



Childhood Cancer Survivor Study (U24 CA55727)

Report of the
Cancer Control & Intervention Working Group
Melissa Hudson, M.D.

CCSS Investigator Meeting
Williamsburg, VA
June 9-10, 2010

Objectives

- Establish priorities for cancer control and intervention research within the CCSS
- Monitor/facilitate progress of ongoing CCSS cancer control research initiatives
- Engage and mentor new/ junior investigators in CCSS cancer control research initiatives

Co-Chairs:

- Melissa Hudson/Kevin Oeffinger

Members

- Jackie Casillas, Children's Hospital L.A.
- Sharon Castellino, Wake Forest University
- Tara Henderson, University of Chicago
- Paul Nathan, Sick Kids, Toronto
- Kirsten Ness, St. Jude Children's Research Hospital
- Emily Tonorezos, Memorial Sloan Kettering

- 21 approved concept proposals
 - 16 manuscripts published/in press
 - 5 manuscripts under review (3 revised/resubmit)
 - 4 manuscripts under development
- 7 applications of intent pending concepts
- 9 ancillary studies
 - 4 closed; 5 manuscripts published
 - 6 in progress

Research priorities and focus

- Health status
- Health care utilization
- Health knowledge
- Health behavior
- Health screening

Health status

- Hudson et al. **Health status** of adult long-term survivors of childhood cancer. JAMA, 2003.
- Castellino et al. **Minority adult survivors** of childhood cancer: a comparison of long-term outcomes, health care utilization, and health-related behaviors. J Clin Oncol, 2005.
- Park et al. **Health insurance** coverage in survivors of childhood cancer. J Clin Oncol, 2005.

Health status

- Krull et al. **Adolescent** psychopathology and adult health outcomes in long-term survivors of childhood cancer. J Cancer Survivor, 2010.
- Kirchhoff et al. **Unemployment** among Adult Survivors of Childhood Cancer: A report from the Childhood Cancer Survivors Study. Medical Care (in press).
- Casillas et al. The impact of **insurance** type on survivor and general **preventive health** care utilization in childhood cancer survivors. Cancer (revise/resubmit).

Health status

- Kirchoff et al. **Occupational outcomes** of adult childhood cancer survivors. Social Science Med. Submitted
- Hudson et al. **Longitudinal** changes in **health status**. AOI approved. Concept draft. Awaiting 2007 data.

Health care & health care utilization

- Oeffinger KC et al. **Health care** of young adult survivors of childhood cancer. Ann Fam Med, 2004.
- Yeazel MW et al. An examination of the **dental utilization** practices of adult survivors of childhood cancer. J Public Health Dent, 2004.
- Nathan PC et al. **Medical care** in long-term survivors of childhood cancer. J Clin Oncol, 2008.

Health care & health care utilization

- Kurt et al. Rates of **hospitalization** among adult survivors of childhood and adolescent cancer. J Natl Cancer Inst (revise/resubmit).
- Caplin et al. Influence of **regional access on follow-up care** for adult survivors of pediatric cancer (manuscript in preparation).
- Casillas et al. Understanding **health care utilization patterns** and changes occurring over a decade. AOI approved. Concept draft. Awaiting 2007 data.

Health behaviors – Tobacco

- Emmons et al. **Predictors of smoking** initiation and cessation among childhood cancer survivors J Clin Oncol, 2002.
- Emmons et al. Long-term **smoking cessation outcomes** among childhood cancer survivors in the Partnership for Health Study. J Clin Oncol, 2009.
- Kahalley et al. **Attentional and executive dysfunction** as predictors of smoking within the Childhood Cancer Survivor Study cohort. Nicotine Tob Res, 2010.

Health behaviors – Tobacco

- Kahalley et al. **Psychosocial vulnerabilities** increase **smoking risk** for adolescent cancer survivors (under review by J Cancer Survivorship).
- Klosky et al. Predictors of **smokeless tobacco** use among survivors of childhood cancer. Concept proposal submitted.
- Klesges et al. **Prevalence and predictors of smoking cessation** in childhood cancer survivors. AOI approved.

