

# Epidemiology/Biostatistics Working Group Report

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Yutaka Yasui, PhD

St. Jude Children's Research Hospital

yutaka.yasui@stjude.org

**CCSS**

Childhood Cancer  
Survivor Study



St. Jude Children's  
Research Hospital

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An NCI-funded Resource

# To get involved in CCSS => Discuss with Working Group Chairs

CCSS



Daniel-San, catch fly  
with chopstick,  
accomplish anything.



**Childhood Cancer  
Survivor Study**  
An NCI-funded  
resource



# Catch & Discuss with Working Group Chairs

ccss



Catch WG Chairs,  
discuss utilization  
of CCSS resource  
for your research!



**Childhood Cancer  
Survivor Study**  
An NCI-funded  
resource

# Scope of Epi/Biostat Working Group

CCSS

1. **To lead and support investigations on population sciences relevant to CCSS**, such as mortality, cost-effectiveness, characterization of primary treatment exposures (including temporal changes), and disadvantaged/minority populations
2. **To encourage and support methodological research.** This includes developing innovative epidemiological and biostatistical methods and applying state-of-the-art methodologies

# Working Group Membership

CCSS

Wendy Leisenring, Fred Hutchinson Cancer Research Center  
Ann Mertens, Emory University  
Kiri Ness, 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

Yutaka Yasui (Chair), St. Jude Children's Research Hospital

**Anyone  
interested in  
Scope 1) and 2)  
is welcome!**

- 7** Published/In Press Manuscripts (since 1/1/2020)  
(10+ as Secondary WG)
- 4** Currently Submitted Manuscripts
- 10** Analysis/Manuscript in Process
- 3** Concepts in development
- 8** New AOs (total, since 1/1/2020)

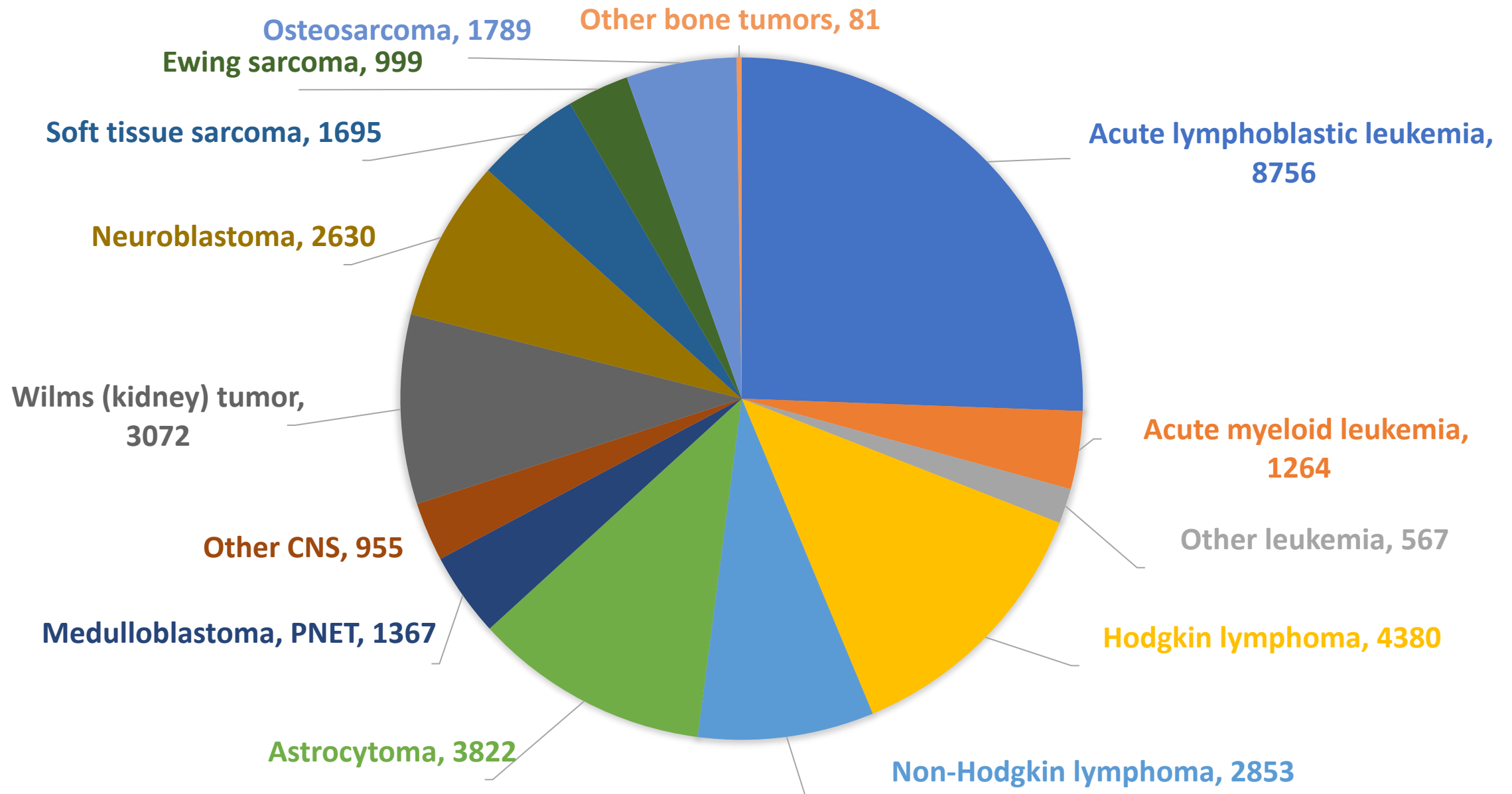
## Mortality among 5-year survivors of childhood cancer: results over five decades of follow-up

Stephanie Dixon, MD  
St. Jude Children's Research Hospital

Qi Liu, Matthew Ehrhardt, Eric Chow, Kevin Oeffinger, Ann Mertens, Paul Nathan, Rebecca Howell, Wendy Leisenring, Kevin Krull, Kirsten Ness, Melissa Hudson, Leslie Robison, Yutaka Yasui, **Gregory Armstrong**

