

The rise of early-onset colorectal cancer: an emerging population

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Disclosures

- Dr. Cimino has received an honorarium from G1 Therapeutics.
- All financial relationships listed for this individual have been mitigated.



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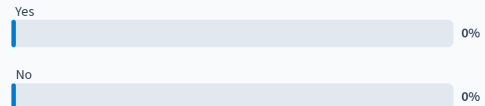
Objectives

- Describe recent trends in the incidence of early-onset colorectal cancer (EOCRC)
- Discuss proposed etiologies for EOCRC
- Identify guideline-supported screening recommendations for EOCRC



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Have you ever treated an adult patient with cancer who was <50 years old?

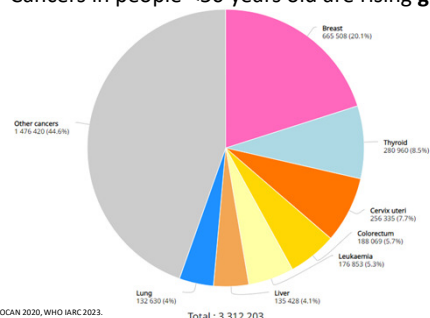


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Early-Onset Cancer: A Future Pandemic?

- Cancers in people <50 years old are rising **globally**



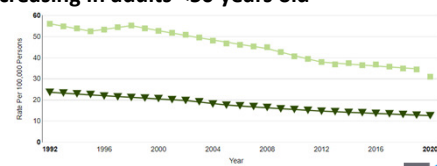
GLBOCAN 2020, WHO IARC 2023.



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Colorectal Cancer (CRC)

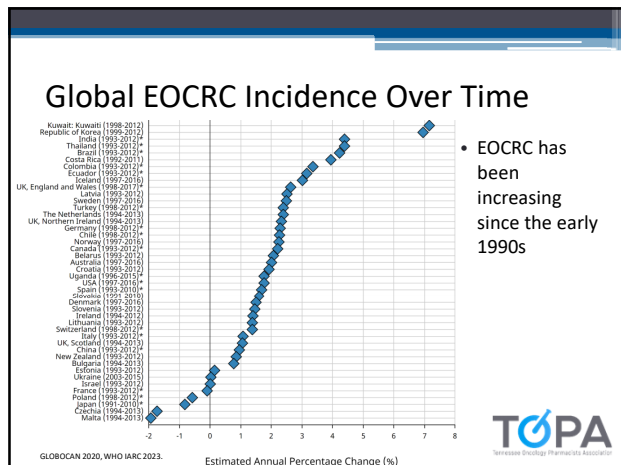
- 3rd most common; 2nd cause of deaths globally
- Median age of diagnosis = 66 years old
- **Incidence & mortality** are decreasing overall, but are **increasing in adults <50 years old**



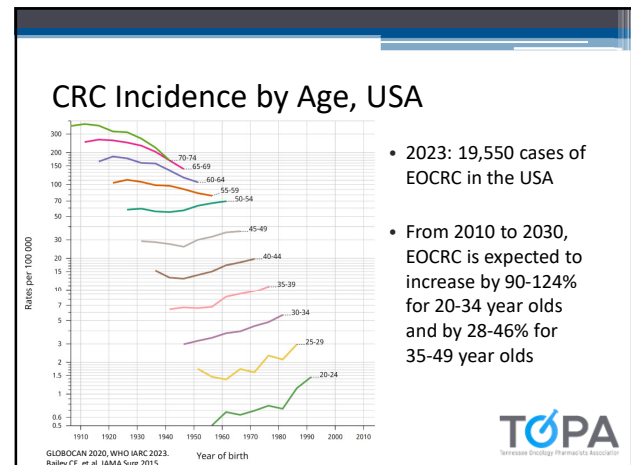
Xi Y, et al. Transl Oncol 2021.
GLBOCAN 2020, WHO IARC 2023.
SEER database.