Health behaviors – Physical activity

- Florin et al. **Physical activity** in adult survivors of childhood **ALL**. Cancer Epidemiol Biomarkers Prev, 2007.
- Cox et al. **Promoting physical activity** in childhood cancer survivors. Cancer, 2009.
- Wampler et al. Factors associated with **inactivity** in survivors of **lower extremity sarcoma**. Medicine and Science in Sports (under review).

Health behaviors – Physical activity

- A comparison of **functional outcomes** between **sarcoma** survivors with **surgery or radiation** as their local control. AOI approved. Concept under development.
- A comparison of **functional outcomes** between **upper extremity and lower extremity sarcoma** survivors. AOI approved. Concept under development.

Health screening

- Yeazel et al. The **cancer screening** practices of adult survivors of childhood cancer. *Cancer*, 2004.
- Cox et al. **Medical screening** participation in the Childhood Cancer Survivor Study. *Arch Intern Med*, 2009.
- Nathan PC et al. Screening and surveillance for **second malignant neoplasms** in adult survivors of childhood cancer. *Ann Intern Med* (revise/resubmit).

Health screening – breast cancer

- Oeffinger et al. **Breast cancer surveillance practices** among women previously treated with chest radiation for a childhood cancer. JAMA, 2009.
- Cox et al. **Determinants of mammography screening** participation in adult childhood cancer survivors. Oncol Nurs Forum, 2009.
- Smith et al. **Inconsistent mammography perceptions and practices** among women at risk of breast cancer following a pediatric malignancy. Cancer Causes & Control (in press).
- Cox et al. **Identifying intervention targets** to increase mammography screening among at-risk childhood cancer survivors. AOI approved.

Health behaviors - Alcohol

- Lown et al. **Alcohol consumption patterns** and risk factors among childhood cancer survivors compared to siblings and general population peers. *Addiction*, 2008.

Health knowledge

- Kadan-Lottick et al. Childhood cancer survivors' knowledge about their **past diagnosis and treatment**. JAMA, 2002.
- Lansdale M, Castellino S, Marina N, et al. Knowledge of **hepatitis C virus screening** in long-term pediatric cancer survivors: a report from the Childhood Cancer Survivor Study. Cancer, 2009.



Evaluation of Cardiovascular Health Outcomes among Survivors: The ECHOS Study

Melissa Hudson & Cheryl Cox

Co-Principal Investigators

R01NR011322

ECHOS

- Aim #1: To assess efficacy of two interventions in increasing CV screening.
- Aim #2: To measure behavioral changes induced by intervention and their mediating effects on CV screening.
- Aim #3: To evaluate the cost-effectiveness of intervention.

ECHOS

- Primary outcome: completion of imaging evaluation of LV systolic function (e.g., echo).
- Hypothesis: Survivors randomized to standard care + APN phone counseling will have greater proportion completing CV screening.
- Eligibility: CCSS participant, age > 25 years, reporting no cancer-related follow-up in previous 5 years.
- Stratification: age (< 30 years v. \geq 30 years), sex, frequency of recommended CV screening

ECHOS Study

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Baseline assessment

Standard Care

Individualized Treatment Summary

- Cancer therapy
- Cancer-related health risks
- CV health screening recommendations
- Risk reduction behaviors

