Epidemiology/Biostatistics Working Group Report

Wendy Leisenring, ScD Cindy Im, PhD

CCSS
Childhood Cancer Survivor Study

St. Jude Children's Research Hospital

An NCI-funded Resource

Scope of Research

CCSS

- To lead and support investigations on population sciences relevant to CCSS including:
  - Mortality
  - Cost-effectiveness
  - Characterization of primary treatment exposures (including temporal changes, radiation dosimetry)
  - Minority populations
- To encourage and support methodological research associated with enhancing the follow-up and evaluation of the CCSS cohort

Working Group Membership: CCSS Weekly Call

CCSS

Meetings to maintain the integrity of CCSS methods, including sampling and recruitment, survey design, and analysis

St. Jude Children's Research Hospital
- Greg Armstrong (CCSS PI)
- Kumar Srivastava (Statistics & Data Center)
- Yutaka Yasui
- Sadie Mirzaei Salehabadi
- Kendrick Li
- Yan Chen
- Shani Alston
- Chris Vukadinovich
- Mingjuan Wang
- Zhuo Qu
- Grace Zhuo
- Nivya George
- Vikki Nolan
- Aaron McDonald

Fred Hutchinson Cancer Center
- Wendy Leisenring (WG Co-Chair)
- Kayla Stratton

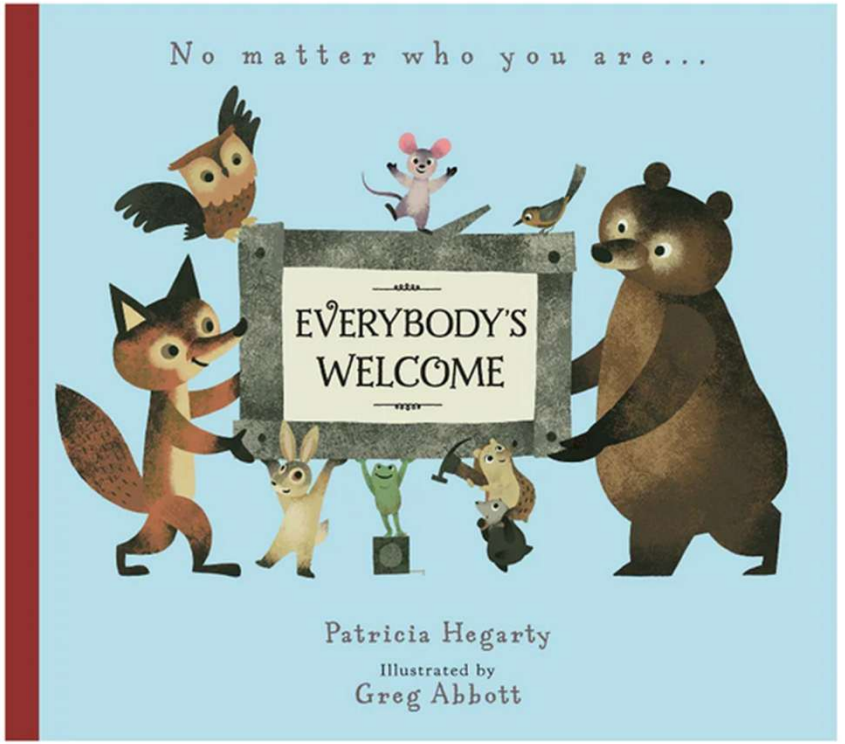
University of Minnesota
- Cindy Im (WG Co-Chair)

University of Texas MD Anderson Cancer Center
- Rebecca Howell (Radiation Dosimetry Center)
- Susan Smith

Working Group Membership: Active Methodological Projects

CCSS

- Greg Armstrong, St. Jude Children's Research Hospital
- James Bates, Emory University
- I-Chan Huang, St. Jude Children's Research Hospital
- Rebecca Howell, MD Anderson Cancer Center
- Cindy Im, University of Minnesota
- Xu Ji, Emory University
- Anne Kirchhoff, University of Utah
- Wendy Leisenring, Fred Hutchinson Cancer Center
- Arin Madenci, Boston Children's Hospital
- Sadie Mirzaei Salehabadi, St. Jude Children's Research Hospital
- Chaya Moskowitz, Memorial Sloan Kettering Cancer Center
- Kiri Ness, St. Jude Children's Research Hospital
- Kumar Srivastava, St. Jude Children's Research Hospital
- Lennie Wong, City of Hope
- Yutaka Yasui, St. Jude Children's Research Hospital
- Jennifer Yeh, Boston Children's Hospital
- Yan Yuan, University of Alberta



Working Group Progress

CCSS

15 Published/In Press Manuscripts (since 1/1/2023)

6 Currently Submitted Manuscripts

11 Analysis/Manuscript in Process

2 Concepts approved

4 New AOIs (where Epi/Biostats is primary; total since 1/1/2023)

Highlights of recently completed research and ongoing analyses

CCSS

(1) Methodological research

(2) Administrative or registry data linkages

(3) Risk prediction

(4) Health outcome comparative modeling

(5) Conditional mortality

Highlights of recently completed research and ongoing analyses

CCSS

(1) Methodological research

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(4) Health outcome comparative modeling

(5) Conditional mortality

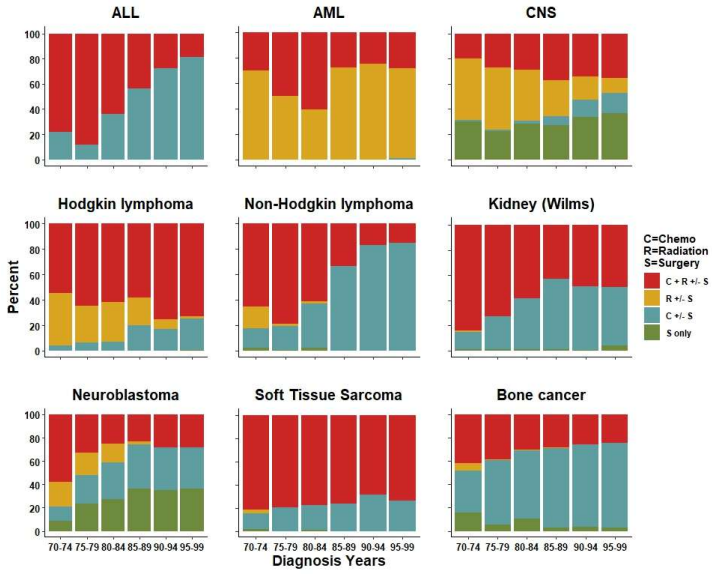
Methods: CCSS Cohort Methodology Paper

CCSS

Temporal Changes in Treatment of Childhood Cancer 1970-1999: Study Design and Cohort Characteristics of the Childhood Cancer Survivor Study Cohort

Wendy Leisenring, Yutaka Yasui, Kayla Stratton, Vikki Nolan, Aaron McDonald, Cindy Im, Greg Armstrong et al.

- Eligible and participant cohort characteristics
- Treatment changes across three decades
- Response and ongoing engagement
- Statistical approaches to reduce bias due to dropout / non-participation



Childhood Cancer Survivor Study

An NCI-funded resource

Methods: CCSS Cohort Methodology Paper

CCSS

Participation and continuing engagement

Baseline participation more likely:

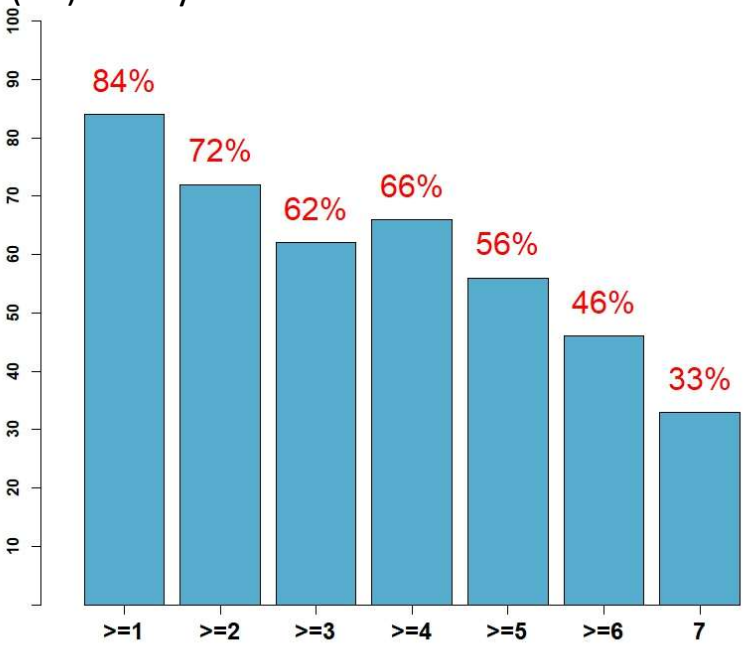
- Females
- Older survivors
- Alive at baseline
- Later diagnosis years (vs. 1970-1986)
- Some variations by diagnosis and institution

Higher FU Survey completion(s) associated with **same variables** plus:

- Higher Socioeconomic status (income, education, health insur)
- Fewer severe chronic conditions
- Better self-reported health status (perception of health)
- Healthier behaviors

Paper describes use of Inverse Probability Weighting to account for participation bias

Percent of Survivors with at least N Follow-up (FU) surveys contributed*



*Among those eligible to contribute at least N FU surveys

Childhood Cancer Survivor Study

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Methods: Approaches to reduce bias in CCSS analyses

CCSS

Statistical analysis of self-reported health conditions in cohort studies: handling of missing onset age

Sedigheh Mirzaei[a,*], José Miguel Martínez[b], Shizue Izumi[c], Motomi Mori[a], Gregory T. Armstrong[d], Yutaka Yasui[d]

Journal of Clinical Epidemiology

Published online 9 July 2024

Sedigheh (Sadie) Mirzaei, PhD (St. Jude)

- Practical methods to analyze self-reported time-to-event data when onset age is missing can lead to bias
  - E.g., complete-data analysis; simple replacement with survey age
- Interval-censored regression: Shown to result in measures of association with reduced bias and smaller SDs

Highlights of recently completed research and ongoing analyses

CCSS

(1) Methodological research

(2) Administrative or registry data linkages

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(5) Conditional mortality

Linkage: Center for International Blood and Marrow Transplant (CIBMTR)

CCSS

Objective: Supplement hematopoietic cell transplantation (HCT) data

Longitudinal outcomes for US/international patients who receive cellular therapies

- Center reporting for all allogeneic HCTs has been mandatory in US since 2008
- Voluntary center reports for autologous HCT, CART, gene therapy; covers >80%

blood® 5 JANUARY 2023 | VOLUME 141, NUMBER 1

Chronic conditions, late mortality, and health status after childhood AML: a Childhood Cancer Survivor Study report

Lucie M. Turcotte,[1] Jillian A. Whitton,[2] Wendy M. Leisenring,[2] Rebecca M. Howell,[3] Joseph P. Neglia,[1] Rachel Phelan,[4,5] Kevin C. Oeffinger,[6] Kirsten K. Ness,[7] William G. Woods,[8] E. Anders Kolb,[9] Leslie L. Robison,[7] Gregory T. Armstrong,[7] and Eric J. Chow[2]

- CIBMTR data used to assess chronic graft-versus-host disease (matched 114/238 survivors)

