

Examining the Etiology of Young-onset Breast Cancer

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10/26/2022



CanPath

Canadian Partnership
for Tomorrow's Health



Outline

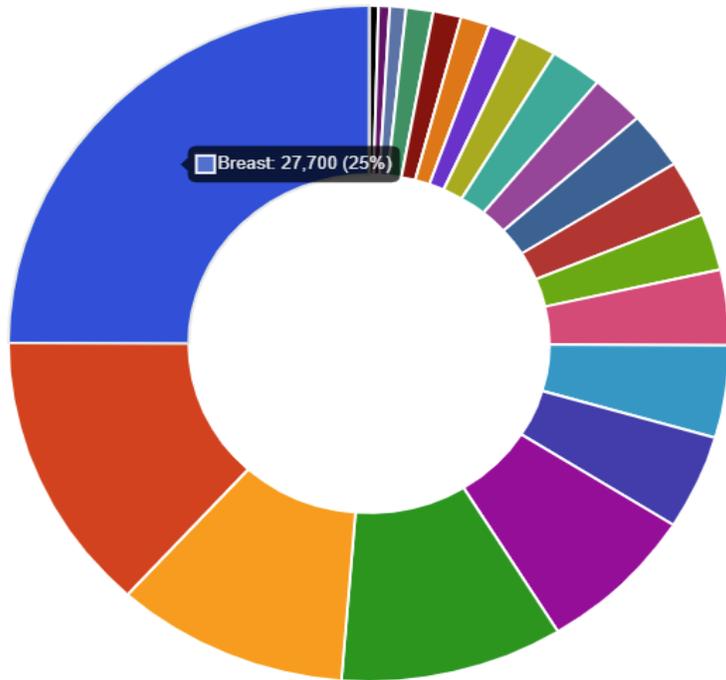
- 1** Epidemiology of Breast Cancer
- 2** Early-Onset Breast Cancer
- 3** Using CanPath to examine EoBC
- 4** Next Steps



Canadian
Cancer Statistics
2021

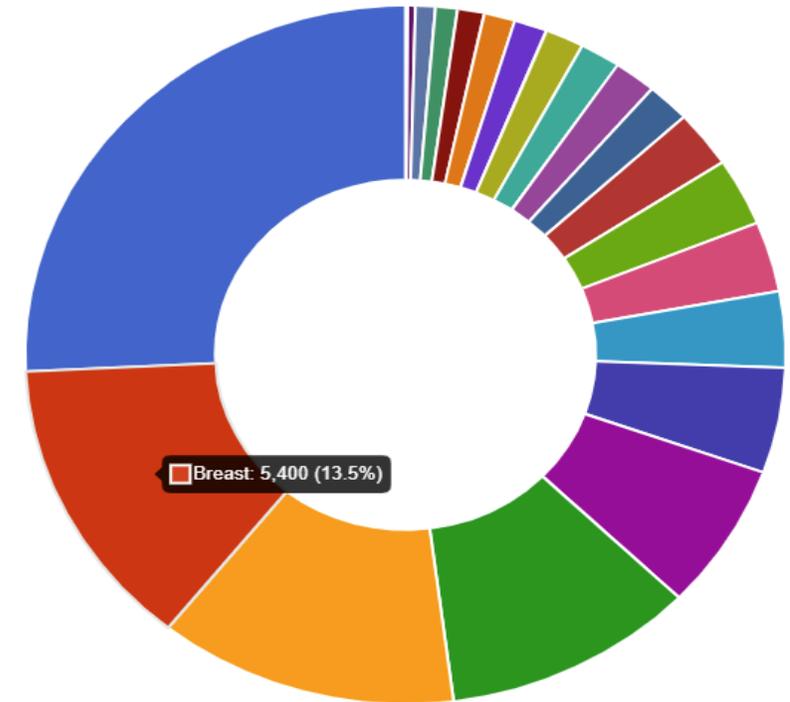
Breast Cancer Incidence, 2021

- Hodgkin lymphoma ■ Esophagus ■ Liver ■ Brain/CNS ■ Stomach ■ Cervix
- Multiple myeloma ■ Head and neck ■ Kidney and renal pelvis ■ Leukemia
- Ovary ■ Pancreas ■ Bladder ■ Melanoma ■ Thyroid ■ Non-Hodgkin lymphoma
- Uterus (body and NOS) ■ Colorectal ■ All other cancers ■ Lung and bronchus
- Breast

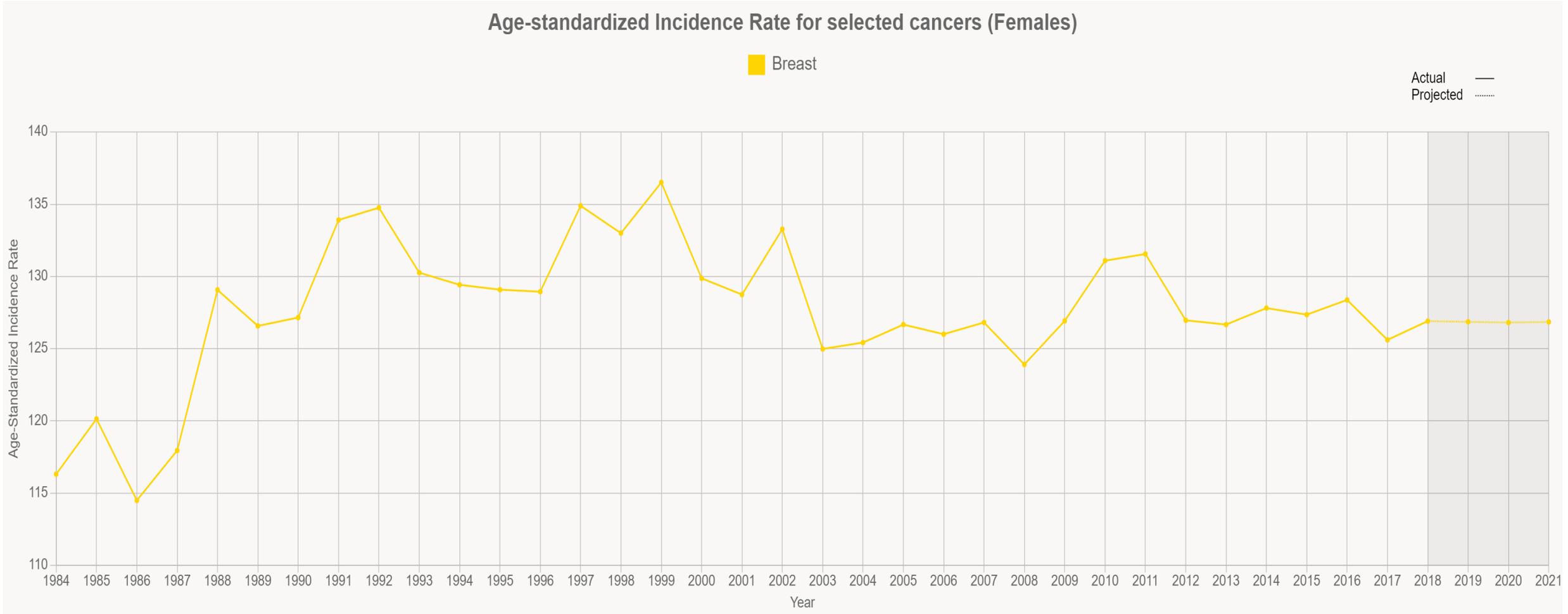


Breast Cancer Mortality, 2021

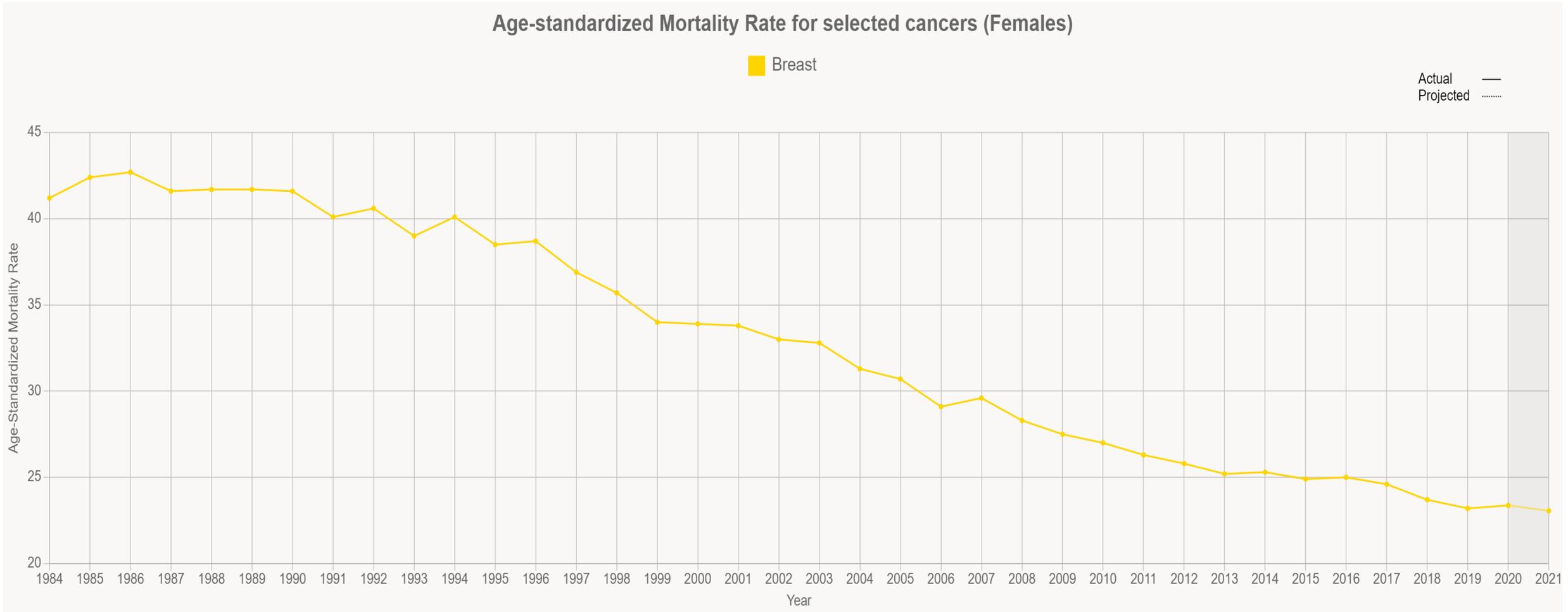
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Breast Cancer Incidence (ASIR), 2021, Canadian Cancer Society



