Epidemiology/Biostatistics Working Group

CCSS PI Meeting
June 6-7, 2012

WG Committee

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

- **Yeh et al. A Model-Based Estimate of Cumulative Excess Mortality in Survivors of Childhood Cancer. Ann Intern Med, 2010**
- **Ness et al. Characteristics of responders to a request for a buccal cell specimen among survivors of childhood cancer and their siblings. Pediatr Blood Cancer, 2010**
- **Watt et al. Radiation-related risk of basal cell carcinoma in childhood cancer survivors. Accepted J Nat Cancer Inst, 2012.**

Progress on active analyses/projects

Use of inverse probability censored weighting to evaluate and handle impact of dropout bias in the CCSS (Di/Stratton/ Leisenring)

- **Evaluate whether subjects dropping out over time differ**
- **Use information about missing subjects to adjust analyses**
- **Apply to previously published analyses and determine potential for bias in our results**
- **Analyses largely complete and manuscript being drafted**

Progress on active analyses/projects

Missing data imputation (Martin/Liu/Adewale/Yasui)

- **Missing treatment data due to not signing the medical record release form or incomplete abstraction**
- **Account for uncertainty in missing treatment data in analyses**
- **Manuscript is 80% complete with Wilms' and HL examples (departure of a postdoc, replaced by another postdoc to complete)**
- **Need to impute for other diagnosis groups**

Progress on active analyses/projects

Estimating effects of anthracycline exposure on late cardiac outcomes (Ryerson/Mertens)

- **What fraction of early cardiac outcomes among childhood cancer survivors treated with anthracyclines could be prevented by improving physical fitness.**
- **direct effect - effect of anthracyclines on the outcome**
- **indirect effect - is the effect of anthracycline exposure explained by subsequent exercise deconditioning.**
- **Draft manuscript complete, under preliminary review**

Progress on active analyses/projects

Cost Effectiveness of Cardiac Guideline for Survivors of Pediatric Cancers (Wong) – Abstract at ASCO, draft manuscript underway

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

Conditional Survival in CCSS (Wasilewski) – Draft manuscript underway

- **Comparative analysis of conditional survival in the original CCSS cohort and the Surveillance, Epidemiology and End Results (SEER) database.**

Progress on active analyses/projects

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

- **Evaluate other potential comparisons groups for CCSS survivors (NHANES, BRFSS)**

Impact of health behaviors and health perceptions on subsequent mortality (Cox/Nolan) – Manuscript in preparation

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

Progress on ancillary studies

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

- **Methodology development**

Feasibility of recruiting CCSS participants to participate in clinical evaluation (Mertens/Green) – Analyses underway

- **For use as preliminary data in future ancillary grant applications**

Current approved AOI

- **Assessing bias associated with missing data from CCSS (Gurney)**
- **Prediction of risk of serious health conditions (Salz)**
- **Cost effectiveness of breast cancer screening guideline for pediatric cancer survivors (Wong)**
- **Predictors of healthy aging in the CCSS cohort (Ness)**
- **Statistical analysis of recurrent event and panel count data (Zhu)**

Future Research Projects

- **Differences in participant characteristics between the original and expanded studies (Whitton - waiting for Expansion data)**
- **Changes in treatment characteristics from the original to the expanded studies (Whitton - waiting for Expansion data)**
- **Methods related to longitudinal analysis of CCSS data (Leisenring)**
- **Handling of death between questionnaires, a mixed censoring/competing risk problem (Leisenring/Ness/Yasui)**

Recent findings - Feasibility of recruiting CCSS participants for clinical evaluations

- Risk-based health evaluations are recommended by the Children's Oncology Group for childhood cancer survivors
- Data from CCSS suggests that a minority of adult survivors of childhood cancer seek regular preventive medical care
- Need to conduct research designed to
  - increase utilization of risk-based assessments
  - evaluate the efficacy of exposure specific interventions
- Interventions would require on site evaluation of eligible survivors to initiate the intervention and evaluate its effectiveness.

