What is your GUT telling you?

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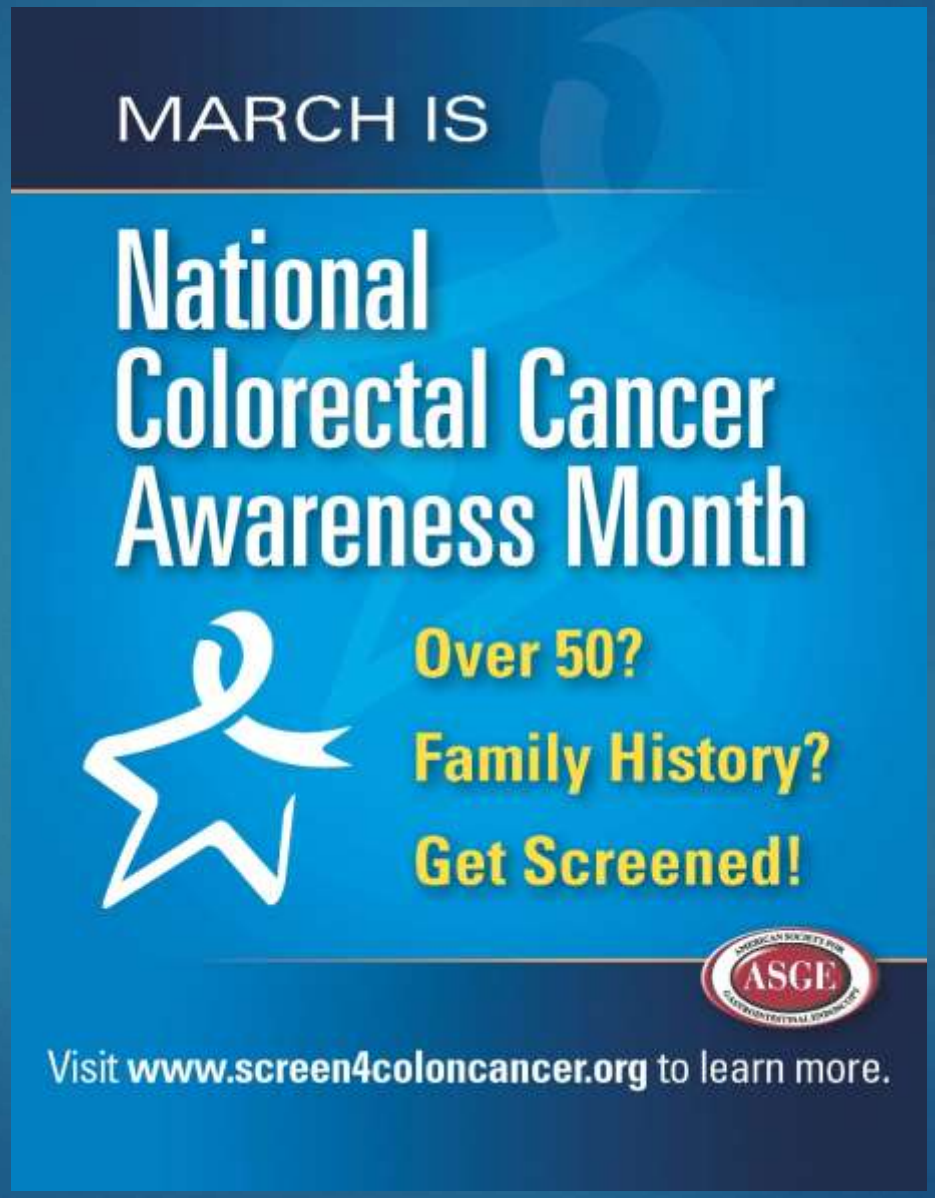
About me

- No financial disclosures.
- Practicing gastroenterology 24 years
- GI Fellowship: Yale University/YNHH/Norwalk Hospital
- Advanced Endoscopic Procedure Training: Beth Israel Deaconess Medical Center.
- Colorectal Cancer Screening, advanced biliary and pancreatic endoscopy.
- Consultative GI practice.

