UC San Diego Health

Colorectal Cancer Before 50: What Physicians Need to Know

Samuel Eisenstein, M.D.

Associate Professor of Surgery

University of California San Diego

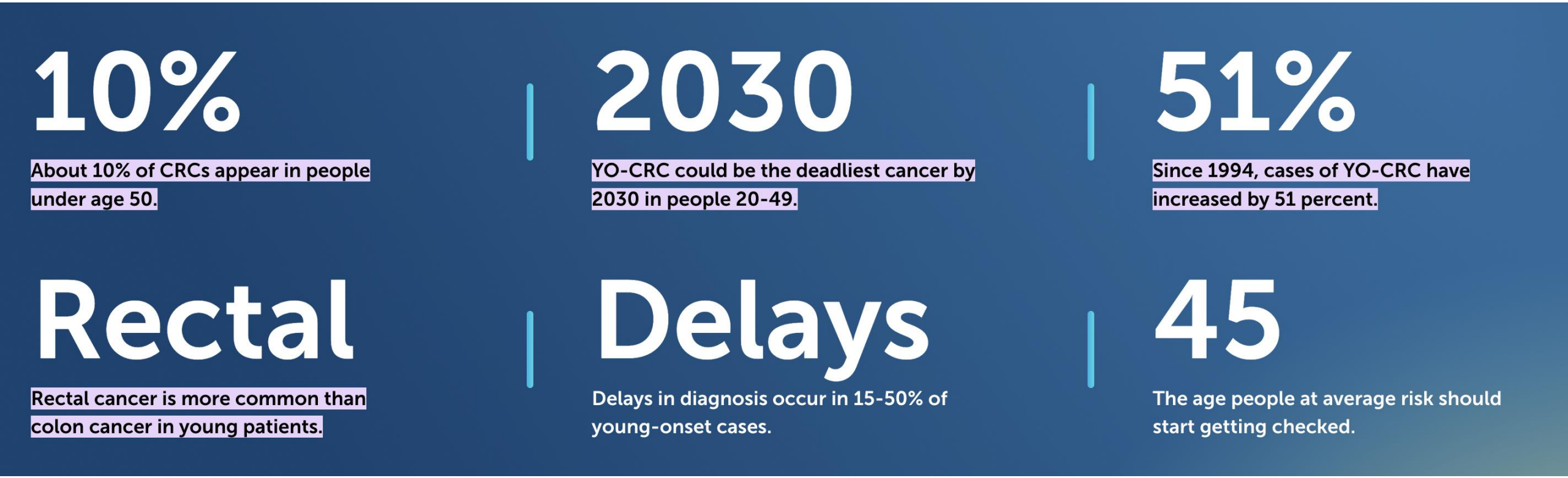
Disclosures

- Takeda – consulting
- Crohn’s and Colitis Foundation – research support

Young Onset Colorectal Cancer (CRC)

Young onset colorectal cancer is colon cancer or rectal cancer diagnosed before the age of 50

Young Onset CRC: Facts and Figures



Important role for primary care in early recognition

Objectives

- Colorectal cancer trends
- Epidemiology and risk factors
- Clinical presentation and diagnostic challenges
- Screening and early detection
- Management and multidisciplinary approach
- Key takeaways & call to action

