Epidemiology/Biostatistics Working Group Report

Yutaka Yasui, PhD

Wendy Leisenring, PhD

CCSS
Childhood Cancer Survivor Study

St. Jude Children's Research Hospital

An NCI-funded Resource

Scope of Research

CCSS

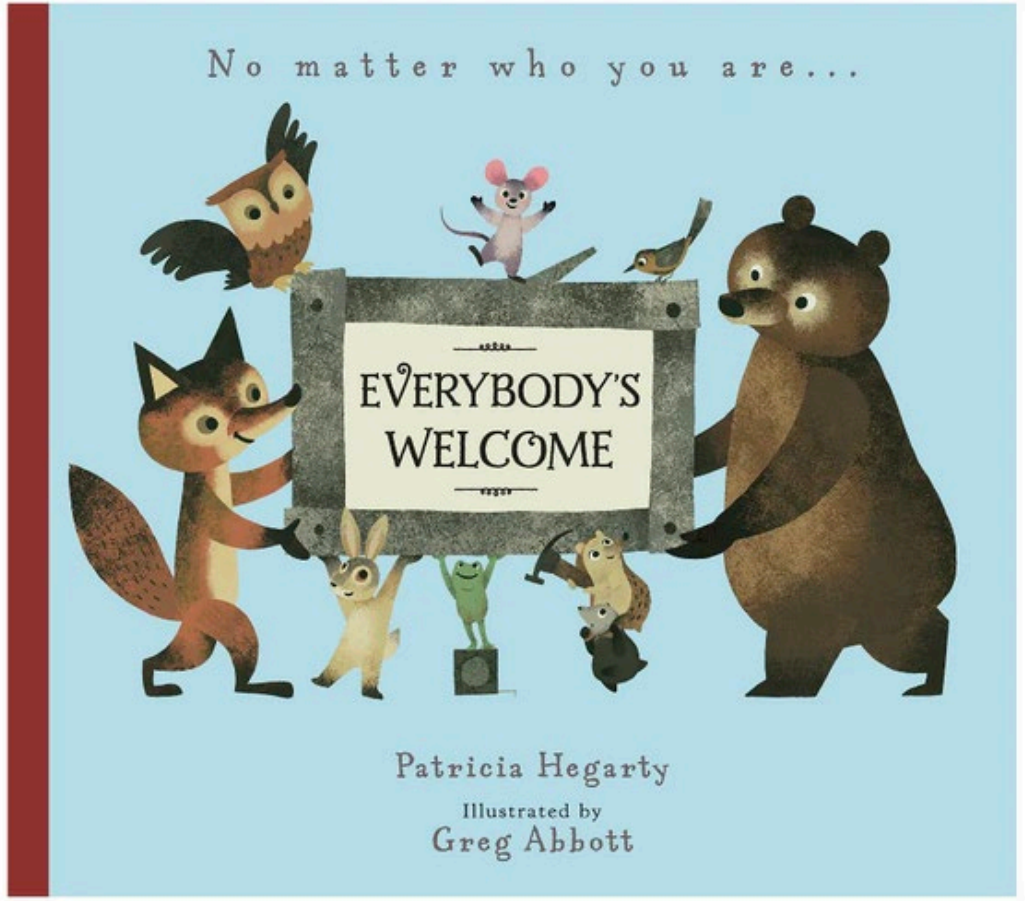
- To lead and support investigations on population sciences relevant to CCSS, such as mortality, cost-effectiveness, characterization of primary treatment exposures (including temporal changes, radiation dosimetry), and minority populations

- To encourage and support methodological research associated with enhancing the follow-up and evaluation of the CCSS cohort

Working Group Membership

CCSS

Ann Mertens, Emory University
Kiri Ness, St. Jude Children's Research Hospital
Greg Armstrong, St. Jude Children's Research Hospital
Leslie Robison, St. Jude Children's Research Hospital
Kumar Srivastava, St. Jude Children's Research Hospital
Sadie Mirzaei Salehabadi, St. Jude Children's Research Hospital
Yan Yuan, University of Alberta
Cindy Im, University of Alberta
Chaya Moskowitz, Memorial Sloan Kettering Cancer Center
Jennifer Yeh, Boston Children's Hospital
Arin Madenchi, Boston Children's Hospital
Stephanie Dixon, St. Jude Children's Research Hospital
Anne Kirchhoff, University of Utah
Xu Ji, Emory University
Rebecca Howell, MD Anderson Cancer Center
James Bates, Emory University
Wendy Leisenring (Co-Chair), Fred Hutchinson Cancer Research Center
Yutaka Yasui (Co-Chair), St. Jude Children's Research Hospital



Working Group Progress

CCSS

4 **Published/In Press Manuscripts** (since 1/1/2022)
2 **Currently Submitted Manuscripts**
8 **Analysis/Manuscript in Process**
2 **Concepts in development**
1 **New AOIs** (total, since 1/1/2022)

Highlights of Recently Completed Research

CCSS

1. Excess mortality and modifiable risk factors
2. Cardiac substructure dosimetry
3. Tx-specific genetic risk

Highlights of Recently Completed Research

CCSS

1. Excess mortality and modifiable risk factors
2. Cardiac substructure dosimetry
3. Tx-specific genetic risk

Excess Mortality & Modifiable Risk Factors

CCSS

Specific causes of excess late mortality and association with modifiable risk factors among survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort

Stephanie B Dixon, Qi Liu, Eric J Chow, Kevin C Oeffinger, Paul C Nathan, Rebecca M Howell, Wendy M Leisenring, Matthew J Ehrhardt, Kirsten K Ness, Kevin R Krull, Ann C Mertens, Melissa M Hudson, Leslie L Robison, Yutaka Yasui, Gregory T Armstrong

Stephanie Dixon
St. Jude Children's Research Hospital

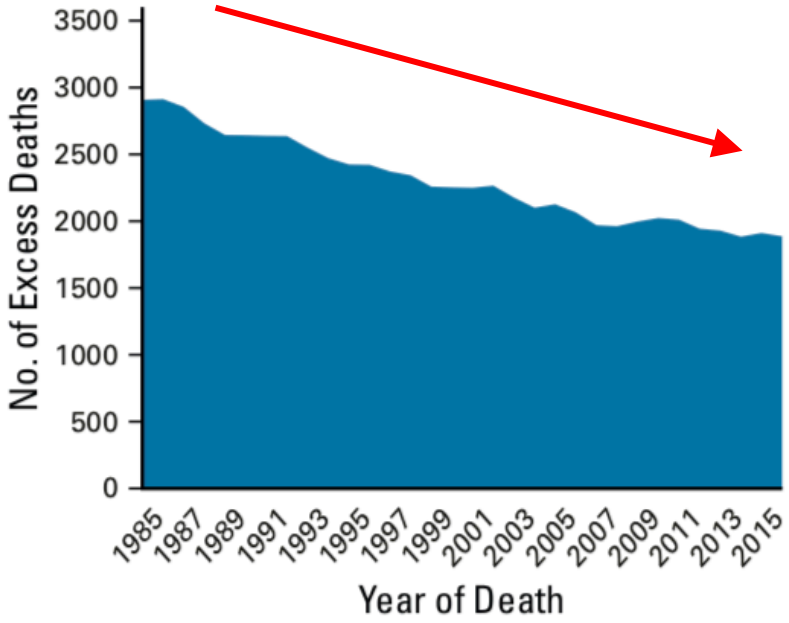
THE LANCET

Volume 401, Issue 10386, 29 April–5 May 2023, Pages 1447-1457

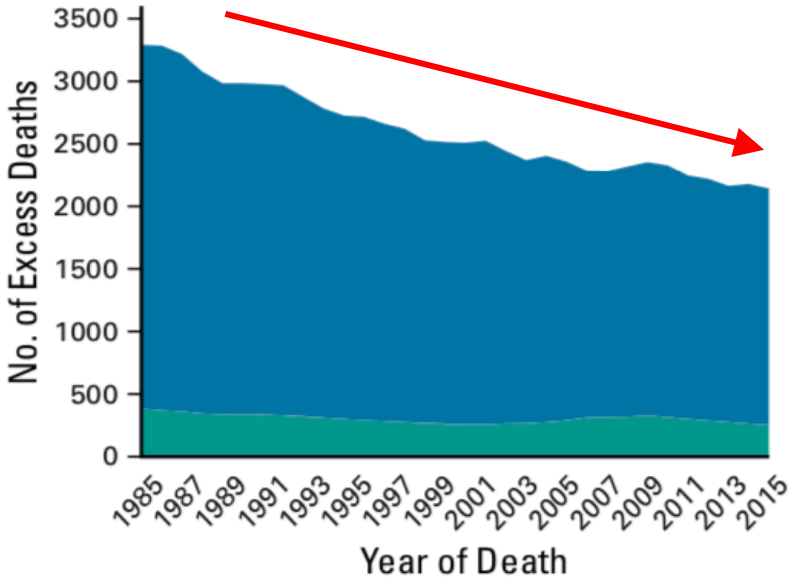
Excess death compared to the general population

ccss

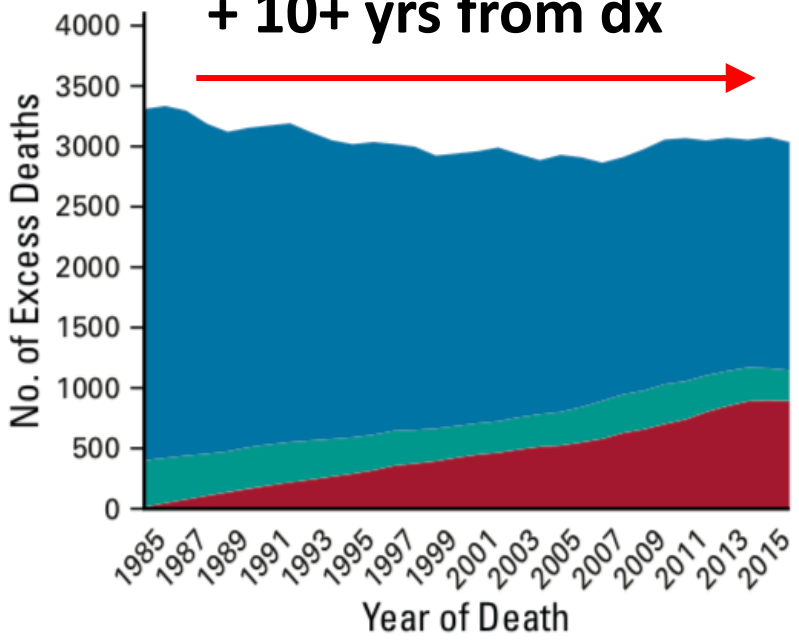
< 5 years from dx



< 5 yrs + 5-9 yrs from dx



< 5 yrs + 5-9 yrs + 10+ yrs from dx



Annalynn M. Williams, Ph.D.
Univ. of Rochester

Rethinking Success in Pediatric Oncology: Beyond 5-Year Survival

AnnaLynn M. Williams, PhD[1]; Qi Liu, MSc[2]; Nickhill Bhakta, MD, MPH[1,3]; Kevin R. Krull, PhD[1,4]; Melissa M. Hudson, MD[1,5]; Leslie L. Robison, PhD[1]; and Yutaka Yasui, PhD[1]

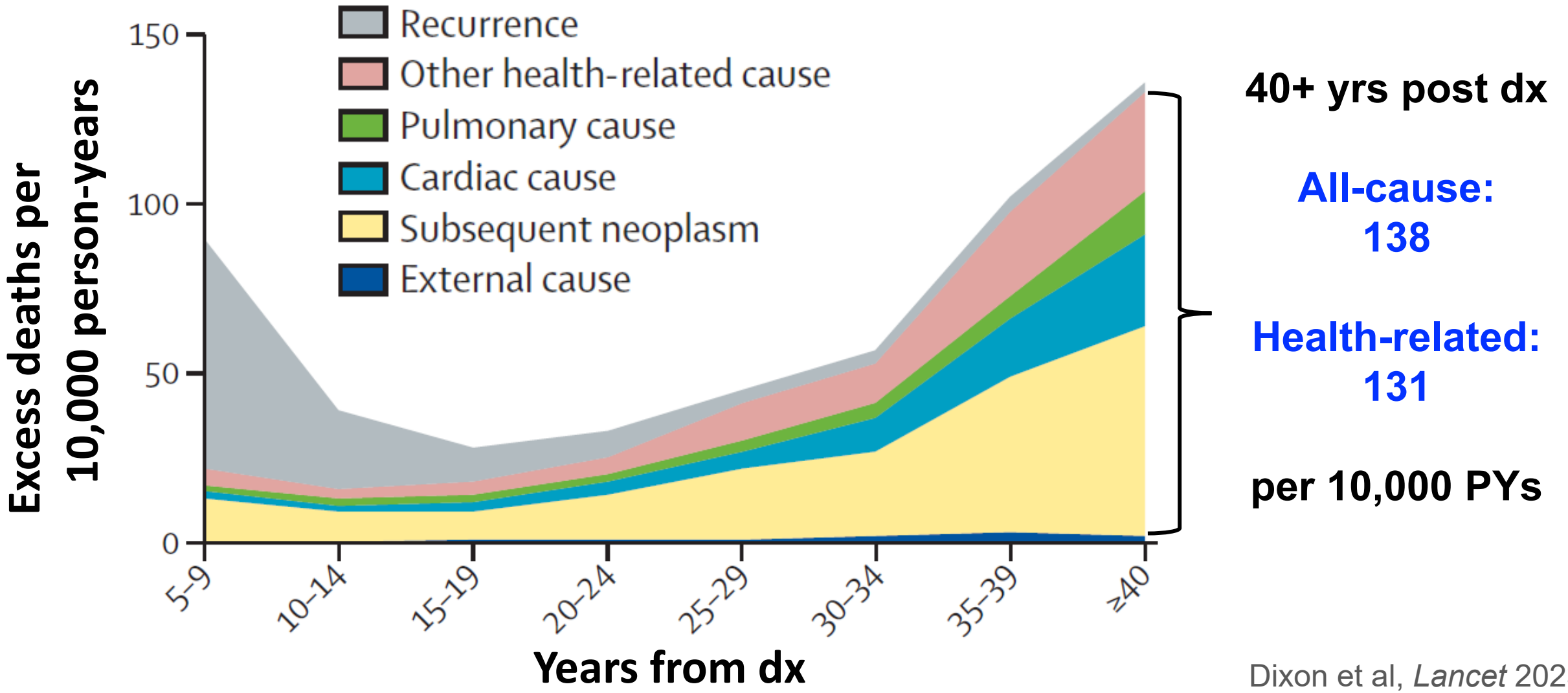
Methodological/Population-Science Question #1

CCSS

- **What causes of death are in excess among survivors?**
- **How are they changing over time/aging?**
- **Are lifestyle and modifiable risk factors associated with the excess death?**

Excess Death in Survivors of Childhood Cancer

CCSS



40+ yrs post dx

All-cause: 138

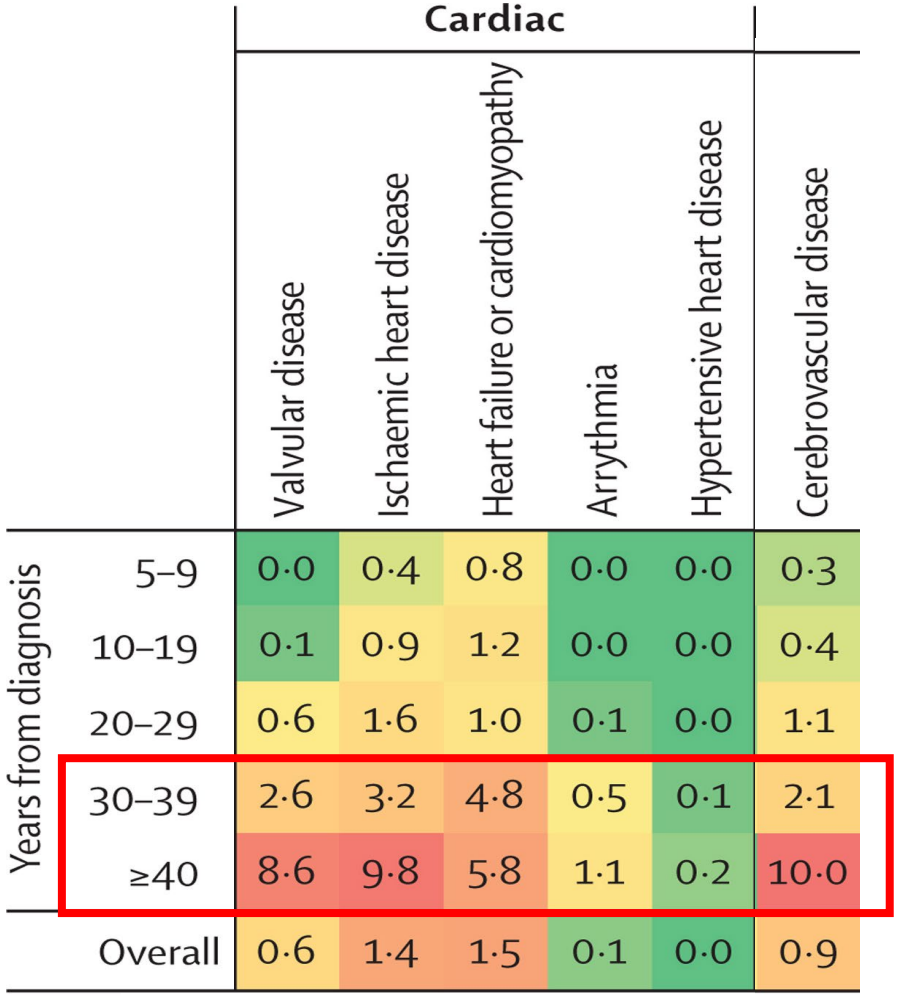
Health-related: 131

per 10,000 PYs

Dixon et al, *Lancet* 2023.

