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Updates in Colorectal Cancer Screening

Elisabeth R. Evans, MSN, FNP-BC
San Diego, CA

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Disclosures

Elisabeth R. Evans, MSN, FNP-BC

Exact Sciences Corporation Employee July 2019 – Present

Sr. Medical Science Liaison and AOPH Scientific Specialist

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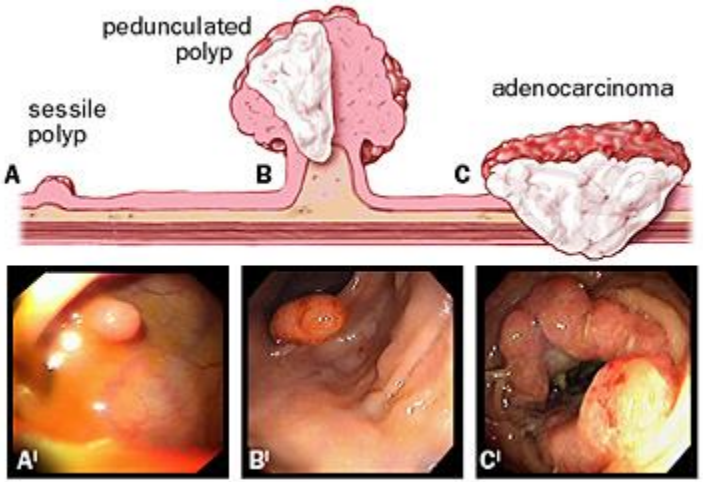
Outline

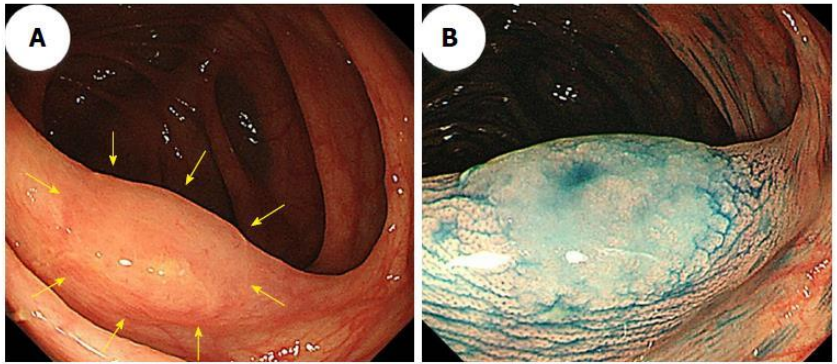
- What is Colorectal Cancer?
- Colorectal Cancer Risk Factors
- Pathogenesis of Colorectal Cancer
- Symptoms and Diagnosis
- Colorectal Cancer in Younger Populations

What Is Colorectal Cancer?

Polyp/Cancer

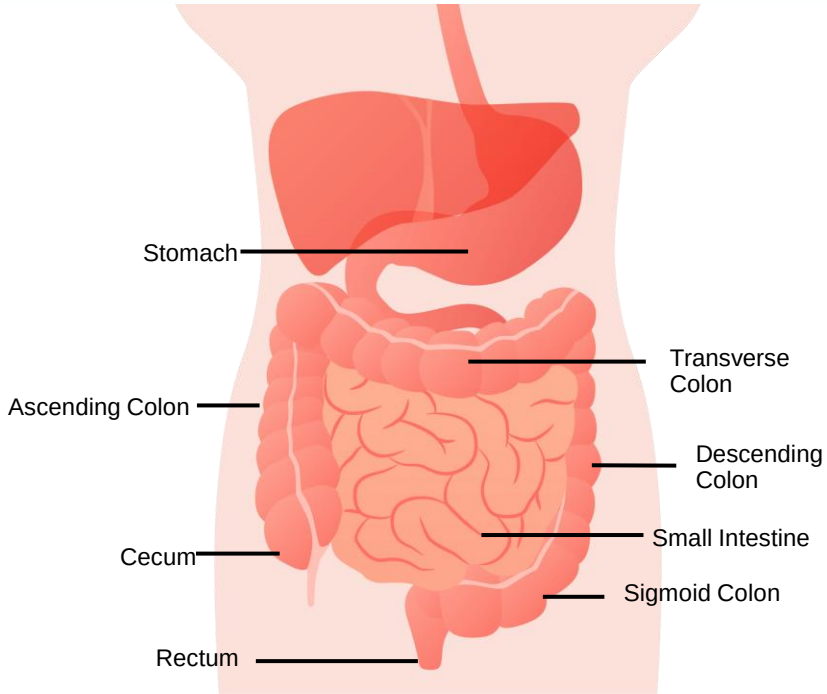


Sessile Serrated Adenoma/polyp



Basic Anatomy of Colon and Rectum

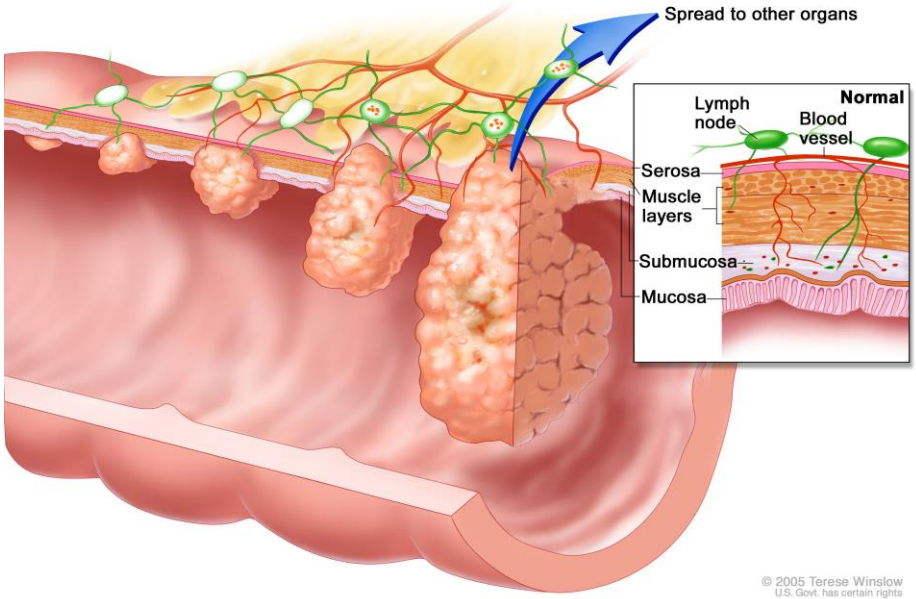
- The colon is a muscular tube about 5 feet long (1.5 meters) that is divided into 4 sections:
  - Ascending
  - Transverse
  - Descending
  - Sigmoid
- Rectum is the final 6 inches (15 cm) of the large intestine



