Early Onset Cancers

Arkhjamil Angeles

BC Cancer Surrey

Disclosures

Honorarium: Pfizer, Eisai
Advisory Board: Eisai

Objectives

1. Define early onset cancer (EOC)
2. Summarize the epidemiology and trends of EOC
3. Review potential risk factors for EOC
4. Review differences between EOC and later onset cancers
5. Summarize outcomes for patients with EOC
6. Clinical practice considerations for patients with EOC

Definition

- **Early onset cancer (EOC)**—defined as malignancies diagnosed before age 50

Epidemiology

- EOCs have shown a marked increase in incidence in Canada and globally over the past two decades, particularly for colorectal, breast, thyroid, and certain GI cancers
- Compared with the 1943 birth cohort, persons born circa 1988 had approximately 5- and 2-fold greater risks of rectal cancer and colon cancer
- Early onset CRC accounts for ~10% of all new diagnoses of CRC, which has shifted the median age at diagnosis from 72 years in the early 2000 to 66 years at present

Veer et al. Cancer. Aug 2020.
Sinicrope. NEJM. Apr 2022.

Cancer
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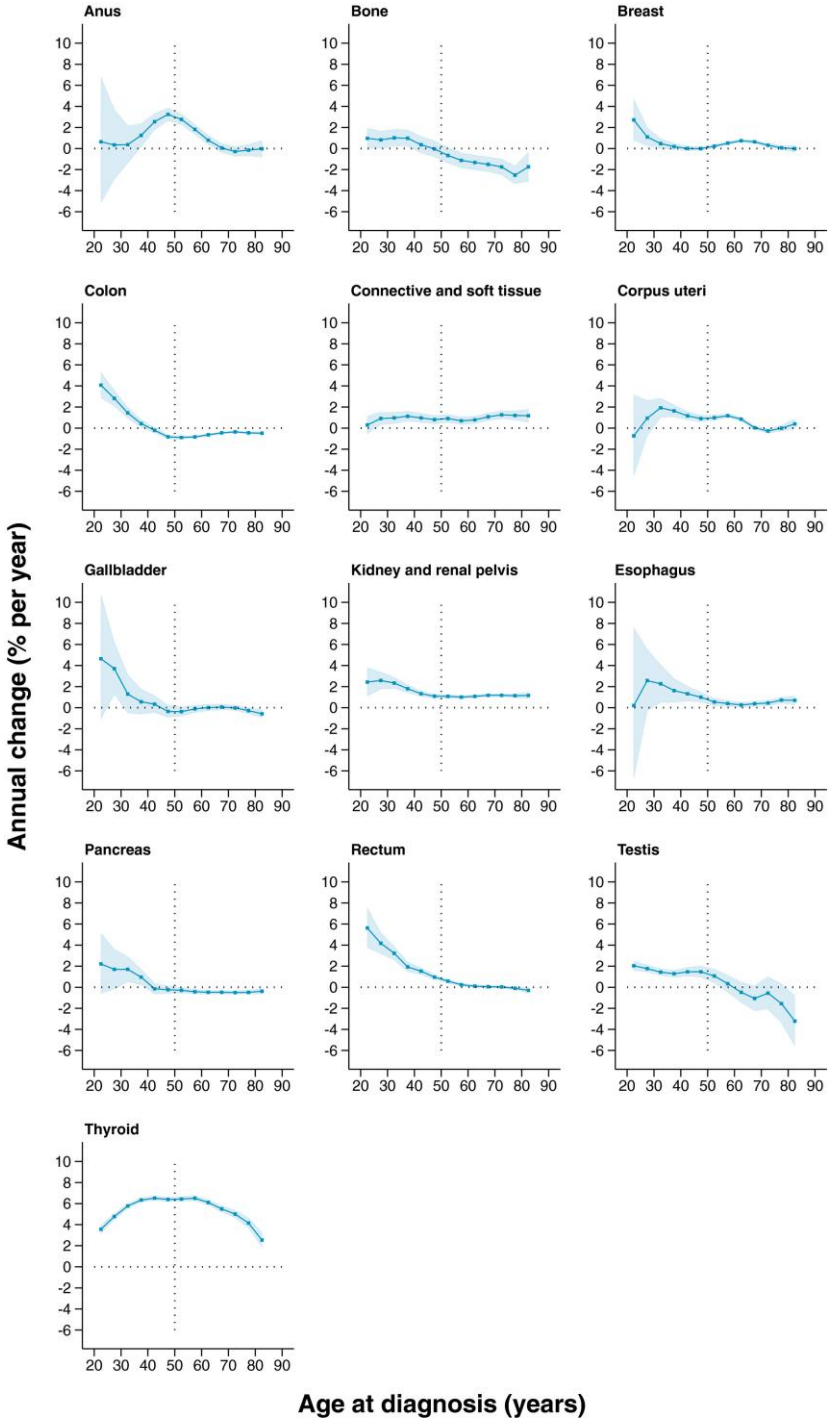
Emerging cancer incidence trends in Canada: The growing burden of young adult cancers

Emily V. Heer MSc, Andrew S. Harper MSc, Hyuna Sung PhD, Ahmedin Jemal PhD, Miranda M. Fidler-Benaoudia PhD

Age-specific average annual percentage changes for cancers that are **increasing** in young adults, 1983-2012



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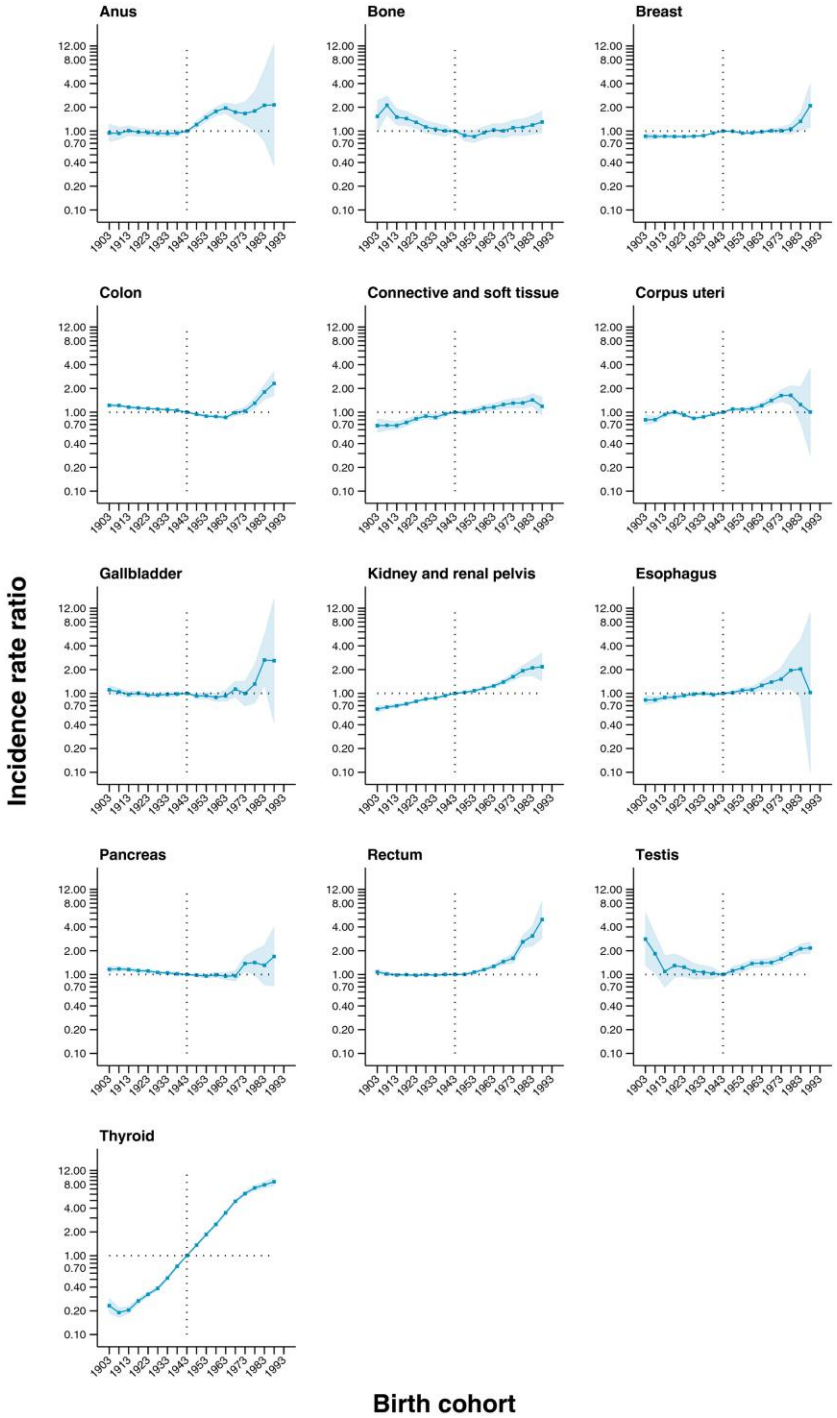
Incidence rate ratios by birth cohort from 1903 to 1993 for cancers that are **increasing** in young adults, 1983-2012