Breast Cancer Mortality (ASMR), 2021, Canadian Cancer Society

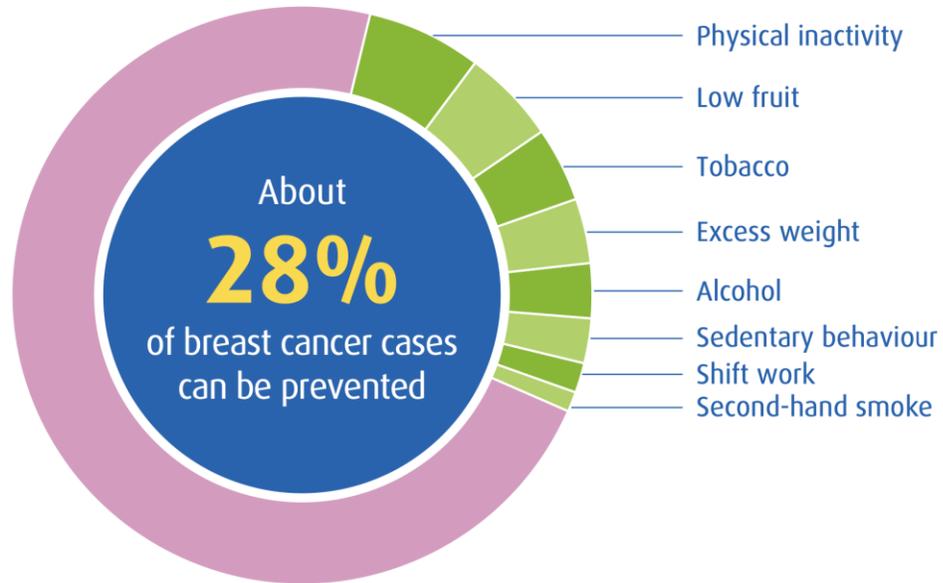


Known modifiable exposures

Preventing breast cancer in Canada



Breast cancer is the most commonly diagnosed cancer among Canadian women.



Prevent.cancer.ca

Many cancers due to Non-modifiable exposures



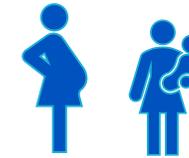
Family History



Genetic mutations and Inherited Genes



Age at menarche, child birth



Reproductive factors



Ethnicity



Age

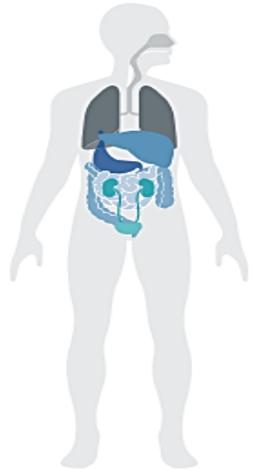


Hormonal Therapies



Personal Health History

Preventable Cancers



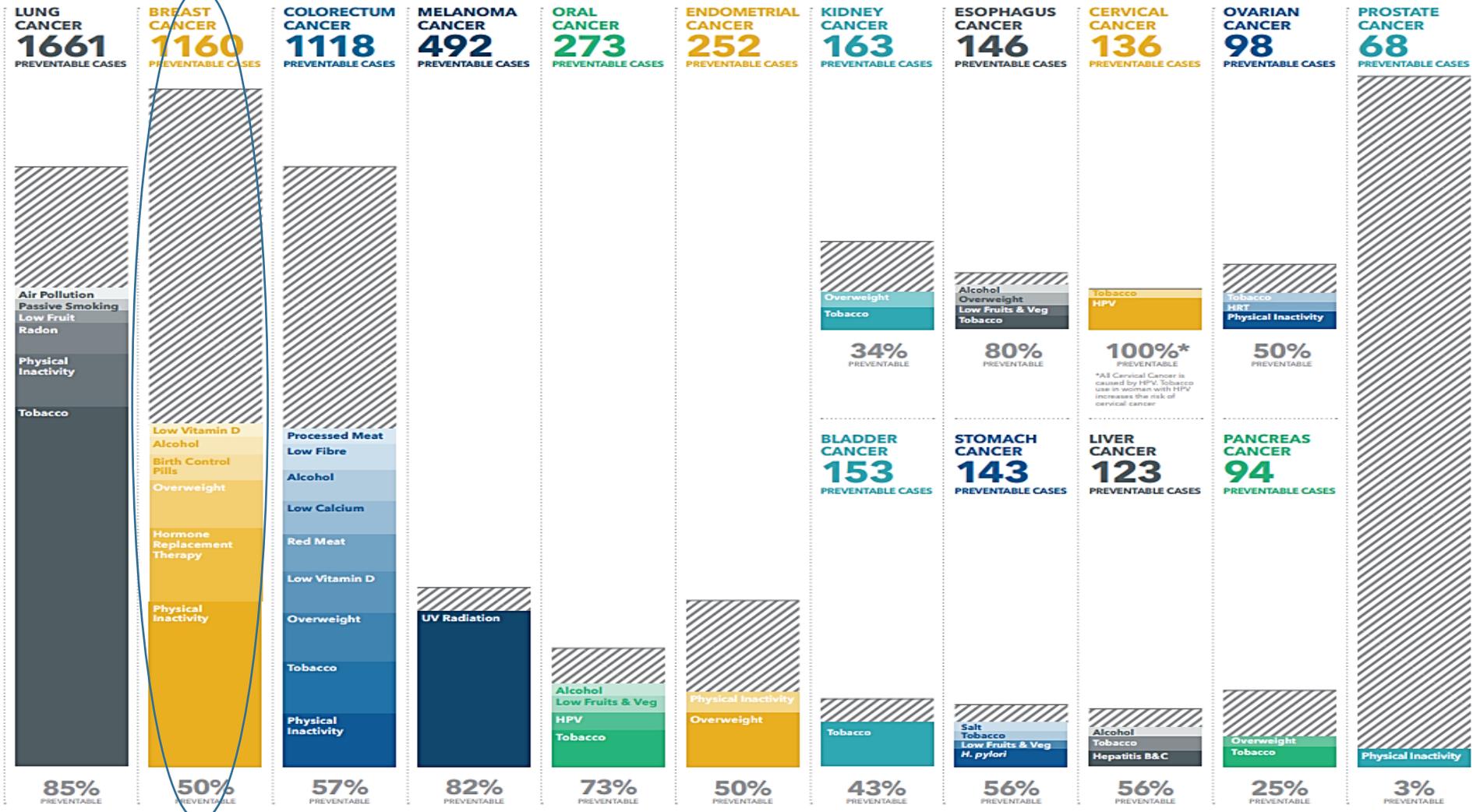
PREVENTABLE CANCER IN ALBERTA

About 45% of cancer in Alberta is caused by factors we can change. That's about 6,700 cancer cases we could prevent each year, if we work together. Some types of cancer are more preventable than others. This graphic shows the cancers in Alberta that could be prevented if we work together. Visit HealthierTogether.ca for more information.