American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020.

Stages of Colorectal Cancer

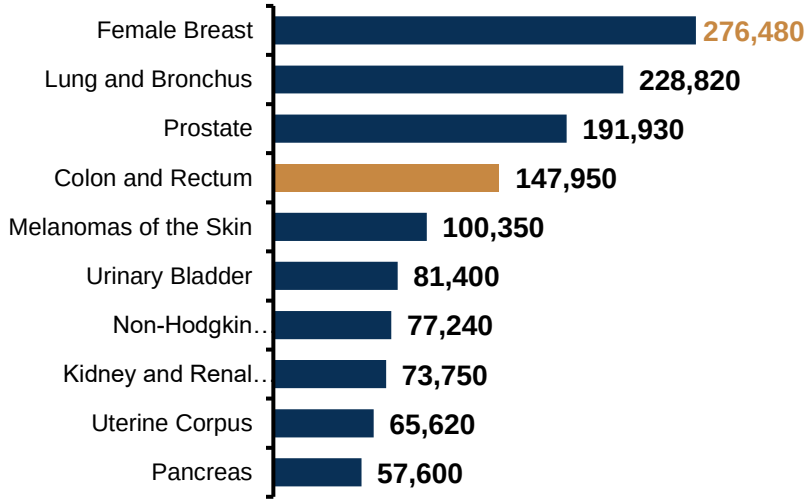
- CRC usually begins as a polyp
- When a polyp progresses to cancer, it can grow into the wall of the colon/rectum (local)
- It may invade lymph vessels and spread to nearby lymph nodes (regional)
- Cancer cells may also be carried via blood vessels to other organs such as the liver or lung (distant)



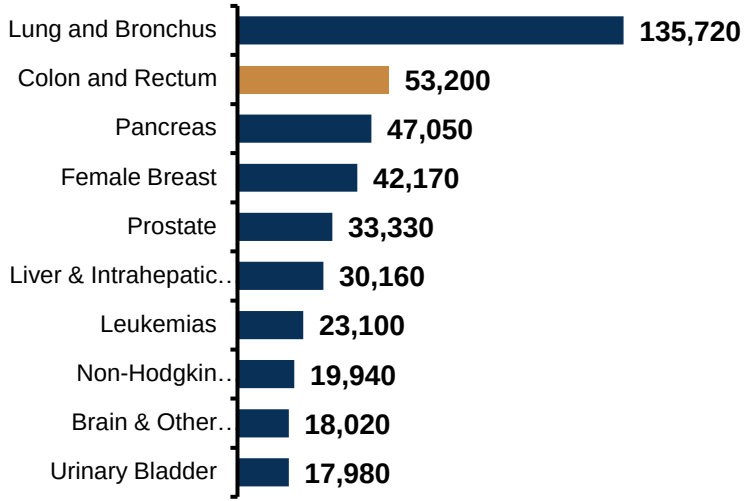
American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020.

Estimated CRC Incidence and Mortality, US 2020

Top 10 Cancers by Number of New Cancer Cases (United States, 2020)



Top 10 Cancers by Number of Cancer Deaths (United States, 2020)



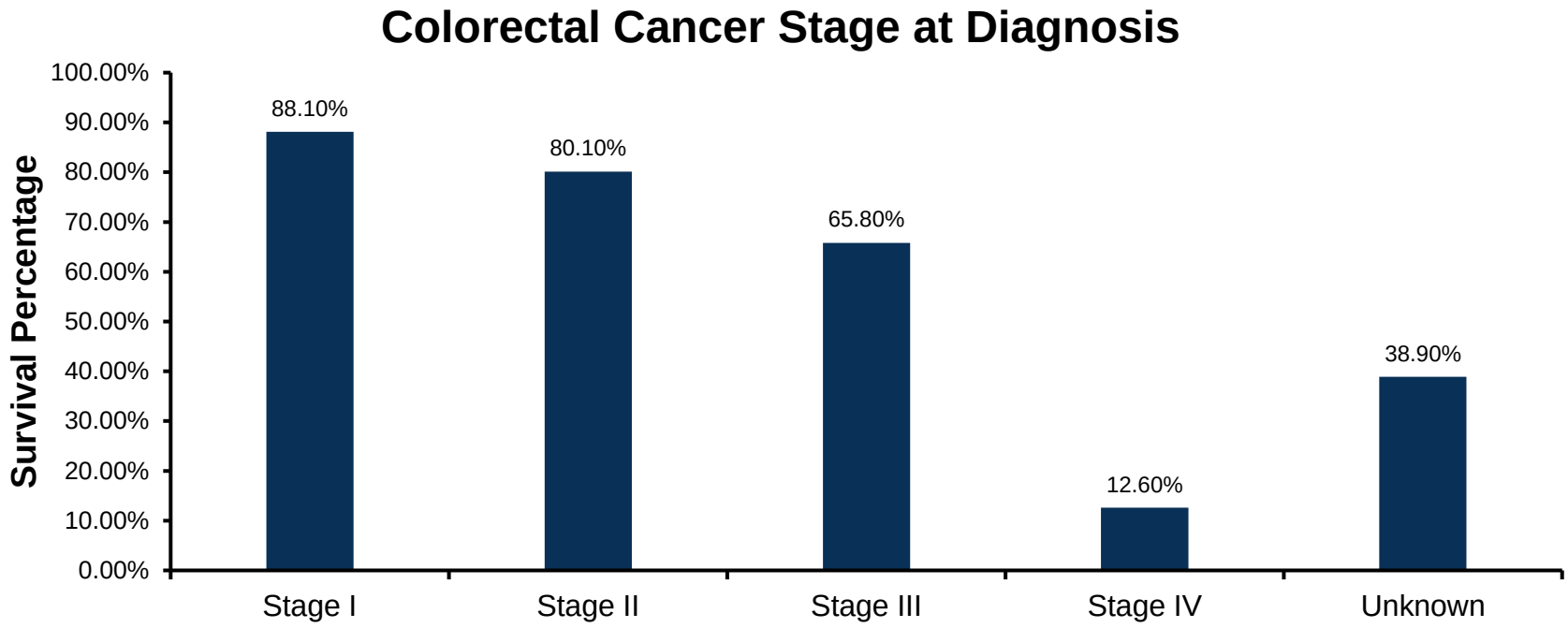
Overall Lifetime Risk of CRC:

4.4% for men

4.1% for women

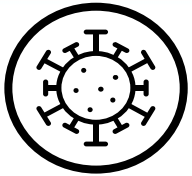
Siegel RL, Miller KD, Jemal A. *CA Cancer J Clin.* 2020;70(1):7-30.

5-Year CRC Relative Survival for Men and Women (2007-2013)

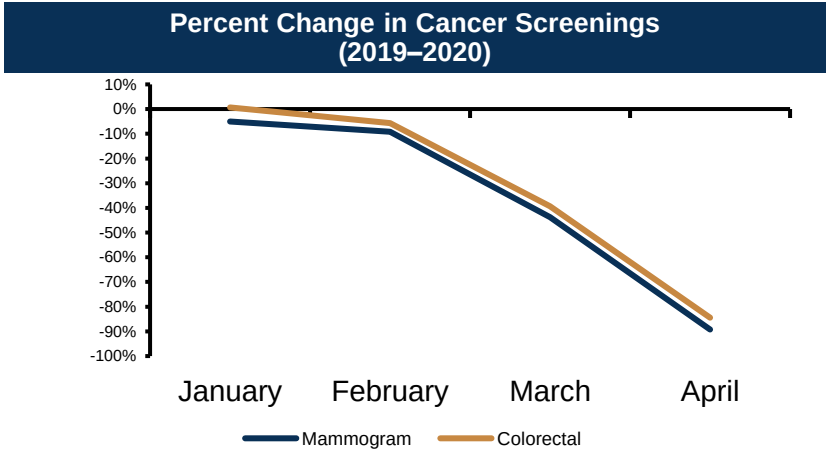


American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Atlanta: American Cancer Society; 2020.

The Effects of COVID-19 on Cancer Screening



- Retrospective cohort study of COVID and Cancer Research Network (CCRN) data compared patient encounter data from January to April 2019 vs the same month in 2020
- Network of 20 institutions across the US with over 28 M patients
- **April displayed the greatest drop:** screening of patients with colorectal cancer **fell by −84.5%** when comparing 2020 with 2019



Month	Mammograms	Colorectal
January	-5.0%	0.7%
February	-9.1%	-5.6%
March	-43.8%	-39.4%
April	-89.2%	-84.5%

London JW et al. *JCO Clin Cancer Inform*. 2020;4:657-665.

CRC Screening Recommendations – Fall 2020

The AGA gathered 60 experts in gastroenterology and research to envision how screening could reach its full potential.

Their conclusion: To significantly reduce the number of colorectal cancer cases and deaths would require a universal approach to screening that reaches more people and offers alternatives in addition to colonoscopy.

- Offer noninvasive testing upfront, such as stool testing, and integrate these options with colonoscopy.
- Share decision-making with the patient and consider personal risk factors: colonoscopy for those at high risk, or initial noninvasive testing for those at lower risk.
- Assign colonoscopy when it would provide the greatest benefit, rather than as the default screening method. This would improve access to patients who most need a colonoscopy.
- Systematically initiate screening, follow-up testing and surveillance, rather than rely only on a physician's recommendation.
- Ensure appropriate screening is readily available to at-risk individuals, with no social, racial or economic disparities.

Komanduri S, Melson JE. https://www.medscape.com/viewarticle/935288.

