

# Birth defects in offspring of adolescents and young adults diagnosed with cancer

Caitlin C. Murphy, PhD, MPH  
UTHealth Houston School of Public Health

ACTCR Meeting  
Texas Cancer Registry  
Monday, October 23, 2023

**July 2018:** “Notes from call with Philip”

**August 2018:** Data Discovery Workshop, DSHS

**September 2018:** Submit grant proposal to U.S. Department of Defense (thanks to Melanie for her letter of support)

**June 2019:** Proposal funded!

**March 2020:** COVID-19 shuts down our work

**November 2020:** Receive data linkage from TCR (many, many thanks to Erin)

**All the days since:** learn and analyze linked data (thanks to Sandi and Philip for their ongoing guidance)

notes from call with Philip - Word


Layout References Mailings Review View Help Tell me what you want to do

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Health and Human  
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**Texas Department of State Health Services**

John Hellerstedt, M.D.  
Commissioner

September 7, 2018

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Department of Clinical Science  
University of Texas Southwestern  
Harold C. Simmons Comprehensive  
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Dear Dr. Murphy:



## My goals for today

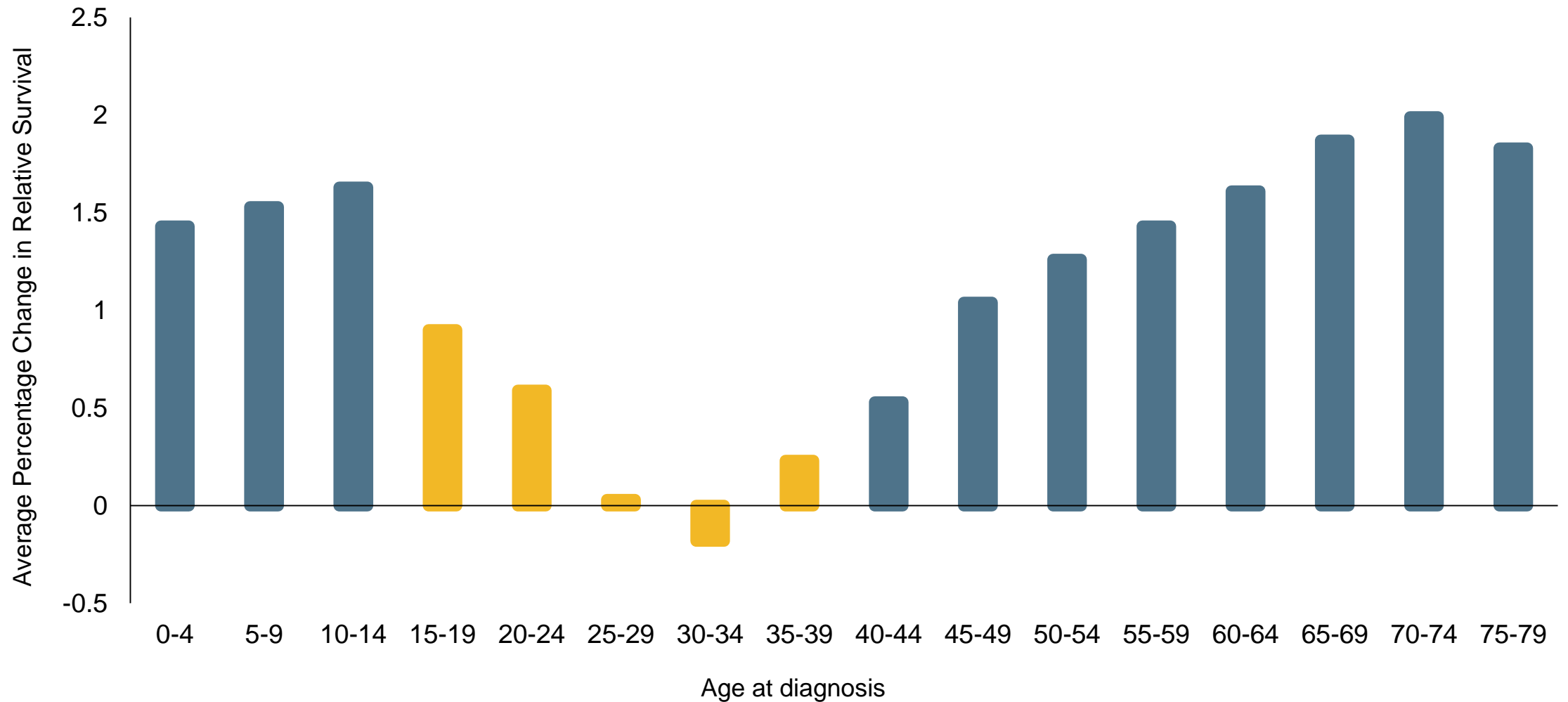
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To showcase the awesomeness of TCR data

- Birth defects in offspring of adolescents and young adults with cancer
- Differences in birth defects by cancer-related factors

To identify opportunities to expand this work

## Adolescents and young adults with cancer: a unique but understudied population



## Fertility and reproductive health present challenges to AYAs

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Gonadotoxic effects of cancer treatment

Reduced fertility or infertility

Access to fertility preservation and ART

Predisposed to poor maternal and perinatal outcomes

Uncertainty surrounding reproductive potential

Fears related to pregnancy and adverse outcomes

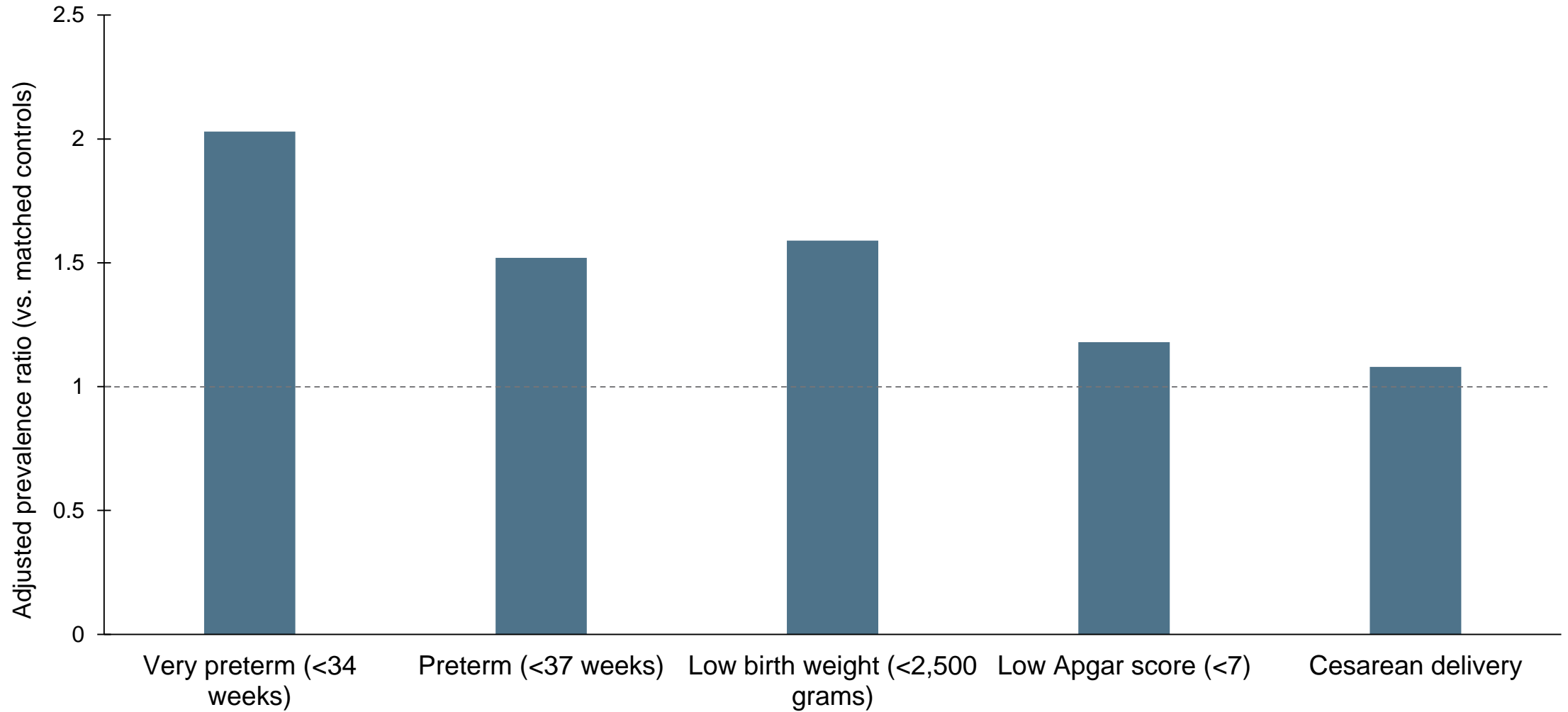
## Clinical practice guidelines on fertility preservation for AYAs