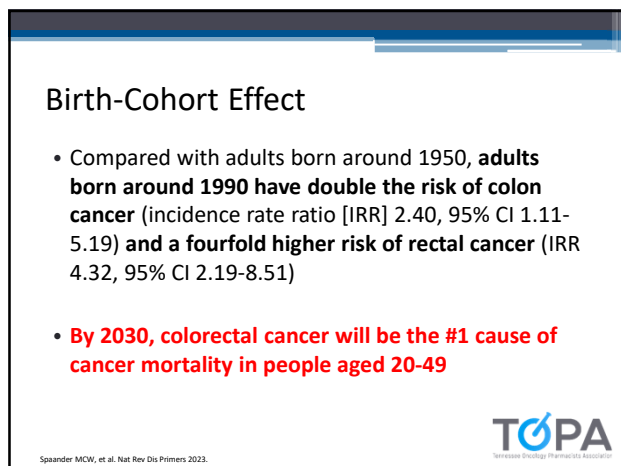
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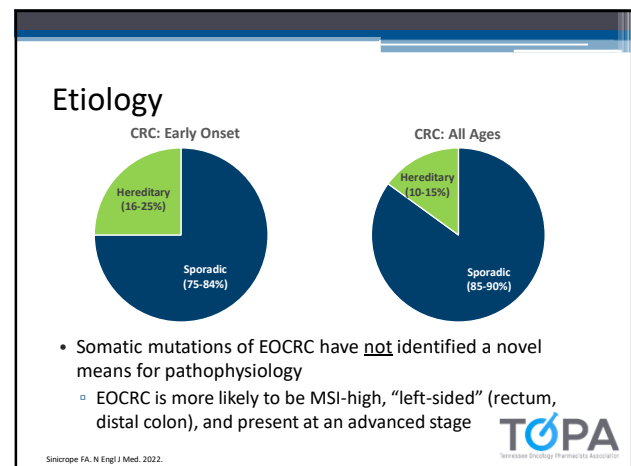
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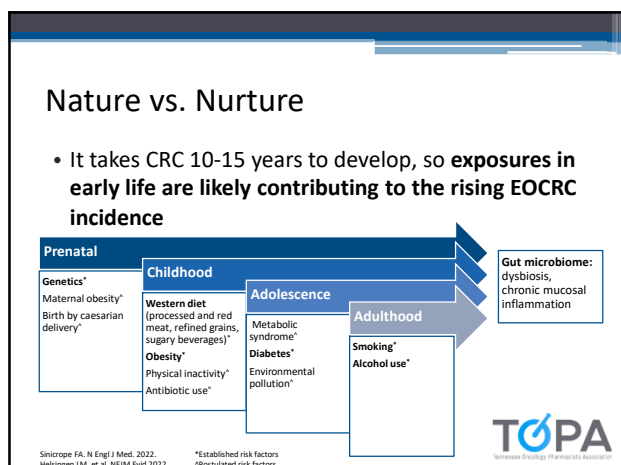
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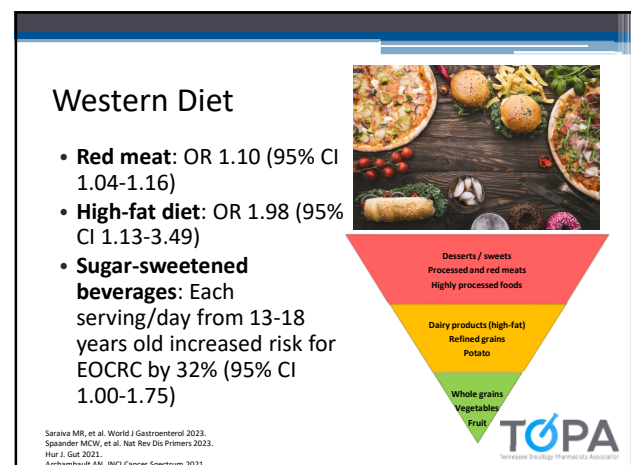
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Obesity

- **Higher body fatness at an early age is associated with a higher risk of EOCRC**
- BMI ≥ 30 kg/m² (obesity) at ages 20 years, 30 years, and 10 years prior to diagnosis had approximately double the risk of EOCRC (OR 2.56, 95% CI 1.20-5.44; OR 2.06, 95% CI 1.25-3.40; OR 1.88, 95% CI 1.30-2.73)



Saravia MR, et al. World J Gastroenterol 2023.
Li H. Gastroenterol 2022.

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Diabetes

- Diagnosis of type 2 DM before 50 years old has a 3.5 fold (95% CI 2.3-5.1) increased risk of EOCRC



Saravia MR, et al. World J Gastroenterol 2023.
Spaander MCW, et al. Nat Rev Dis Primers 2023.

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Alcohol & Tobacco

- **Alcohol:**
 - 1-2 drinks per week: 7% increased risk
 - 3-4 drinks per week: 14% increased risk
 - ≥ 5 drinks per week: 27% increased risk
- **Tobacco**
 - Smoking was associated with 1.57 times (95% CI 1.20-2.04) increased odds of developing EOCRC

Saravia MR, et al. World J Gastroenterol 2023.
Spaander MCW, et al. Nat Rev Dis Primers 2023.
Jin EH, et al. J Clin Oncol 2023.
Li H, et al. J Clin Cancer Specr 2023.