Young Onset CRC: Trends

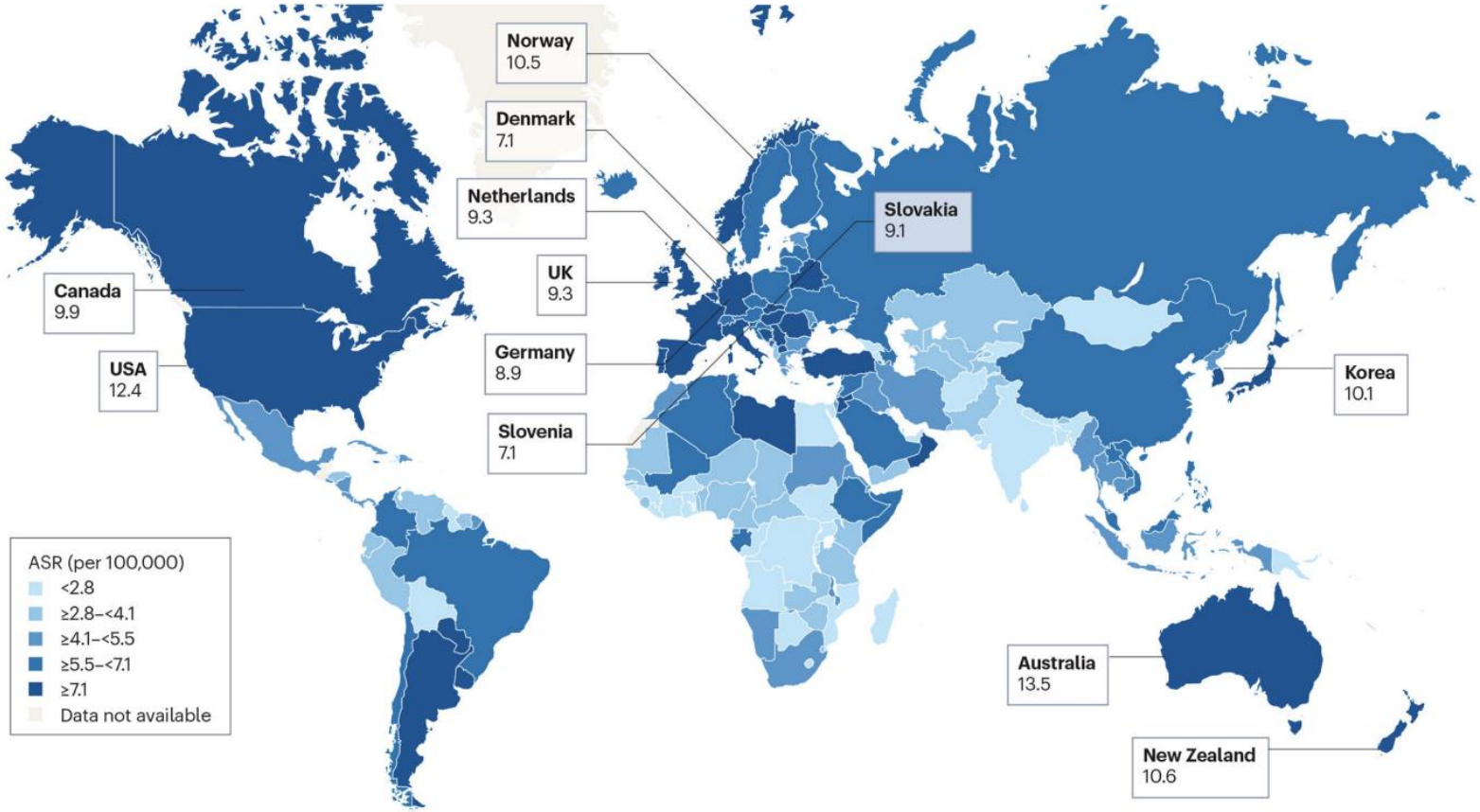
