

# Air Pollution and Respiratory Healthcare Events Among Childhood Cancer Survivors

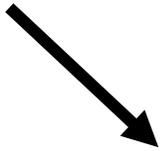
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University of Utah School of Medicine

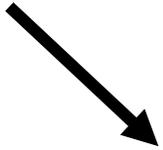
Collaborative on Health and the Environment Webinar

*I have no conflicts of interest.*

**Environmental  
exposure**



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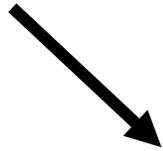
Childhood leukemias

*Filippini, 2019*

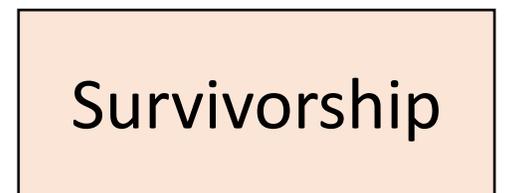
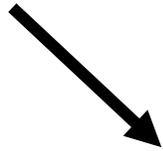
Childhood central nervous system  
tumors

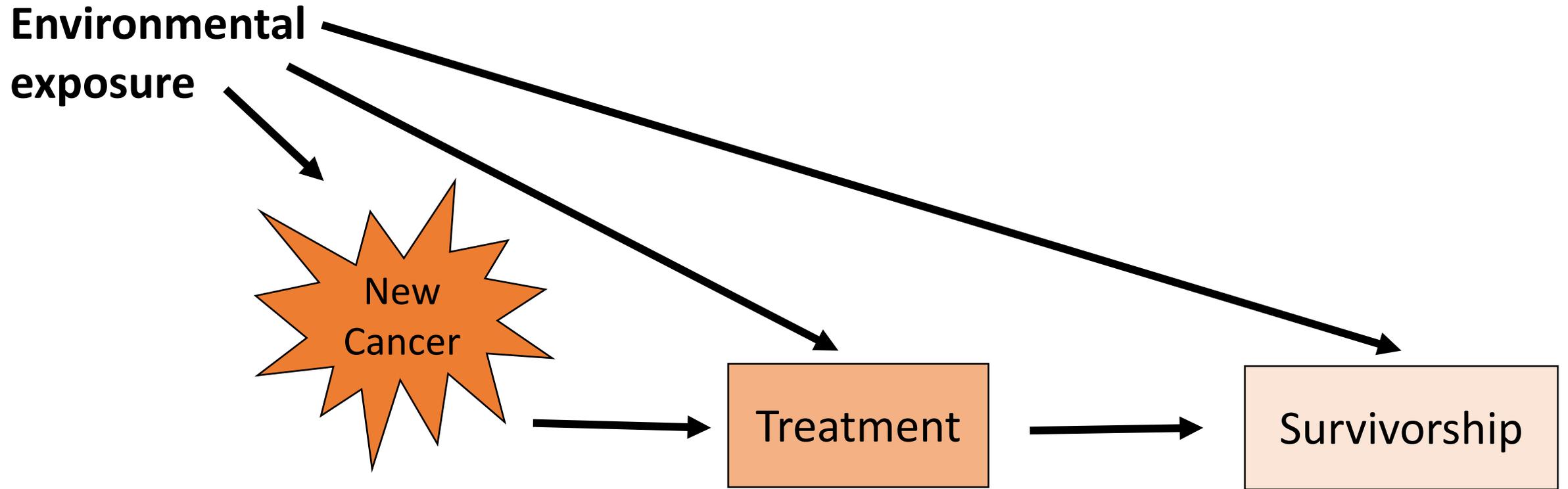
*Ehrenstein, 2016*

**Environmental  
exposure**



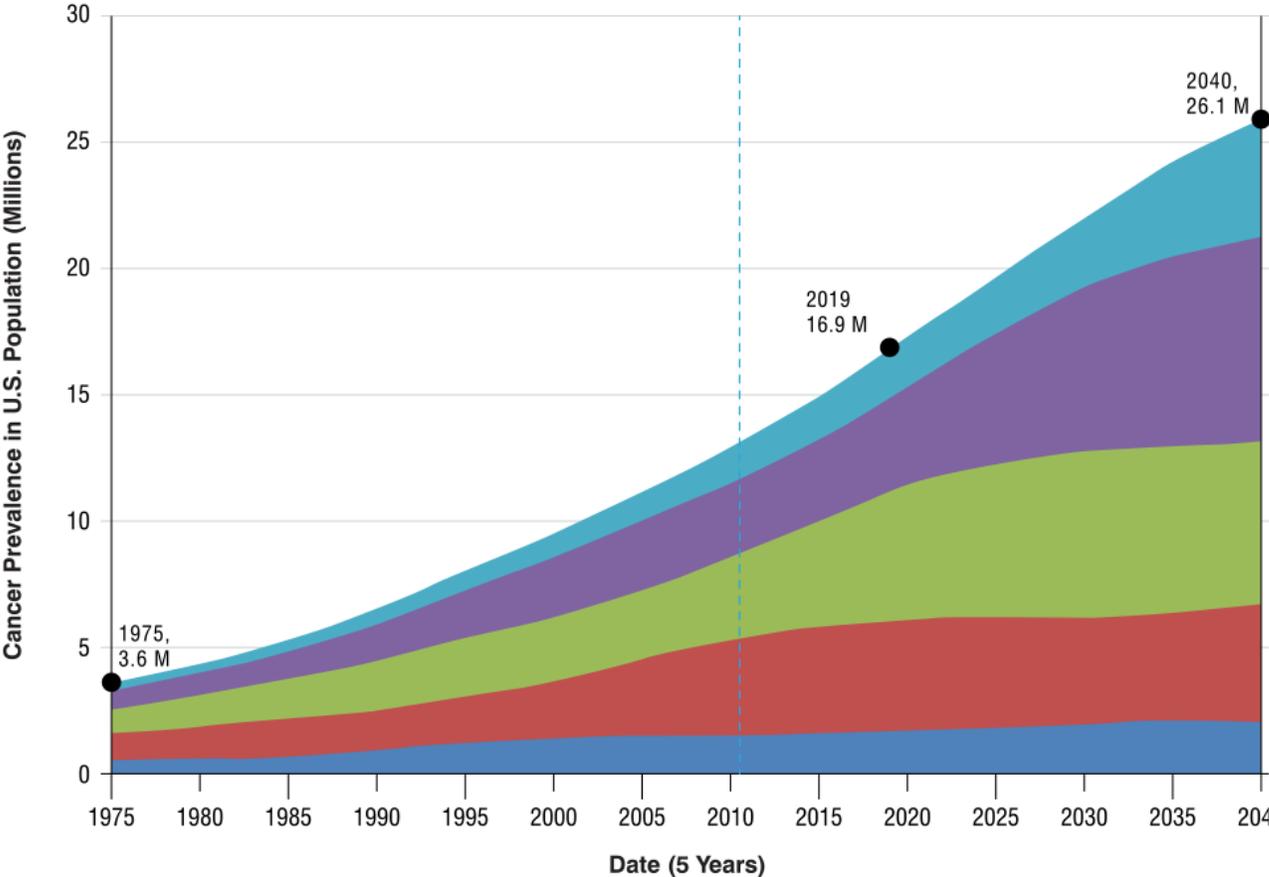
**Environmental  
exposure**





