221

ORIGINAL RESEARCH | Annals of Internal Medicine

## Cost-Effectiveness of the Children's Oncology Group Long-Term Follow-up Screening Guidelines for Childhood Cancer Survivors at Risk for Treatment-Related Heart Failure

F. Lennie Wong, PhD; Smita Bhatia, MD, MPH; Wendy Landier, PhD, RN; Liton Francisco, BS; Wendy Leisenring, ScD; Melissa M. Hudson, MD; Gregory T. Armstrong, MD; Ann Mertens, PhD; Marilyn Stovall, PhD; Leslie L. Robison, PhD; Gary H. Lyman, MD, MPH; Steven E. Lipshultz, MD; and Saro H. Armenian, DO, MPH

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

***Schedule for Echocardiogram or MUGA Scans***

| Age at treatment* | Chest radiation | Total anthracycline dose** | Recommended frequency of ECHO or MUGA*** |
|---|---|---|---|
| < 1 year | Yes | Any | Every year |
| | No | < 200 mg/m$^2$ | Every 2 years |
| | | ≥ 200 mg/m$^2$ | Every year |
| 1 to 4 years old | Yes | Any | Every year |
| | No | < 100 mg/m$^2$ | Every 5 years |
| | | ≥ 100 to < 300 mg/m$^2$ | Every 2 years |
| | | ≥ 300 mg/m$^2$ | Every year |
| ≥ 5 years old | Yes | < 300 mg/m$^2$ | Every 2 years |
| | | ≥ 300 mg/m$^2$ | Every year |
| | No | < 200 mg/m$^2$ | Every 5 years |
| | | ≥ 200 to < 300 mg/m$^2$ | Every 2 years |
| | | ≥ 300 mg/m$^2$ | Every year |

*age at first treatment with anthracycline or chest radiation (whichever was given first)

**based on total doses of doxorubicin/daunorubicin or the equivalent doses of other anthracyclines

***MUGA scans may be used for patients who received anthracycline chemotherapy without radiation; ***Echocardiograms are the preferred test for those who received radiation*** involving the heart because the test provides more detailed information regarding structural issues, including valve structures.