 Cases not linked to modifiable factors

HEALTHIER TOGETHER

HEALTHIERTOGETHER.CA

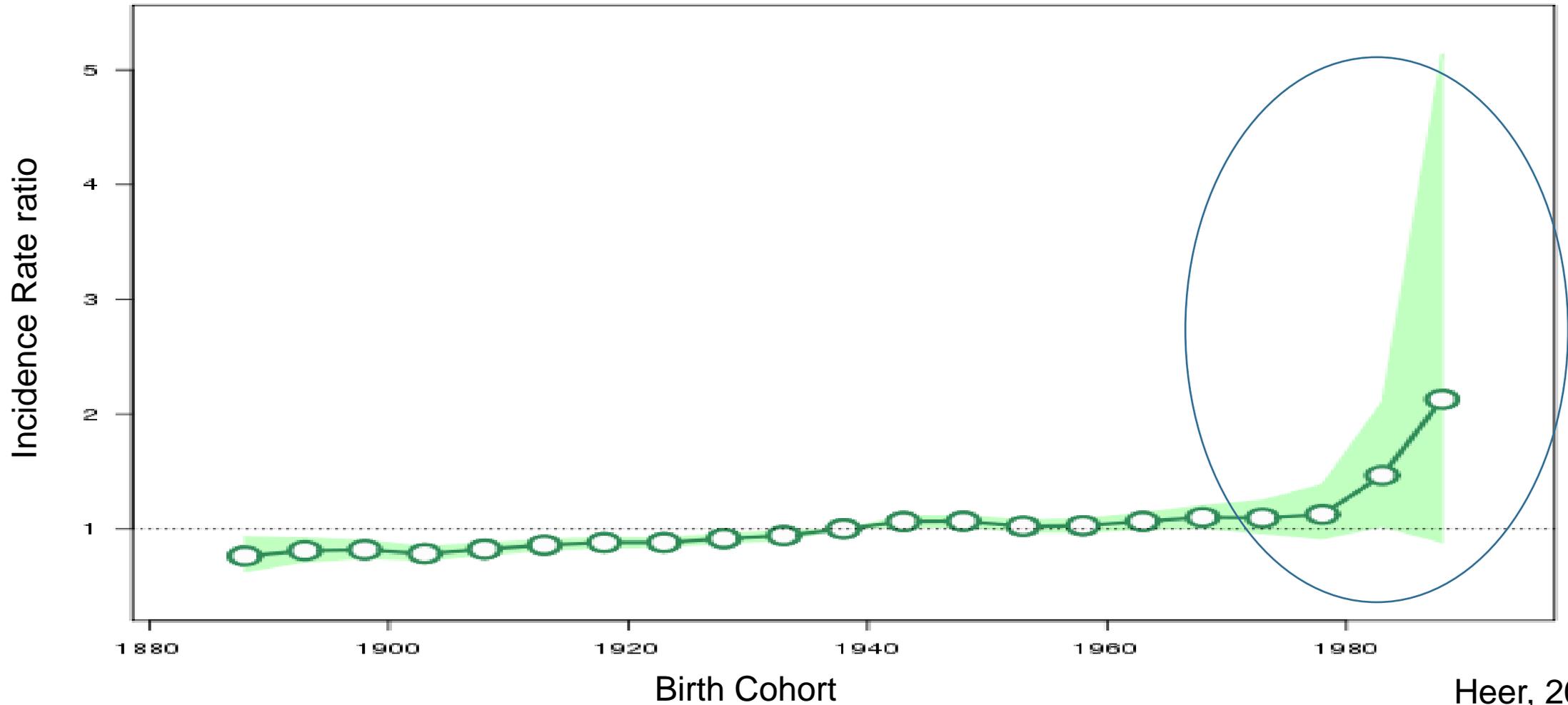


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EoBC – Changing Trends?

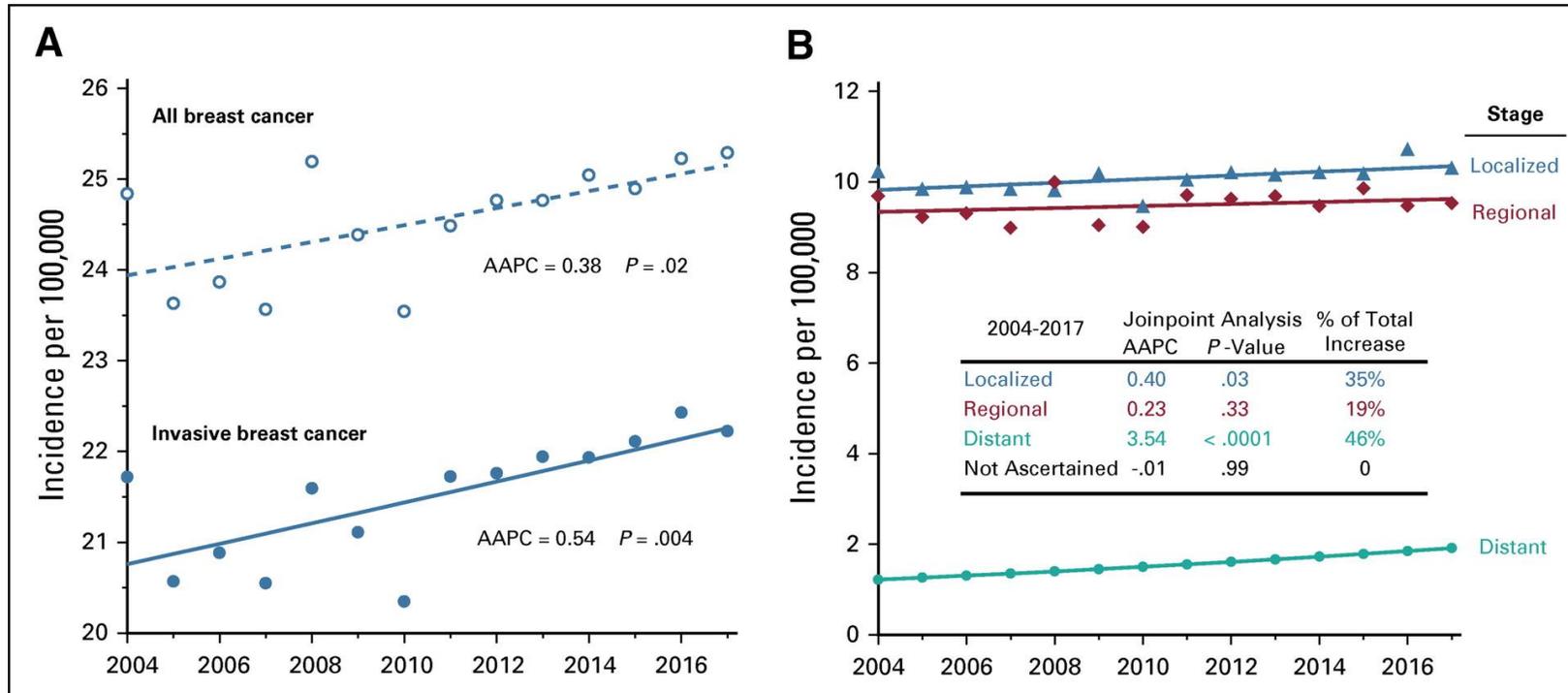
Risk of Breast Cancer by Birth Cohort (1888-1988) in Canada



Heer, 2019, CJPH

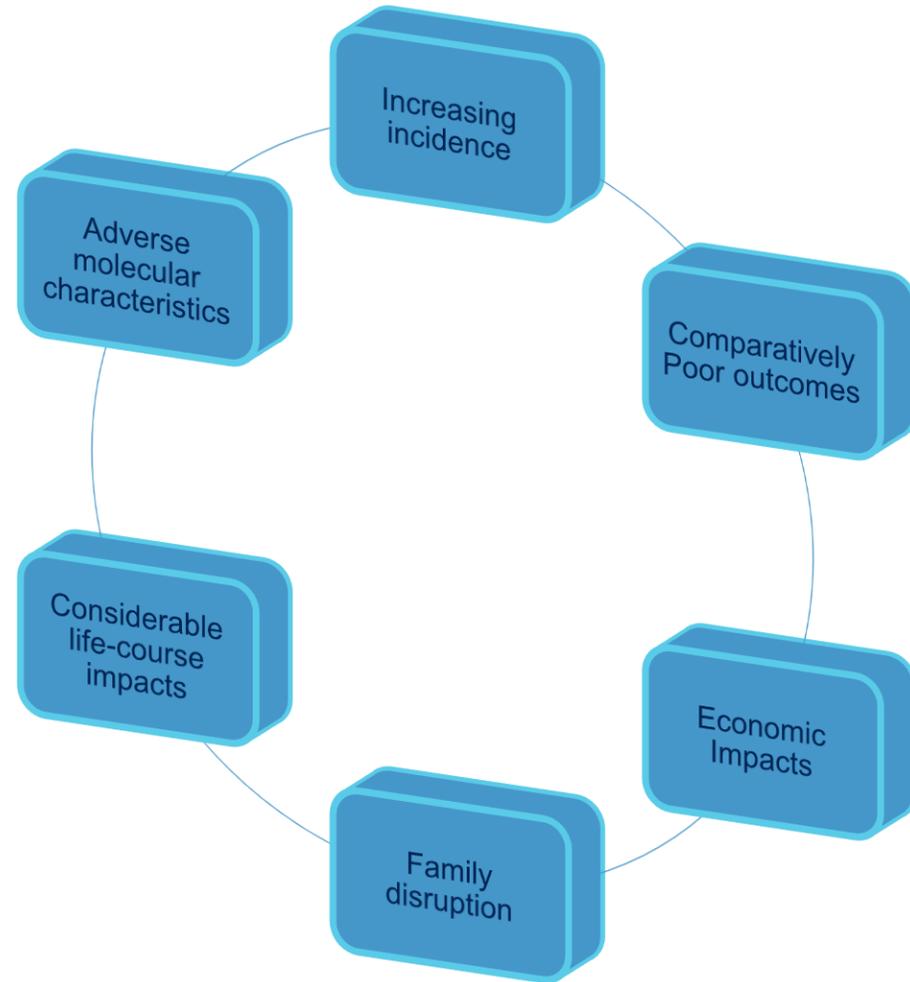
EoBC – Changing Trends?

Annual incidence of breast cancer in women, age 15-39, 2004-2017 in the US



Cathcart-Rake, 2021

EoBC – Major Clinical and Population Health Issue



Article

The Impact of Organised Screening Programs on Breast Cancer Stage at Diagnosis for Canadian Women Aged 40–49 and 50–59

Anna N. Wilkinson ^{1,*} , Jean-Michel Billette ², Larry F. Ellison ², Michael A. Killip ³, Nayaar Islam ⁴ 
and Jean M. Seely ⁵ 



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Healthy Communities.
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AHS lowers recommended age for breast cancer screening

October 18, 2022

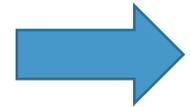
Many Alberta women are now able to start biennial (every two years) breast cancer screening sooner following changes to clinical practice guidelines.

The recommended age for biennial screening for average-risk women has been lowered to 45 from 50. Alberta is the first province in Canada to make these changes, which expand the benefits of routine screening to more people.