Excess Cardiovascular Death in Survivors

CCSS



Years from diagnosis	Cardiac: Valvular disease	Cardiac: Ischaemic heart disease	Cardiac: Heart failure or cardiomyopathy	Cardiac: Arrythmia	Cardiac: Hypertensive heart disease	Cerebrovascular disease
5–9	0·0	0·4	0·8	0·0	0·0	0·3
10–19	0·1	0·9	1·2	0·0	0·0	0·4
20–29	0·6	1·6	1·0	0·1	0·0	1·1
30–39	2·6	3·2	4·8	0·5	0·1	2·1
≥40	8·6	9·8	5·8	1·1	0·2	10·0
Overall	0·6	1·4	1·5	0·1	0·0	0·9

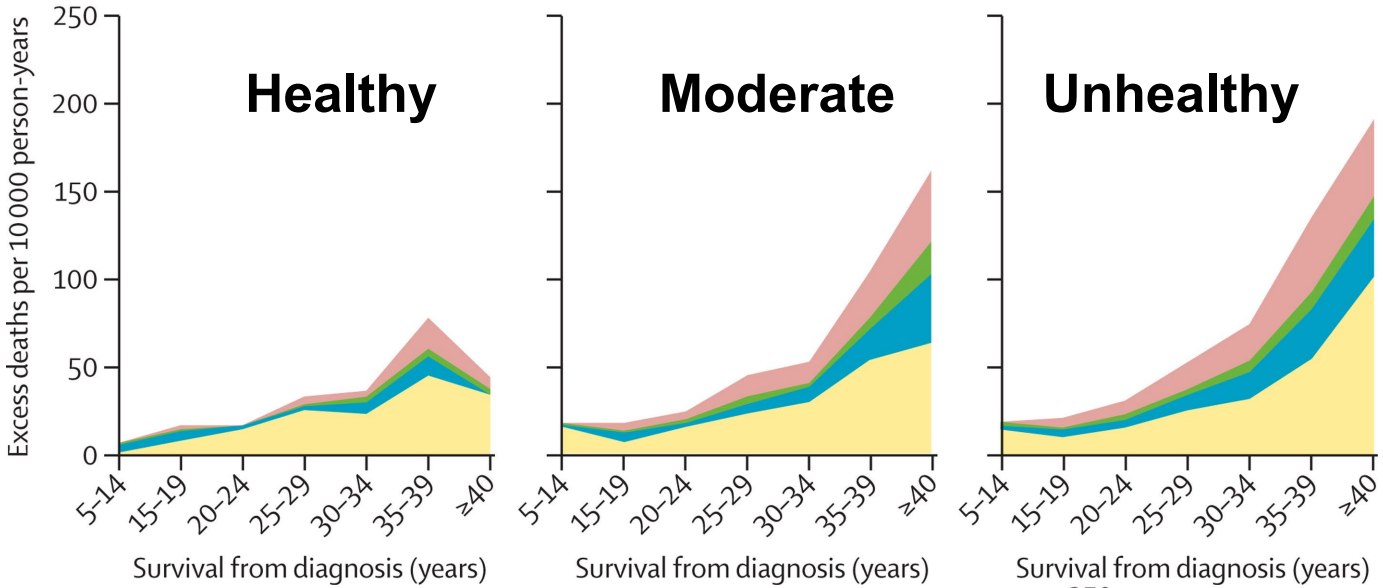
Absolute excess risk per 10,000 person-years

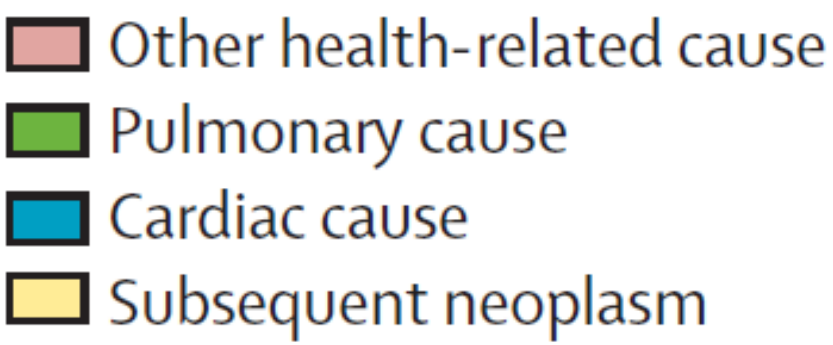
- Leading causes
  - **Similar to the general population, occurring at a younger age and higher rate**
- The largest non-cancer contributors:
  - **Stroke**
  - **Ischemic heart disease**
  - **Valvular heart disease**
  - **Heart failure**

Dixon et al, *Lancet* 2023.

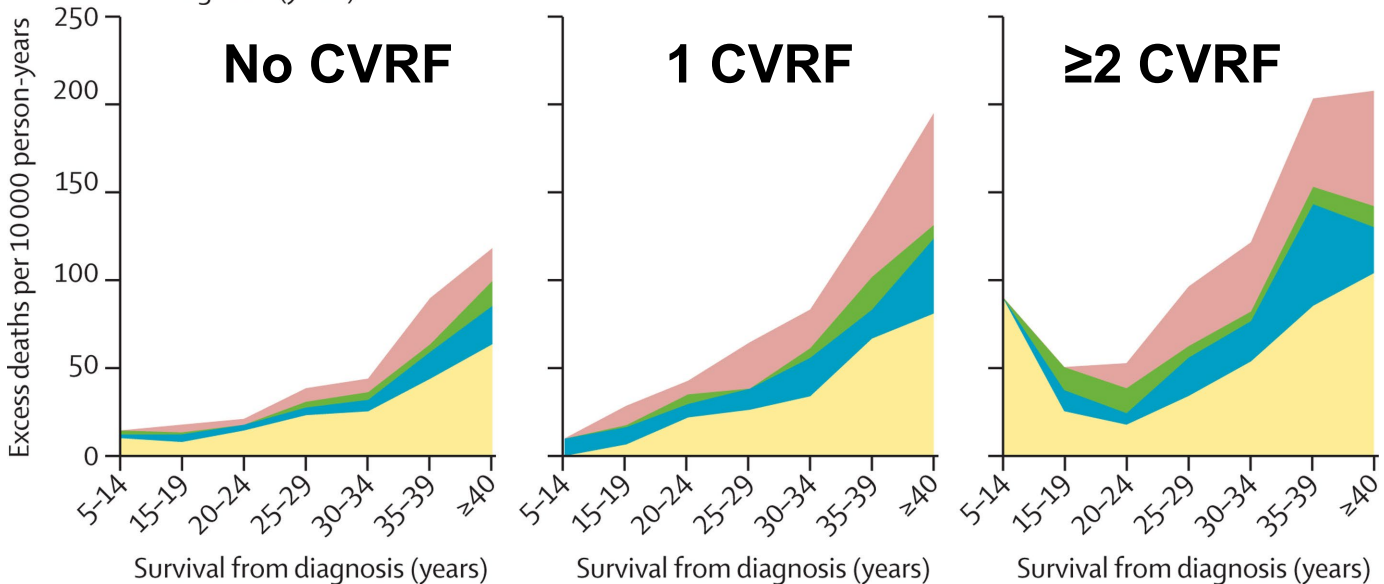
Excess Death & **Lifestyle and CVRFs**

CCSS





Unhealthy lifestyle and presence hypertension or diabetes were each associated with excess health-related mortality, independent of prior cancer tx



Dixon et al, *Lancet* 2023.

Related publication

CCSS

JAMA Network Open™ February 10, 2023

Original Investigation | Oncology

Association of Modifiable Health Conditions and Social Determinants of Health With Late Mortality in Survivors of Childhood Cancer

Matthew J. Ehrhardt, MD, MS; Qi Liu, MS; Stephanie B. Dixon, MD, MS; Eric Caron, MSN; Debbie Redd, MSN; Kyla Shelton, MS; I-Chan Huang, PhD; Nickhill Bhakta, MD, MPH; Kirsten K. Ness, PhD; Daniel A. Mulrooney, MD, MS; Tara M. Brinkman, PhD; Wassim Chemaitilly, MD; Angela Delaney, MD; Gregory T. Armstrong, MD, MSCE; Deo Kumar Srivastava, PhD; Alia Zaidi, MD; Leslie L. Robison, PhD; Yutaka Yasui, PhD; Melissa M. Hudson, MD

Highlights of Recently Completed Research

CCSS

1. Excess mortality and modifiable risk factors
2. Cardiac substructure dosimetry
3. Tx-specific genetic risk

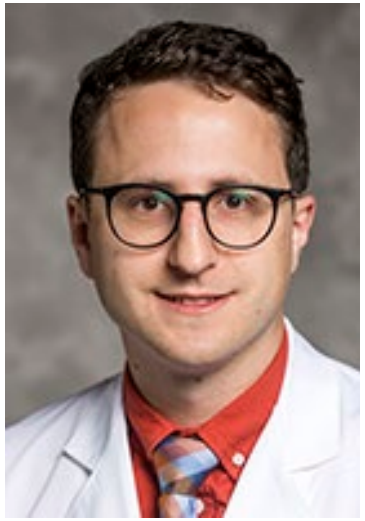
Ancillary Studies: R01

ccss

Principal Investigator: Rebecca Howell (MD Anderson), Dan Mulrooney, Yutaka Yasui (St. Jude Children's Research Hospital)
Title: **Personalized Risk Prediction to Reduce Cardiovascular Disease in Childhood Cancer Survivors**
Proposed Funding Source: National Institutes of Health (R01)
Study Aims: Develop a prediction model for cardiac outcomes using cardiac substructures

Rebecca Howell, PhD
MD Anderson Cancer Center

Dan Mulrooney, MD, MS
St. Jude Children's Res. Hosp.



James E Bates, MD
Emory University

Childhood Cancer Survivor Study
An NCI-funded resource

Substructure Cardiac Dosimetry & Cardiac Event Risk

ccss

Original Reports | Pediatric Oncology

Cardiac Substructure Radiation Dose and Risk of Late Cardiac Disease in Survivors of Childhood Cancer: A Report From the Childhood Cancer Survivor Study

James E. Bates, MD[1]; Suman Shrestha, PhD[2]; Qi Liu, MSc[3]; Susan A. Smith, MPH[2]; Daniel A. Mulrooney, MD, MS[4,5]; Wendy Leisenring, ScD[6]; Todd Gibson, PhD[7]; Leslie L. Robison, PhD[4]; Eric J. Chow, MD, MPH[6]; Kevin C. Oeffinger, MD[8]; Gregory T. Armstrong, MD, MSCE[4]; Louis S. Constine, MD[9,10]; Bradford S. Hoppe, MD, MPH[11]; Choonsik Lee, PhD[7]; Yutaka Yasui, PhD[4]; and Rebecca M. Howell PhD[2]

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Methodological/Population-Science Question #2

CCSS

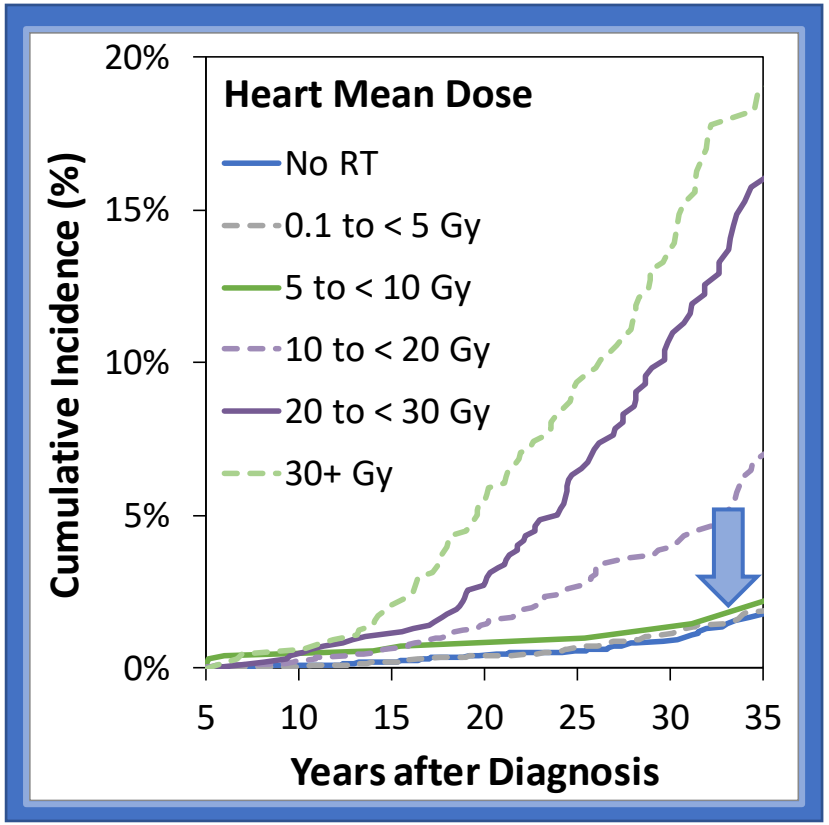
- **How are the RT doses to substructures of the heart associated with cardiac late effects risks?**

  Is there a threshold?

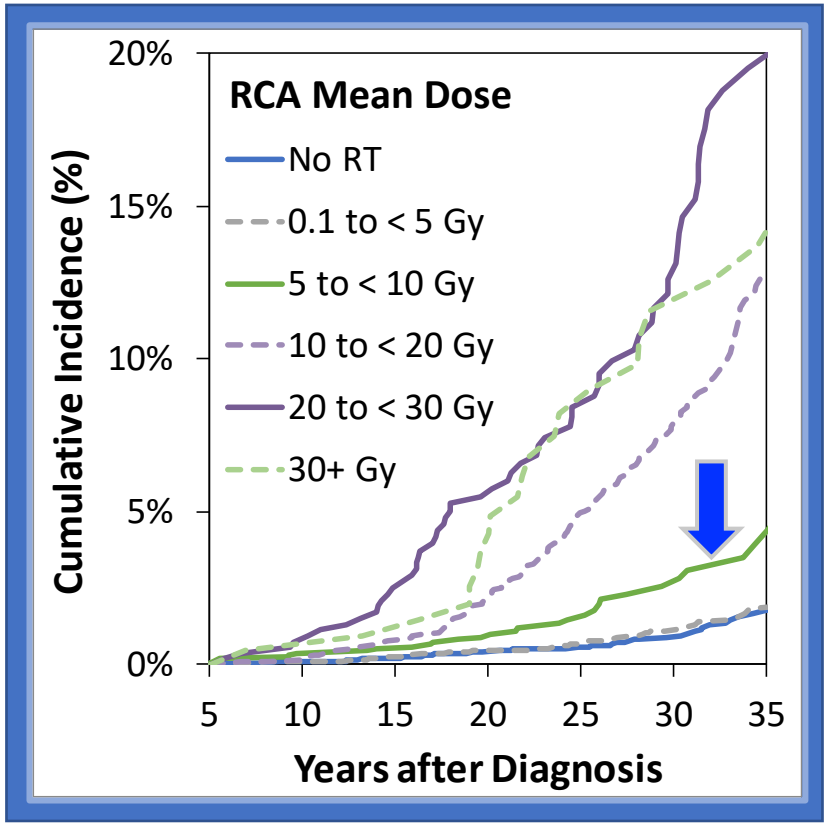
Coronary Artery Disease & Substructure dose