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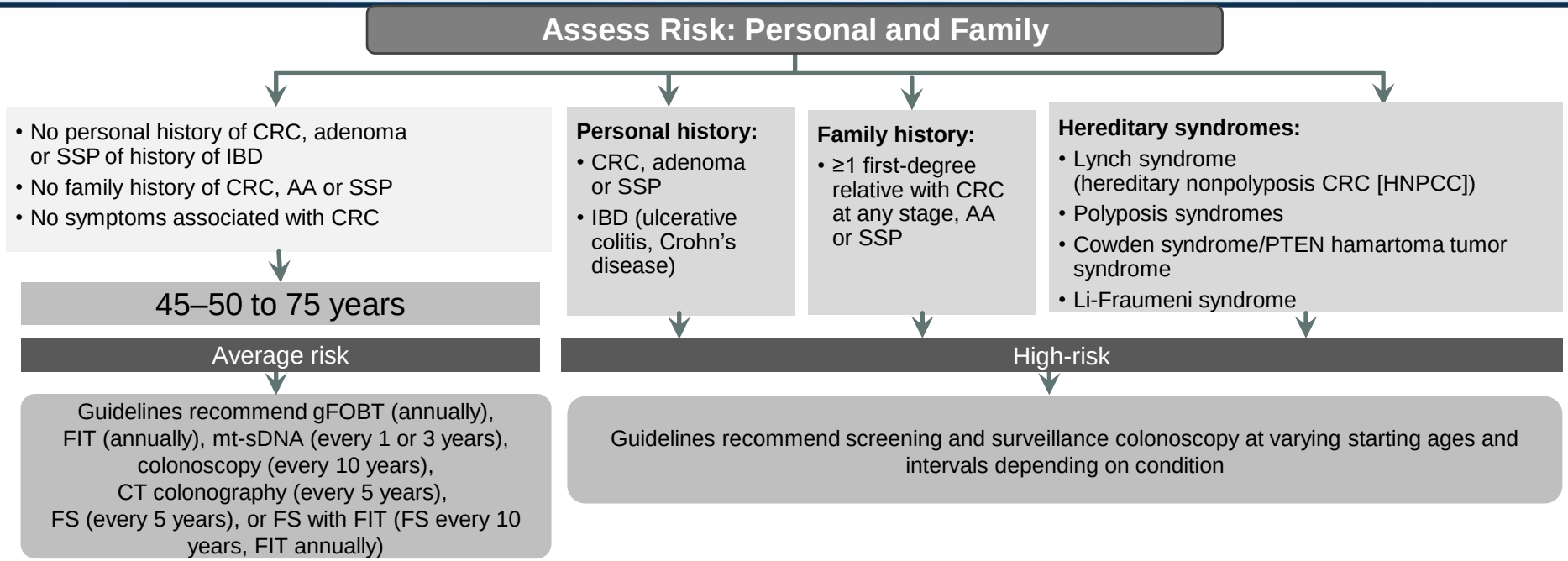
Risk Factors

Colorectal Cancer

Assessing Risk



1. Bibbins-Domingo K et al. *JAMA*. 2016;315(23):2564-2575; 2. Wolf AMD et al. *CA Cancer J Clin*. 2018;68(4):250-281;
3. National Comprehensive Cancer Network. Colorectal Cancer Screening (Version 2.2020);
https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf. Accessed August 24, 2020;
4. Rex DK et al. *Am J Gastroenterol*. 2017;112(7):1016-1030; 5. National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Colorectal (Version 1.2020). https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf. Accessed August 24, 2020; 6. Gupta et al. *Gastroenterology*. 2020; DOI:10.1053/j.gastro.2019.10.026.

Risk Factors for Colorectal Cancer[1]

- Non-Modifiable risk factors include:
  - Personal or family history of CRC or adenomas
  - Inflammatory Bowel Disease
  - Type 2 Diabetes
- In the United States ~55% of all CRCs are attributable to modifiable lifestyle factors:
  - High alcohol consumption
  - Being overweight or obese
  - Unhealthy diet (red/processed meat)
  - Smoking

Factors that increase risk	Relative risk*
Heredity and medical history	
Family history of CRC	
1 or more first-degree relatives	2.2
1 or more first-degree relatives diagnosed before age 50	3.6
2 or more first-degree relatives	4.0
1 or more second-degree relatives	1.7
Inflammatory bowel disease	1.7
Type 2 diabetes	
Male	1.4
Female	1.2[†]
Modifiable Factors	
Heavy alcohol (daily average > 3 drinks)	1.3
Obesity (Body Mass Index ≥30 kg/m^2)	1.3
Red meat (100 g/day)	1.1
Processed meat (50 g/day)	1.2
Smoking	
Current vs. Never	1.5
Former vs. Never	1.2
Factors that decrease risk	
Physical activity	0.7
Dairy (400 g/day)	0.9

Vitamin D and Colorectal Cancer Risk

- Pooled 17 cohorts with Vit D 25(OH) levels
- 5706 CRC patients and 7107 control
- Each 25(OH) nmol/L increment:
  - CRC decreased by 19% in women (significant)
  - CRC decreased by 7% in men (not significant)
- No difference in age, race, region
- No benefit in Vit D 25(OH) levels > 100nmol/L

McCullough ML et al. *J Natl Cancer Inst.* 2019;111(2):158-169.

2020 Post Colonoscopy Follow Up

Tubular Adenoma

- 1-2 TA: 7-10yr (vs 5yr)
- 3-4 TA: 3-5yr (vs 3 yr)
- >10mm or +histology: 3yr (same)
- >10 TA: 1yr (new)
- Piecemeal resection: (6 months)

Serrated Polyps

- 1-2 SSP <10mm: 5-10yr (new)
- 3-4 SSP <10mm: 3-5yr (new)
- >5 SSP, >10mm, +histology: 3yr (same)
- Piecemeal resection if >20mm: 6 months (same)

Gastroenterology. 2020 Feb 14.

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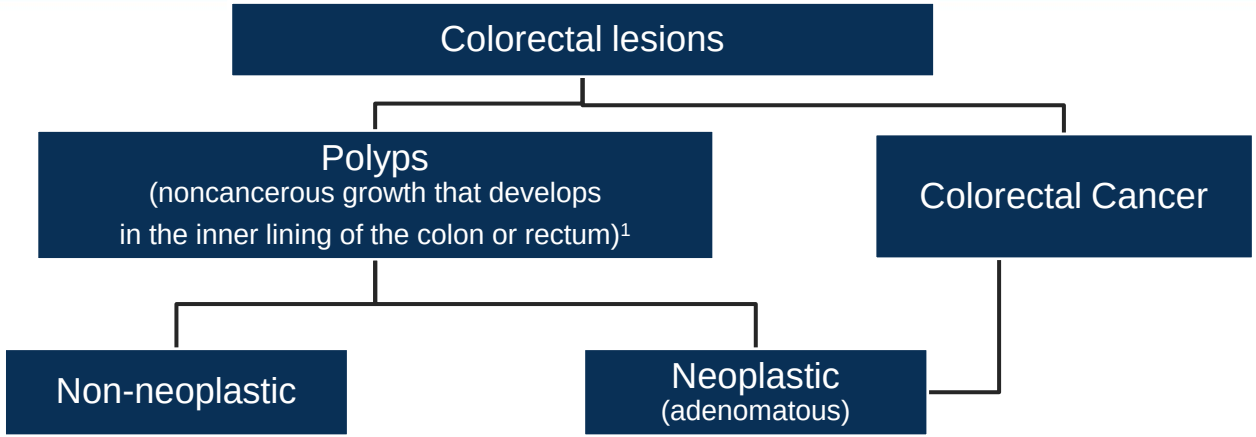
Pathogenesis