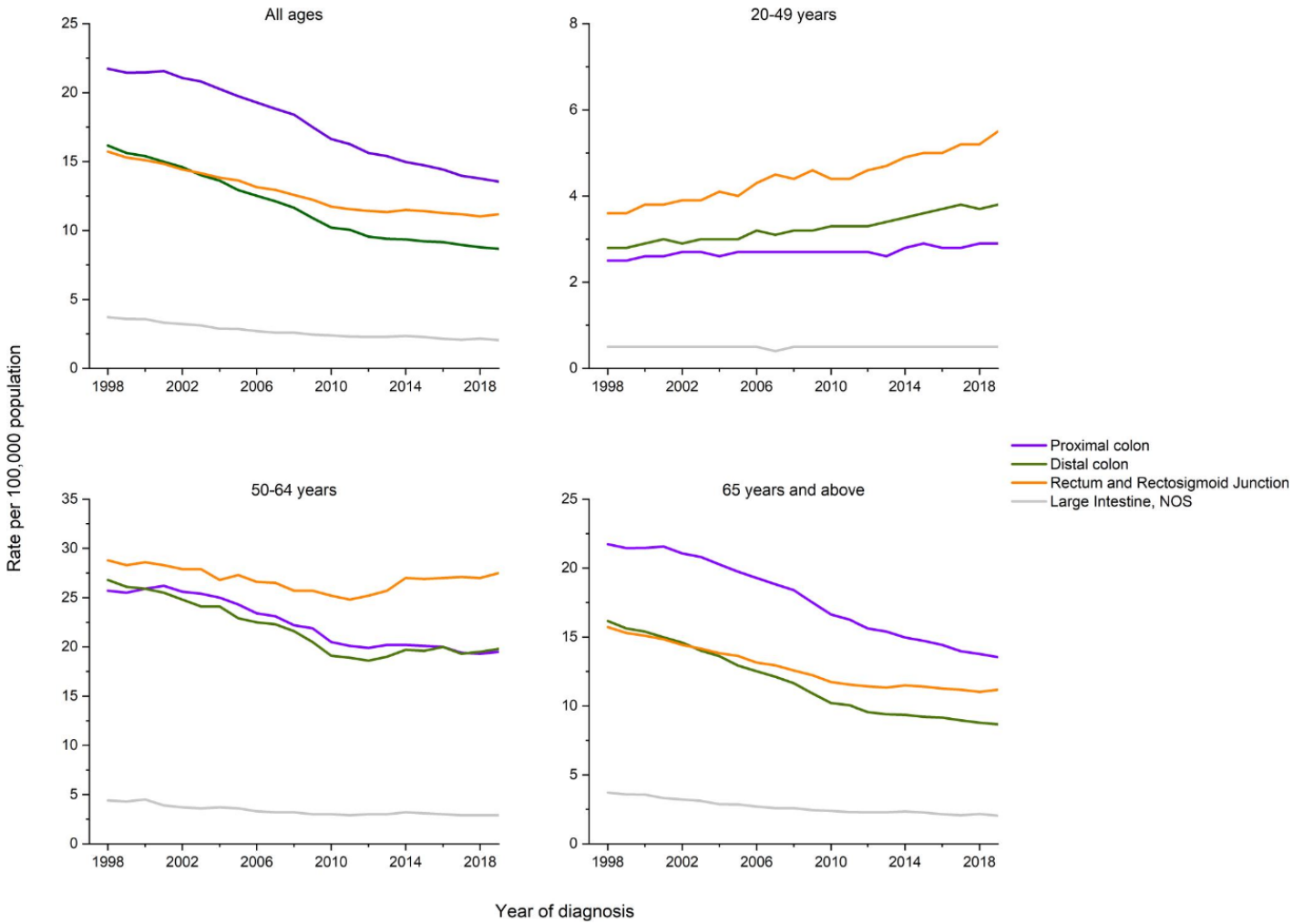