ccss

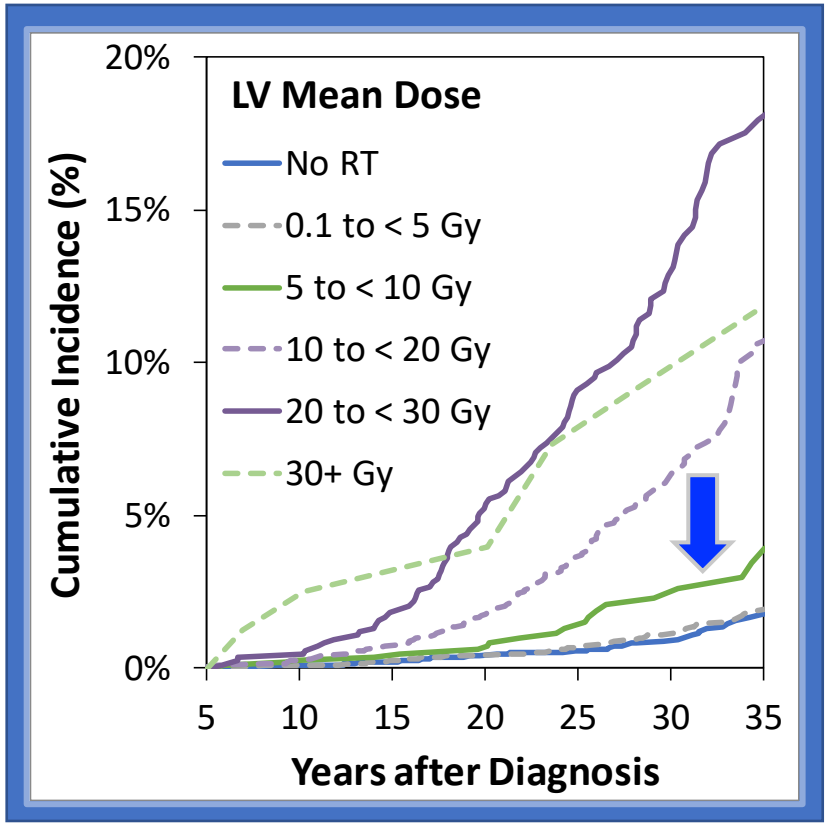
Whole Heart



Right Coronary Artery



Left Ventricle



Coronary Artery Disease & Substructure dose

ccss

Mean RT Dose	Entire Heart	RCA	Left Ventricle
No RT	Ref	Ref	Ref
0.1 – 4.9 Gy	1.1 (0.8 – 1.6)	1.1 (0.8 – 1.6)	1.1 (0.8 – 1.6)
5 – 9.9 Gy	**1.3 (0.6 – 2.9)**	**2.6 (1.6 – 4.1)***	**2.2 (1.3 – 3.7)***
10 – 19.9 Gy	3.7 (2.6 – 5.2)*	5.3 (3.9 – 7.2)*	4.8 (3.5 – 6.6)*
20 – 29.9 Gy	6.8 (4.8 – 9.6)*	8.5 (5.9 – 12.2)*	7.7 (5.5 – 10.9)*
≥30 Gy	8.2 (5.7 – 11.9)*	5.1 (2.9 – 8.9)*	2.7 (1.0 – 7.9)

Coronary Artery Disease & Mean Whole Heart Dose

ccss

Excess Relative Risk(Rate) Model

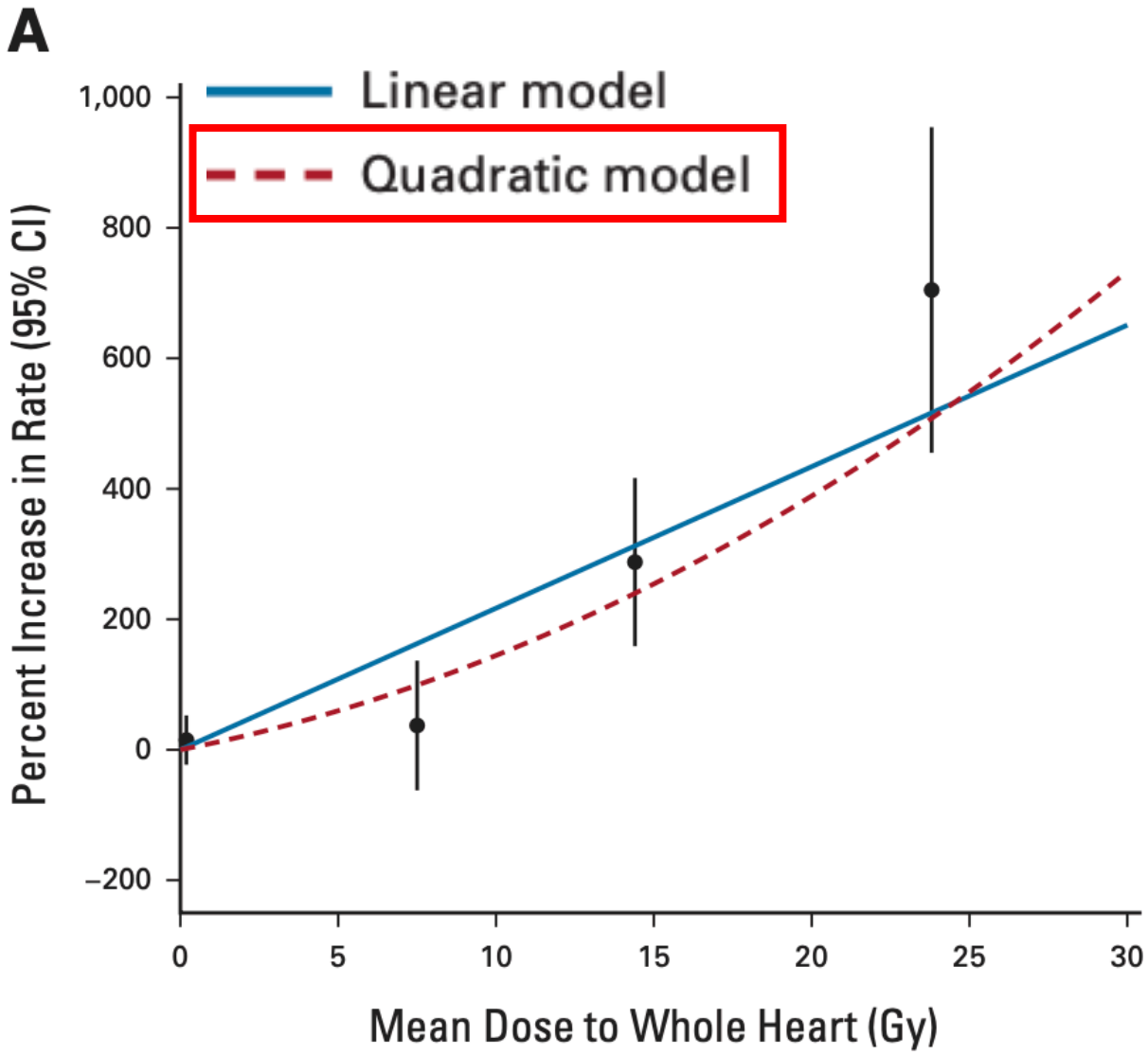
Rate = (non-RT effects)
x (1+ RT effects)

Cox & Piecewise Exp. Model

Rate = (non-RT effects)
x (RT effects)

Coronary Artery Disease & Mean Whole Heart Dose

ccss



Excess Relative Risk(Rate) Model

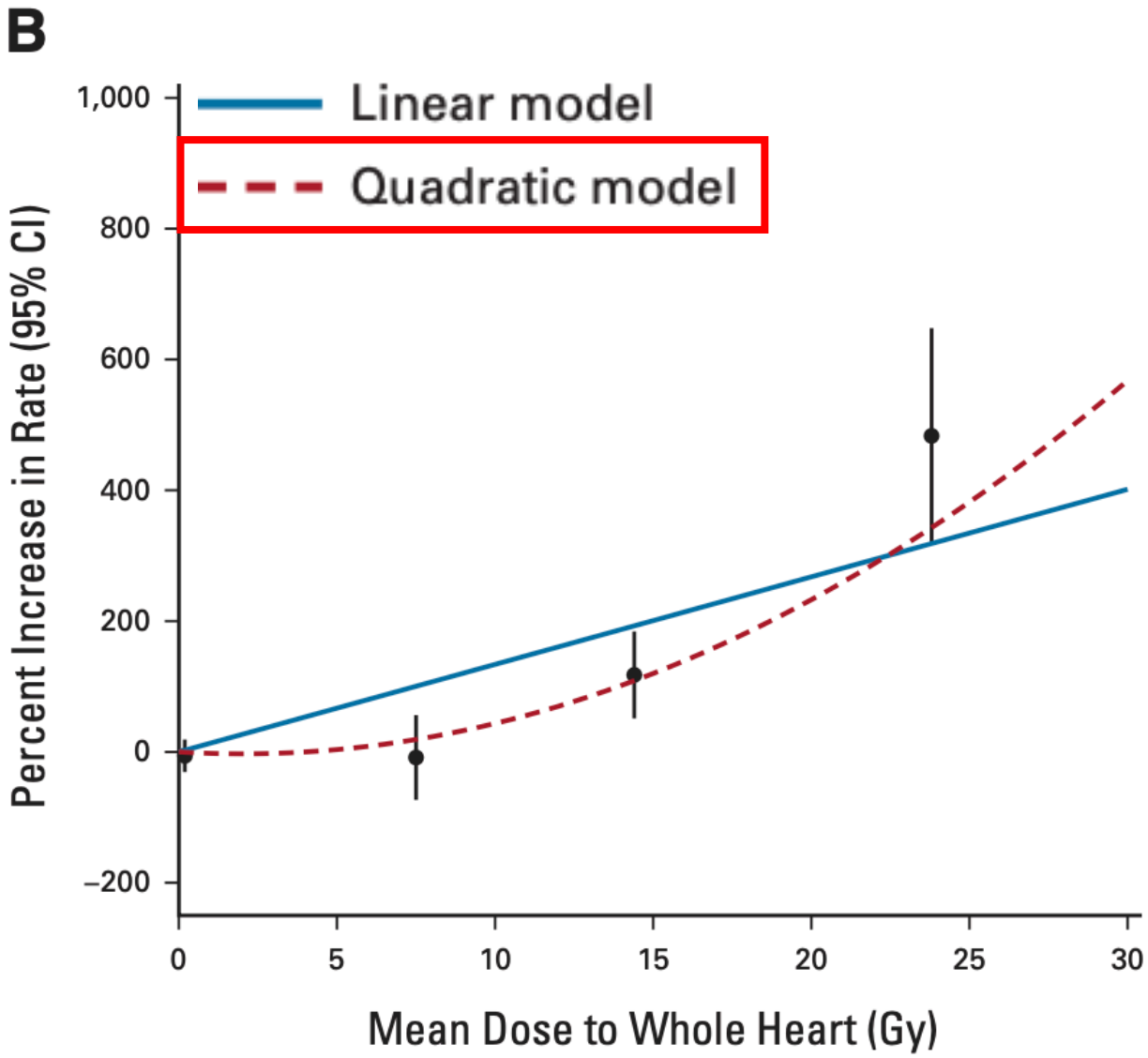
Rate = (non-RT effects) x (1+ RT effects)

Cox & Piecewise Exp. Model

Rate = (non-RT effects) x (RT effects)

Heart Failure & Mean Whole Heart Dose

CCSS



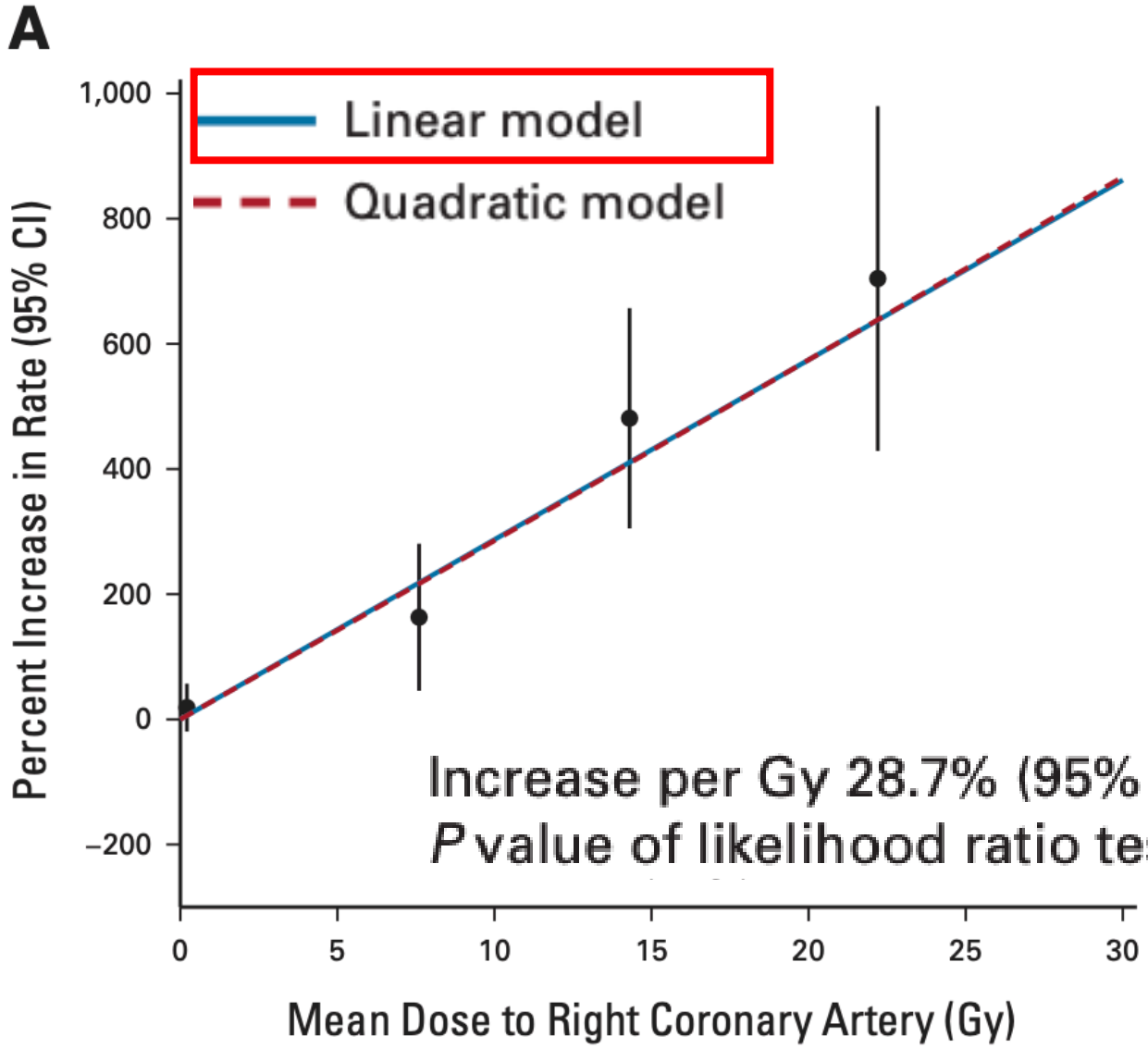
Excess Relative Risk(Rate) Model

Rate = (non-RT effects)

x (1+ RT effects)

Coronary Artery Disease & RCA dose

CCSS

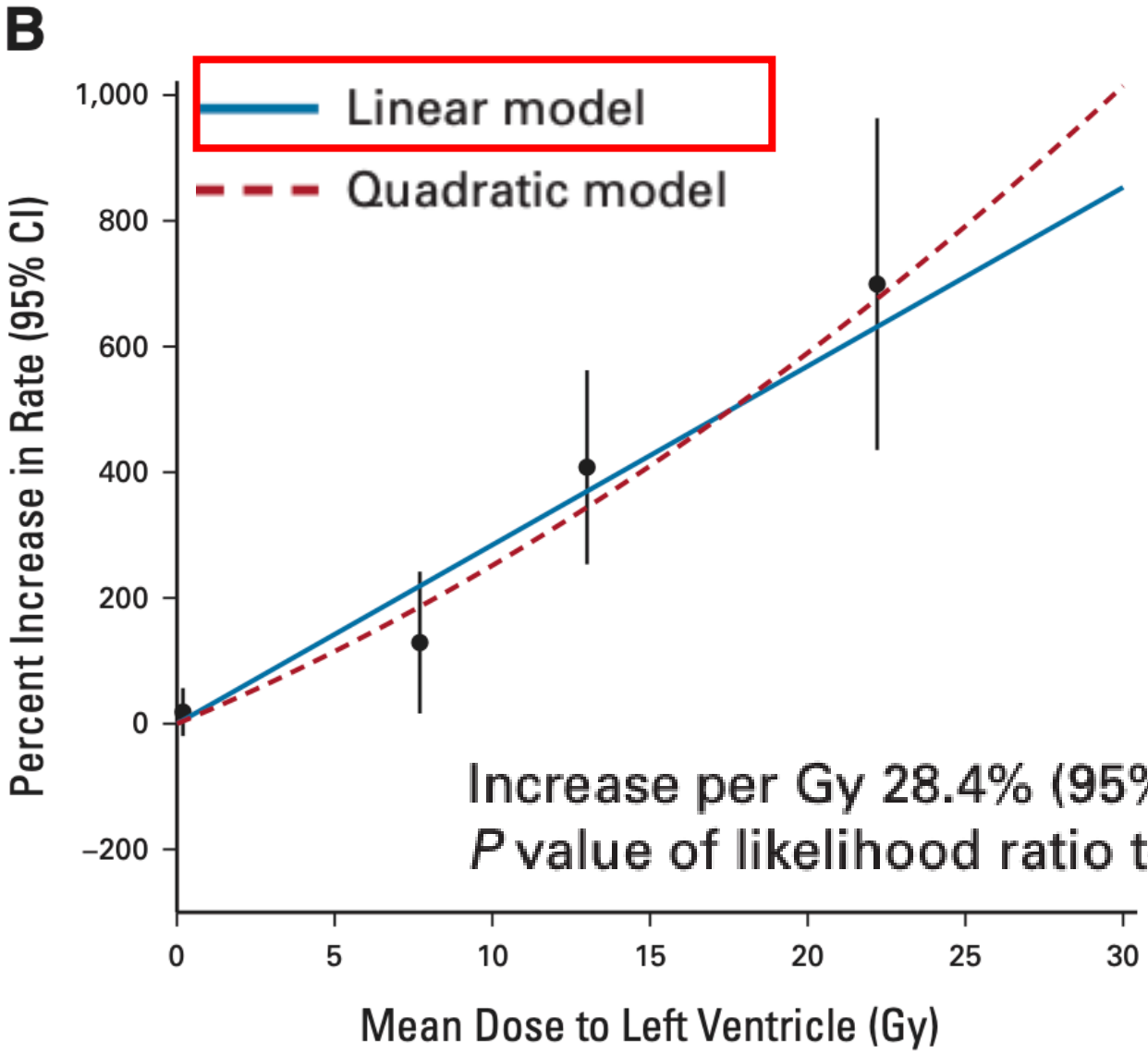


Excess Relative Risk(Rate) Model

Rate = (non-RT effects) x (1+ RT effects)

