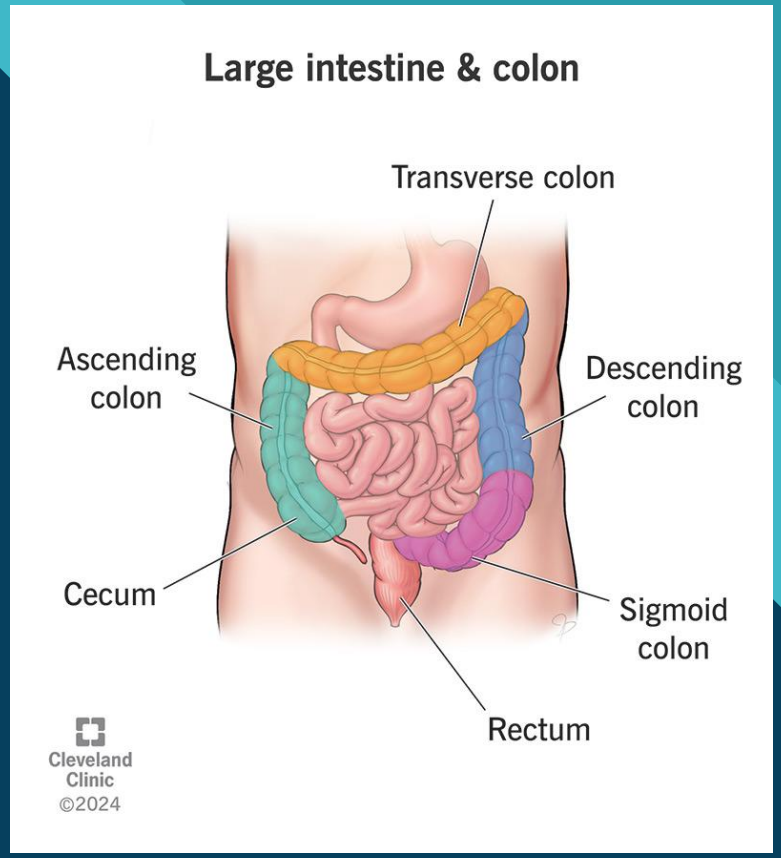
Early Onset Colorectal Cancer

Jared Marquardt, MD

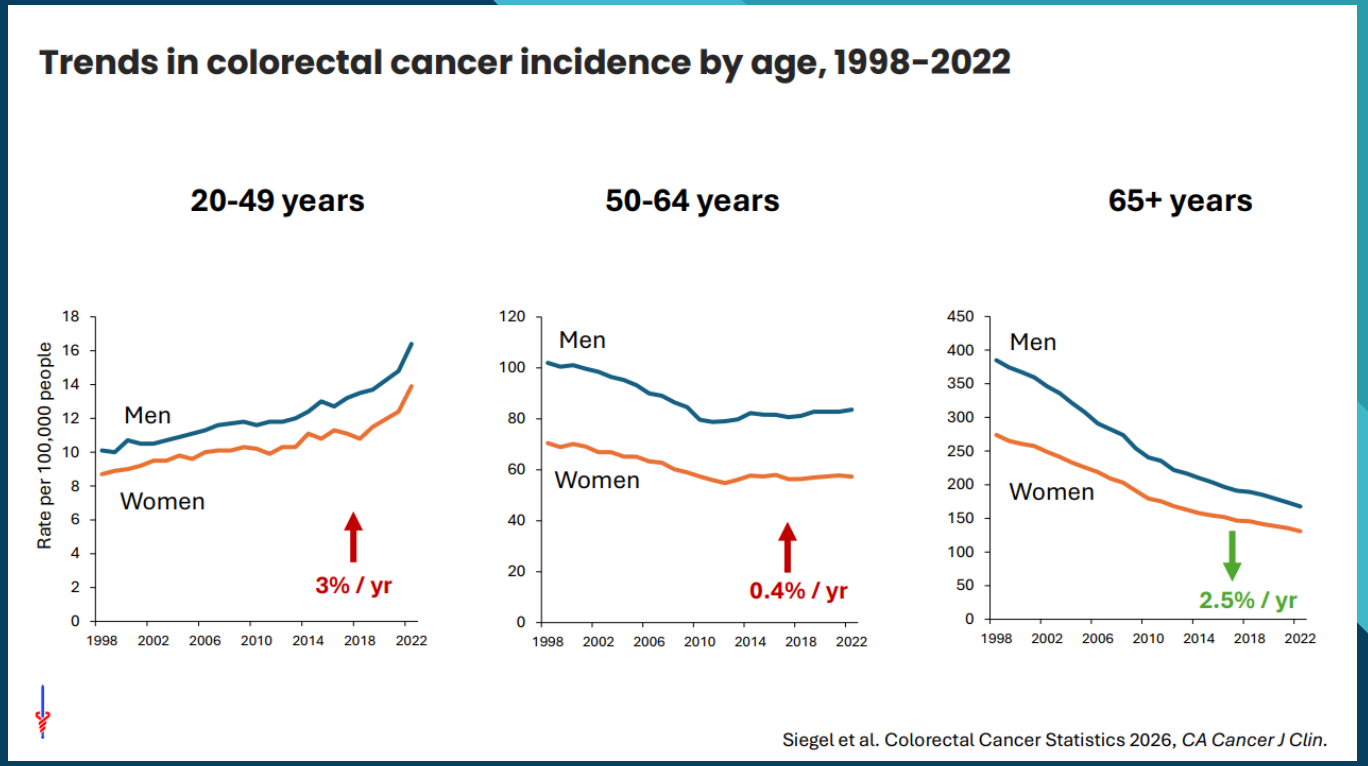
Colorectal Cancer

- ~150,000 cases each year in the U.S.
  - 1.9 million globally (900,000 deaths)
- 2026 projections
  - 158,850 new CRC cases in 2026
  - 108,860 new cases of colon cancer (55,410 in men and 53,450 in women)
  - 49,990 new cases of rectal cancer (28,750 in men and 21,240 in women)
- Estimated that 45% of these will be under age 65 (27% in 1995)