Colorectal Cancer

Understanding CRC Pathology

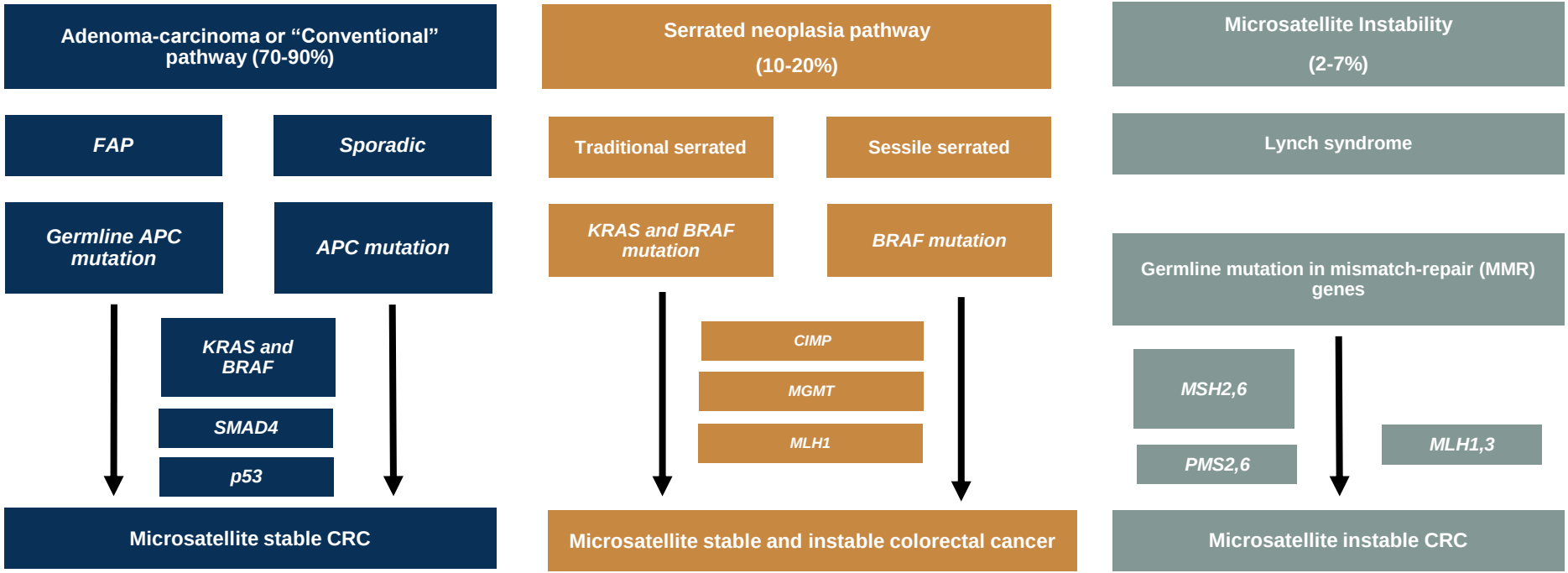


- Usually no malignant potential
- Include:
  - **Hyperplastic polyps**
    - Subgroup of Serrated Polyps: has malignant potential
  - **Inflammatory polyps**
  - **Hamartomatous polyps**

- Have malignant potential
- **Adenomas:** may be found anywhere throughout the colon
- Histological appearance:
  - **Tubular**
  - **Tubule-villous adenomas**
  - **Villous adenoma**

1. American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022; Atlanta: American Cancer Society. 2020;
2. Shussman N Wexner SD. *Gastroenterol Rep (Oxf).* 2014;2(1):1-15.

Pathogenesis: Genetic and Epigenetic Events

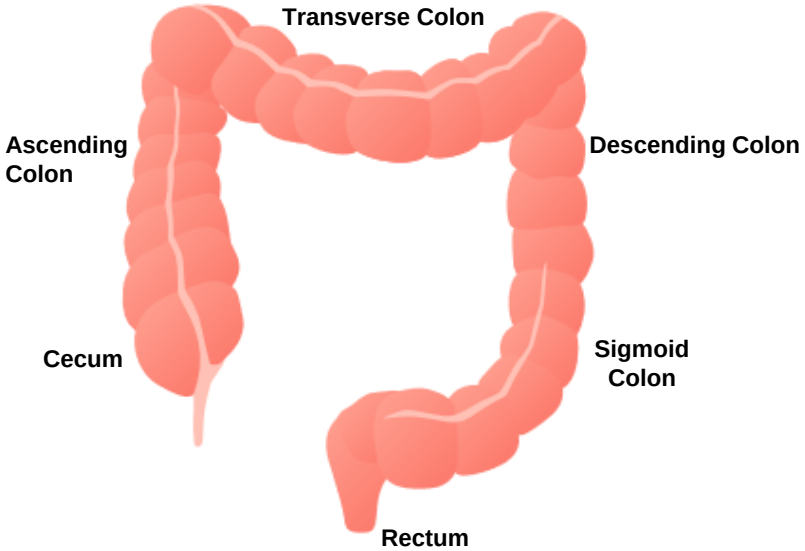


Dekker et al. *Lancet*. 2019; 394: 1467–80.