Coronary Artery Disease & LV dose

ccss



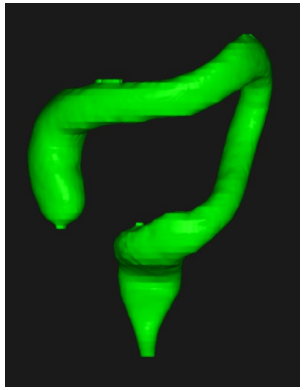
Excess Relative Risk(Rate) Model

Rate = (non-RT effects)

x (1+ RT effects)

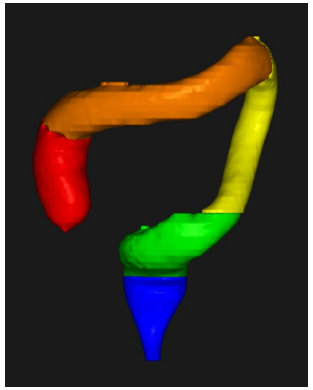
Colorectal SMN total & substructure dosimetry

CCSS



Total colorectal RT metrics

- Mean dose
- V_5, V_{10}, V_{20}, V_{30}, V_{40}
- V_5 with $d_{max} < 20$
- V_{10} with $d_{max} < 20$



Substructure RT metrics

- Mean dose

Constance Owens, BS
MD Anderson Cancer Center

Rebecca Howell, PhD
MD Anderson Cancer Center

Highlights of Recently Completed Research

CCSS

1. Excess mortality and modifiable risk factors
2. Cardiac substructure dosimetry
3. Tx-specific genetic risk

Ancillary Studies: R21

ccss

Principal Investigator: Cindy Im & Yan Yuan
Title: **Treatment-specific genetic risk scores for late effects prediction in childhood, AYA cancer survivors**
Dates of Funding: 9/21 – 8/24
Funding Source: National Institutes of Health **R21CA261833**
Award: $279,068
Study Aims: Create a reference TX-G Effects Catalog for a range of treatments and subsequent malignant neoplasm, cardiovascular, and endocrine phenotypes and develop TX-G polygenic risk scores among childhood/AYA cancer survivors.

Cindy Im, PhD
University of Minnesota

Yan Yuan, PhD
University of Alberta

Childhood Cancer Survivor Study
An NCI-funded resource

Method: Development of Tx-specific PRS

ccss

Leveraging Therapy-Specific Polygenic Risk Scores to Predict Restrictive Lung Defects in Childhood Cancer Survivors

Cindy Im[1], Yan Yuan[1], Eric D. Austin[2], Dennis C. Stokes[2], Matthew J. Krasin[3], Andrew M. Davidoff[4], Yadav Sapkota[5], Zhaoming Wang[5], Kirsten K. Ness[5], Carmen L. Wilson[5], Gregory T. Armstrong[5,6], Melissa M. Hudson[5,6], Leslie L. Robison[5], Daniel A. Mulrooney[5,6], and Yutaka Yasui[1,5]

Volume 82, Issue 16

15 August 2022

General-pop.'s results do not apply to survivors

ccss

AJHG

ARTICLE | VOLUME 107, ISSUE 4, P636-653, OCTOBER 01, 2020

Generalizability of "GWAS Hits" in Clinical Populations: Lessons from Childhood Cancer Survivors

Cindy Im • Na Qin • Zhaoming Wang • Weiyu Qiu • Carrie R. Howell • Yadav Sapkota • Wonjong Moon • Wassim Chemaitilly • Todd M. Gibson • Daniel A. Mulrooney • Kirsten K. Ness • Carmen L. Wilson • Lindsay M. Morton • Gregory T. Armstrong • Smita Bhatia • Jinghui Zhang • Melissa M. Hudson • Leslie L. Robison • Yutaka Yasui • Show less

Open Archive • Published: September 17, 2020 • DOI: https://doi.org/10.1016/j.ajhg.2020.08.014 •

Methodological/Population-Science Question #3

CCSS

- **Can we derive useful Tx-specific PRS for survivors?**

Tx-specific Polygenic Risk Scores (PRS) for Survivors

ccss

Weighted sum of risk alleles:

$$PRS = \sum_{k=1}^{K} \beta_k X_k$$

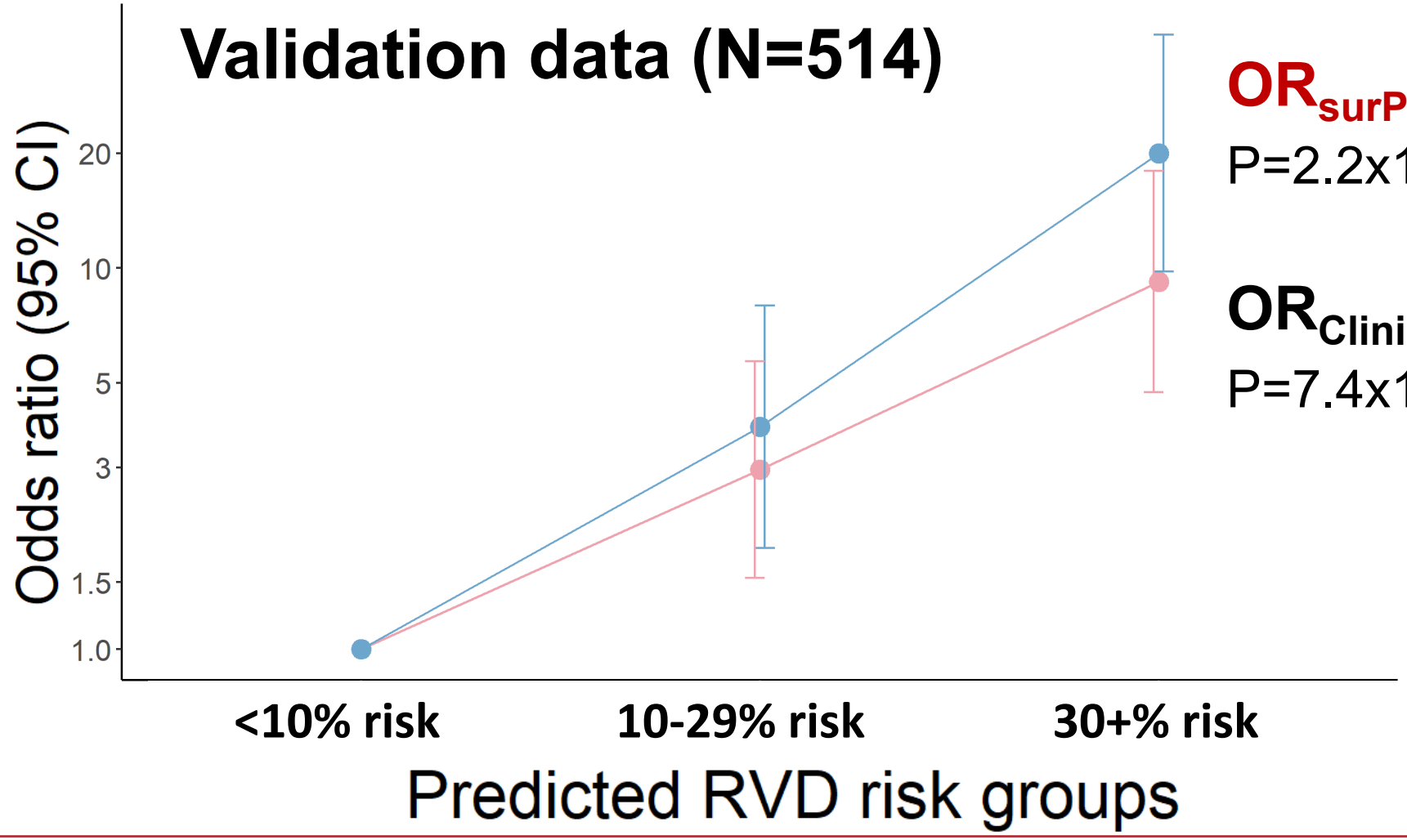
β_k = weights (e.g., log odds ratios) estimated in GWAS

X_k = number of risk alleles (0, 1, 2) individual at genetic locus k

Consider this for Tx-specific subgroups of survivors

Chest-RT-, Bleomycin-, Dactinomycin- specific PRSs

CCSS



OR_{surPRS}= 20.0

P=2.2x10^{-16}

$OR_{Clinical}$= 9.2

P=7.4x10^{-11}

Childhood Cancer Survivor Study

An NCI-funded resource

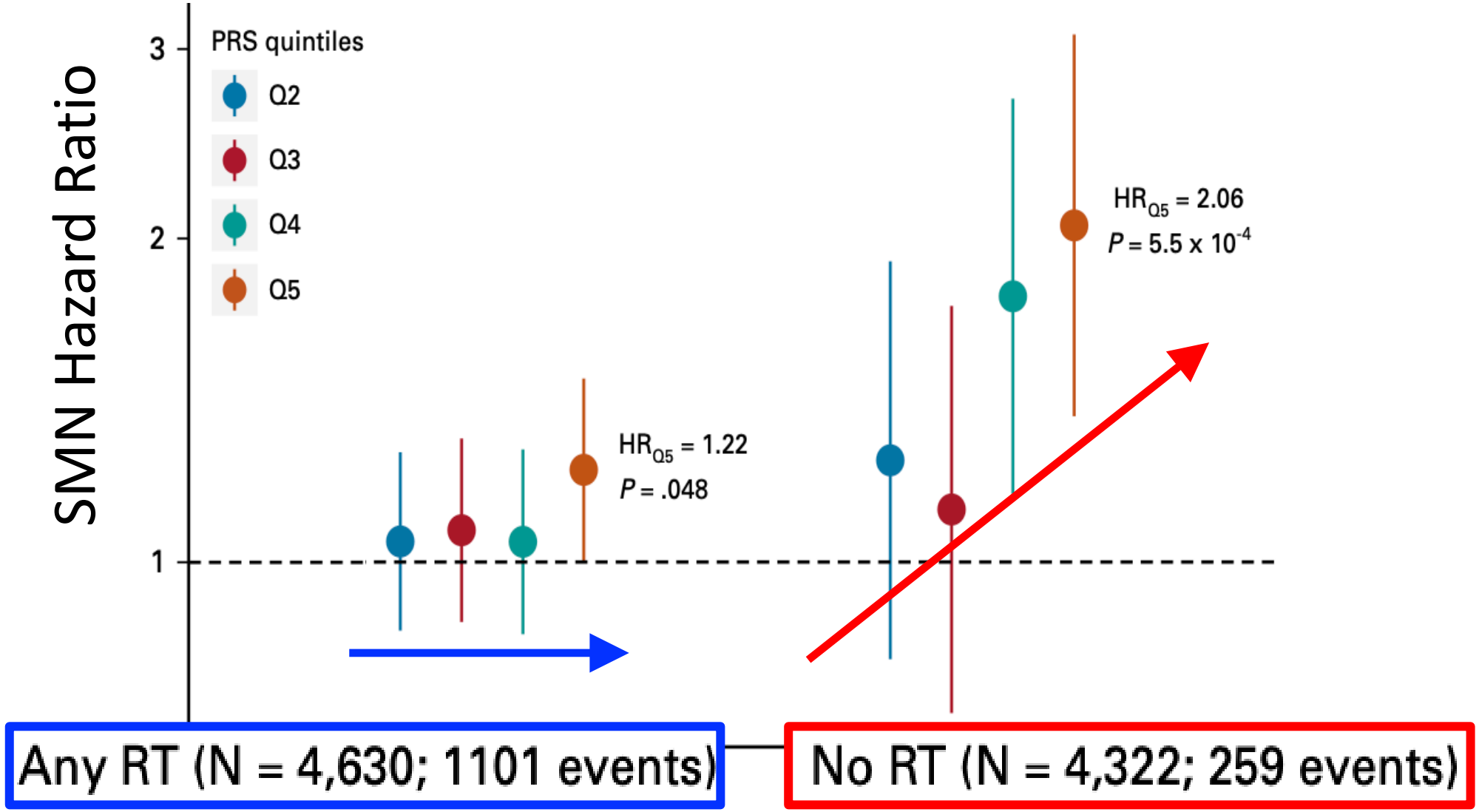
Polygenic Risk and Chemotherapy-Related Subsequent Malignancies in Childhood Cancer Survivors: A Childhood Cancer Survivor Study and St Jude Lifetime Cohort Study Report

Cindy Im, PhD[1]; Noha Sharafeldin, PhD[2,3]; Yan Yuan, PhD[4]; Zhaoming Wang, PhD[5,6]; Yadav Sapkota, PhD[5]; Zhanni Lu, DrPH[1]; Logan G. Spector, PhD[1]; Rebecca M. Howell, PhD[7]; Michael A. Arnold, MD[8]; Melissa M. Hudson, MD[5,9]; Kirsten K. Ness, PhD[5]; Leslie L. Robison, PhD[5]; Smita Bhatia, MD[3]; Gregory T. Armstrong, MD[5,9]; Joseph P. Neglia, MD[1]; Yutaka Yasui, PhD[4,5]; and Lucie M. Turcotte, MD[1]

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

Lucie Turcotte, MD, MPH, MS
University of Minnesota

General population 179-variant pleiotropic cancer PRS: Associated with SMNs in survivors?