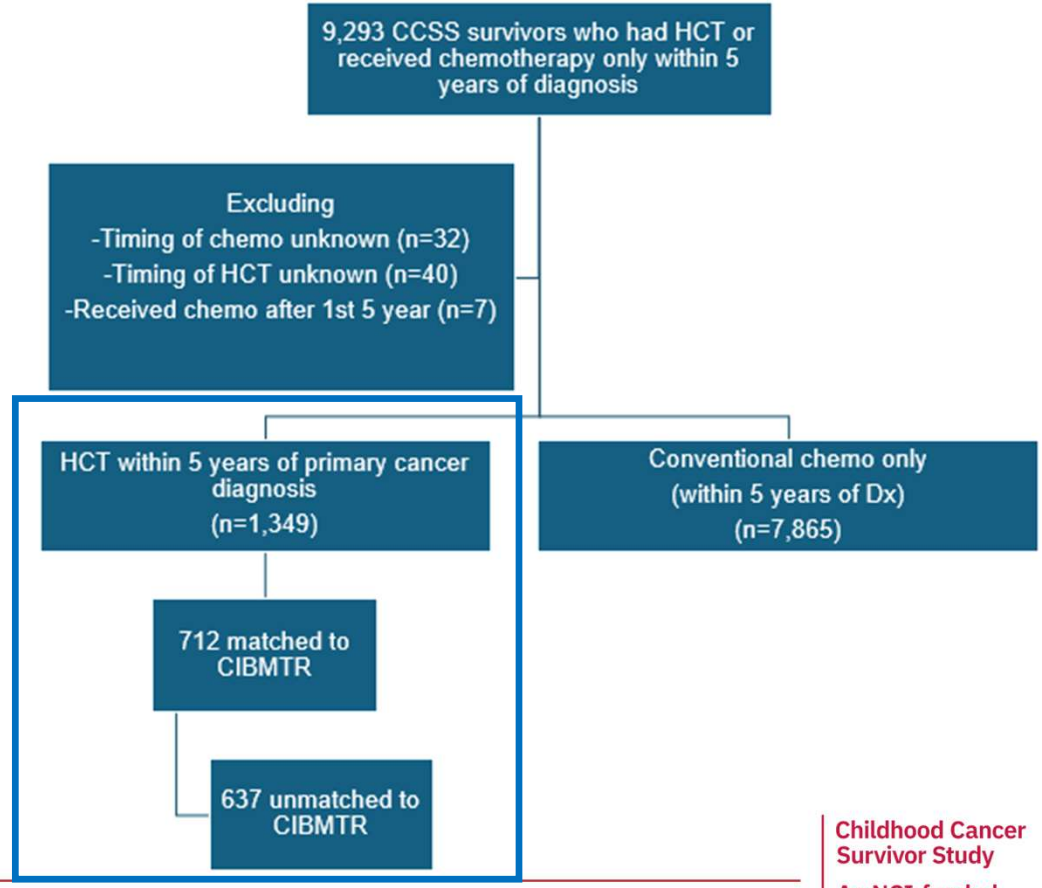
Linkage: Center for International Blood and Marrow Transplant (CIBMTR)

CCSS

Cardiovascular risk factors in survivors of childhood HCT and their role in development of cardiovascular disease: A CCSS-CIBMTR Analysis

Danielle Friedman, MD
(MSKCC)

Presenting at ISLCCC on Friday, 10:35a!



Childhood Cancer Survivor Study
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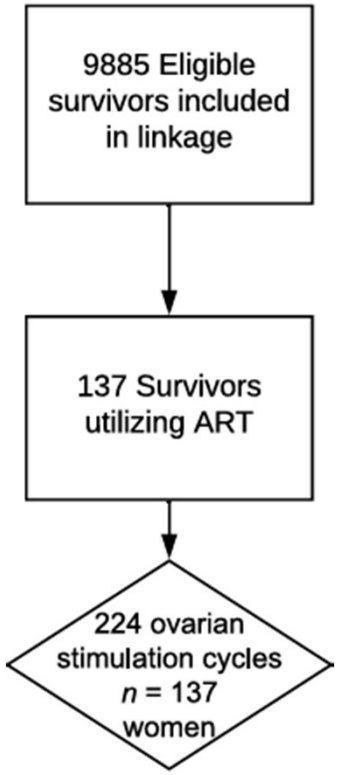
Linkage: Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS)

CCSS

Assisted reproductive technology use and outcomes in childhood cancer survivors

Cancer. 2024;130:128–139.

Kimberly W. Keefe MD[1] | Andrea Lanes PhD[1] | Kayla Stratton MS[2] | Daniel M. Green MD[3] | Eric J. Chow MD, MPH[2] | Kevin C. Oeffinger MD[4] | Sara Barton MD[5] | Lisa Diller MD[6] | Yutaka Yasui PhD[3] | Wendy M. Leisenring ScD[2] | Gregory T. Armstrong MD, MSCE[3] | Elizabeth S. Ginsburg MD[1]

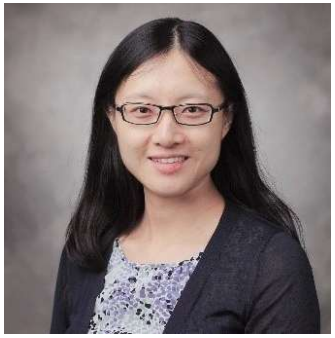


Linkage: Medicaid administrative claims data

CCSS

CCSS ancillary studies:

1) Examine Medicaid uptake, coverage continuity, longitudinal patterns of health service utilization, and associated policy/system level factors (**NCI R03 CA267456**)
2) Assess survivor experiences with insurance and care within the Medicaid system, and identify sources of disparities (**NIMHD K01 MD018637**)



Xu Ji, PhD (Emory)

Linkage: Medicaid administrative claims data

CCSS

Ji et al.: Medicaid enrollment changes among adult survivors of childhood cancer following Medicaid expansion: a report from the Childhood Cancer Survivor Study

(In revision, *JCO Oncology Practice*)

Established linkage of CCSS participants with 100% national Medicaid claims:

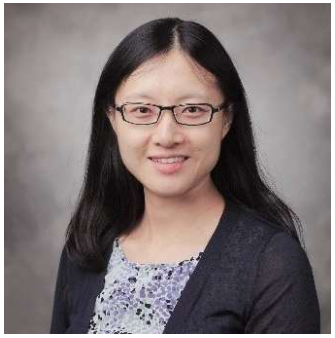
CCSS Data:

- Age, sex, race/ethnicity
- Household income, education attainment
- Chronic conditions
- Cancer type

SSN
DOB
Sex

Medicaid Data:

- Monthly Medicaid enrollment status
- Healthcare & pharmacy claims



Xu Ji, PhD (Emory)

Analysis: **13,355** survivors and **1,752** siblings

Childhood Cancer Survivor Study
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Linkage: Affordable Care Act Medicaid expansion

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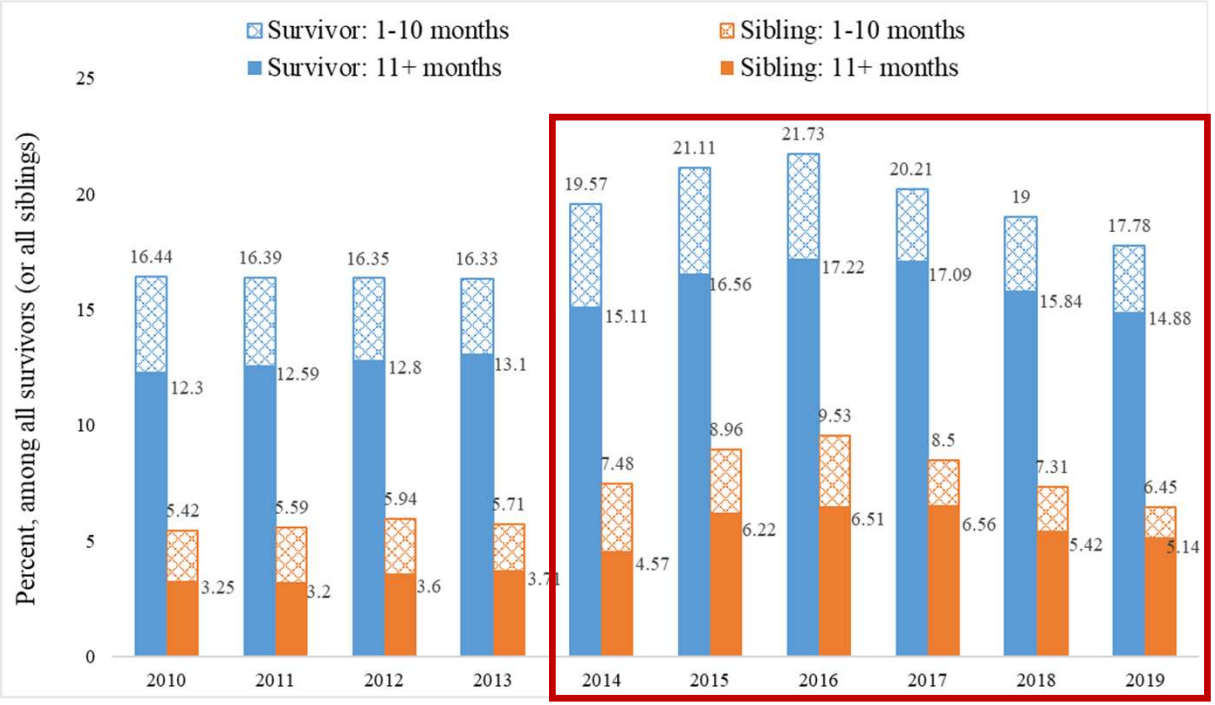
Trends in Medicaid enrollment, by annual coverage duration

- Continuous (11-12 months) vs. non-continuous (≤10 months)



- ACA Medicaid expansion associated with increased Medicaid participation and coverage among survivors vs. siblings
- Benefit greatest for survivors in minority racial and ethnic groups, with lower SES

Ji et al, 2025 (in revision, *JCO Oncol Pract*)

Linkage: Other studies among Medicaid-enrolled survivors

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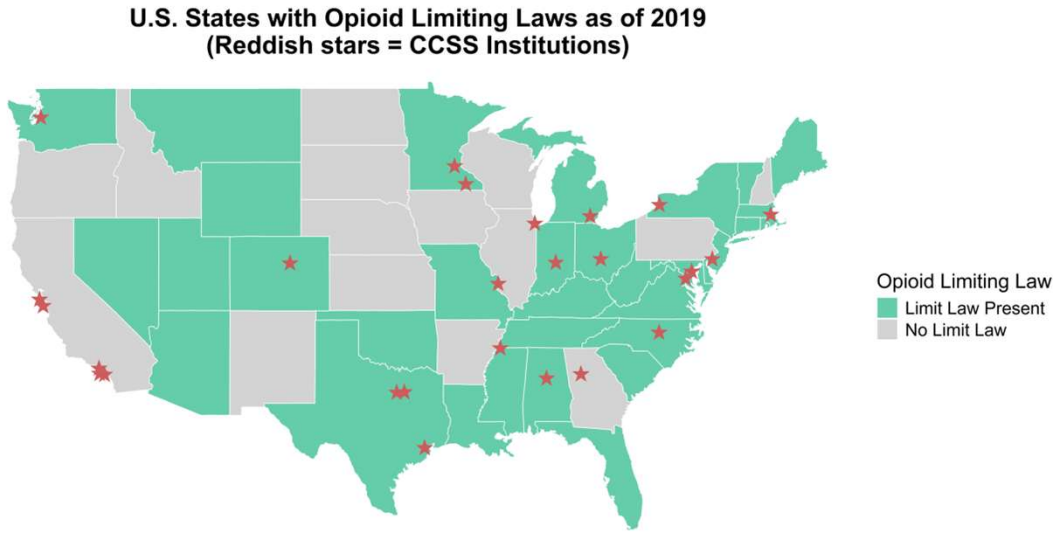
Xin Hu, PhD (Emory)