Figure 1. Global incidence of YO-CRC.
Age-standardized incidence of young-onset colorectal cancer (YO-CRC; age 20–49 years) in both sexes worldwide **for the year 2020. Countries/regions with the** greatest **percentage increase for years 2008–2012** are depicted in red.[8]

Young Onset CRC: Trends

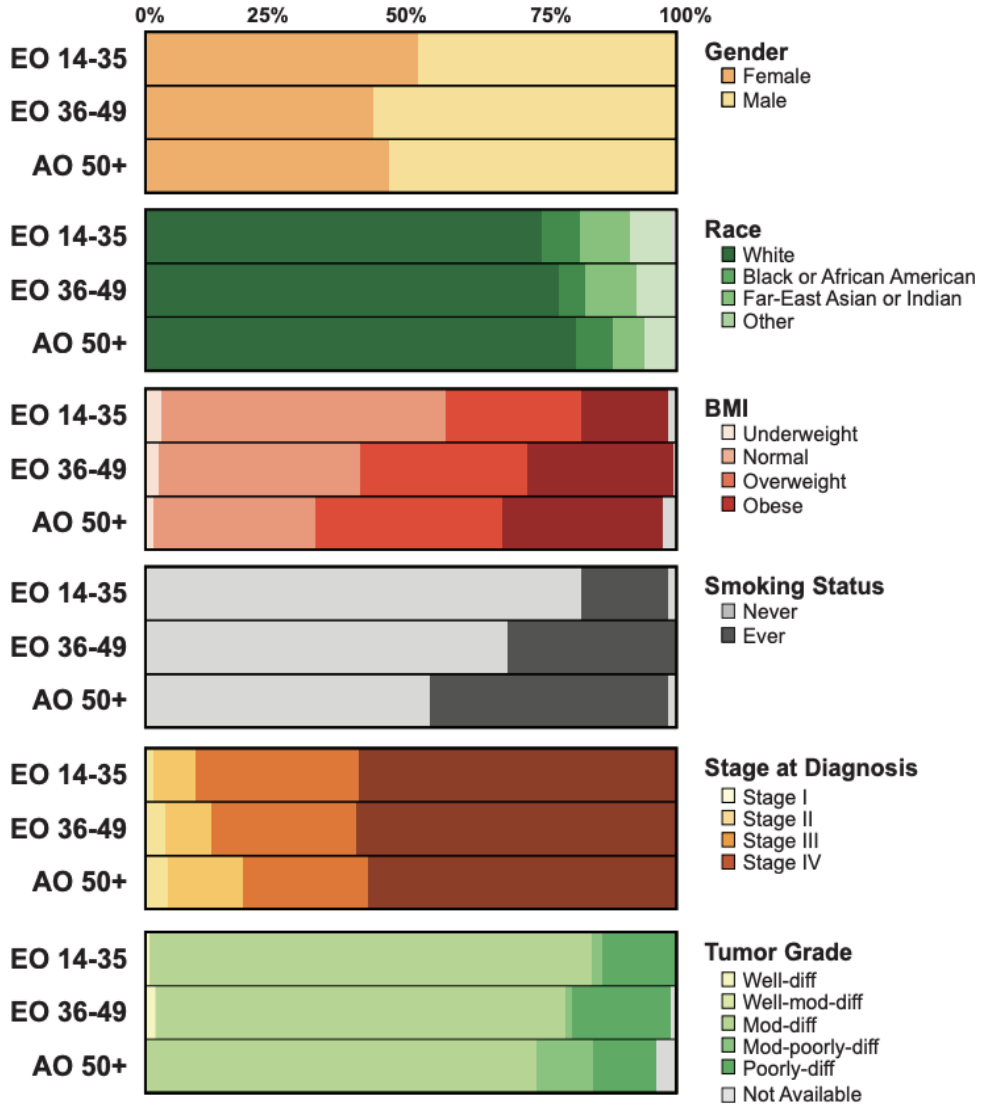
- In all ages, incidence is decreasing
- Incidence in young adults is increasing
  - Doubled since 1990s
  - Predominantly left-sided



Young Onset CRC: Epidemiology

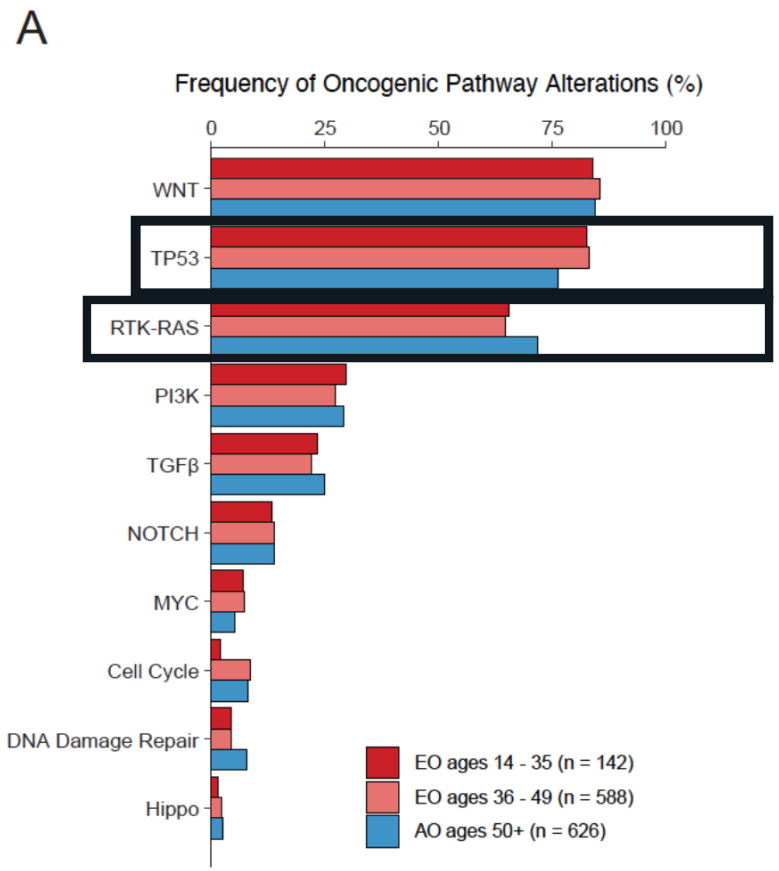
- Women>Men
- Non-white race
- Normal BMI
- Non-smokers
- Present with advanced disease
  - Delay in diagnosis
- More aggressive pathologic features
  - LVI, T3/T4, N+
  - Poorly differentiated