# Publications 221 Wong *et al.*

- **Research Question**

  **Is the COG guideline for screening asymptomatic left ventricular dysfunction (AVLF) cost effective?**

- **Measure of cost effectiveness**

  **Incremental Cost Effectiveness Ratio [$ / QALY]**

# Publications 221 Wong *et al.*

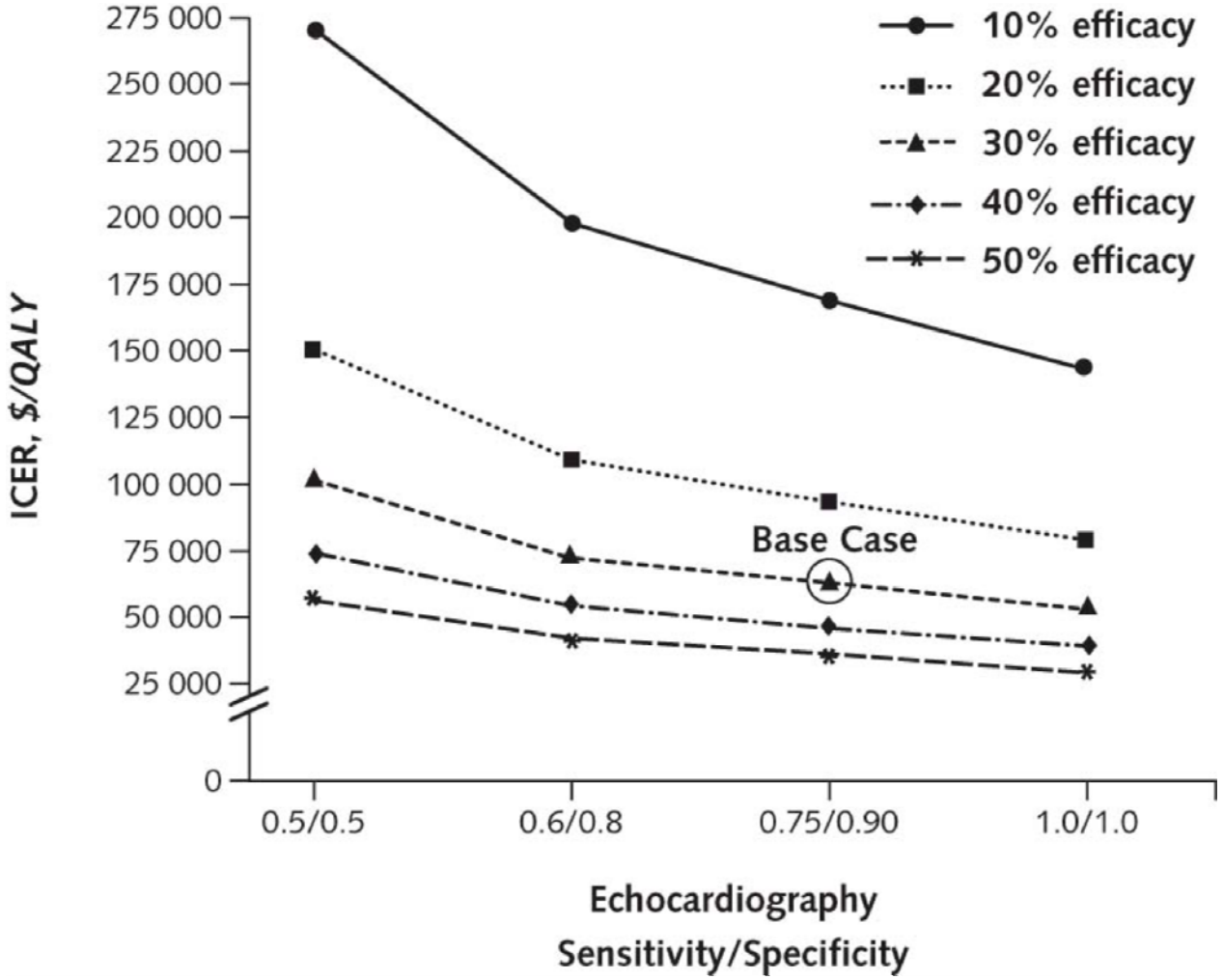
- **Complex Mathematical Modeling/Simulation using Markov State Transition Models**
- **Used CCSS as the realistic cohort of childhood cancer survivors**

# Publications 221 Wong *et al.*

- **The COG Guidelines = Cost effective**
  **ICER $61,500/QALY**

- **A screening with approximately 1/2 the frequency of the COG guidelines:**
  **ICER $33,200/QALY**

# Publications 221 Wong *et al.*



CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

## Publications 241

Cancer

American Cancer Society

Original Article

### Conditional Survival in Pediatric Malignancies: Analysis of Data From the Childhood Cancer Survivor Study and the Surveillance, Epidemiology, and End Results Program

Ann C. Mertens, PhD[1]; Jian Yong, MS[2]; Andrew C. Dietz, MD, MS[3]; Erin Kreiter, MSc[2]; Yutaka Yasui, PhD[2]; Archie Bleyer, MD[4]; Gregory T. Armstrong, MD, MSCE[5]; Leslie L. Robison, PhD[5]; and Karen Wasilewski-Masker, MD, MSCR[1]