**Environmental exposures occur along the entire cancer continuum, from diagnosis to survivorship**

# Cancer Prevalance and Projections in U.S. Population from 1975–2040



**KEY**

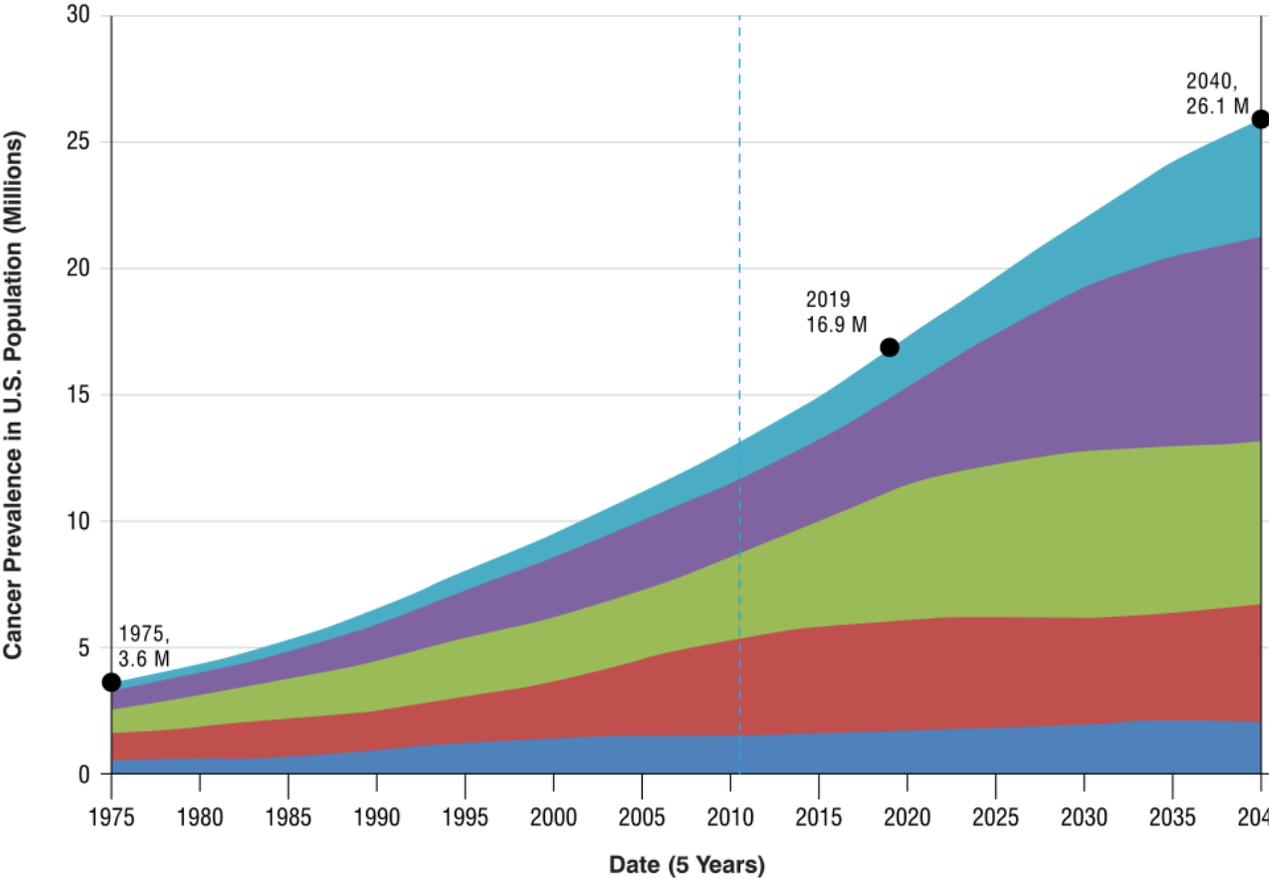
Signifies the year at which the first baby boomers (those born 1946–1964) turned 65 years old.

**Age**

- <50
- 50–64
- 65–74
- 75–84
- 85+

REFERENCE: Bluethmann SM, Mariotto AB, Rowland, JH. Anticipating the “Silver Tsunami”: Prevalence Trajectories and Comorbidity Burden among Older Cancer Survivors in the United States. Cancer Epidemiol Biomarkers Prev. 2016;25:1029-1036.

# Cancer Prevalance and Projections in U.S. Population from 1975–2040



**Estimated 16.9 million persons diagnosed with cancer in 2019**

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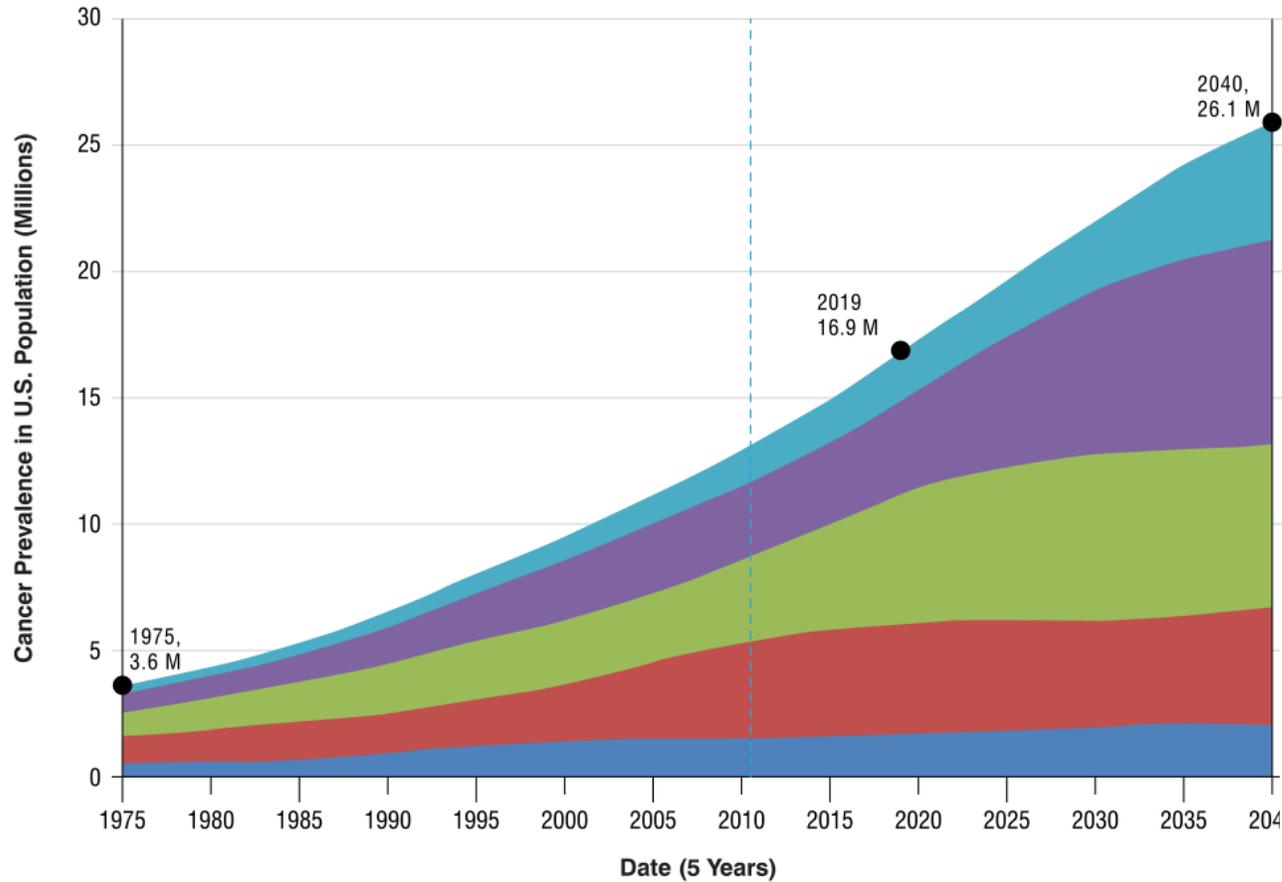
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# Cancer Prevalance and Projections in U.S. Population from 1975–2040