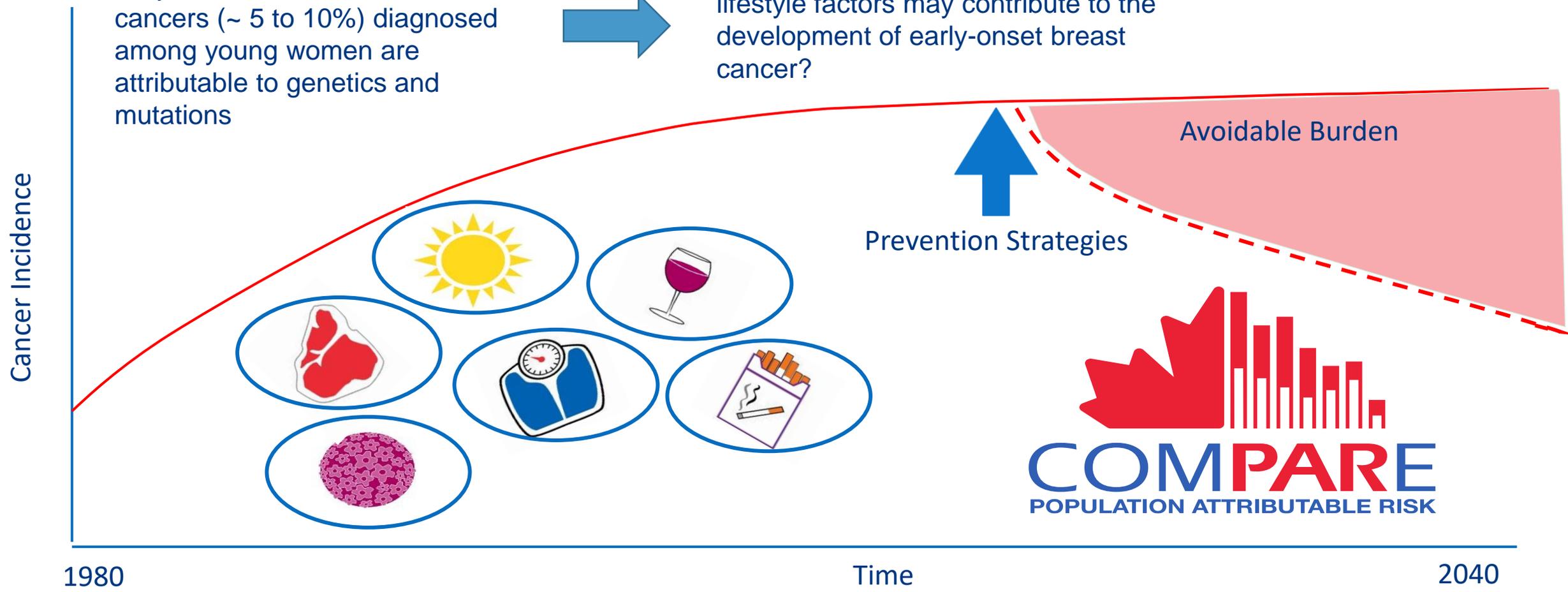
“Early detection and treatment give people with cancer the best chance to survive this disease. Alberta is leading the country by making breast cancer screening available to more women, at a younger age, saving lives in the process,” says Health Minister Jason Copping.

Why is Early-onset Breast Cancer on the Rise?

Only a small number of breast cancers (~ 5 to 10%) diagnosed among young women are attributable to genetics and mutations



Suggests environmental and/or lifestyle factors may contribute to the development of early-onset breast cancer?

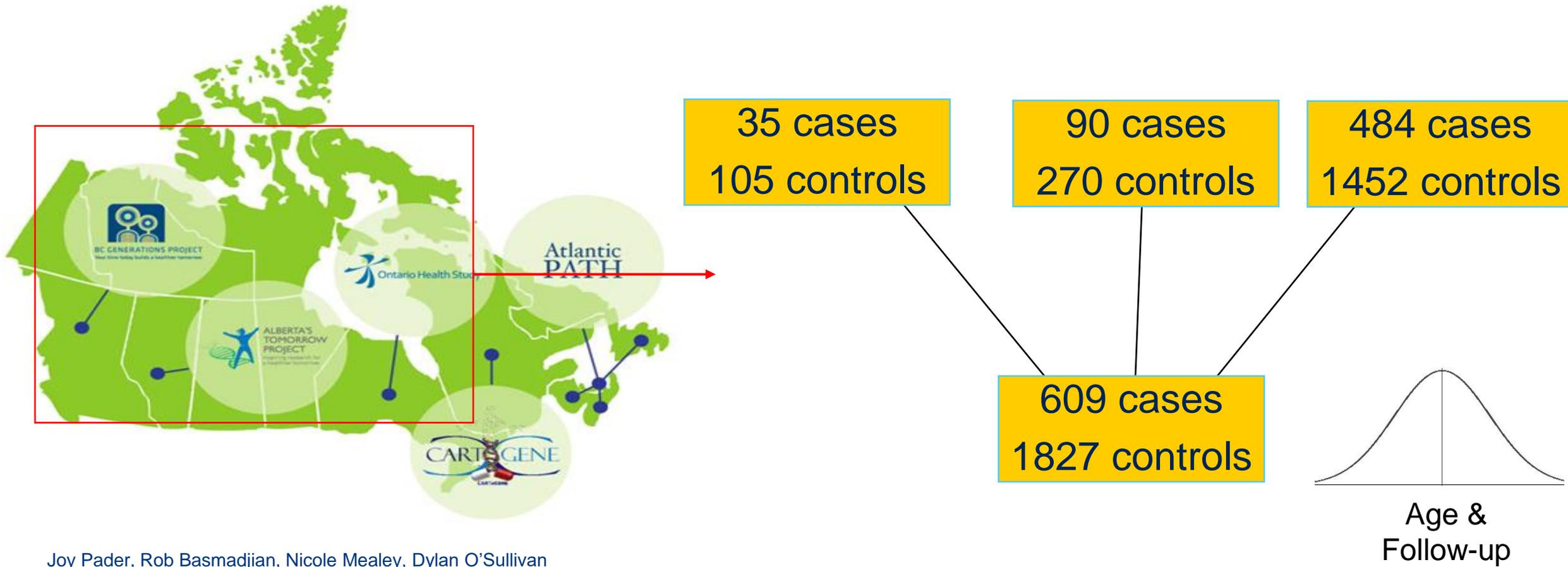


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Examining the Etiology of Young-Onset Breast Cancer in the Canadian Partnership for Tomorrow's Health (CanPath)



Joy Pader, Rob Basmadjian, Nicole Mealey, Dylan O'Sullivan

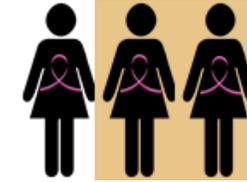
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Cases



Examine Risk

Factors



Controls



Examine Risk

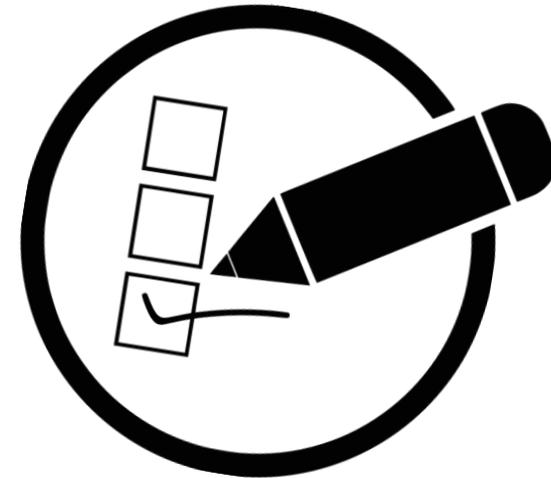
Factors



Pader et al., 2021

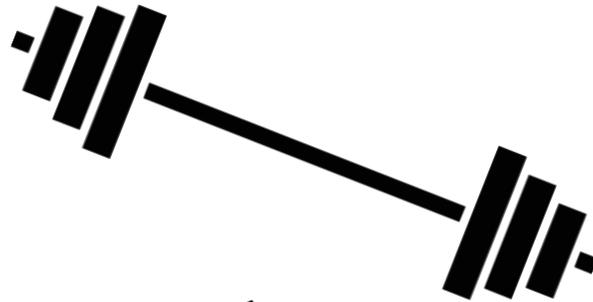
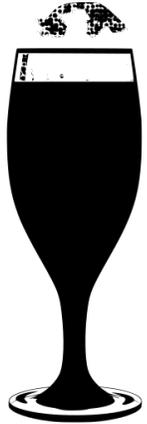
Examining the Etiology of Young-Onset Breast Cancer in the Canadian Partnership for Tomorrow's Health (CanPath)

- Exposure information - Health and Lifestyle Questionnaires
- Case data – Linkage Provincial Cancer Registries