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In 2006, the American Society of Clinical Oncology recommended:

- Discuss infertility risks and fertility preservation with all patients of reproductive age
- Refer patients to reproductive specialists
- Address fertility preservation as early as possible, before treatment
- Document discussions in the medical record

## Excess risk of adverse birth outcomes in AYAs



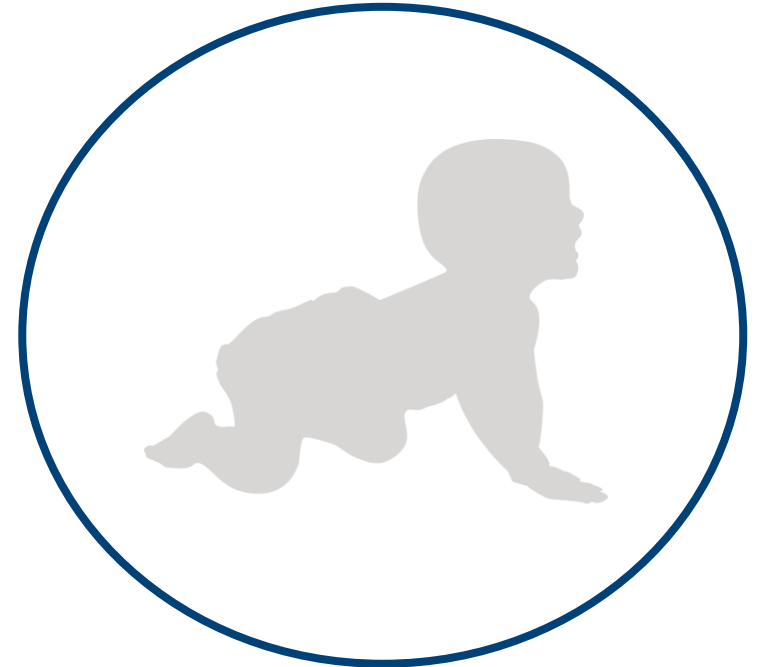
## ...but what about risk of birth defects in offspring?



**3-5%** of pregnancies complicated by birth defects



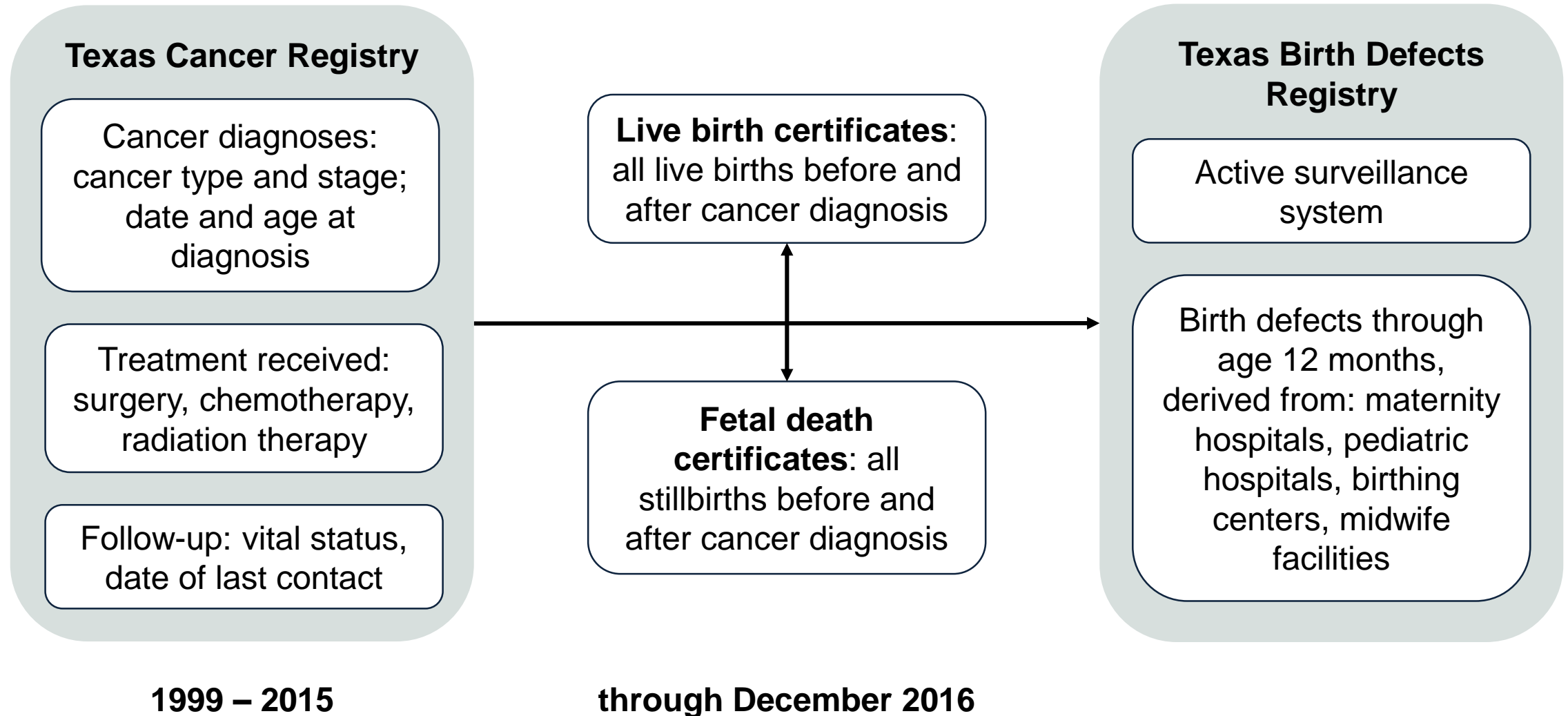
**120,000** infants born with birth defects in the U.S. each year



**20%** of infants deaths are caused by birth defects



# Linking Texas Cancer Registry, vital statistics, and Texas Birth Defects Registry



## Identifying first singleton birth to female AYAs after cancer diagnosis

**56,292** female AYAs linked with live birth and fetal death certificates

**11,066** live births and **76** stillbirths to female AYAs after cancer diagnosis

Exclude:

- **16** missing gestational age
- **586** multiple births
- **1,291** births from diagnoses during pregnancy
- **2,357** second or later births

**6,840** singleton live births and **42** stillbirths to **6,882** female AYAs after cancer diagnosis

Match 3:1 by maternal race/ethnicity, maternal age, year of birth

**20,520** singleton live births and **126** stillbirths to **20,646** female AYAs without cancer

## Characteristics of 6,882 female AYAs and 20,646 without cancer

	Female AYAs		Without cancer	
	n	(%)	n	(%)
<b>Maternal age</b>				
15-19	126	(1.8)	378	(1.8)
20-24	812	(11.8)	2435	(11.8)
25-29	1757	(25.5)	5272	(25.5)
30-34	2272	(33.0)	6821	(33.9)
35-39	1532	(22.7)	4682	(22.7)
≥40	353	(5.1)	1058	(5.1)
<b>Race and ethnicity</b>				
Non-Hispanic White	3894	(56.6)	11683	(56.6)
Non-Hispanic Black	611	(8.9)	1831	(8.9)
Hispanic	2048	(29.8)	6146	(29.8)
Other	329	(4.8)	986	(4.8)

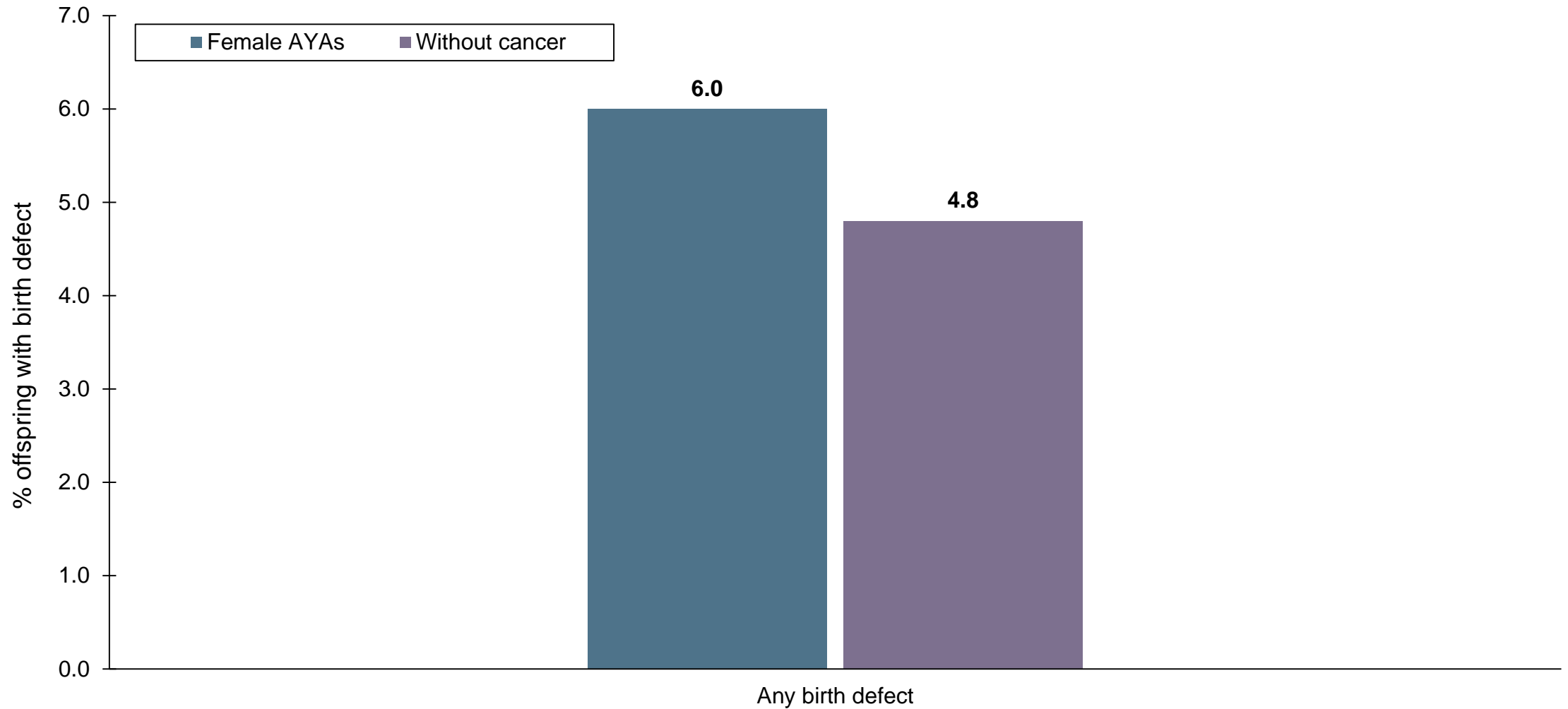
## Characteristics of 6,882 female AYAs and 20,646 without cancer

	Female AYAs		Women without cancer	
	n	(%)	n	(%)
Infant sex				
Male	3527	(51.3)	10544	(51.1)
Female	3355	(48.8)	10102	(48.9)
Gestational age				
< 32 weeks	168	(2.4)	337	(1.6)
32 - <37 weeks	702	(10.2)	1525	(7.4)
≥37 weeks	6012	(87.4)	18784	(91.0)
Parity				
Nulliparous	2866	(41.8)	6456	(31.4)
Primiparous	3997	(58.2)	14140	(68.7)
<i>Missing</i>	19		50	

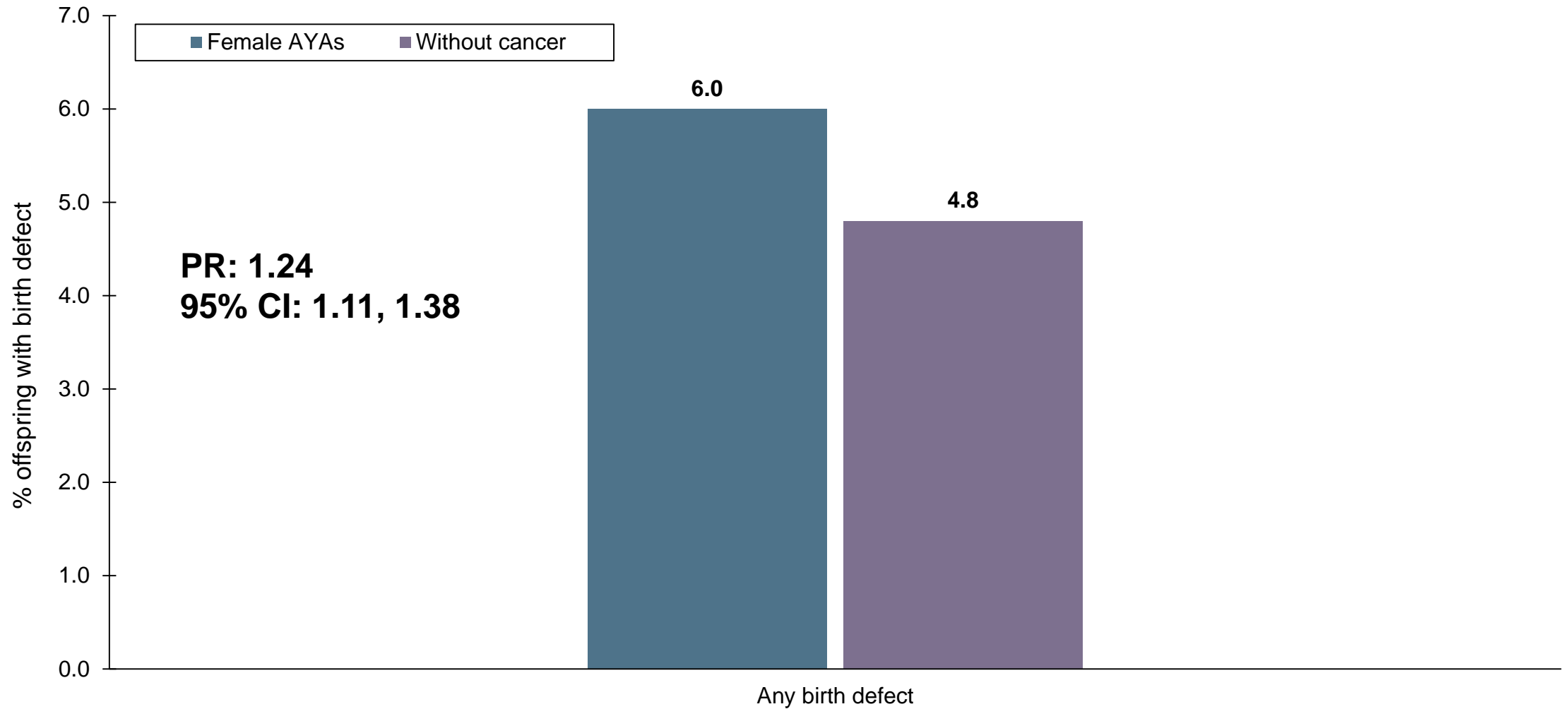
## Cancer-related characteristics of 6,882 female AYAs