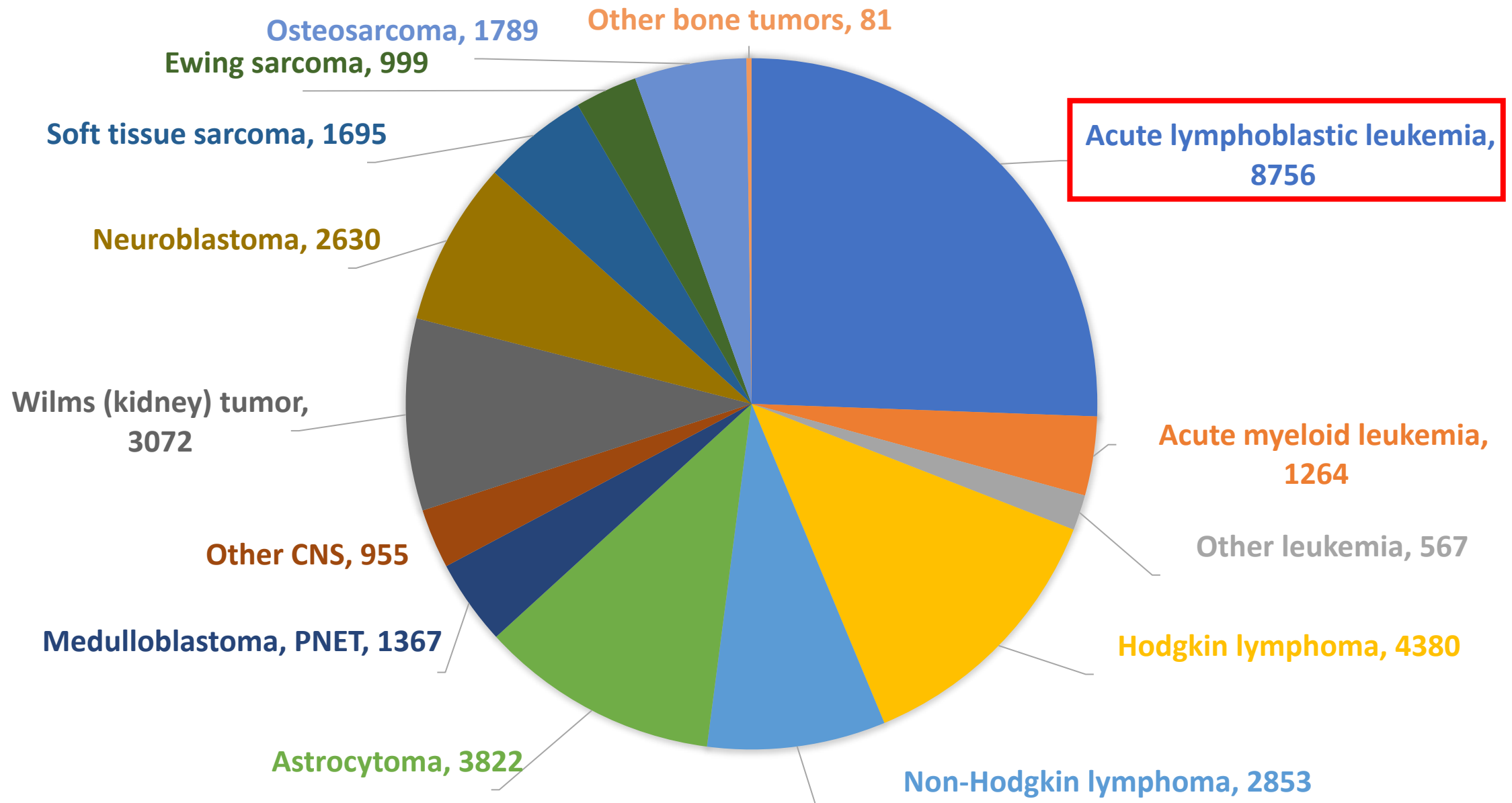


34,230 survivors w/ median time from diagnosis 29.1 years, range 5.0 - 48.0

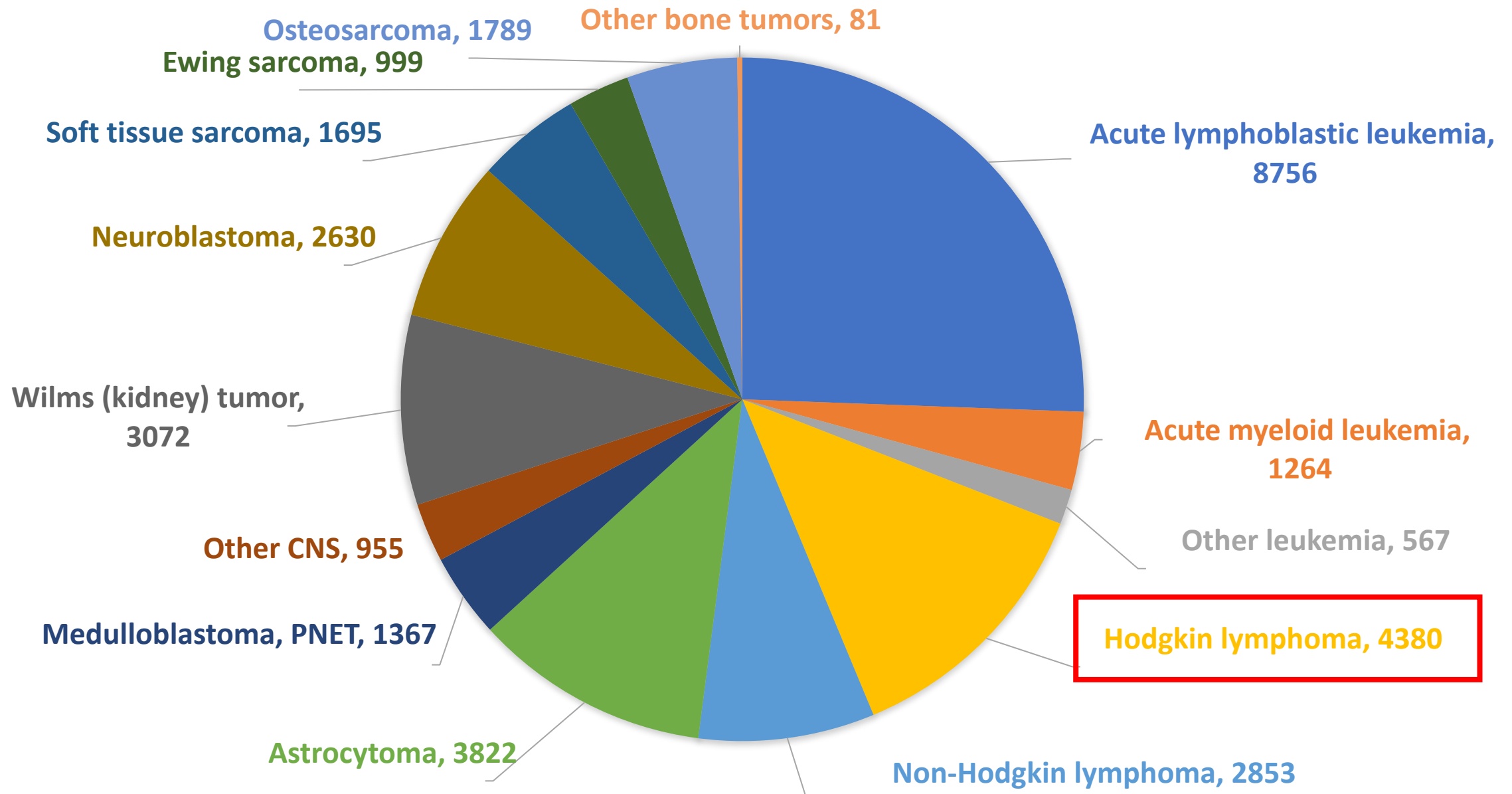




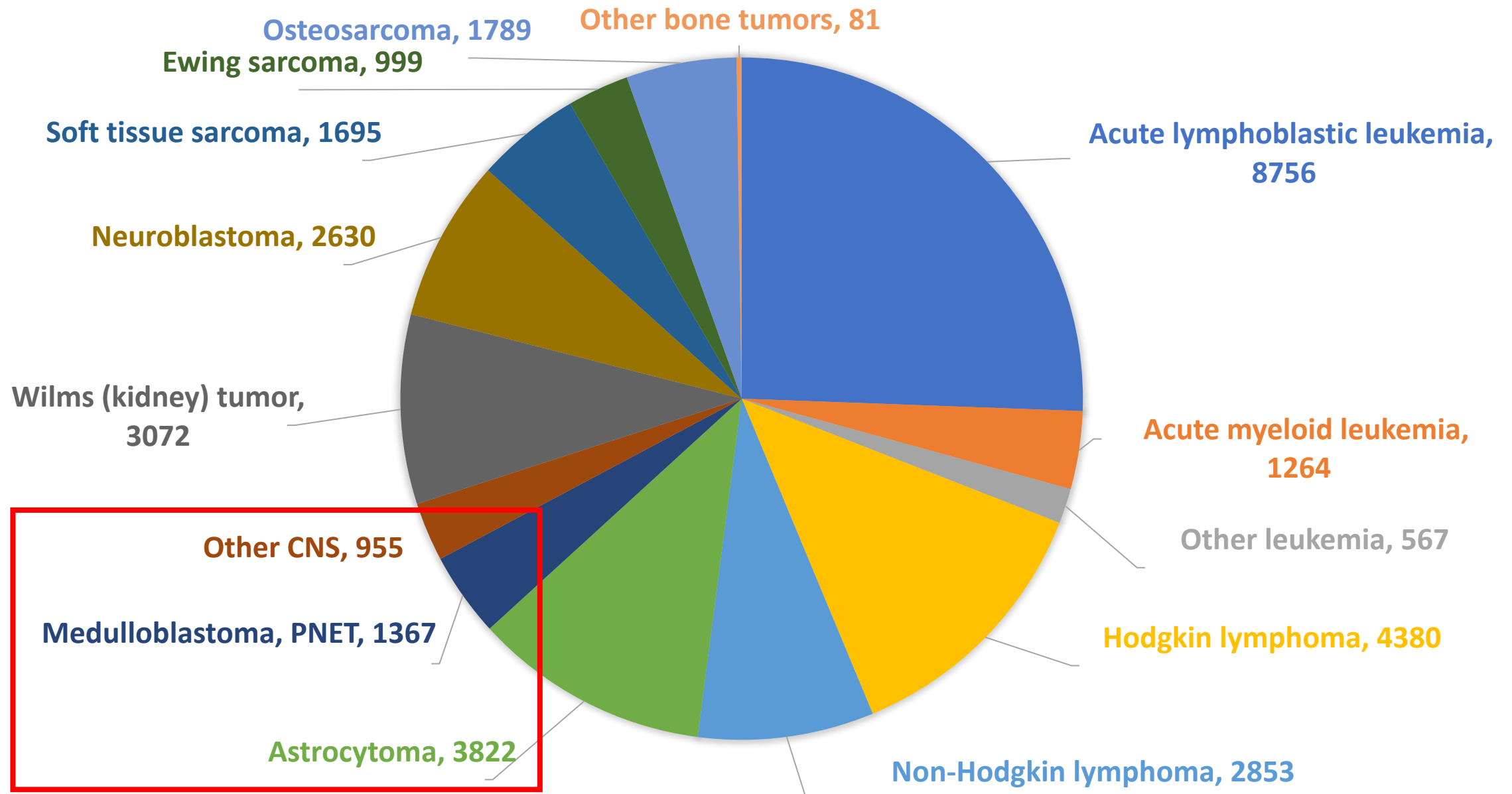
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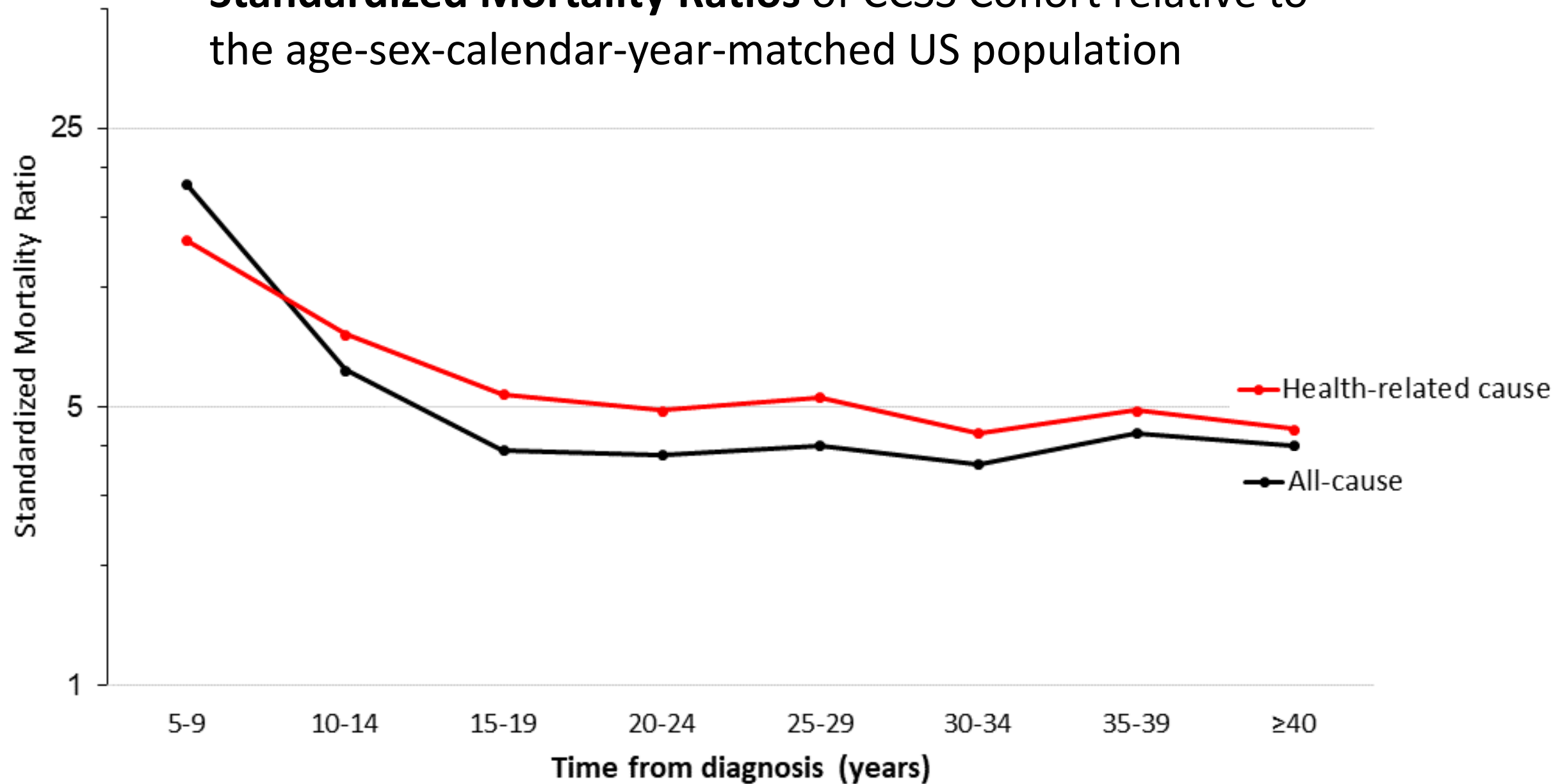
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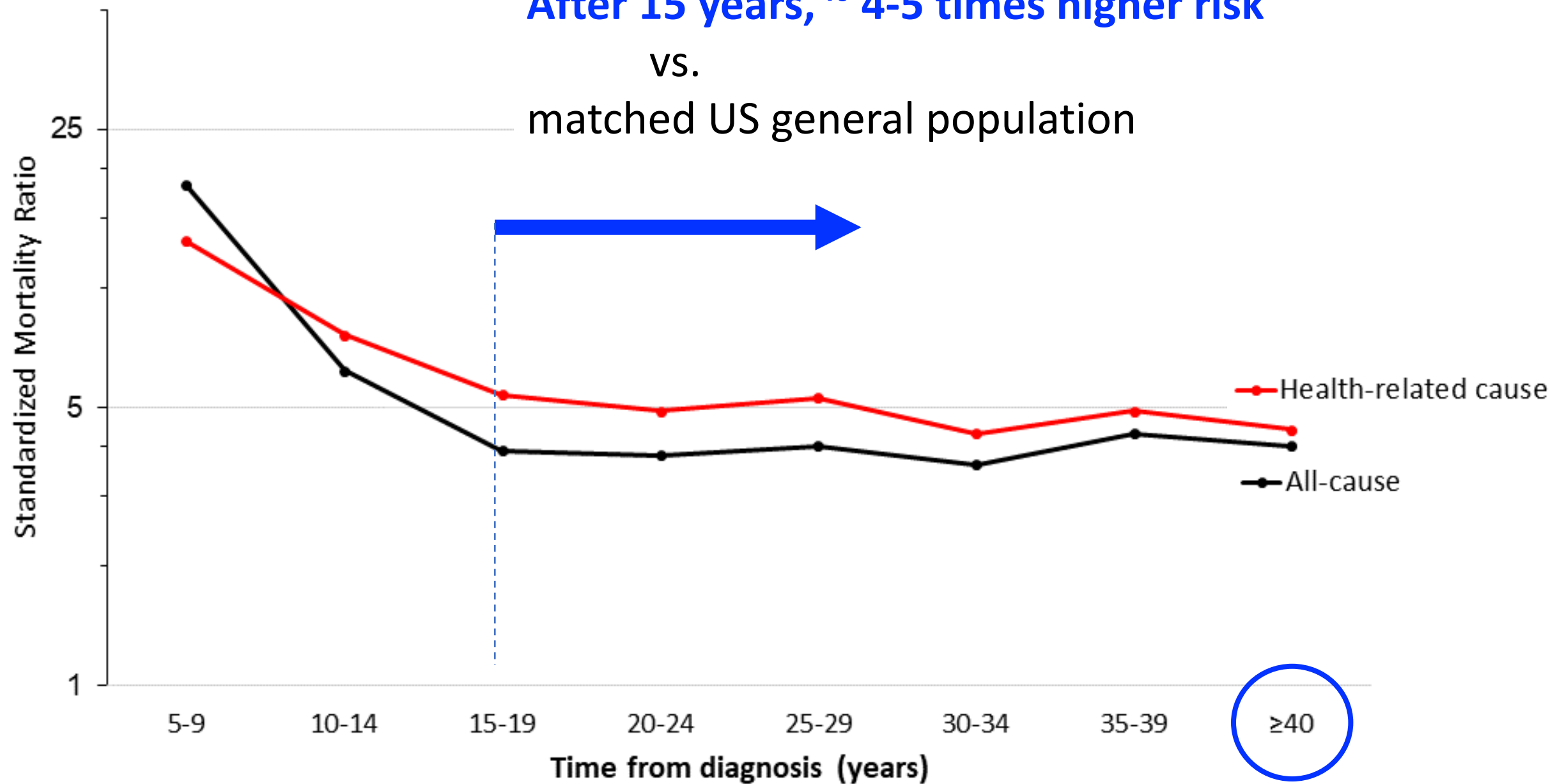
## Standardized Mortality Ratios of CCSS Cohort relative to the age-sex-calendar-year-matched US population