Feasibility of recruiting CCSS participants for clinical evaluations

- **A prerequisite for such intervention research is identification and characterization of CCSS participants who would agree to return to an appropriate center for a risk-based evaluation.**
- **Needs assessment survey to determine barriers and motivators for successful recruitment into clinical research projects**
- **Preliminary data from this project could be used for grant applications.**

Feasibility study – Eligibility

Participants within 100 miles of one of the five CCSS institutions - 1713 eligible CCSS participants

Hospital for Sick Children	Survivors	Siblings
≤ 50 mile	379	160
50-100 mile	119	45
St Jude Children's Research Hospital		
≤ 50 mile	108	30
50-100 mile	95	28
University of Michigan		
≤ 50 mile	182	60
50-100 mile	116	48
City of Hope National Medical Center		
≤ 50 mile	400	95
50-100 mile	67	29
Emory/Children's Healthcare at Atlanta		
≤ 50 mile	154	38
50-100 mile	93	21

Feasibility study – Methods

- **Eligible participants sent a recruitment packet from the CCSS Coordinating Center**
- **Recruitment packet -introductory letter and a brief survey evaluating preferences and potential barriers to participation in an intervention study that would require a clinic visit.**
- **Completed surveys returned to CCSS Coordinating Center**
- **If the completed survey is not received, a follow-up telephone call and/or a second recruitment packet was sent.**

Feasibility study – Participation rates

Outcome	Survivors (%)	Siblings (%)
MAILED	831	374
Completed	444 (53.4%)	133(35.6%)
PENDING	381 (45.8%)	239 (63.9%)
Refused	1 (0.1%)	1 (0.3%)
Ineligible-moved beyond 100 mi	1 (0.1%)	1 (0.3%)
Refused all else	2 (0.2%)	
Deceased	2 (0.2%)	
NOT MAILED	462	13
Pre-study Refused all else	1	
On hold burden	461	13

Feasibility study – Results

	Survivors (%)	Siblings (%)
Interest in participating in clinical research		
Very interested	238 (54%)	46 (35%)
Interested	168 (38%)	58 (43%)
Not interested	36 (8%)	29 (22%)
Where medical evaluation would take place		
Pediatric outpatient clinic	10 (2%)	0 (0%)
Adult out-patient clinic	180 (42%)	51 (38%)
Either clinic	214 (49%)	52 (39%)
Neither clinic	39 (6%)	30 (23%)

Feasibility study – Results

Indicate how important each item is when deciding whether to participate in a clinic visit (%)

	Very important	Important	Not important
Coming to [Institution] for a medical check-up	38	39	23
Visiting with the individuals involved in my care	78	19	3
Learning about possible health problems that may occur later in life related to my previous treatment for childhood cancer	62	29	9
Helping other survivors of childhood cancer or a similar illness	77	22	1
Needing more information related to my diagnosis and/or treatment of childhood cancer	35	42	23
Needing help in knowing how best to communicate with my primary care doctor	54	42	22
Receiving a check for my participation	16	29	55

Feasibility study – Results

Survivors: What things might make it hard for you to take part in a research study at [Institution]? (Mark all that apply)

	Survivors – Checked (%)	Survivors - Ranked #1 (%)
Need for childcare	7	11
Cannot travel alone, need assistance	5	11
Missing work (workload, difficulty getting permission)	22	66
Missing school	2	4
None of the above	23	4
Other	5	4

Feasibility study – Results

Survivors - What aspects of a visit to [Institution] would be least appealing? (Mark all that apply)

	Survivors – Checked (%)	Survivors - Ranked #1 (%)
Traveling	17	33
Being in a hospital setting	7	8
Having tests run	10	21
Bringing up old memories of when I was sick	11	10
Being asked to go to a hospital other than the one at which I received my treatment for cancer	7	10
None of the above	42	15
Other	5	3

Future priorities

- **Short-term (1 year)**
  - **Complete our projects**
  - **Engage new investigators interested in methodology**
  - **Work with investigators for analyses with more complex methodologies (e.g., longitudinal, CCSS I vs. II)**

- **Long-term (5 years)**
  - **Assess representativeness of participants retained**
  - **Prepare for the next grant cycle with sound methods**