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# Publications 241

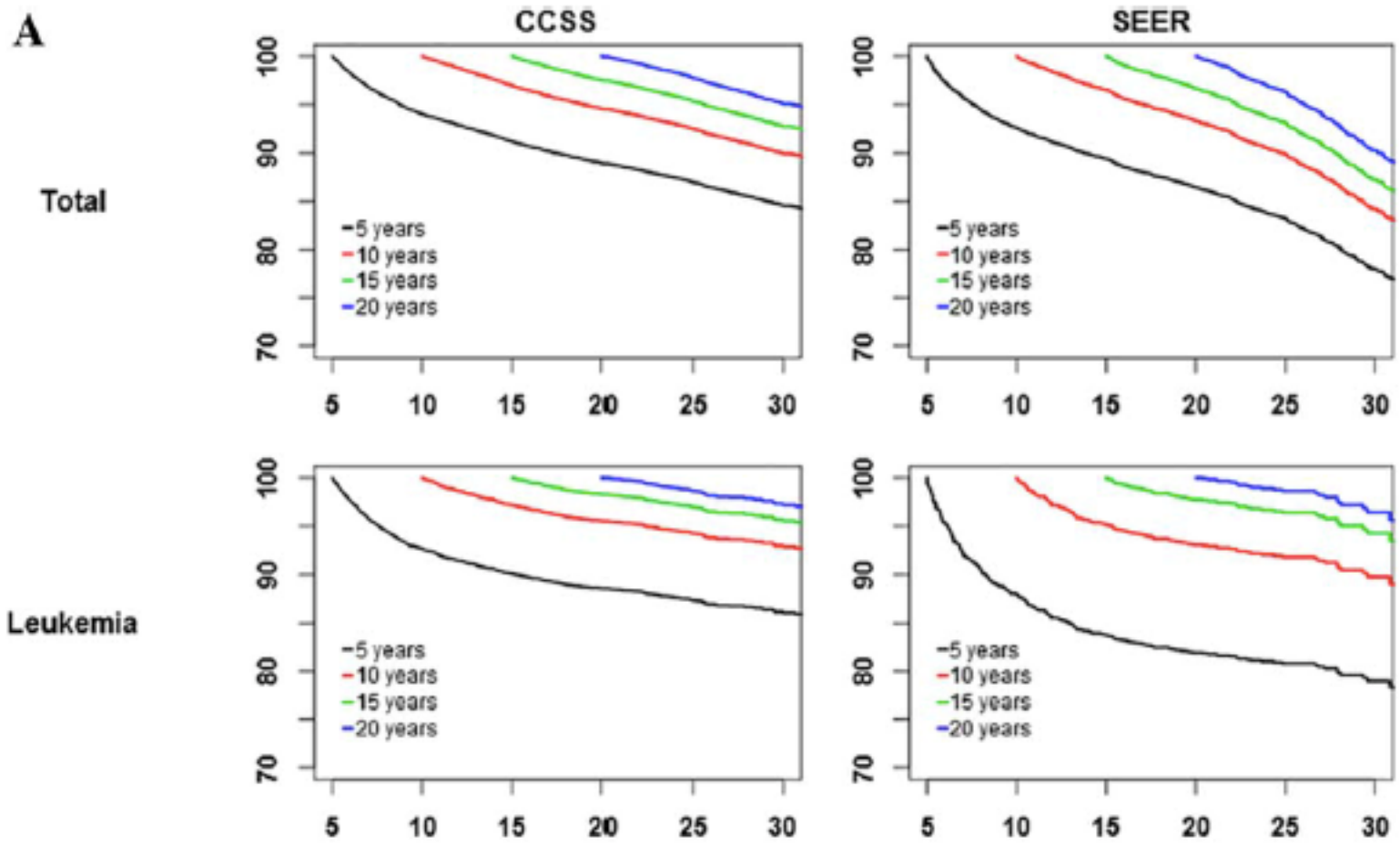


**TABLE 2.** Probability of Death Within the Next 10 Years for CCSS Patients Who Survived 5 Years After Their Cancer Diagnosis by Cause of Death and Cancer Type

| | | | Cause-Specific Death[a] | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Survival Probability | | All-Cause of Death | | Neoplasms | | Infectious | |
| Diagnosis Group | % | 95% CI | % | 95% CI | % | 95% CI | % | 95% CI |
| Total | 91.2 | 90.8-91.6 | 8.8 | 8.4-9.2 | 6.3 | 6.0-6.7 | 0.3 | 0.2-0.4 |
| Leukemia | 90.1 | 89.3-90.9 | 9.9 | 9.1-10.7 | 7.4 | 6.7-8.1 | 0.4 | 0.2-0.5 |
| Kidney tumors | 97.4 | 96.5-98.2 | 2.6 | 1.8-3.5 | 1.5 | 0.9-3.9 | 0 | – |
| CNS | 87.1 | 85.8-88.5 | 12.9 | 11.5-14.2 | 9.5 | 8.3-10.7 | 0.3 | 0.1-0.5 |
| Lymphoma | 93.1 | 92.3-94.0 | 6.9 | 6.0-7.7 | 4.4 | 3.7-5.1 | 0.3 | 0.1-0.5 |
| Neuroblastoma | 95.8 | 94.6-97.0 | 4.2 | 3.0-5.4 | 2.9 | 1.9-3.9 | 0.1 | 0-0.3 |
| Soft tissue sarcoma/Ewing sarcoma | 89.2 | 87.8-90.6 | 10.8 | 9.4-12.2 | 8.1 | 6.8-9.3 | 0.2 | 0-0.3 |
| Osteosarcoma/Other bone tumors | 90.5 | 88.7-92.4 | 9.5 | 7.6-11.3 | 6.7 | 5.1-8.2 | 0.4 | 0-0.8 |