	n	(%)		n	(%)
Age at diagnosis			Stage at diagnosis		
15-19	803	(11.7)	Local	3568	(62.3)
20-24	1542	(22.4)	Regional	1464	(25.6)
25-29	2176	(31.6)	Distant	698	(12.2)
30-34	1700	(24.7)	Cancer types		
35-39	661	(9.6)	Thyroid	1990	(28.9)
Time from diagnosis to birth			Breast	738	(10.7)
<2 years	1033	(15.0)	Lymphoma	861	(12.5)
2-5 years	4210	(61.2)	Gynecologic	651	(9.5)
>5 years	1639	(23.8)	Melanoma and skin	574	(8.3)
Received chemotherapy	1440	(24.0)	Sarcoma	316	(4.6)
			Leukemia	215	(3.1)

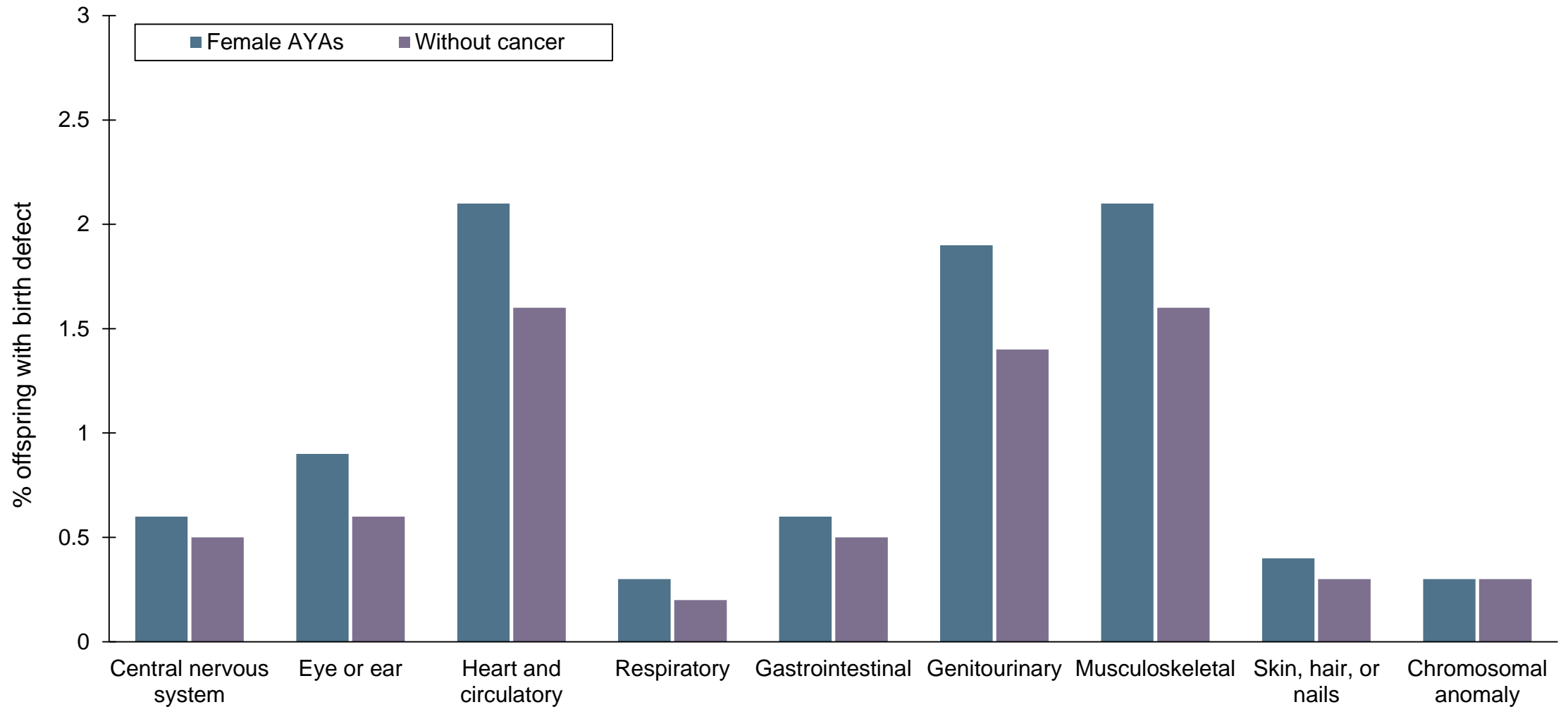
## Any birth defect in offspring of female AYAs with and without cancer