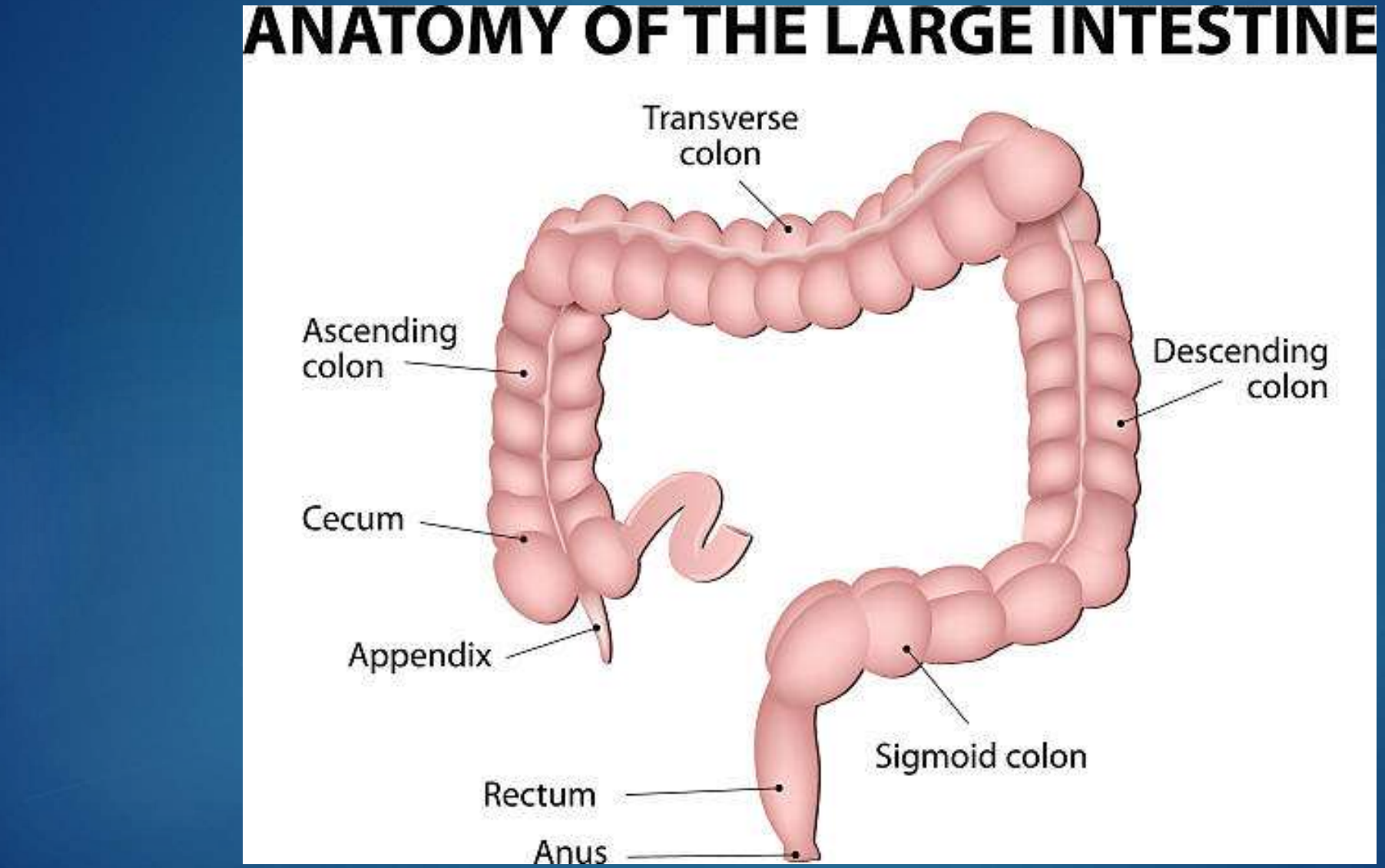
Emerson Health Gastroenterology


MARCH IS
National Colorectal Cancer Awareness Month
Over 50?
Family History?
Get Screened!
ASGE
Visit www.screen4coloncancer.org to learn more.

COLORECTAL CANCER IS

PREVENTABLE.
TREATABLE.
BEATABLE.

Colorectal cancer is the third most common cancer diagnosed in both men and women in the United States. But you can prevent it with a colonoscopy.


ANATOMY OF THE LARGE INTESTINE
Transverse colon
Ascending colon
Descending colon
Cecum
Appendix
Sigmoid colon
Rectum
Anus

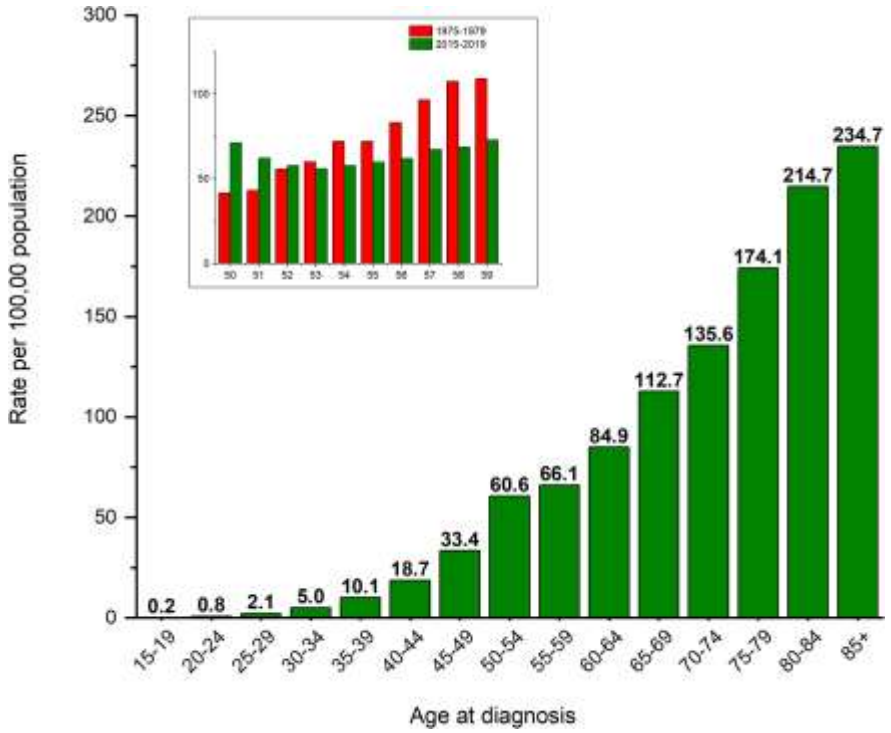
Colon cancer

- How common is it, what is the scope of the issue?
- Rationale: Why is colon cancer appropriate for screening?
- Methods: What are the options available?

Colorectal Cancer

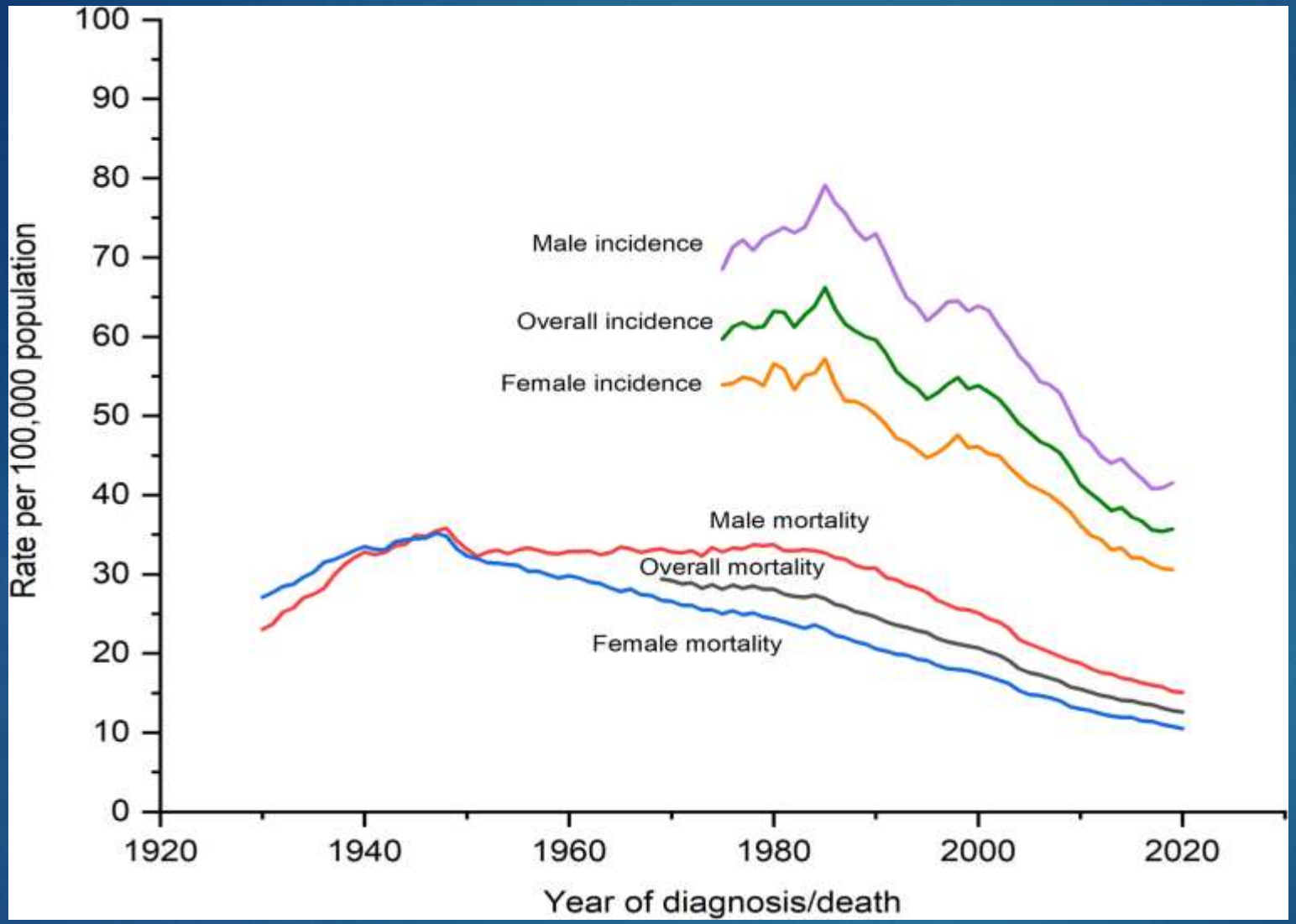
- Lifetime incidence 1:23 men, 1:25 women.
- 153,020 diagnosed, 52,550 die (USA)
- 19,550 diagnosed and 3750 die <50.