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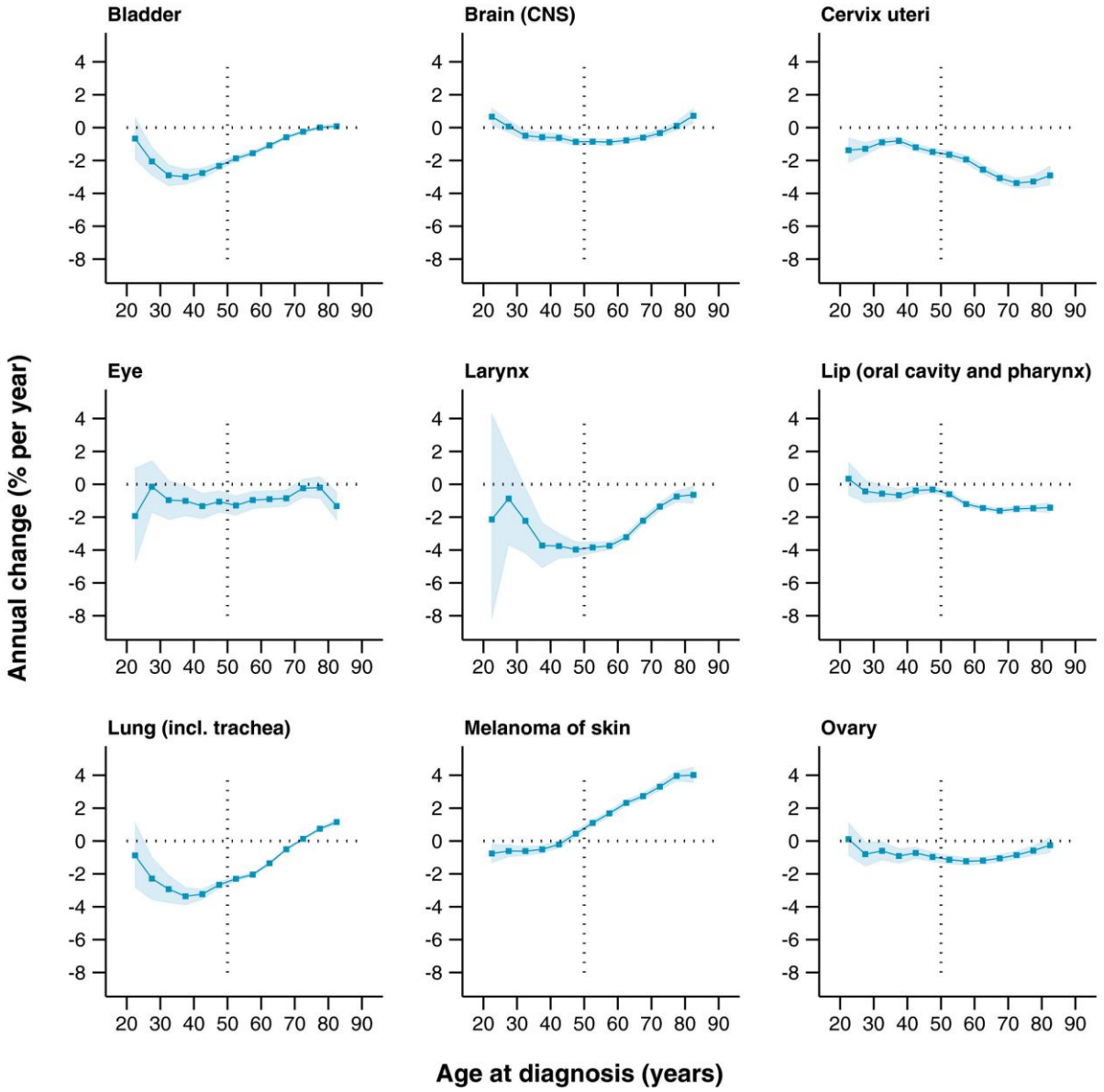
Age-specific average annual percentage changes for cancers that are **decreasing** in young adults, 1983-2012



Veer et al. Cancer. Aug 2020.

› Am J Gastroenterol. 2022 Sep 1;117(9):1502-1507. doi: 10.14309/ajg.0000000000001884. Epub 2022 Jun 10.

Early-Onset Colorectal Cancer Incidence, Staging, and Mortality in Canada: Implications for Population-Based Screening

Dylan E O'Sullivan [1 2 3], Yibing Ruan [4], Winson Y Cheung [1 5], Nauzer Forbes [1 3 5], Steven J Heitman [1 3 5], Robert J Hilsden [1 3 5], Darren R Brenner [1 2 3 4]

Affiliations + expand

PMID: 35973186 DOI: 10.14309

› Cancer Epidemiol. 2024 Oct:92:102640. doi: 10.1016/j.canep.2024.102640. Epub 2024 Aug 5.

Age-specific colorectal cancer incidence trends in Canada, 1971-2021

Emily Heer [1], Yibing Ruan [2], Matthew T Warkentin [3], Robert J Hilsden [4], Linda Rabeneck [5], Dylan E O'Sullivan [2], Darren R Brenner [6]

Affiliations + expand

PMID: 39106619 DOI: 10.1016/j.canep.2024.102

› Can Assoc Radiol J. 2024 Nov;75(4):847-854. doi: 10.1177/08465371241246422. Epub 2024 Apr 25.

Incidence of Breast Cancer in Younger Women: A Canadian Trend Analysis

Jean M Seely [1], Larry F Ellison [2], Jean-Michel Billette [2], Shary X Zhang [2], Anna N Wilkinson [3]

Affiliations + expand

PMID: 38664982 DOI: 10.1177/084653712412464

› J Natl Cancer Inst. 2025 Aug 23:djaf238. doi: 10.1093/jnci/djaf238. Online ahead of print.

Increase of early-onset colorectal cancer: a cohort effect

Laura Downham [1], Mathieu Laversanne [2], Sandra Perdomo [3], Adalberto M Filho [2], Freddie Bray [2], Paul Brennan [3]

Affiliations + expand

PMID: 40848248 DOI: 10.1093/jnci/djaf238

The NEW ENGLAND JOURNAL of MEDICINE

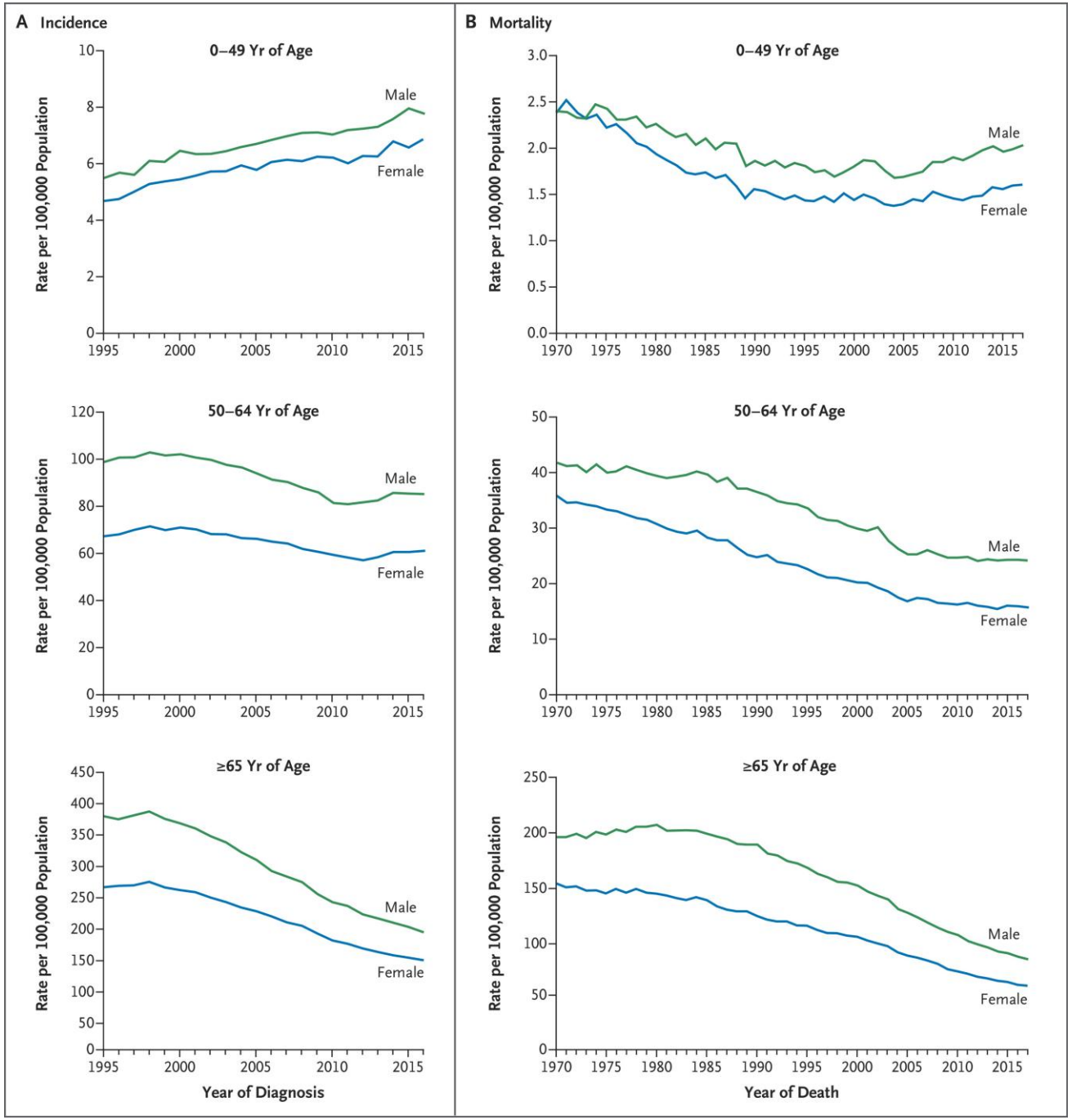
REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Increasing Incidence of Early-Onset Colorectal Cancer

Frank A. Sinicrope, M.D.