After 15 years, ~ 4-5 times higher risk

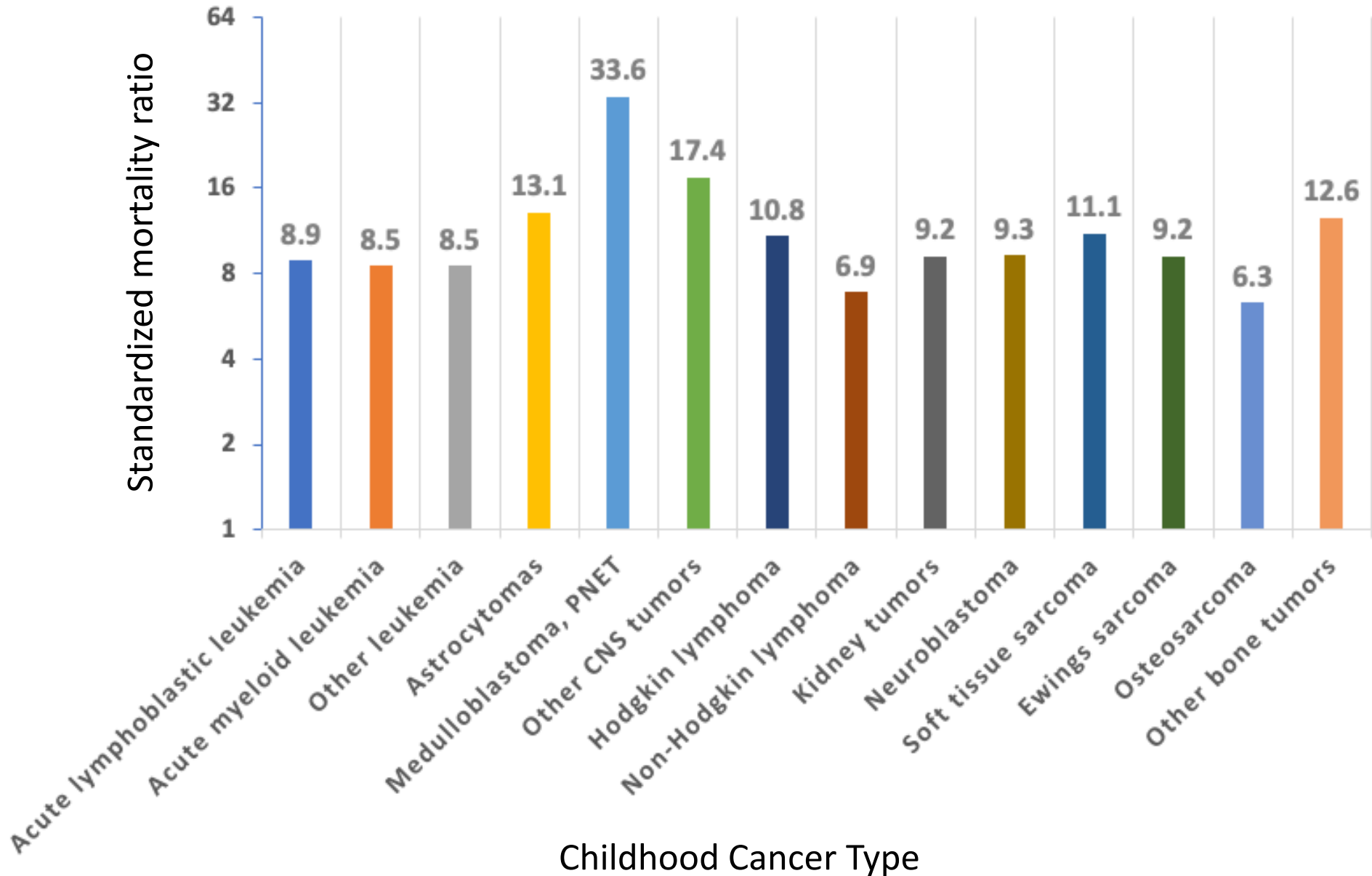
vs.

matched US general population

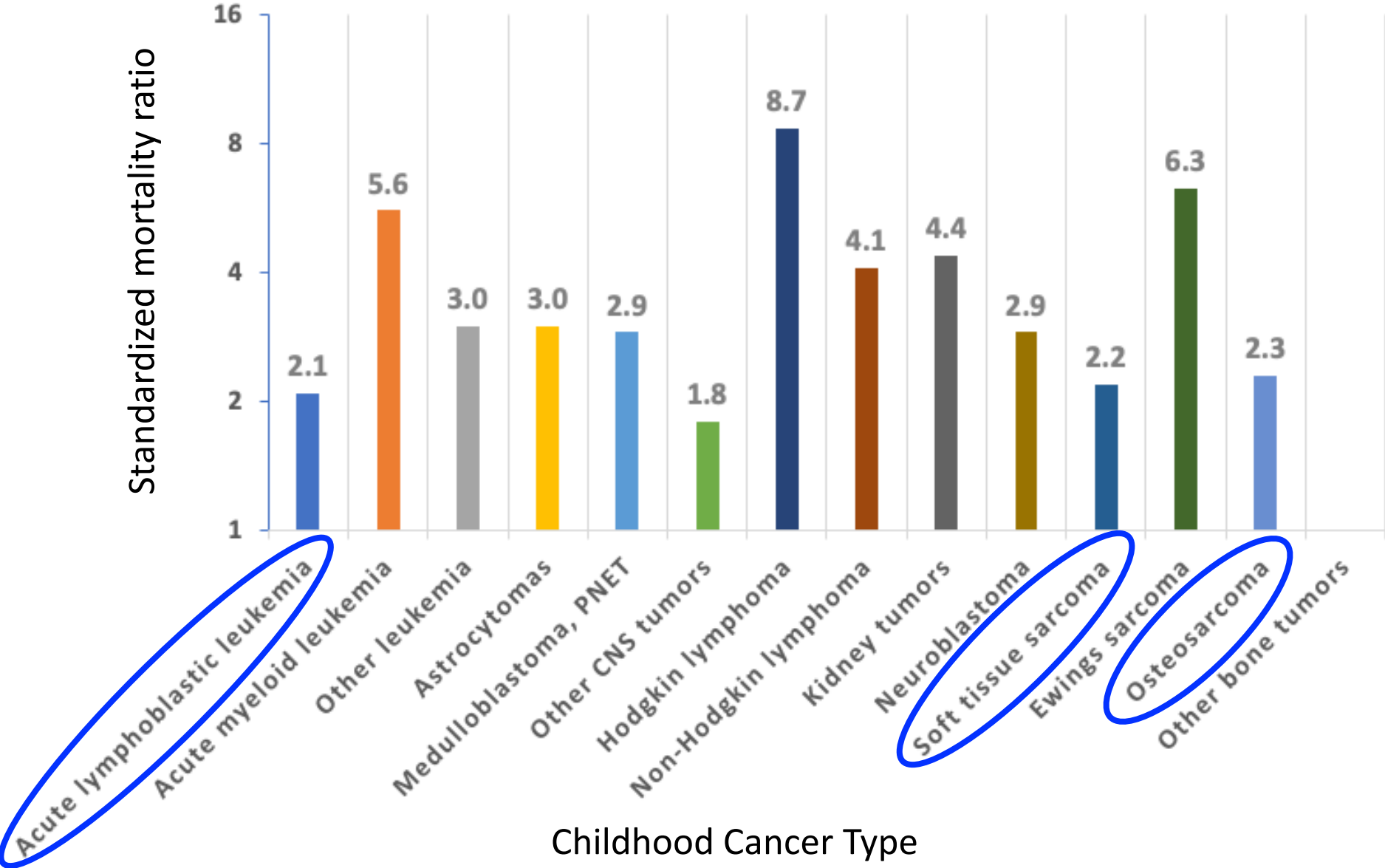




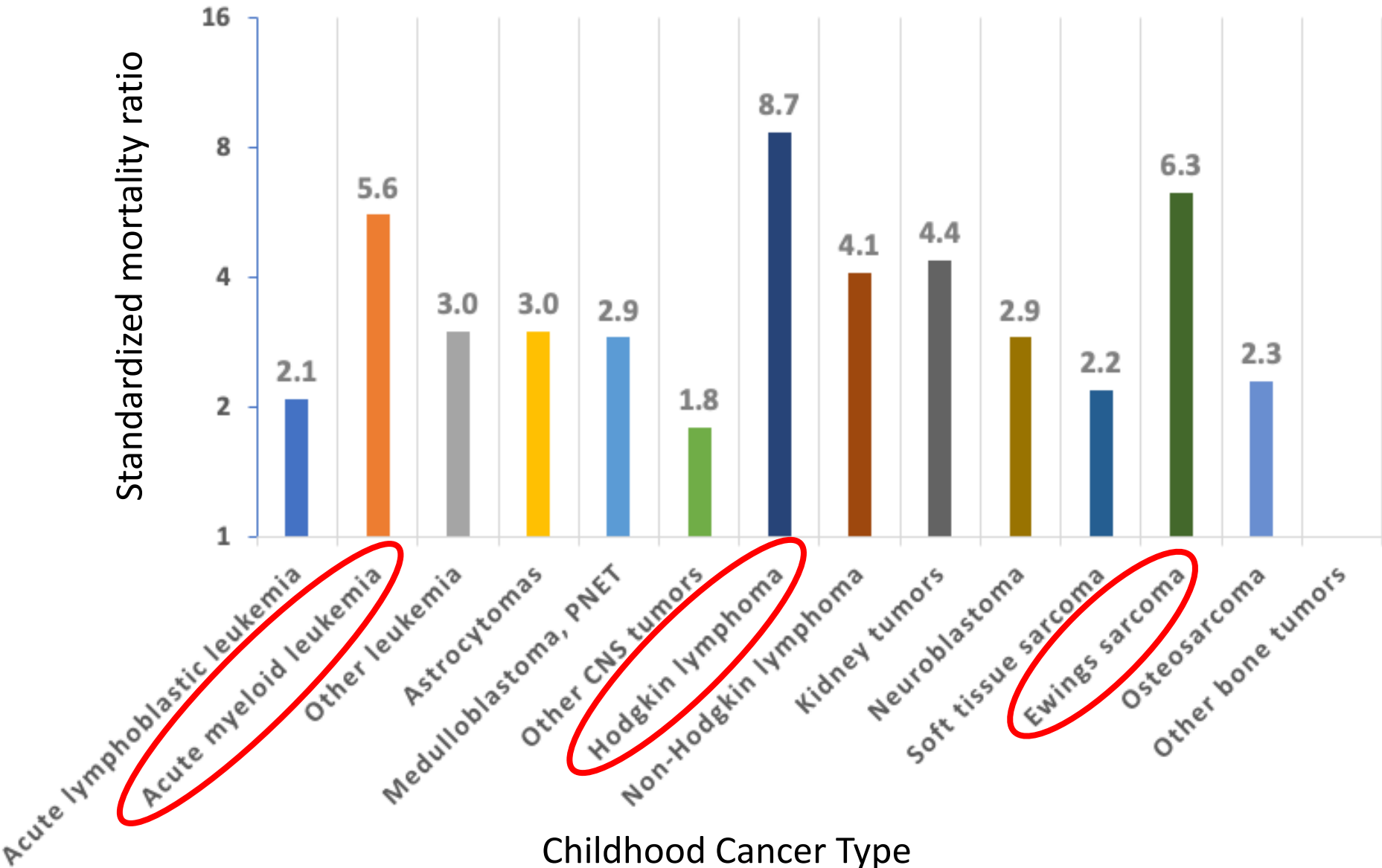
Standardized Mortality Ratios of **Death** due to Second Malignant Neoplasms



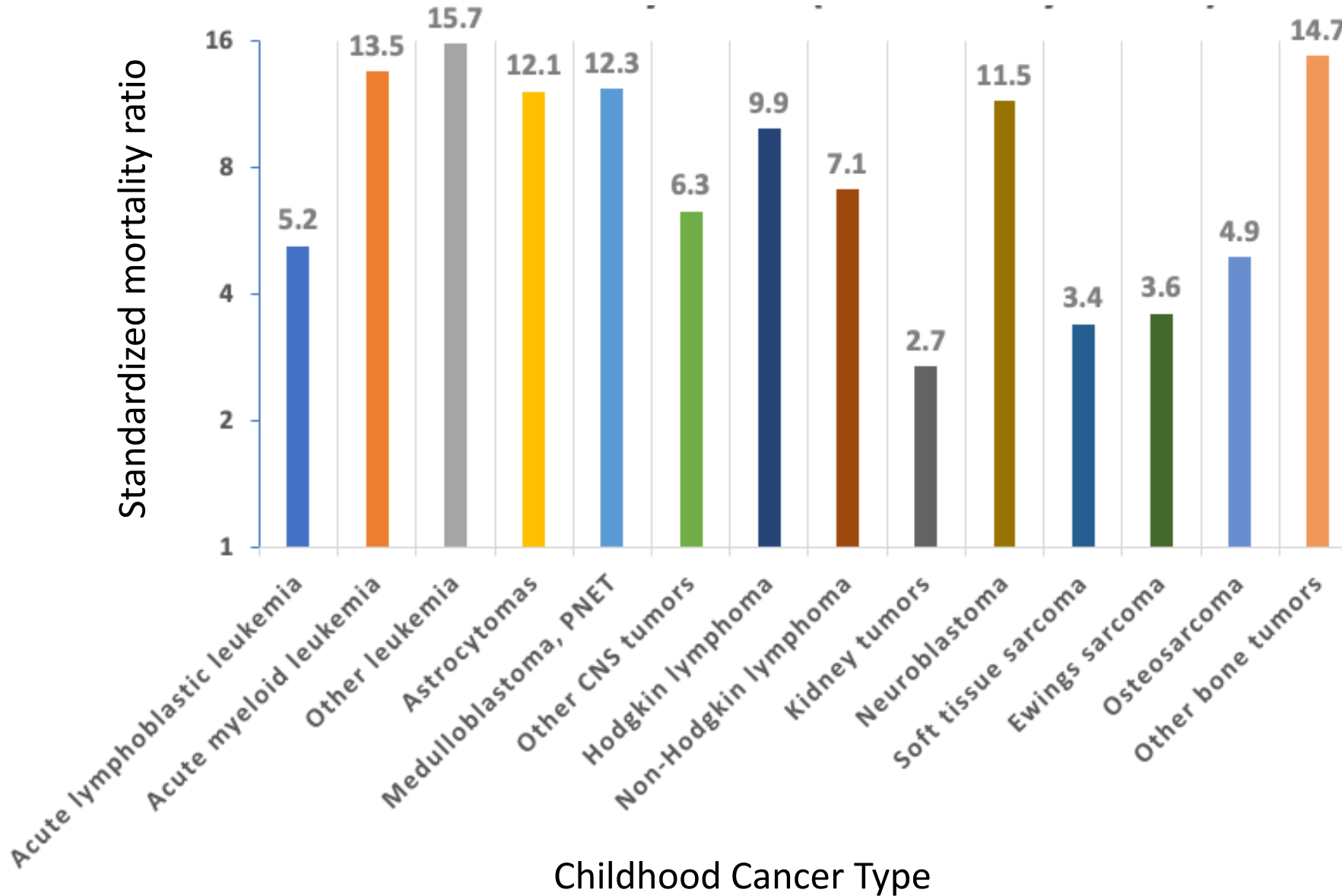
# Standardized Mortality Ratios of **Death due to Cardiac Diseases**