CCSS Career Development Award (mentor: Xu Ji)

Association Between State Opioid Limiting Laws and Opioid Prescription Among Medicaid-enrolled Survivors of Childhood Cancer: A CCSS-Medicaid Analysis

Presenting at ISLCCC on Friday, 5p



Linkage: Neighborhood-level social determinants of health (SDOH)

CCSS

Objective: Look beyond individual-level risk factors and supplement CCSS participant data with neighborhood-level SDOH classifications

Approved CCSS Concepts:

- Chronic health conditions (C. Howell, 20-07)
- Sleep health (M. Navarrette, 24-07)
- Subsequent neoplasm risk (T. Ghosh, 24-14)
- Healthcare utilization, health status, and rurality (L. Strange, 24-07)
- Late mortality (C. Im, 24-08)

Linkage: SDOH classification in CCSS

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Eligible CCSS 5-year survivors
N=34,204

Completed baseline survey
N=25,725

Geocoded residential address available for ≥1 time point
N=22,700

- Baseline (N=19,446)
- Any follow-up (N=17,447)
- Both (N=14,193)

I-Chan Huang, PhD (St. Jude)

CCSS-SDOH classifications among survivors:

- Social Vulnerability Index (SVI): N=20,912
- Area Deprivation Index (ADI): N=18,751
- Persistent poverty: N=19,446
- Rural Urban Commuting Area Codes (RUCA): N=17,560

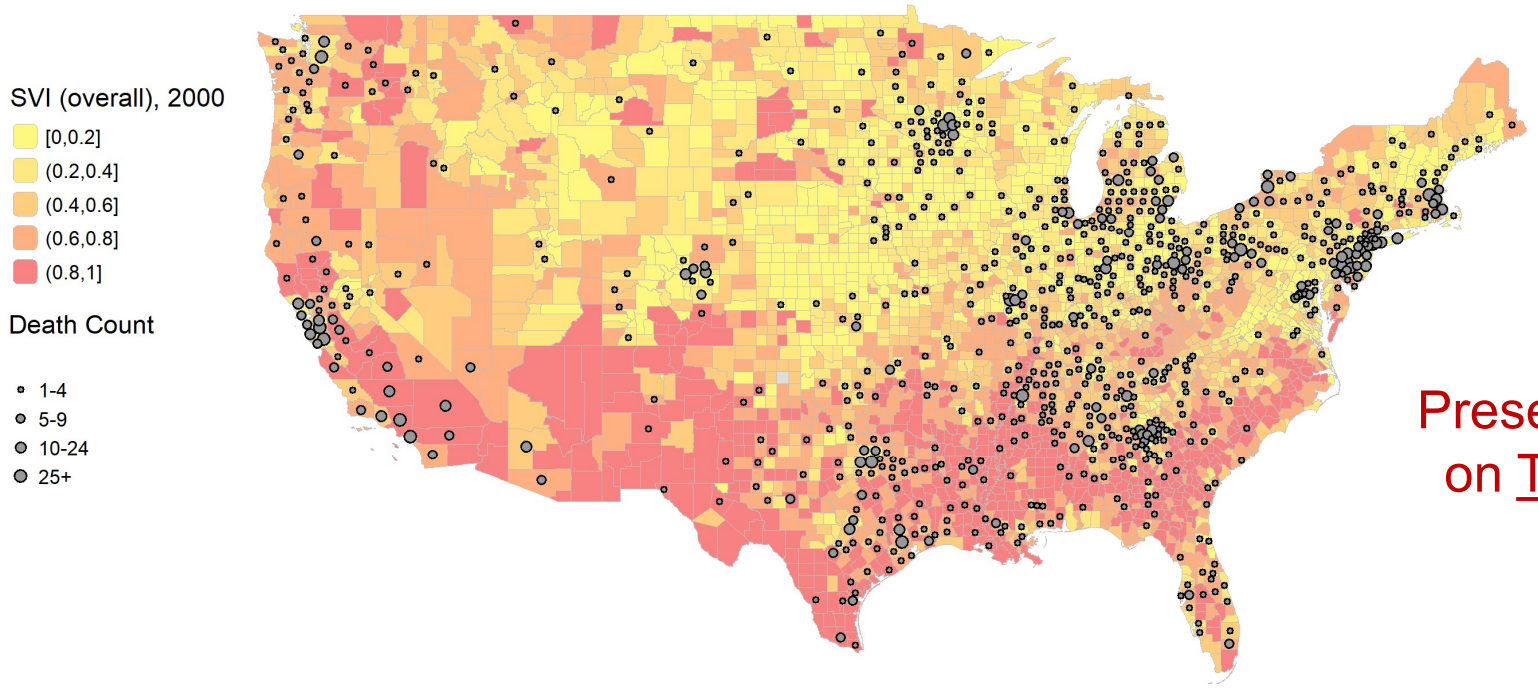
Among CCSS siblings:

- 5,045 with baselines; 4,086 have geocodes

Linkage: Neighborhood-level social determinants of health (SDOH)

CCSS

SDOH and late mortality among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study



Cindy Im, PhD

Presenting at ISLCCC on Thursday, 5:25p!

Childhood Cancer Survivor Study

An NCI-funded resource

Highlights of recently completed research and ongoing analyses

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(1) Methodological research

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(5) Conditional mortality

Risk prediction: Development and validation of novel late effects risk stratification tools

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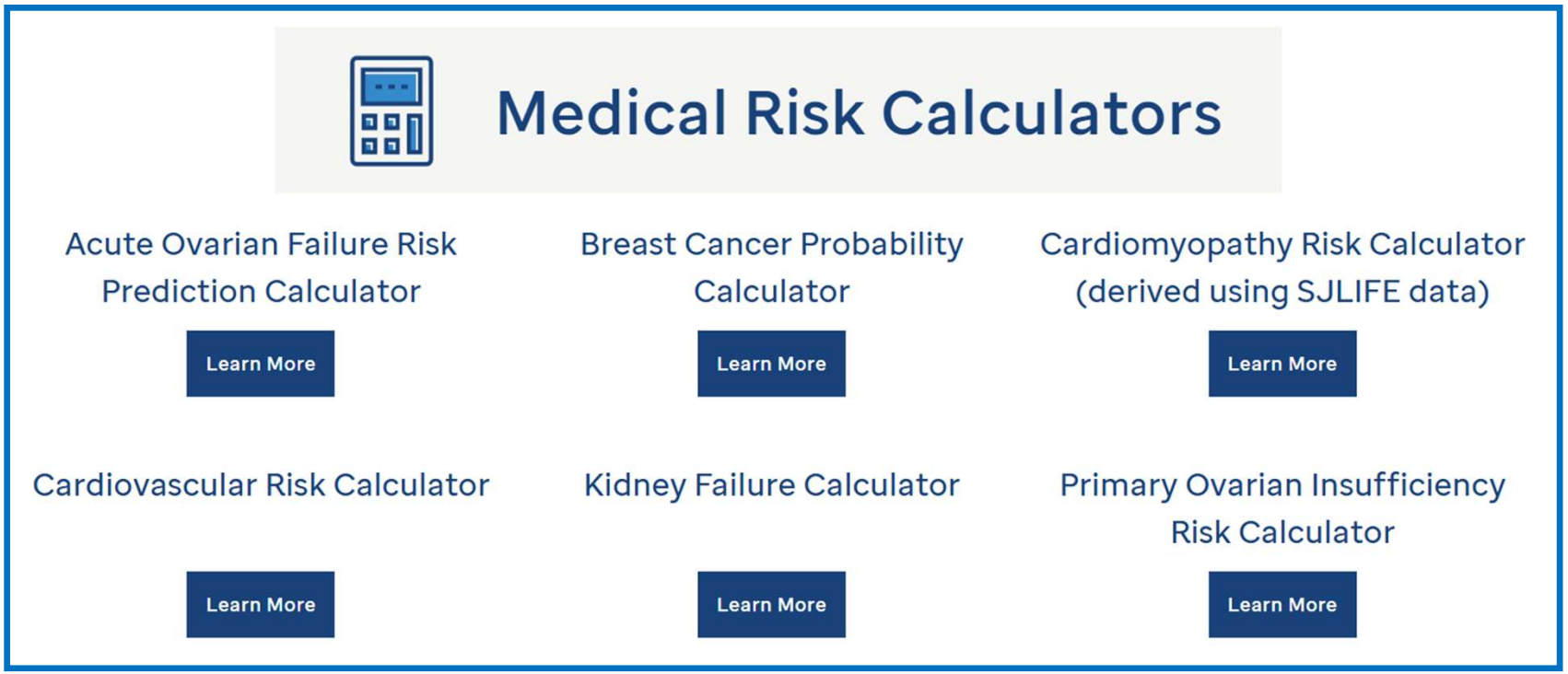
CCSS Website



Risk prediction (+linkage!): Estimate kidney failure risk by age 40y

CCSS

Journal of Clinical Oncology

Development and Validation of a Prediction Model for Kidney Failure in Long-Term Survivors of Childhood Cancer

Natalie L. Wu, MD, MS[1,2,3]; Yan Chen, MMath[4]; Bryan V. Dieffenbach, MD[5]; Matthew J. Ehrhardt, MD, MS[6]; Sangeeta Hingorani, MD, MPH[2,3]; Rebecca M. Howell, PhD[7]; John L. Jefferies, MD[8]; Daniel A. Mulrooney, MD, MS[6]; Kevin C. Oeffinger, MD[9]; Leslie L. Robison, PhD[6]; Brent R. Weil, MD, MPH[5]; Yan Yuan, PhD[4]; Yutaka Yasui, PhD[6]; Melissa M. Hudson, MD[6]; Wendy M. Leisenring, ScD[3]; Gregory T. Armstrong, MD, MSCE[6]; and Eric J. Chow, MD, MPH[2,3]

ORIGINAL REPORTS | February 16, 2023

Natalie Wu, MD
UCSF Benioff Children's Hospitals

Eric Chow, MD
Fred Hutchinson Cancer Center

Model development data: 25,483 CCSS survivors (204 cases)

- 50/52 kidney transplants corroborated by OPTN (through 12/31/2013)
- NDI used to ascertain death related to chronic kidney disease or kidney failure

Risk prediction: POI risk estimates by ages 21y through 40y

CCSS

R21CA261833, MPI: C Im, Y Yuan
R01CA216354, MPI: Y Yasui, J Zhang

THE LANCET
Oncology

Development and validation of age-specific risk prediction models for primary ovarian insufficiency in long-term survivors of childhood cancer: a report from the Childhood Cancer Survivor Study and St Jude Lifetime Cohort

Cindy Im, Zhe Lu*, Sogol Mostoufi-Moab, Angela Delaney, Lin Yu, Jessica L Baedke, Yutong Han, Yadav Sapkota, Yutaka Yasui, Eric J Chow, Rebecca M Howell, Smita Bhatia, Melissa M Hudson, Kirsten K Ness, Gregory T Armstrong, Paul C Nathan†, Yan Yuan†*

Yan Yuan, PhD
University of Alberta

Paul Nathan, MD
SickKids, University of Toronto

Model development data: 7,891 CCSS female survivors (922 cases)

Predictors: Race/ethnicity, age at cancer diagnosis, 20 different chemotherapy agents, HCT, TBI, abdominal/pelvic RT (ovarian RT)

Highlights of recently completed research and ongoing analyses

CCSS

(1) Methodological research

(2) Administrative or registry data linkages

(3) Risk prediction

(4) Health outcome comparative modeling

(5) Conditional mortality

Health outcome comparative modeling : Accelerated Aging in Survivors

CCSS

JAMA Oncology | Original Investigation

Accelerated Aging in Survivors of Childhood Cancer—Early Onset and Excess Risk of Chronic Conditions

Jennifer M. Yeh, PhD; Zachary J. Ward, PhD; Kayla L. Stratton, MS; Mercedes V. McMahon, MPH; Chelsea S. Taylor, BA; Gregory T. Armstrong, MD, MSCE; Eric J. Chow, MD, MPH; Melissa M. Hudson, MD; Lindsay M. Morton, PhD; Kevin C. Oeffinger, MD; Lisa R. Diller, MD; Wendy M. Leisenring, ScD

Published online March 20, 2025.