Rising incidence of colorectal cancer diagnoses in patients aged **<50 years** in the US

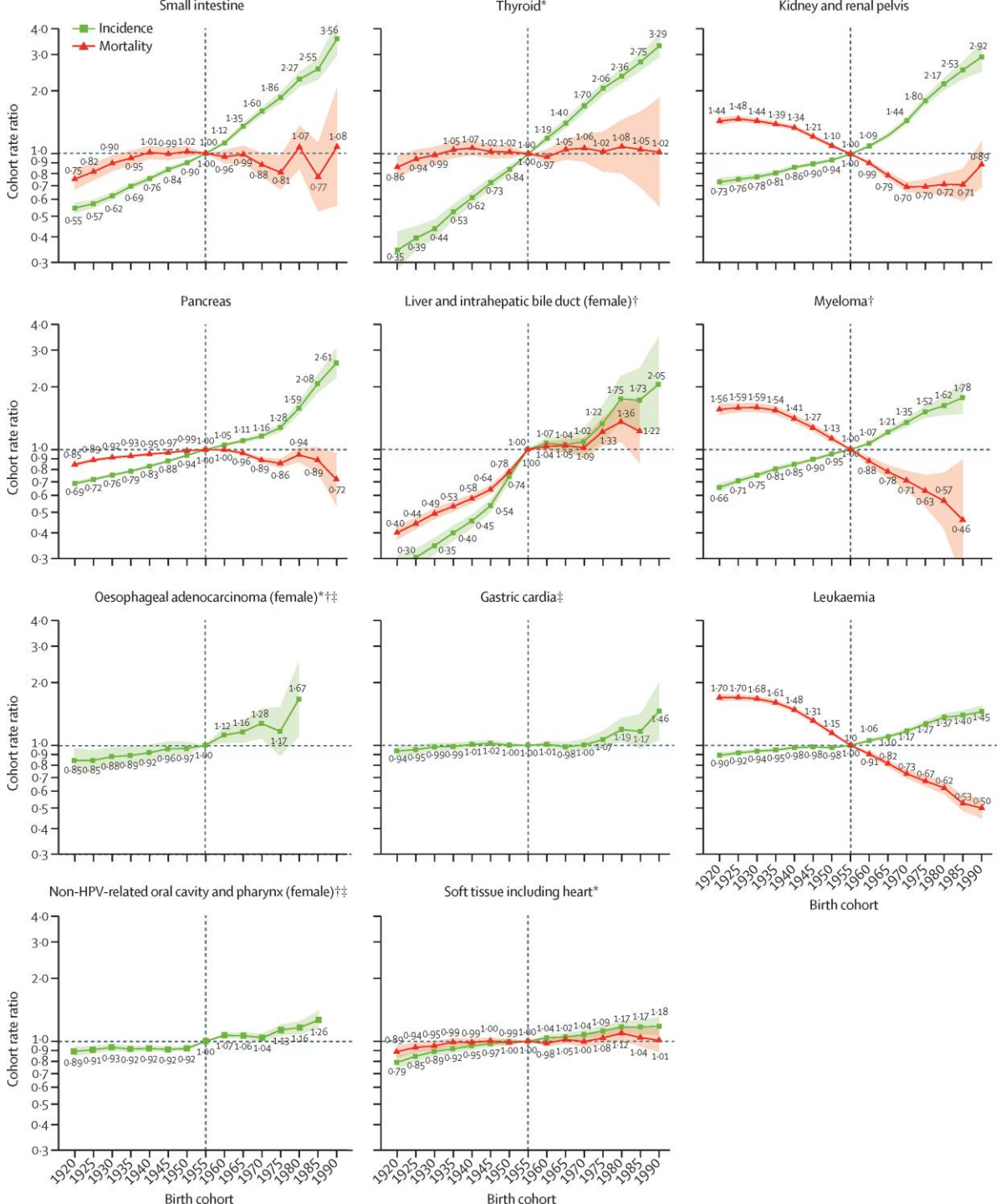


Sinicrope. NEJM. Apr 2022.

Differences in cancer rates among adults born between 1920 and 1990 in the USA: an analysis of population-based cancer registry data

Hyuna Sung, Chenxi Jiang, Priti Bandi, Adair Minihan, Miranda Fidler-Benaoudia, Farhad Islami, Rebecca L Siegel, Ahmedin Jemal

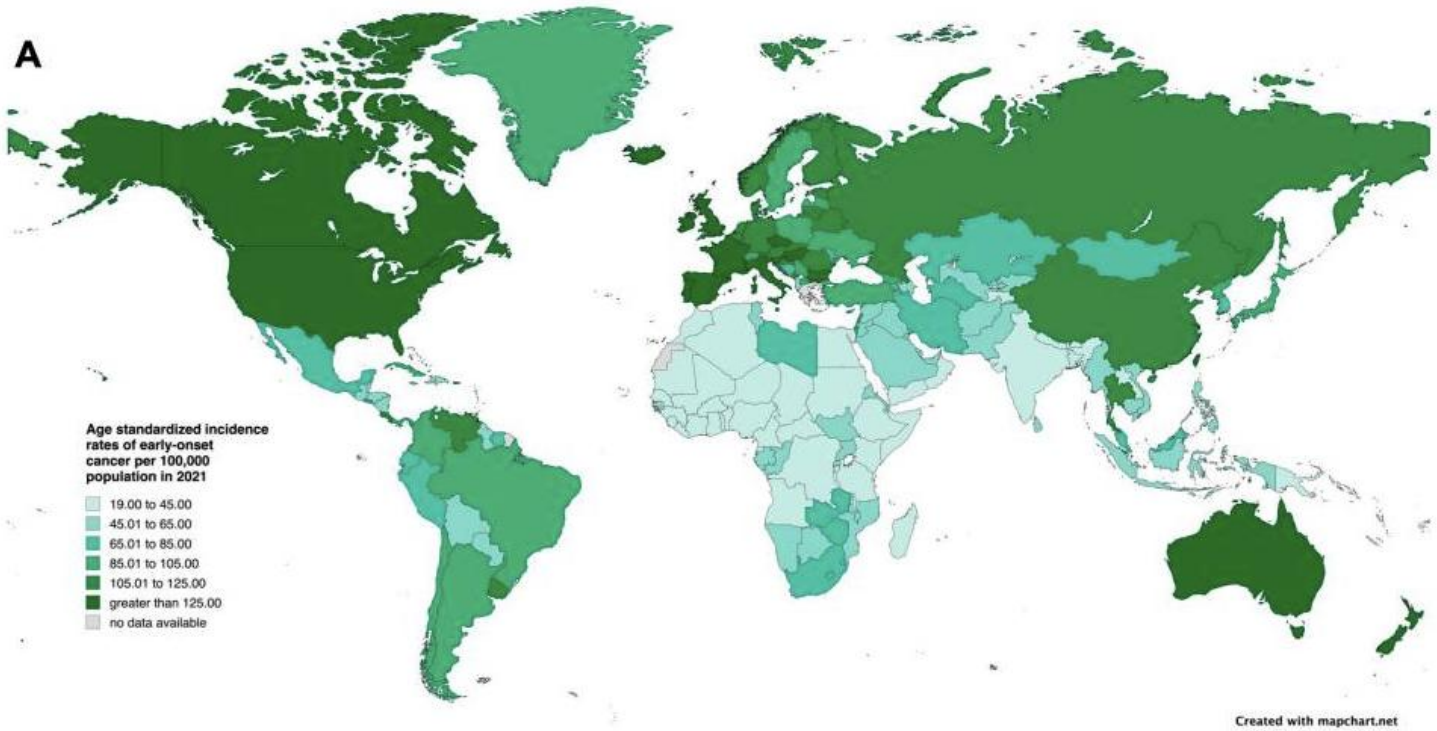
Birth cohort incidence and mortality rate ratio trends from 1920 to 1990 for 11 cancers with a **consistent increase in incidence** across birth cohorts in the USA