# Standardized Mortality Ratios of **Death due to Cardiac Diseases**



# Standardized Mortality Ratios of Death due to Pulmonary Diseases



# Afternoon Epi/Biostat WG Breakout Session

CCSS

## 1. Mortality Data/Analysis

### Mortality among 5-year survivors of childhood cancer: results over five decades of follow-up

Stephanie Dixon, MD  
St. Jude Children's Research Hospital



Qi Liu, Matthew Ehrhardt, Eric Chow, Kevin Oeffinger, Ann Mertens, Paul Nathan, Rebecca Howell, Wendy Leisenring, Kevin Krull, Kirsten Ness, Melissa Hudson, Leslie Robison, Yutaka Yasui, **Gregory Armstrong**

## 2. Prediction Modeling w/ Genetic Variables



Cindy Im, PhD  
University of Alberta

R21 (Impact Score 19): MPI (Cindy Im, Yan Yuan)  
"Treatment-specific genetic risk scores for late effects prediction in childhood, adolescent, and young adult cancer survivors"

## 3. Linking w/ External Data: Medicaid

### Association via Medicaid Outcomes/Healthcare data

- Disadvantaged population studies
- Uniformly verified (non self-report) late effects outcomes
- Cost studies
- Ancillary Study grant opportunity

Xu Ji, PhD  
Emory University



### R03 application:

Understanding the effect of the Affordable Care Act Medicaid Expansion in Adult Survivors of Childhood Cancer

Anne Kirchhoff, PhD  
University of Utah



## 4. Other Discussions, Q&A



## Mortality after cardiovascular (CV) disease in the Childhood Cancer Survivor Study

Wendy Bottinor, MD, MSCI

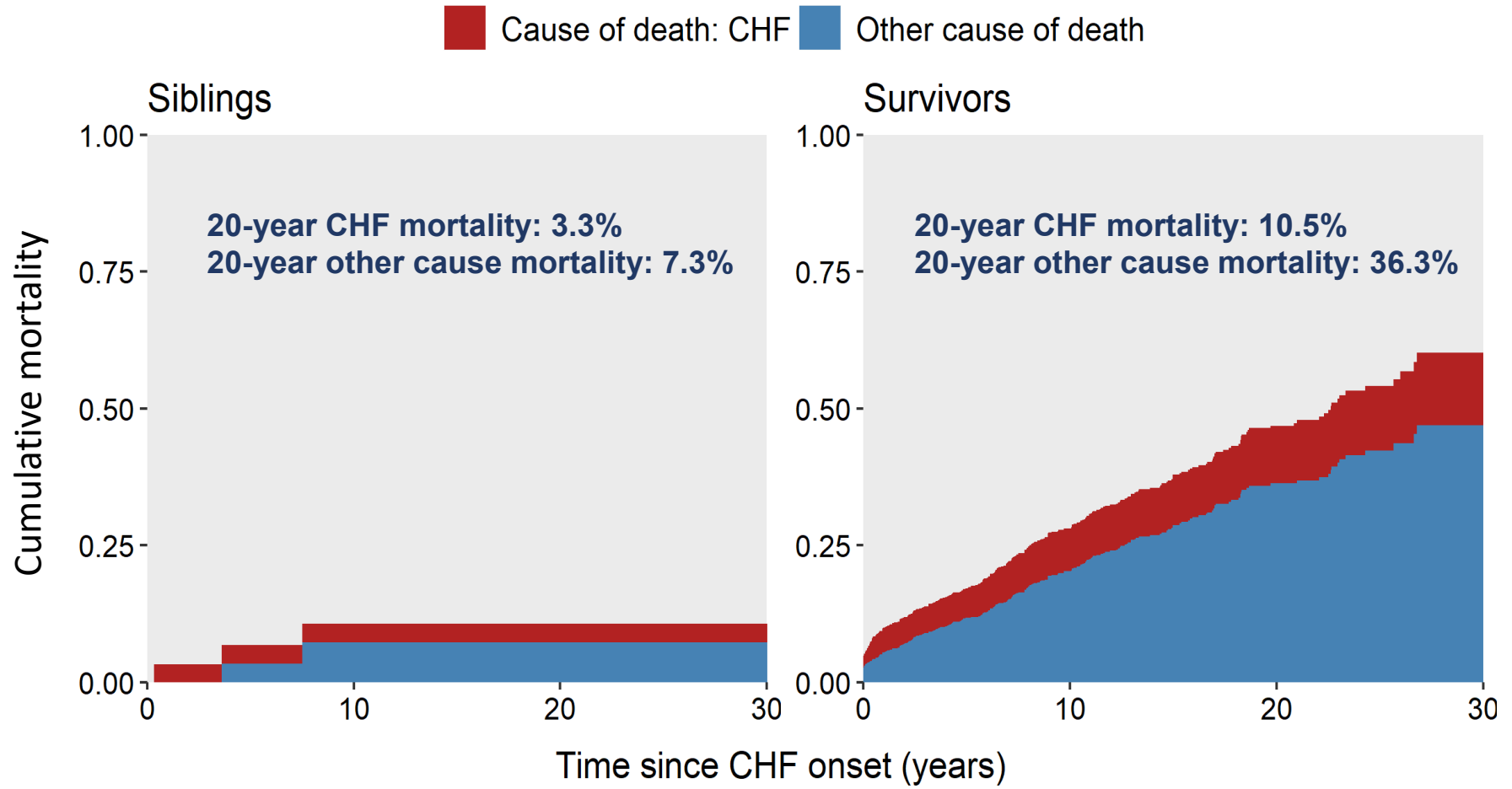
Virginia Commonwealth University

Cindy Im, Saro H. Armenian, Borah Hong, Rebecca  
M. Howell, Kirsten K. Ness, Kevin C. Oeffinger,  
Gregory T. Armstrong, Yutaka Yasui, **Eric J. Chow**

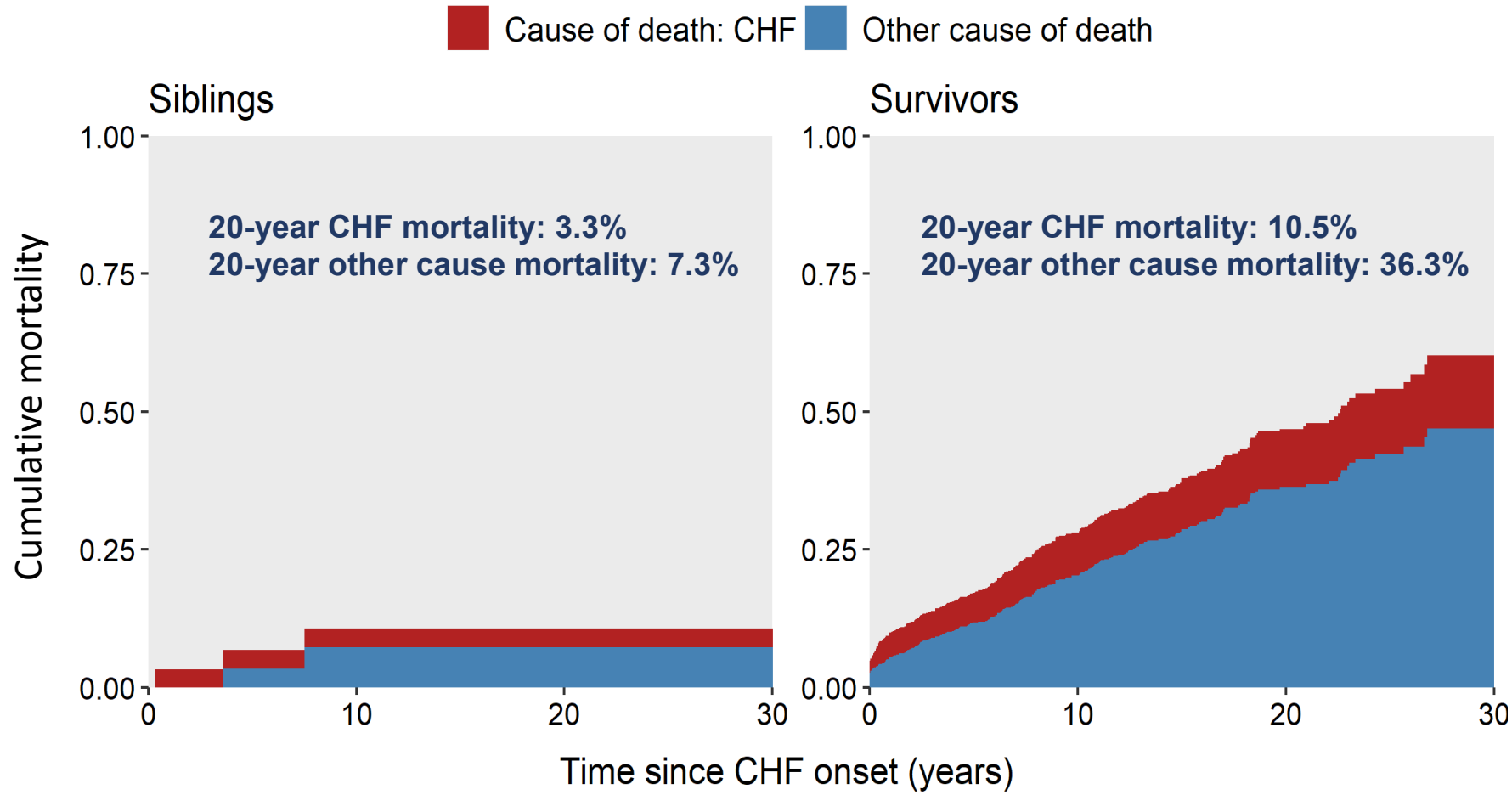


**Congestive Heart Failure (CHF):** 847 survivors (38% deceased); 31 siblings (16% deceased)

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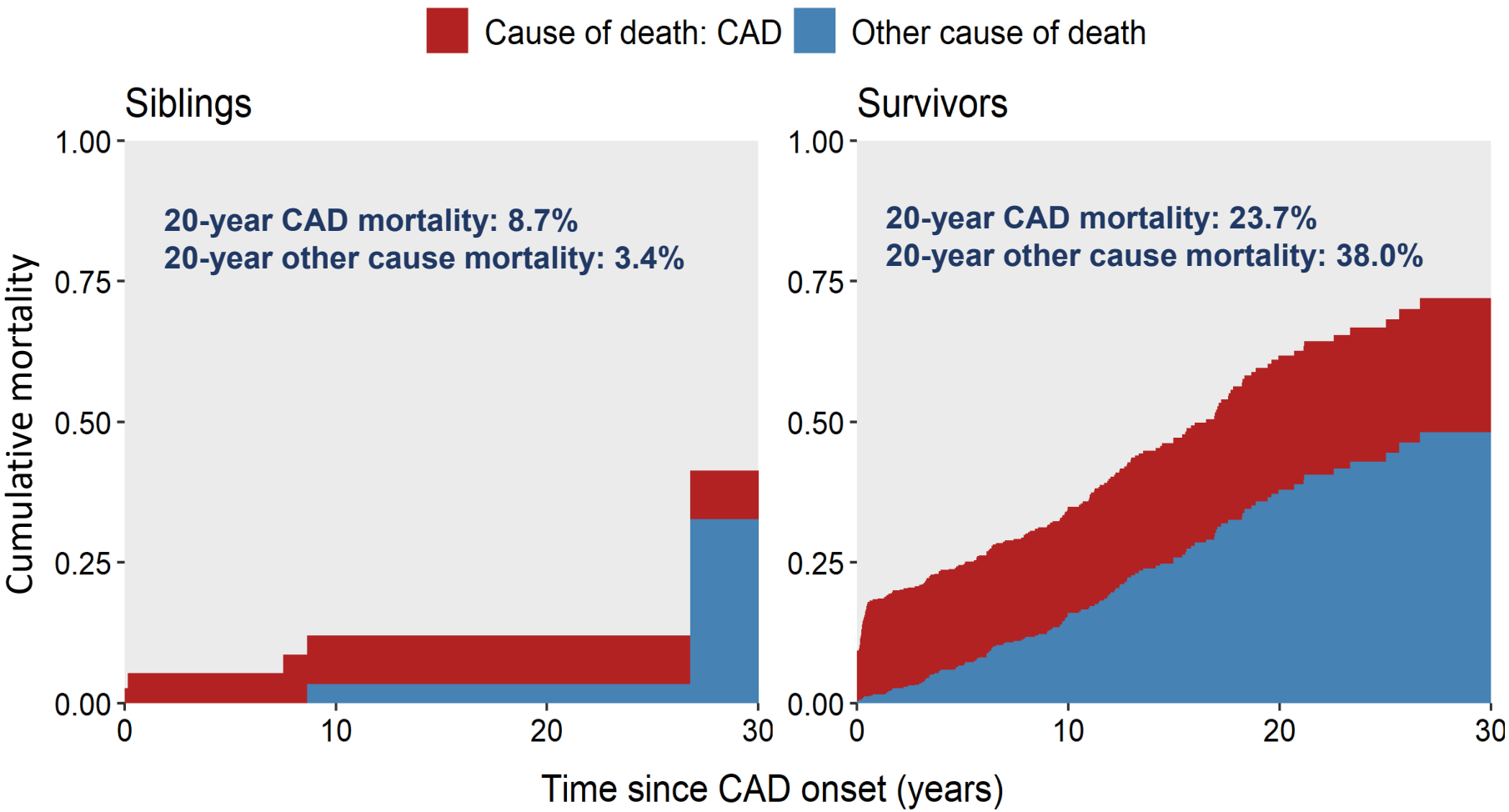
*Adjusted for age, sex, race, index year, smoking, CV risk conditions (hypertension, dyslipidemia, diabetes)*