- 55,230 will die from CRC



EOCRC

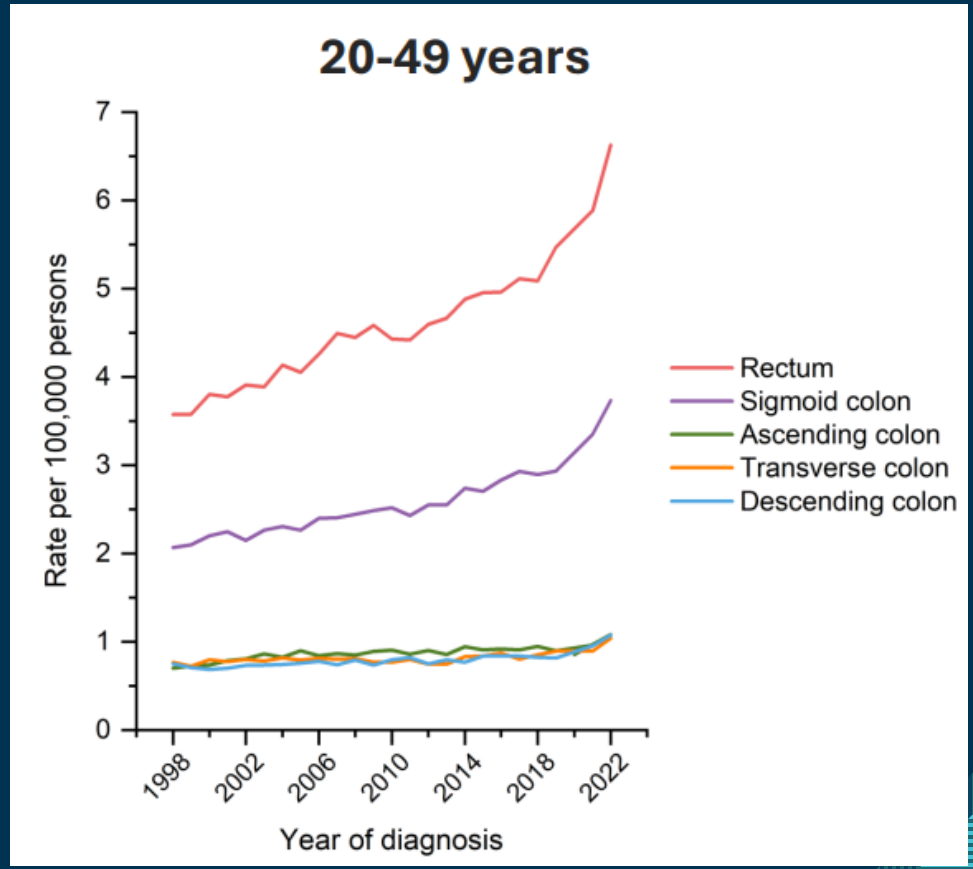
- **What is Early-Onset Colorectal Cancer (EOCRC)?**
- CRC diagnosed before age 50
- Accounts for 14% of all CRC cases in the U.S.
- Most rapidly increasing early-onset cancer in the country
- **Key Statistic:**
  - CRC is **the leading** cause of cancer death among U.S. men aged 20-49 and second leading cause among women in that age group
  - Overall, CRC is the 3rd most common cancer in men and women in U.S.