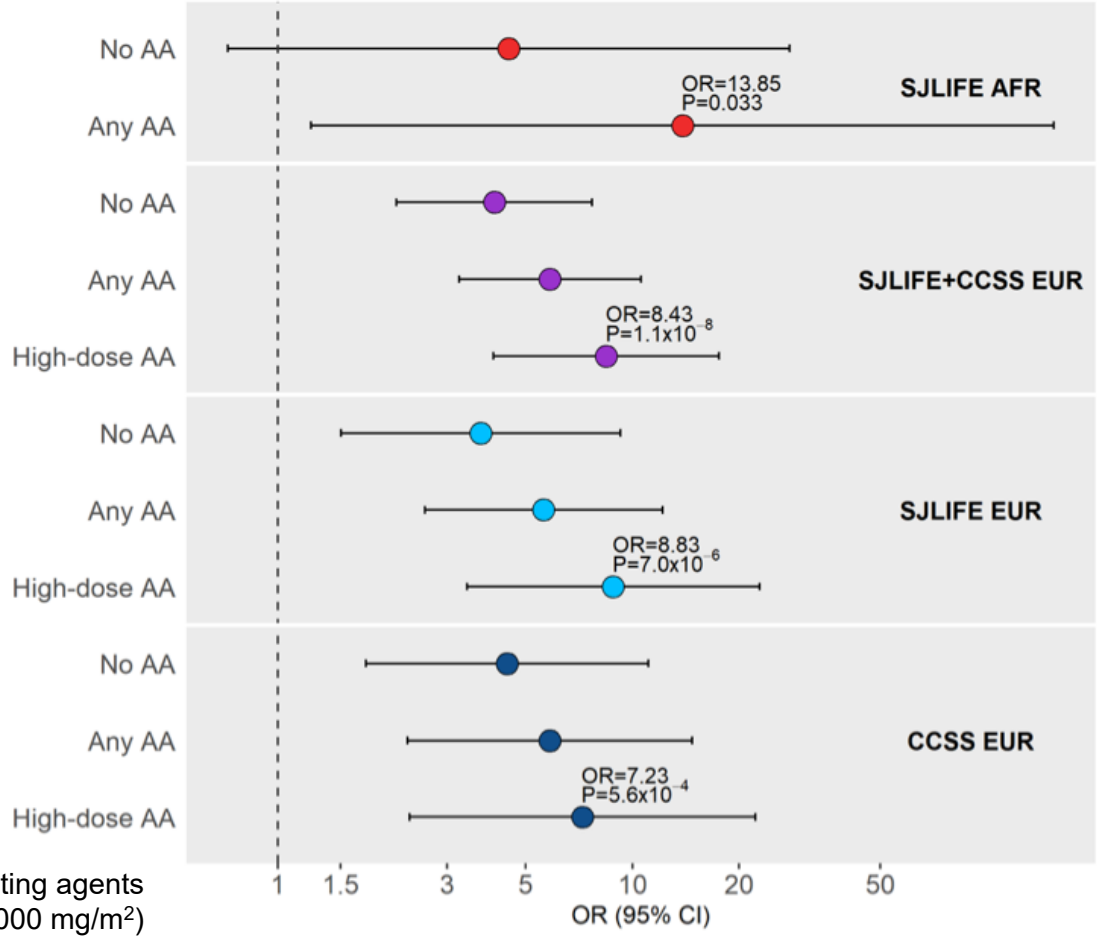


Similar findings in an ISLCCC talk

Yadav Sapkota, PhD
St. Jude Children's Research Hospital

"Genetic study of diabetes mellitus risk in diverse populations of survivors of childhood cancer: a report from the St. Jude Lifetime Cohort (SJLIFE) and the Childhood Cancer Survivor Study (CCSS)"

Cindy Im,[1] Achal Neupane,[2] Jessica L. Baedke,[2] Angela Delaney,[2] Stephanie B. Dixon,[2] Eric J. Chow,[3] Sogol Mostoufi-Moab,[4] Melissa A. Richard,[5] M. Monica Gramatges,[5] Philip J. Lupo,[5] Noha Sharafeldin,[6] Smita Bhatia,[6] Gregory T. Armstrong,[2] Melissa M. Hudson,[2] Kirsten K. Ness,[2] Leslie L. Robison,[2] Yutaka Yasui,[2] Carmen L. Wilson,[2*] Yadav Sapkota[2*]



AA=alkylating agents
(high-dose: ≥4000 mg/m^2)

Approved Concept Proposals

CCSS

Area-level socioeconomic variables

ccss

Geocoded residential & local social- and physical-environmental data

Carrie Howell, PhD
University of Alabama at Birmingham

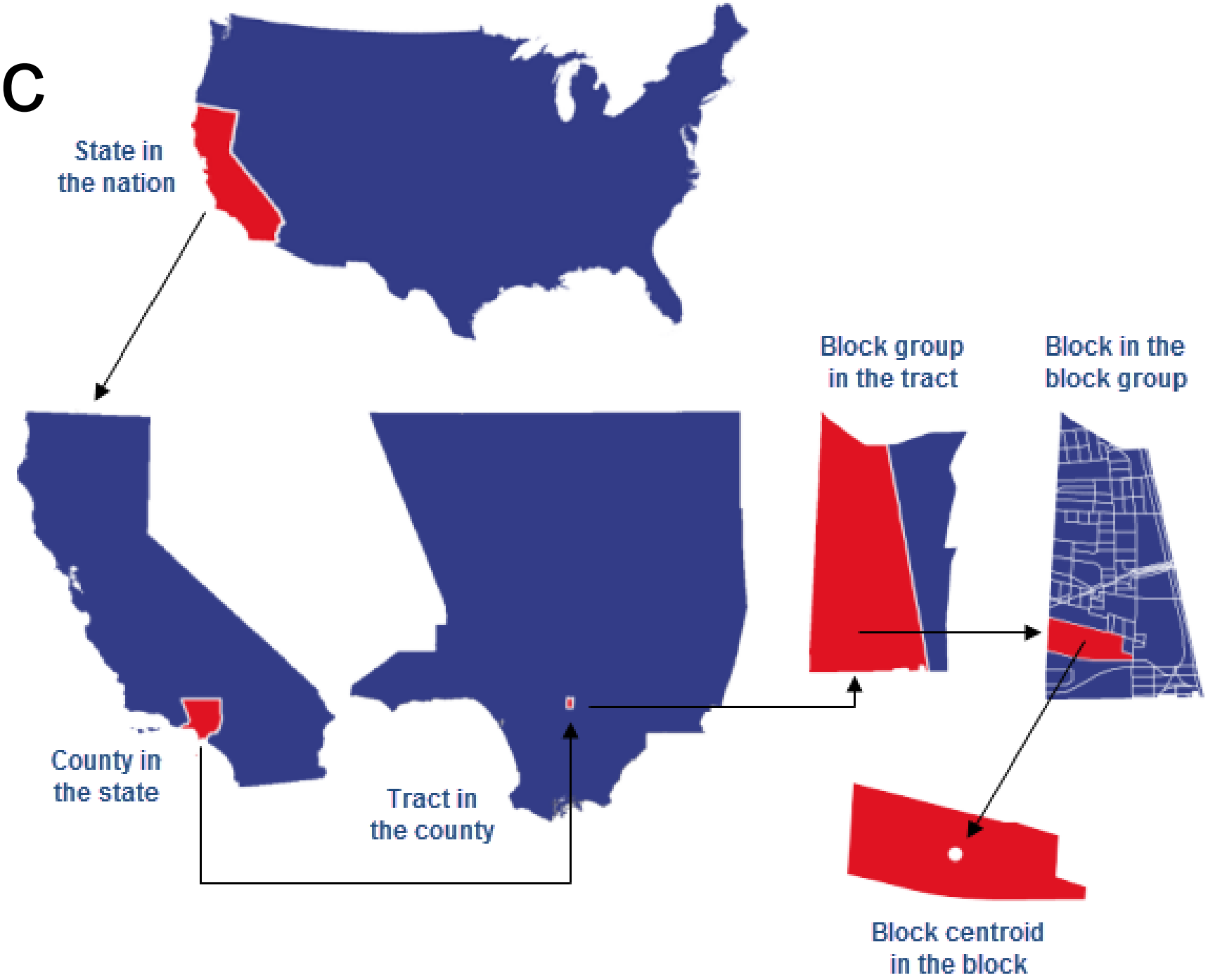
Lena Winestone, MD
University of California, San Francisco

Methodological/Population-Science Question #4

CCSS

- **How do area-level Social Determinants of Health influence survivors' health and survivorship care?**

Geographic Units



Available Area-level Measures

CCSS

Rurality (2000, 2010)

- Classified using the USDA Rural-Urban Commuting Codes (RUCA) based on census tract of residence

Yost SES Index (2000, 2010-2019)

- Uses seven census tract indicator variables
  - Education, employment, income
- Use the weighted linear combination of variables (principle component analysis) to create a value for each census tract
  - Categorized into quintiles from low to high SES

Available Area-level Measures

CCSS

Social Vulnerability Index (CDC SVI) [2000, 2010, 2014, 2016, 2018]

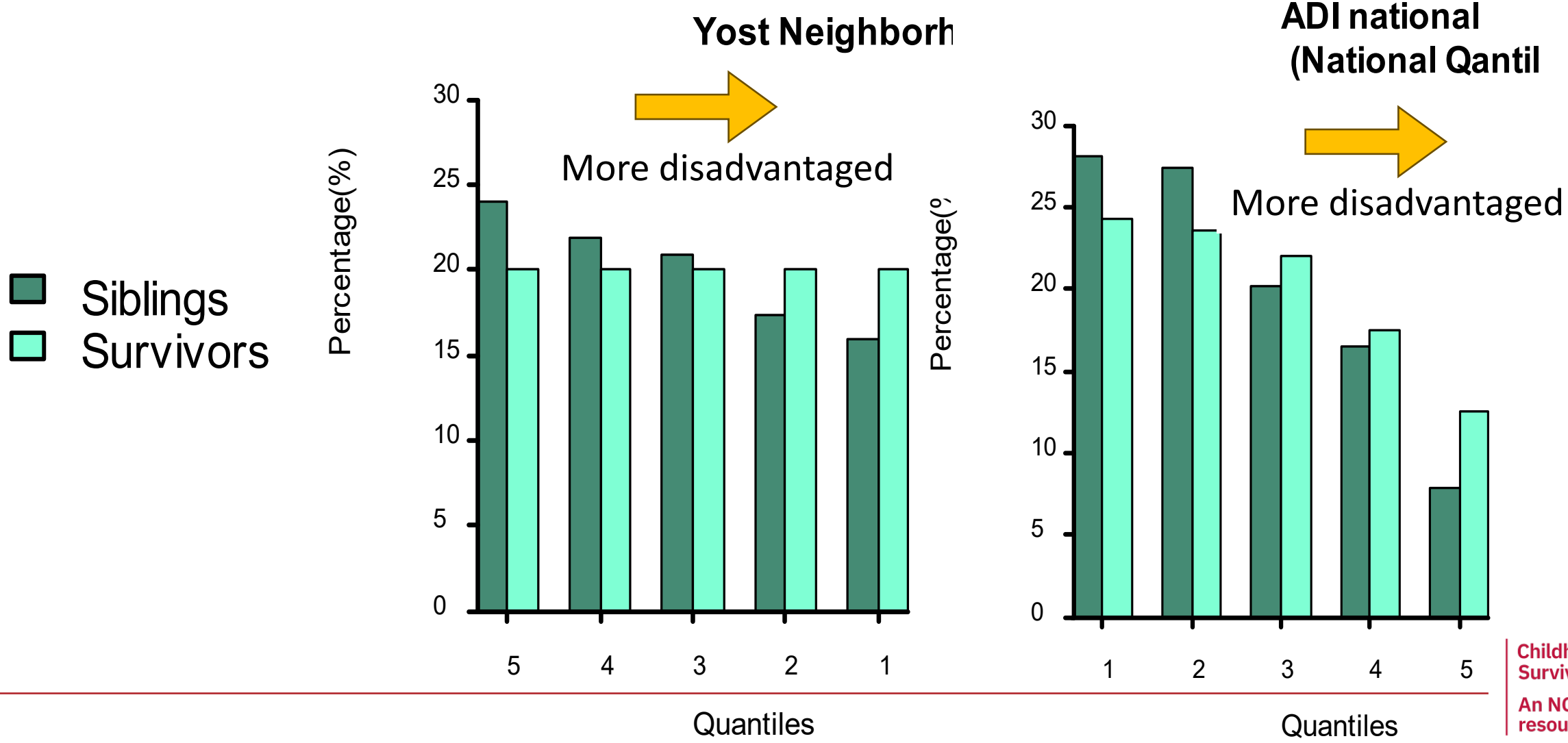
- Score of 0-100 (national or state rank)
- Higher = more social vulnerabilities in census tract of residence
- Low (0.0-<0.33), moderate (0.33-<0.66), and high vulnerability (≥0.66)
- Overall and 4 subscales: SES, Household composition, Minority, Housing

Area Deprivation Index (ADI) [2015, 2019]