Survivor risk after CHF (vs. siblings)		
	HR (95% CI)	P
All-cause mortality	7.32 (2.56 - 20.89)	<0.001
Mortality due to CHF	3.62 (0.48 - 27.29)	0.21

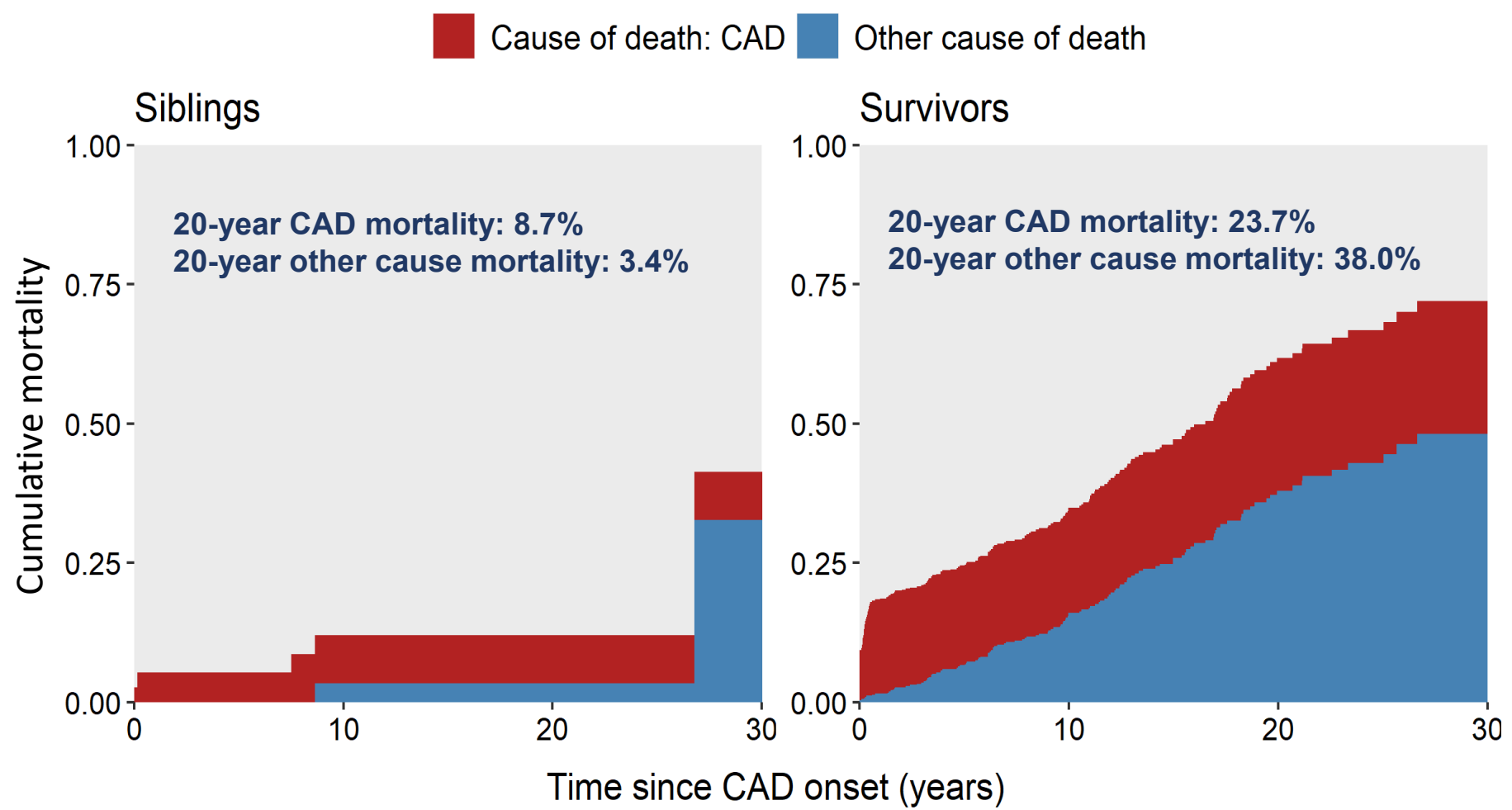
**Coronary Artery Disease (CAD):** 510 survivors (46% deceased); 39 siblings (18% deceased)



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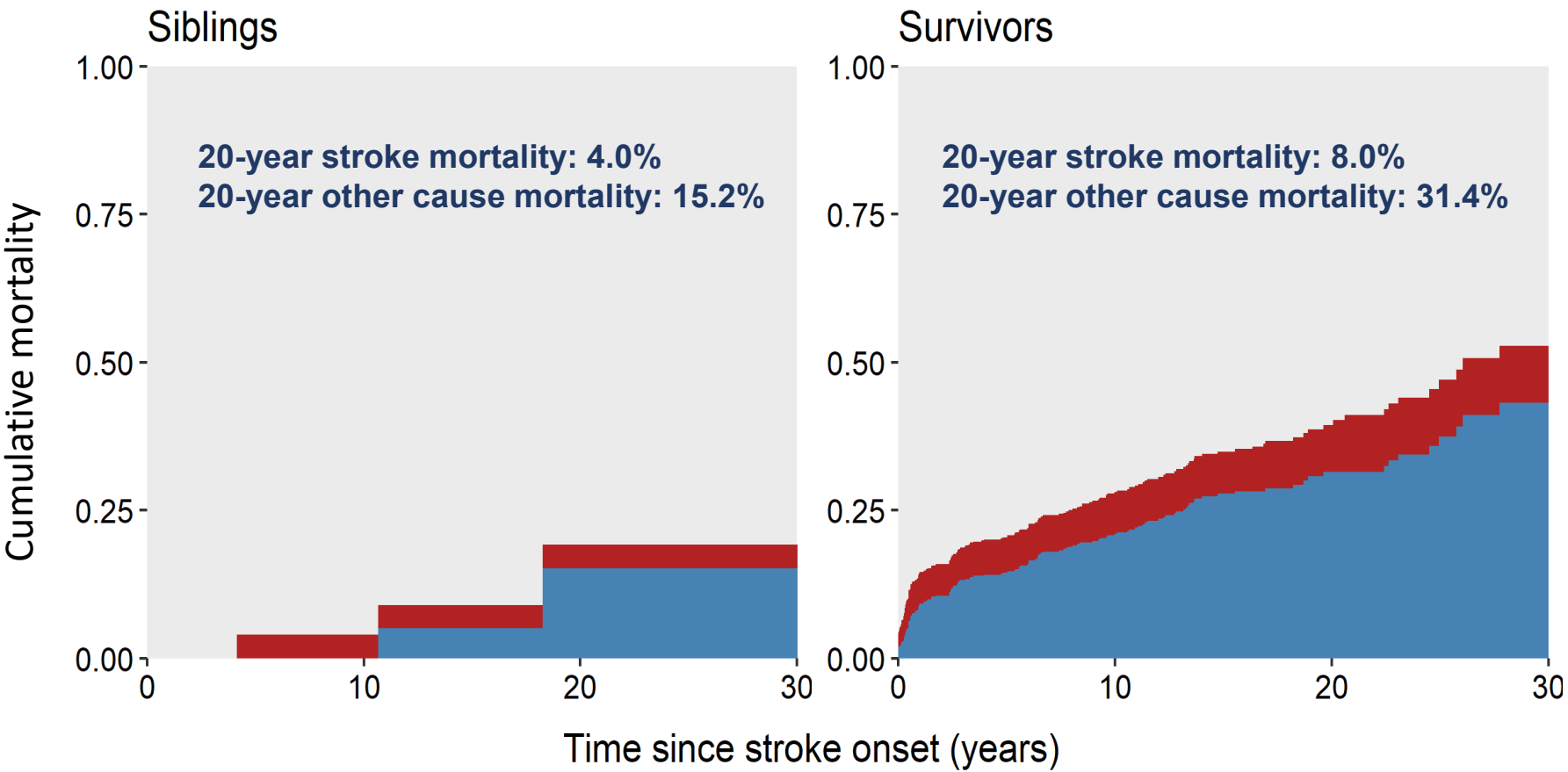
*Adjusted for age, sex, race, index year, smoking, CV risk conditions (hypertension, dyslipidemia, diabetes)*

Survivor risk after CAD (vs. siblings)*		
	HR (95% CI)	P
All-cause mortality	5.54 (2.37 - 12.93)	<0.001
Mortality due to CAD	3.70 (1.05 - 13.02)	0.04

**Stroke:** 568 survivors (34% deceased); 27 siblings (11% deceased)

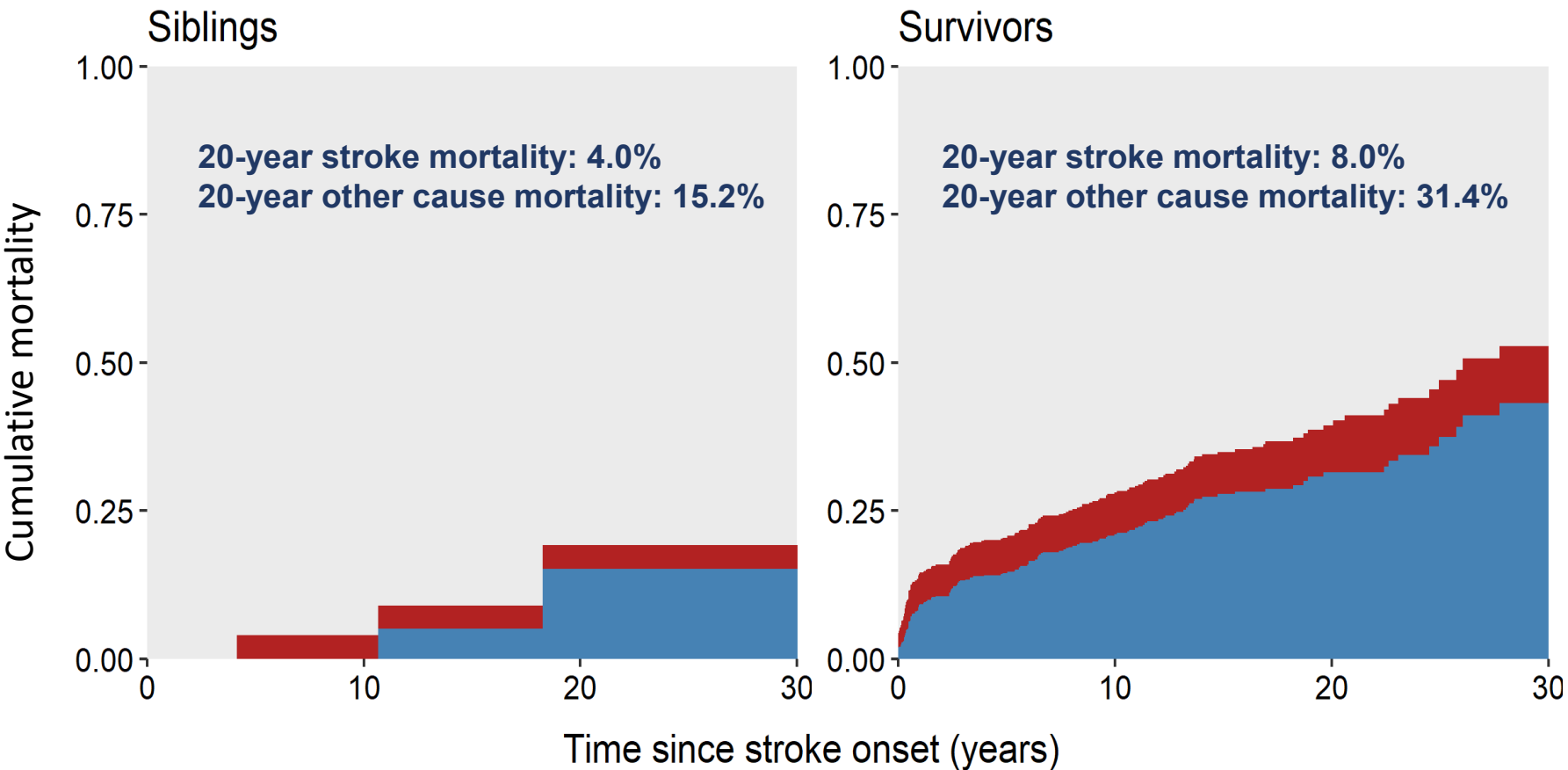
**Stroke:** 568 survivors (34% deceased); 27 siblings (11% deceased)

Cause of death: Stroke    Other cause of death



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Cause of death: Stroke    Other cause of death



*Adjusted for age, sex, race, index year, smoking, CV risk conditions (hypertension, dyslipidemia, diabetes)*

Survivor risk after stroke (vs. siblings)		
	HR (95% CI)	P
All-cause mortality	3.57 (1.12 - 11.37)	0.03
Mortality due to stroke	3.12 (0.40 - 24.32)	0.28