Estimated 26.1 million persons diagnosed with cancer in 2040



Estimated 16.9 million persons diagnosed with cancer in 2019

### KEY

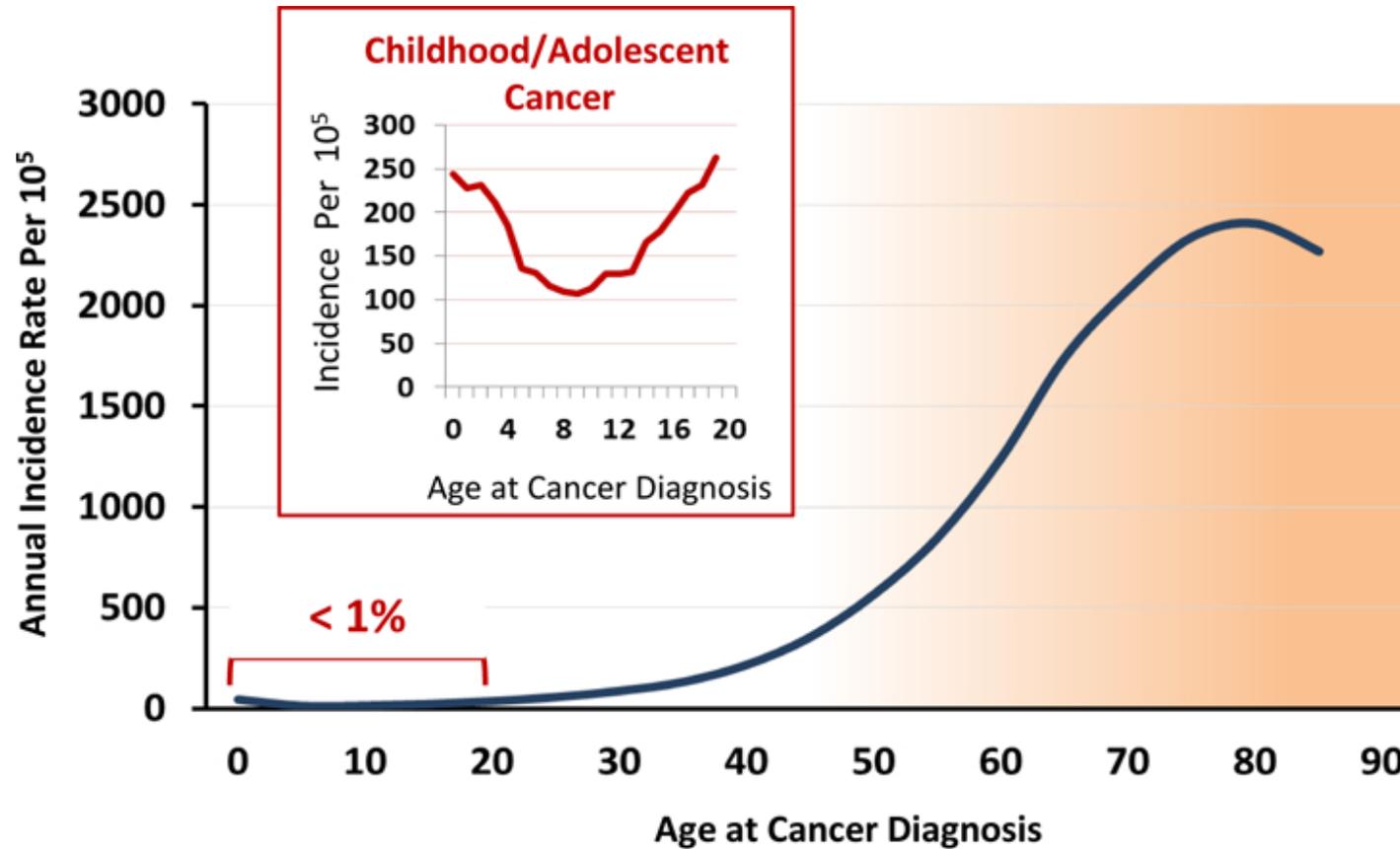
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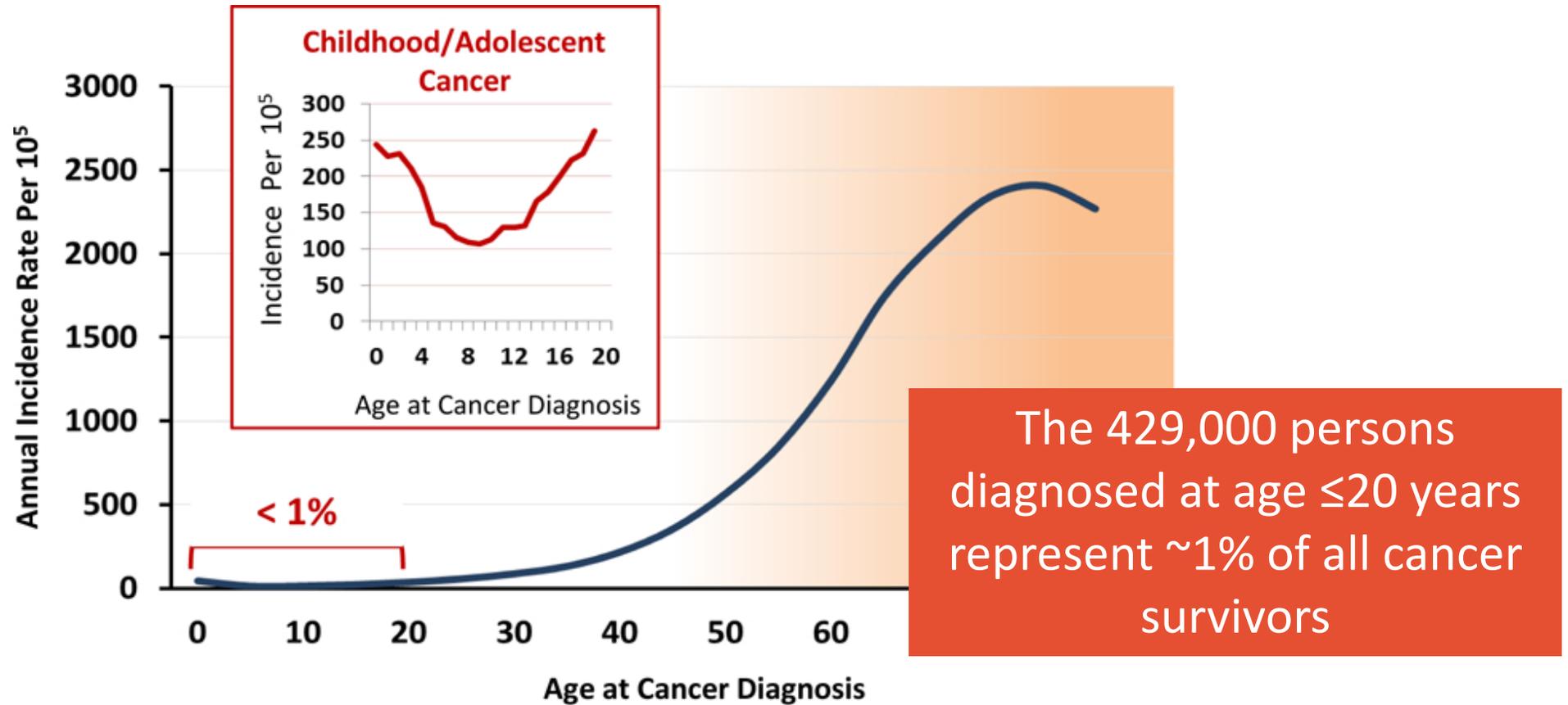
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# Age-specific cancer incidence rates



Robison & Hudson. 2014. Nature Reviews Cancer.

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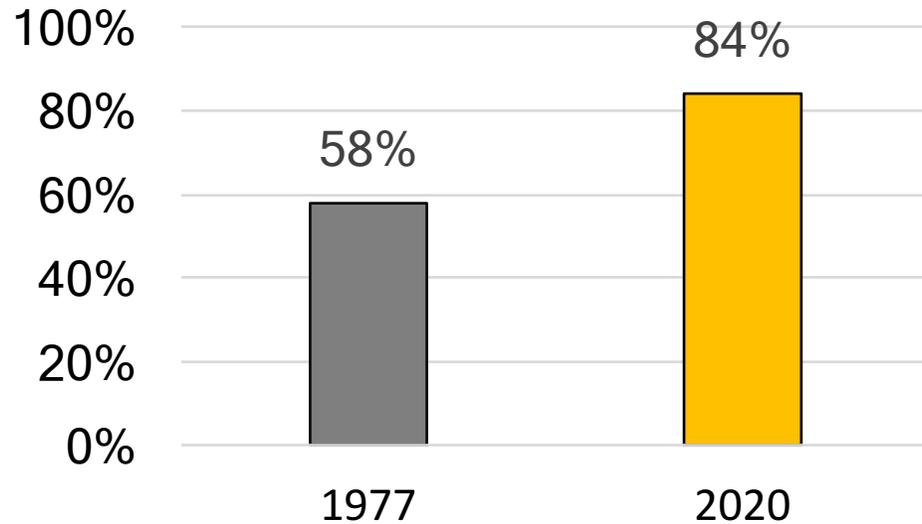


Robison & Hudson. 2014. Nature Reviews Cancer.

Phillips et al. 2015. Cancer epidemiology, biomarkers & prevention

# Treatment efficacy has improved, but survivors pay a price in treatment-related health effects (late effects)

5-year survival for certain childhood cancers has improved,

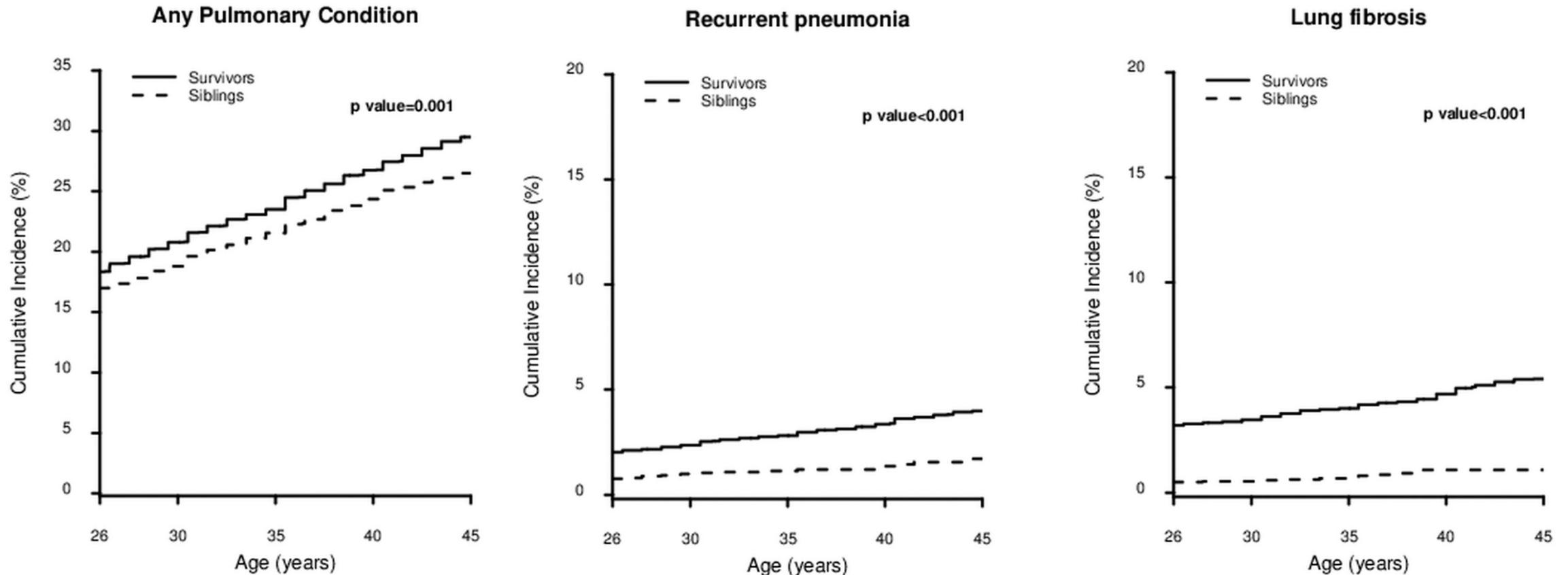


<https://www.acco.org/us-childhood-cancer-statistics/>  
<https://www.cancer.org/cancer/cancer-in-children/key-statistics.html>

but 2/3 of survivors experience health problems due to cancer treatment:

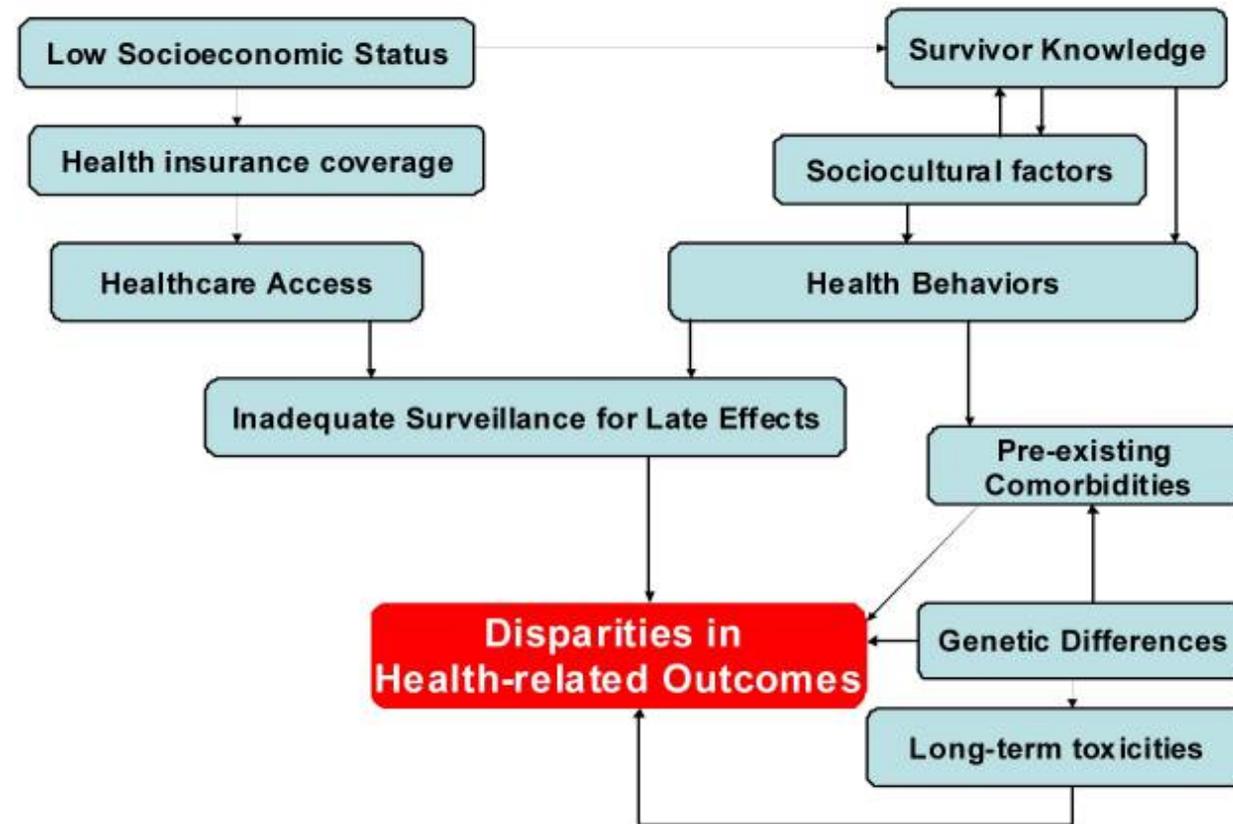
- Lung damage
- Heart damage
- Second cancers
- Infertility
- Endocrine disorders
- Impaired cognitive function
- Immunosuppression

# Cumulative Incidence of Lung Conditions among Childhood Cancer Survivors



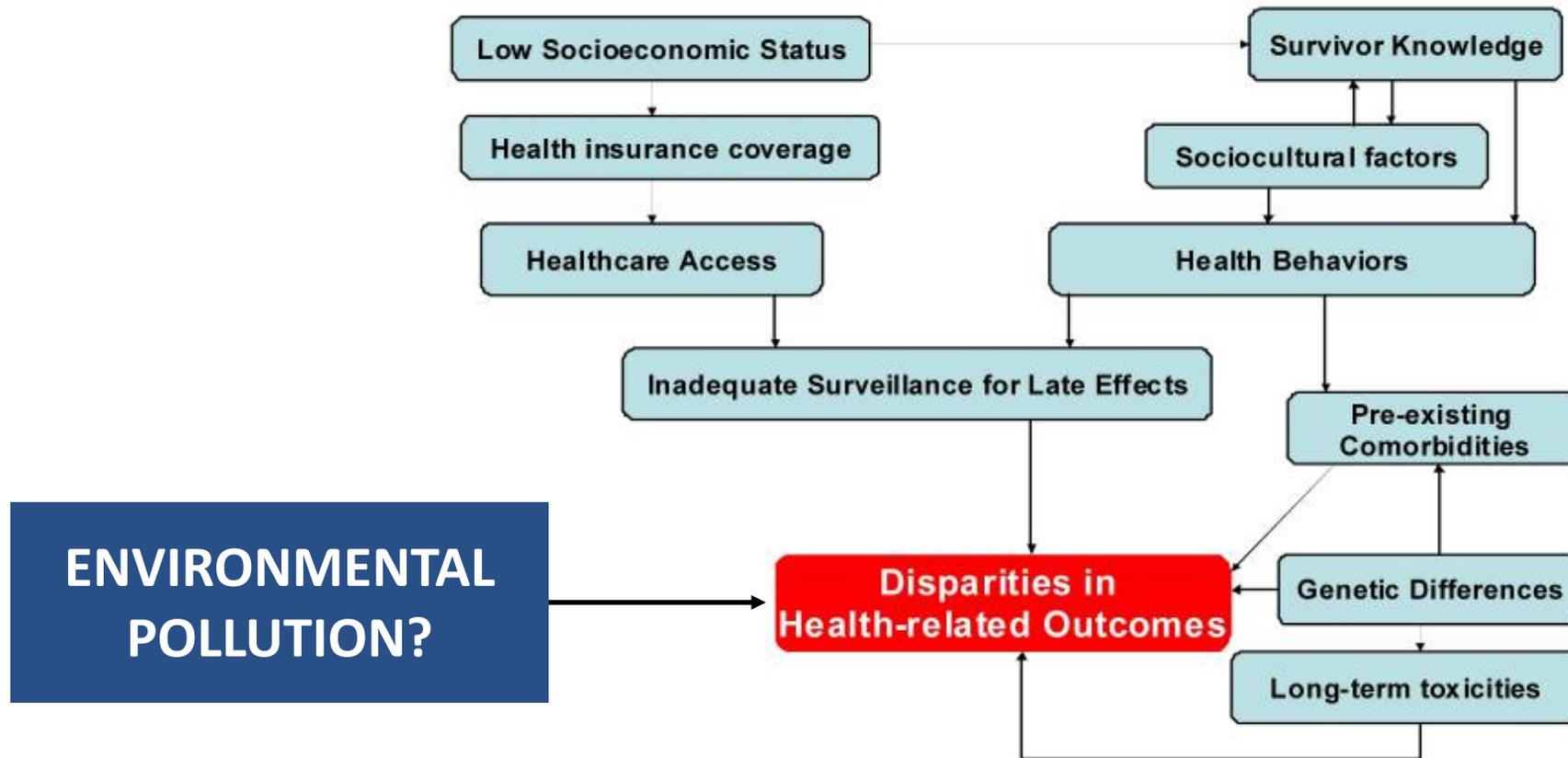
Dietz et al. 2016. *Cancer*. 2016 Dec 1; 122(23): 3687–3696.