- Census block group
- Not available on those in earlier follow-ups

Survivors vs. Siblings at FU6/FU5

ccss



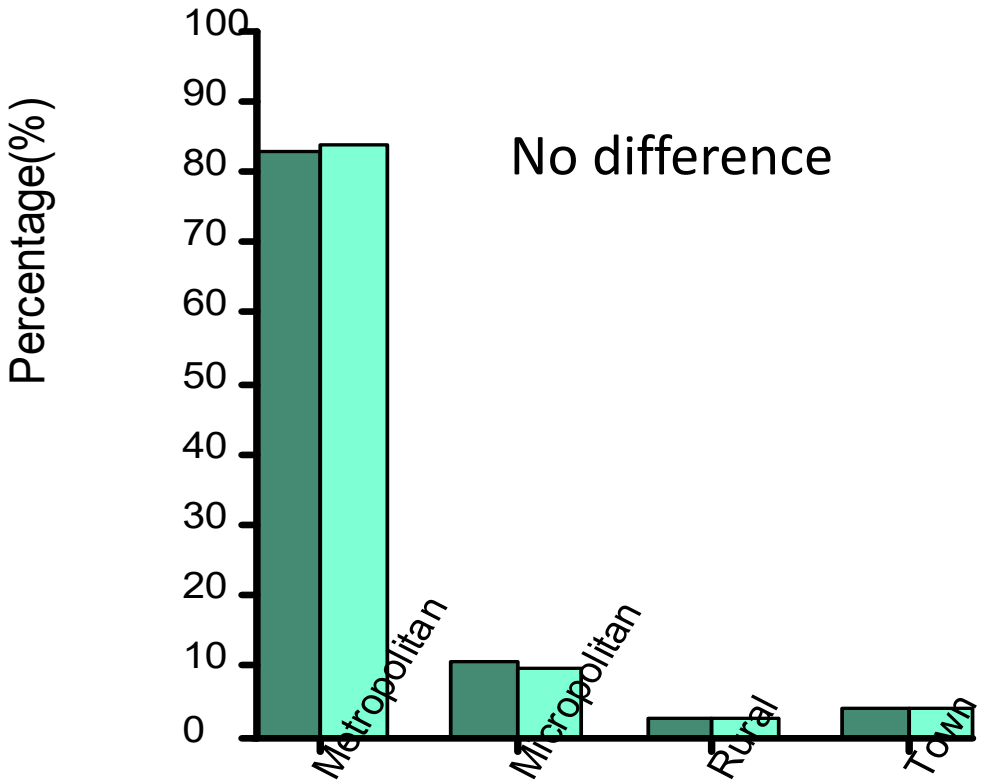
Childhood Cancer Survivor Study

An NCI-funded resource

Survivors vs. Siblings at FU6/FU5

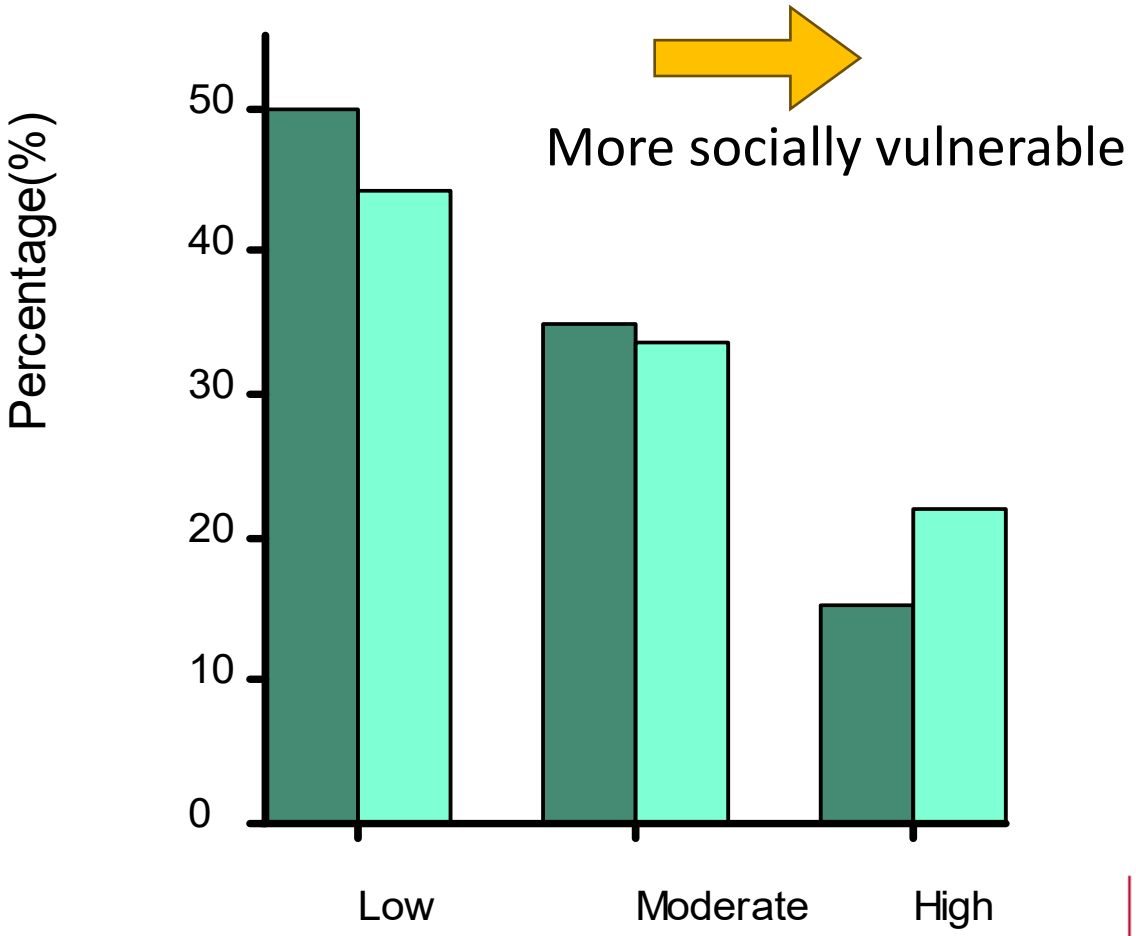
ccss

Rurality



No difference

SVI Overall



More socially vulnerable

Childhood Cancer Survivor Study

An NCI-funded resource

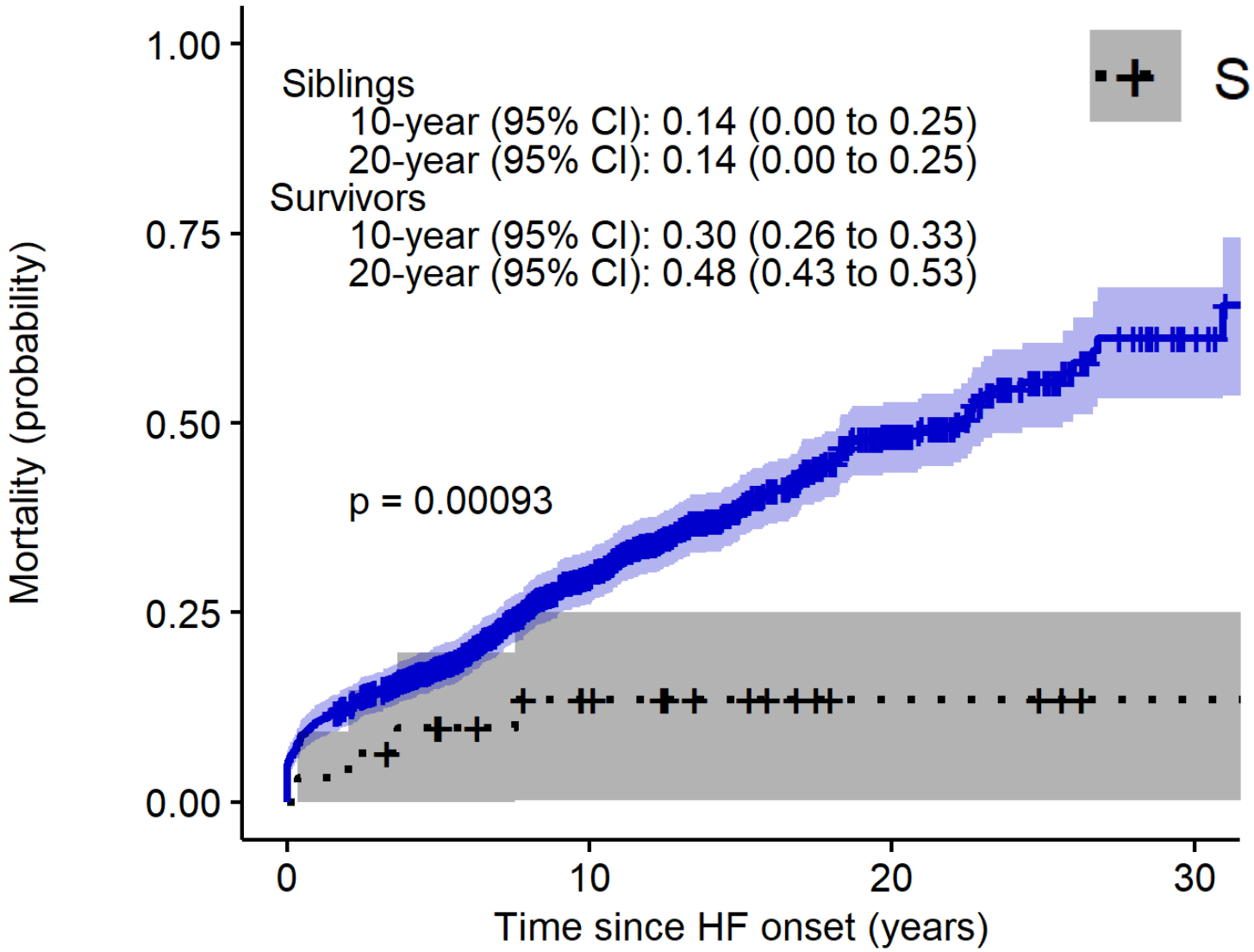
Methodological/Population-Science Question #5

CCSS

- **Do survivors have higher mortality rates than the general population <u>after developing a specific chronic health condition</u>?**

Mortality after a serious cardiovascular event

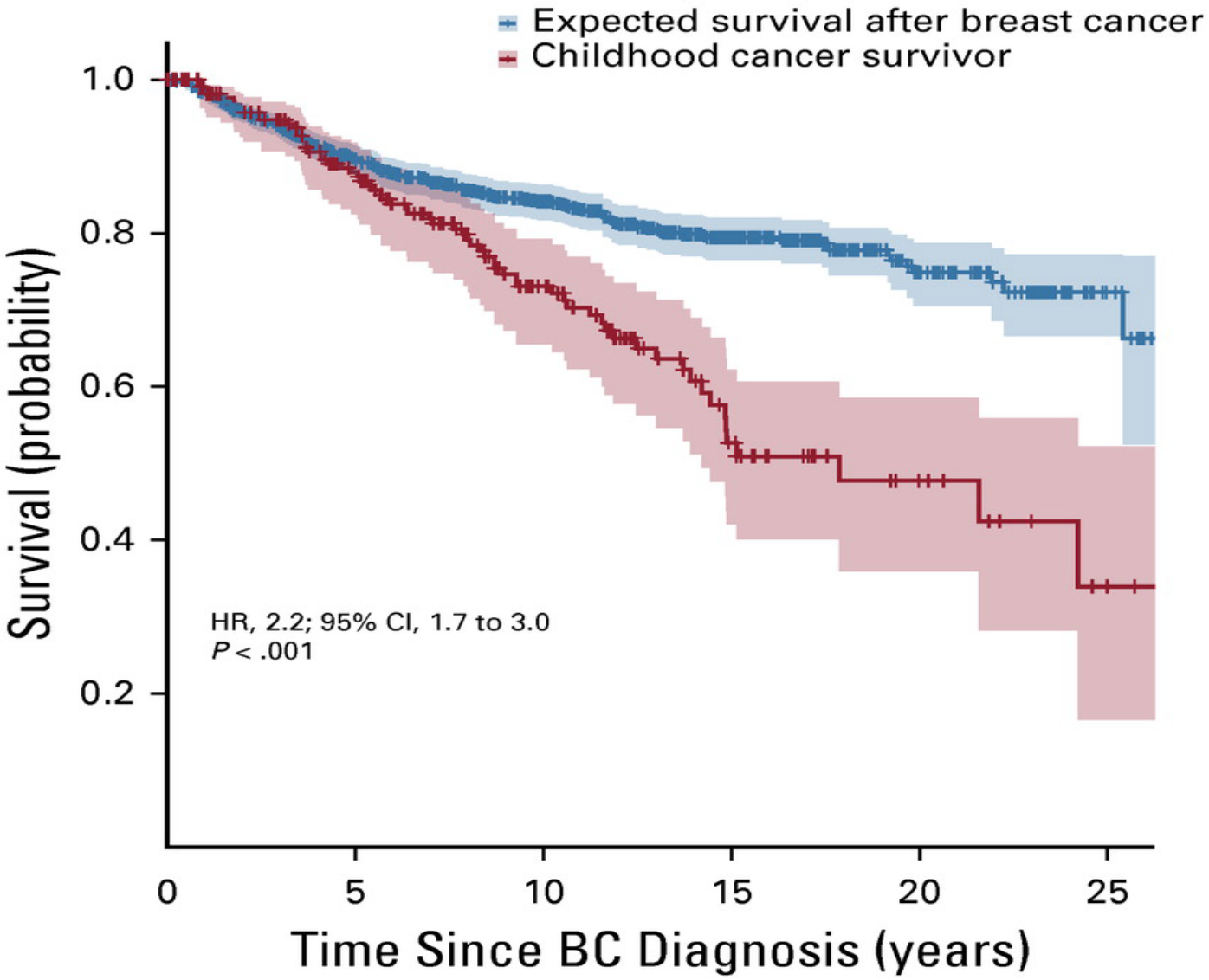
CCSS



Wendy Bottinor, MD, MSCI
Virginia Commonwealth Univ.

Mortality after a breast subsequent neoplasm

ccss

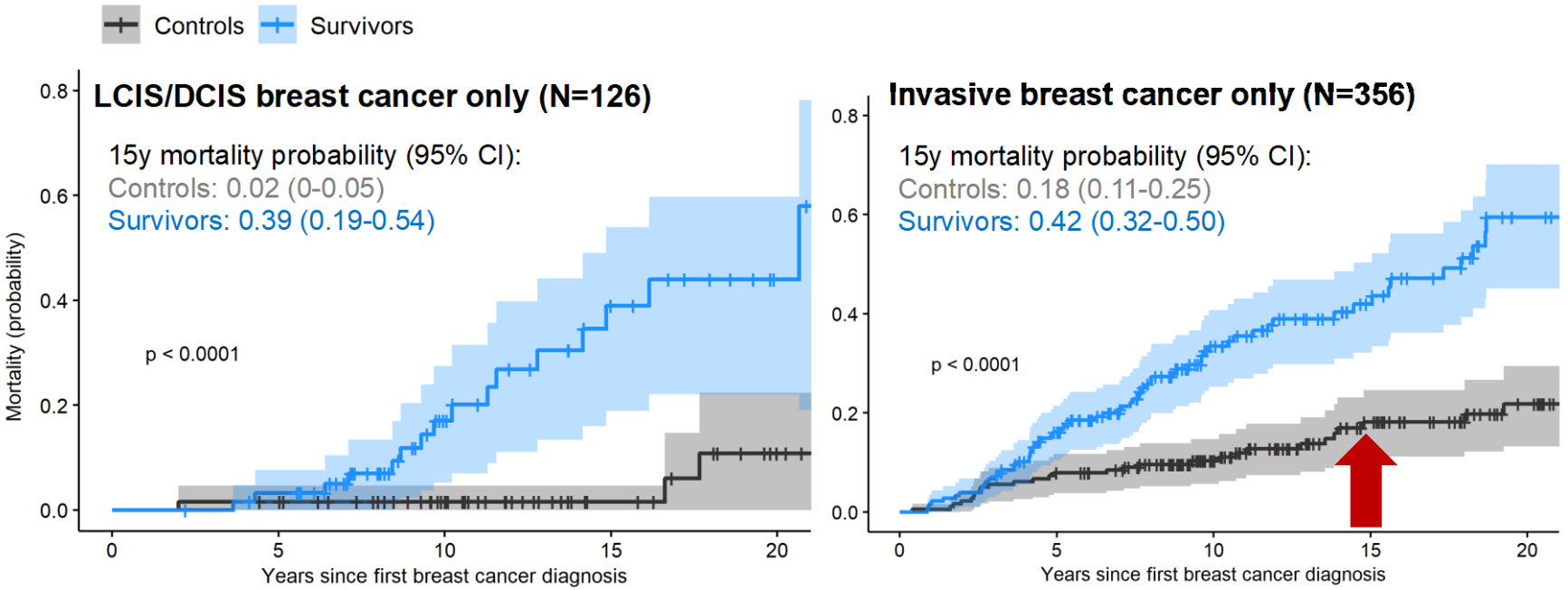


Chaya Moskowitz, PhD
Memorial Sloan Kettering Cancer Center

JCO 2019

Mortality after a breast subsequent neoplasm

CCSS



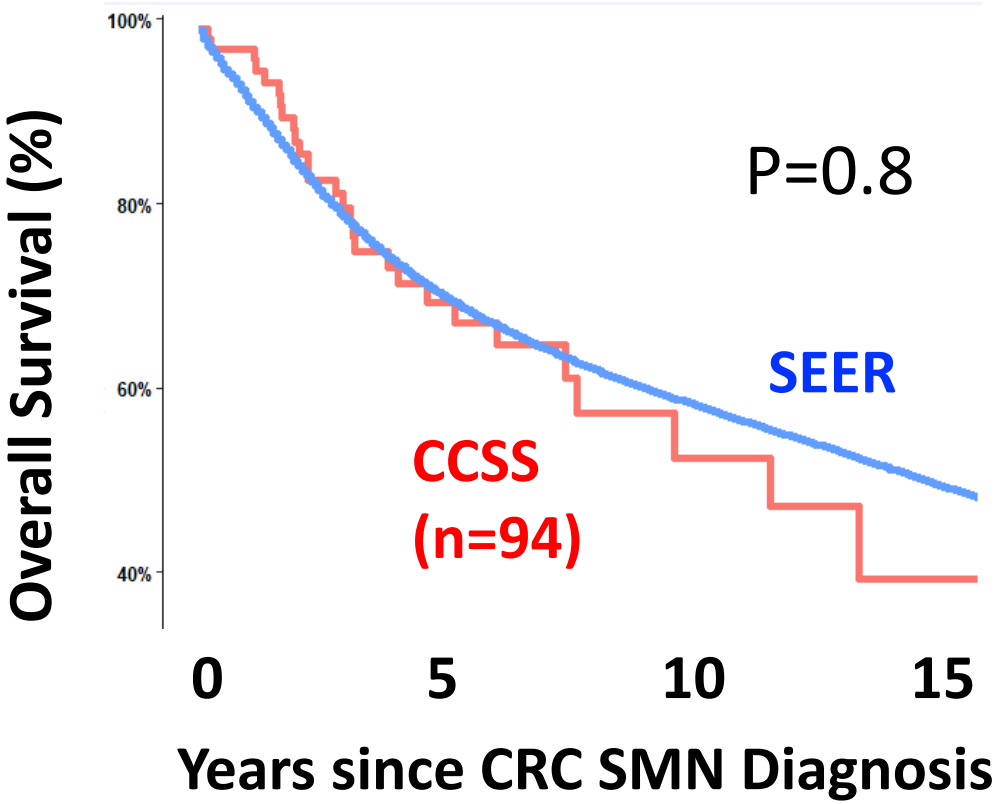
Details of BCa tx as well as mortality in an ISLCCC talk by Cindy Im

Cindy Im, PhD
University of Minnesota

Lucie Turcotte, MD, MPH, MS
University of Minnesota

Mortality after a colorectal subsequent neoplasm

CCSS



- Median 30 yrs after Childhood Ca. dx
- Abdominal RT (n=45, 52%)
- Pelvic RT (n=41, 47%)

Tara Henderson, MD, MPH
University of Chicago

Chaya Moskowitz, PhD
Memorial Sloan Kettering Cancer Center

Methodological/Population-Science Question #6

CCSS

- **How can we represent the longitudinal CHC burden for evaluating its effect on other survivorship outcomes?**

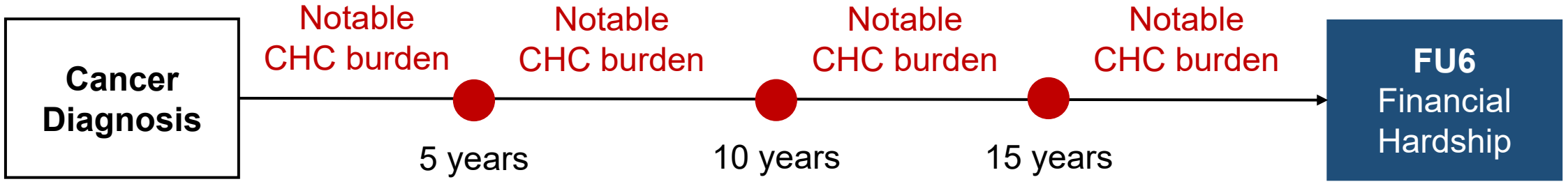
I-Chan Huang, PhD
St. Jude Children's
Research Hospital

Severity of Individual Global CHC Burden

ccss

Global Burden	CTCAE Grade 4	CTCAE Grade 3	CTCAE Grade 2	CTCAE Grade 1
Very high burden	≥2	Any count	Any count	Any count
	1	≥2	Any count	Any count
High burden	1	0 or 1	Any count	Any count
	0	≥2	Any count	Any count
Medium burden	0	1	Any count	Any count
	0	0	≥1	Any count
Low burden	0	0	0	≥1
No burden	0	0	0	0

Geenen et al, JAMA 2007



Severity of global CHC burden	n (%)
No/low	1154 (33.8)
Medium	1689 (45.5)
High	587 (15.5)
Very high	208 (5.2)

"Notable" Global CHC burden

Years from Dx to developing notable global CHC burden	n (%)
Not present	1154 (33.8)
< 5 years	1297 (34.6)
5-9.9 years	252 (7.2)
10-14.9 years	250 (6.7)
≥ 15 years	685 (17.6)

Early vs. late CHC burden

Progression of Global CHC Burden

ccss

Change of global CHC burden between 10 years post-diagnosis and before the completion of the hardship survey

Progression of global CHC burden	n (%)
Persistent no or low burden	1154 (31.7)
Persistent medium burden	1023 (28.1)
Moderate burden change†	666 (18.3)
Significant burden change‡	546 (15.0)
Persistent high or very high burden	249 (6.9)