| | Cause-Specific Death[a] | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Cardiac/Vascular | | External | | Other | | Unknown | |
| Diagnosis Group | % | 95% CI | % | 95% CI | % | 95% CI | % | 95% CI |
| Total | 0.3 | 0.2-0.4 | 0.5 | 0.4-0.6 | 0.4 | 0.3-0.5 | 1.0 | 0.9-1.1 |
| Leukemia | 0.1 | 0-0.2 | 0.3 | 0.2-0.5 | 0.4 | 0.3-0.6 | 1.3 | 1.0-1.6 |
| Kidney tumors | 0.4 | 0.1-0.8 | 0.3 | 0-0.6 | 0.3 | 0-0.6 | 0.1 | 0-0.2 |
| CNS | 0.2 | 0-0.3 | 0.6 | 0.3-0.9 | 0.6 | 0.3-0.9 | 1.7 | 1.3-2.3 |
| Lymphoma | 0.7 | 0.4-1.0 | 0.6 | 0.3-0.8 | 0.4 | 0.2-0.6 | 0.5 | 0.3-0.8 |
| Neuroblastoma | 0.2 | 0-0.4 | 0.4 | 0-0.7 | 0.2 | 0-0.4 | 0.4 | 0-0.9 |
| Soft tissue sarcoma/Ewing sarcoma | 0.5 | 0.2-0.8 | 0.5 | 0.2-0.9 | 0.4 | 0.2-0.9 | 1.1 | 0.6-1.5 |
| Osteosarcoma/Other bone tumors | 0.4 | 0-0.8 | 0.8 | 0.3-1.4 | 0.3 | 0-0.7 | 0.9 | 0.3-1.5 |

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

## Publications 223


### Regression analysis of mixed recurrent-event and panel-count data

LIANG ZHU

*Department of Biostatistics, St. Jude Children's Research Hospital, Memphis, TN 38105, USA*

XINWEI TONG

*School of Mathematical Sciences, Beijing Normal University, Beijing 100875, China*

JIANGUO SUN*

*Department of Statistics, University of Missouri, Columbia, MO 65211, USA and School of Mathematics, Jilin University, Changchun 130012, China*

sunj@missouri.edu

MAN-HUA CHEN

*Department of Statistics, Tamkang University, Tamsui, New Taipei 25137, Taiwan*

DEO KUMAR SRIVASTAVA

*Department of Biostatistics, St. Jude Children's Research Hospital, Memphis, TN 38105, USA*

WENDY LEISENRING

*Department of Biostatistics, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA*

LESLIE L. ROBISON

*Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital, Memphis, TN 38105, USA*

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# Publications 237


## Regression Analysis of Mixed Recurrent-Event and Panel-Count Data with Additive Rate Models

Liang Zhu,[1] Hui Zhao,[2,*] Jianguo Sun,[3,4] Wendy Leisenring,[5] and Leslie L. Robison[6]

# Publications 223

$$L_n(\theta) = \prod_{i=1}^{n} \left\{ e^{-\Lambda(C_i)\, e^{X_i'\beta}}\, e^{K_i X_i'\beta} \prod_{j=1}^{K_i} \lambda(T_{ij}) \right\}^{r_i} \left[ e^{N_{iK_i} X_i'\beta}\, e^{-\Lambda(T_{iK_i})\, e^{X_i'\beta}} \prod_{j=1}^{K_i} \{\Lambda(T_{ij}) - \Lambda(T_{ij-1})\}^{\Delta N_{ij}} \right]^{1-r_i},$$

where $T_{i0} = 0$, $N_{iK_i} = N_i(T_{iK_i})$, and $\Delta N_{ij} = N_i(T_{ij}) - N_i(T_{ij-1})$ for $j = 1, \ldots, K_i$, $i = 1, \ldots, n$. Correspondingly, the log-likelihood function has the form

$$\sum_{i=1}^{n} \sum_{j=1}^{K_i} r_i \log \lambda(T_{ij}) + \sum_{i=1}^{n} \left[ -r_i \Lambda(C_i)\, e^{X_i'\beta} + r_i K_i X_i'\beta + (1 - r_i) N_{iK_i} X_i'\beta \right.$$

$$\left. - (1 - r_i) \Lambda(T_{iK_i})\, e^{X_i'\beta} + \sum_{j=1}^{K_i} (1 - r_i) \Delta N_{ij} \log\{\Lambda(T_{ij}) - \Lambda(T_{ij-1})\} \right]. \qquad (2.2)$$