# Potential Causes of Disparities in Health-related Outcomes in Long-term Survivors of Childhood Cancer



*Bhatia. Pediatr Blood Cancer. 2011. Jun;56(6):994-1002.*

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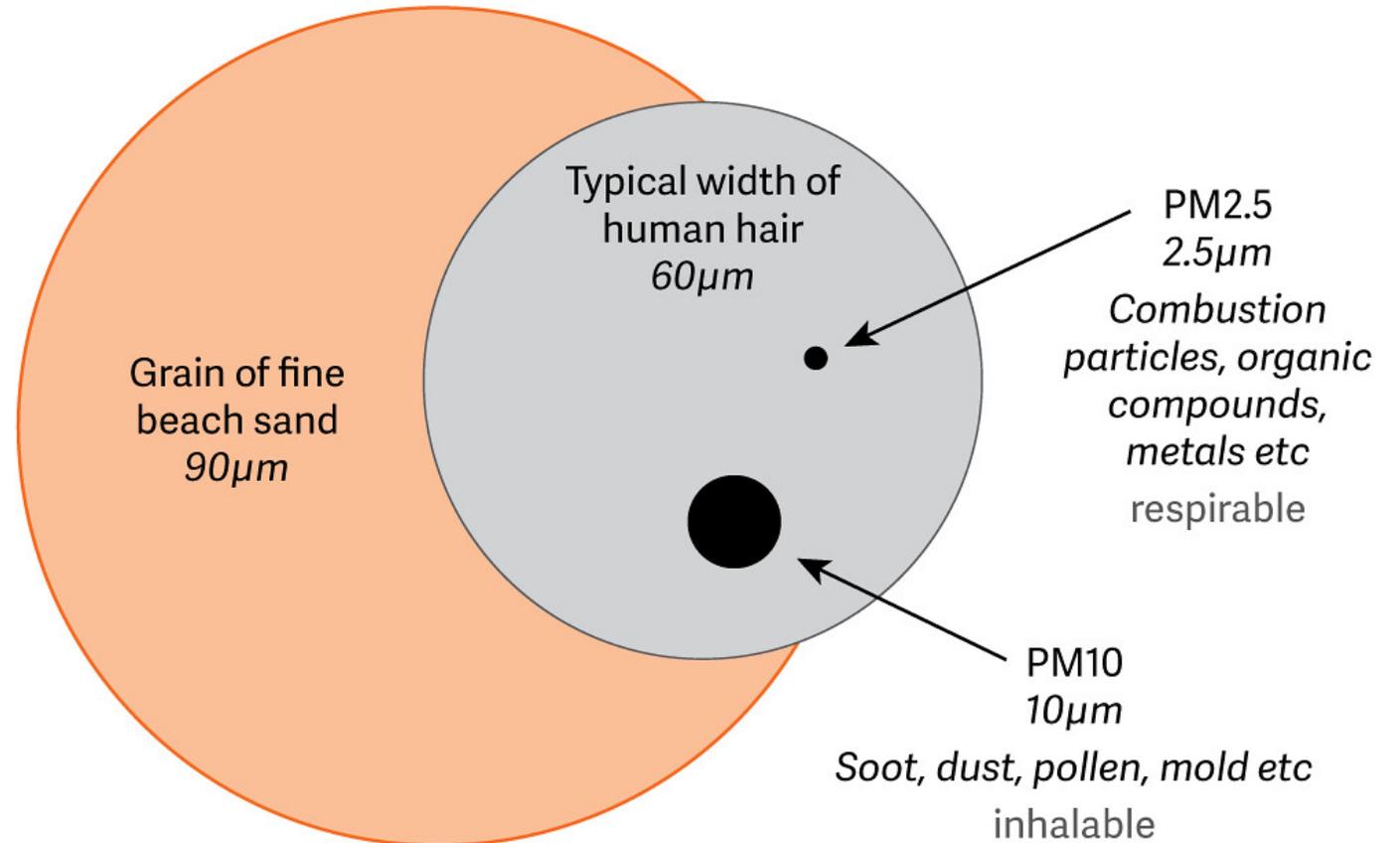
Bhatia. *Pediatr Blood Cancer*. 2011. Jun;56(6):994-1002.

# Fine Particulate Matter Air Pollution (PM<sub>2.5</sub>)

Children and persons with pre-existing lung illness are highly susceptible to air pollution

PM<sub>2.5</sub> is associated with decreased survival among adult cancer patients (Eckel, 2016; Xu, 2013; Huo, 2013; DuPré, 2020).

Effect of PM<sub>2.5</sub> on morbidity among childhood cancer survivors is unknown.



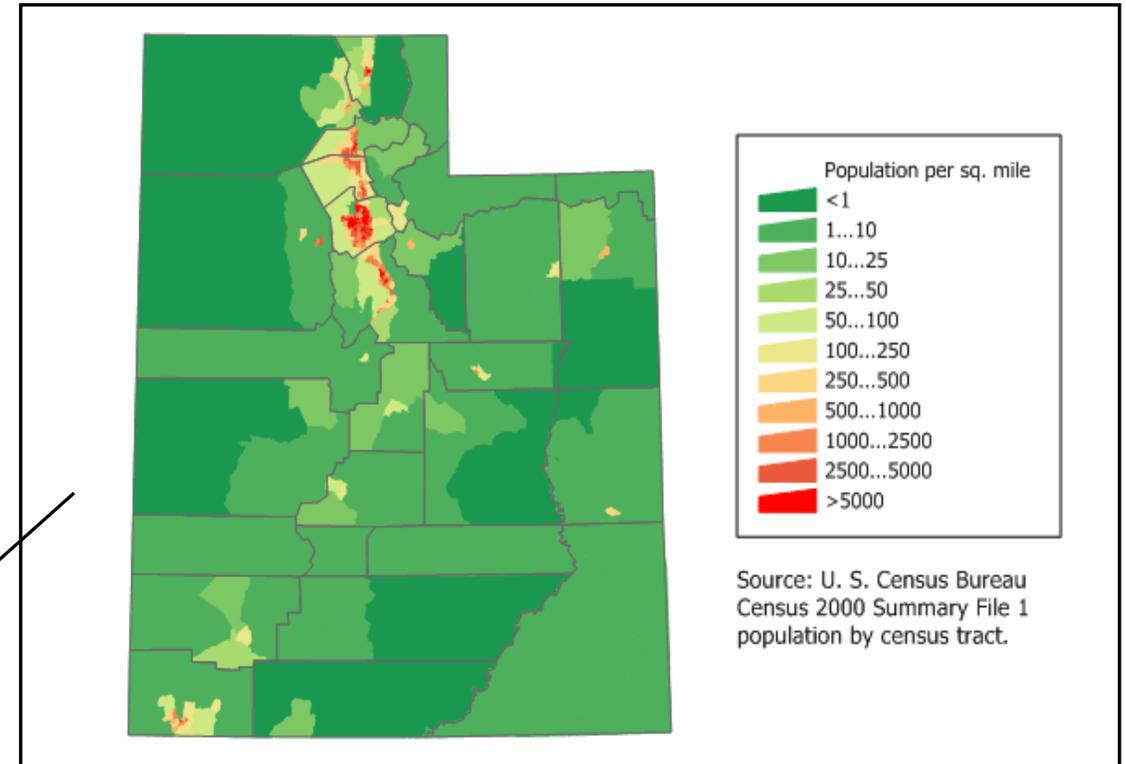
GRID-Arendal. <https://www.grida.no/resources/8282>

**Aim:** Examine the association between short-term PM<sub>2.5</sub> and respiratory health events among survivors of childhood cancers in Utah



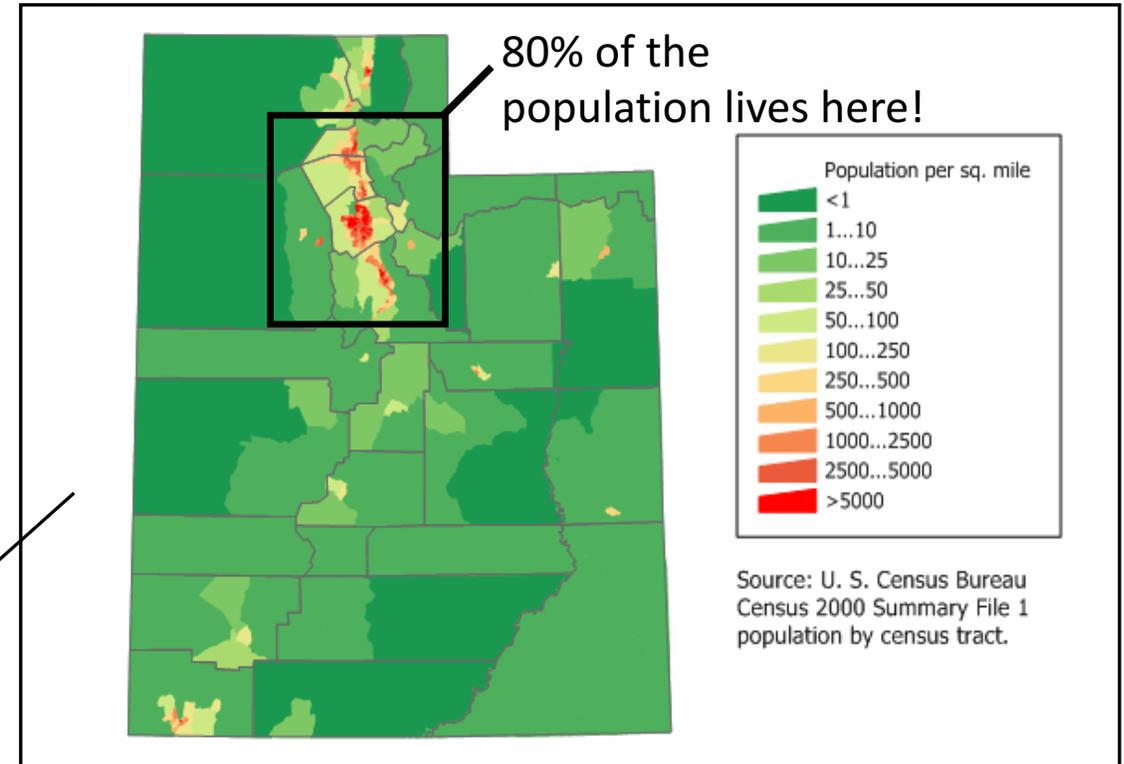
# Air pollution is a public health problem in Utah