Importance of early recognition, critical role for primary care



Young Onset CRC: Genetic risk

- Most cases before 50 years are sporadic
- MSK: EOCRC (759) vs. AOCRC (687)
  - Exclude hereditary, MSI, IBD
- Inherited component ~30% (first degree relative)
- Pathogenic germline variant ~20%
- Somatic genomically indistinguishable from average onset
  - No significant differences in TMB, fraction of genome altered, whole-genome duplication, LOH



Young Onset CRC: Established and Emerging Risk Factors

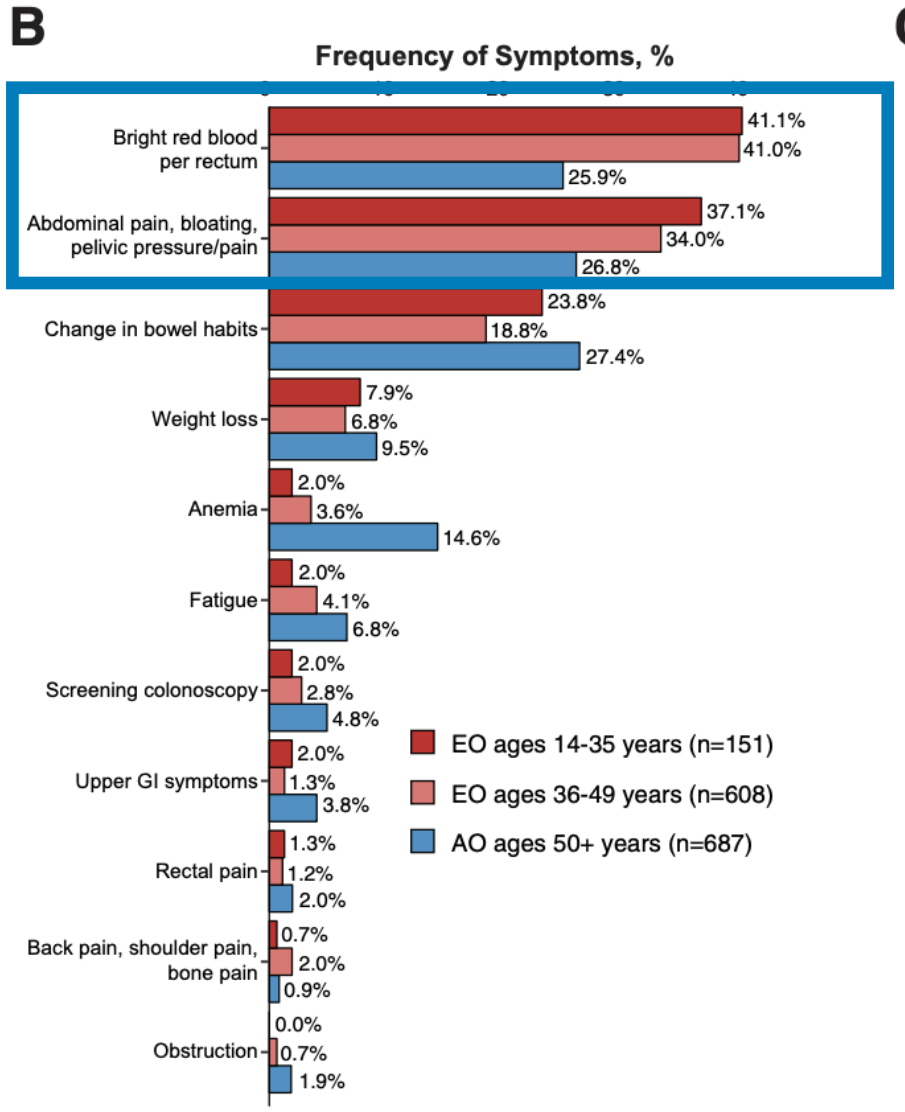
- Lifestyle
  - Sedentary lifestyle
  - Diet: sugar, red/processed meat, processed foods, low fiber
  - Obesity
  - Smoking and alcohol
- Exposures
  - Antibiotics
  - Agricultural runoff
  - Industrial pollution
  - Occupational exposures