Standard Care + APN Tailored Care

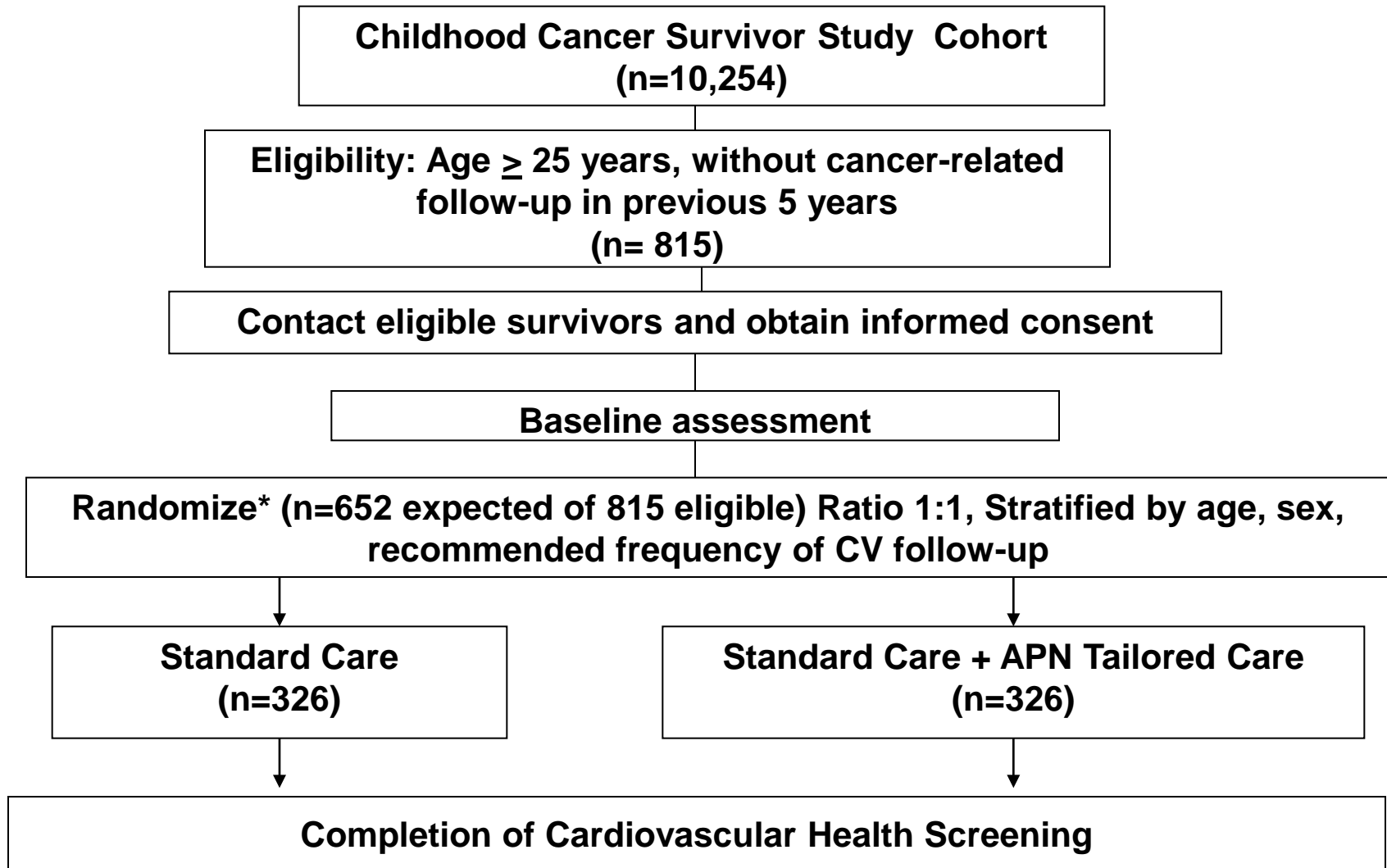
- 2 Motivational interviewing sessions by telephone @ 1 and 3 weeks
- 2 Follow-up letters summarizing counseling session content

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12-month assessment:

- Primary outcome: Cardiac imaging of LV function (yes/no)
- Secondary outcomes: Moderating/mediating factors; barriers to completing CV screening; replicating costs of intervention

Study Design





**Encouraging Mammography/MRI and Preventive
Opportunities for Women Exposed to Radiation.
The EMPOWER Study**

Kevin Oeffinger
Principal Investigator
R01CA134722
9/23/2009 – 7/31/2014

EMPOWER

- **Primary aim:** Determine the efficacy of an intervention, consisting of mailed tailored print materials followed by a telephone-delivered Brief MI, on mammogram screening rates compared with an attention control.
- **Hypothesis:** Women in the intervention group will have a 20% higher rate of screening mammography than women in the attention control group.