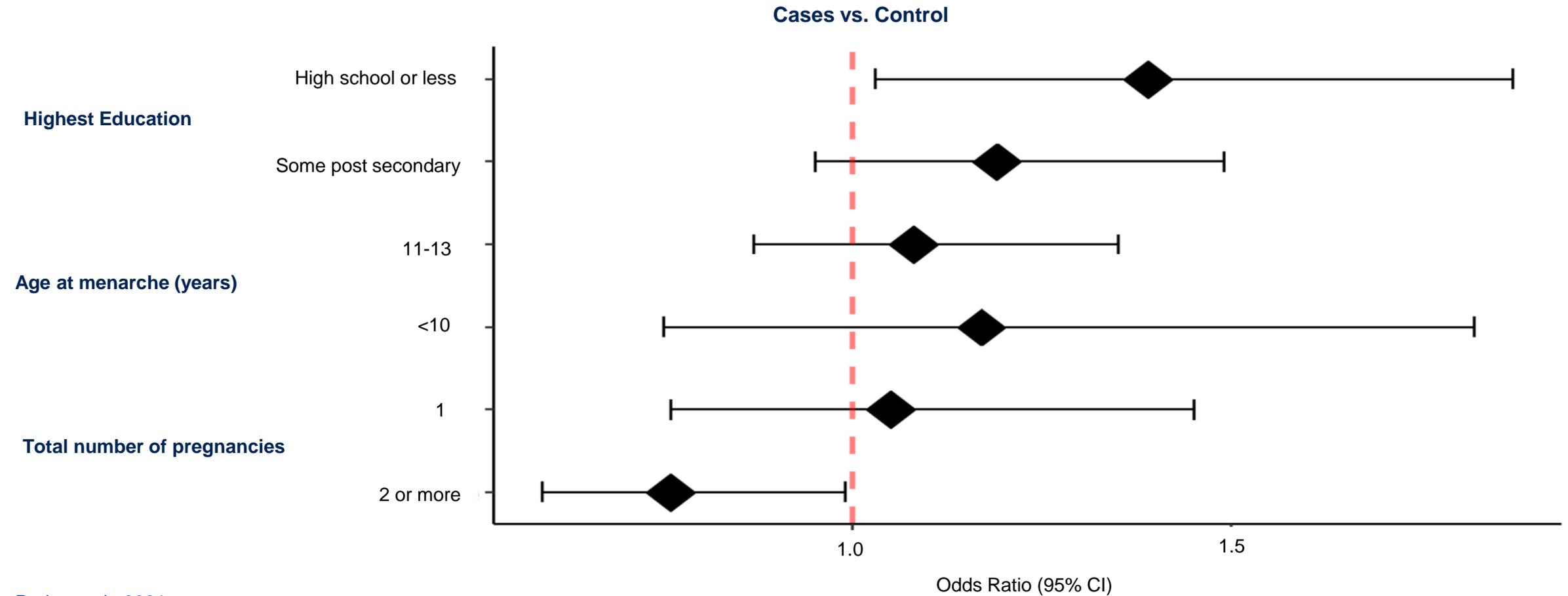
Pader et al., 2021

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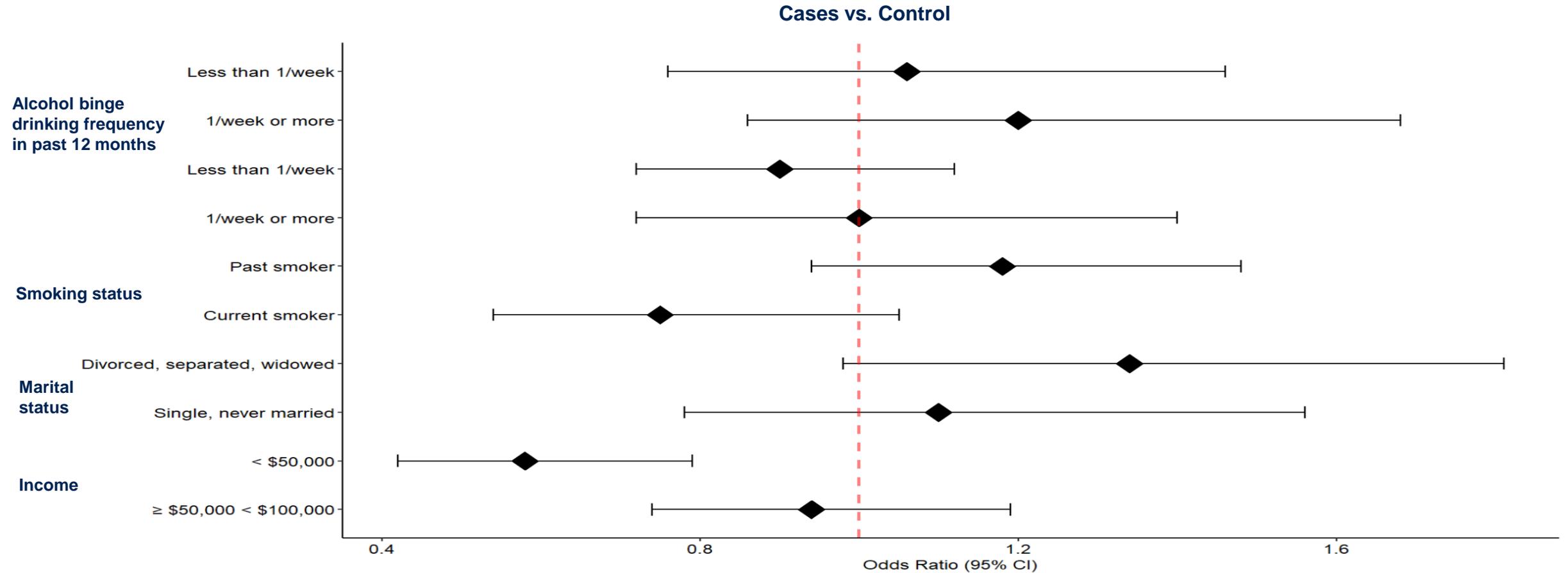
Pader et al., 2021

Examining the Etiology of Young-Onset Breast Cancer in the Canadian Partnership for Tomorrow's Health (CanPath)



Pader et al., 2021

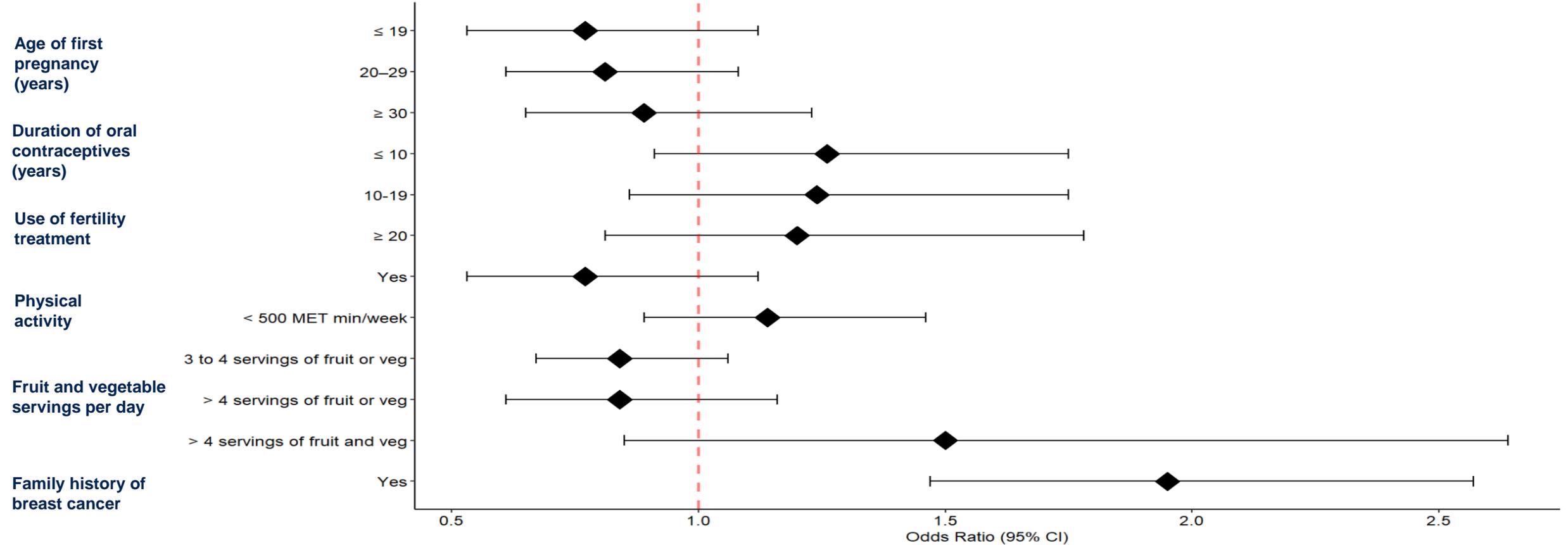
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Pader et al., 2021

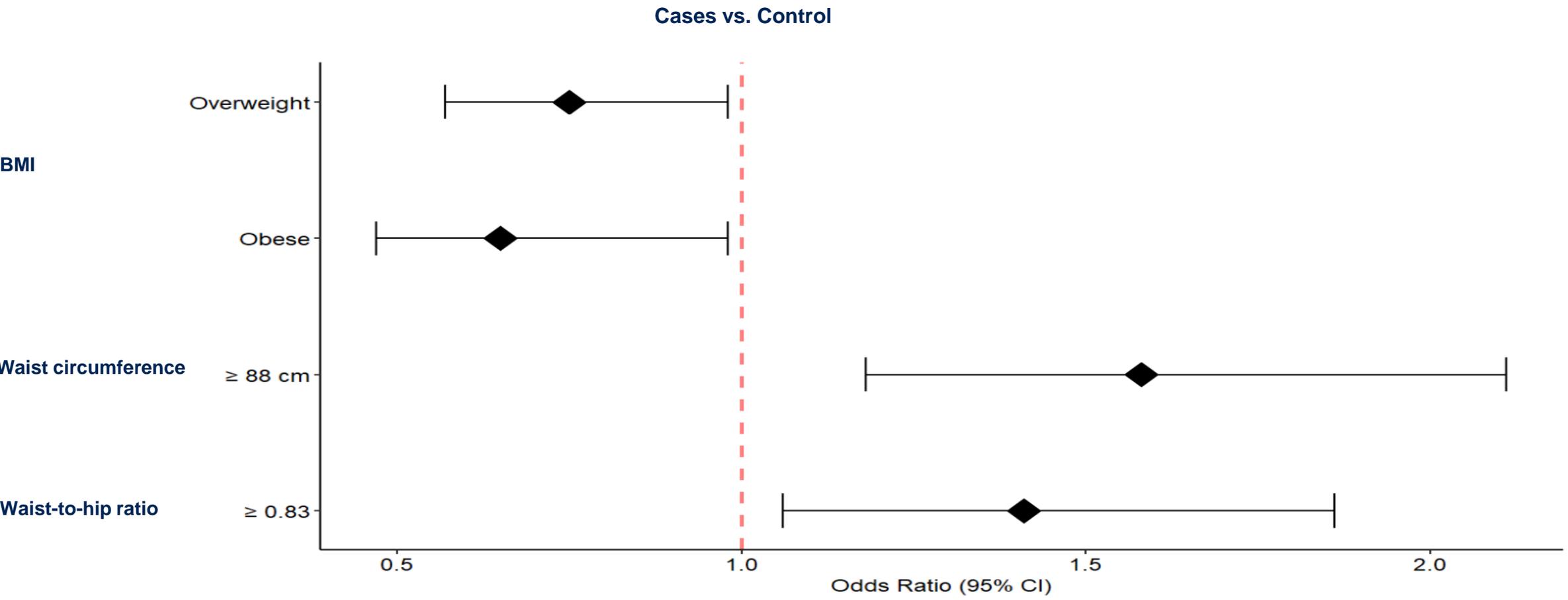
Examining the Etiology of Young-Onset Breast Cancer in the Canadian Partnership for Tomorrow's Health (CanPath)