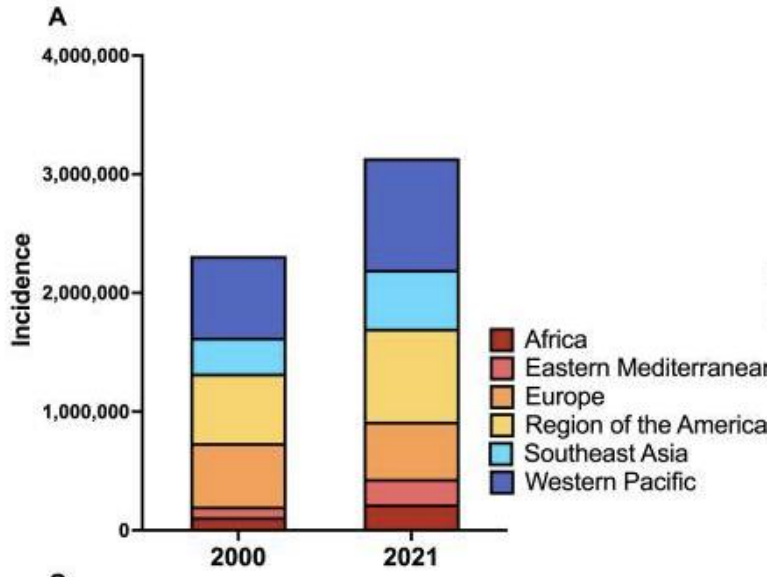


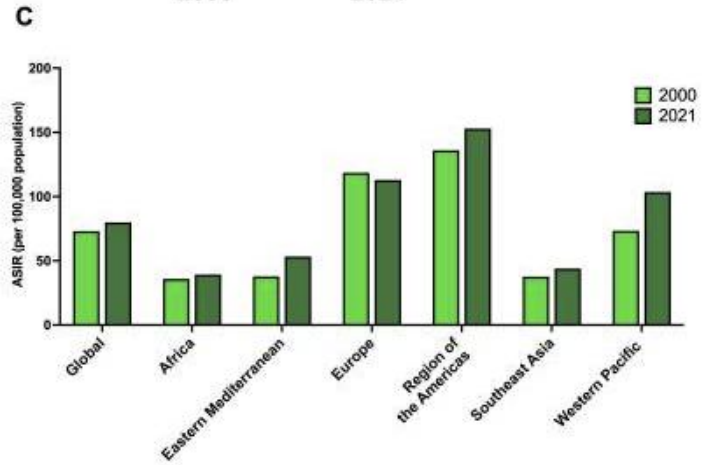
Sung et al. The Lancet Public Health. Aug 2024.

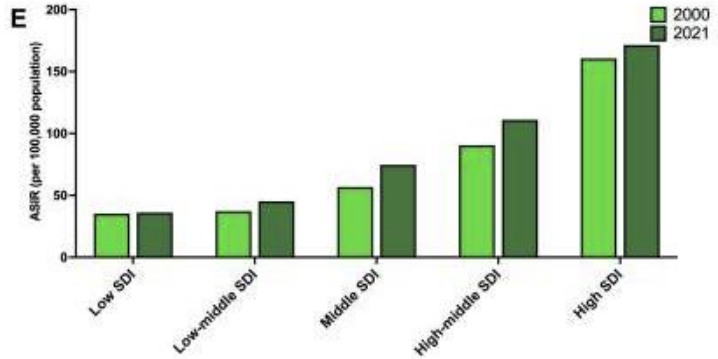
Contemporary Changes in Global Trends in Early-Onset Cancer: Incidence and Mortality (2000–2021)

Pojsakorn Danpanichkul [1,†], Yanfang Pang [2,3,4,†], Supapitch Sirimangklanurak [5], Thanida Auttapracha [5], Thanawin Pramotedham [6], Chun Wei Pan [7], Benjamin Koh [8], Zhen Yu Wong [9], Sakditad Saowapa [1], Shyna Zhuoying Gunalan [8], Kwanjit Duangsonk [10], Chanakarn Kanitthamniyom [1], Donghee Kim [11], Karn Wijarnpreecha [12,13,14], Amit G Singal [15], Daniel Q Huang [6,*,‡], Ju Dong Yang [16,*,‡]







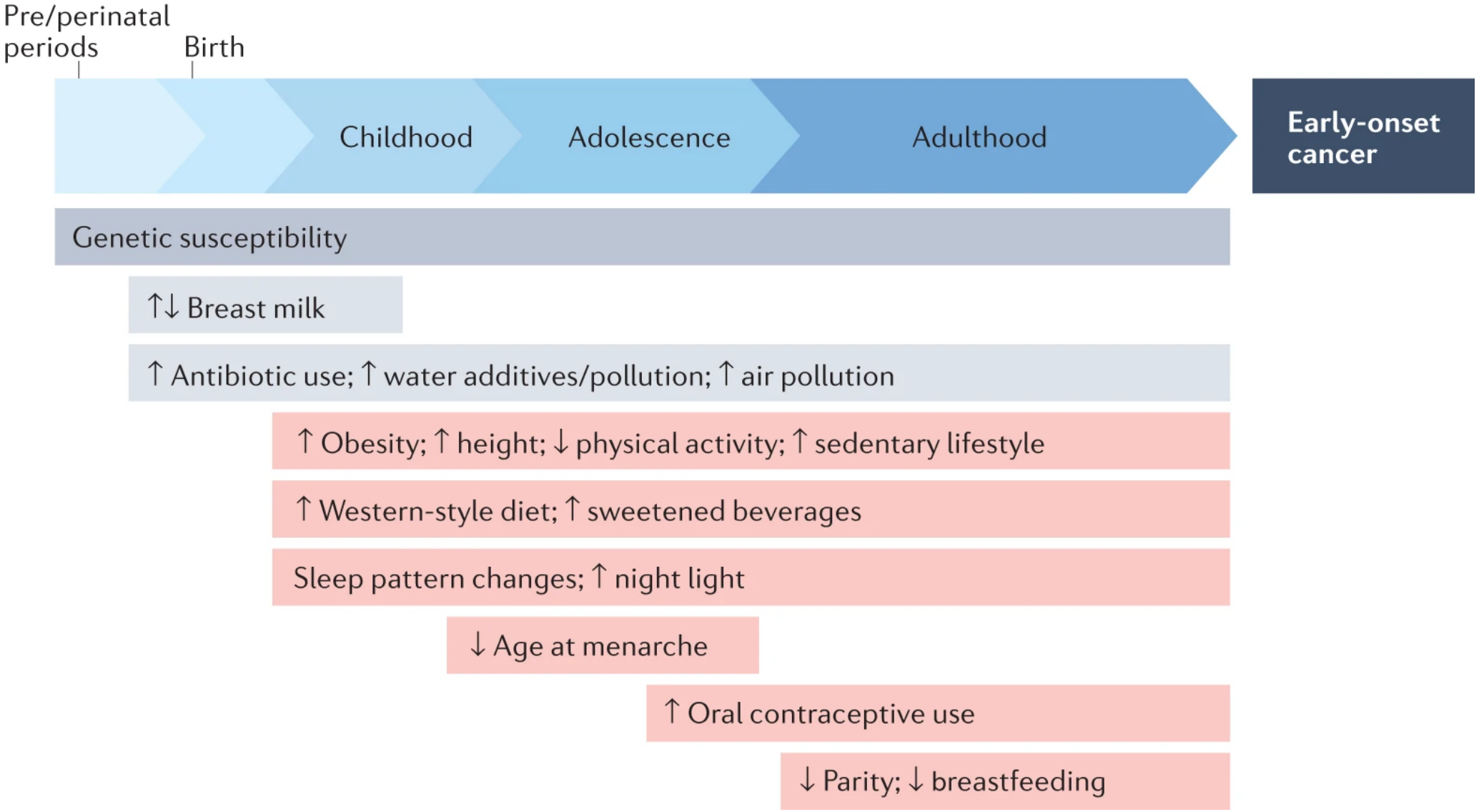


Danpanichkul et al. Cancers. Aug 2025.

What is the cause of EOCs?

- The etiology of early-onset cancers is multifactorial
- Hereditary syndromes account for only a minority of cases (10-15%), and germline genetics are mostly stable across generations
- Most cases appear to be sporadic and are likely related to cumulative exposures (exposome) beginning early in life and epigenetics
- Other potential contributors to earlier diagnosis include enhanced imaging technologies, and updated screening guidelines (ie. intensified screening of high-risk populations)

Individual life-course exposures and their relationship with the development of early-onset cancers



Ugai et al. Nature Reviews Clinical Oncology. Sep 2022.