Jennifer Yeh, Ph.D.
Boston Children's Hospital
Harvard Medical School

Illustrates accelerated aging in terms of early onset and excess risk at age 65

- COMPASS model: Simulation model based on CCSS data and population-based databases to estimate **lifetime** risks of 8* treatment-related CHCs & mortality
- Relative risks, excess risks compared with general population

*6 aging-related conditions (breast cancer, colorectal cancer, heart failure, MI/CAD, valvular disease, stroke) and 2 common, life-threatening SMN among survivors (sarcoma, glial tumors)

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Health outcome comparative modeling : Accelerated Aging in Survivors

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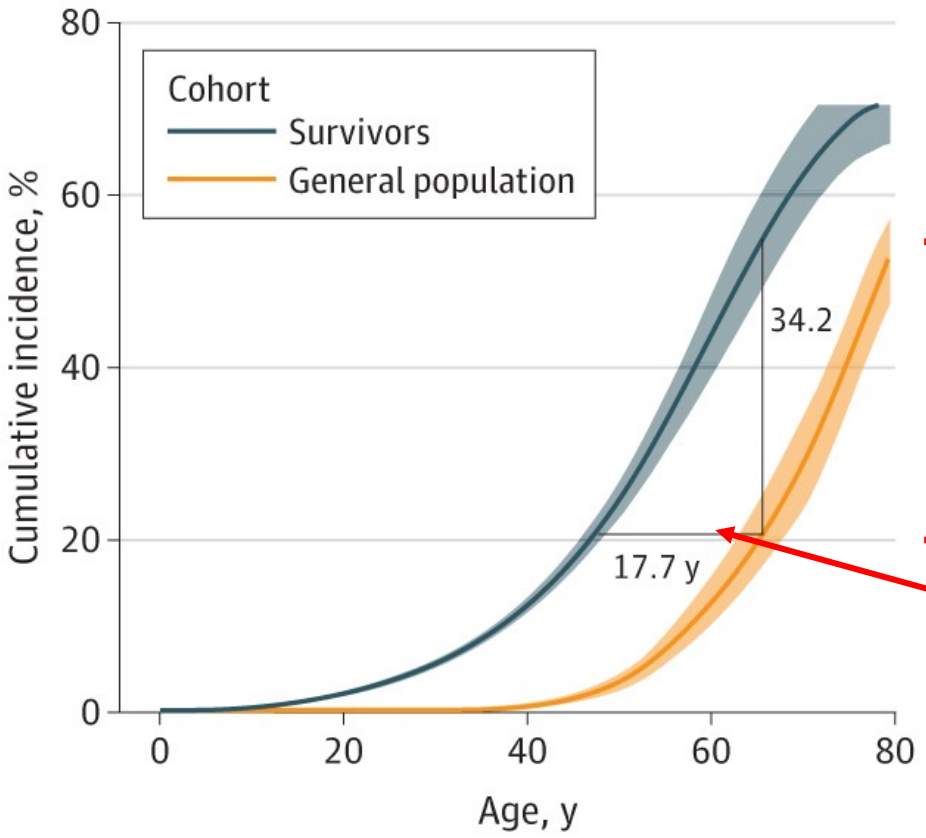

Predicted excess morbidity of at least 1 of the 8 chronic health conditions

34.2% higher risk at age 65

17.7 years earlier onset

Projected risks are higher among survivors treated with radiation

But regardless of radiation exposure or diagnosis, all survivors are projected to experience accelerated aging

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Health outcome comparative modeling : Trends in outcomes among ALL survivors

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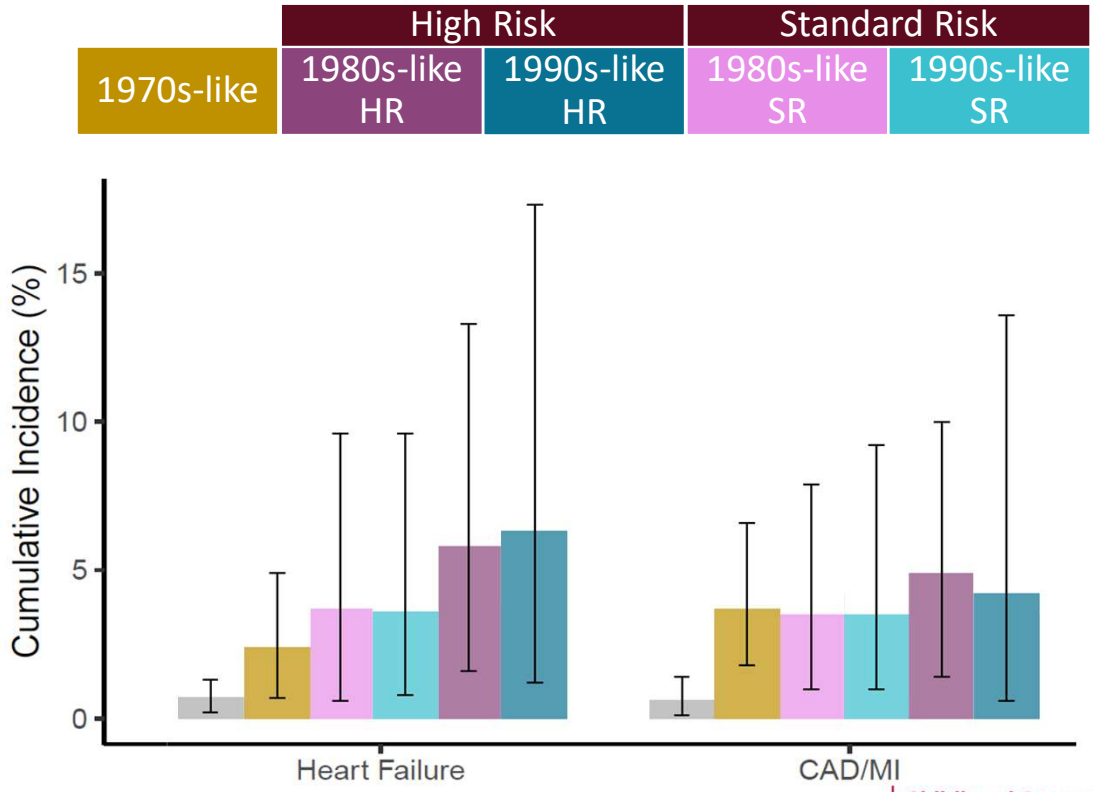
Project long-term outcomes for ALL treatment exposure subgroups using the COMPASS model

- Presented at ASPHO 2025

Trend toward higher cumulative incidence of cardiac late-effects among HR subgroups, particularly for heart failure



Additional papers to examine:

- HL survivors by treatment (breast cancer, CV)
- Medulloblastoma survivors (stroke)

Childhood Cancer Survivor Study

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Highlights of recently completed research and ongoing analyses

CCSS

(1) Methodological research

(2) Administrative or registry data linkages

(3) Risk prediction or decision modeling

(4) Health outcome comparative modeling

(5) Conditional mortality

Mortality after major cardiovascular events

CCSS

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 83, NO. 8, 2024

Mortality After Major Cardiovascular Events in Survivors of Childhood Cancer

Wendy Bottinor, MD, MSCI,[a] Cindy Im, PhD,[b] David R. Doody, MS,[c] Saro H. Armenian, DO, MPH,[d] Alexander Arynchyn, MD, PhD,[e] Borah Hong, MD,[f] Rebecca M. Howell, PhD,[g] David R. Jacobs, Jr, PhD,[b] Kirsten K. Ness, PhD,[h] Kevin C. Oeffinger, MD,[i] Alexander P. Reiner, MD, MSc,[j] Gregory T. Armstrong, MD, MSCE,[h] Yutaka Yasui, PhD,[h] Eric J. Chow, MD, MPH[c,f,j]

Wendy Bottinor, MD
VCU

Mortality risk of childhood cancer survivors after 1st major CV event is <u>comparable</u> to individuals in the general population <u>who are >20 years older</u>

Median age at first major CV event:

- CCSS survivors: 31 years
- CARDIA: 57 years

Mortality after subsequent breast cancer

CCSS

Lucie Turcotte, MD
UMN

nature communications

Article

https://doi.org/10.1038/s41467-025-58434-w

Treatment, toxicity, and mortality after subsequent breast cancer in female survivors of childhood cancer

Cindy Im[1], Hasibul Hasan[1], Emily Stene[1], Sarah Monick[2], Ryan K. Rader[3], Jori Sheade[4], Heather Wolfe[5], Zhanni Lu[1], Logan G. Spector[1], Aaron J. McDonald[6], Vikki Nolan[6], Michael A. Arnold[7], Miriam R. Conces[8], Chaya S. Moskowitz[9], Tara O. Henderson[10], Leslie L. Robison[6], Gregory T. Armstrong[6], Yutaka Yasui[6], Rita Nanda[11], Kevin C. Oeffinger[12], Joseph P. Neglia[1], Anne Blaes[13] & Lucie M. Turcotte[1]

New CCSS ancillary study data: subsequent breast cancer treatment and outcomes

Mortality after subsequent breast cancer

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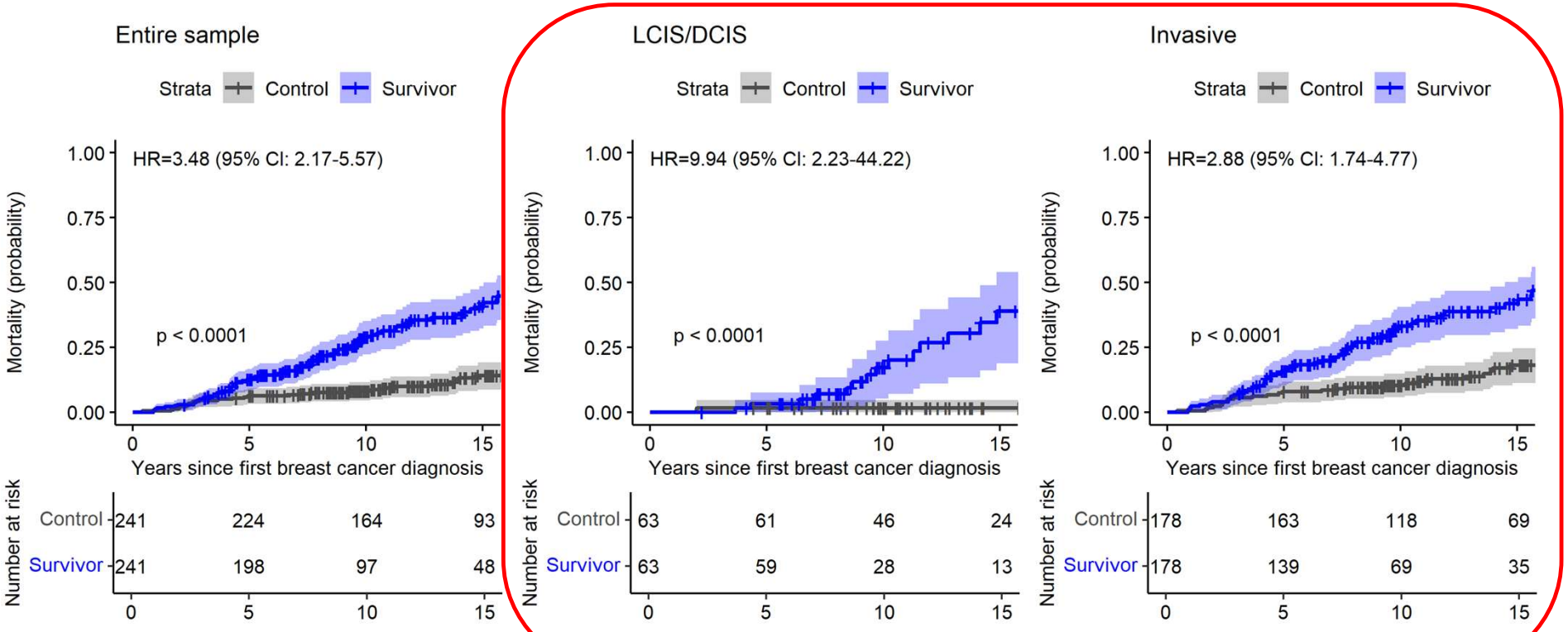