Colorectal cancer statistics, 2023



CA A Cancer J Clinicians, Volume: 73, Issue: 3, Pages: 233-254, First published: 01 March 2023, DOI: (10.3322/caac.21772)

Colorectal cancer statistics, 2023



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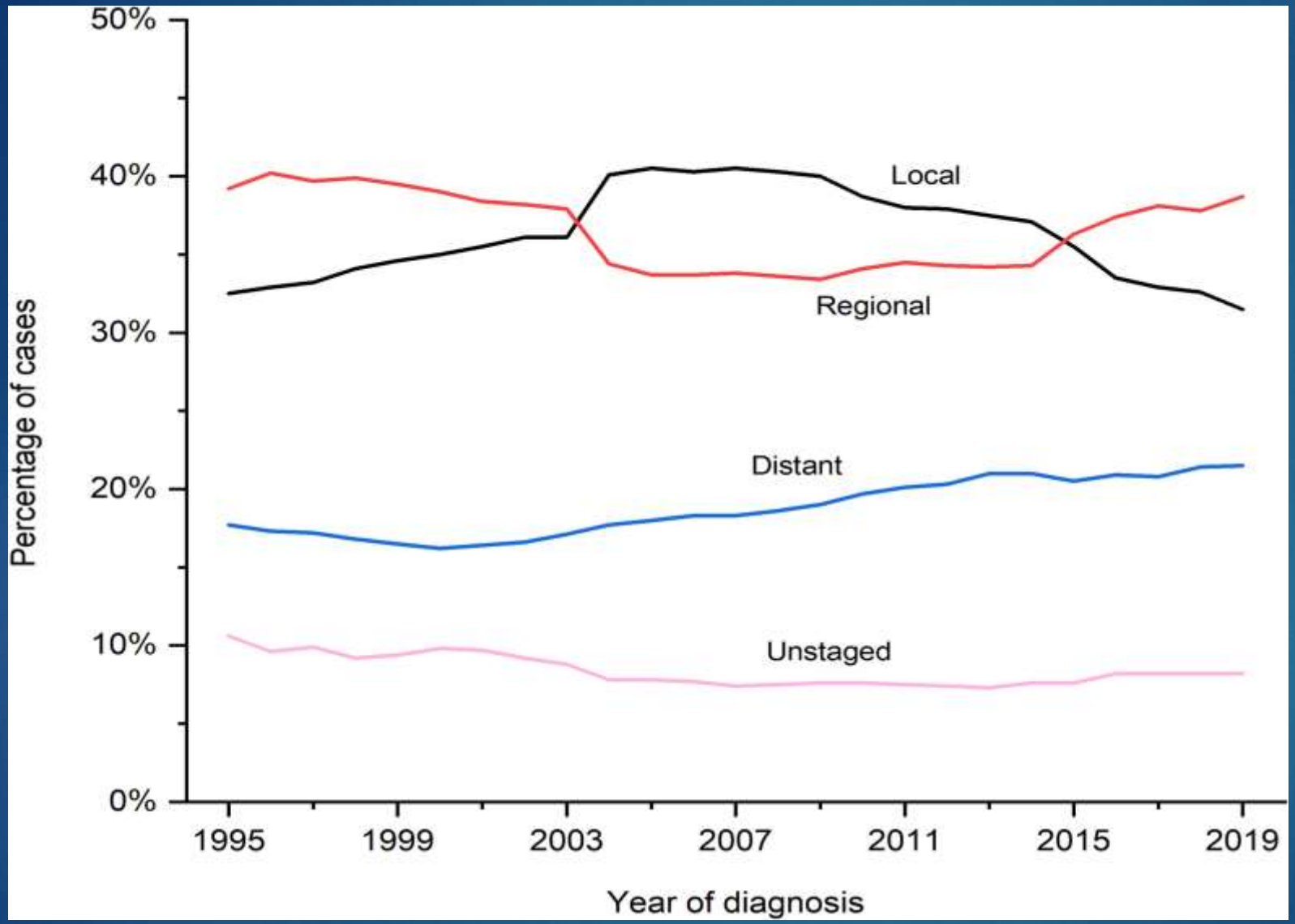