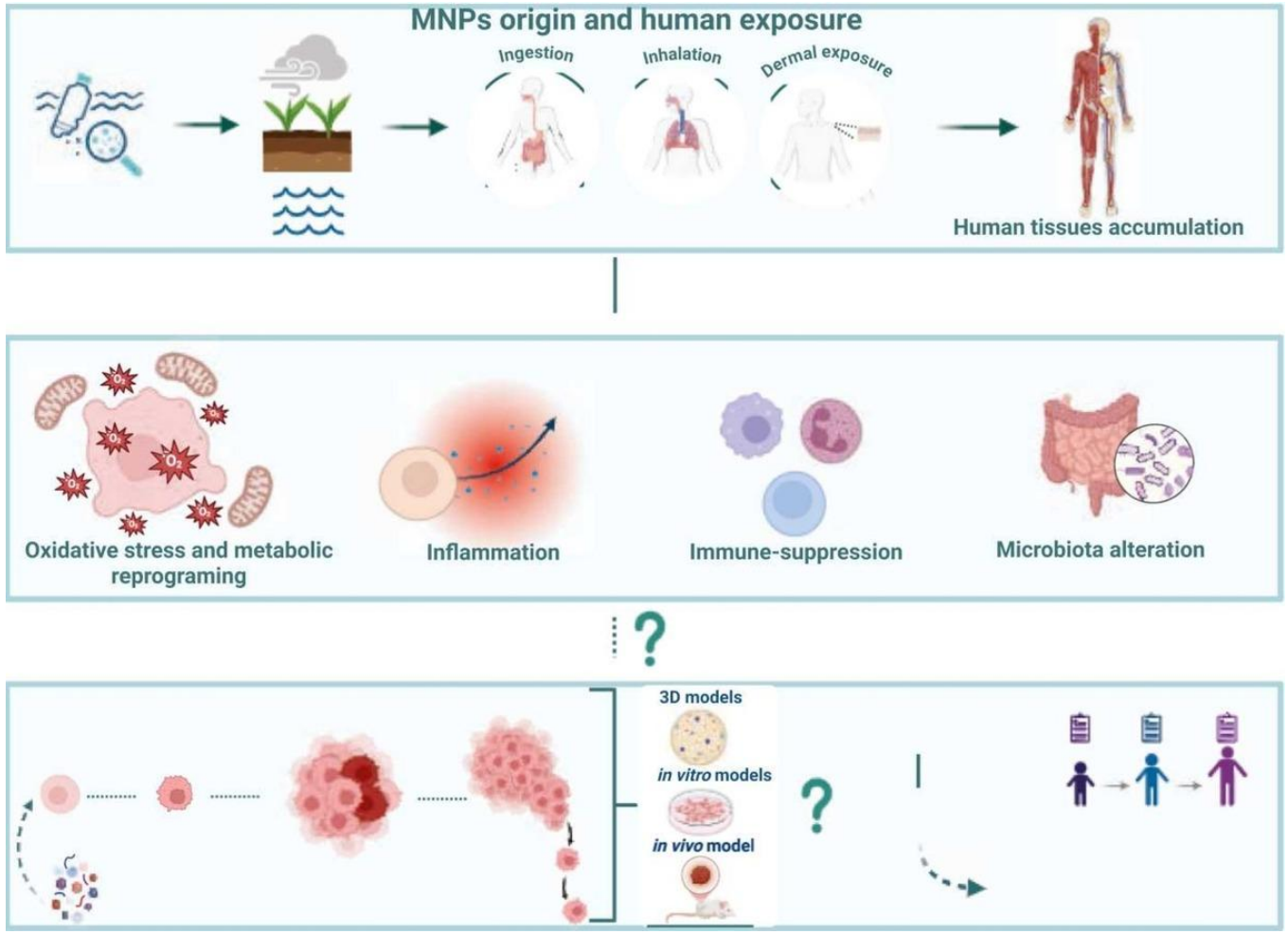
Possible risk factors for early-onset cancers

Cancer type	Risk factors with increasing temporal trend	Risk factors with stable temporal trend	Risk factors with decreasing temporal trend
Breast	Earlier menarche, OCP use, nulliparity, older age at first birth, never breastfeeding, obesity, physical inactivity, ETOH consumption	Family history of breast cancer	Smoking
CRC	Obesity, sedentary behaviour, metabolic syndromes, T2DM, DLD, Western diet, low vitamin D intake, ETOH use, IBD	Family history of CRC	Smoking
Endometrial	Obesity		
Esophageal	Obesity, recurrent GERD		Smoking
Head and neck	ETOH use, HPV infection (in areas without vaccination)		
Kidney	Obesity, chemical exposure (PFAS)		
Liver		Family history of liver cancer	Chronic HBV
Pancreatic	Obesity, ETOH use		Smoking
Stomach		Family history of gastric cancer	H. Pylori infection
Prostate		Family history of prostate cancer	
Myeloma	Obesity		

Ugai et al. Nature Reviews Clinical Oncology. Sep 2022.

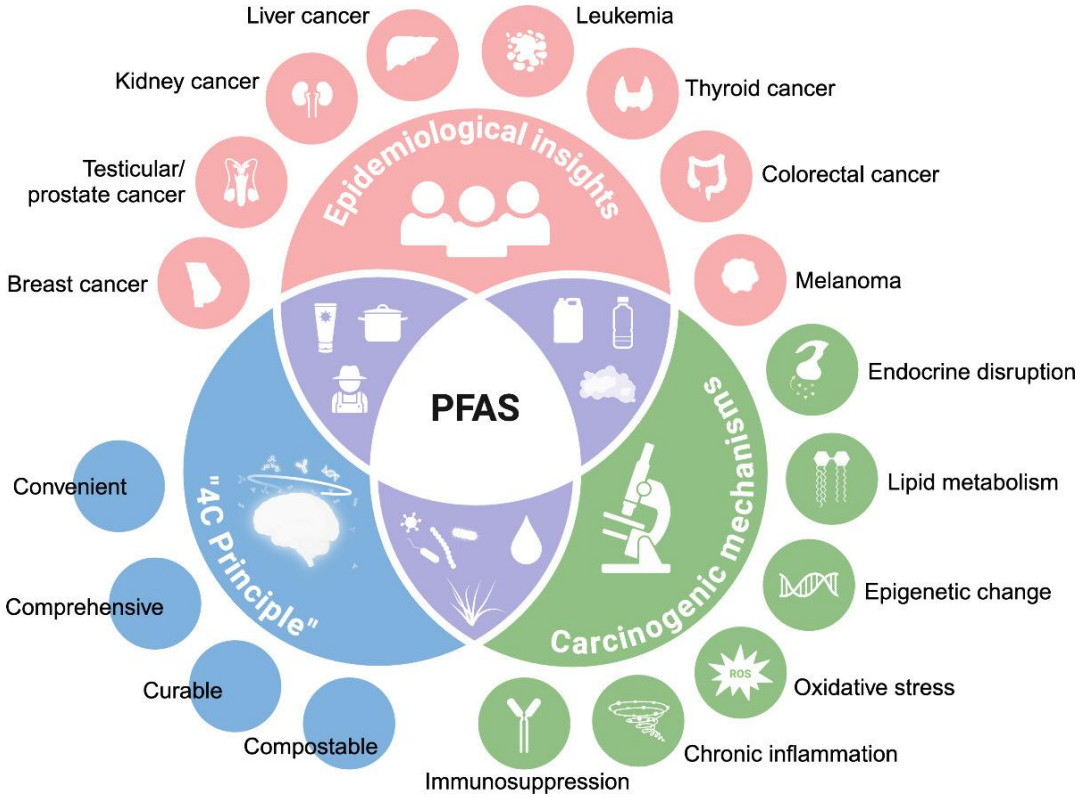
Possible risk factors for early-onset cancers: Environmental exposures

Micro- and nanoplastics



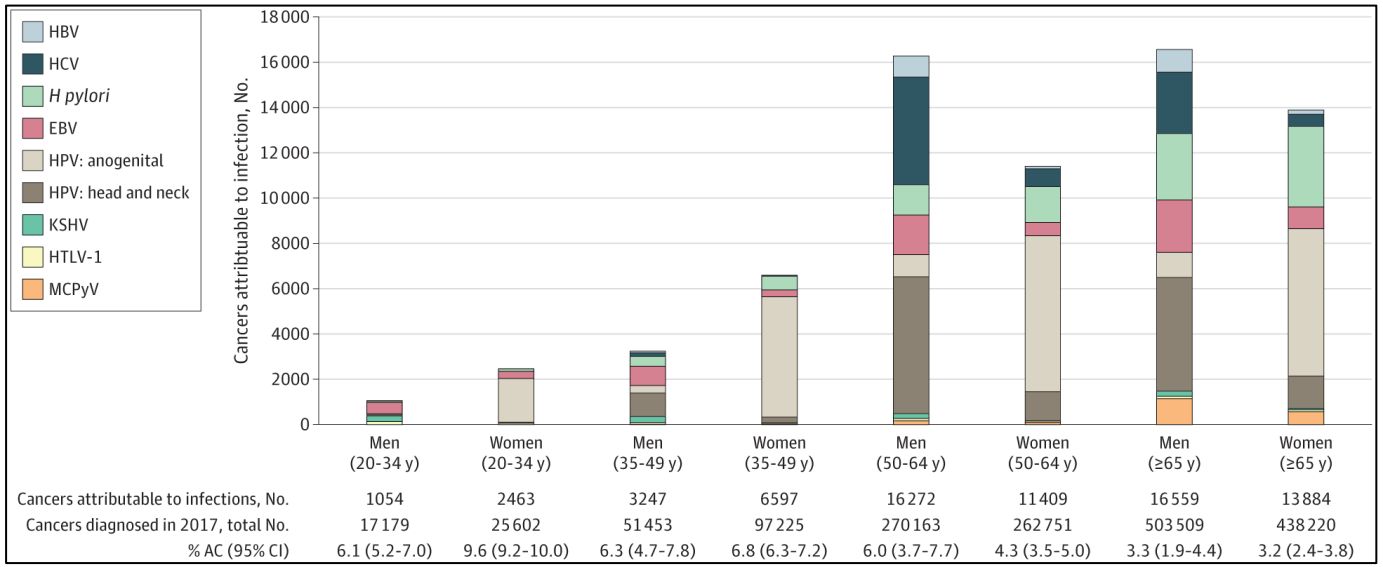
Cirillo et al. Journal of Hazardous Materials. Mar 2026.

“Forever chemicals”



Zheng et al. Science of the Total Environment. Nov 2024.