Left-Sided vs. Right-Sided CRC

Right-sided (proximal)

- Microsatellite Instability (MSI)
- Hypermutated (BRAF mutations)
- Occurs in older ages
- Tumors have flat morphology



Left-sided (distal)

- Chromosomal Instability Pathway (CSI/CIN)
- ***KRAS*** **mutations**
- Occurs in younger ages
- Tumors have polyploid-like morphology

1. Baran B et al. *Gastroenterol Res.* 2018;11(4):264-273; 2. Bylsma LC, et al. *Cancer Med*. 2020;9(3):1044-1057;
3. Siegel R, et al*. CA Cancer J Clin*. 2020;70:7-30.

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Symptoms and Diagnosis

Colorectal Cancer

Symptoms of CRC

- Early CRC often has no symptoms, which is why screening is so important
- As the tumor grows, it may bleed or block the intestine causing:
  - Bleeding from the rectum
  - Blood in the stool or in the toilet
  - Dark or black stools
  - Change in bowel habit or shape of the stool
  - Cramping or pain in the lower abdomen
  - Constipation or diarrhea that persists more than a few days
  - Decreased appetite
  - Unintentional weight loss
  - Anemia/Fatigue/Weakness/Short of breath

American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022; Atlanta: American Cancer Society. 2020.

Guidelines Recommend Routine CRC Screening

	Recommendations	USPSTF 2016[1]	ACS 2018[2]	NCCN® 2019[3,*]	MSTF 2017[4]
	Choice of test	Screening for CRC with several different methods can accurately detect early stage CRC and adenomatous polyps	• High-sensitivity stool-based test or a structural (visual) exam, depending on patient preference and test availability • *All positive results on non-colonoscopy screening tests should be followed up with timely colonoscopy*	• Multiple modalities exist, and the choice should be based on patient preference and resource availability • Any screening is better than none	Recommended colonoscopy every 10 years or annual FIT as first-tier options for screening *(strong recommendation; moderate-quality evidence)*
Direct Visual Examination	**Colonoscopy**	Every 10 years	Every 10 years	Every 10 years	Every 10 years (Tier 1)
	CT colonography	Every 5 years	Every 5 years	Every 5 years	Every 5 years (Tier 2)
	FS	Every 5 years	Every 5 years	Every 5–10 years	Every 5 or 10 years (Tier 2)
	FS with FIT	FS every 10 years with annual FIT	--	FS every 10 years with annual FIT is an alternative strategy	--
	Capsule colonoscopy	--	--	--	Every 5 years (Tier 3)
Stool-based Tests	**gFOBT or hs-gFOBT**	Annual gFOBT	Annual hs-gFOBT	Annual hs-gFOBT	--
	FIT	Annual	Annual	Annual	Annual (Tier 1)
	mt-sDNA	Every 1 or 3 years	Every 3 years	Every 3 years	Every 3 years (Tier 2)

1. Bibbins-Domingo K et al. *JAMA*. 2016;315(23):2564-2575; 2. Wolf AMD et al. *CA Cancer J Clin*. 2018;68(4):250-281;
3. National Comprehensive Cancer Network. Colorectal Cancer Screening (Version 2.2020). https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf. Accessed August 24, 2020;
4. Rex DK et al. *Am J Gastroenterol*. 2017;112(7):1016-1030.

Guidelines Recommend Routine CRC Screening

	US Preventive Services Task Force (USPSTF) 2016[1]	American Cancer Society (ACS) 2018[2]	National Comprehensive Cancer Network® (NCCN®)† 2020[3]	US Multi-Society Task Force (USMSTF) 2017[4]
Age to Start Screening	50 years	with average risk of CRC: 45 years (qualified*) or 50 years (strong)	50 years	50 years overall; 45 years for African Americans (weak)
Age to Stop Screening	75 years	75 years (qualified*)	75 years	75 years or when life expectancy is <10 years
After 75 years	Individualized decision for screening	Individualized decision for screening at ages 76-85 years	Individualized decision for screening at ages 76-85 years (include a discussion of the risks and benefits based on comorbidity status and estimated life expectancy)	Stop screening when life expectancy is <10 years; recommendation to stop screening can be based on patient age and comorbidities

1. Bibbins-Domingo K et al. *JAMA*. 2016;315(23):2564-2575; 2. Wolf AMD et al. *CA Cancer J Clin*. 2018;68(4):250-281;
3. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology - colorectal cancer screening; Version 2. 2020. Updated June 8, 2020. https://www.nccn.org/professionals/physician_gls/pdf/colorectal_screening.pdf Accessed July 22, 2020; 4. Rex DK et al. *Am J Gastroenterol*. 2017;112(7):1016-1030.

CRC Screening Tests Overview – Visual Examinations

Screening Test	Benefits	Performance & Complexity*	Limitations	Test Time Interval
Colonoscopy	• Examines entire colon • Can biopsy and remove polyps • Can diagnose other diseases • Required for abnormal results from all other tests	Performance: Highest Complexity: Highest	• Full bowel cleansing • Can be expensive • Sedation usually needed, necessitating a chaperone to return home • Patient may miss a day of work • Highest risk of bowel tears or infections compared with other tests	10 years
Computed tomographic colonography (CTC)	• Examines entire colon • Fairly quick • Few complications • No sedation needed • Noninvasive	Performance: High (for large polyps) Complexity: Intermediate	• Full bowel cleansing • Cannot remove polyps or perform biopsies • Exposure to low-dose radiation • Colonoscopy necessary if positive • Not covered by all insurance plans	5 years
Flexible Sigmoidoscopy (FS)	• Fairly quick • Few complications • Minimal bowel preparation • Does not require sedation or a specialist	Performance: High for rectum & lower one-third of the colon Complexity: Intermediate	• Partial bowel cleansing • Views only one-third of colon • Cannot remove large polyps • Small risk of infection or bowel tear • Slightly more effective when combined with annual fecal occult blood testing • Colonoscopy necessary if positive • Limited availability	5 years

American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022; Atlanta: American Cancer Society. 2020.