Im et al., Nat Commun (2025)

Childhood Cancer Survivor Study
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Mortality after breast cancer recurrence

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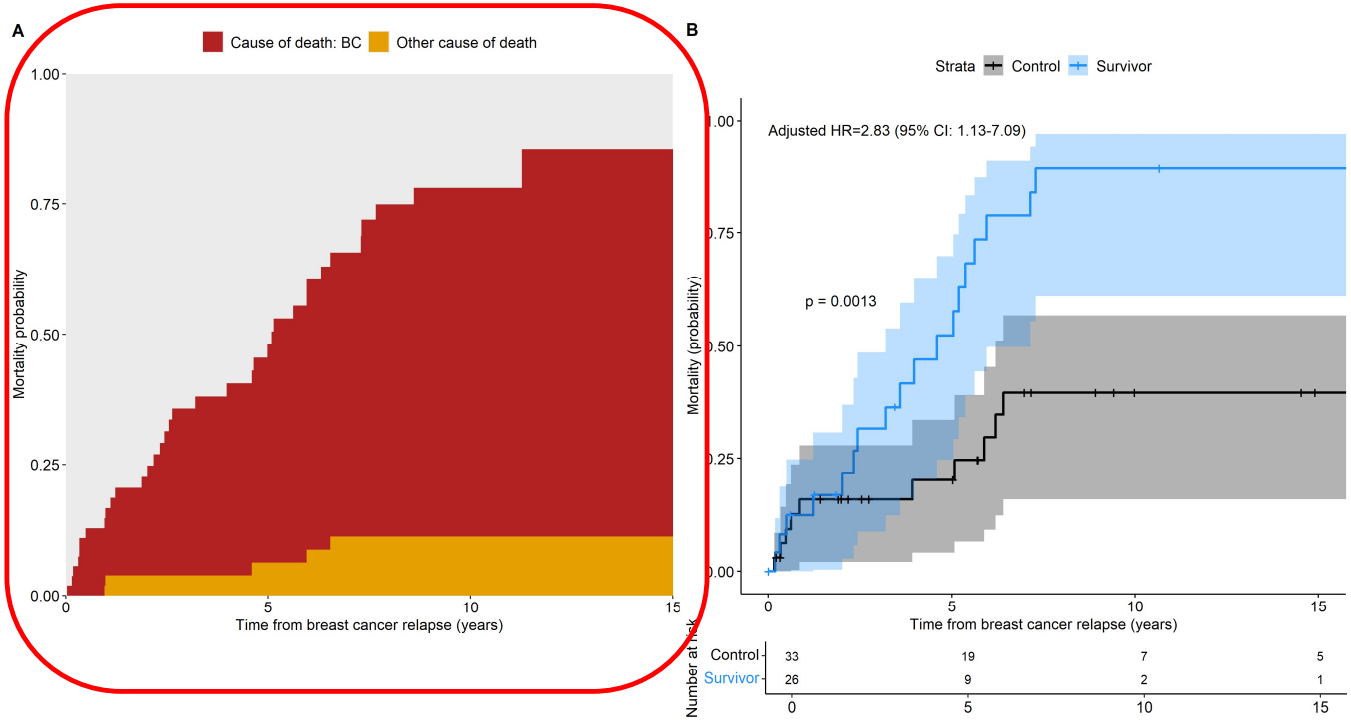
Lucie Turcotte, MD
UMN

Presenting at ISLCCC on Friday, 1:45!



Childhood Cancer Survivor Study
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Mortality after subsequent thyroid cancer

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Oral abstract at ASCO 2025; Poster will be presented at ISLCCC!

Mortality in survivors of childhood cancer diagnosed with subsequent thyroid cancer: A report from the Childhood Cancer Survivor Study

Dana Barnea, Qi Liu, Emily Tonorezos, Paul Nathan, Sogol Mostoufi-Moab, Shizue Izumi, Joseph P. Neglia, Gregory T. Armstrong, Kevin Oeffinger, Yutaka Yasui, Lucie M. Turcotte

Ancillary Studies: Recently completed or ending in 2025

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PIs	Ancillary studies
Xu Ji Emory University	NCI R03 CA267456 (completed): Understanding the **impact of the Affordable Care Act** on healthcare coverage, utilization, and outcomes for childhood cancer survivors
Jennifer Yeh Boston Children's Hospital	NCI R01 CA227576 (ending 8/2025): Genetic testing to guide pediatric cancer care and follow up: using anthracycline-associated cardiac toxicity as a model for the future (ending 8/2027) • **Cancer Outcomes Microsimulation: Pediatric and Adolescent SurvivorShip (COMPASS) model**
Cindy Im University of Minnesota **Yan Yuan** University of Alberta	NCI R21 CA261833 (ending 8/2025): **Treatment-specific genetic risk scores** for late effects prediction in childhood, adolescent, and young adult cancer survivors

Ancillary Studies: Ongoing or new

CCSS

PIs	Ancillary studies
Rebecca Howell University of Texas MD Anderson Cancer Center **Daniel Mulrooney** **Yutaka Yasui** St. Jude Children's Research Hospital	NCI R01 CA261750 (ending 4/2026): **Personalized Risk Prediction** to Reduce Cardiovascular Disease in Childhood Cancer Survivors
Jennifer Yeh Boston Children's Hospital	NCI R01 CA261874 (ending 8/2027): Can risk-reducing medications improve breast cancer prevention in childhood and adolescent cancer survivors? **Comparative modeling** to inform care • **BrEAst Cancer Outcomes iNsight (BEACON) study**
Xu Ji Emory University	NIMHD K01 MD018637 (ending 1/2028): **Disparities in Quality Healthcare** Among Childhood Cancer Survivors: Role of Medicaid
Yadav Sapkota St. Jude Children's Research Hospital **Cindy Im** University of Minnesota	R01HL173881 (ending 4/2028): Developing and validating **race-specific cardiomyopathy risk prediction models** in African American survivors of childhood cancer

Ancillary Studies: Ongoing or new

CCSS

PIs	Ancillary studies
Rebecca Howell University of Texas MD Anderson Cancer Center **Daniel Mulrooney** **Yutaka Yasui** St. Jude Children's Research Hospital	NCI R01 CA261750 (ending 4/2026): Personalized Risk Prediction to Reduce Cardiovascular Disease in Childhood Cancer Survivors

Predicting valvular heart disease in adult survivors of childhood cancer: a report from the Childhood Cancer Survivor Study and St. Jude Lifetime Cohort

Daniel Mulrooney, MD
St. Jude

Presenting at ISLCCC on Saturday, 10:40a!

Utilizing FU7 Frozen Data

CCSS

- Population-level burden of morbidity among survivors of childhood cancer in the United States
  - Led by AnnaLynn Williams, Cindy Im, Wendy Leisenring
- Attribution of neighborhood-level social determinants of health on late mortality
  - Led by Cindy Im, Greg Armstrong, I-Chan Huang
- Disability Adjusted Life Years (DALYs) in childhood cancer survivors
  - Led by Lennie Wong and Greg Armstrong

Plan for Concept Development Using FU8 Survey Data Focused on Aging

CCSS

- Analysis approaches to multiple Short Surveys (Full Survey OR 3 versions of Short Survey)
  - Response rate differences across 3 Short Surveys (insights on types of questions for higher response rates)

- Novel analyses of unmet needs of survivors (a new section re: Health Services)

- Drop-out/Participation analysis (continued evaluation of weighted analyses)

Opportunities for Collaboration with Other Working Groups

CCSS

We interact with all WGs

Our WG is a secondary assignment for many concepts

Value Added and Special Considerations to our WG by a 2000-2025 Cohort Expansion

CCSS

Solving methodological challenges that will arise…

- Sampling efficiency to meet Aims of the study
- Maximizing the participation rate
- Evaluation for early late effects (including mortality) of new therapies (small sample sizes, shorter follow-up)
- Different methods of collecting data (e.g., VPR or registry linkage in general; EHR) => Impact on analyses (comparability between old and new methods)

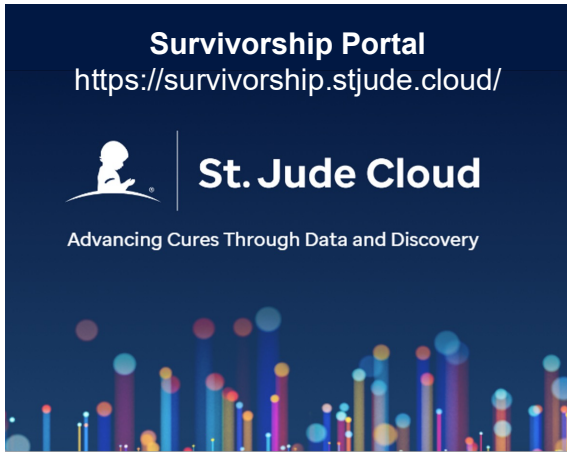
Future Top Priorities

CCSS

- Shorter surveys, rotating survey content
- VPR (Virtual Pooled Registry) cancer incidence data utilization
- Maximizing and maintaining other registry data linkages (e.g., Medicare, CIBMTR, OPTN)
- Analysis of new BIG personal digital health data (wearables, mobile health)
- LEAP protocol (COG-CCSS partnership)

Major updates: St. Jude Cloud Survivorship Portal

CCSS



St. Jude Survivorship Portal: Sharing and Analyzing Large Clinical and Genomic Datasets from Pediatric Cancer Survivors

Gavriel Y. Matt; Edgar Sioson; Kyla Shelton; Jian Wang; Congyu Lu; Airen Zaldivar Peraza; Karishma Gangwani; Robin Paul; Colleen Reilly; Aleksandar Acić; Qi Liu; Stephanie R. Sandor; Clay McLeod; Jaimin Patel; Fan Wang; Cindy Im; Zhaoming Wang; Yadav Sapkota; Carmen L. Wilson; Nickhill Bhakta; Kirsten K. Ness; Gregory T. Armstrong; Melissa M. Hudson; Leslie L. Robison; Jinghui Zhang; Yutaka Yasui; Xin Zhou

CANCER DISCOVERY AUGUST 2024

CCSS Statistical Center (Kumar Srivastava's Team)
Seattle Group (Wendy Leisenring's Team)