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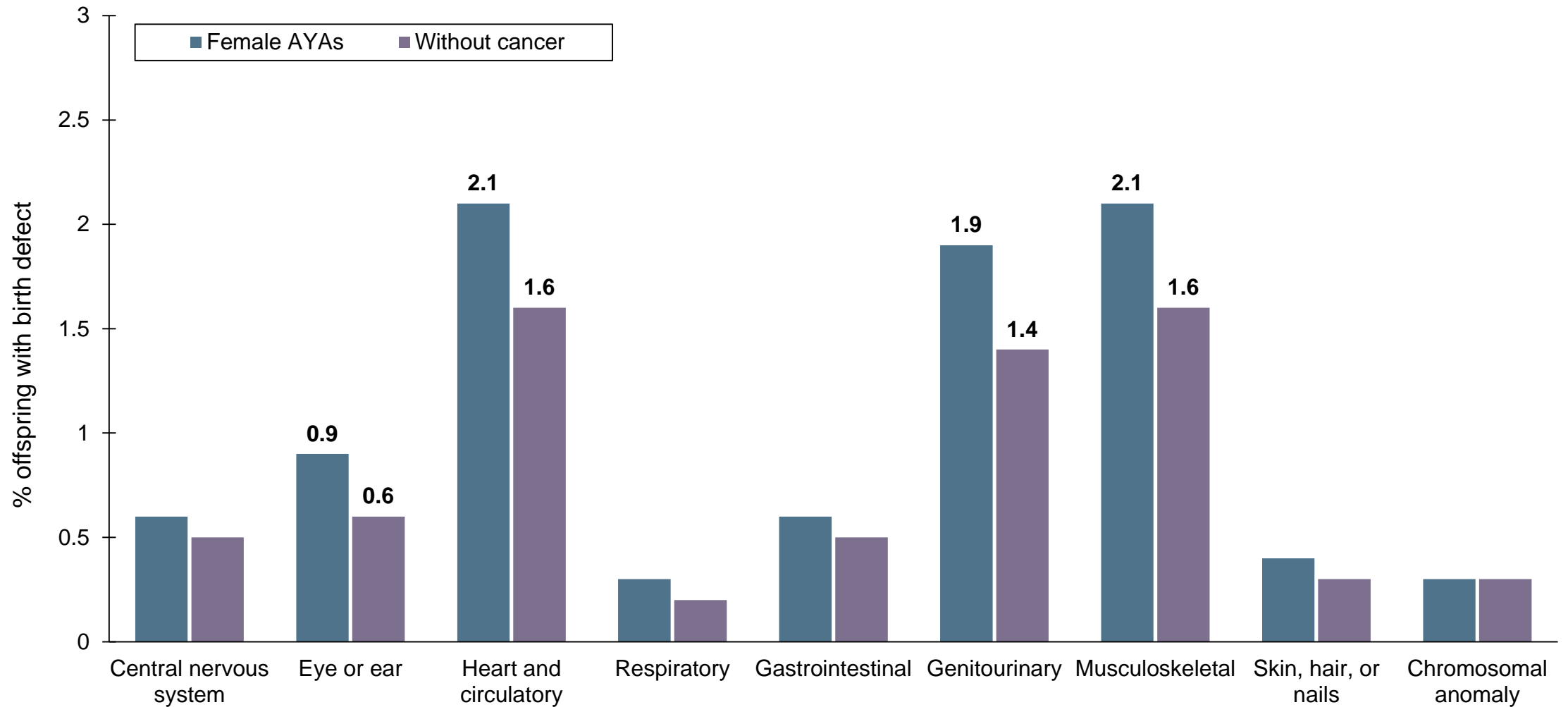