CRC Screening Tests Overview – Stool Tests

Screening Test	Benefits	Performance & Complexity*	Limitations	Test Time Interval
Fecal immunochemical test (FIT)	• No bowel cleansing or sedation • Performed at home • Low cost • Noninvasive	Performance: Intermediate for cancer Complexity: Low	• Requires multiple stool samples • Will miss most polyps • May produce false-positive test results • Slightly more effective when combined with a flexible sigmoidoscopy every five years • Colonoscopy necessary if positive	Annual
High-sensitivity guaiac-based fecal occult blood test (gFOBT)	• No bowel cleansing or sedation • Performed at home • Low cost • Noninvasive	Performance: Intermediate for cancer Complexity: Low	• Requires multiple stool samples • Will miss most polyps • May produce false-positive test results • Pre-test dietary limitations • Slightly more effective when combined with a flexible sigmoidoscopy every five years • Colonoscopy necessary if positive	Annual
mt-sDNA	• No bowel cleansing or sedation • Performed at home • Requires only a single stool sample • Noninvasive	Performance: Intermediate for cancer Complexity: Low	• Will miss most polyps • More false-positive results than other tests • Higher cost than gFOBT and FIT • Colonoscopy necessary if positive	3 years

American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022; Atlanta: American Cancer Society. 2020.

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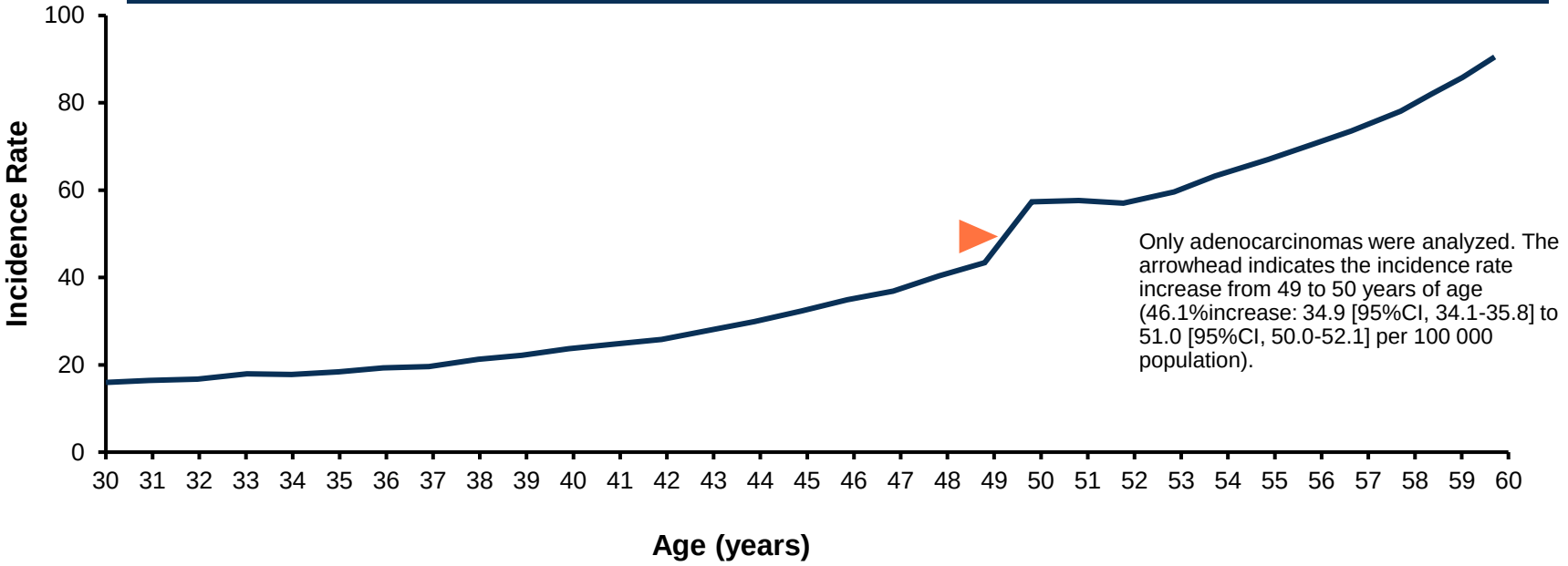
Younger (<50 Years) Populations