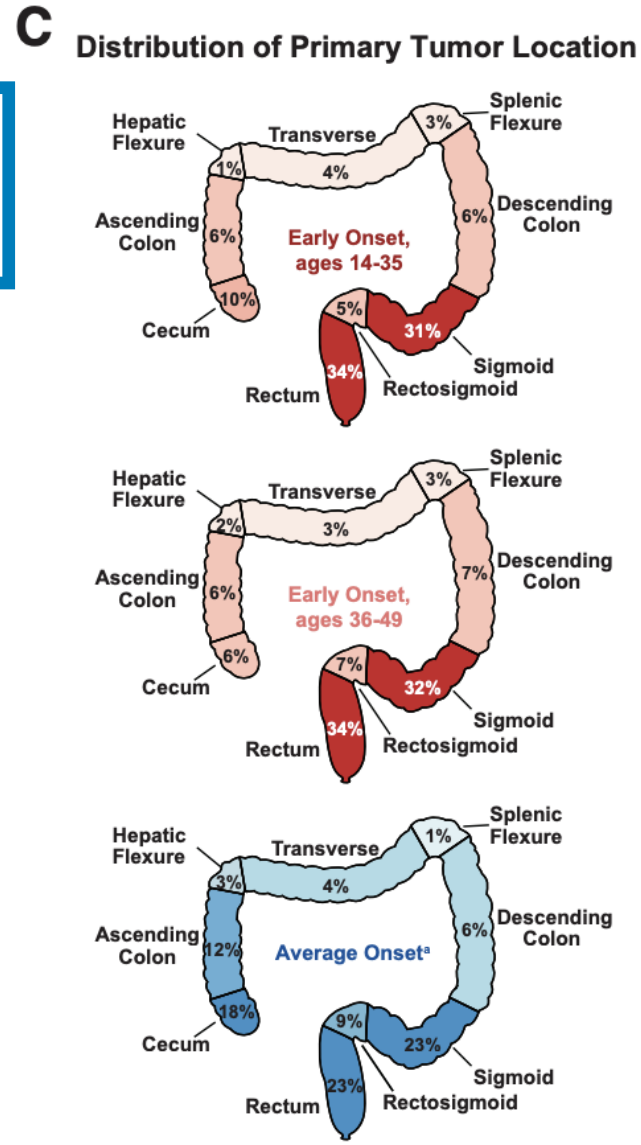
- Effect on Microbiome
  - Dysbiosis
  - Loss of protective microbiota
  - Production of oncogenic metabolites
    - Secondary bile acids
    - Nitrosamines
    - Formate

- Intestinal Effects
  - Proinflammatory environment
  - Suppression of immunity
  - Induction of tumor growth

Young Onset CRC: Clinical Presentation and Challenges

- Bright red blood per rectum
- Abdominal/pelvic pain/bloating
  - Related to more commonly left sided disease
- Delay in diagnosis approximately 6 months
  - *Importance of keeping CRC in the differential for younger patients*