† From no/low burden to medium burden; ‡ E.g., from no/low burden to high or very high burden

Methodological/Population-Science Question #7

CCSS

- **How can we best measure prediction performance?**

Yan Yuan, PhD
University of Alberta

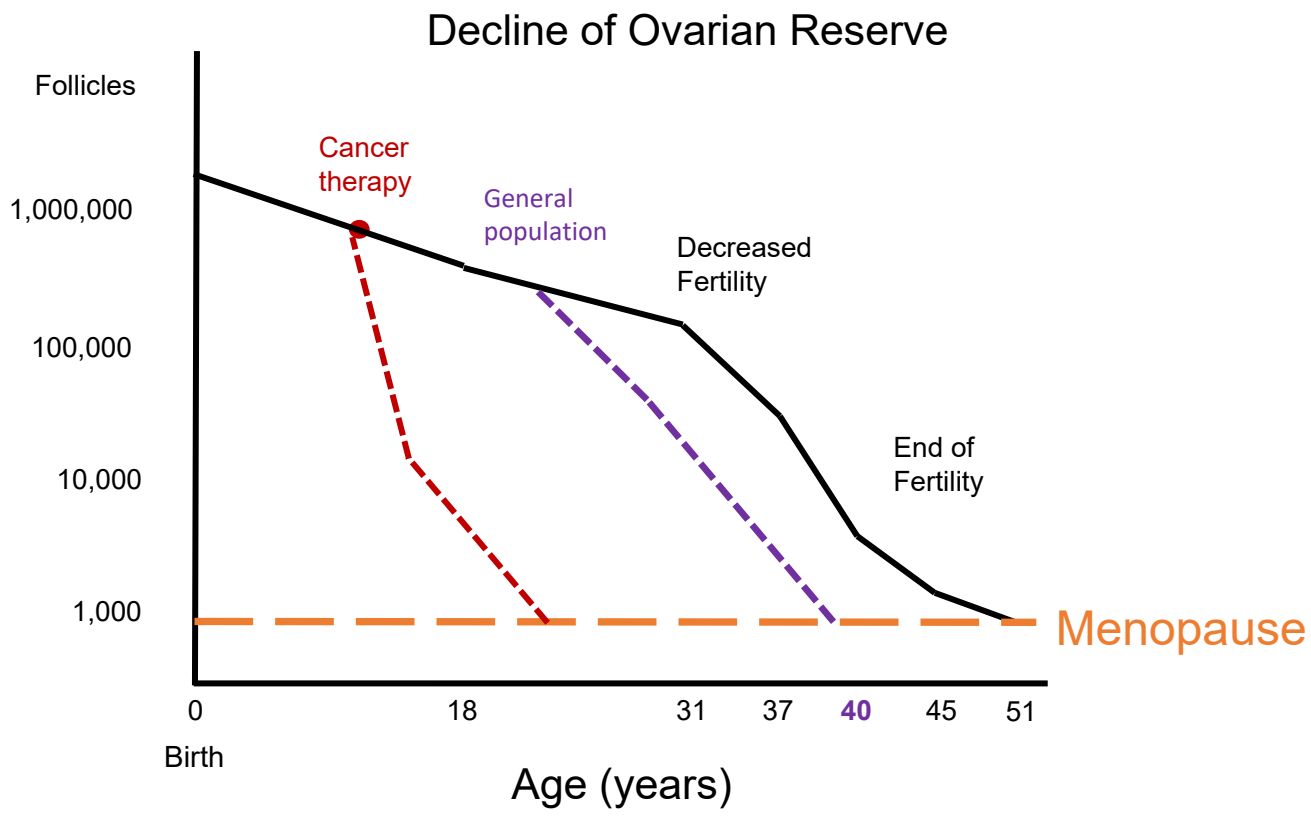
Predicting acute ovarian failure in female survivors of childhood cancer: a cohort study in the Childhood Cancer Survivor Study (CCSS) and the St Jude Lifetime Cohort (SJLIFE)

Rebecca A Clark, Sogol Mostoufi-Moab, Yutaka Yasui, Ngoc Khanh Vu, Charles A Sklar, Tarek Motan, Russell J Brooke, Todd M Gibson, Kevin C Oeffinger, Rebecca M Howell, Susan A Smith, Zhe Lu, Leslie L Robison, Wassim Chemaitilly, Melissa M Hudson, Gregory T Armstrong, Paul C Nathan, Yan Yuan**

THE LANCET Oncology
Volume 21, Issue 3, March 2020, Pages 436-445

Prediction of Primary Ovarian Insufficiency

ccss



POI

compromised ovarian function before age 40

Prevalence

General population 1%

(Torrealday, et al. EMCNA, 2015)

Childhood Cancer Survivors 15%

(Levine, et al. Cancer, 2018, Chemaitilly, et al. JCEM, 2006)

Modified from http://oncofertility.northwestern.edu/resources/assessing-ovarian-reserve-after-cancer-treatments

Prediction-performance metric

ccss

Survivor-Specific PRS

Risk prediction metrics	Without	With	
Any ovarian RT and chemotherapy (n=158; POI prevalence[a]: 58%)			P-value
SBrS (95% CI)	-1.4% (-31.6% to 16.3%)	20.0% (1.0% to 35.0%)	0.018
AUPRC (95% CI)	0.76 (0.63 to 0.89)	0.87 (0.80 to 0.94)	0.029
AUROC (95% CI)	0.70 (0.57 to 0.82)	0.78 (0.70 to 0.87)	0.12
Spiegelhalter-z (95% CI)	2.43 (0.47 to 4.39)	1.63 (-0.33 to 3.59)	0.98
True positive rate[c]	38.0%	78.3%	--
Positive predictive value[d]	71.6%	70.2%	--

Prediction-performance metric

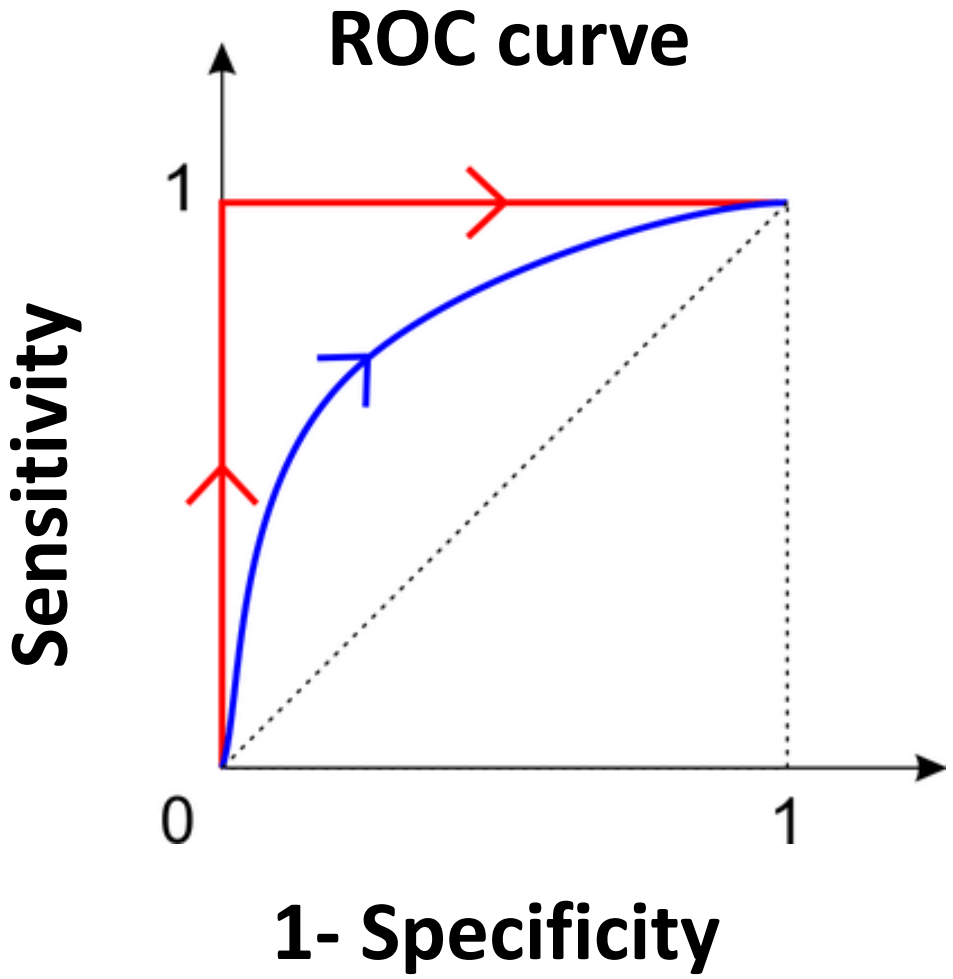
ccss

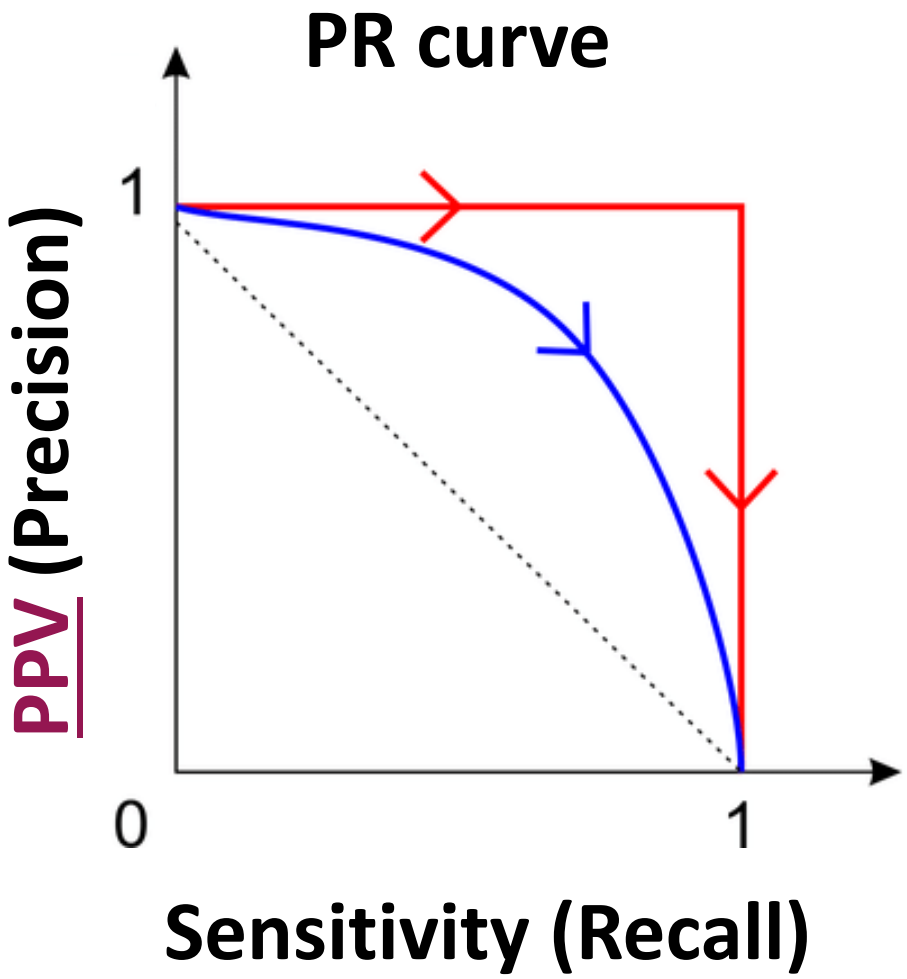
Survivor-Specific PRS

Risk prediction metrics	Without	With	
Any ovarian RT and chemotherapy (n=158; POI prevalence[a]: 58%)			P-value
SBrS (95% CI)	-1.4% (-31.6% to 16.3%)	20.0% (1.0% to 35.0%)	0.018
AUPRC (95% CI)	0.76 (0.63 to 0.89)	0.87 (0.80 to 0.94)	0.029
AUROC (95% CI)	0.70 (0.57 to 0.82)	0.78 (0.70 to 0.87)	0.12
Spiegelhalter-z (95% CI)	2.43 (0.47 to 4.39)	1.63 (-0.33 to 3.59)	0.98
True positive rate[c]	38.0%	78.3%	--
Positive predictive value[d]	71.6%	70.2%	--

Prediction-performance metric

ccss





Ines Dedovic, PhD Thesis 2017

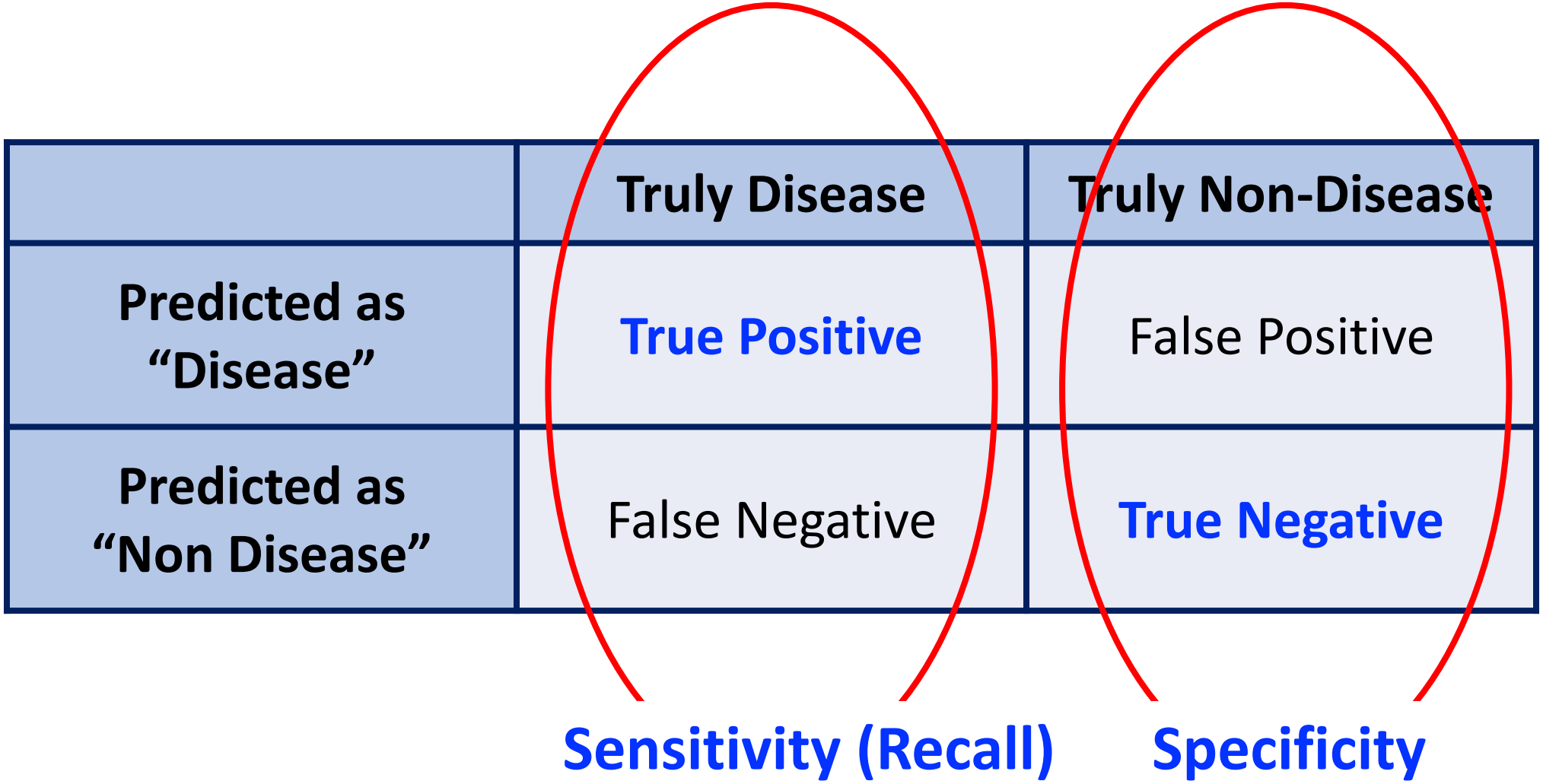
Precision Recall vs. Sensitivity Specificity

CCSS

	Truly Disease	**Truly Non-Disease**
Predicted as "Disease"	True Positive	False Positive
Predicted as "Non Disease"	False Negative	True Negative