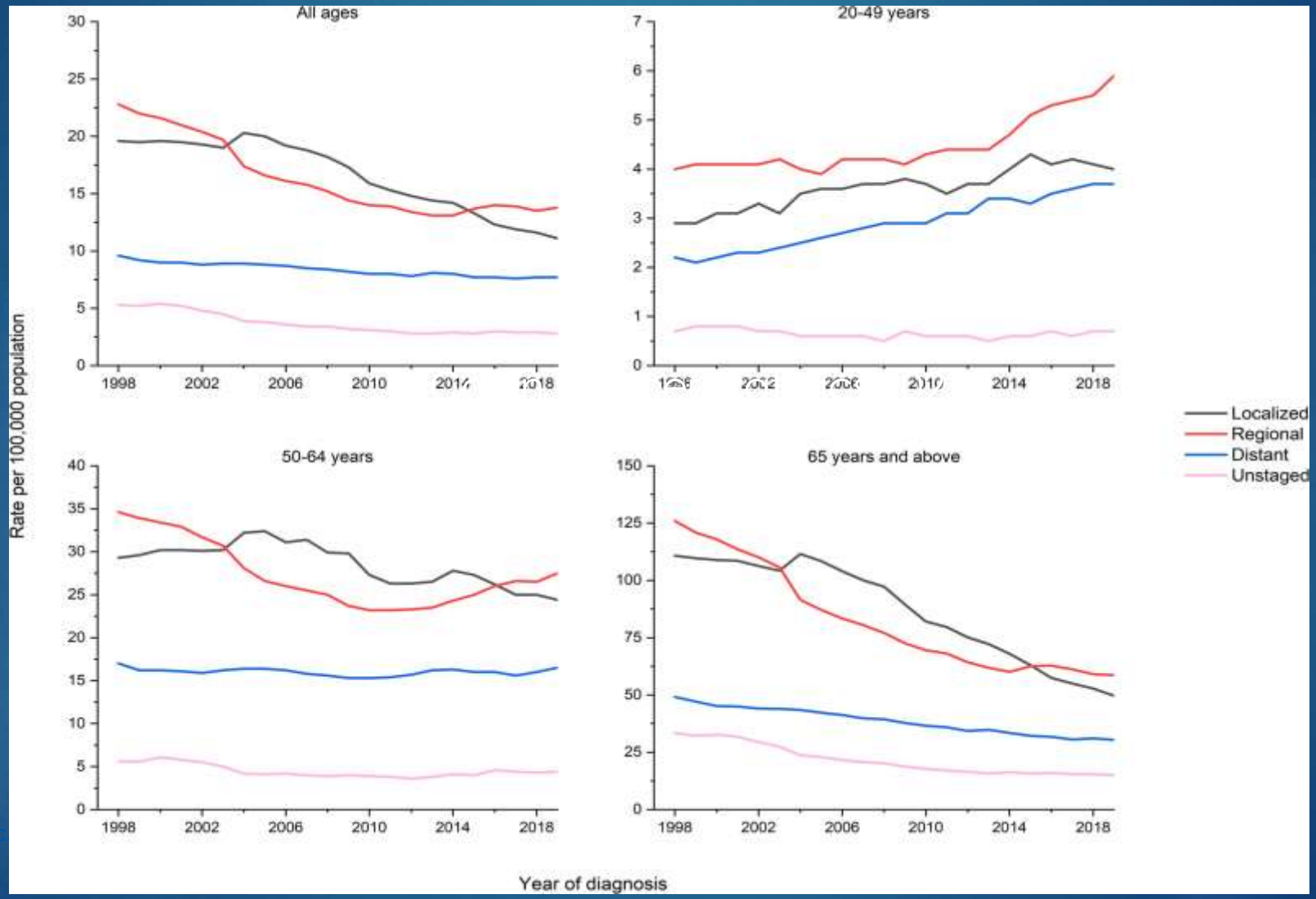
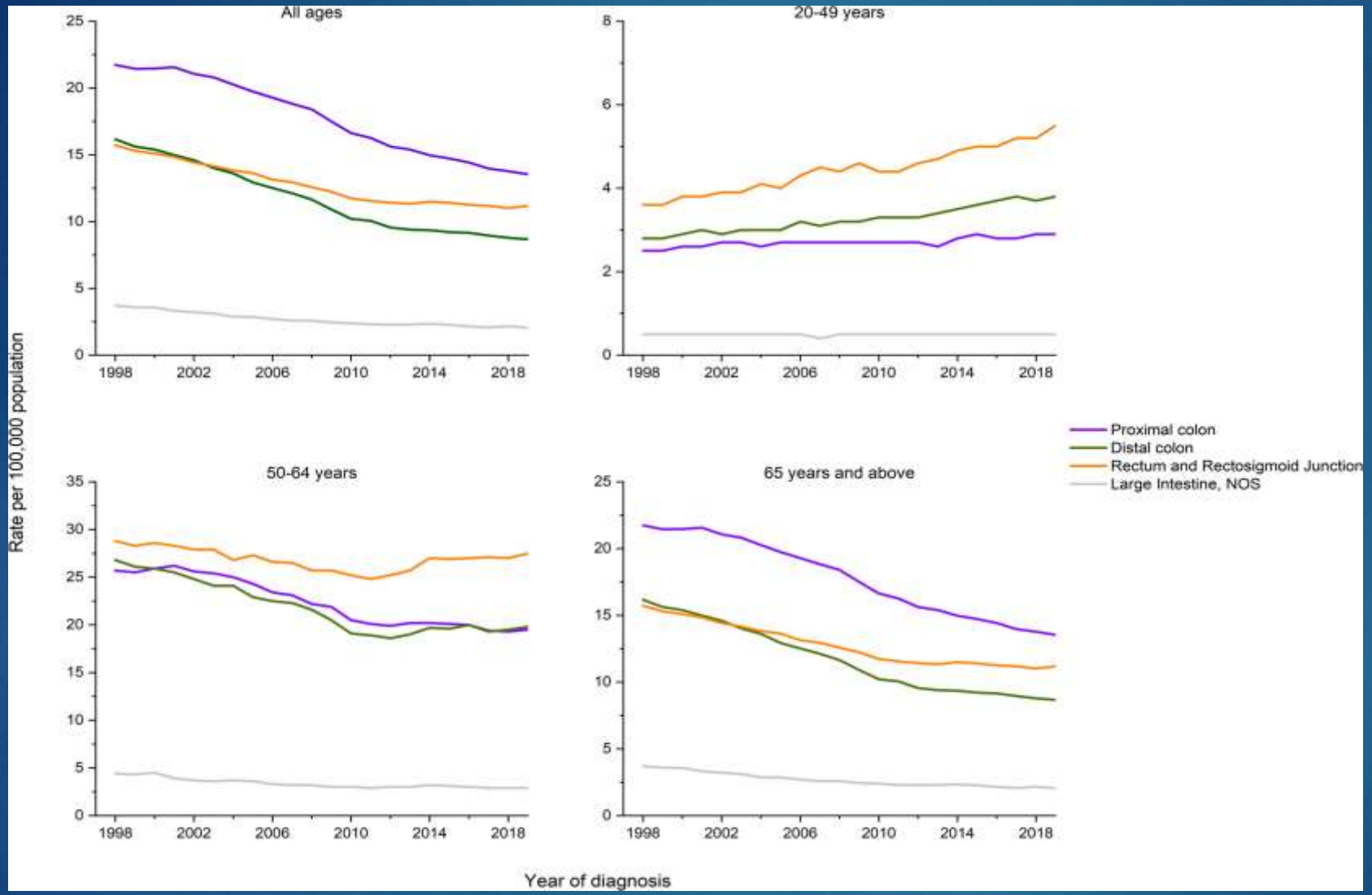
Colon Cancer Statistics 2023

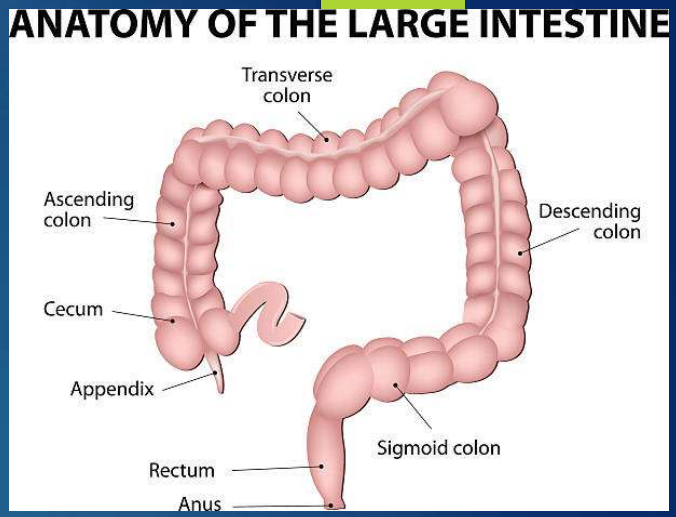


Colon Cancer Statistics 2023



Colon Cancer Statistics 2023





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Why is colon cancer increasing in young adults?