Incidence

Rising Incidence:

- 2-3% annual increase ages <50 since late 1980s
  - Only 0.4% increase in ages 50-64
  - People born around 1950 have lowest risk of CRC
    - Highest risk→ people born in 1990s (5x higher than 1950s)
- Rectal cancer incidence increasing by 1% per year after many years of declining incidence
  - 75-80% left colon and rectum (vs. 60% in later-onset)
- Rectal cancer now accounts for 1/3 of CRC, previously ¼
- Alaska Native people have highest CRC incidence
  - Twice as high as white people
  - American Indian have the 2nd highest incidence
- **Projections by 2030:**
  - 1 in 4 rectal cancers will be diagnosed in individuals <50
  - 1 in 10 colon cancers will be diagnosed in individuals <50



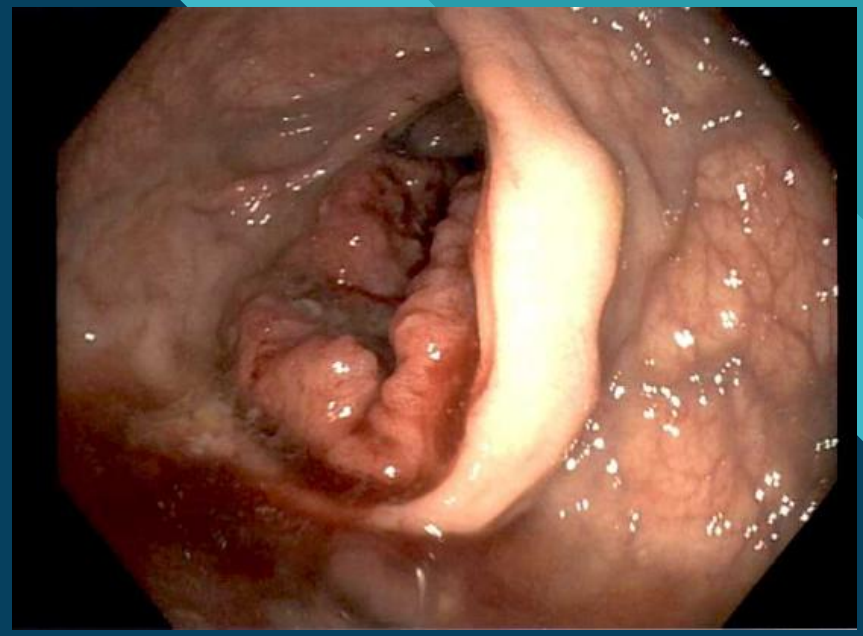
Mortality

Divergent Mortality Patterns:

- Overall CRC mortality declining by 1.7% per year (due to screening in older adults)
- EOCRC mortality INCREASING by 1% per year (2011-2020)
- 75% EOCRC are advanced stage at time of diagnosis
    - More likely to be rectal or left sided cancer

Contrast with Later-Onset CRC:

- Ages 65+: Mortality declining 2.0-2.3% annually
- Ages 50-64: Mortality increasing 1% annually since 2019
- Ages <50: Mortality increasing 1% annually since 2004



Why is this happening?

Multiple proposed mechanisms/theories

- Hereditary syndromes, family history of CRC, family history advanced adenomas
- Inflammatory bowel disease (Crohn's, ulcerative colitis)
- Metabolic dysregulation
  - Poor diet, obesity, lack of exercise
- Smoking
- EtOH
- Lack of Vit D?
- Less NSAID/ASA use?
- Gut microbiome?
  - *Fusobacterium nucleatum, Colibactin-producing (pks+) Escherichia coli, Enterotoxigenic Bacteroides fragilis* (ETBF)
  - Antibiotic use
- Occupation, socioeconomic status, health disparities, access to screening

Risk Factors

Modifiable Risk Factors

- **Lifestyle and Dietary Factors:**
  - **Obesity:** BMI >30, childhood obesity, maternal obesity
  - **Western dietary pattern:** High processed meat, red meat, refined grains, sugar
  - **Sugar-sweetened beverages:** ≥2 servings/day associated with 2-fold increased risk
  - **Sedentary lifestyle**
  - **Smoking**
  - **Alcohol**
- **Many of these risks start early in life (childhood/adolescence)**