# Publications 223

- **N=3,966 CCSS pregnancy questionnaire: one or more pregnancies => a detailed questionnaire**
- **697 did not return the pregnancy questionnaire: we only know counts of pregnancies (panel-count data)**
- **3269 returned the detailed questionnaire, providing calendar times of pregnancies (recurrent-event data)**
- **Regression analysis on associations**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# Publications 220

J Cancer Surviv (2014) 8:460–471
DOI 10.1007/s11764-014-0353-7

## Noncancer-related mortality risks in adult survivors of pediatric malignancies: the childhood cancer survivor study

**Cheryl L. Cox · Vikki G. Nolan · Wendy Leisenring · Yutaka Yasui · Susan W. Ogg · Ann C. Mertens · Joseph P. Neglia · Kirsten K. Ness · Gregory T. Armstrong · Les L. Robison**

## Publications 220

- **Nested case-control study**
- **445 cases: Died from causes other than recurrence or non-health-related events**
- **Matched on primary diagnosis, age at baseline questionnaire, time from diagnosis to baseline questionnaire, and time at-risk**
- **Adjust for treatment exposures & demogr.**

| | OR (95 % CI) | *P* value |
|---|---|---|
| Physical activity | | |
| 0 days per week | 1.72 (1.27–2.34) | <0.001 |
| 1–2 days per week | 1.65 (1.17–2.31) | 0.004 |
| 3+ days per week | 1.00 | |
| Health worry and concern[b] | | |
| Current health status | | |
| Good or excellent | 1.00 | |
| Fair or poor | 1.98 (1.45–2.71) | <0.001 |

# Publications 220

| | | |
|---|---|---|
| BMI | | |
| Underweight | 2.58 (1.55–4.28) | <0.001 |
| Normal | 1.00 | |
| Overweight | 1.12 (0.84–1.50) | 0.43 |
| Obese | 1.03 (0.71–1.49) | 0.88 |