Colon cancer risk factors. Average Risk vs High Risk

- A personal history of colorectal cancer or certain types of polyps
- A family history of colorectal cancer or advanced polyps
- A personal history of inflammatory bowel disease (ulcerative colitis or Crohn's disease)
- Confirmed hereditary colorectal cancer syndrome, such as familial adenomatous polyposis (FAP) or Lynch syndrome (hereditary non-polyposis colon cancer or HNPCC)*
- A personal history of radiation exposure to the abdomen (belly) or pelvic area to treat a prior cancer

Colon Cancer Risk Factors

- Uncontrollable
  - Family history/genetics 1.79
  - IBD 2.93
  - Age
  - Race

- Controllable
  - BMI 1.10
  - Smoking 1.06
  - Physical activity 0.88
  - Red meat consumption 1.13 (5 servings/week)
  - Vegetable consumption 0.86 (5 servings/day)

Cancer Causes Control. 2013 Jun; 24(6): 1207–1222.

Characteristics of an Effective Screening Test

- Cost: to apply to a population the cost must be reasonable. $/QALY
- Ease of use: The test should be easy to administer.
- Safe: Associated with minimal discomfort and mortality.
- Accurate: Provide valid results (high sensitivity and specificity)
- Alter the natural history of the disease.

Detection vs Prevention

- Tests for early detection of CRC
  - FIT annually
  - *Multitargeted stool DNA test aka* Cologuard every three years.
  - Virtual Colonoscopy every 5 years.
  - Positive results require a colonoscopy for follow up.
- Tests for early detection AND prevention of CRC.
  - Colonoscopy if normal every 10 years.

Current Colorectal Cancer Screening Guidelines

- Average risk screening starts at 45* and continues to 75*.
- Ages 76-85* individualized.

- High risk screening starts at 10 years earlier than youngest first degree relative at age of diagnosis.

Colorectal Cancer Screening by state.

Top 10

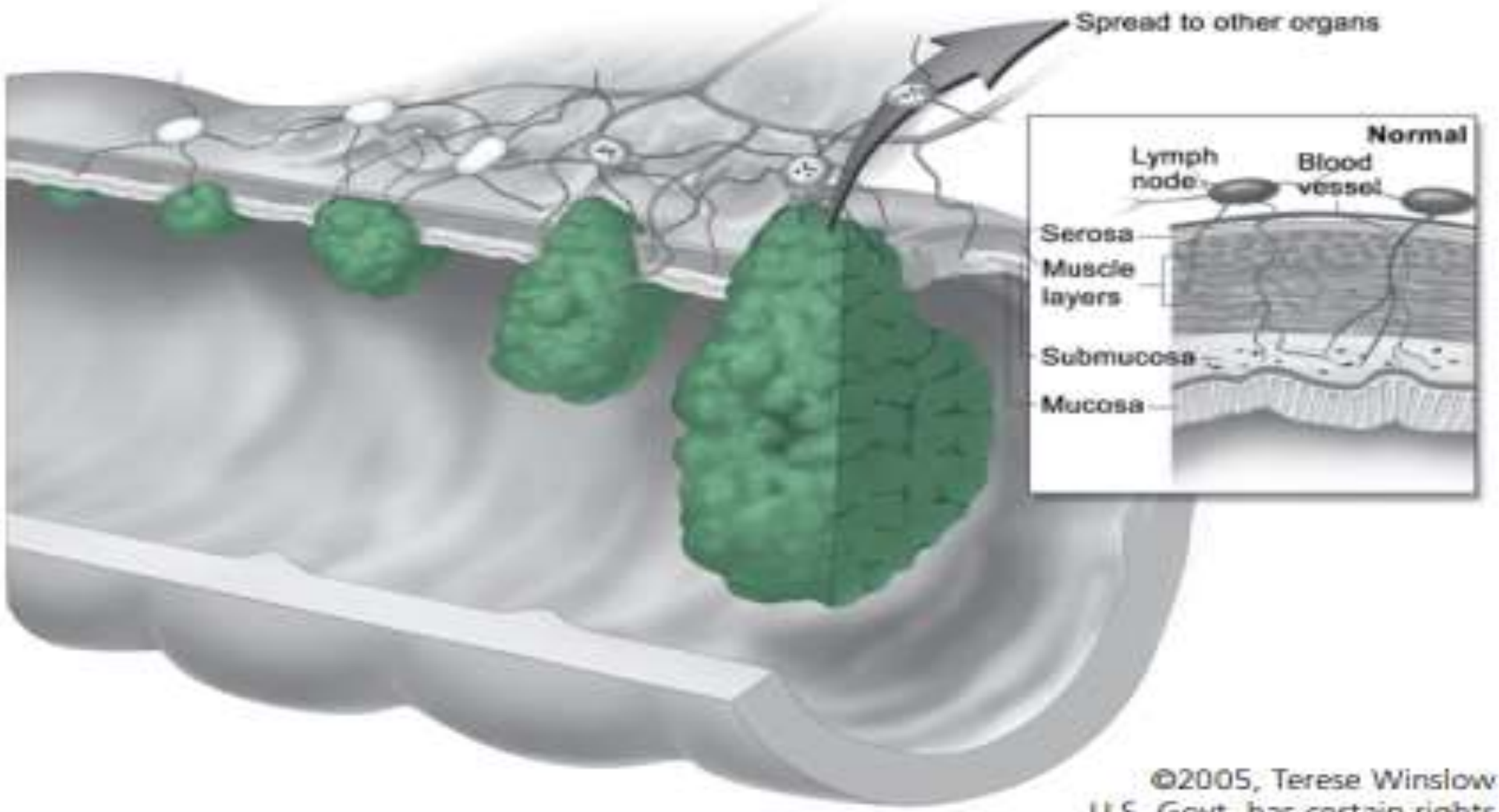
- 1. Maine: 68.9%
- 2. Rhode Island: 66.2%
- 3. Connecticut: 65.6%
- 4. **Massachusetts: 65.4%**
- 5. Wisconsin: 65%
- 6. Delaware: 64.7%
- 7. West Virginia: 64.4%
- 8. Iowa: 64.1%
- 8. Virginia: 64.1%
- 10. Kentucky: 64%