# Radiation dose is associated with increased all-cause and CV-specific mortality risk among survivors\*

CV disease	Radiation (per 10 Gy)	All Cause mortality		Cause Specific mortality		
		HR (95% CI)	P		HR (95% CI)	P
After CHF	Heart RT dose	1.27 (1.12 - 1.44)	<0.001	CHF-specific	1.43 (1.10 - 1.85)	0.01
After CAD	Heart RT dose	1.22 (1.06 - 1.41)	0.01	CAD-specific	1.35 (1.08 - 1.68)	0.01
After stroke	Heart RT dose	1.46 (1.00 - 2.12)	0.05	Stroke-specific	3.05 (1.28 - 7.28)	0.01
	Brain RT dose	1.24 (1.13 - 1.37)	<0.001	Stroke-specific	1.12 (0.92 - 1.38)	0.26

\*Adjusted for age, sex, race, index year, smoking, CV risk conditions (hypertension, dyslipidemia, diabetes), age at diagnosis, anthracycline dose

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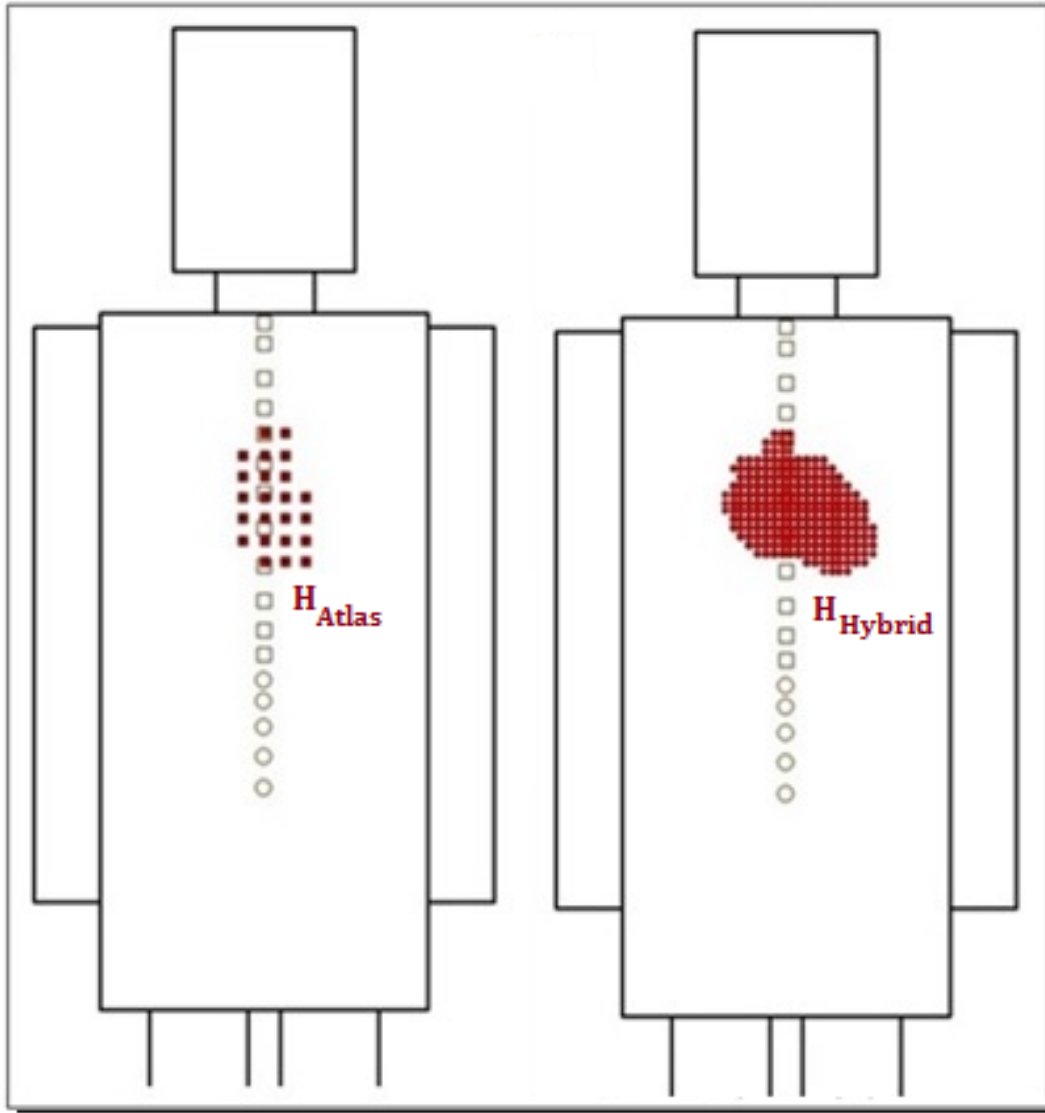
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## Radiation Therapy Related Cardiac Disease Risk in Childhood Cancer Survivors: Updated Dosimetry Analysis

Rebecca Howell, PhD, Suman Shrestha, MS  
MD Anderson Cancer Center

**James E. Bates**, Qi Liu, Susan A. Smith, Kevin Oeffinger, Eric Chow, Aashish C. Gupta, Constance A. Owens, Louis S. Constine, Bradford S. Hoppe, Wendy Leisenring, Ying Qiao, Rita E. Weathers, Laurence E. Court, Chelsea C. Pinnix, Stephen F. Kry, Daniel Mulrooney, Gregory T. Armstrong, Yutaka Yasui

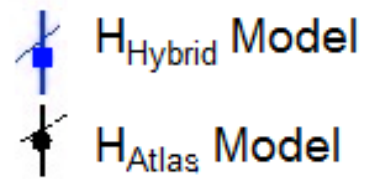




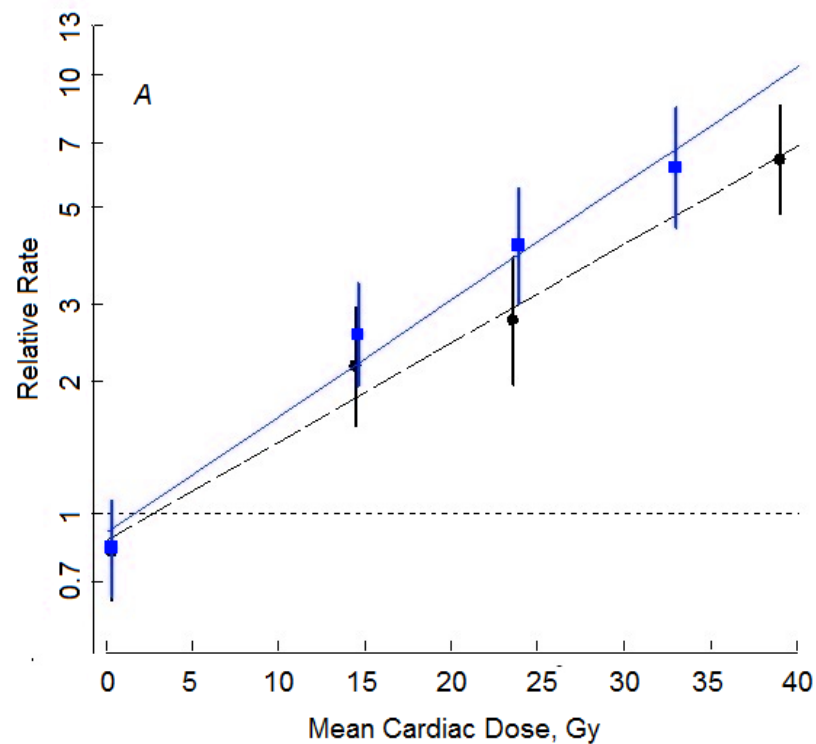
A simple atlas-based heart model ( $H_{Atlas}$ )

vs.

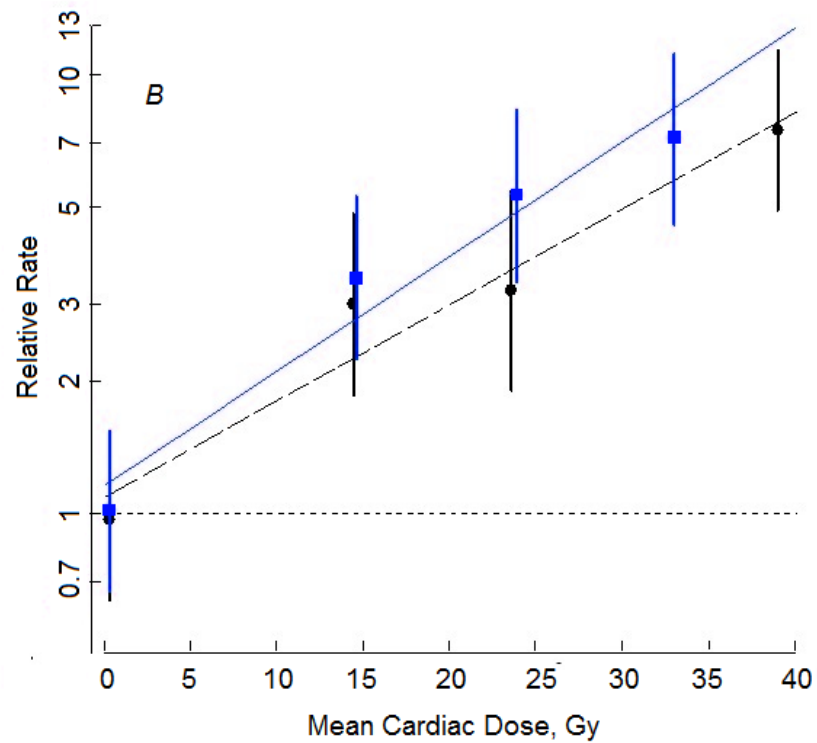
A high-resolution CT-based anatomically realistic age-scalable cardiac model ( $H_{Hybrid}$ )



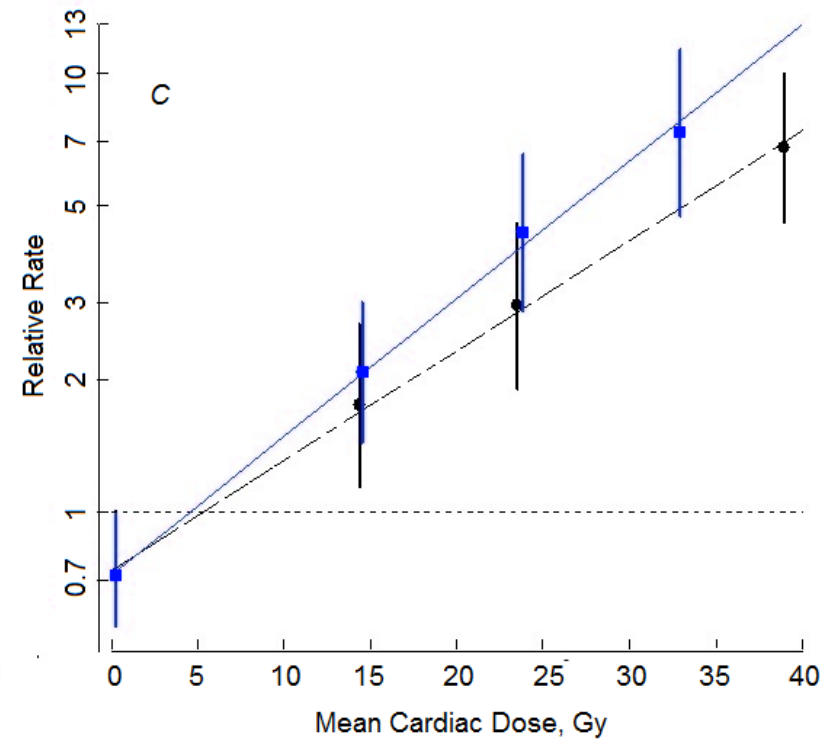
Any Cardiac Disease



Coronary Artery Disease



Congestive Heart Failure



# Associations of mean heart RT dose with cardiac disease risk

	Any Cardiac Disease			Coronary Artery Disease			Congestive Heart Failure		
Dose (Gy)	Relative Rates (95% CI)		P	Relative Rates (95% CI)		P	Relative Rates (95% CI)		P
	H <sub>Atlas</sub> (Bates et al.)	H <sub>Hybrid</sub> (This Work)		H <sub>Atlas</sub> (Bates et al.)	H <sub>Hybrid</sub> (This Work)		H <sub>Atlas</sub> (Bates et al.)	H <sub>Hybrid</sub> (This Work)	
No RT	Ref	Ref		Ref	Ref		Ref	Ref	
0.1 – 9.9	0.8 (0.6 – 1.1)	0.8 (0.6 - 1.1)	0.348	1.0 (0.6 – 1.5)	1.0 (0.7 - 1.5)	0.254	0.7 (0.5 – 1.0)	0.7 (0.5 - 1.0)	0.548
10 – 19.9	2.2 (1.6 – 2.9)	2.6 (2.0 - 3.3)	0.066	3.0 (1.9 – 4.8)	3.4 (2.2 - 5.3)	0.286	1.7 (1.1 – 2.7)	2.1 (1.4 - 3.0)	0.148
20 – 29.9	2.8 (2.0 – 3.8)	4.1 (3.0 - 5.5)	0.012	3.2 (1.9 – 5.4)	5.3 (3.4 - 8.3)	0.018	2.9 (1.9 – 4.6)	4.3 (2.9 - 6.5)	0.064
≥ 30	6.4 (4.8 – 8.5)	6.1 (4.5 - 8.4)	0.618	7.5 (4.9 – 11.4)	7.1 (4.6 - 11.2)	0.372	6.7 (4.6 – 9.9)	7.3 (4.7-11.4)	0.580



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# Approved Concept Proposal #1

CCSS

## Association of Individual and Neighborhood Characteristics and Adverse Outcomes in Childhood Cancer Survivors

Carrie Howell, PhD  
University of Alabama  
at Birmingham



Lena Winestone, MD  
University of California  
San Francisco



# Approved Concept Proposal #1

CCSS

Geocoded residential & local social-  
and physical-environmental data  
(e.g., small area SES) of CCSS  
participants will be soon available!