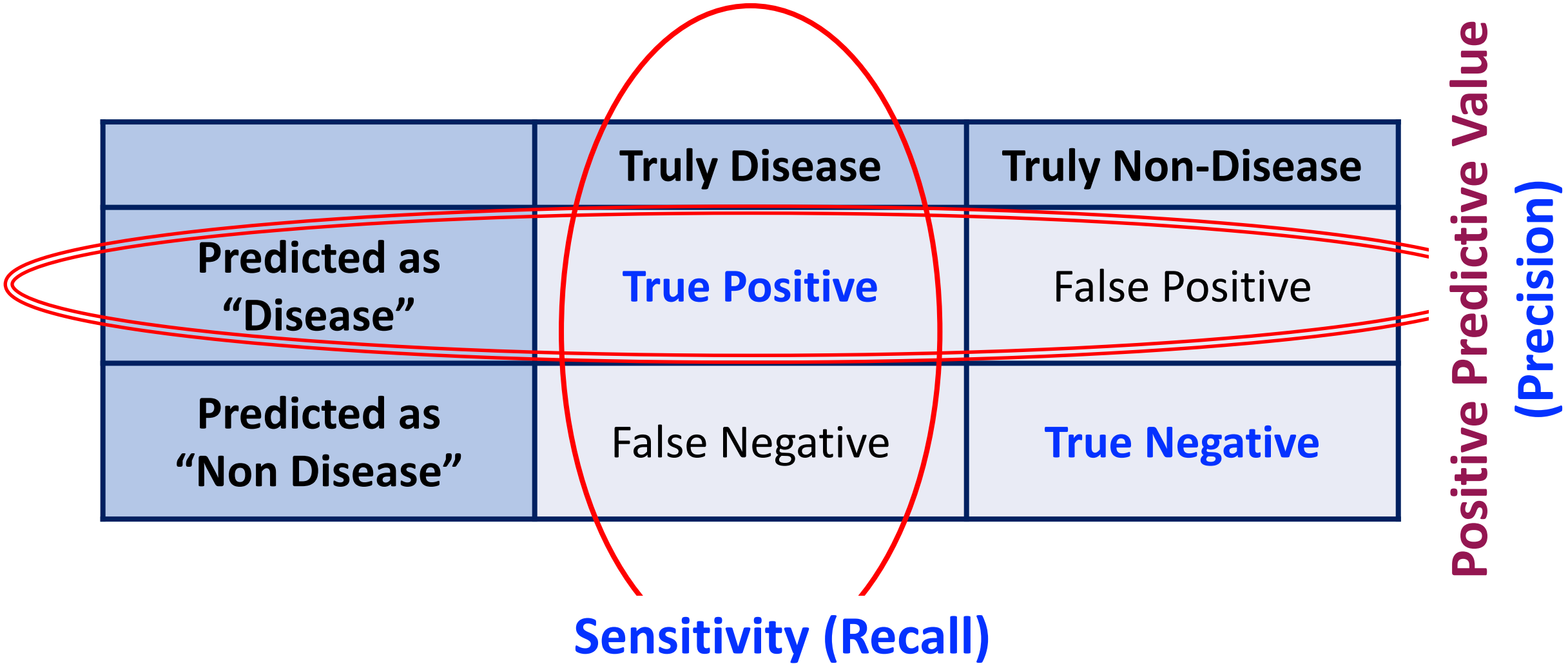
ROC is based on Sensitivity & Specificity

ccss



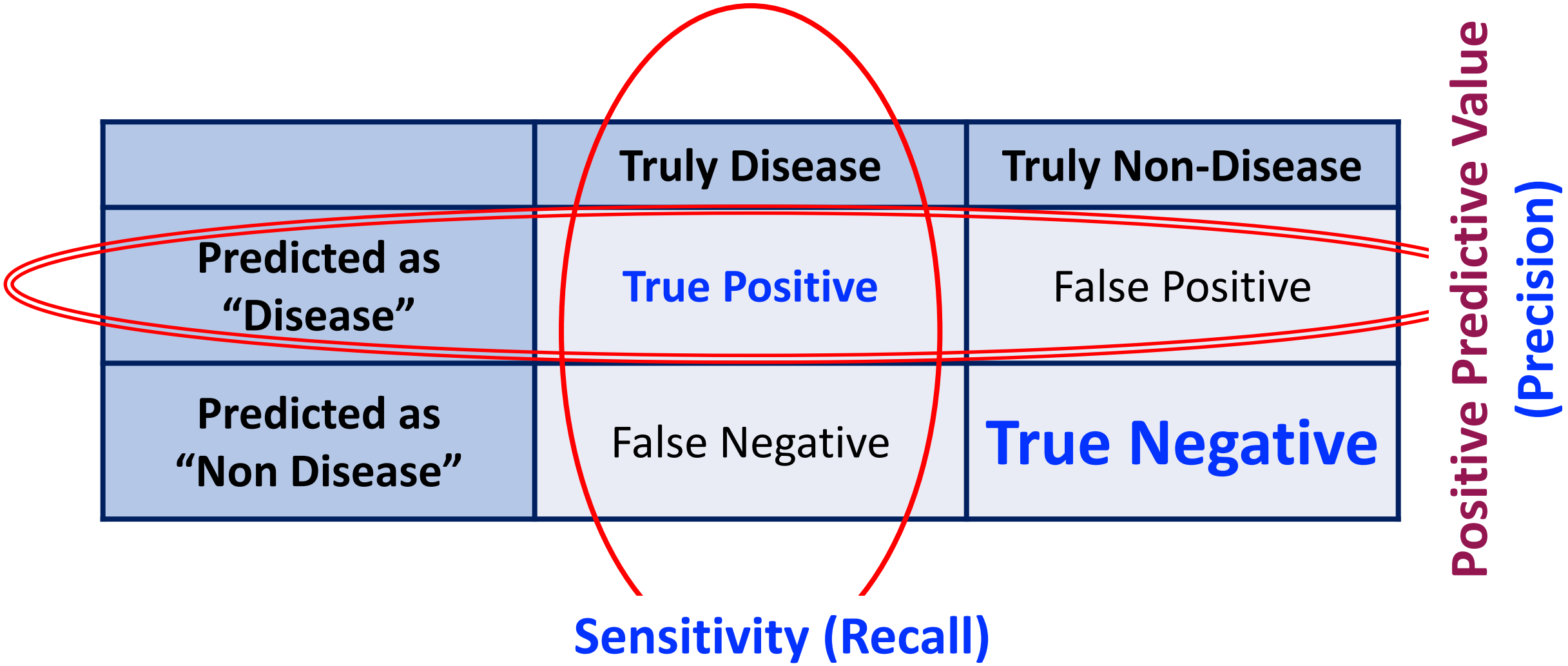
PR is based on PPV & Sensitivity

ccss



PR is based on PPV & Sensitivity

ccss



Methodological/Population-Science Question #8

CCSS

- **How to address the potential inaccuracy of self-report vs. clinically-assessed CHCs?**
- **How to address the missing onset age of CHCs?**

Sadie Mirzaei, PhD
St. Jude Children's Research Hospital

Additional Ancillary Studies

CCSS

Ancillary Studies

ccss

Principal Investigator: Jennifer Yeh (Harvard University)
Title: Can Risk Reducing Medications Improve Breast Cancer Prevention in Childhood and Adolescent Cancer Survivors? Comparative Modeling to Inform Care.
Dates of Funding: 9/22 – 8/27
Funding Source: National Institutes of Health (R01)
Award: $13,228,808

Jennifer Yeh, PhD
Boston Children's Hospital
Harvard Medical School

Ancillary Studies

ccss

Principal Investigator: Xu Ji (Emory University)
Title: Understanding the impact of the Affordable Care Act on Healthcare Coverage, Utilization and Outcomes Among Survivors of Childhood Cancer
Dates of Funding: 12/21 - 12/23
Funding Source: National Institutes of Health **R03CA267456**
Award: $171,872
Study Aims: Linkage with national Medicaid data to evaluate how the Affordable Care Act Medicaid expansion affects insurance coverage, health service utilization, and mortality for adult survivors of childhood cancer.

Xu Ji, PhD
Emory University

Five Year Plan: Progress Update

ccss

Enhance Data Sharing

To maximize access to the CCSS resource we will leverage a cloud-based sharing platform (SJ Cloud Survivorship Portal) to develop a data analysis ecosystem with tools for data access, visualization and analysis of genetic, treatment exposure and outcome data. (http://survivorship.stjude.cloud/)

Xin Zhou, PhD
St. Jude Children's Res. Hospital

June 15th 5:30pm – 6:00pm Demo (ISLCCC)

ccss

Data content

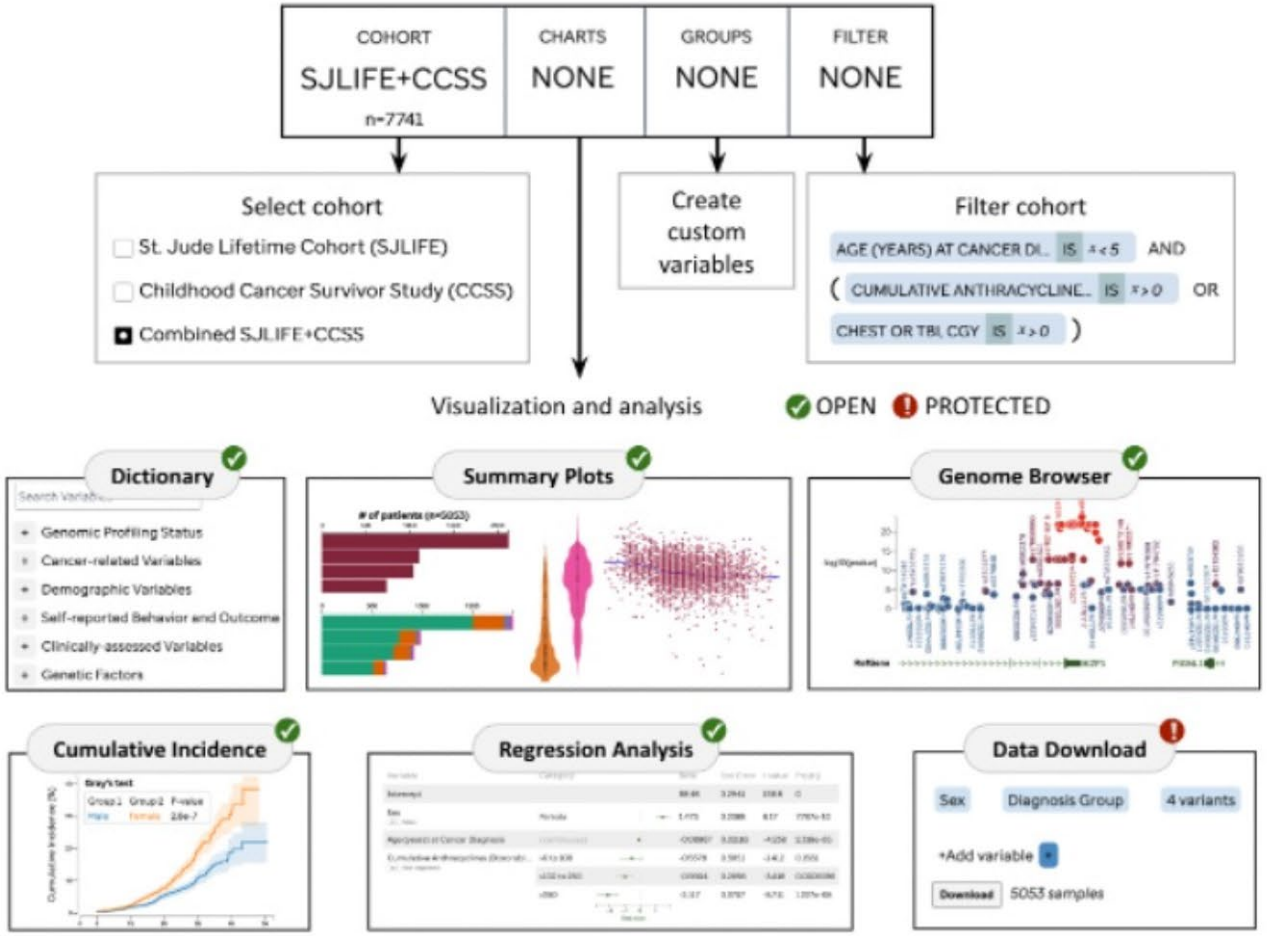
COHORT
St. Jude Lifetime Study (SJLIFE), n=5,053
Childhood Cancer Survivor Study (CCSS), n=2,688

PHENOTYPES / EXPOSURES
Demographics, n=36
Cancer diagnosis, n=4
Cancer treatment, n=95
Clinical assessments, n=350
Chronic health conditions, n=400
Self-reported and questionnaire, n=776

WHOLE-GENOME SEQUENCING
Genotypes for >400 million variants
Polygenic risk scores, >500 traits
Genetic ancestries
Ancestry principal components
Linkage disequilibrium

Visit the Survivorship Portal on St. Jude Cloud
https://survivorship.stjude.cloud/

Visualization and analysis features



St. Jude Survivorship Portal

https://survivorship.stjude.cloud/

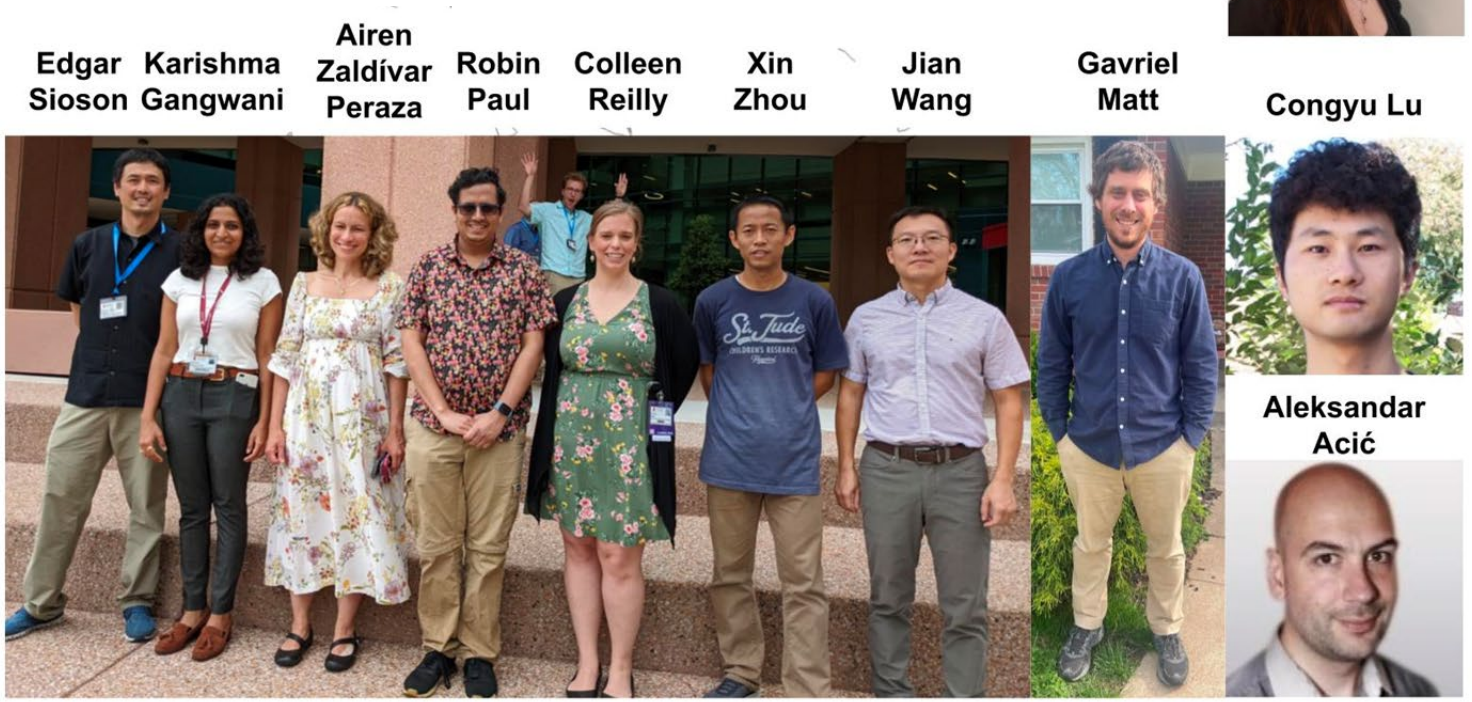
Xin Zhou, PhD
Assistant member
Department of Computational Biology

Jinghui Zhang, PhD
Chair/Member
Department of Computational Biology

Zhou Lab

- **5 PhD staffs**
- **4 Web developers**
- **1 Postdoc**
- **1 Student**

in collaboration with Department of Epidemiology & Cancer Control



Discussion: Opportunities

CCSS

- Discover/support **junior researchers w/ method interest**
- **Separate tx (era) effects and aging effects** – Application of age-period-cohort models
- **Minority-applicable PRS** – Transferability of PRS
- **Incorporation of other genetic variations (rare variants, haplotypes, CNV, …)**

Discussion: Opportunities

CCSS

- International comparisons (tx and outcomes)
- Address cohort attrition
- Recruit/retention of minority survivors and survivors with lower educational attainment
- Data linkage (too soon to link to Medicare?)

Contact us for any inquiry/interest

CCSS

- **Yutaka Yasui**
  yutaka.yasui@stjude.org
- **Wendy Leisenring**
  wleisenr@fredhutch.org