## Specific types of birth defects in offspring of female AYAs with and without cancer

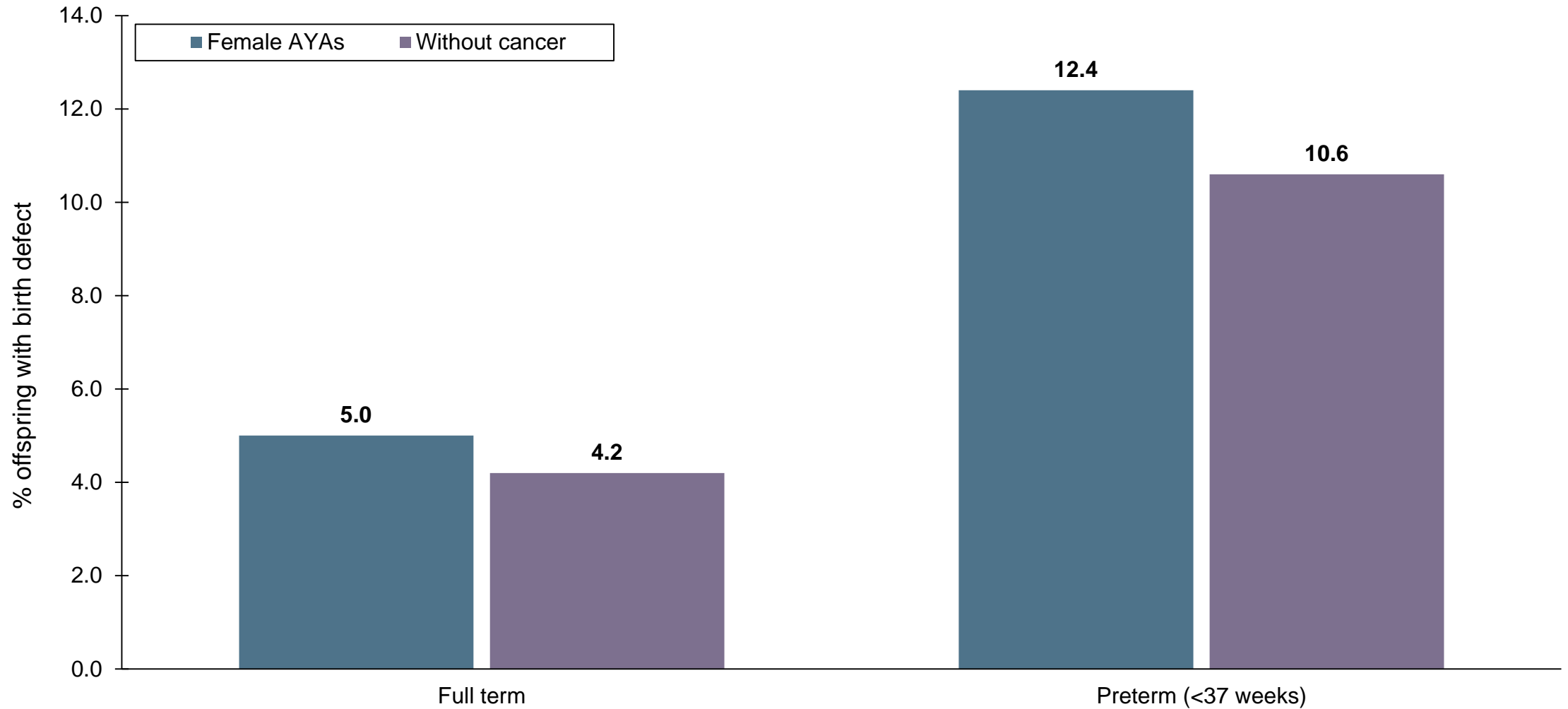




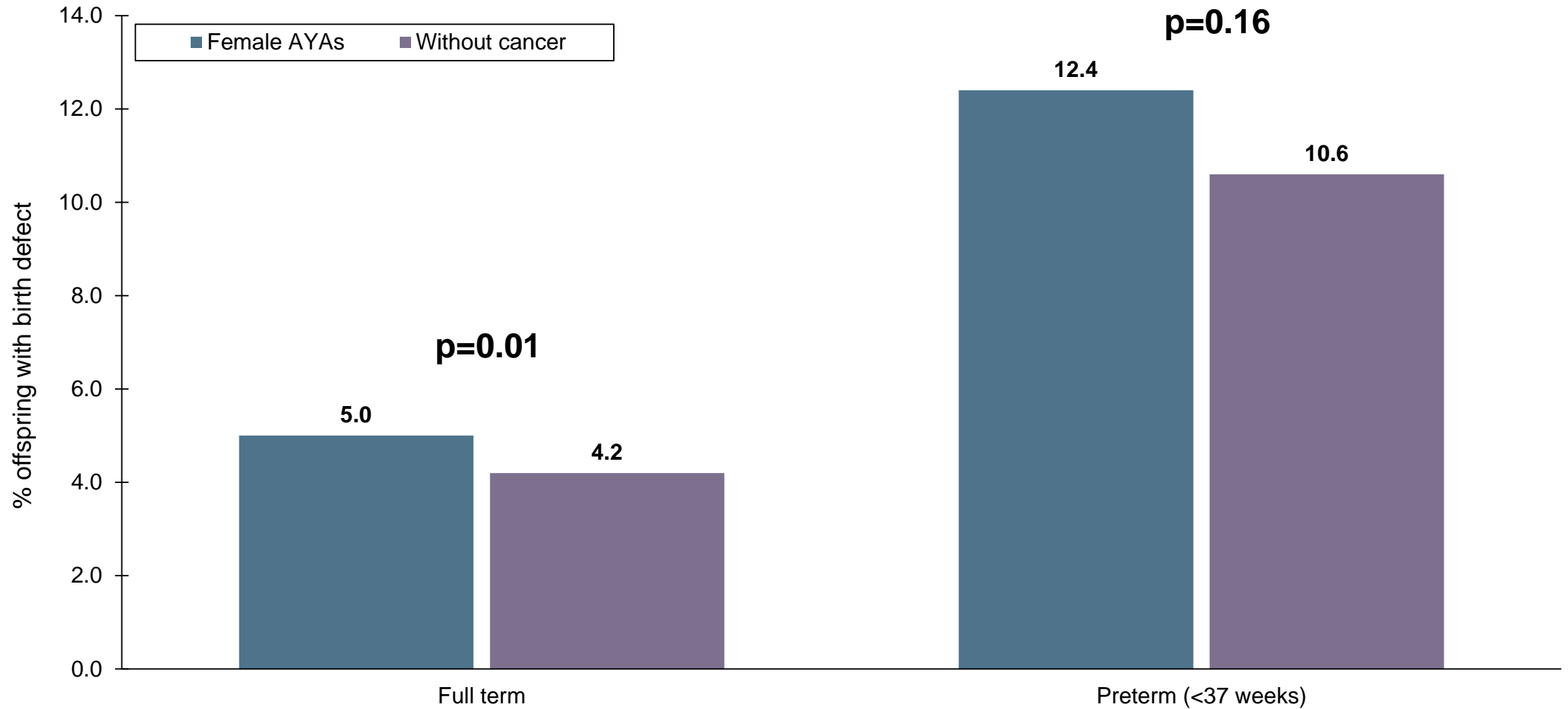
## Specific types of birth defects in offspring of female AYAs with and women without



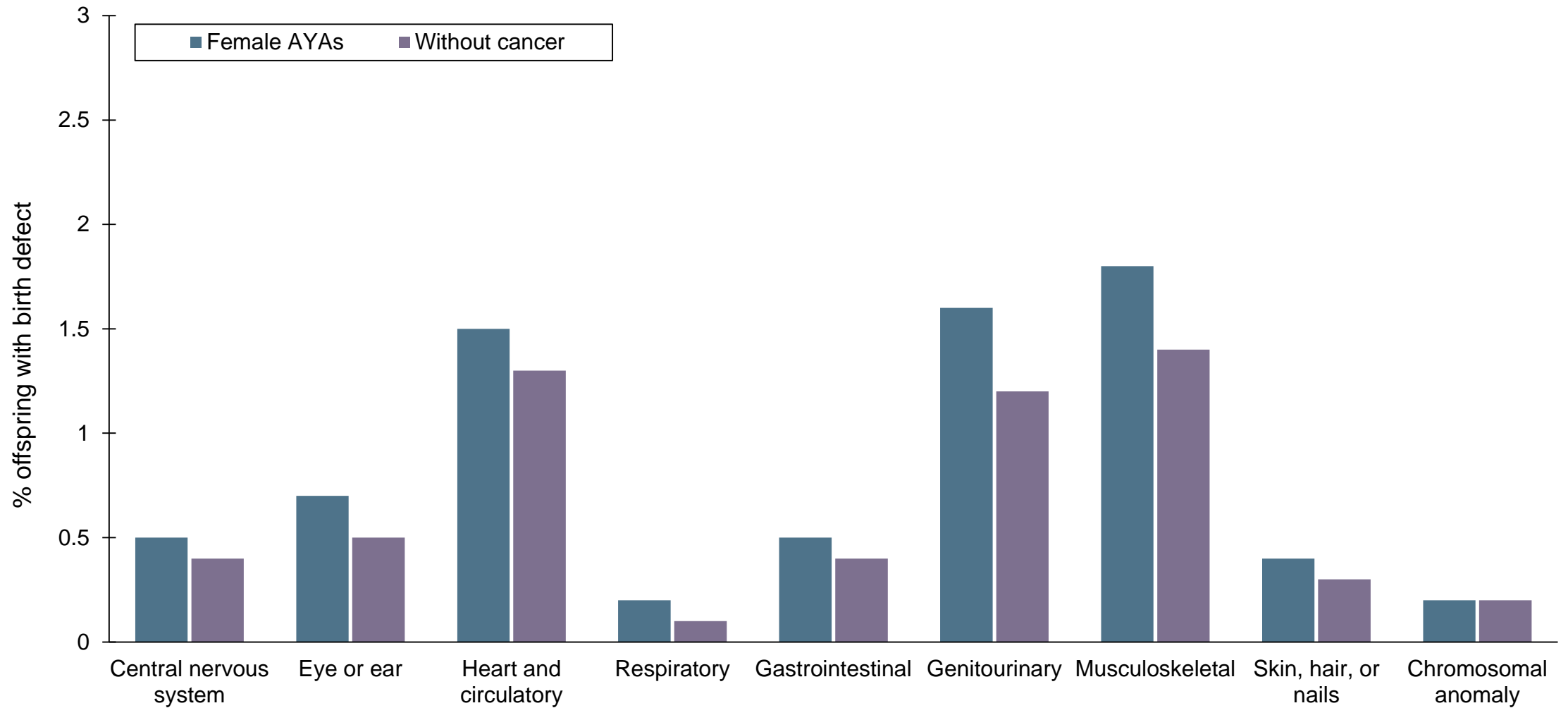
## Any birth defect for full term vs. preterm



