CCSS

An NCI-funded Resource

Childhood Cancer Survivor Study (U24 CA55727)

Report of the

Statistical Center

Wendy Leisenring, PhD

CCSS Investigator Meeting

Williamsburg, VA

June 9-10, 2010

Statistical Center sites

- FHCRC, Seattle - Wendy Leisenring
  ~4 FTE
- U of Alberta, Edmonton - Yutaka Yasui
  ~1.6 FTE
- St Jude, Memphis - Kumar Srivastava
  ~4 FTE
- Gives rise to new issues around uniformity of analyses and need for excellent communication between sites.

Statistical Center Overview

Key Activities

- Database Management
- Proposal Development
- Statistical Analyses

- Weekly Conf Call w/ Coordinating Center and Radiation Dosimetry Center

1. Database Management

Data Management

- Bulk of management occurs at St Jude coordinating center
- After each questionnaire a “Data Freeze” takes place
- Involves error checks on new data elements
  - Internal checks (outliers, impossible values)
  - Some external comparisons to existing data
  - Decision making regarding resolution of discrepancies
- Working with St Jude to transition Data Freezing there

Public Use Data Tables

- Quicker access to summary data

- By Disease, Age, Gender, FU, Tx:

  - Baseline: smoking, thyroid conditions, diabetes, GH deficiency, osteoporosis, hormone related conditions, insurance, health status measures, physical limitations, BSI, BMI, education, pregnancy, chronic conditions grade
  - MRAF: chemotherapy drugs, radiation sites, surgery sites
  - Mortality

- On CCSS Website:
  http://ccss.stjude.org/data-and-analysis/public-access-data-tables

Multiple Imputation Project

- Imputation of missing treatment data by diagnosis group

- Wilms Tumor and Hodgkin Disease groups have been imputed with close discussions with MDs
  - Defined key clinical factors required for each Dx imputiation
- Draft methodological paper has been written
- Continue imputations in remaining dx groups

Proposals, Ancillary studies

- Assist with development of all analysis proposals
  - More tomorrow on process during “CCSS 101”
- Collaborate on ancillary study grant proposals
- Please include us early in process

Selected Recent Key Projects

Cardiac Outcomes	Published BMJ
Cardiovascular RF	Published CEBP
Late Recurrence	Published JNCI
Neuropsychological	Published Neuropsychology
Male/Female Fertility (2)	Published JCO
Ocular Outcomes	Published Pediatric Blood Cancer
Unemployment	Medical Care
ALL Neurologic	Published JCO
HCV screening	Published Cancer
SMN Update	In Press, JNCI
Disease Specific	NB (JNCI), CNS (JNCI), Ewings (JNCI), Osteosarcoma (Cancer), HL (To Blood)

CCSS projects with Statistical Center Involvement

	N
Published (ever)	111
- 2008-2010	58
Submitted	11
In final draft form	8
Manuscript in preparation	12
Abstracts submitted (for 2010)	17
Analyses Ongoing	23
In Queue waiting for Statistician	2

- Detailed listing in Meeting Notebook

Longitudinal Analyses

- Common Elements between Baseline and Follow-up 2007 (and other questionnaires)

- Invites longitudinal analyses of data

- In February, statisticians and others met in Seattle to discuss arising issues

Conceptualize your Question

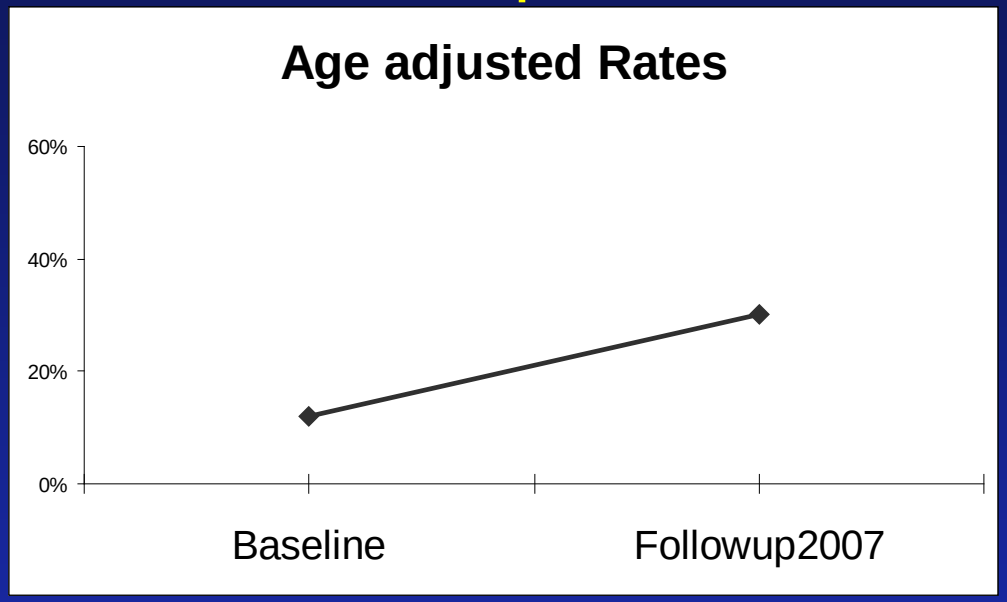
- Different types of analyses utilize “Longitudinal Data”