Bottom 10

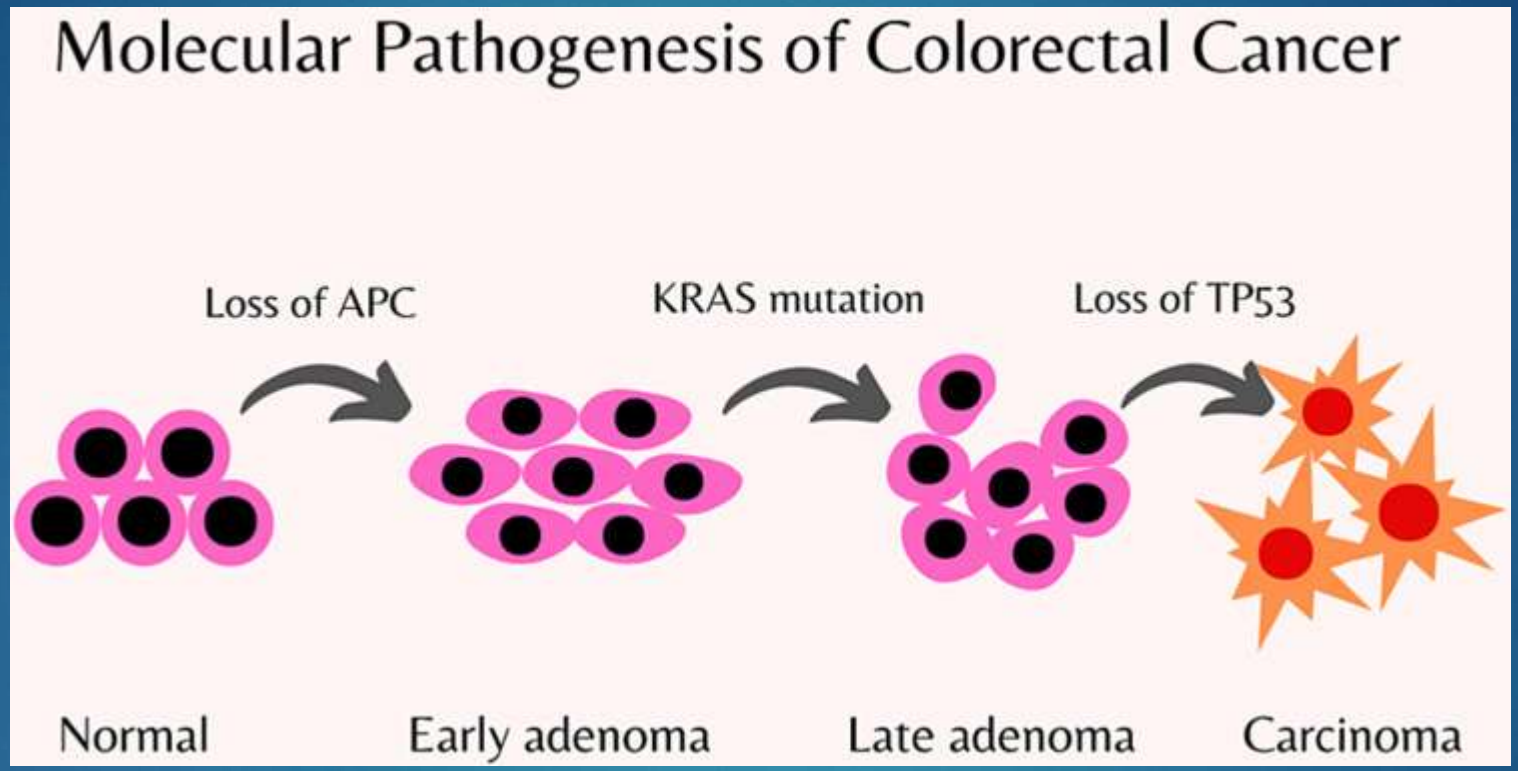
- 41. Arkansas: 56.4%
- 42. Alaska: 56.2%
- 43. New Jersey: 55.9%
- 44. Arizona: 55.8%
- 44. Oklahoma: 55.8%
- 46. Wyoming: 55.4%
- 47. Nevada: 55.3%
- 47. New Mexico: 55.3%
- 49. Texas: 53.8%
- 50. California: 52.4%

CDC Behavioral Risk Factor Surveillance System 2022

Figure 2. Stages of Colorectal Cancer Growth



Multi hit theory of carcinogenesis.



The polyp to cancer sequence can take 5-15 years

Comparison of most commonly used CRC screening tests.

Test	Advanatages	Disadvantages
FIT	Non invasive,High sensitivity (74) and specificity (95)for cancer Inexpensive $20, no prep	Frequency (annually) Low sensitivity for advanced (25%) adenomas and SSL (5%)
Cologaurd (FIT and fecal DNA)	Non Invasive, High sensitivity for colon cancer (92%) and large sessile lesion (40%). Every three years, no prep	Low specificity (87%) Cost ($600)
Colonoscopy	Gold standard for sensitivity and specificity. Can Prevent colon cancer.	Invasive, bowel prep required, operator dependent. Cost.

Comparison (continued)

Test	Advantages	Disadvantages
Virtual colonoscopy	High sensitivity 92% for lesions > 1 cm, frequency every 5 years.	Prep required, Radiation exposure Lower sensitivity for smaller lesions, flat lesions, SSA
Flexible sigmoidoscopy	Every 5 years, no sedation required, less expensive than colonoscopy.	No sedation, misses all lesions other than left sided lesions.

Colonoscopy vs FIT-fecal DNA vs FIT

Table 1. Sensitivity and Specificity of the Multitarget Stool DNA Test and the Fecal Immunochemical Test (FIT) for the Most Advanced Findings on Colonoscopy.

Most Advanced Finding	Colonoscopy (N=9989)	Multitarget DNA Test (N=9989)		FIT (N=9989)	
		Positive Results	Sensitivity (95% CI)	Positive Results	Sensitivity (95% CI)
	no.	*no.*	%	*no.*	%
Colorectal cancer					
Any	65	60	92.3 (83.0–97.5)	48	73.8 (61.5–84.0)
Stage I to III*	60	56	93.3 (83.8–98.2)	44	73.3 (60.3–83.9)
Colorectal cancer and high-grade dysplasia	104	87	83.7 (75.1–90.2)	66	63.5 (53.5–72.7)
Advanced precancerous lesions†	757	321	42.4 (38.9–46.0)	180	23.8 (20.8–27.0)
Sessile serrated polyps ≥ 1cm			42.4		5.1
			Specificity (95% CI)		Specificity (95% CI)
All nonadvanced adenomas, non-neoplastic findings, and negative results on colonoscopy	9167	1231	86.6 (85.9–87.2)	472	94.9 (94.4–95.3)
Negative results on colonoscopy	4457	455	89.8 (88.9–90.7)	162	96.4 (95.8–96.9)