Protective Factors:

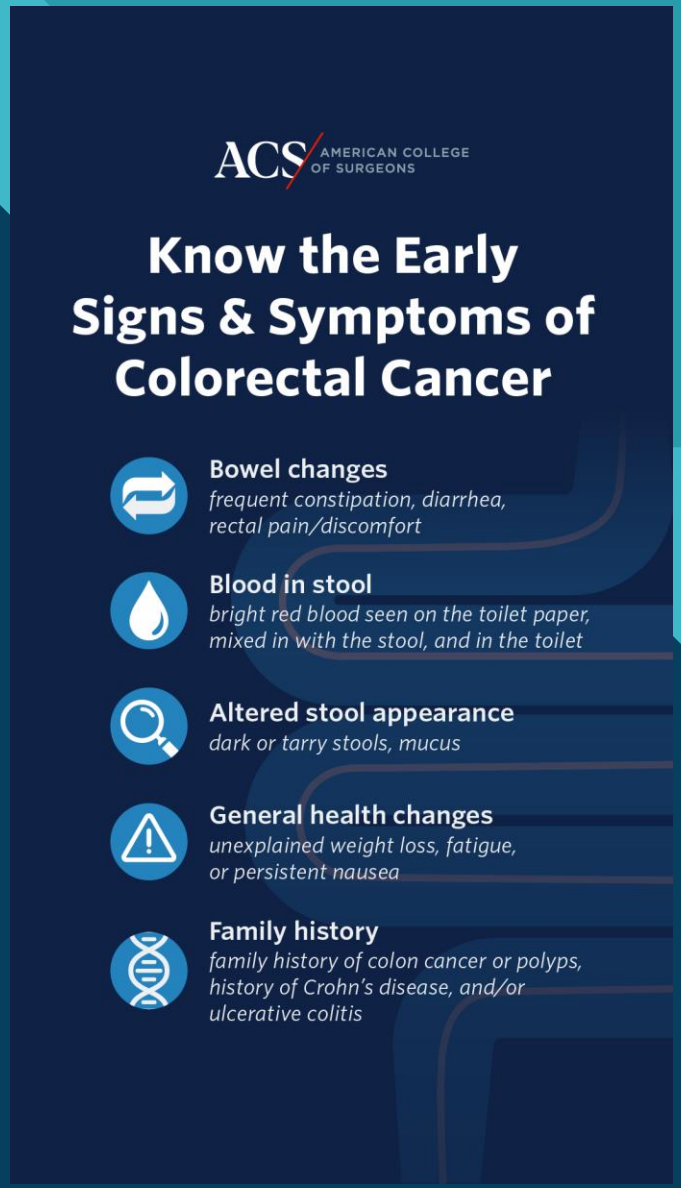
- Physical activity
- Vitamin D intake ≥450 IU/day

Non-modifiable Risk Factors

- **Genetics and Medical History**
- **Family history:**
  - Present in 14-34% of EOCRC vs. 8-19% of later-onset
- **Hereditary syndromes:**
  - Pathogenic germline variants in 16-25% (vs. ~10% in later-onset)
  - Primarily **Lynch Syndrome** (MSH2, MLH1, MSH6, PMS2)
  - Also FAP, MUTYH-associated polyposis
- **Inflammatory bowel disease:** present in 3% of EOCRC vs. 0.4% of later-onset

Clinical Aspects of EOCRC

- **Common Symptoms:**
  - Hematochezia (45%)
  - Abdominal pain (40%)
  - Altered bowel habits (27%)
- **Diagnostic Delays:**
  - Median time from symptoms to diagnosis: 128 days (vs. 79 days in older patients)
  - Clinicians may not suspect CRC in younger individuals
- **Tumor Location:**
  - 75-80% left colon and rectum (vs. 60% in later-onset)
  - More likely to be advanced stage (III-IV) at diagnosis
- **Prognosis:**
  - Similar or slightly better survival compared to late-onset CRC
  - Very young (ages 18-30) may have worse prognosis due to aggressive types



Screening

- USPSTF changed screening age to 45 in 2021
  - Or 10 years before 1st degree relative diagnosis, whichever is first
- Screen or test for genetic/familial risk factors
- Screen earlier if IBD
- Any positive stool or blood-based test → timely colonoscopy to complete screening
  - NCCN – scope within 9 months
  - AGA – 80% within 3 months, 100% within 6 months
- Any symptoms? → diagnostic colonoscopy ASAP

Can colorectal cancer be prevented?