Young Onset CRC: Screening and Detection Strategies

Warning signs

- Rectal bleeding
- Abdominal pain
- Change in bowel habits

Young Onset CRC: Screening and Detection Strategies

Stool-based tests

- Fecal immunochemical test (FIT): A common stool-based test that checks for microscopic blood in stool
  - Low sensitivity for detecting CRC (70%-75% vs colonoscopy)
  - Low sensitivity for precursor lesions
    - 20% to 25% for advanced adenomas
    - <5% for advanced sessile serrated adenomas
- Multitarget Stool DNA test (mt-sDNA): Also known as Cologuard, this test checks for abnormal DNA in stool
  - Better sensitivity for detecting CRC (92%)
  - Low sensitivity for precursor lesions (40-50%)
- Limitations: Less effective than a colonoscopy, and may require a follow-up colonoscopy

Colonoscopy

- Benefits: Can detect and remove precancerous polyps before they turn into cancer
- Drawbacks
  - Requires sedation and bowel preparation
  - Invasive/risk of complications

Recommended intervals for colorectal cancer screening tests include

- High-sensitivity gFOBT or FIT every year
- sDNA-FIT every 1 to 3 years
- CT colonography every 5 years
- Flexible sigmoidoscopy every 5 years
- Flexible sigmoidoscopy every 10 years + FIT every year
- Colonoscopy screening every 10 years

Young Onset CRC: Risk Reduction

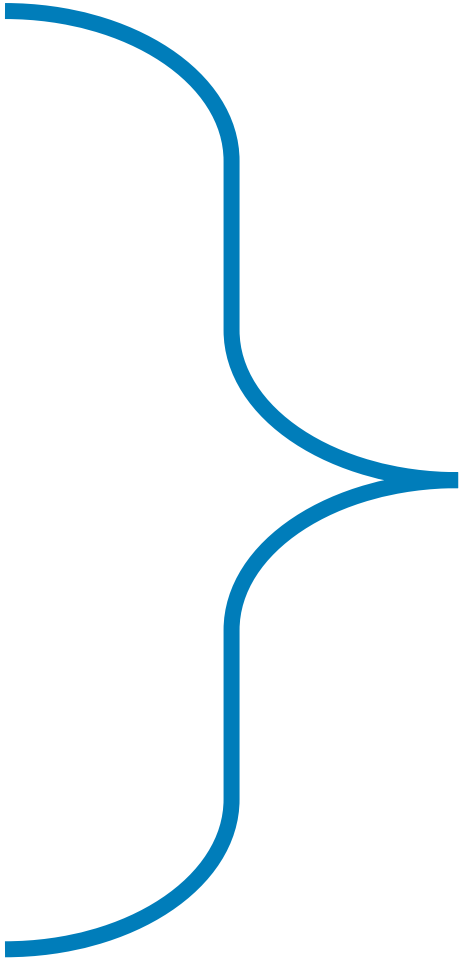
- Increase physical activity
  - 150 minutes of moderate exercise or 75 minutes of vigorous exercise each week
- Limit red meat processed meat
- High proportion of plant-based foods in the diet
  - Fiber supplement
- Limit alcohol
- Don't smoke
- Supplements may benefit: Folate, selenium, omega-3 fatty acids, vitamin D, NSAIDs, curcumin, green tea, soy

Young Onset CRC: Treatment Strategies

- Surgery
  - May require temporary or permanent ostomy
- Chemotherapy
- Radiation
  - For rectal cancer only
  - Some patients with rectal cancer have a complete response to neoadjuvant therapy and have close surveillance with surgery only for regrowth

Management Considerations for Young Adults with Cancer

- Fertility
  - Cancer during pregnancy
- Sexual and urinary function
- Long-term impact of therapies on QOL and function
  - Neuropathies
  - XRT
- Secondary cancer
- Psychological and mental health impact on patient and family



Role of primary care in survivorship, surveillance, and addressing long-term effects

Key Takeaways and Call to Action

- CRC is increasingly prevalent among young adults, particularly left sided disease
- Delays in diagnosis are common

Have a high index of suspicion with bleeding and abdominal symptoms

- Quality of life is significantly altered by treatment and there are unique considerations for young adults who are likely best served at specialty centers

Thank you

Samuel Eisenstein, M.D.
Associate Professor of Surgery

seisenstein@health.ucsd.edu

UC San Diego Health