Possible risk factors for early-onset cancers: Infectious pathogens

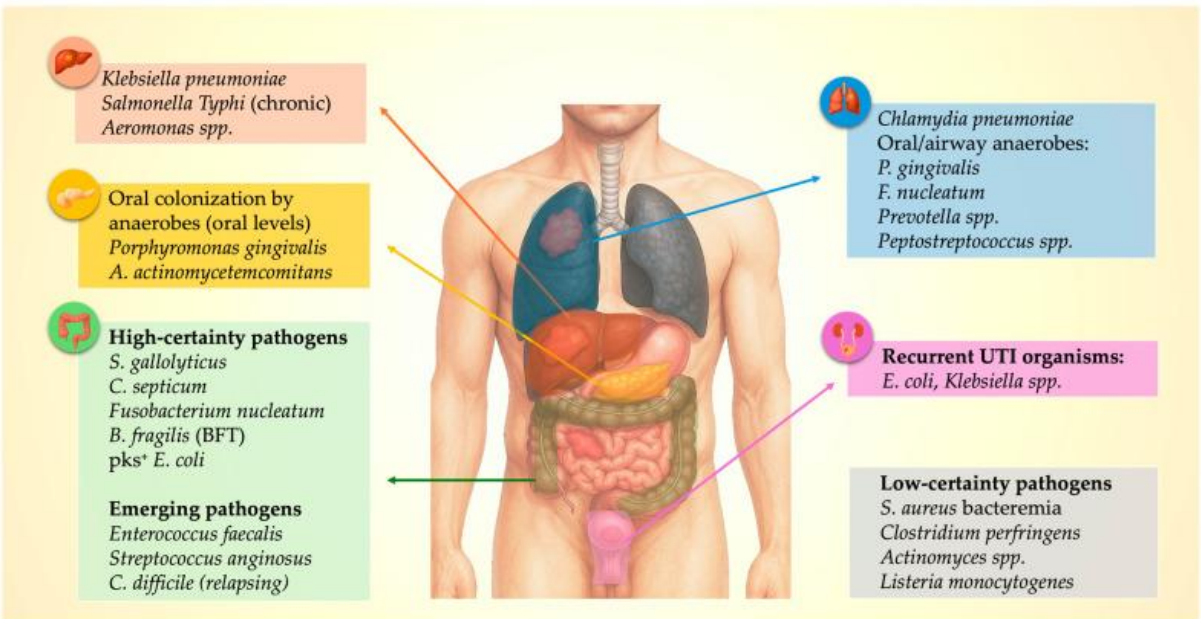


More cancers were attributed to oncogenic infections in younger than older patients (6-9% vs 3-6%)

Volesky-Avellaneda et al. JAMA Oncology. Oct 2023.

Reduced bacterial diversity in the gut, and enrichment of specific bacterial populations have been associated with EOC

Mocibob et al. Cancers. Dec 2025.



Differences between EO and LO cancers

- Clinical: Presenting with more advanced stages
- Pathologic: Often poorer histopathologic/tumor features
- Genomic: Differences in mutational burden

Clinical: More Canadian patients with EOC are being diagnosed at a later stage compared to average screening age patients for CRC

Age-specific (5-year age groups) risk of being diagnosed with a late-stage (III and IV versus I and II) early-onset colorectal, colon, or rectal cancer compared with the average screening age (50–74 years) from 2011 to 2017 in Canada (excluding Quebec)

	Colorectal cancer RR (95% CI)	Colon cancer RR (95% CI)	Rectal cancer RR (95% CI)
Sex			
Female	Ref (1.0)	Ref (1.0)	Ref (1.0)
Male	1.02 (1.00–1.04)	0.98 (0.95–1.00)	1.05 (1.02–1.09)
Age			
50–74	Ref (1.0)	Ref (1.0)	Ref (1.0)
20-24	0.54 (0.42–0.68)	0.30 (0.21–0.42)	0.61 (0.37–1.02)
25-29	0.89 (0.76–1.04)	0.68 (0.55–0.84)	1.30 (1.04–1.64)
30-34	1.11 (1.02–1.22)	1.03 (0.91–1.16)	1.16 (1.01–1.33)
35-39	1.16 (1.08–1.25)	1.09 (0.99–1.21)	1.21 (1.08–1.35)
40-44	1.13 (1.07–1.19)	1.10 (1.02–1.18)	1.16 (1.08–1.26)
45-49	1.18 (1.13–1.22)	1.17 (1.11–1.24)	1.17 (1.10–1.24)

CI = confidence interval; RR = relative risk.

O'Sullivan et al. American Journal of Gastroenterology. Sep 2022.

Potential reasons for higher rates of late-stage diagnoses in younger patients

1. Lower clinical suspicion by medical staff
2. Lack of screening programs
3. Health-care access and system delays
4. Younger patients may underestimate symptoms
5. Competing life priorities
6. Psychological drivers such as fear, denial, and stigma
7. Differences in tumor biology

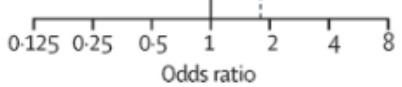
Pathologic: Tumour-specific differences in early-onset versus later-onset cancers

Cancer type	Tumor characteristics
Breast	High tumor grade, triple negative subtypes, high Ki-67
CRC	MSI-H status, LVI and PNI, signet ring cell histology, lower lymphocytic immune reaction
Endometrial	Poor differentiation, high mitotic rates, deep myometrial invasion
Pancreatic	Poor differentiation, PNI
Prostate	Fewer AR, SPOP, ASXL1 alterations
Gastric	High grade, signet ring cell or diffuse histology, somatic alterations (CDH1, BANP, TGFBR1, MUC5B)

Ugai et al. Nature Reviews Clinical Oncology. Sep 2022.

Genomic: Differences in gene mutation frequencies and mutation rates between EO and LO CRC

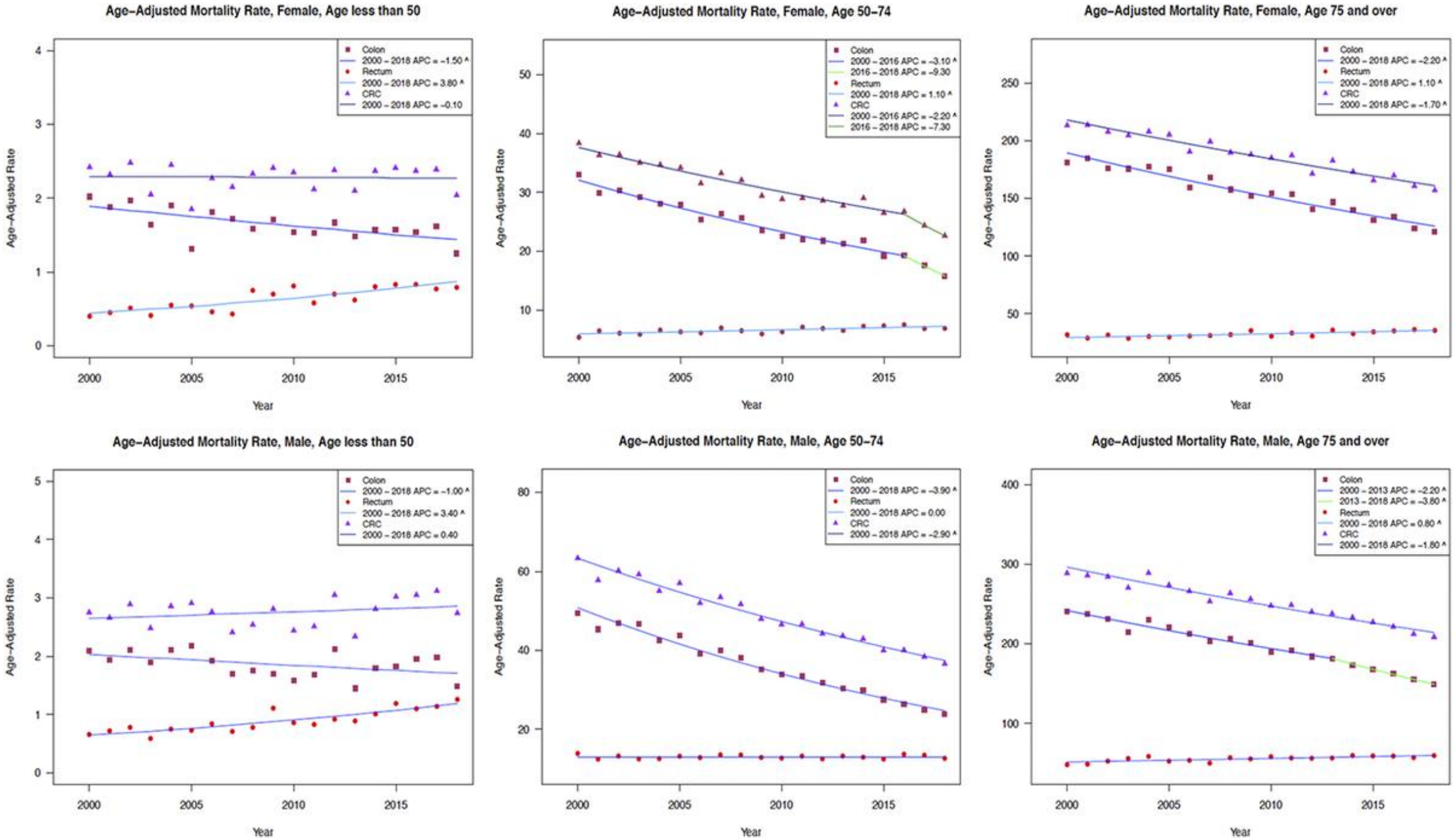
	Frequency (LOCRC *vs* EOCRC)	Odds ratio (95%CI)	Adjusted p value	Mutation rate (LOCRC *vs* EOCRC)	Adjusted p value
AKT3	6·0% *vs* 12·7%	2·11 (1·51–2·97)	0·0015	0·1% *vs* 0·2%	<0·0001
APC	58·6% *vs* 75·0%	2·00 (1·59–2·51)	<0·0001	3·0% *vs* 3·4%	<0·0001
BRAF	44·2% *vs* 15·6%	0·27 (0·21–0·35)	<0·0001	1·1% *vs* 0·3%	<0·0001
BRCA1	16·3% *vs* 25·1%	1·59 (1·24–2·03)	0·012	0·4% *vs* 0·5%	0·00038
BRCA2	33·6% *vs* 42·2%	1·46 (1·19–1·80)	0·02	0·9% *vs* 1·2%	0·014
CDC73	10·1% *vs* 16·2%	1·77 (1·32–2·37)	0·0091	0·2% *vs* 0·3%	0·0097
CDH1	13·0% *vs* 18·7%	1·64 (1·25–2·15)	0·019	0·3% *vs* 0·4%	0·033
CTNNB1	18·0% *vs* 31·6%	2·15 (1·70–2·72)	<0·0001	0·4% *vs* 0·7%	<0·0001
ERBB3	19·3% *vs* 25·9%	1·50 (1·18–1·91)	0·038	0·4% *vs* 0·5%	0·039
FAT1	43·1% *vs* 51·6%	1·43 (1·15–1·78)	0·045	1·3% *vs* 1·5%	0·067
FLT1	15·2% *vs* 23·3%	1·55 (1·20–1·99)	0·037	0·3% *vs* 0·4%	0·0012
FOXP1	9·3% *vs* 15·7%	1·97 (1·40–2·77)	0·0086	0·2% *vs* 0·3%	0·01
IRF2	6·9% *vs* 14·6%	2·60 (1·49–4·54)	0·038	0·2% *vs* 0·3%	0·027
KRAS	32·0% *vs* 53·3%	2·35 (1·91–2·89)	<0·0001	1·1% *vs* 1·4%	<0·0001
LATS1	14·6% *vs* 22·6%	1·65 (1·22–2·23)	0·045	0·3% *vs* 0·4%	0·019
MET	12·8% *vs* 19·0%	1·68 (1·28–2·19)	0·011	0·3% *vs* 0·3%	0·024
MLH1	17·8% *vs* 26·2%	1·60 (1·26–2·04)	0·009	0·4% *vs* 0·6%	0·0011
MSH2	16·5% *vs* 26·9%	1·76 (1·38–2·24)	0·00074	0·4% *vs* 0·5%	<0·0001
NF1	25·6% *vs* 35·6%	1·56 (1·25–1·94)	0·0058	0·7% *vs* 0·9%	0·0028
PALB2	13·6% *vs* 20·3%	1·59 (1·22–2·08)	0·032	0·3% *vs* 0·4%	0·012
PHOX2B	5·7% *vs* 9·5%	1·91 (1·30–2·81)	0·042	0·1% *vs* 0·2%	0·043
PIK3CA	40·2% *vs* 54·8%	1·74 (1·42–2·14)	<0·0001	1·2% *vs* 1·5%	<0·0001
RNF43	53·9% *vs* 39·3%	0·61 (0·49–0·76)	0·0015	1·7% *vs* 1·1%	<0·0001
SETD2	25·2% *vs* 36·3%	1·62 (1·30–2·01)	0·0015	0·6% *vs* 0·8%	0·00011
TCF7L2	35·0% *vs* 51·2%	2·01 (1·62–2·50)	<0·0001	0·8% *vs* 1·1%	<0·0001