Imperiale TF, New Engl J Med

Cologuard

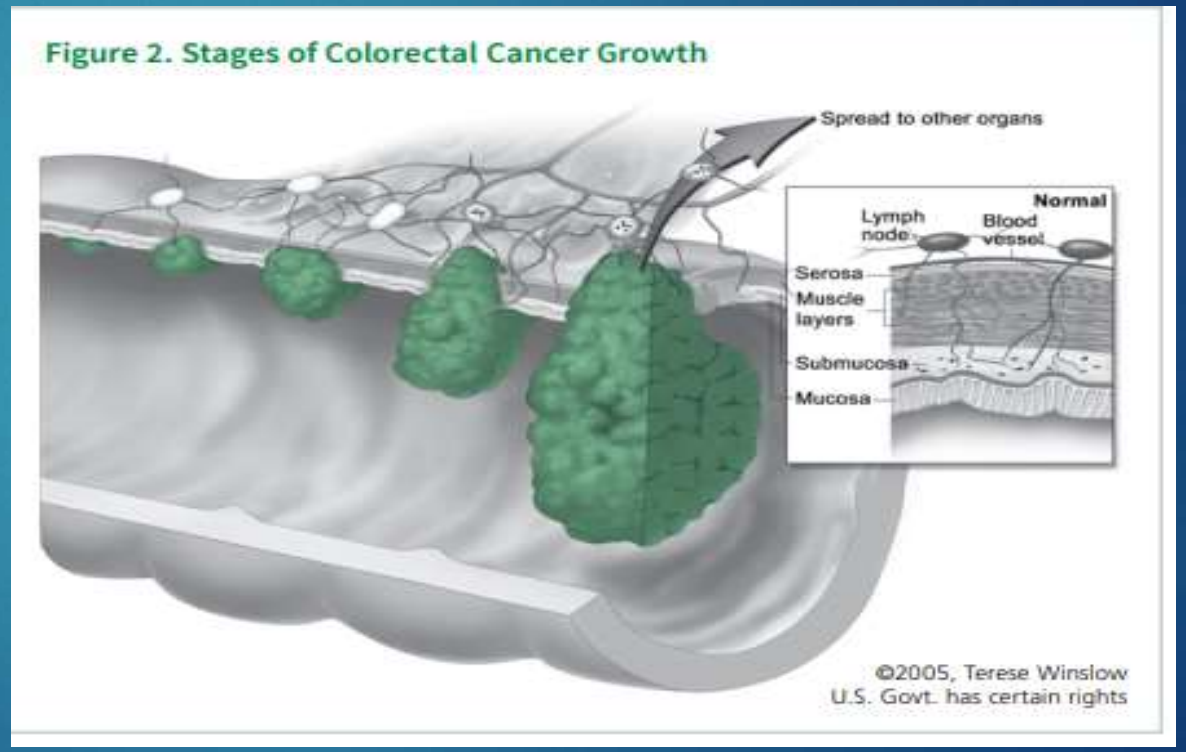
- Tests for blood in the stool and DNA associated with colon cancer.
- No prep required.
- Detects large polyps 42% of time. 95% detected by colonoscopy.
- Detects cancer up to 92% of the time.
- 13% False positive rate.
- ONLY FOR AVERAGE RISK PATIENTS.

Symptoms of colon cancer

- NONE (*in early stages)*
- Rectal bleeding.
- Change in bowel habits.
- Weight loss (unexplained).
- Abdominal pain and bloating.
- Symptoms related to anemia (breathlessness, fatigue, etc).

Survival vs CRC stage (colon/rectal) (AJCC).

- Stage O Cis.
- Stage I 92/88
- Stage II 65-87/50-81
- Stage III 53-90/58-83
- Stage IV 12/13



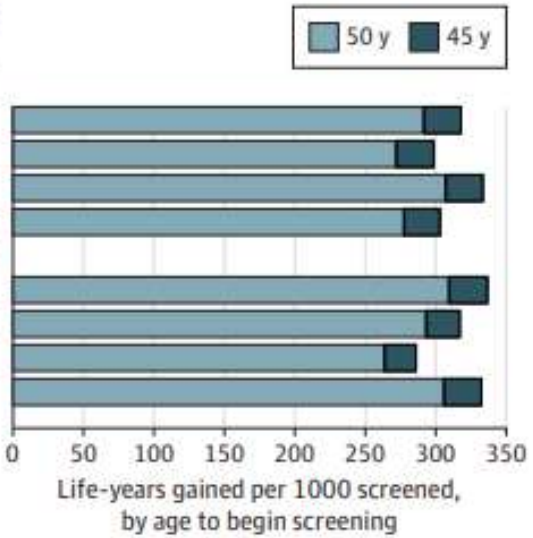
Estimated Life years saved by various screening methods.

USPSTF 2022

Figure 2. Benefits of Colorectal Cancer Screening

A Benefit: Estimated life-years gained per 1000 individuals screened[a]

Screening modality and frequency	Mean life-years gained if start screening[b]		Additional life years gained if start screening at age 45 y
	At age 50 y	At age 45 y	
Stool tests			
FIT every year	292	318	26
HSgFOBT every year[c,d]	272	298	26
sDNA-FIT every year	307	333	26
sDNA-FIT every 3 y[d]	278	303	25
Direct visualization tests			
COL every 10 y	310	337	27
CT colonography every 5 y	293	317	24
Flexible SIG every 5 y	264	286	22
Flexible SIG every 10 y plus FIT every year	306	332	26