↓

St. Jude Epidemiology & Cancer Control Data Wranglers (Kyla Shelton's Team)

↓

St. Jude Computational Biology (Xin Zhou's Team)

Childhood Cancer Survivor Study

An NCI-funded resource

Contact us for any inquiry/interest

CCSS

- **Wendy Leisenring**
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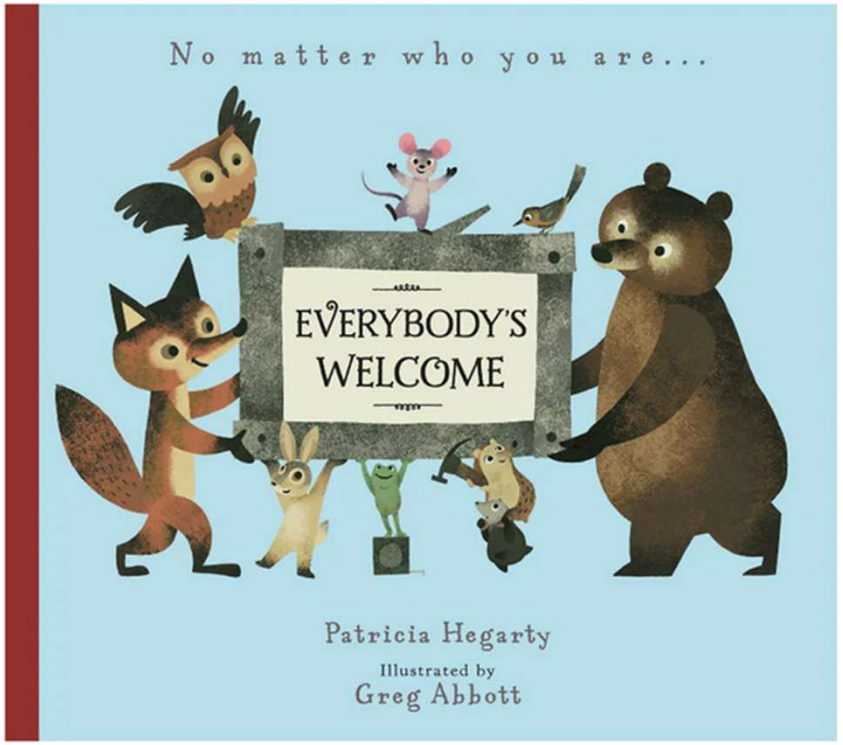


CCSS

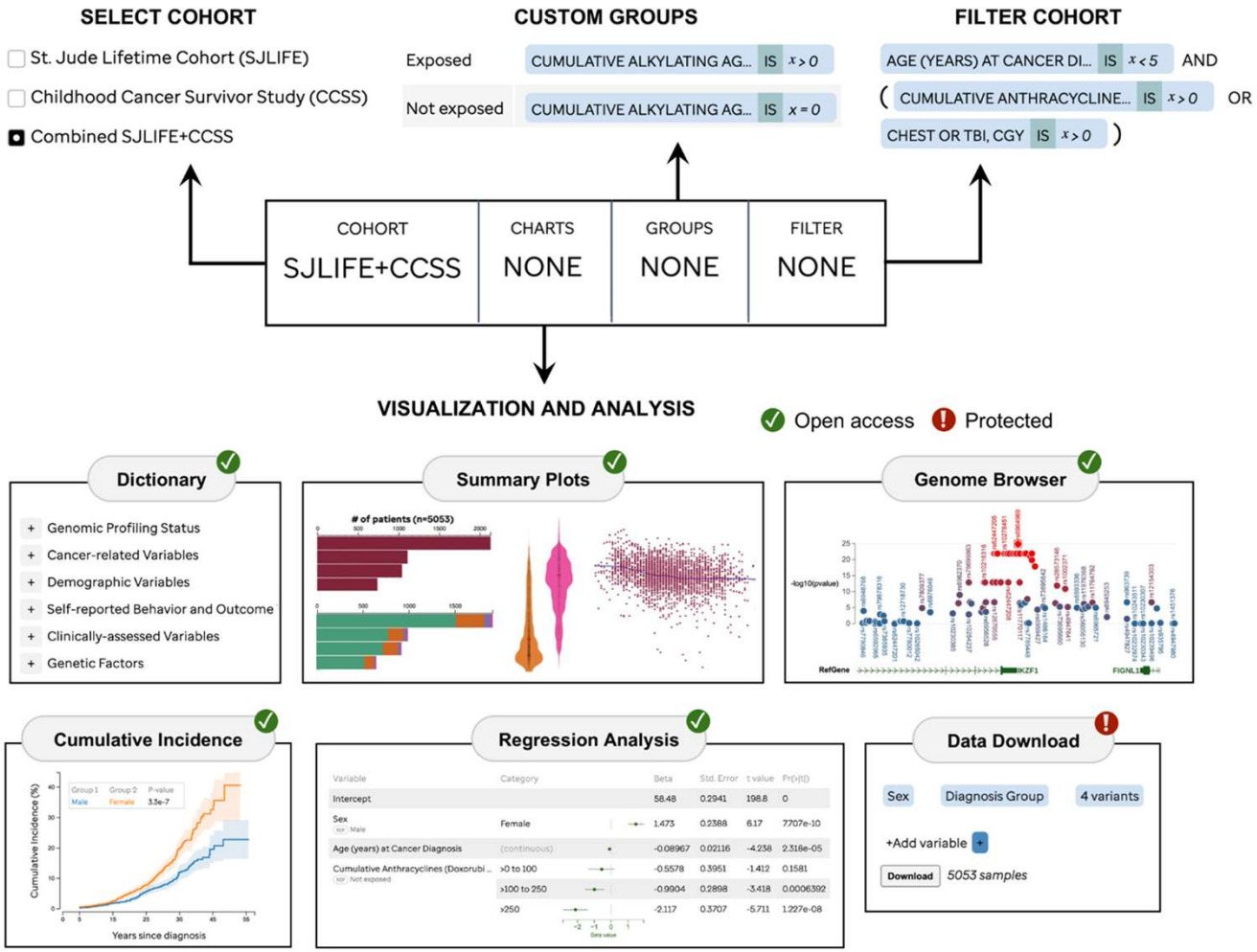
- DISCARDED SLIDES FOLLOW

Select a survivor cohort and proceed to the "CHARTS" tab at the top to explore the data.

- [ ] St. Jude Lifetime Cohort (SJLIFE)
- [ ] Childhood Cancer Survivor Study (CCSS)
- [x] Combined SJLIFE+CCSS*

Survivorship Portal

Feature	St. Jude Lifetime Cohort Study	Childhood Cancer Survivor Study
Data freeze	December 2018	December 2023
Survivors on portal	5,053 (2,288 shared with CCSS)	25,735 (2,288 shared with SJLIFE)
Criteria for inclusion on portal	Availability of WGS data or campus visit	Completion of questionnaire
Survival duration	Survived ≥ 5 years since cancer diagnosis	Survived ≥ 5 years since cancer diagnosis
Cancer diagnosis	All diagnoses	Leukemia, CNS, HL, NHL, neuroblastoma, soft tissue sarcoma, Wilms, bone tumors
Year of cancer diagnosis	1962-2012	1970-1999
Age at cancer diagnosis	<25 years	<21 years
Cancer treatment	Chemotherapy, radiation, surgery	Chemotherapy, radiation, surgery
Study design	Retrospective cohort with prospective follow-up, hospital-based	Retrospective cohort with prospective follow-up, hospital-based
Institution(s)	St. Jude Children's Research Hospital	31 pediatric oncology institutions across the U.S. and Canada
Methods of contact	Clinic visits and surveys	Surveys
Methods for ascertainment of outcomes	Clinical assessments, medical records, self-report, NDI	Self-report, pathology reports (subsequent neoplasm), NDI
Source of sequenced germline DNA	Blood	Saliva or blood



Survivorship Portal

PHENOTYPIC DATA

Demographics, 36 variables
Cancer diagnosis and treatment, 99 variables
Clinical assessments, 350 variables
Chronic health conditions, 400 variables
Self-reported and questionnaire, 776 variables
Over 8.6M data points

GENETIC DATA

Whole-genome sequencing
>400M genotyped variants
>81M polygenic risk scores for >500 traits
Genetically defined ancestries
Ancestry-specific PCs and LD
~1.5TB genotype data

Methods: Approaches to reduce bias in CCSS analyses

CCSS

Hazard ratios and 95% confidence intervals for associations with diabetes mellitus risk

Covariates	Observation-deletion (n=25,429)		Simple replacement (n=25,656)		Interval censored (n=25,656)	
	HR	95% CI	HR	95% CI	HR	95% CI
No pancreatic tail RT	Ref.		Ref.		Ref.	
Any to <10 Gy	0.94	(0.76, 1.17)	0.97	(0.82, 1.14)	1.03	(0.87, 1.23)
10 to <15 Gy	**3.19**	**(2.36, 4.31)**	**2.23**	**(1.71, 2.91)**	**2.31**	**(1.74, 3.06)**
15 to <20 Gy	**2.77**	**(1.61, 4.77)**	**2.13**	**(1.32, 3.44)**	**2.34**	**(1.41, 3.91)**
20 Gy or more	**2.83**	**(1.81, 4.43)**	**2.21**	**(1.50, 3.26)**	**2.57**	**(1.75, 3.78)**

Linkage: SDOH measures

CCSS

- **Social Vulnerability Index (CDC SVI) [2000, 2010, 2014, 2016, 2018]**
  - Score of 0-100 (national percentile ranks) where higher = more social vulnerability
  - Based on census tract of residence
  - Overall and 4 thematic domains: neighborhood-level SES, household composition/disability, minority status, housing/transportation
- **Area Deprivation Index (ADI) [2015, 2019]**
  - Focuses on overall neighborhood-level SES
  - Uses census block group
  - Limited to later baselines/follow-ups

Linkage: SDOH measures

CCSS

- **Persistent poverty [1980, 1990, 2000, 2007-2011]**
  - Neighborhood-level poverty across multiple time points
  - Counties with at least 20% of residents living below the federal income poverty level for ~30 years, using USDA Economic Research Service decennial census data
- **Rurality (RUCA) [2000, 2010]**
  - Urbanization measure using USDA Rural-Urban Commuting Codes
  - Based on census tract of residence

Health outcome comparative modeling : Tamoxifen for breast cancer prevention

CCSS

BEACON model (~CISNET + CCSS): Estimate clinical benefits and harms of adding tamoxifen to screening among survivors

Presented at ASCO 2024

Pediatric lymphoma survivors previously treated with mediastinal RT

Before age 50

No screening or tamoxifen → 20% will develop breast cancer; 2-3% will die of breast cancer

Annual mammo/MRI screening starting at age 25 → 56% of breast cancer deaths averted

Screening with addition of tamoxifen before age 35 → 67% of breast cancer deaths averted; <1% risk of serious side-effects; Reduction in childbearing years

Tamoxifen for 5 years further reduces breast cancer mortality when combined with recommended screening

As CCSS Engages with Participants This Year What Would You Like to Learn From Them?

CCSS

- How to improve continued participation/engagement, in particular, among minorities/disadvantaged populations and sustain diversity (e.g., younger survivors)?

- How do survivors perceive their contribution to CCSS research and the survivorship community?