**Carrie Howell, PhD**  
University of Alabama  
at Birmingham



**Kiri Ness, PT, PhD, FAPTA**  
St. Jude Children's  
Research Hospital

The screenshot shows the Geocodio website. At the top is the Geocodio logo and a navigation bar with links for Pricing, Customers, Compare, Product, Security, Privacy, Help, and Contact. There are buttons for 'LOG IN' and 'SIGN UP'. The main heading is 'Hassle-free geocoding', followed by two buttons: 'UPLOAD SPREADSHEET' and 'GET AN API KEY'. Below this is a paragraph: 'Straightforward and easy-to-use geocoding, reverse geocoding, and data matching for US and Canadian addresses.' A section titled 'Used by thousands of happy customers' displays a grid of logos for various companies including Oracle, Associated Press, Bonobos, Stanford, ProPublica, McKesson, Expedia, Nielsen, Amazon, OdysseyRE, TransUnion, PitchBook, American Red Cross, Aetna, AAA, FORTER, and Sodexo. At the bottom, a section titled 'Geocoding is only one step of your process. Geocodio makes it fast and painless.' lists six features: Batch Geocoding API, Flexible Terms of Use, Geocode Spreadsheets, Spelling Correction and Address Parsing, Enrich Your Data, and Reverse Geocoding.

geocodio

Pricing Customers Compare Product Security Privacy Help Contact LOG IN SIGN UP

## Hassle-free geocoding

UPLOAD SPREADSHEET GET AN API KEY

Straightforward and easy-to-use geocoding, reverse geocoding, and data matching for **US and Canadian** addresses.

Used by thousands of happy customers

ORACLE AP Associated Press BONOBOs Stanford PROPUBLICA

McKESSON Expedia nielsen amazon OdysseyRE TransUnion PitchBook

American Red Cross aetna AAA FORTER sodexo

### Geocoding is only one step of your process. Geocodio makes it fast and painless.

- Batch Geocoding API**  
Whether you have 100 or 100,000,000 addresses, we can help you.
- Flexible Terms of Use**  
Store, share, and reuse the data however you want with no restrictions.
- Geocode Spreadsheets**  
Upload a spreadsheet of addresses or coordinates and enrich data all in one go.
- Spelling Correction and Address Parsing**  
Parse, standardize, and complete addresses. Correct minor typos and inconsistencies.
- Enrich Your Data**  
Add FIPS codes, time zones, Congressional districts, and more to addresses or coordinates.
- Reverse Geocoding**  
Turn latitude/longitude coordinates into approximate addresses.

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# Approved Concept Proposal #2

CCSS

## Use of an Incentive to Increase Biologic Sample (Oragene) Return

Aaron McDonald, PhD  
**Project Director of CCSS**  
St. Jude Children's Research Hospital



# Approved Concept Proposal #3

CCSS

Long-term cost-effectiveness of cancer predisposition syndrome identification strategies in survivors of pediatric leukemia, brain tumors or bone/soft-tissue sarcomas

Catherine Goudie, MD, FRCPC  
McGill University



## Efficacy and Cost-effectiveness of the Children's Oncology Group Long-term Follow-up Screening Guidelines for Childhood Cancer Survivors at Risk of Colorectal Cancer

Van T. Nghiem, PhD  
University of Alabama at Birmingham





# Approved Concept Proposal #5

CCSS

## Mortality Due to Colorectal Cancer Among Survivors of Childhood Cancer

Ajay Major, MD, MBA  
University of Chicago





# Ancillary Study #1

CCSS

**Title:** Cost effectiveness of breast cancer screening guidelines for female survivors of pediatric cancers

**Dates of Funding:** 7/17 - 6/20

**Funding Source:** American Cancer Society

**Award:** \$527,000

**Study Aims:** 1) Examine the cost-effectiveness of 1) annual clinical breast examination, 2) annual breast tomosynthesis vs. MRI as adjunct to mammography.

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Principal Investigator

**Lennie Wong, PhD**

City of Hope



# Ancillary Study #2

CCSS

**Title:** Innovative Statistical Analysis for Genome-Wide Data with Interval-Censored Outcomes of Oral Health

**Dates of Funding:** 05/20 - 04/22

**Funding Source:** National Institutes of Health (R03)

**Award:** \$189,729

**Study Aims:** Develop nonparametric screening method for ultrahigh-dimensional interval-censored data

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Co-Principal Investigator

**Yimei Li, PhD**

St. Jude Children's  
Research Hospital



Co-Principal Investigator

**Ryan Sun, PhD**

MD Anderson Cancer  
Center



Childhood Cancer  
Survivor Study  
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resource

# Ancillary Study #3

CCSS

**Title:** Late Effects Prediction using Clinical Phenotypes and Whole Genome Sequencing

**Dates of Funding:** 4/17 - 3/22

**Funding Source:** National Institutes of Health (RO1)

**Award:** \$3,457,455

**Study Aims:** 1) Build individual risk prediction models with the SJLIFE cohort for 11 outcomes including meningioma, basal cell carcinoma, and multiple subsequent neoplasms, 2) Validate the risk prediction models in a larger cohort study with higher SN counts (CCSS).

---

Co-Principal Investigator

**Yutaka Yasui, PhD**

St. Jude Children's  
Research Hospital



Co-Principal Investigator

**Jinghui Zhang, PhD**

St. Jude Children's  
Research Hospital



Childhood Cancer  
Survivor Study  
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resource

# Current Top Priorities

CCSS

- (1) Close collaboration with CCSS Genetics Working Group and the NCI's DCEG in analyses of SNP array and whole genome/exome sequencing data evaluating genetic susceptibility to a variety of late effects, including gene main effects and gene by treatment/environment interactions
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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 Chemaïtilly • 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>



Cindy Im, PhD  
University of Alberta



R21 (Impact Score 19): MPI (Cindy Im, Yan Yuan)

“**Treatment-specific genetic risk scores** for late effects prediction in childhood, adolescent, and young adult cancer survivors”

Childhood Cancer  
Survivor Study  
An NCI-funded  
resource

# Afternoon Epi/Biostat WG Breakout Session

CCSS

## 1. Mortality Data/Analysis

Mortality among 5-year survivors of childhood cancer:  
results over five decades of follow-up

Stephanie Dixon, MD  
St. Jude Children's Research Hospital



Qi Liu, Matthew Ehrhardt, Eric Chow, Kevin Oeffinger, Ann Mertens, Paul Nathan, Rebecca Howell, Wendy Leisenring, Kevin Krull, Kirsten Ness, Melissa Hudson, Leslie Robison, Yutaka Yasui, Gregory Armstrong

## 2. Prediction Modeling w/ Genetic Variables



Cindy Im, PhD  
University of Alberta

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## 3. Linking w/ External Data: Medicaid

Association via Medicaid Outcomes/Healthcare data

- Disadvantaged population studies
- Uniformly verified (non self-report) late effects outcomes
- Cost studies
- Ancillary Study grant opportunity

Xu Ji, PhD  
Emory University



R03 application:

Understanding the effect of  
the Affordable Care Act  
Medicaid Expansion in Adult  
Survivors of Childhood Cancer

Anne Kirchhoff, PhD  
University of Utah



## 4. Other Discussions, Q&A



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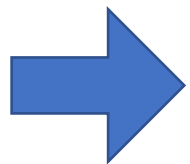
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CCSS

Title: Improving Cancer Screening Guidelines for Survivors of Childhood Cancer

Dates of Funding: 9/16-3/22

Funding Source: American Cancer Society

Title: Genetic testing to guide pediatric cancer care and follow up: using anthracycline-associated cardiac toxicity as a model for the future

Dates of Funding: 9/18-8/23

Funding Source: NIH (R01)



**Jennifer Yeh, PhD**

Boston Children's Hospital  
Harvard Medical School

Title: Cost effectiveness of breast cancer screening guidelines for female survivors of pediatric cancers  
Dates of Funding: 7/17 - 6/20  
Funding Source: American Cancer Society  
Award: \$527,000  
Study Aims: 1) Examine the cost-effectiveness of 1) annual clinical breast examination, 2) annual breast as adjunct to mammography.

Principal Investigator  
**Lennie Wong, PhD**  
City of Hope



Long-term cost-effectiveness of cancer predisposition syndrome identification strategies in survivors of pediatric leukemia, brain tumors or bone/soft-tissue sarcomas

**Catherine Goudie, MD, FRCPC**  
McGill University



Efficacy and Cost-effectiveness of the Children's Oncology Group Long-term Follow-up Screening Guidelines for Childhood Cancer Survivors at Risk of Colorectal Cancer

**Van T. Nghiem, PhD**  
University of Alabama at Birmingham



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# Current Top Priorities

CCSS

## 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)

THE LANCET  
Oncology

*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\**

### Age-specific Risk Prediction for Premature Ovarian Insufficiency in Childhood Cancer Survivors

A report from the Childhood Cancer Survivor Study

---

Presented by Yan Yuan PhD

School of Public Health, University of Alberta, Canada

Authors: Zhe (Michael) Lu, Sogol Mostoufi-Moab, Yutaka Yasui, Eric Chow, Rebecca Howell, Gregory T. Armstrong, Paul Nathan\*, Yan Yuan\*

Elastic Net  
Extreme Gradient Boosting  
Ensemble

Yan Yuan, PhD  
University of Alberta





## Prediction of Health-related Quality of Life from Longitudinal Self-reported Symptom Patterns in Adults Survivors of Childhood Cancer



**ML4H: Machine Learning for Health**

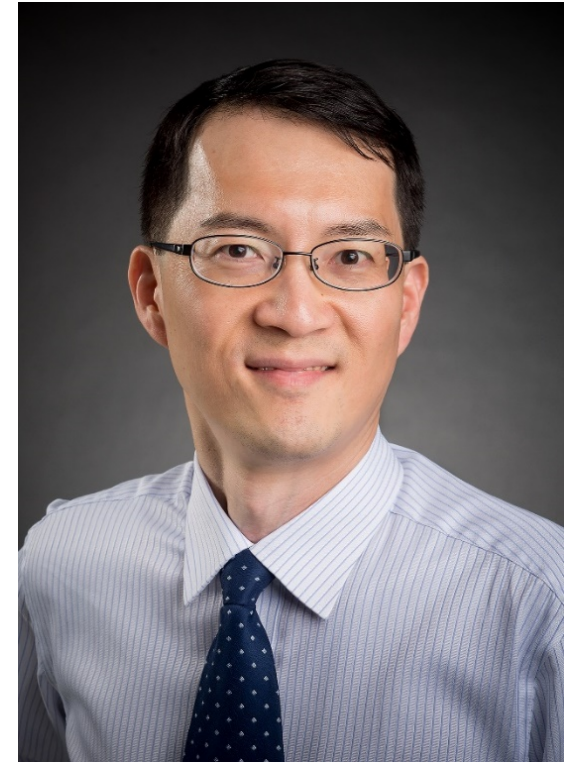
Workshop at NeurIPS 2019

[papers](#) [extended abstracts](#) [organizers](#) [program committee](#) [schedule](#) [speakers](#)

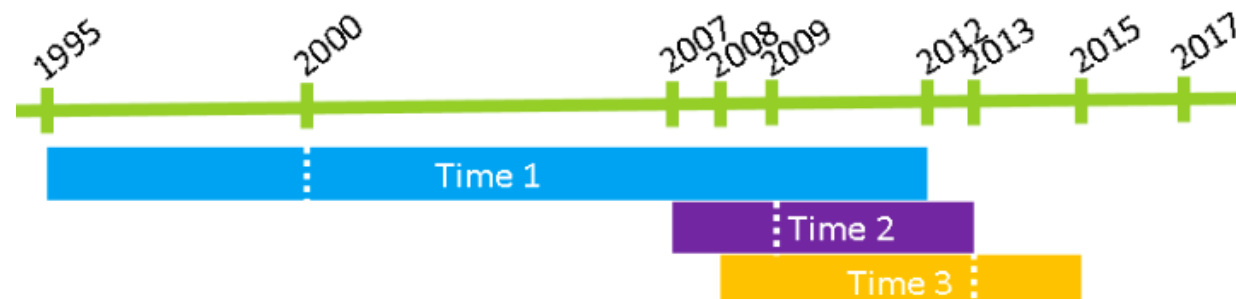
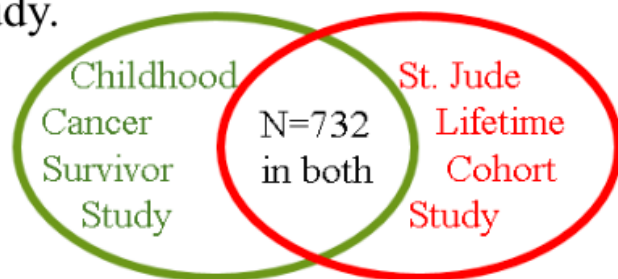