Cases vs. Control



Pader et al., 2021

Examining the Etiology of Young-Onset Breast Cancer in the Canadian Partnership for Tomorrow's Health (CanPath)



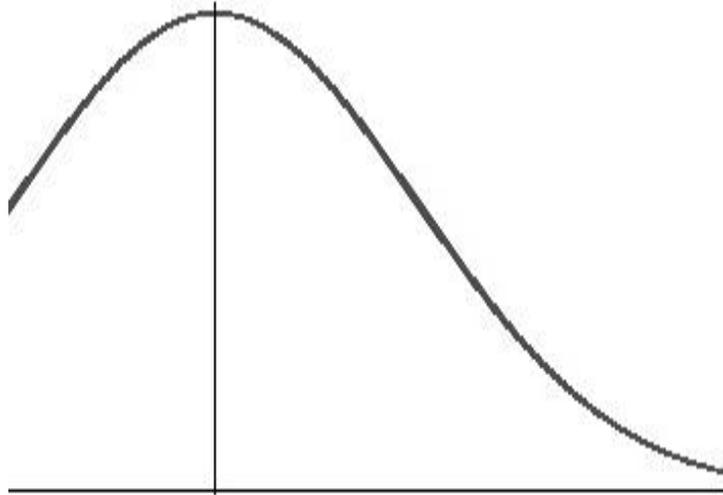
Pader et al., 2021



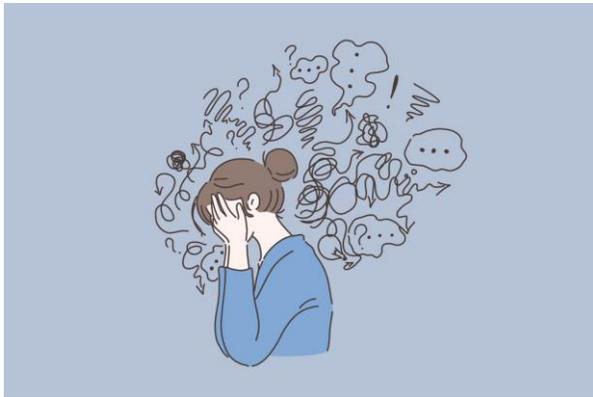
Initial Interpretations

- Energy Balance is involved in EoBC risk – but a complex story
- Family and personal history may be key markers of risk to help guide primary care
- More to do!

Limitations of the Study?



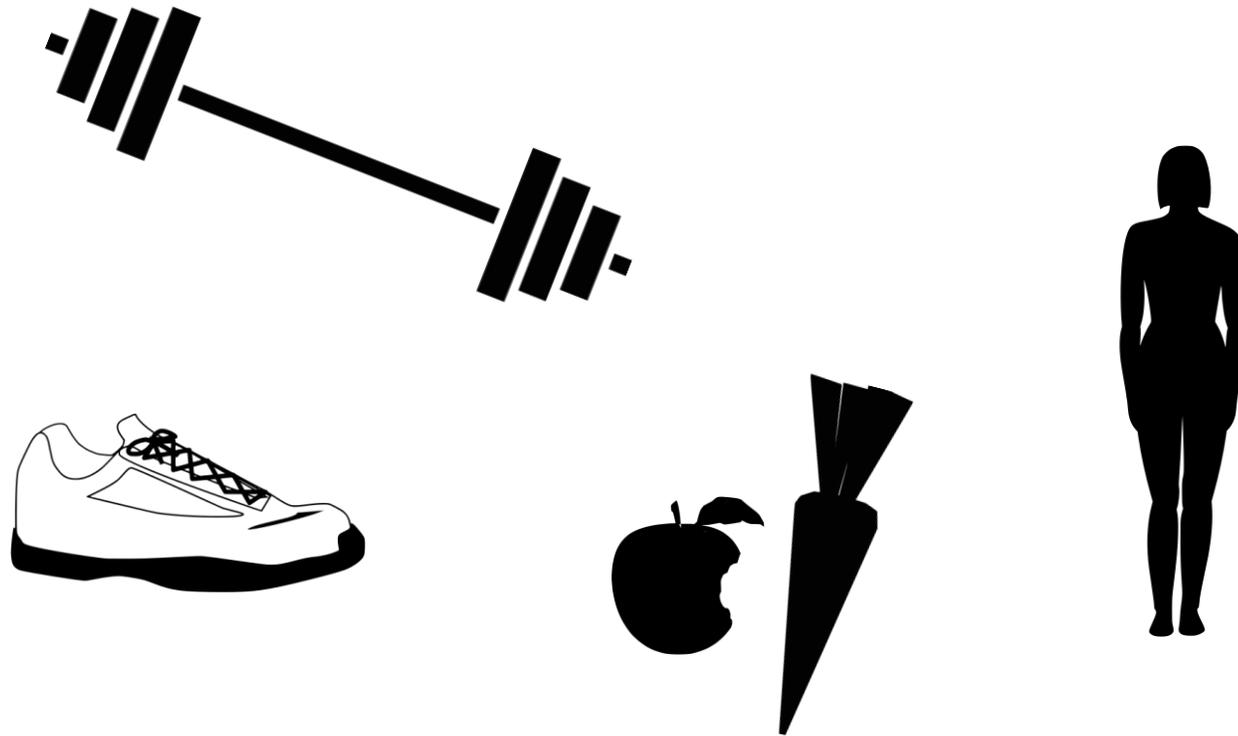
Examining novel exposures?



How can we use these cohorts to better understand these associations?



Biomarkers of inflammation, insulin resistance and breast cancer risk: a nested case-control study from Alberta's Tomorrow Project cohort



Cancer Causes & Control (2020) 31:1057–1068
<https://doi.org/10.1007/s10552-020-01329-6>

ORIGINAL PAPER



High-sensitivity C-reactive protein, hemoglobin A1c and breast cancer risk: a nested case-control study from Alberta's Tomorrow Project cohort

Tiffany R. Price¹ · Christine M. Friedenreich² · Paula J. Robson³ · Haocheng Li⁴ · Darren R. Brenner²

Received: 1 December 2019 / Accepted: 24 July 2020 / Published online: 21 September 2020
© Springer Nature Switzerland AG 2020

Abstract

Purpose Our aim is to examine the associations between high-sensitivity C-reactive protein (hsCRP) and hemoglobin A1c (HbA1c), common biomarkers of inflammation and insulin resistance, respectively, with breast cancer risk, while adjusting for measures of excess body size.

Methods We conducted a nested case-control study within the Alberta's Tomorrow Project cohort (Alberta, Canada) including 197 incident breast cancer cases and 394 matched controls. The sample population included both pre- and postmenopausal women. Serum concentrations of hsCRP and HbA1c were measured from blood samples collected at baseline, along with anthropometric measurements, general health and lifestyle data. Conditional logistic regression was used to evaluate associations between hsCRP, HbA1c, and breast cancer risk adjusted for excess body size (body fat percentage) and other risk factors for breast cancer.

Results Higher concentrations of hsCRP were associated with elevated breast cancer risk (odds ratio [OR] 1.27; 95% confidence interval [95% CI] 1.03–1.55). The observed associations were unchanged with adjustment for body fat percentage. Higher HbA1c concentrations were not significantly associated with an increased breast cancer risk (OR 1.22; 95% CI 0.17–8.75).

Conclusion These data suggest that hsCRP may be associated with elevated breast cancer risk, independent of excess body size. However, elevated concentrations of HbA1c did not appear to increase breast cancer risk in apparently healthy women.

Keywords Breast cancer · High-sensitivity C-reactive protein · Hemoglobin A1c · Alberta's Tomorrow Project cohort · Nested case-control study

Introduction

Breast cancer is the most common malignancy affecting women in Canada. In 2019, breast cancer represented 25% of all new cancers among Canadian women and 13% of all cancers [1, 2]. Average 5-year survival for breast cancer in Canada is 87%, with health outcomes varying substantially across subtypes of breast cancer and stage at diagnosis [1, 2]. Obesity has been associated with postmenopausal breast cancer risk [3]. The mechanisms relating excess body size to postmenopausal status and breast cancer risk may involve elevated estrogen production associated with fat tissue and subsequent elevation of circulating concentrations of estradiol. However, several other biological mechanisms have

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s10552-020-01329-6>) contains supplementary material, which is available to authorized users.