**Smoking status was not associated.**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

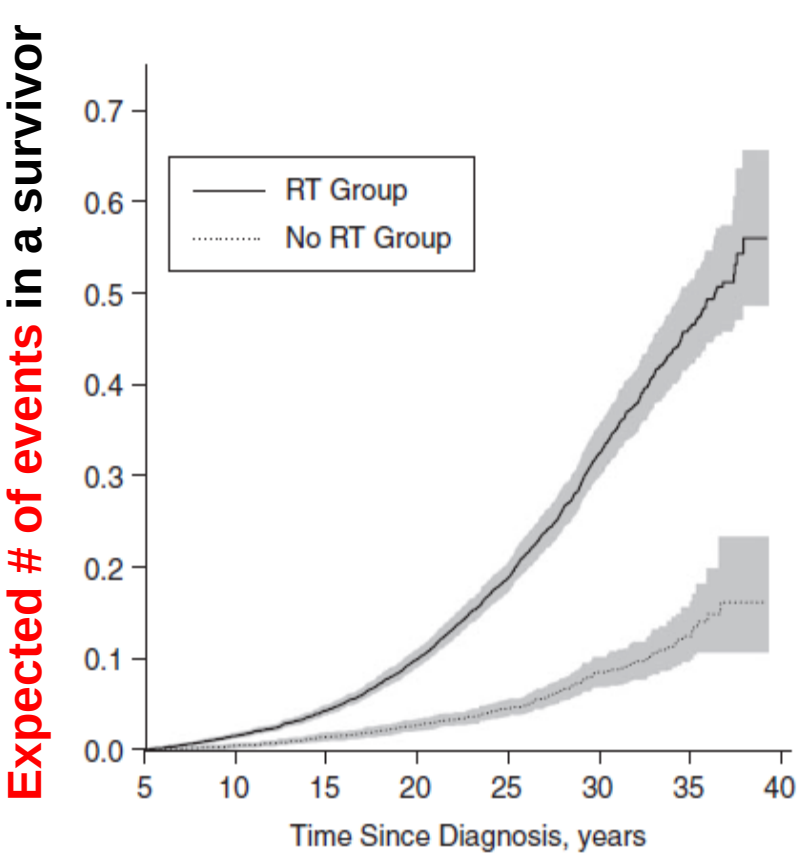
# Publications 239

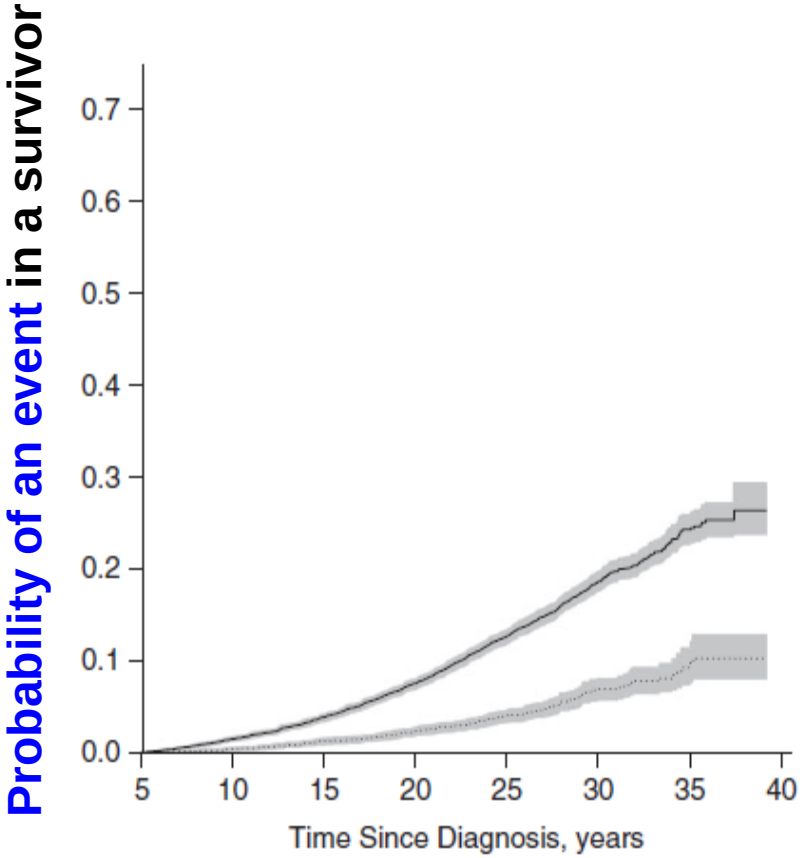
American Journal of EPIDEMIOLOGY

## Estimating the Burden of Recurrent Events in the Presence of Competing Risks: The Method of Mean Cumulative Count

Huiru Dong, Leslie L. Robison, Wendy M. Leisenring, Leah J. Martin, Gregory T. Armstrong, and Yutaka Yasui*

# Occurrence of Subsequent Neoplasms by RT



# Publications 239 Dong *et al.*

- **Two estimates differ in the influence of censoring**

  **Ghosh and Lin (Biometrics 2000)**
  **Our sum of CIs**

- **Censoring after 1st SN**

  **In Ghosh and Lin, it affects CIs of 1st SN, 2nd SN, …**
  **in our sum of CIs, it affects CIs of 2nd SN, …**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# Publications 227

Pediatric Blood & Cancer

## Factors Associated With Recruiting Adult Survivors of Childhood Cancer Into Clinic-Based Research

Ann C. Mertens, PhD,[1]* Wei Liu, PhD,[2] Kirsten K. Ness, PhD,[3] Aaron McDonald, PhD,[3] Melissa M. Hudson, MD,[3,4] Karen Wasilewski-Masker, MD, MSCR,[1] Smita Bhatia, MD,[5] Paul C. Nathan, MD,[6] Marcia Leonard, NP,[7] Kumar Srivastava, PhD,[2] Leslie L. Robison, PhD,[3] and Daniel M. Green, MD[3]