Chronic and acute exposure to fine particulate matter (PM<sub>2.5</sub>)



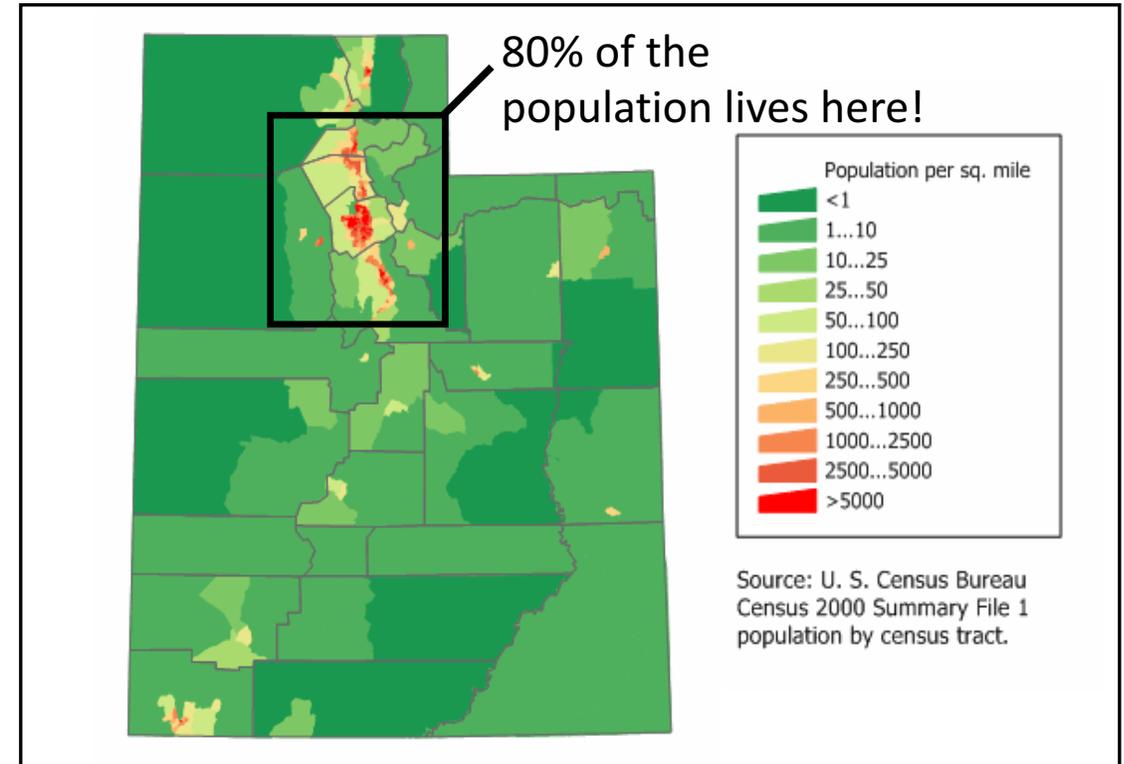
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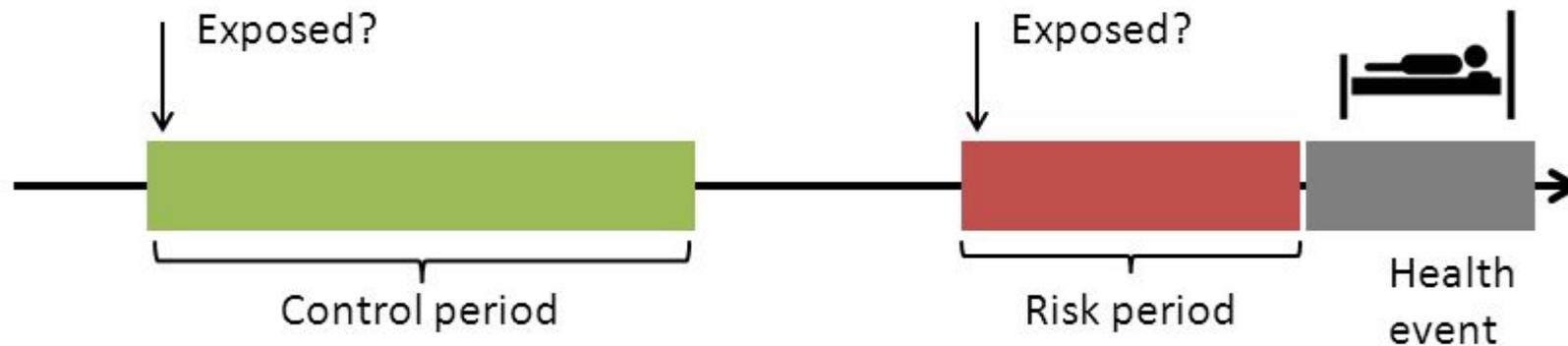
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# Case-crossover design

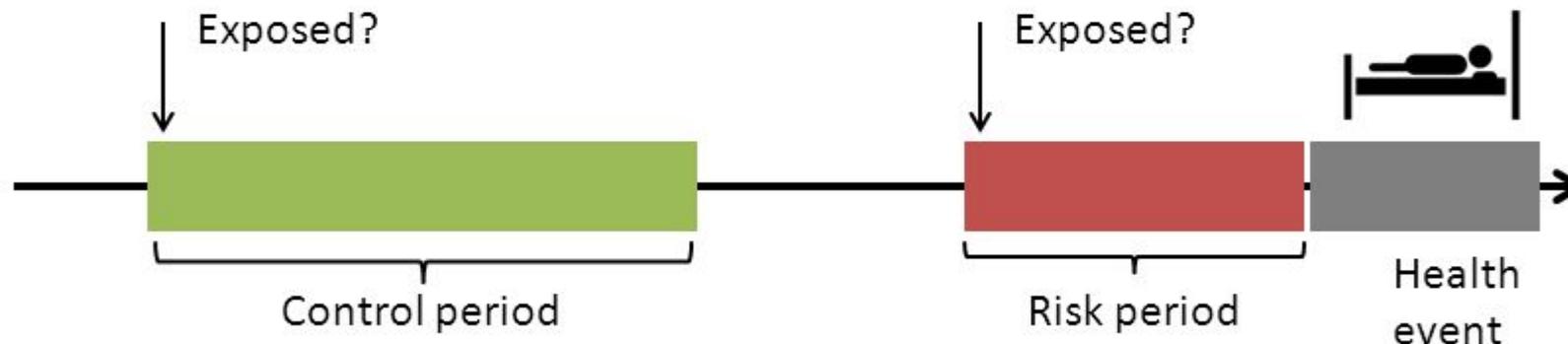
Used to study the effects of transient exposure on the risk of acute events



*Tobías, Armstrong, & Gasparrini. 2014. Presentation: "Analysis of time-stratified case-crossover studies in environmental epidemiology using Stata"*

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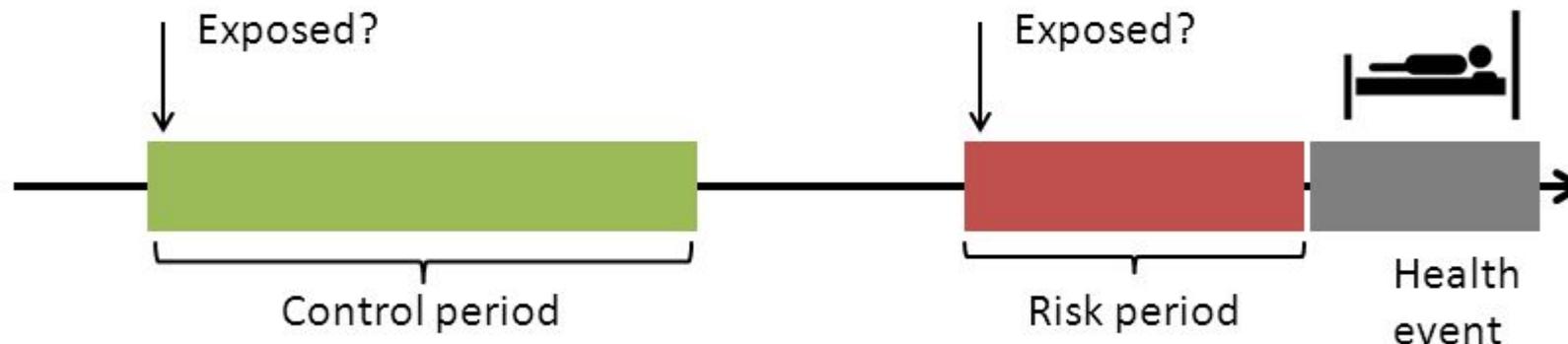