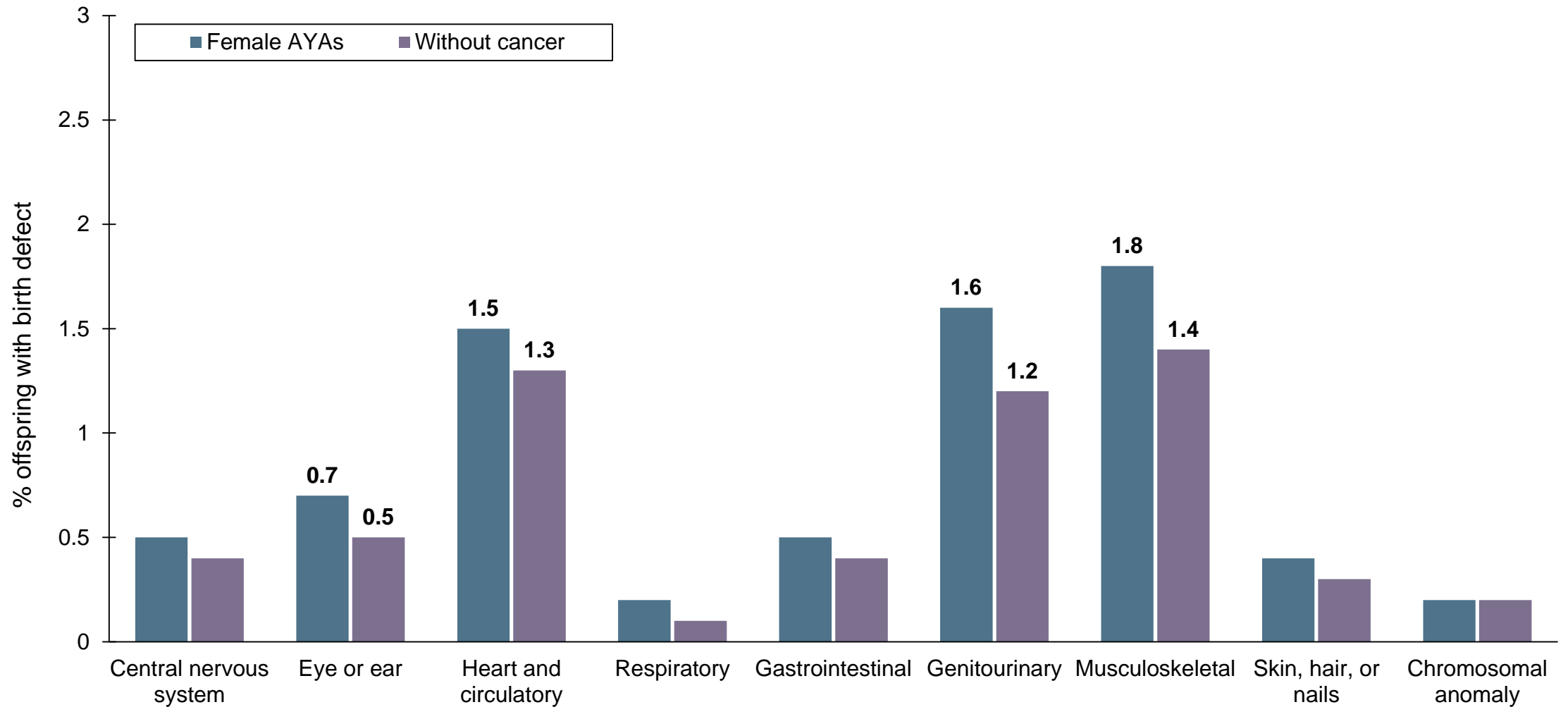
## Any birth defect for full term vs. preterm



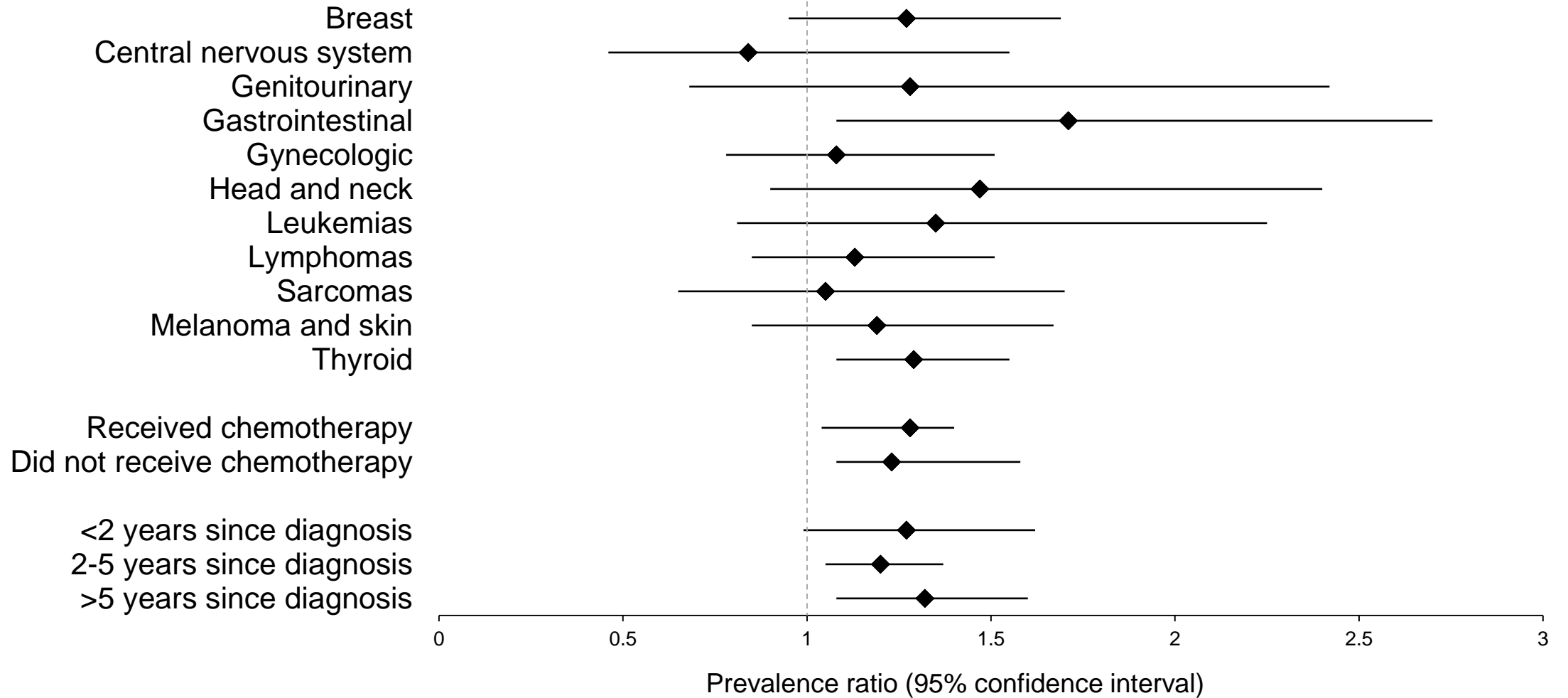
## Specific types of birth defects among full term births



## Specific types of birth defects among full term births



# Differences in prevalence of any birth defect by cancer-related characteristics



## Key takeaways

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Prevalence of birth defects was higher in liveborn and stillborn offspring of AYAs compared to age- and race/ethnicity-matched women without cancer, although rare in both groups

No difference in prevalence of birth defects by receipt of chemotherapy or time since cancer diagnosis, implicating factors contributing to the development of cancer vs. cancer treatment

# A birth defects-cancer-birth defects cycle?



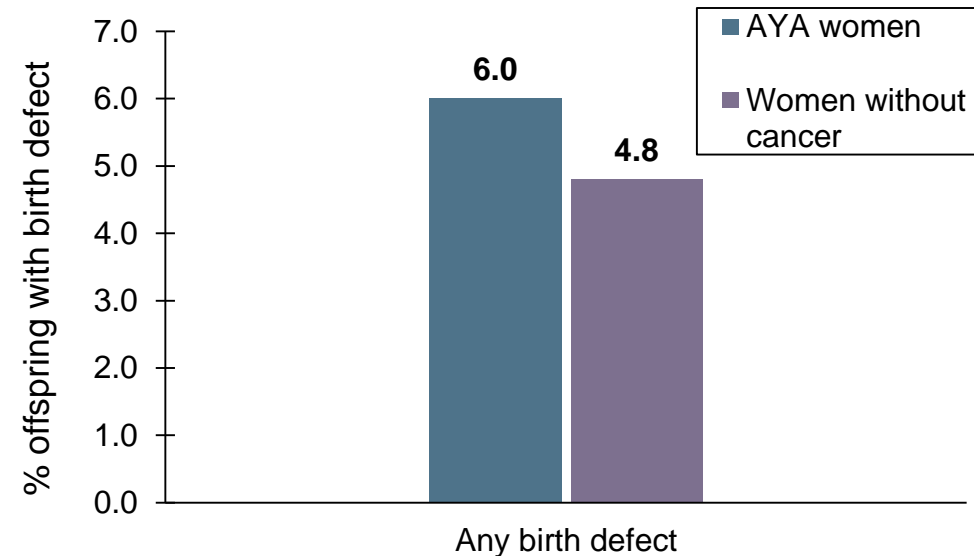
JAMA Oncology | Original Investigation

## Association Between Birth Defects and Cancer Risk Among Children and Adolescents in a Population-Based Assessment of 10 Million Live Births