Risk prediction: Estimate kidney failure risk by age 40y

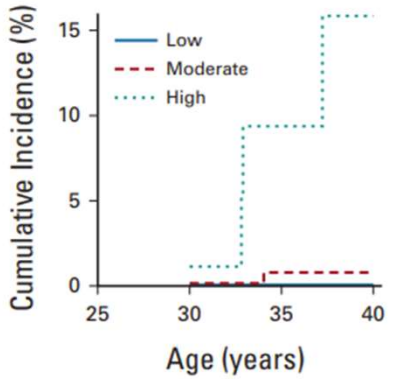
CCSS

Predictors: Race/ethnicity, age at cancer diagnosis, nephrectomy, nephrotoxic chemotherapy, abdominal RT (kidney RT dose), congenital genitourinary anomalies, hypertension (within 5y dx)

TABLE 3. Integer Risk Scores Associated With Late Kidney Failure and Corresponding Prediction Model Performance (continued)

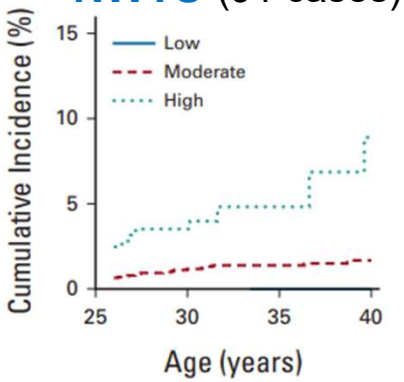
Variable	Simple Model	Dose-Specific Model
SJLIFE (validation)		
AUC	0.83 (95% CI, 0.73 to 0.96)	0.88 (95% CI, 0.72 to 0.98)
C-statistic	0.86 (95% CI, 0.75 to 0.96)	0.88 (95% CI, 0.71 to 0.98)
NWTS (validation)		
AUC	0.62 (95% CI, 0.54 to 0.68)	0.67 (95% CI, 0.61 to 0.77)
C-statistic	0.63 (95% CI, 0.56 to 0.70)	0.64 (95% CI, 0.59 to 0.73)

SJLIFE (8 cases)



No. at risk:				
Low	1,750	457	327	212
Moderate	652	139	88	46
High	88	20	10	8

NWTS (91 cases)

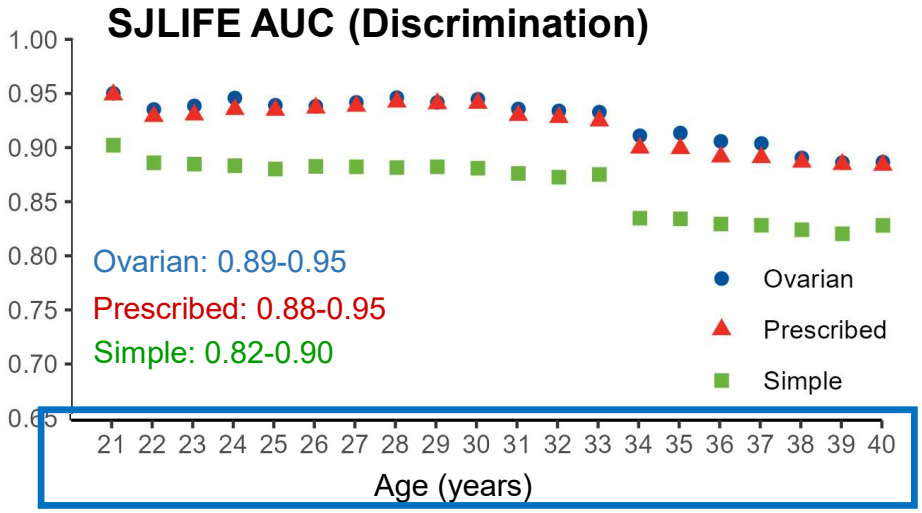


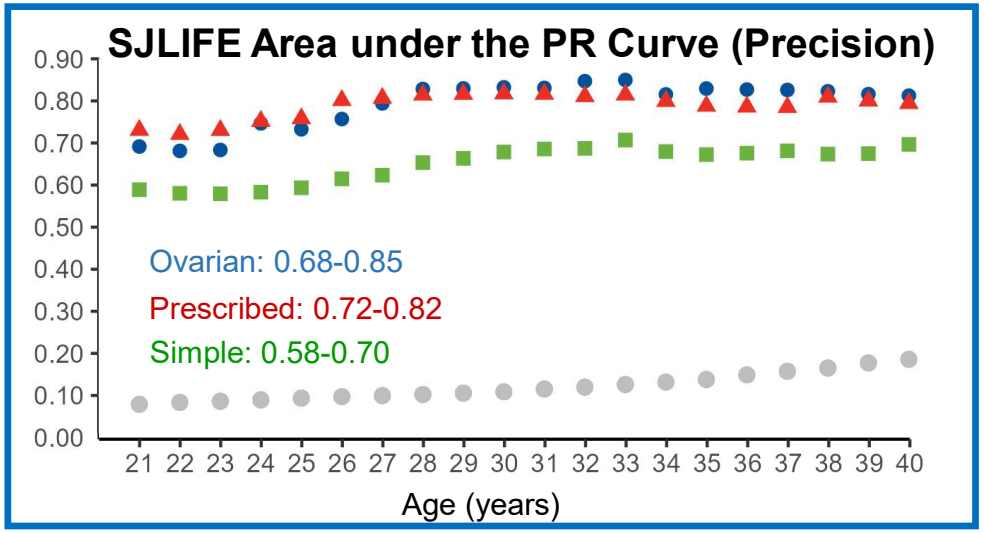
No. at risk:				
Low			65	44
Moderate	5,817	1,474	1,034	421
High	969	244	67	45

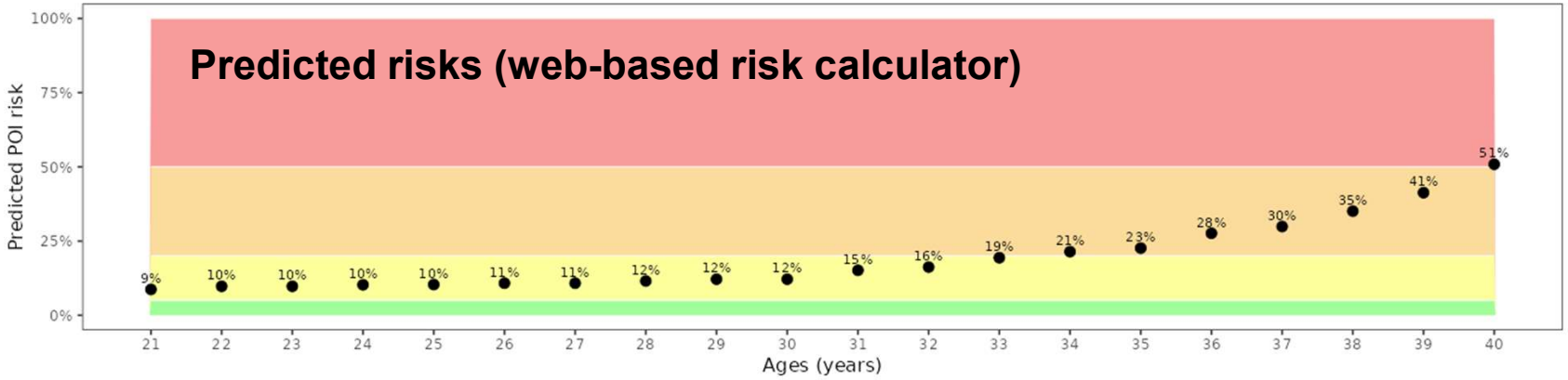
Wu et al., J Clin Oncol (2023)

Risk prediction: Age-specific POI risk estimates

CCSS







Im et al., Lancet Oncol (2023)

Childhood Cancer Survivor Study

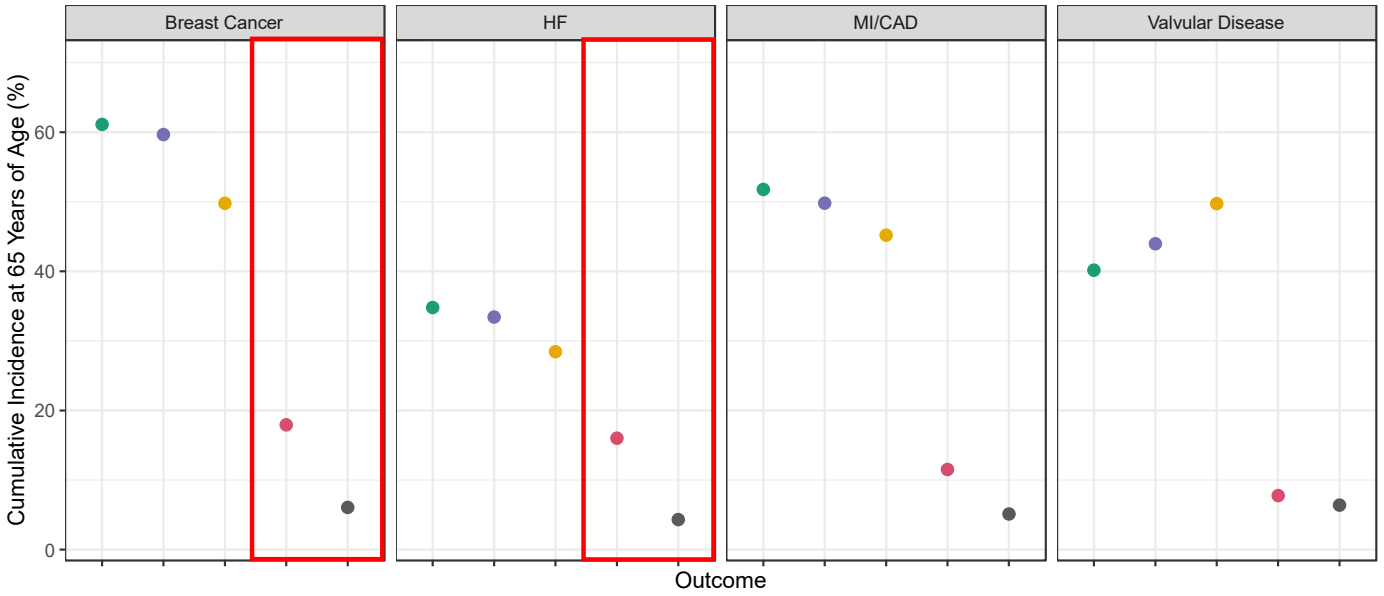
An NCI-funded resource

Health outcome comparative modeling : Trends in outcomes among HL survivors

CCSS

Building upon Oeffinger et al. (JCO 2021), project long-term outcomes for HL treatment exposure subgroups using the COMPASS model

- Presented at SMDM 2025



Extended−field RT
Chest RT ≥ 35 Gy
Chest RT < 35 Gy
Chemo Only
General Population

Improved outcomes are projected for HL survivors treated without chest RT, but survivors will still face elevated risks for breast cancer and heart failure