# Motivators to participate

- Visiting with individuals involved in their care (77%)
- Wanting additional health information
  - Learning about health problems (35%)
  - How to communicate with primary care doctors (36%)
  - Information on health screening (51%)
- Altruistic factors
  - Helping other pediatric cancer survivors (76%)
  - Helping other children with cancer (76%)

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

1. Recent publications
2. **Ongoing work**
3. Future focus

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# High Priority Expansion Studies

| EPIDEMIOLOGY / BIOSTATISTICS | | |
|---|---|---|
| 01.20.14 | Late Mortality by Treatment Era | Armstrong/SJCRH |
| 04.02.14 | Differences in participant characteristics and changes in treatment characteristics from the original to the expanded cohorts | Mertens/Emory |
| 01.14.14 | Association between key therapeutic exposures and outcomes - gaps in knowledge | Bhatia/City of Hope |
| 01.14.14 | Risk of Cardiovascular disease and Second Malignancies attributable to therapeutic exposures by Treatment Era | Bhatia/City of Hope |

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# High Priority Expansion Studies

**ASSOCIATED PRESENTATION**

Meeting: **2015 ASCO Annual Meeting**

Presenter: **Gregory T. Armstrong**

**View Video**

Late Mortality by Treatment Era — Armstrong/SJCRH

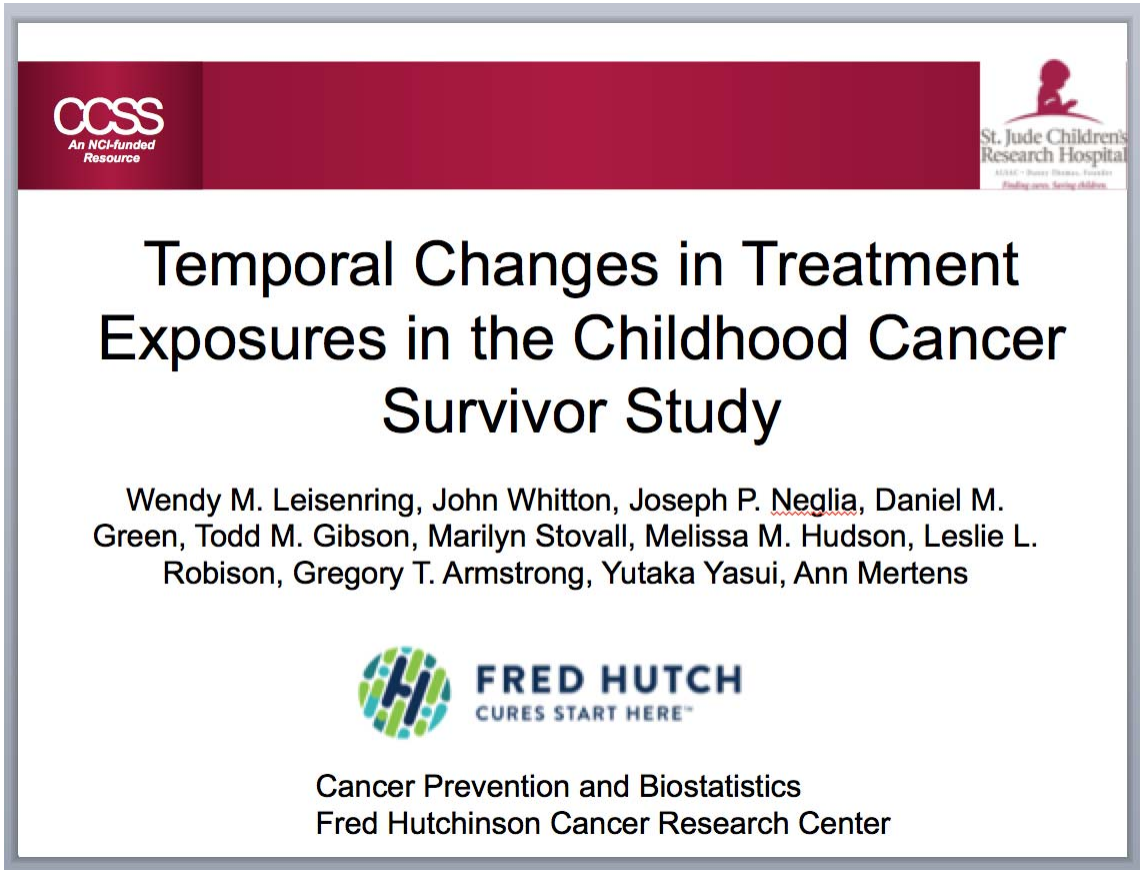
CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