Articles

THE LANCET • Vol 355 • January 15, 2000

### Risks of leukaemia and solid tumours in individuals with Down's syndrome





## **A big thank you to TCR!**

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Four peer-reviewed publications

Seven presentations at scientific meetings

Four student-led projects, including two doctoral dissertations

Preliminary data for new R01 funding (PI Rauh-Hain)

# Thank you!

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Collaborators:

Marlyn Allicock, PhD, MPH  
Andrea Betts, PhD, MPH  
Barbara Cohn, PhD  
Philip Lupo, PhD, MPH  
Sandi Pruitt, PhD, MPH  
Aubree Shay, PhD, MSSW  
Jennifer Wang, MPH



## Questions?

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## Disease classification codes for birth defects

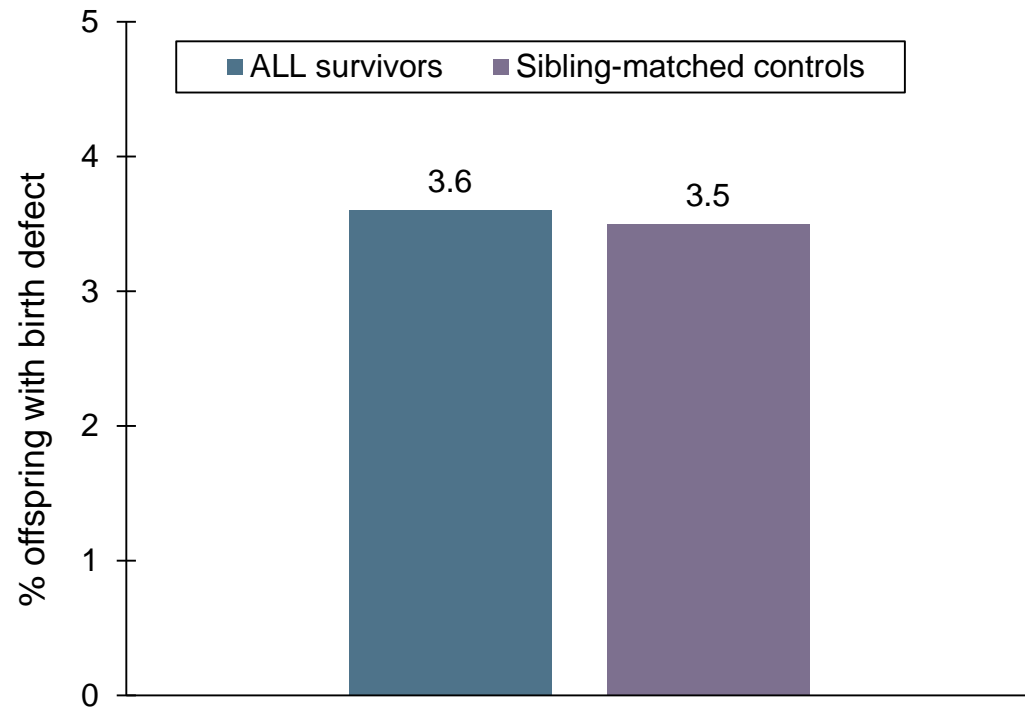
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Type of birth defect	BPA codes	Examples
Chromosomal anomalies	758.000 – 758.990	<ul style="list-style-type: none"><li>• Trisomy 21</li></ul>
Central nervous system	740.000 – 742.990	<ul style="list-style-type: none"><li>• Spina bifida</li><li>• Anencephaly</li></ul>
Eye or ear	743.000 – 744.910	<ul style="list-style-type: none"><li>• Anotia, microtia</li><li>• Congenital cataract</li></ul>
Heart and circulatory system	745.000 – 747.900	<ul style="list-style-type: none"><li>• Pulmonary atresia</li></ul>
Respiratory system	748.000 – 748.900	<ul style="list-style-type: none"><li>• Choanal atresia</li></ul>
Gastrointestinal system	750.000 – 751.900	<ul style="list-style-type: none"><li>• Pyloric stenosis</li></ul>
Genitourinary system	752.000 – 753.990	<ul style="list-style-type: none"><li>• Hypospadias</li></ul>
Musculoskeletal system	754.000 – 756.990	<ul style="list-style-type: none"><li>• Clubfoot</li><li>• Limb deficiency</li></ul>
Skin, hair, or nails	757.000 – 757.990	<ul style="list-style-type: none"><li>• Congenital ichthyosis</li></ul>

## ...but what about risk of birth defects in offspring?

Some evidence from studies of childhood cancer:

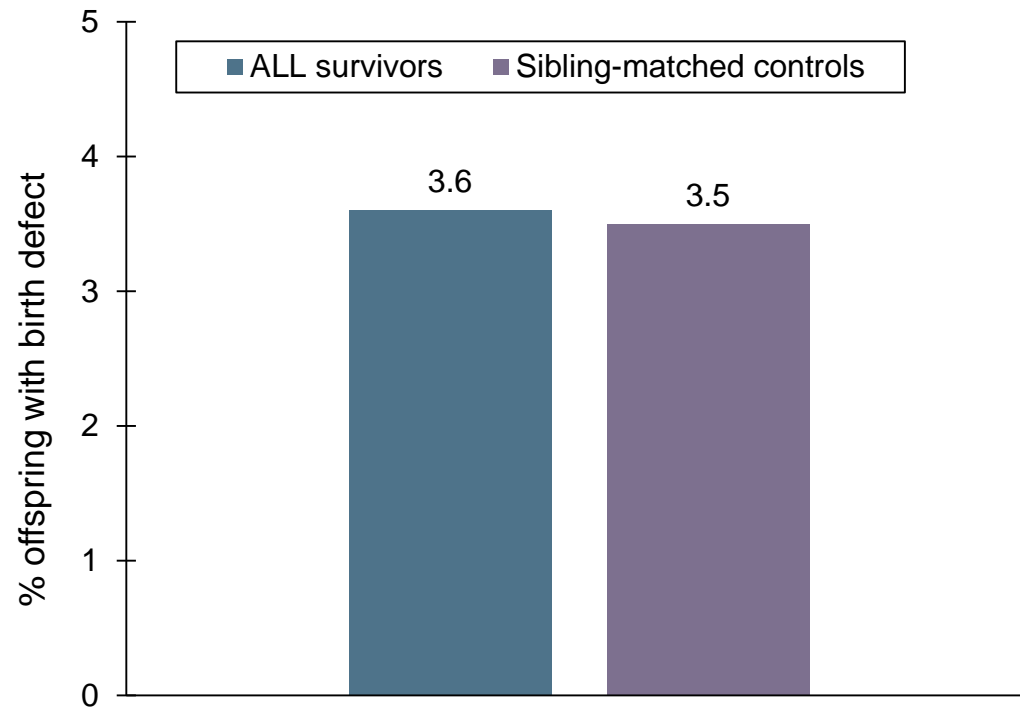
### Kenney LB, et al. Cancer 1996



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### Kenney LB, et al. Cancer 1996



### Signorello LB, et al. J Clin Oncol 2012