1. Compare difference in rates (or means) between two time points

2. Evaluate pattern of outcomes as a function of time (or age) using data from multiple questionnaires

3. Time-to-event analyses utilizing data from most recently completed questionnaire per subject.

1. Compare difference in rates (or means) between two time points

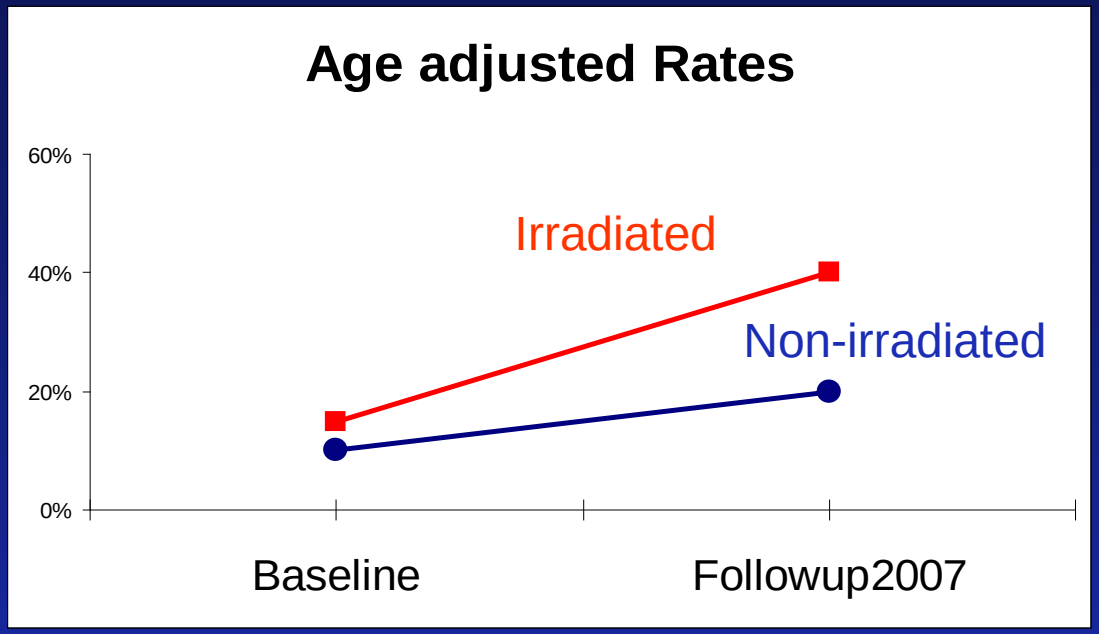


• Potential Hypothesis 1: Rate has increased between Baseline and Follow-up2007.

•Analyses:

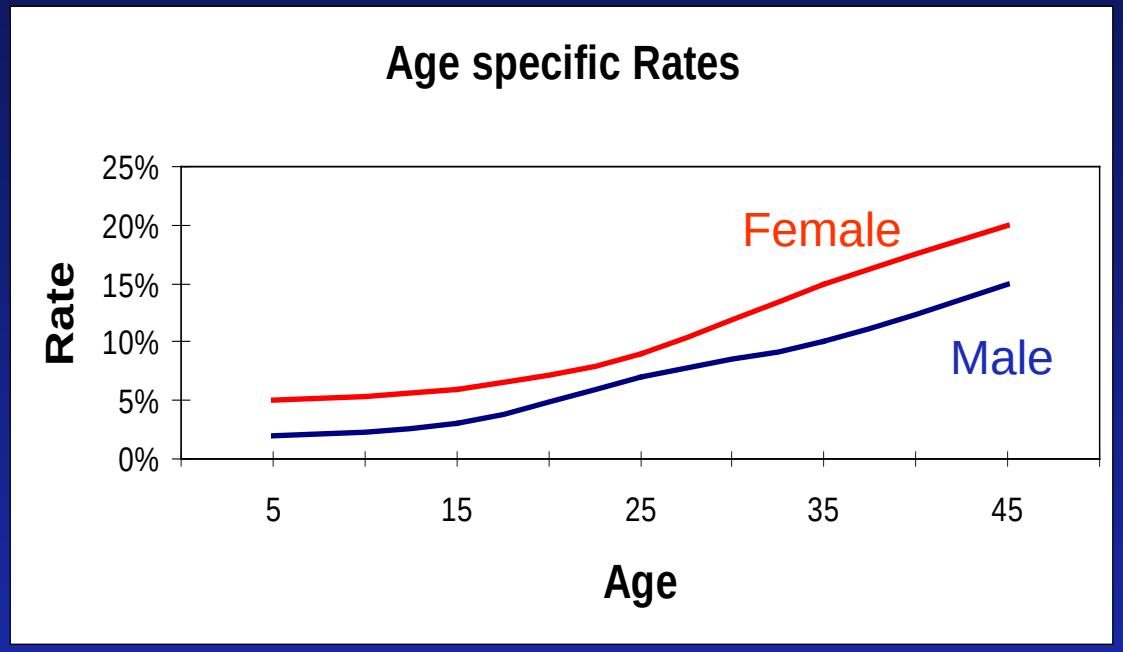
- •Estimate rates at each time point
- •Might use paired data from time points, using delta change as outcome.
- •Adjustment for age, time, other factors

Comparisons Between Groups



- Potential Hypothesis 2: Slope is steeper for irradiated subjects than for non-irradiated subjects
- Analyses:
  - Evaluate impact of covariate (e.g. Radiation) on change between two time points.

2. Evaluate pattern of rates (means) as a function of time (or age).

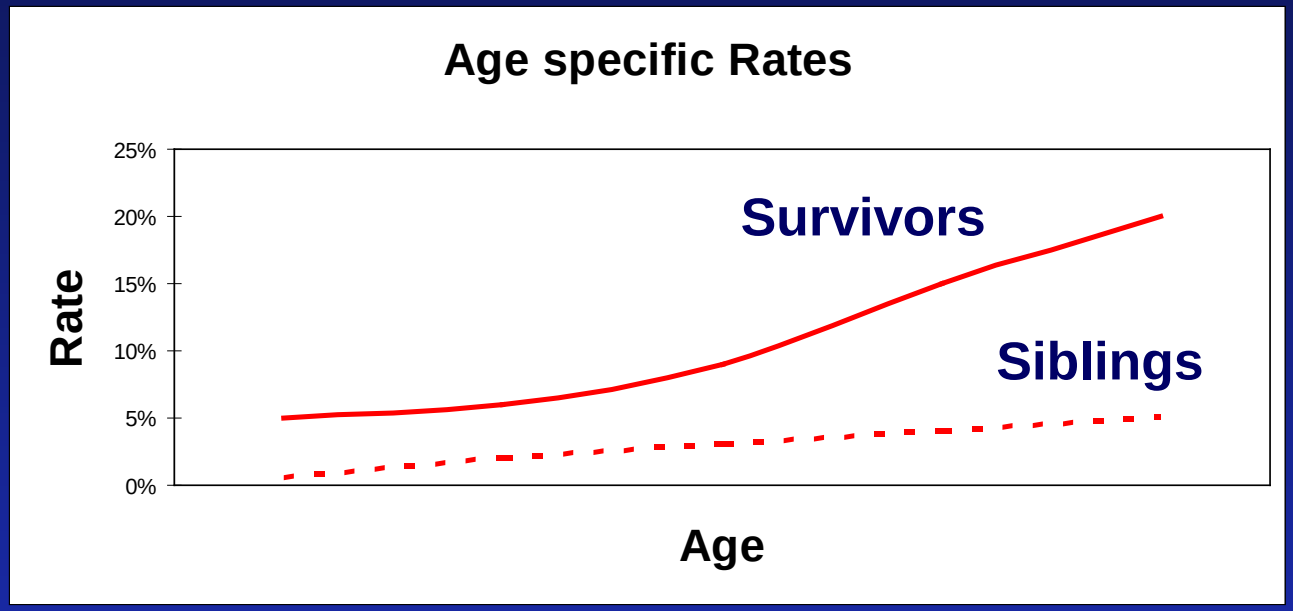


- Potential Hypothesis 1: Average rate across time is higher for females than for males