Li et al. The Lancet Oncology. Aug 2025.

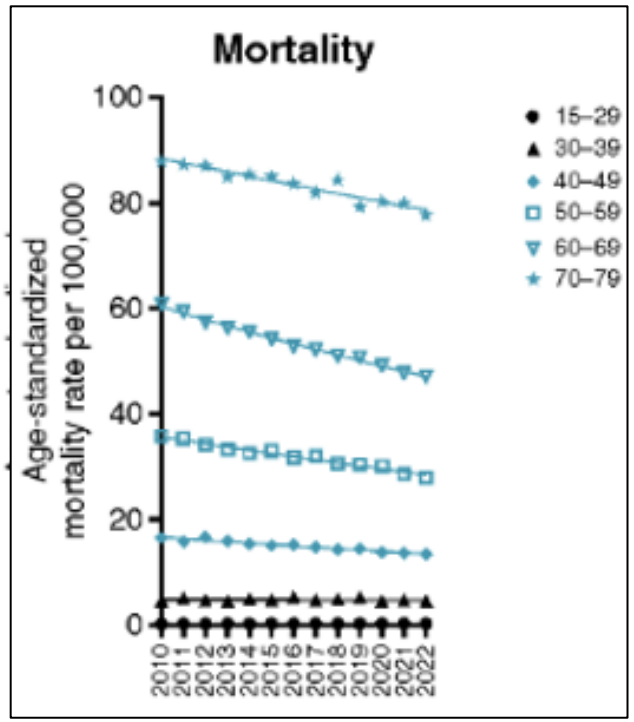
EOC and survival outcomes

- For most cancers, outcomes for patients with EOC have remained unchanged likely due to advances in treatment and care
- Mortality rates are improving for patients with later onset cancers likely due to better treatments and broader implementation of screening programs allowing for earlier detection

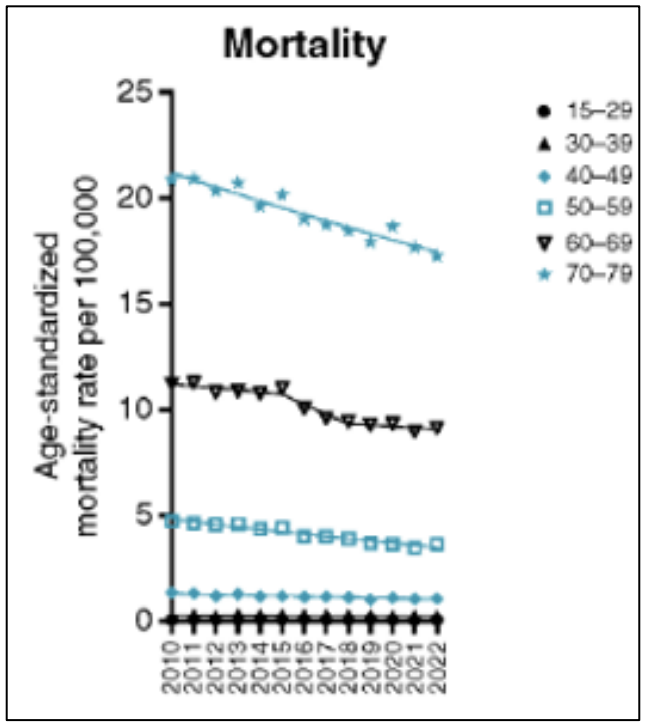


O'Sullivan et al. American Journal of Gastroenterology. Sep 2022.

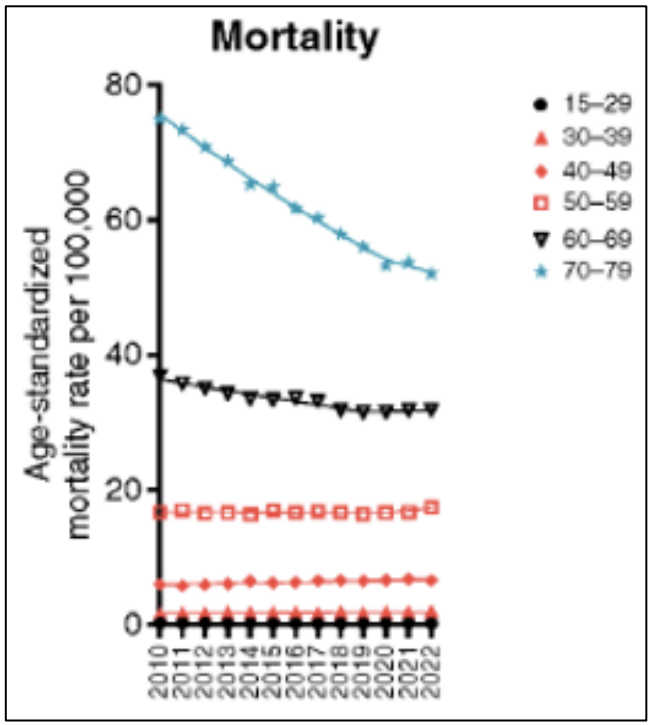
Female Breast



Kidney



Colorectal



Shiels et al. Cancer Discovery. Jul 2025.

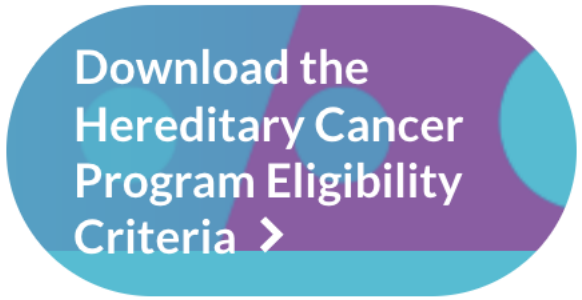
Clinical considerations

- Primary care providers
  1. Recognize red flag symptoms
     - All adults with hematochezia should be considered for colonoscopy, as hemorrhoids do not exclude additional pathology
     - Refer for colonoscopy any patient with hematochezia, abdominal pain, altered bowel habits, unexplained iron deficiency anemia, or unintentional weight loss
     - Be alert to persistent or unexplained symptoms in younger patients, especially when multiple consultations occur
     - Teenagers and young adults with cancer consult more frequently (≥4 times in 3 months) before diagnosis compared to controls

Demb et al. JAMA Network Open. May 2024.
Saatci et al. British Journal of Cancer. Oct 2024.