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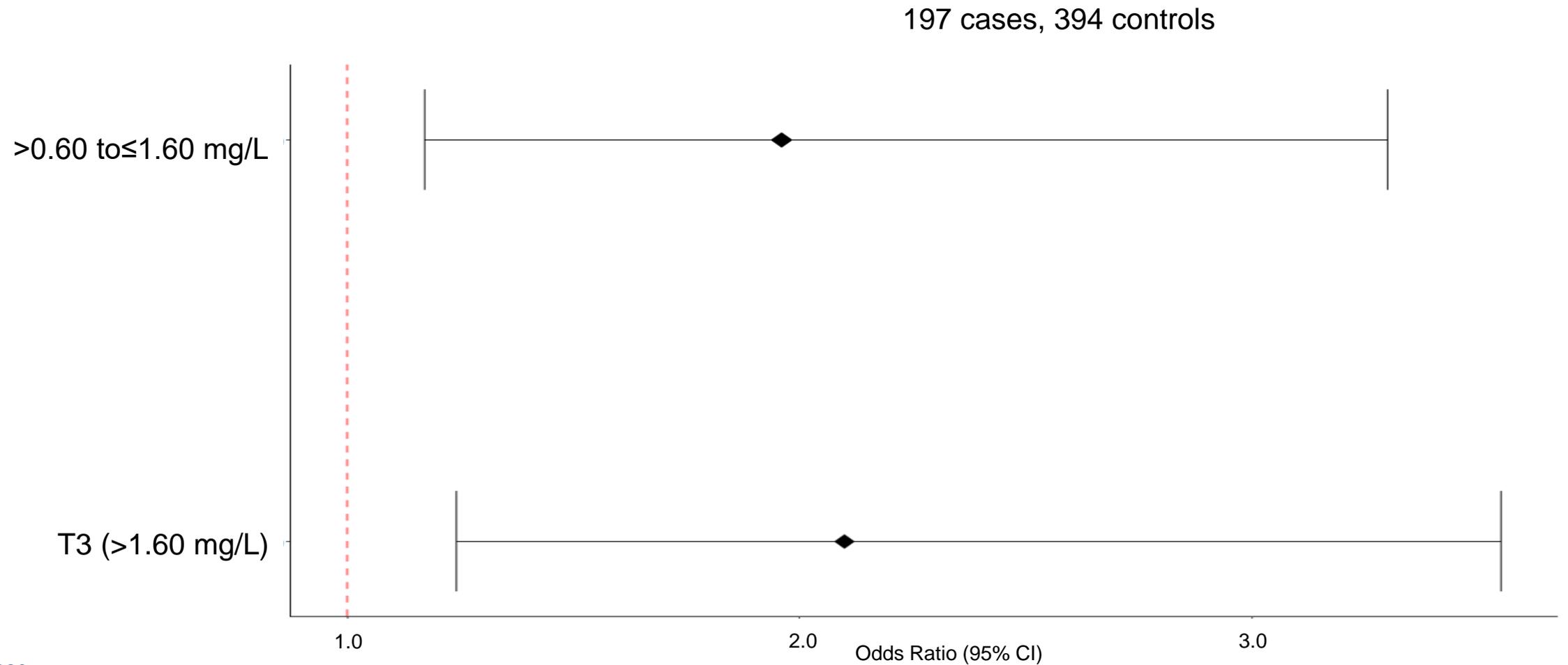
¹ Community Health Sciences, University of Calgary, Calgary, AB, Canada

² Department of Cancer Epidemiology and Prevention Research, Alberta Health Services, Calgary, AB, Canada

³ Cancer Research & Analytics, CancerControl Alberta.

Price T. et al., 2020

Biomarkers of inflammation, insulin resistance and breast cancer risk: a nested case-control study from Alberta's Tomorrow Project cohort



Price T. et al., 2020

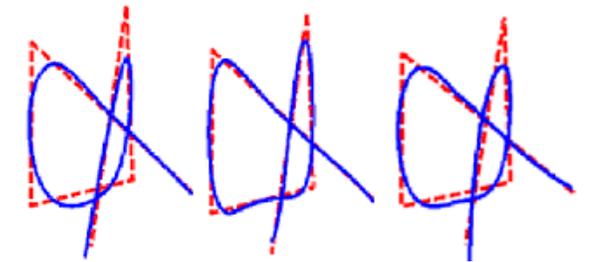
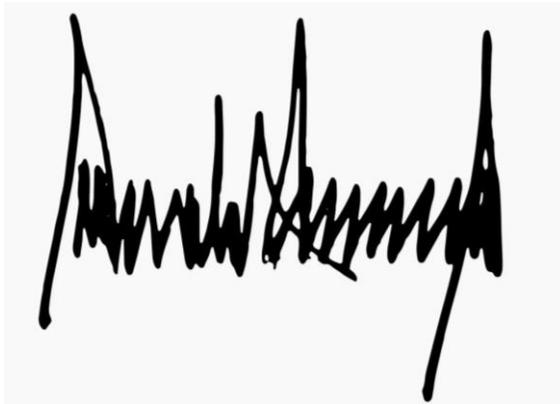
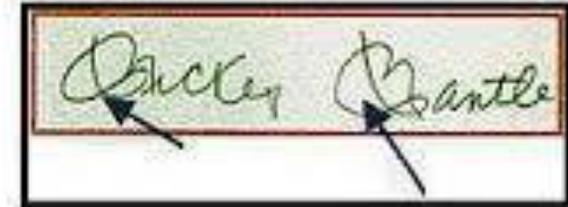
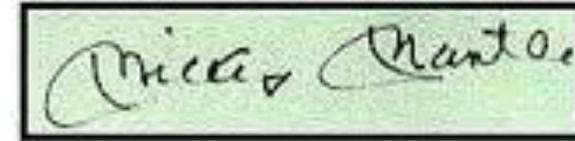
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What about exposures we haven't measured?

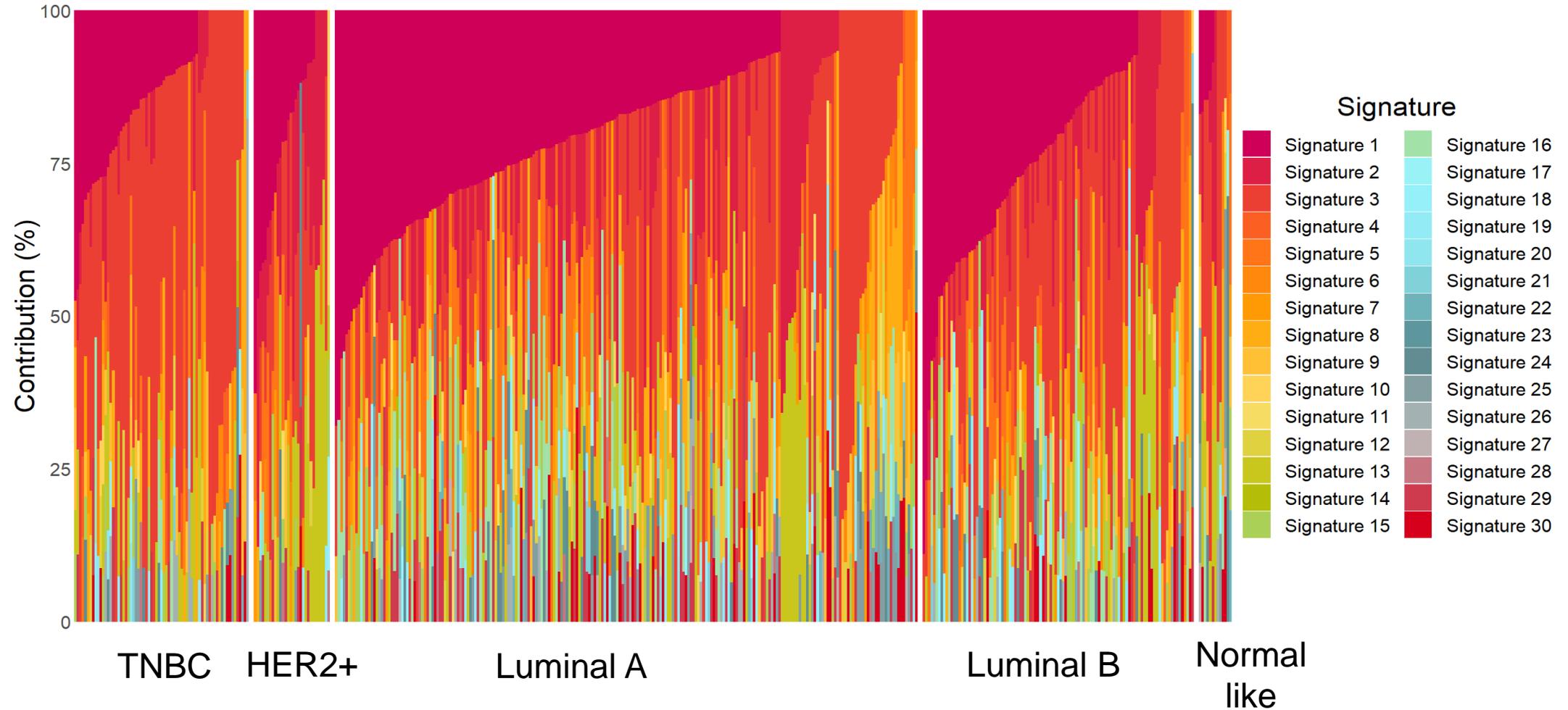


Can we use the genome to identify “causes” of cancer?