- Utilizes all available data from each questionnaire (≥1)

- Clinically relevant

Comparison to Siblings

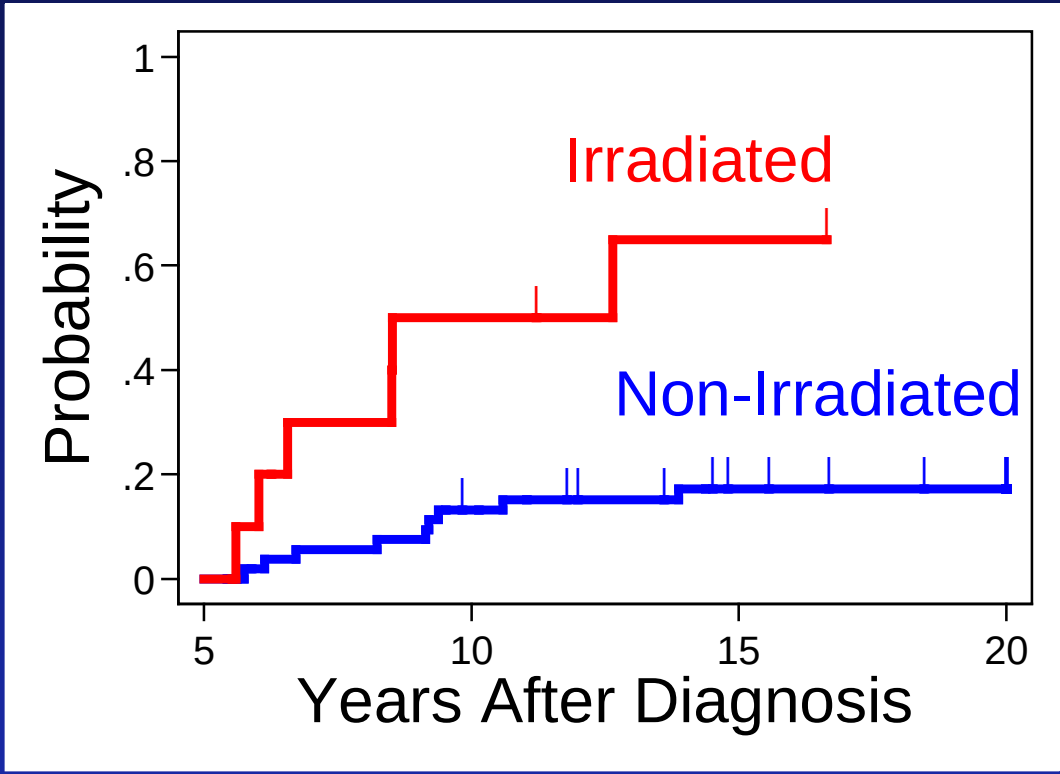


- Potential Hypothesis 2 Slope is steeper for Survivors than for Siblings.
- Analyses:

  Multivariable generalized linear models to evaluate impact of covariates on slope (or shape) of curves.

  (e.g. interaction between age and survivor/siblings)

3. Time-to-event analyses utilizing data from most recent questionnaire



- Potential Hypothesis: Cumulative incidence is higher for Irradiated subjects than non-irradiated subjects.
- Analyses
  - Cumulative incidence/Survival curves
  - Multivariable regression models

Statistical Issues for all analyses

- Handling drop-out – multiple imputation for outcomes at follow-up

- Death between questionnaires
  - Requires assumptions and sensitivity analyses about events between last questionnaire and death
  - Potential use of COD from death certificate

Planning such analyses

- Challenge you to carefully consider what type of question you wish to ask
  - Clinical relevance?
  - How is question asked on survey? i.e. need age of onset for time-to-event.
- Initial stages of proposal planning – schedule a conference call with statistician(s) and key investigators to ensure common goals and understanding.

Future Plans

- Focus on publications
  - Complete “drafts”
- Establish methodological standards (longitudinal analyses, missing data)
- Add siblings and SMN data to FU2007 data freeze with St Jude
- Expanded Cohort
  - Questionnaire and MRAF Data checking