EMPOWER

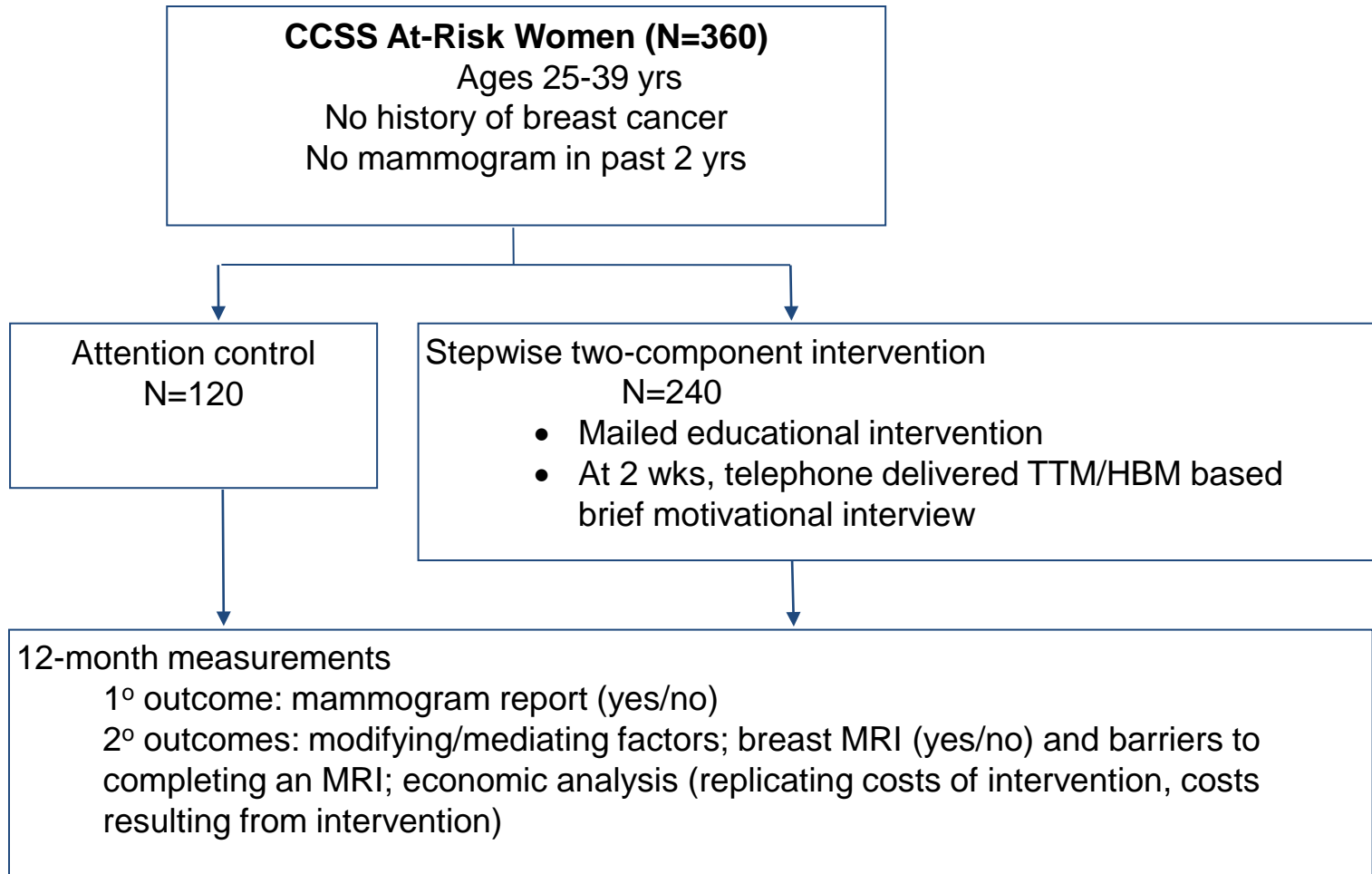
Secondary Aims:

- Explore moderating and mediating factors that predict mammogram completion and timing of the obtained surveillance.
- Determine the percent of women who have an adjunct breast MRI and explore barriers to completing this imaging test (e.g., insurance/cost, physician authorization).
- Estimate (1) the replication costs of the intervention and (2) costs resulting from the intervention.