Differences in participant characteristics and changes in treatment characteristics from the original to the expanded cohorts

Mertens/Emory



CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

**Epidemiology/Biostatistics Working Group**

# High Priority Expansion Studies

| | |
|---|---|
| Association between key therapeutic exposures and outcomes - gaps in knowledge | Bhatia/City of Hope |
| Risk of Cardiovascular disease and Second Malignancies attributable to therapeutic exposures by Treatment Era | Bhatia/City of Hope |

## Multiple concept proposals

# Manuscripts Submitted/Circulated

- **Derivation of anthracycline equivalence to doxorubicin in relation to late cardiotoxicity (Lieke Feijen, JCO review)**
- **Direct and indirect effects of anthracycline exposure on cardiac outcomes (Blythe Ryerson/Rebecca Williamson/Mertens)**
- **Access to Health Information Technology and Health Information Seeking (Mechelle Claridy/Mertens)**

# Manuscripts Submitted/Circulated

- **Inverse Probability Weighting to Adjust for Selection Bias and Drop Out (Chonghzi Di/Leisenring)**
- **Differences in Long-Term Outcomes by Race/Ethnicity in Childhood Cancer Survivors (Qi Liu/Bhatia/Yasui, ASCO)**
- **Handling Missing Data due to No Consent for Medical Record Abstraction by Multiple Imputation (Leah Martin/Qi Liu/Yasui)**

# Concepts Approved/Submitted

- **Tiled study design: using temporal overlap as a method to extend longitudinal follow-up among carefully selected time-limited cohorts (Chow)**
- **Use of an incentive to increase biologic sample (Oragene) return rate (McDonald)**
- **Cost Effectiveness of COG Breast Cancer Screening Guidelines for Female Survivors of Pediatric Cancers (Wong)**
- **Radiation dose reconstruction methods for intensity modulated radiation therapy (Howell/Stovall)**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

# Epidemiology/Biostatistics Working Group

1. Recent publications
2. Ongoing work
3. **Future focus**

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

## Epidemiology/Biostatistics Working Group

**PLEASE FEEL FREE TO CONTACT ME IF YOU HAVE ANY INTEREST OR IDEA ON POTENTIAL EPI/BIOSTAT PROJECTS**

**yyasui@ualberta.ca**

## Enabling methodology work

- **Develop epi/biostat methods that enable promote (CCSS) late effects research**
- **Lead methodologically-involved investigations that provide a template**

## Address key quantitative issues in (CCSS) late-effects research

- **Prediction modeling and its evaluation**

- **GWAS analysis framework**

  **Gene sets/Pathway/Epistasis methodologies**

  **G x T interaction evaluattion**

- **Prediction modeling and its evaluation**

- **GWAS analysis framework**

  **Gene sets/Pathway/Epistasis methodologies**

  **G x T interaction evaluation**

**Table 1: Summary of SNP-set interaction signals overlapping with WTCCC single-SNP strong signals and single-SNP meta-analysis signals**[¥]

| Disease | Logic-Based SNP-set Interaction | WTCCC single-SNP | | Meta-Analysis | |
|---|---|---|---|---|---|
| | # of Strong Signals | # of Strong Signals | Overlap | # of Significant Loci | Overlap[*] |
| BD | **13** | 1 | 0/1 (0%) | 1 | 1/1(100%) |
| CAD | **16** | 1 | 1/1 (100%) | 23 | 7/23 (30%) |
| HT | **15** | 0 | NA | 27 | 8/27 (30%) |
| RA | **72** | 2 | 2/2(100%) | 10 | 6/10 (60%) |
| T1DM | **105** | 5 | 5/5(100%) | 41 | 12/41 (29%) |
| T2DM | **19** | 3 | 3/3 (100%) | 7 | 4/7 (57%) |

CCSS
An NCI-funded Resource

Childhood Cancer Survivor Study

## Epidemiology/Biostatistics Working Group

**PLEASE FEEL FREE TO CONTACT ME IF YOU HAVE ANY INTEREST OR IDEA ON POTENTIAL EPI/BIOSTAT PROJECTS**

**yyasui@ualberta.ca**