**Events (Case days):** Respiratory hospitalizations and emergency department (ED) visits from January 1996 – December 2015

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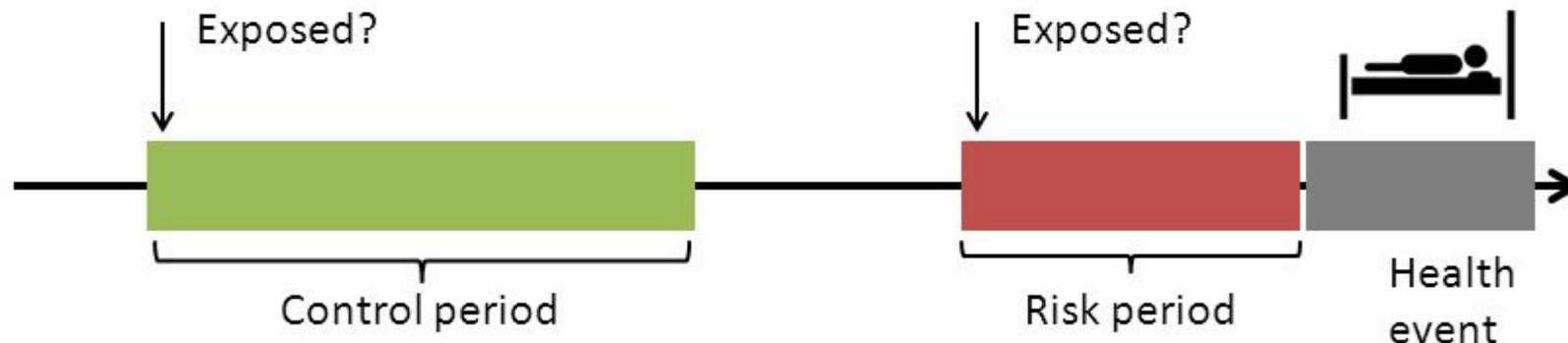
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**PM<sub>2.5</sub> exposure:** Cumulative 3-day average PM<sub>2.5</sub> by residential ZIP code

*Tobías, Armstrong, & Gasparrini. 2014. Presentation: "Analysis of time-stratified case-crossover studies in environmental epidemiology using Stata"*

# Source population

## Cancer survivor cohort:

- Diagnosed at age 0-25 years with a childhood cancer
- Diagnosed or treated at the only pediatric oncology center in the Mountain West
- Survivors alive  $\geq 5$  years from diagnosis
- Had a respiratory health event between 5 years after diagnosis and age 39

## Cancer-free persons:

- Matched by age and sex
- Had events in same time frame and ages as survivors

# Results

		Health events	
	Total	Hospitalization	ED visit
	N	n	n
Childhood cancer survivors	335	68	267
Cancer-free persons	378	59	319

# Results

	Survivors with health events	
	n	%
Total	185	
Female	75	40.5
White, Non-Hispanic	154	83.2
5 to 9 years since diagnosis	115	62.2
Previous chemotherapy	120	64.9
	Mode	
Age at hospitalization (years)	8	
Age at ED visit (years)	9	

# Main and Stratified Effects of a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ with Respiratory Health Events among Survivors of Childhood Cancers

	Hospitalizations		ED visits	
	Odds Ratio	95% CI	Odds Ratio	95% CI
<b>Main effect</b>	1.84*	1.13–3.00	1.04	0.86–1.26
<b>Cause of admission</b>				
Respiratory infection	2.09*	1.06–4.14	1.02	0.80–1.29
<b>Race/ethnicity</b>				
Hispanic	2.22	0.93–5.27	1.28	0.86–1.89
White, Non-Hispanic	1.64	0.88–3.05	0.98	0.79–1.22
<b>Previous chemotherapy</b>				
No	1.35	0.50–3.66	0.86	0.62–1.20
Yes	2.03*	1.14–3.61	1.16	0.92–1.45

Models controlled for temperature; \* Significant 95% CI

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	Odds Ratio	95% CI
<b>Main effect</b>	1.08	0.86–1.36
<b>Race/ethnicity</b>		
Hispanic/Other	1.61*	1.04–2.49
White, Non-Hispanic	0.93	0.71–1.23
<b>Previous chemotherapy</b>		
No	0.89	0.62–1.29
Yes	1.24	0.92–1.67
<b>Age at diagnosis (years)</b>		
0 to 3	1.63*	1.03–2.58
4 to 10	1.08	0.66–1.77
11 to 18	0.79	0.47–1.33
19 to 26	0.96	0.60–1.56

Respiratory infections consist of ED visits and hospitalizations

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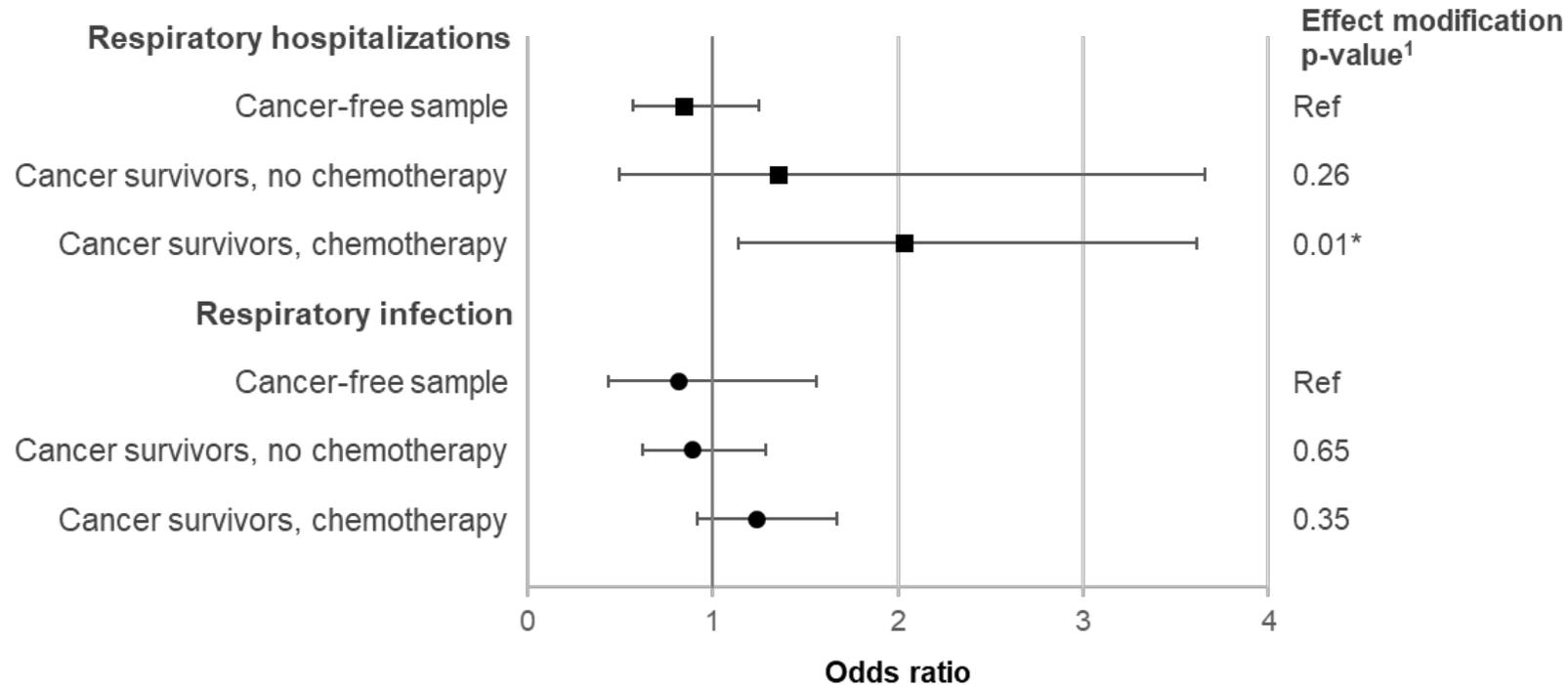
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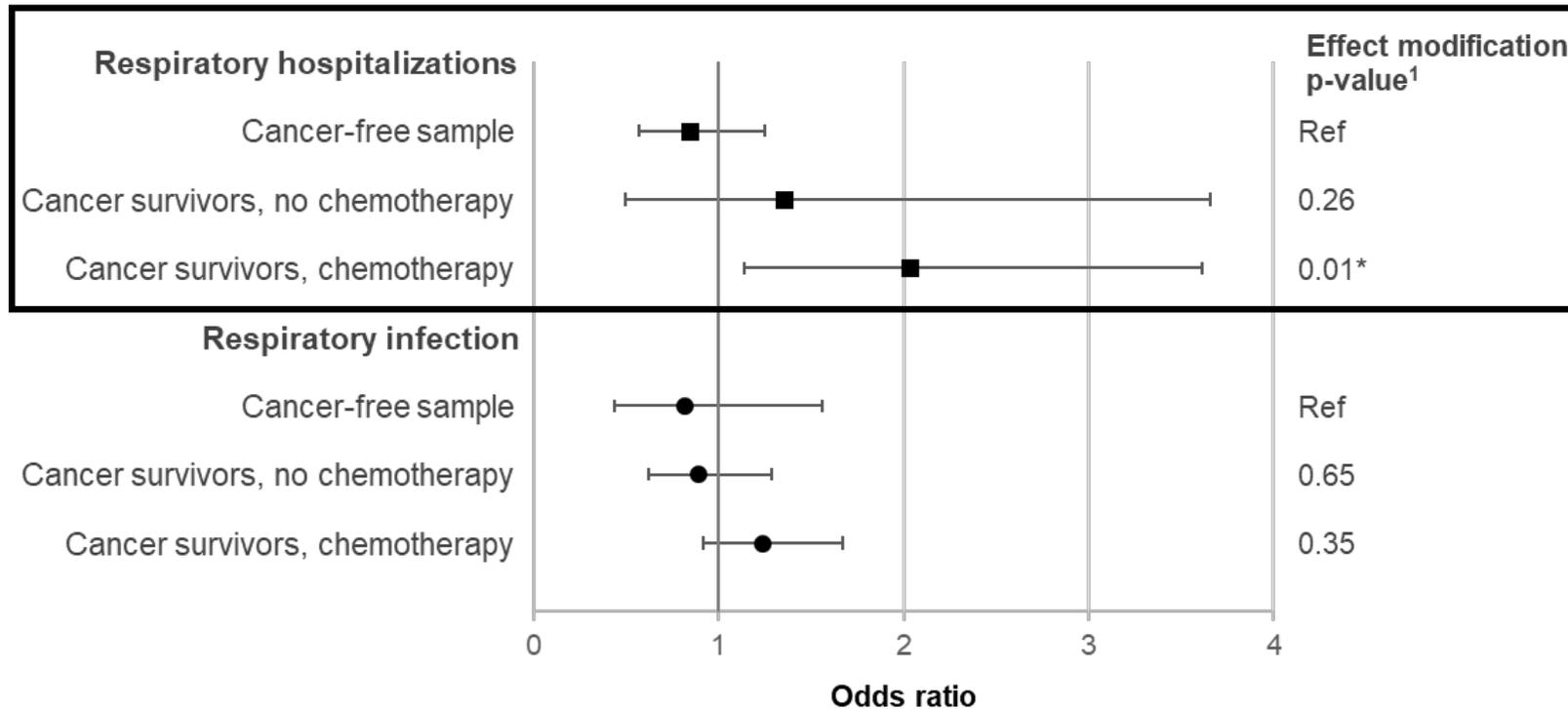
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# PM<sub>2.5</sub> and respiratory events among survivors of childhood cancers and a cancer-free sample