Mutational Signatures – Pilot studies

Later-onset Breast Cancer

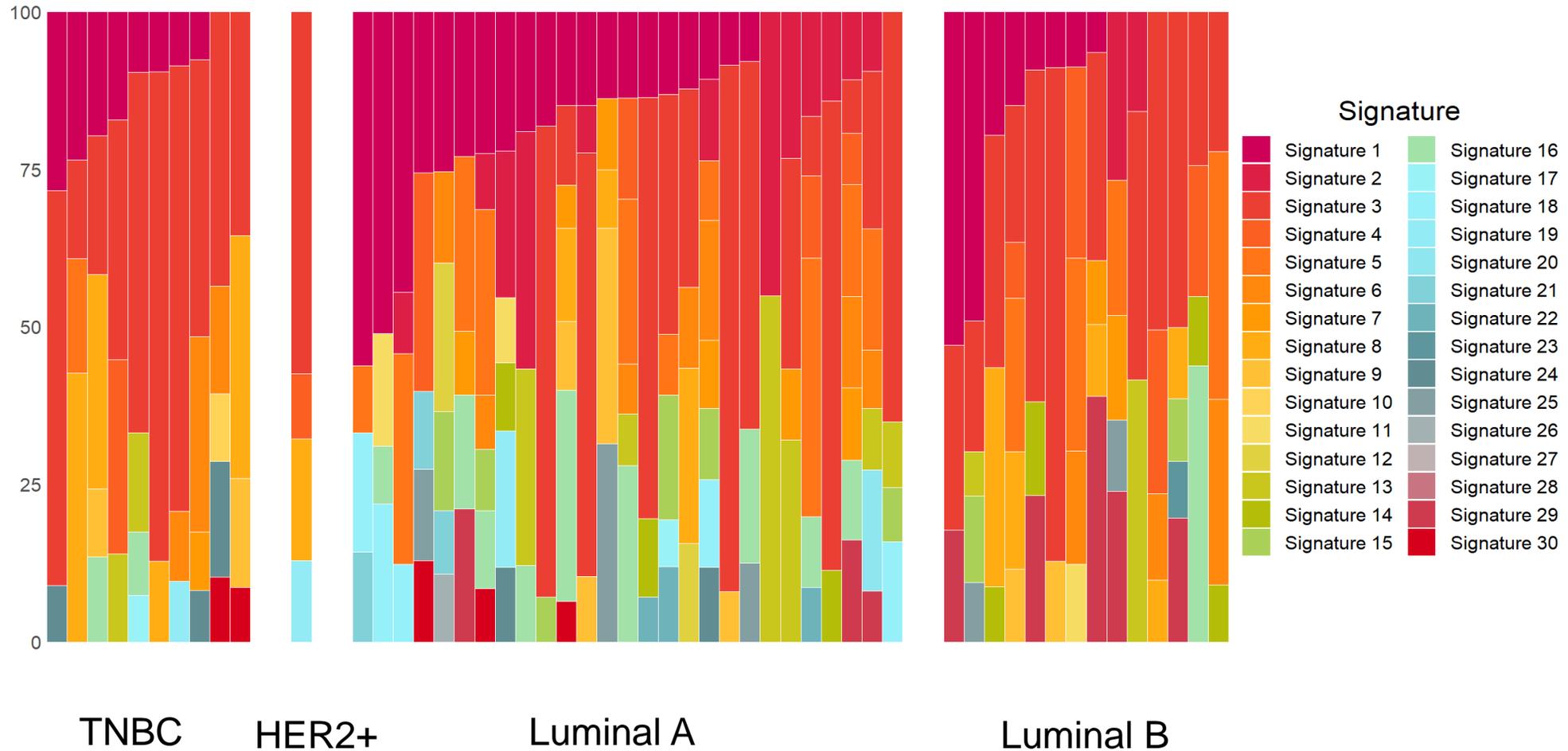


Data from cancer genome atlas

Mealey et al, 2020

Mutational Signatures – Pilot studies

Early-onset Breast Cancer

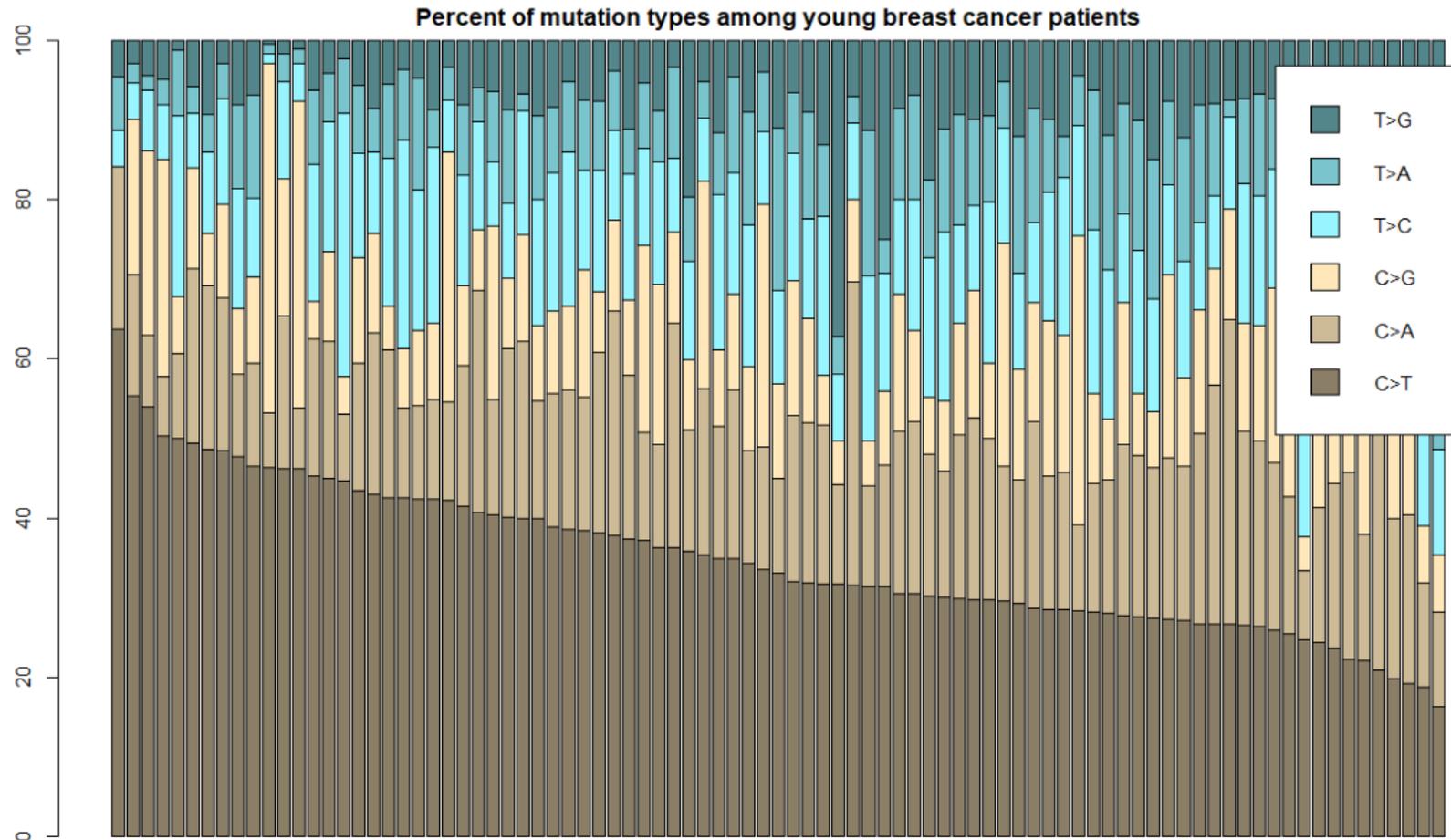


Data from cancer genome atlas

Mealey et al, 2020

Mutational Signatures – Pilot studies

Later-onset Breast Cancer



Significantly higher amount of C>A mutations in younger patients

Difference imply different "processes" driving cancer

Data from cancer genome atlas

Mealey et al, 2020

Mutational Signatures



RUBY 

The Cancer Genome Atlas

- ◀ Excellent starting resource
- ◀ Limited clinical detail and no exposure data for BC



Alberta samples from ACRB

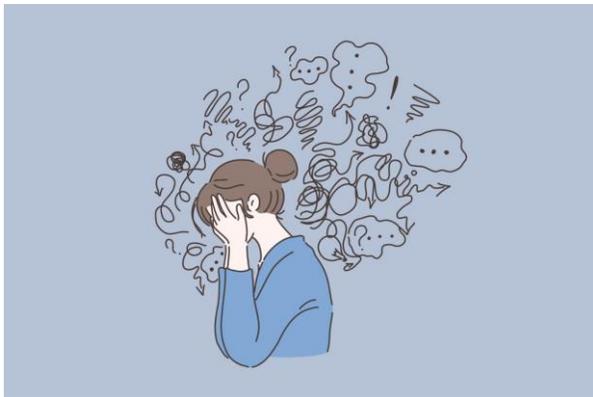
- ◀ Excellent Clinical Data
- ◀ Survival and Outcome Data
- ◀ Exposure data – not ideal



Canadian Partnership for Tomorrow Project RUBY



Mutational Signatures for novel exposures?



Discussion & Next Steps

- CanPath has provided strong framework for large-scale studies of cancer risk
- Additional etiologic research to confirm known and examine novel exposures
- Continued studies of environment and the genome - impact cancer outcomes
- Impact on screening guidelines?
 - Risk stratification & Prediction
- Continued surveillance of emerging trends

Acknowledgements

Calgary Team

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Eliya Farah
Haochang Li

ATP team

Paula Robson
Jennifer Vena
Grace Shen-Tu

BC GEN team
OHS team

CanPath Participants



Q&A



CanPath

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