EMPOWER

- Primary outcome: completion of mammogram
- Eligibility: CCSS female treated with chest radiation, age 25-39 years, reporting breast cancer imaging in previous 2 years and without history of breast cancer
- Randomization stratified by: age 25-33 yrs and 34-39 yrs) and minority status (white, NH and minority)

EMPOWER Schema



**Childhood Cancer Survivor Study
Women post chest radiation**

N=330

Age 25-39 yrs

No mammogram in past 2 yrs

Baseline Survey

Mail or telephone
Administered by CCSS Coordinating Center

Randomize

Intervention Group

N=220

Theoretical foundation: HBM/TTM

Tailored Mailing

- COG breast cancer screening recommendations
- Benefits and other considerations of breast cancer surveillance
- Risk information/laminated placard for physician
- Low cost mammography options

Telephone-delivered Stage-based Brief MI
(*delivered at 2 weeks* by AMC Denver)

- Reinforce screening guidelines
- Assess readiness
- MI-tailored dialogue:
 - Elicit change talk and create ambivalence
 - Resolve ambivalence
 - Change decisional balance
 - Develop action plan
- Tailored follow-up letter post MI with laminated

Attention Control Group

N=110

Generic Mailing

- Standard CCSS Newsletter

Telephone Interview

- (*delivered at 2 weeks* by CCSS Center)
- General interview with standard CCSS questions
 - Embedded questions regarding mammography practices
 - Generic follow-up letter post interview

Mediator Variables

Knowledge
Screening guidelines
Harms/benefits of screening for BC

Health Beliefs
Perception of susceptibility and severity of BC

Decisional Balance
Pros and Cons of mammography

Self-efficacy
Confidence and ability to obtain BC screening

Psychological Factors
Cancer worry
Depressive, anxious or somatic symptoms

Endpoints (12-Month Post-Randomization Assessment)

Mail, telephone, online
Measurements: repeat baseline survey, collect outcomes
Primary outcome: completed mammogram
Secondary outcomes: moderating/mediating factors, breast MRI, replication cost of intervention and costs resulting from the intervention

Post-Study

- Through ongoing CCSS cohort surveys and activities:
- Monitor breast cancer screening practices every two years
 - Track morbidity, all-cause mortality, breast-cancer mortality in participants in both groups

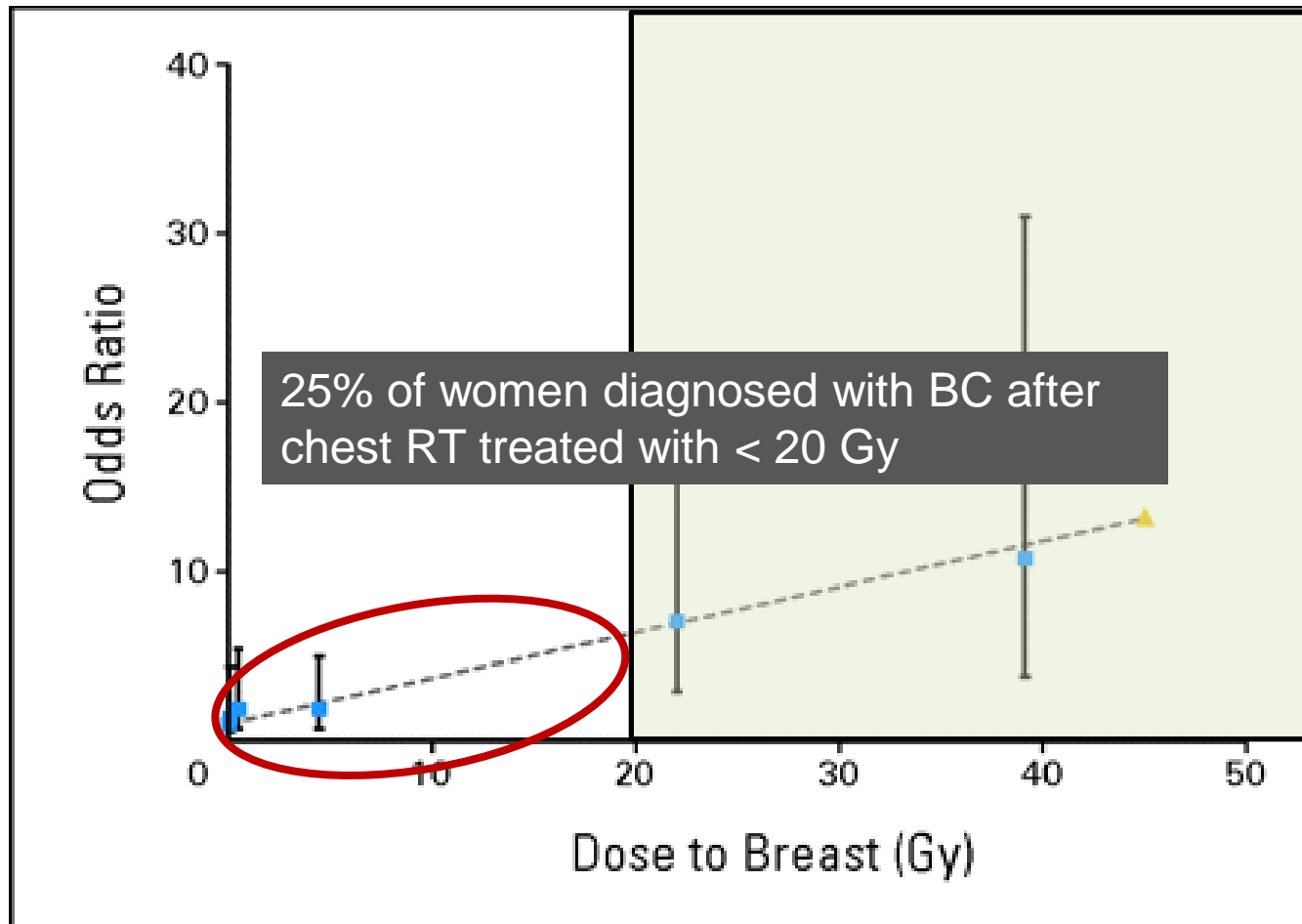
Predicting the Risk of Breast Cancer in Women Who Were Treated With Chest Radiation for a Pediatric Malignancy