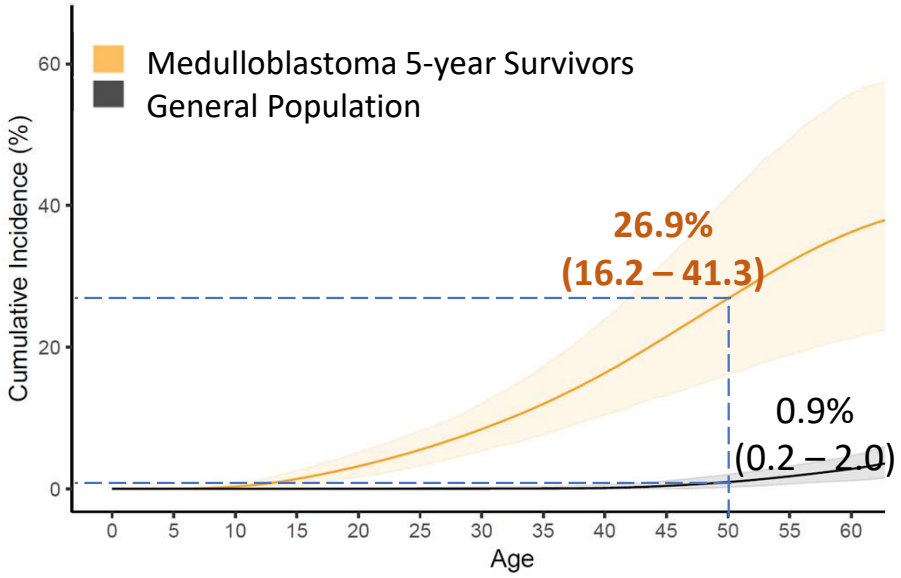
Health outcome comparative modeling : Trends in outcomes among medullo survivors

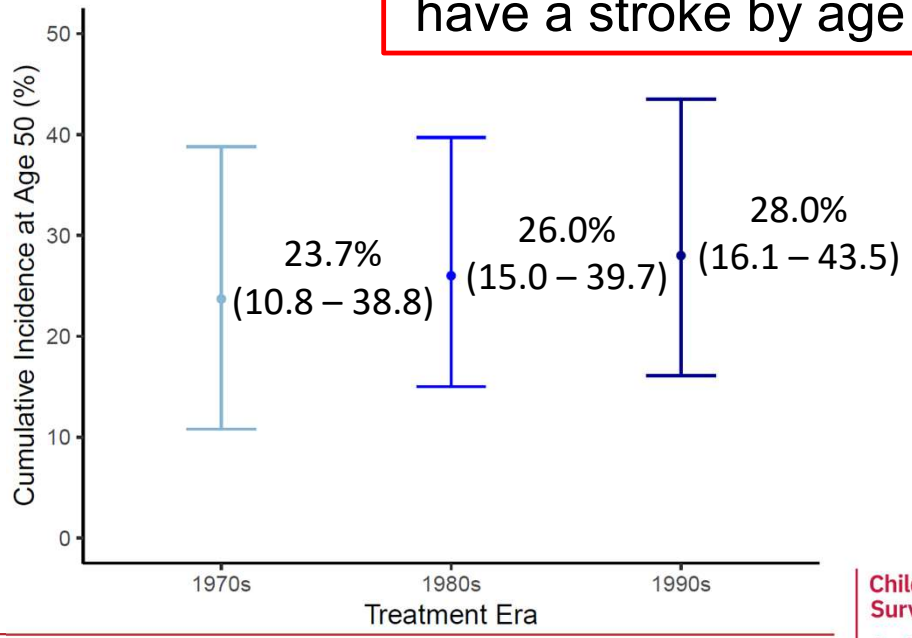
CCSS

Project long-term outcomes for medulloblastoma survivors based on treatment era using the COMPASS model

- Presented at SNO Pediatric-Neuro-Oncology 2025

An estimated 1 in 4 survivors projected to have a stroke by age 50



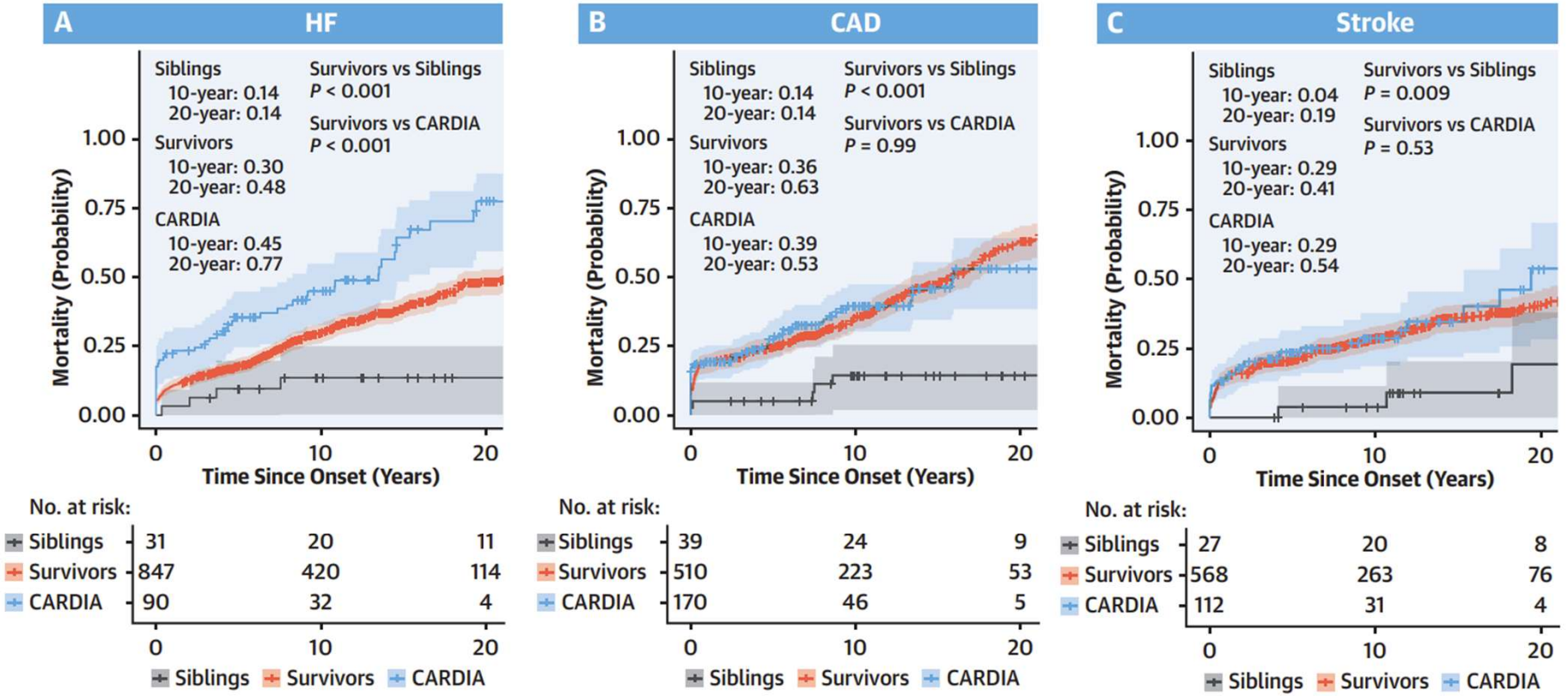


Childhood Cancer Survivor Study

An NCI-funded resource

Mortality after major cardiovascular events: Comparison with CARDIA

CCSS



Bottinor et al., JACC (2024)

Childhood Cancer Survivor Study

An NCI-funded resource

Decision modeling: Subsequent breast cancer screening guidelines

CCSS

Journal of Clinical Oncology

original reports

Health Benefits and Cost-Effectiveness of Children's Oncology Group Breast Cancer Screening Guidelines for Chest-Irradiated Hodgkin Lymphoma Survivors

F. Lennie Wong, PhD[1]; Janie M. Lee, MD, MSc[2]; Wendy M. Leisenring, ScD[3]; Joseph P. Neglia, MD, MPH[4]; Rebecca M. Howell, PhD[5]; Susan A. Smith, MPH[5]; Kevin C. Oeffinger, MD[6]; Chaya S. Moskowitz, PhD[7]; Tara O. Henderson, MD, MPH[8]; Ann Mertens, PhD, MS[9]; Paul C. Nathan, MD, MSc[10]; Yutaka Yasui, PhD[11]; Wendy Landier, PhD[12]; Gregory T. Armstrong, MD[11]; Leslie L. Robison, PhD[11]; and Smita Bhatia, MD, MPH[12]

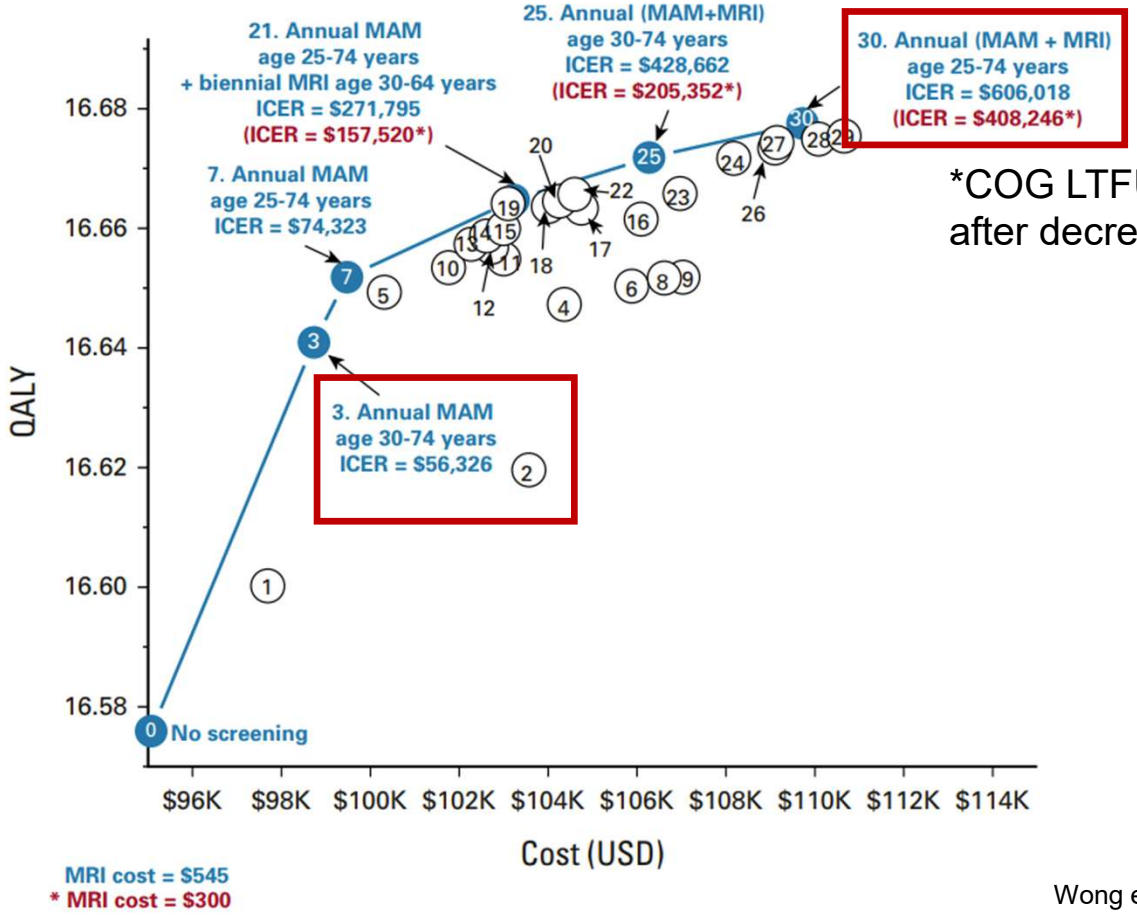
Lennie Wong, PhD
City of Hope

Evaluate multiple breast cancer screening strategies where RCT is not feasible

- Assess COG LTFU Guidelines: annual MAM + MRI at age 25y or 8y after chest RT
- Discrete-event microsimulation modeling using risk estimates from CCSS HL survivors

Decision modeling: Subsequent breast cancer screening guidelines

CCSS



*COG LTFU: not cost-effective even after decreasing breast MRI costs

Wong et al., J Clin Oncol (2022)

Childhood Cancer Survivor Study

An NCI-funded resource