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What are the typical signs and symptoms associated with EOCRC?

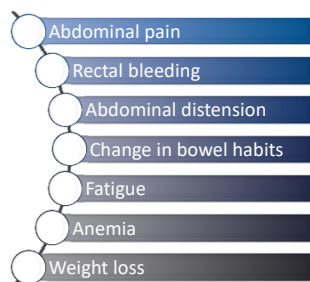
Pale and floating stools	0%
Rectal bleeding and abdominal pain	0%
Anemia and hypercalcemia	0%
Weight loss and lymphedema	0%

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Clinical Presentation

EOCRC diagnosis is often delayed compared to older patients



Saravia MR, et al. World J Gastroenterol 2023.
Srinivasan RA, W Engl J Med. 2022.

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According to the ACS and USPSTF, what age should screening begin for an adult at average risk for colorectal cancer?

40	0%
45	0%
50	0%
55	0%

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Colorectal Cancer Screening Age*

Old Screening Age:
50 years old



New Screening Age:
45 years old

- 2021: American Academy of Family Physicians (AAFP)
- 2023: American College of Physicians (ACP)

- **2018: American Cancer Society (ACS)**
- **2021: US Preventative Services Task Force (USPSTF)**
- 2021: American College of Gastroenterology (ACG)
- 2022: National Comprehensive Cancer Network (NCCN)

American Cancer Society. CA: A Cancer Journal for Clinicians 2018.
US Preventative Services Task Force. JAMA 2021.
American College of Gastroenterology. Am Fam Physician 2022.
American College of Physicians. Ann Intern Med 2023.
National Comprehensive Cancer Network. Colorectal Cancer Screening Version 1.2023.

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*For average-risk adults

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Screening Modalities

	Tool	Description	Sensitivity	
			Cancer	AA
Stool-based	Guaiac fecal occult blood test (gFOBT)*	Detects heme	50-75%	6-21%
	Fecal immunochemical test (FIT)	Detects hemoglobin	74-81%	23-28%
	Multitargeted stool DNA (mt-sDNA)-FIT (Cologuard®)	Detects hemoglobin + aberrantly methylated <i>BMP3</i> and <i>NDRG4</i> promoter regions and mutant <i>KRAS</i>	92-94%	43-47%
Structural examinations	CT colonography (CTC)	Low-dose computed tomography scan	86-100%	86-89%
	Flexible sigmoidoscopy*	Visualizes rectum, sigmoid, and most of descending colon. Can remove polyps if needed.	58-75%	72-86%
	Colonoscopy	Visualizes entire colon. Can remove polyps if needed.	95%	75-95%

Helgert LM, et al. NEJM Evid 2022.

*Reduced incidence of CRC and mortality from CRC in randomized trials
AA: Advanced adenomas

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Screening Recommendations*

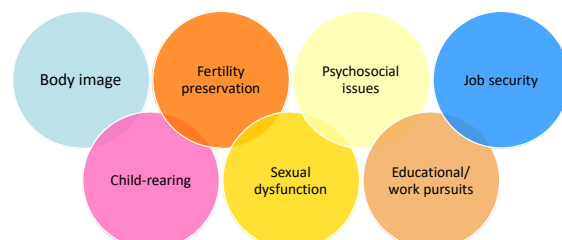
	Tool	ACS	USPSTF
Stool-based	Guaiac fecal occult blood test (gFOBT)	Annually	Annually
	Fecal immunochemical test (FIT)	Annually	Annually
	Multitargeted stool DNA (mt-sDNA)-FIT (Cologuard®)	Every 3 years	Every 1-3 years
Structural examinations	CT colonography (CTC)	Every 5 years	Every 5 years
	Flexible sigmoidoscopy	Every 5 years	Every 5 years (or every 10 years if combined with annual FIT)
	Colonoscopy	Every 10 years	Every 10 years

American Cancer Society. CA: A Cancer Journal for Clinicians 2018.
US Preventative Services Task Force. JAMA 2021.

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*For average-risk adults

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Unique Considerations for the EO CRC Population



Eng C, et al. J Natl Cancer Inst 2021.
Rogers JE, et al. Dig Med Res 2021.

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Summary

- EO CRC is increasing and is expected to be the top cause of cancer-related deaths in adults <50 by 2030
- Western diet, obesity, diabetes, smoking, and alcohol are all known risk factors for EO CRC
- ACS and USPSTF recommend colorectal cancer screening starting at age 45



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