Everyone should start regular screening for colorectal cancer at age 45.*

Stool-based tests

About stool-based tests

- Can be done at home
- Low cost
- No bowel prep or sedation
- Need to be done more often than visual tests
- Will need a colonoscopy if test is abnormal
- Can miss many polyps and some cancers

Stool-based test options

- Guaiac-based fecal occult blood test (gFOBT) **every year** or
- Fecal immunochemical Test (FIT) **every year** or
- Multi-targeted stool DNA test (MT-sDNA) **every 3 years**

Visual-exam tests

About visual-exam tests

- Done in doctor's office or health facility
- Bowel prep needed
- Only a colonoscopy can remove and test polyps
- Any test other than a colonoscopy will require a colonoscopy if the test is abnormal.

Visual exam test options

- Colonoscopy **every 10 years** or
- CT colonography (virtual colonoscopy) **every 5 years** or
- Flexible sigmoidoscopy **every 5 years**

*If you're at high risk of colorectal cancer based on family history or other factors, you may need to start screening before age 45, be screened more often, or get specific tests.

There are some differences between these tests to consider, but **the most important thing is to get screened, no matter which test you choose.**

More than half of all colorectal cancers are linked to physical inactivity, poor nutrition, excess body weight, tobacco, and alcohol.

- Eat more vegetables, fruits, and whole grains.
- Limit or avoid red and processed meats, sugary drinks, and refined grains.
- Be as physically active as you can.
- Get to a healthy weight range.
- Don't use tobacco, and avoid secondhand smoke.
- Limit or avoid alcohol.

cancer.org/colon | 1.800.227.2345

Future Research and Areas of Need

- Identify early risk factors in childhood and adolescence
  - Study these groups prospectively
- Gut microbiome
  - Can modulation reduce risk?
- Molecular and genomic studies
- Screen, screen, screen!
  - Screening earlier than 45?
- Prevention Strategies
  - Interventional trials targeting modifiable risk factors in adolescents/young adults
  - Public health campaigns on diet, obesity, physical activity starting in childhood
  - Identify higher risk patients at younger age (family history, risk assessments)
- Treatment Issues
  - Prospective trials specifically in EOCRC populations Optimal adjuvant therapy for stage II high-risk disease
  - Long-term survivorship research: late effects, quality of life, psychosocial impact
  - Fertility preservation outcomes and reproductive/sexual health after treatment

Summary

- EOCRC incidence is rising dramatically (2% annually)
- Multifactorial etiology: obesity, Western diet, sedentary lifestyle, gut microbiome
- Studies suggests early-life exposures are critical
- Up to 25% may have hereditary syndromes → universal genetic testing
- Diagnosed at more advanced stages but have similar stage-adjusted survival
- Treatment follows same guidelines as later-onset CRC with special considerations for young patients
- Current screening at age 45 may not capture highest-risk groups
- More research needed
- Symptoms? → timely colonoscopy!

Thank You!

References

- Jayakrishnan T, Ng K. Early-Onset Gastrointestinal Cancers: A Review. *JAMA*. 2025;334(15):1373–1385. doi:10.1001/jama.2025.10218
- Hua H, Jiang Q, Sun P, Xu X. Risk factors for early-onset colorectal cancer: systematic review and meta-analysis. Front Oncol. 2023 May 5;13:1132306. doi: 10.3389/fonc.2023.1132306. PMID: 37213277; PMCID: PMC10196487.
- Increasing Incidence of Early-Onset Colorectal Cancer. NEJM 2022.
- Siegel RL, Wagle NS, Star J, Kratzer TB, Smith RA, Jemal A. Colorectal cancer statistics, 2026. CA Cancer J Clin. 2026;e70067. doi:10.3322/caac.70067
- The fast-growing burden of younger-onset colorectal cancer. Rebecca Siegel, MPH.
- REACCT Collaborative. Characteristics of Early-Onset vs Late-Onset Colorectal Cancer: A Review. JAMA Surg. 2021;156(9):865–874. doi:10.1001/jamasurg.2021.2380
- ACS.org
- UpToDate.org - epidemiology-and-risk-factors-for-colorectal-cancer
- OpenEvidence.com
- Image: https://engl3164.wordpress.com/2013/02/05/uncle-sam-overweight/
- Image: https://my.clevelandclinic.org/health/body/22134-colon-large-intestine
- Image: https://www.cancer.org/cancer/types/colon-rectal-cancer/prevention-infographic.html
- Image: https://stock.adobe.com/search?k=scientist+kid
- Image: https://www.facs.org/for-patients/preparing-for-surgery/symptoms-of-colorectal-cancer/