Clinical considerations

- Primary care providers
  2. Implement age and risk appropriate screening
  3. Obtain family history and refer for genetic testing



https://www.bccancer.bc.ca/health-professionals/clinical-resources/hereditary-cancer

Hereditary Cancer Program Referral Form

BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

Fax completed forms and any attachments to 604-707-5931

Hereditary Cancer Program
Tel: 604.877.6000 local 672198
Email: hereditarycancer@bccancer.bc.ca
www.bccancer.bc.ca/hereditary

Referral Date: _____

Referring Clinician : _____ **Billing #:**_____ **Phone:**_____ **Fax:** _____

Copy to/Second Clinician: _____ **Billing #:**_____ **Phone:** _____ **Fax:** _____

☐ **Self-Referral -** include Primary Care Provider's information in "Copy to" above if available.

Patient				
	Personal Health Number	Date of Birth (yyyy-mmm-dd)	Gender ☐ M ☐ F ☐ X Pronouns: _____	
	Last Name	First and Middle Name	Phone 1	Phone 2
	Address, City, Postal Code:			**Email**

Interpreter Required? ☐ Yes, language: _____

Urgent Referral - Only if impact on ***immediate*** cancer management or patient is palliative. If patient is unwell or prognosis is limited, consider **DNA storage**.
☐ Yes, reason (required): _____
Results required within: ☐ < 1 month ☐ < 3 months ☐ other: _____

Reason for Referral – Select one or more referral categories below and provide short summary of indication
Eligibility criteria are available on the Hereditary Cancer Program website.

☐ **Personal History of Cancer/Polyps -** Attach relevant reports if not available in CAIS/Cerner/CareConnect.
Type(s) of cancer/polyps, age(s) of diagnosis, and relevant details (e.g. bilateral disease, pathology, or cumulative number of polyps):

☐ **Personal History of Pathogenic Variant for Confirmation and/or Follow-up –** Test report required.
eg. from tissue, private pay, out-of-province genetics clinic, clinical trial/research testing

☐ **Family History of Cancer –** May include patient; completed family history form required.
Brief summary (optional):

☐ **Family History of Pathogenic Variant** - Records required if testing occurred outside BC/Yukon

Gene	Clinic/city where testing done *or* HCP family ID	Relative's Name	Relative's Date of Birth	Relationship to referred patient

☐ **Re-assessment** – Patient that was previously seen at HCP
Please describe any new history and/or reason for referral.

☐ **Other**
Please describe or attach supporting letter/medical records.

Date Received at HCP:

Version: March 2026

BC CANCER HEREDITARY CANCER
Provincial Health Services Authority

Name:
PHN:
DOB:

Family History *Complete these pages and give to your doctor/NP's office to attach to your referral**

Please answer the following questions about your **blood** relatives (living and deceased) to help us give you the best care. Your best guesses about ages and other details are fine. This information will become part of your health record.

I agree that personal and family history I provide on these forms can be shared with my relatives for their medical care if they are referred to the HCP or another genetics clinic: ☐ Yes ☐ No

Are you adopted? ☐ No ☐ Yes **Were your parents adopted?** ☐ No ☐ Yes, mother ☐ Yes, father

Are your parents related to each other? (e.g. first cousins) ☐ No ☐ Yes – give relationship: _____

Your Children	How many daughters? ____ How many sons? _____ ☐ I have no biological children
Your Brothers and Sisters ☐ None	How many sisters? ____ How many brothers? ____ How many half-sisters? ____ How many half- brothers? _____ ☐ Same mother ☐ Same father
Your Mother's Side ☐ No info	Is your mother alive? ☐ No ☐ Yes What is her current age or age at death? _____ How many sisters does your mother have? ____ Are any of them your mother's half-sisters? ☐ No ☐ Yes How many brothers does your mother have? ___ Are any of them your mother's half-brothers? ☐ No ☐ Yes Is your grandmother alive? ☐ No ☐ Yes What is her current age or age at death? _____ Is your grandfather alive? ☐ No ☐ Yes What is his current age or age at death? _____
Your Father's Side ☐ No info	Is your father alive? ☐ No ☐ Yes What is his current age or age at death? _____ How many sisters does your father have? ____ Are any of them your father's half-sisters? ☐ No ☐ Yes How many brothers does your father have? ___ Are any of them your father's half-brothers? ☐ No ☐ Yes Is your grandmother alive? ☐ No ☐ Yes What is her current age or age at death? _____ Is your grandfather alive? ☐ No ☐ Yes What is his current age or age at death? _____

Your Family's Ethnic/Ancestral Background: please check all that apply

	Africa/ Caribbean	Asia ☐ East ☐ South/Central	Europe/ UK ☐ Swedish/ Nordic	French Canadian	Indigenous (First Nations, Metis, Inuit)	Jewish ☐ Ashkenazi ☐ Sephardic	Middle East	South and Central America	Other: _____	Don't Know
Mother's mother	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Mother's father	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Father's mother	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐
Father's father	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Previous Cancer Genetics Appointment/Genetic Testing

Has anyone in your family had genetic counselling or genetic testing for the family history of cancer? ☐ No ☐ Yes

If yes, full name of relative(s): _____ Date of Birth or current age (if known): _____

Relationship to you: _____ Name and/or location of genetics clinic: _____

Received Date:

Name:
PHN:
DOB:

Have you ever been diagnosed with cancer? No ☐ Yes ☐ If yes:	Type of Cancer	Age at Diagnosis	City Where Diagnosed

List of any blood relatives who have had cancer. Please include children, brothers, sisters, parents, grandparents, aunts, uncles, and cousins. Your best guesses about their age and other details are fine. You may add another page if you need more space. Please try to print clearly if completing by hand.

Relative's full name	Date of Birth or current age	Age at Death	Relationship to you	Mother's or Father's side	Type of cancer	Age when diagnosed	Location when diagnosed
e.g. Jane Doe	*1941-Nov-08*		*cousin*	*mother's brother's daughter*	*breast*	*65*	*Victoria, BC*

Have you or anyone in your family had any of the following conditions?	No	Yes	Don't Know	If yes, name of your relative and relationship to you
Chronic pancreatitis that started before age 30	☐	☐	☐	
Tumour or growth in the pituitary, parathyroid or adrenal gland	☐	☐	☐	
More than 50 moles/nevi (not freckles)	☐	☐	☐	
More than 10 polyps removed from the colon or rectum (bowel)	☐	☐	☐	

Clinical considerations

- Primary care providers
    4. Assess and counsel on modifiable risk factors
        - Diet and nutrition
            - Encourage balanced diet with fruits, vegetables, whole-grains, healthy fats
            - Limit intake of processed foods, sugar-sweetened beverages
            - Adequate vitamin D intake
            - Limit or avoid alcohol consumption
        - Physical activity and weight
            - Encourage regular moderate to vigorous intensity physical activity
            - Achieve and maintain healthy body weight
        - Other behaviours
            - Smoking cessation
            - Minimize antibiotic overuse/misuse
            - Sun protection
            - Vaccination for eligible patients

Gapstur et al. Cancer Journal for Clinicians. Oct 2018.

Clinical considerations

- Oncologist
  - Discuss hereditary testing
  - No robust data available yet to change treatment guidelines for patients with EOC
  - Unique needs that should be considered and addressed
    - Impacts of treatments on fertility preservation and sexual health
      - Early menopause, POF, ED, family planning
    - Impacts on education/work and finances
    - Impacts on long-term health outcomes, and treatment-related morbidity
      - Renal toxicity, early CV disease, second malignancies, bowel habit changes, bone and endocrine metabolism, chronic pain, neuropathy, chronic fatigue, brain fog
    - Impacts on mental health
      - Depression, anxiety, body image issues, sleep pattern changes

Terry et al. Annual Review of Public Health. Nov 2025.

Clinical considerations

- Public health authorities and policy makers
  - Fund programs promoting healthy lifestyles
  - Re-evaluate screening programs to reflect contemporary data while balancing benefits with cost and potential harms
  - Public education and health literacy

Terry et al. Annual Review of Public Health. Nov 2025.

Research and future directions

- Identify novel and changing risk factors (early life exposures) for EOC
  - Using health records data and early child cohort studies
  - Serial biospecimen collection (blood, urine, stool, saliva, etc) as a tool for identifying genetic changes/risk factors associated with EOC
- Re-evaluating and optimizing screening programs
- Trial design considerations

Summary

- EOC incidence rates are rising globally
- EOC appear to differ from average/later onset cancers often with a more advanced presentation at diagnosis and more aggressive appearing tumor biology
- Outcomes of EOC appear to be unchanged over time likely owing to advances in cancer treatment
- Hereditary causes only account for a small proportion of EOC; changing environmental exposures are likely contributing factors in the development of sporadic EOC
- Optimal management of patients with EOC require a united effort amongst PCP, oncologists, and public health officials, and should address unique challenges