Farideh  
Bagherzadeh-  
Khiabani, MS  
University of Alberta

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



## Childhood Cancer Survivor Study and St. Jude Lifetime Cohort Study.



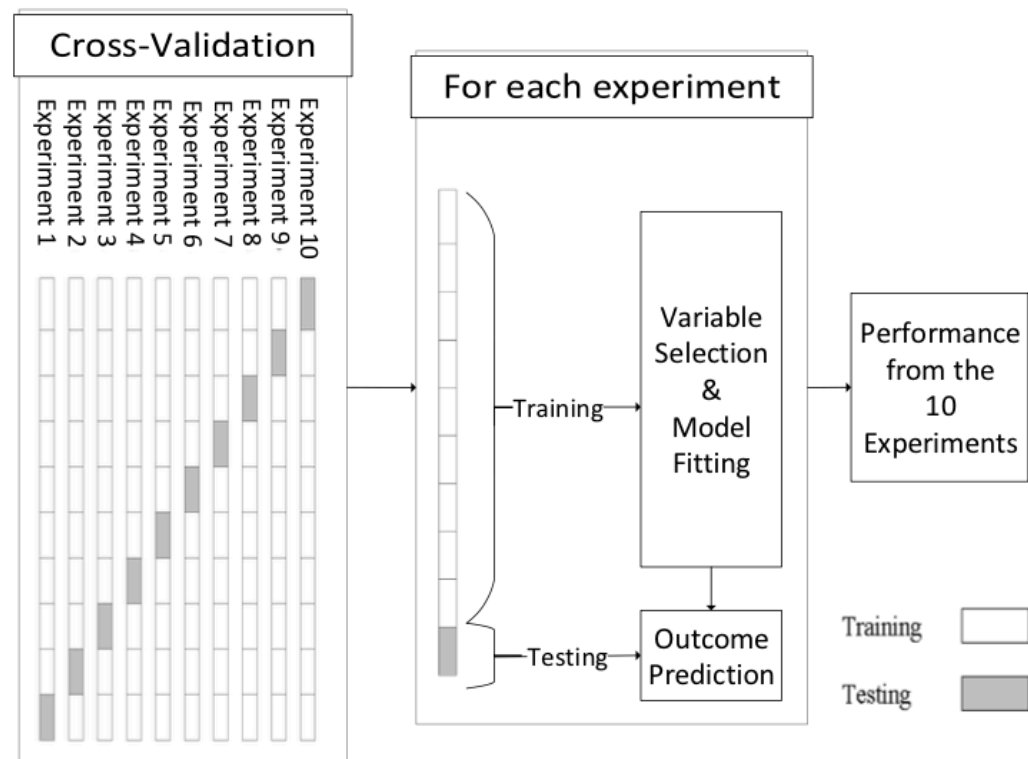
### Machine Learning Procedure

#### Modeling

We used elastic-net for regularized linear regression and Bayesian Information Criterion (BIC) to select its best tuning parameters.

#### Evaluation

We used 10-fold cross-validated Area Under the Curve (AUC) for dichotomous HRQoL status (impaired vs. non-impaired) as performance measure.

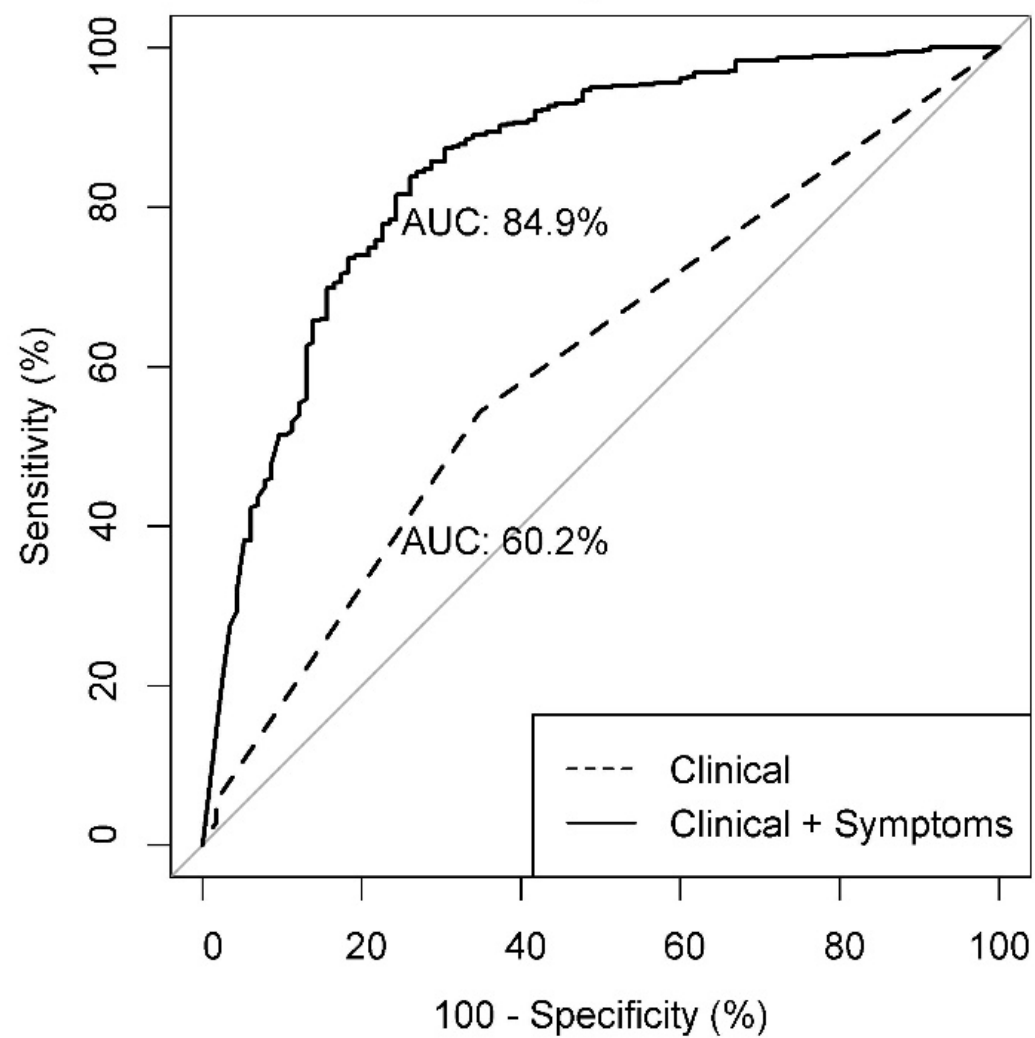


**10-fold cross-validation procedure to obtain cross-validated performance measure at a glance**

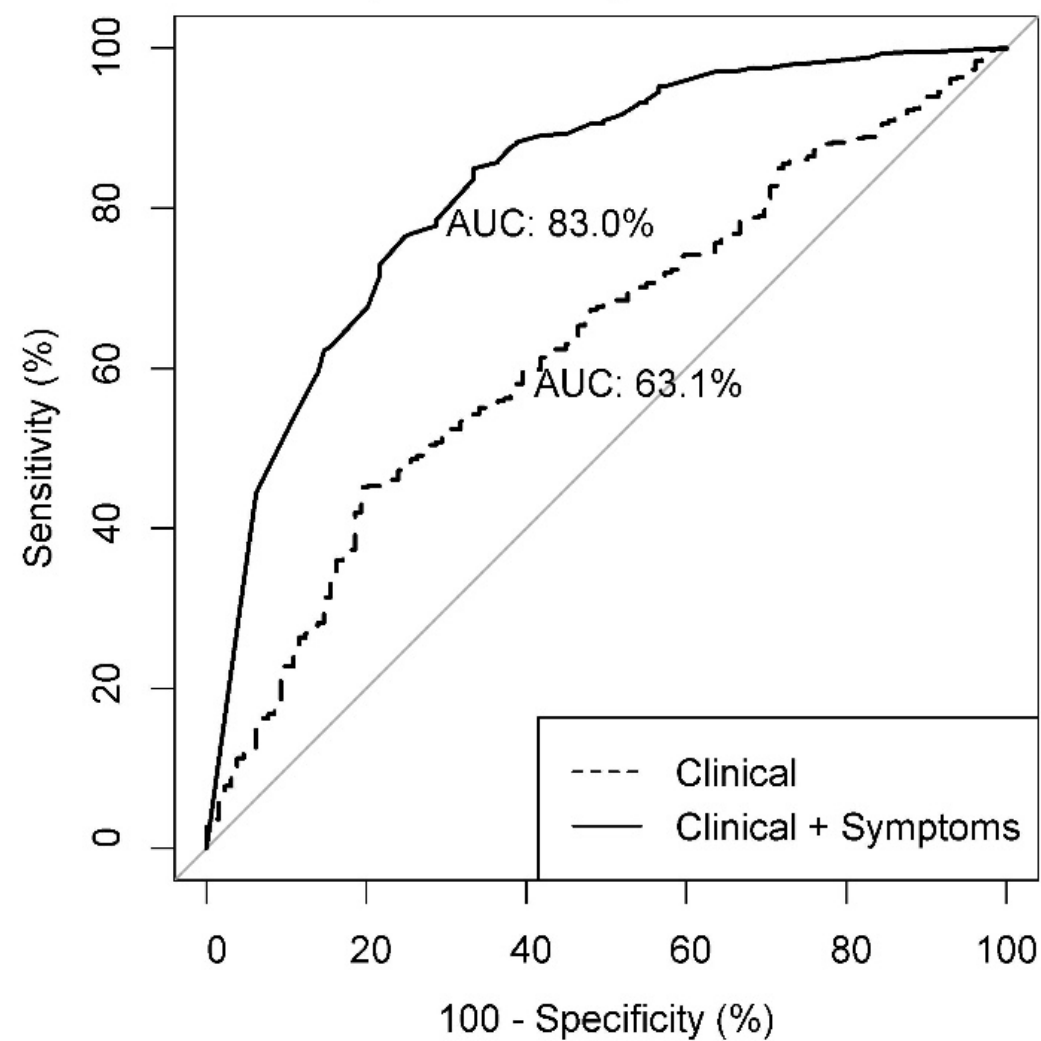


Predictor Category	Predictor Subcategory	Predictor Name	Symptom Pattern Type	Times Involved	Estimate <sup>1</sup>	P-value <sup>1</sup>	Importance <sup>2</sup>
Clinical Model <sup>1</sup>							
(Intercept)					51.265	<0.001	-
Clinical	Demographic	Female (vs. Male)	Feature Engineering		-2.891	<0.001	10
Clinical	Treatment	Amputation			4.42	0.009	4
Symptom Model <sup>2</sup>							
(Intercept)					45.092	<0.001	-
Mental	Domain	Depressive	Increase	T2 to T3	0.151	0.782	5
Mental	Domain	Depressive	Consistent Presence	T1 & T2 & T3	-5.173	<0.001	9
Mental	Item	Depressive : Feeling no interest in things	Consistent Absence	T1 & T2 & T3	2.545	0.009	10
Mental	Item	Depressive : Feeling no interest in things	Consistent Absence	T1& T2	-4.751	0.003	4
Mental	Item	Depressive : Feeling hopeless about the future	Increase	T2 to T3	-2.779	0.113	4
Mental	Item	Depressive : Feeling hopeless about the future	Consistent Absence	T1 & T2 & T3	0.803	0.459	10
Mental	Item	Depressive : Feelings of worthlessness	Consistent Absence	T1 & T2 & T3	1.061	0.322	10
Mental	Domain	Anxiety	Consistent Presence	T2 & T3	-3.331	0.009	4
Mental	Item	Anxiety : Nervousness or shaking inside	Consistent Absence	T1 & T2 & T3	0.73	0.386	9
Mental	Item	Anxiety : Suddenly scared for no reason	Consistent Presence	T1 & T2	-12.536	<0.001	7
Mental	Item	Anxiety : Feeling tense or keyed up	Consistent Presence	T1 & T2 & T3	-2.796	0.075	4
Mental	Item	Anxiety : Feeling tense or keyed up	Consistent Absence	T1 & T2 & T3	1.166	0.172	10
Mental	Item	Anxiety : So restless cannot sit still	Consistent Absence	T1 & T2 & T3	0.668	0.423	7
Mental	Item	Anxiety : So restless cannot sit still	Consistent Presence	T2 & T3	-6.141	0.006	6
Mental	Domains	Summary	Consistent Absence	T1 & T2 & T3	1.304	0.154	9
Physical	Item	Memory: Problems with learning or memory	Consistent Absence	T1 & T2 & T3	1.542	0.014	7
Physical	Domain	Fatigue: Fatigue	Consistent Absence	T1 & T2 & T3	0.764	0.577	6
Physical	Item	Fatigue: Feeling weak	Consistent Absence	T1 & T2 & T3	0.124	0.932	7
Physical	Item	Fatigue: Feeling weak	Consistent Presence	T2 & T3	-4.634	0.008	8
All	Items	Summary	Increase	T2 to T3	-0.345	0.012	10

**Mental Component Score**



**Physical Component Score**



## Major Strength/Opportunity

- Discover, support **junior investigators w/ methodology interest**
- Focus on methodological issues **of high impact**
- **Method webinar or workshop** to expand the use of CCSS data and disseminate accumulated methodological knowledge

## Major Threat/Challenges

- **Abundant demands** on method applications to projects, working with many MS-level analysts
- **Lack of emphasis** on methodological work by methodologists themselves
- **Relatively small number** of methodologists