Colorectal Cancer

Strong Increase in CRC Incidence From 49 – 50 Years

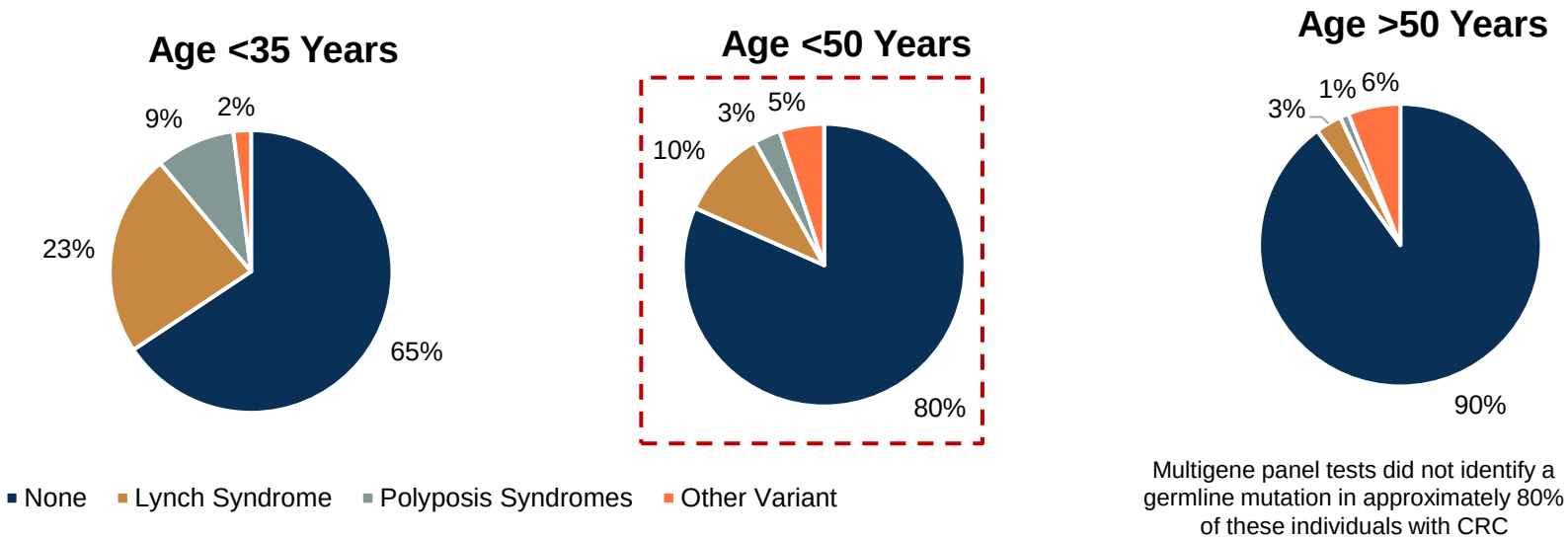
Colorectal Cancer Incidence Rates per 100,000 Population in 1-Year Age Increments in the US Surveillance, Epidemiology, and End Results 18 Registries Among Patients Aged 30 to 60 Years, 2000–2015



Abualkhair WH et al. *JAMA New Open*. 2020;3(1):e1920407.

Genetic Variant Impact on Different Age Groups

Prevalence of pathogenic variants by age at CRC diagnosis



Multigene panel tests did not identify a germline mutation in approximately 80% of these individuals with CRC

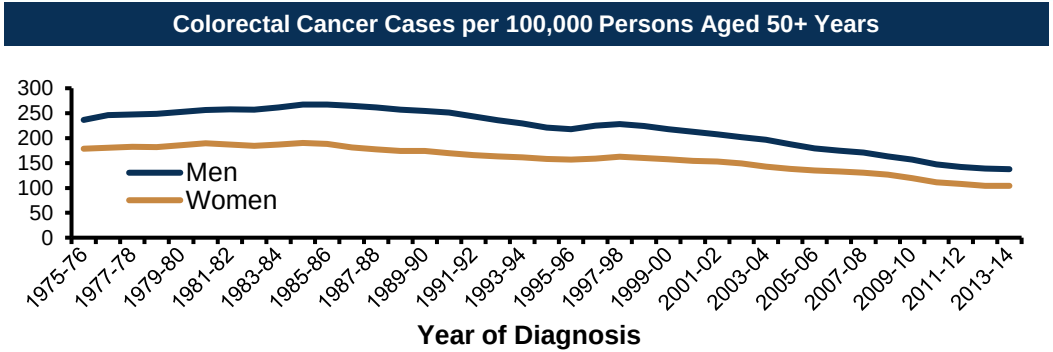
Less than 20% of CRC cases in younger adults (<50) are due to genetic predisposition.

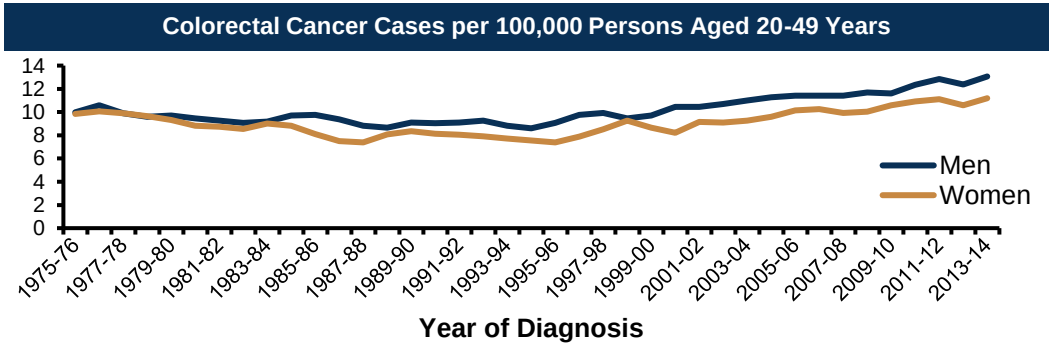
Stoffel EM, Murphy CC. *Gastroenterology*. 2020;158:341–353.

CRC Is a Growing Burden in Adults Younger Than 50 Years

Trends in Colorectal Cancer Incidence Rates by Age (Ages 20-49 and Ages 50+) and Sex, 1975 to 2014

- CRC incidence has gradually declined over the past 20 years in the population ≥50 years due to influence of screening and changes in exposure to risk factors
- There has been a 51% increase in CRC incidence among adults <50 years since 1994
- CRC incidence among adults <50 years increased 2.2% annually from 2012 to 2016





1. Wolf AMD et al. *Ca Cancer J Clin*. 2018;68(4):250-281; 2. American Cancer Society. Cancer Facts & Figures. 2020; Atlanta: American Cancer Society. 2020.

Summary

- CRC is the second most common cause of cancer death in men and women, yet it is the MOST AVOIDABLE
- Both “at risk” and “average risk” patients benefit from a regular CRC screening program
- CRC incidence is increasing in younger populations, and is expected to continue to increase.
- ACS guidelines have a qualified recommendation to begin CRC screening starting at age 45. Other guidelines are expected to follow the same age recommendation