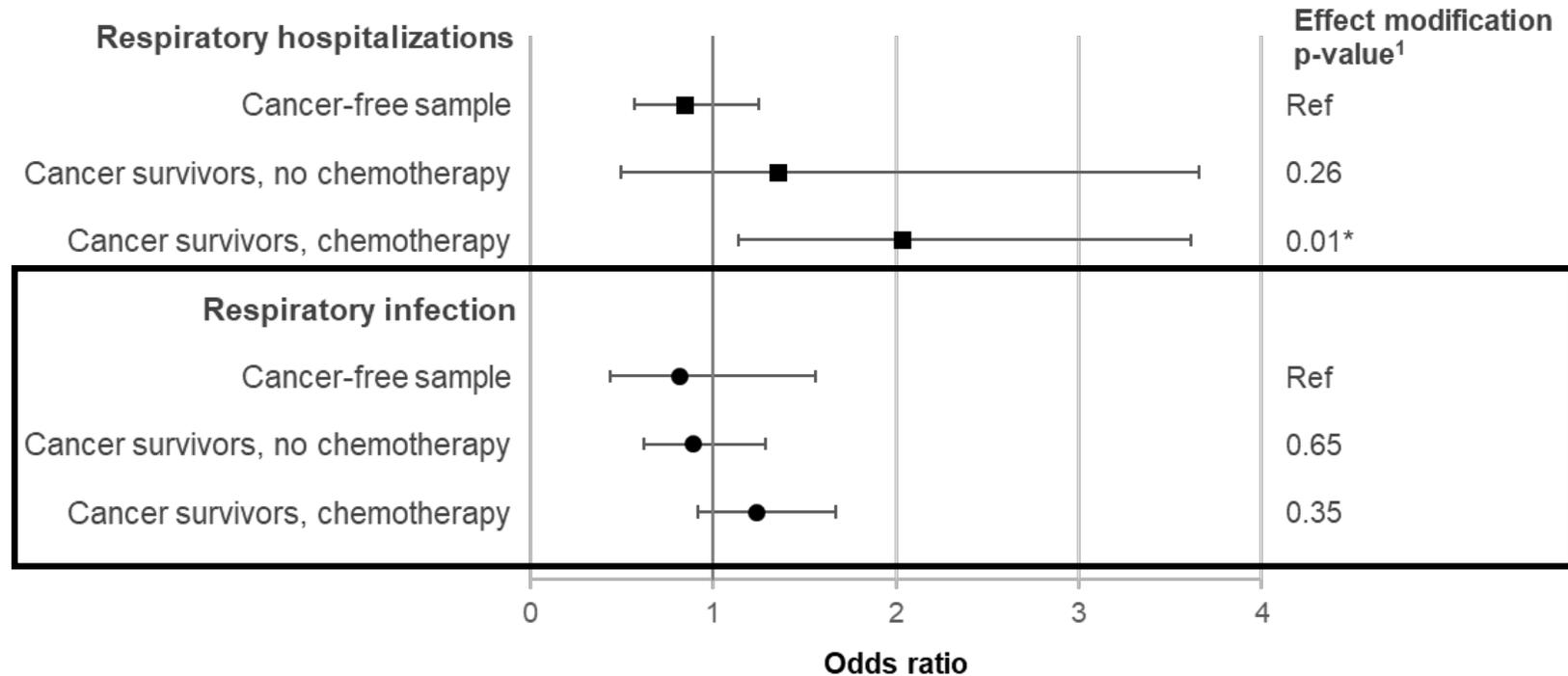
<sup>1</sup>p-value to test for effect modification of association of PM<sub>2.5</sub> on outcome by chemotherapy treatment; cancer-free sample is the reference group; \*Significant at p<0.05

# PM<sub>2.5</sub> and respiratory events among survivors of childhood cancers and a cancer-free sample



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# Discussion

First study to report short-term PM<sub>2.5</sub> is associated with respiratory hospitalization among cancer survivors

- Hospitalizations differ from ED visits

First to report significant effect modification by previous chemotherapy on association of PM<sub>2.5</sub> and respiratory hospitalization

- Residual damage from chemotherapy may sensitize lung tissue to air pollutants

# Information about this topic is desired

Quotes from interviews with parents of childhood cancer survivors:

*“Information, like up and coming [research], something about environmental [exposure]... things that would negatively affect the health of my daughter or any kids that are post-cancer.”*

*“I have never heard of anything of the kind [about air pollution]. If it’s there, it’s just not well put in the news.”*

*Waters et al. 2020. In submission.*

# Next Steps

Conduct study of air pollution and post-treatment respiratory morbidity in a larger sample

- Racial and ethnic minorities and low-income populations

New study - PM<sub>2.5</sub> exposure after diagnosis is associated with mortality among:

- Pediatric patients with lymphoid leukemia, lymphoma, and CNS tumors
- Adolescent and young adult patients with breast, colorectal, and skin melanomas

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## Acknowledgements

### Kirchhoff Research Group:

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### U of Utah collaborators:

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Heidi A. Hanson, PhD  
Claire L. Leiser, MS  
Yue Zhang, PhD  
Utah Population Database

### BYU collaborator:

C. Arden Pope III, PhD

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# Late Effects of the Respiratory System

Cancer therapy	Respiratory Late Effect	Other late effects
Radiation therapy	Reduced FEV, total lung capacity, diffusion capacity	Mortality
Chemotherapy (Bleomycin, doxorubicin, dactinomycin, busulfan, nitrosoureas, platinum-based agents)	Subclinical pulmonary dysfunction; interstitial pneumonitis; pulmonary fibrosis; restrictive lung disease; obstructive lung disease	Mortality
Hematopoietic cell transplantation with any history of chronic GVHD	Pulmonary toxicity (bronchiolitis obliterans, chronic bronchitis, bronchiectasis)	

Late effects are defined as health problems related to cancer therapy