Chaya Moskowitz

Principal Investigator

R01CA136783

Breast cancer risk by radiation dose to the breast



Surveillance Recommendations

- Current guidelines:
 - COG: chest RT \geq 20 Gy, beginning at age 25 or 8 years after radiation treatment
 - ACS and UK guidelines: start at age 30 / 25, not based on radiation dose
 - Dutch: chest RT \geq 20 Gy or TBI, starting at 25; 7 - 19 Gy, starting at age 30
- ~ 25% of women diagnosed with BC after chest RT treated with $<$ 20 Gy
- All exclude other possible risk factors

Develop Risk Calculator

- Build absolute risk (or prediction) model
 - Absolute versus relative risk
 - ➡ No absolute risk models for childhood cancer survivors
- Study a range of different risk factors
- Validate the model
- Develop a web-based calculator

Cohort for Model Development

- Original CCSS cohort
 - All females treated with radiation to the chest for their pediatric cancer
 - Includes participants with diagnoses of HL, NHL, Wilms tumor, neuroblastoma, bone cancer, soft tissue sarcomas, leukemia, CNS tumors
 - Radiation fields: mantle, mediastinal, whole lung, TBI, spinal
 - Wide range of radiation doses
- 1677 women, 187 with BC

Validation

- Expanded CCSS cohort
 - Treated with chest RT between 1987-1999
 - 1225 women, ~37 with BC
- Dutch Childhood Oncology Group (DCOG) Late Effect Registry (LATER) Cohort
 - Population-based cohort diagnosed with pediatric cancer who survived at least 5 years
 - 1087 treated with chest RT between 1970-1999, 60 with BC

Gail Model Predictors

- Age
- Number of 1st degree relatives with breast cancer
- Age at first live birth
- Age at menarche
- Number of previous breast biopsies
- Biopsy with atypical hyperplasia

Treatment Related Factors

- RT dose/volume to the chest
- RT dose fractionation
- RT to the pelvis or abdomen
- Alkylating agent chemotherapy
- Primary childhood cancer diagnosis
- Age at exposure
- Interval from primary cancer diagnosis

Other Risk Factors

- Age at menopause
- Years with intact ovarian function after radiation
- Hormone replacement therapy / oral contraceptive use
- Body mass index

New “priority” projects

- Longitudinal health screening
 - Cancer, cardiovascular, other health outcomes
- Longitudinal health behaviors
 - Smoking, alcohol, physical activity
- Relationship of health behaviors to chronic disease, health status, QOL, etc...
- Follow-up health knowledge