Lifestyle Modifications to Decrease CRC Risk

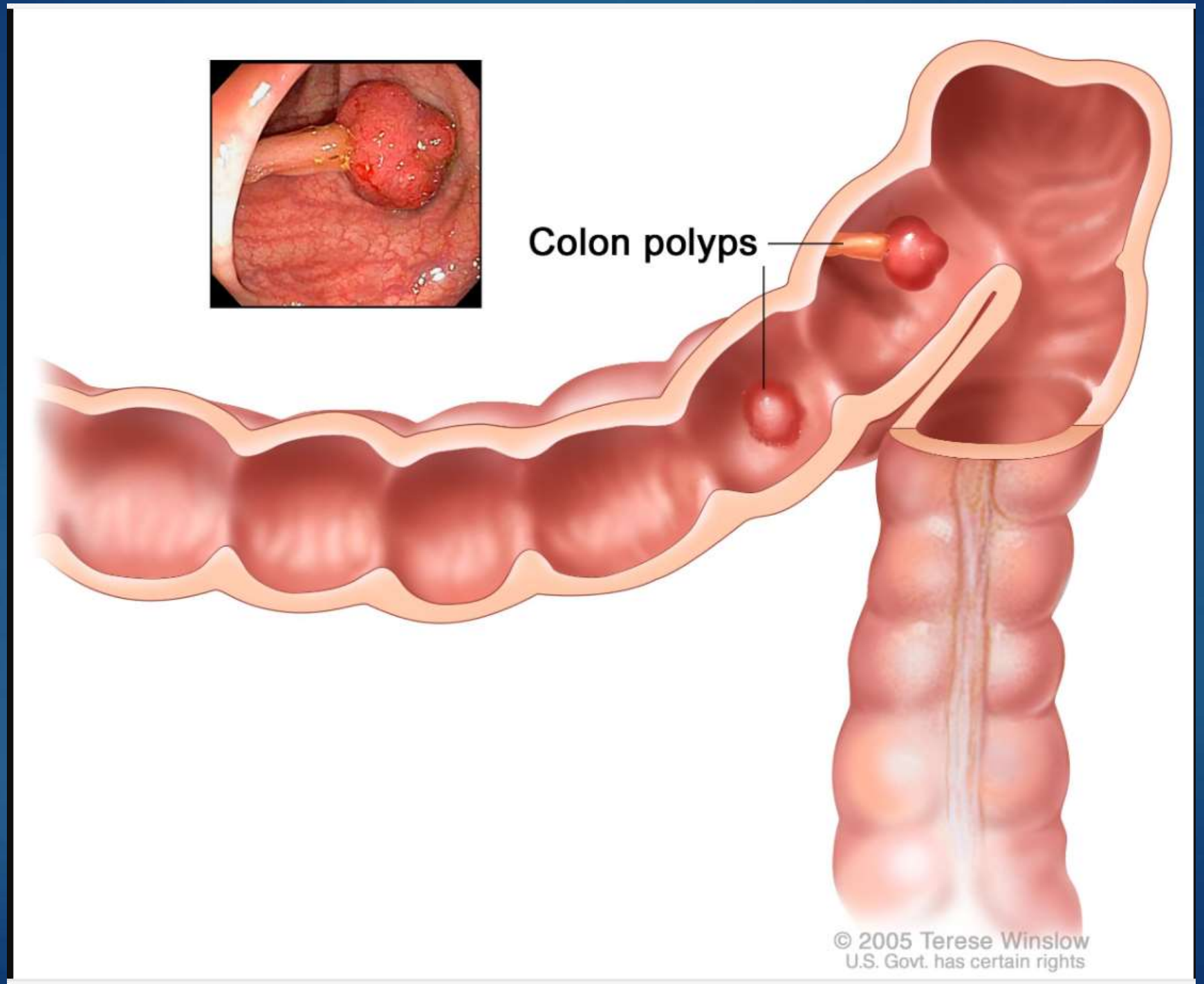
- Varied diet of fruits, vegetables and whole grains. Avoid processed and salt cured foods.
- Alcohol in moderation, if at all.
- Stop Smoking
- Exercise most days of the week.
- Maintain a healthy weight.
- Low dose aspirin
- 2-1/2 cups of coffee per day

Benefits of Using Proven Strategies

More colorectal cancer screening would:

- **DECREASE** the number of people diagnosed with colorectal cancer. Increasing screening prevalence to 80% could reduce the number of people diagnosed with colorectal cancer by 22% by 2030.[6]
- **REDUCE** deaths. Increasing screening prevalence to 80% could reduce deaths from colorectal cancer by 33% by 2030.[5]
- **PREVENT** or detect cancer sooner when it is easier to treat. Almost 88% of adults diagnosed with colorectal cancer at an early stage live for 5 years or more, compared to only 16% of those diagnosed with late-stage cancer.[1]
- **REDUCE** health care spending. Increasing screening prevalence to 70% could reduce Medicare spending by $14 billion* in 2050.[7]

Colonoscopy


Colon polyps
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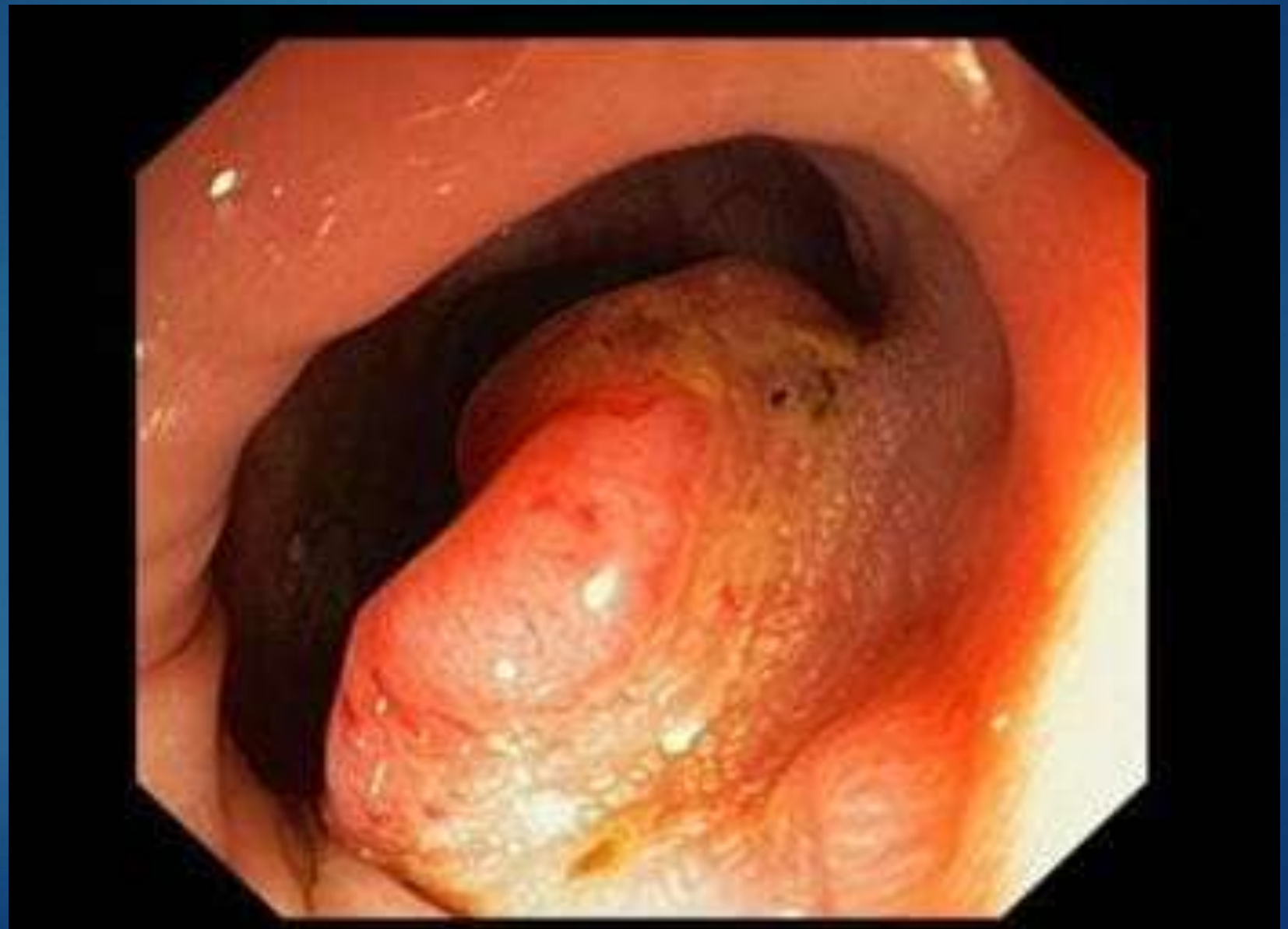
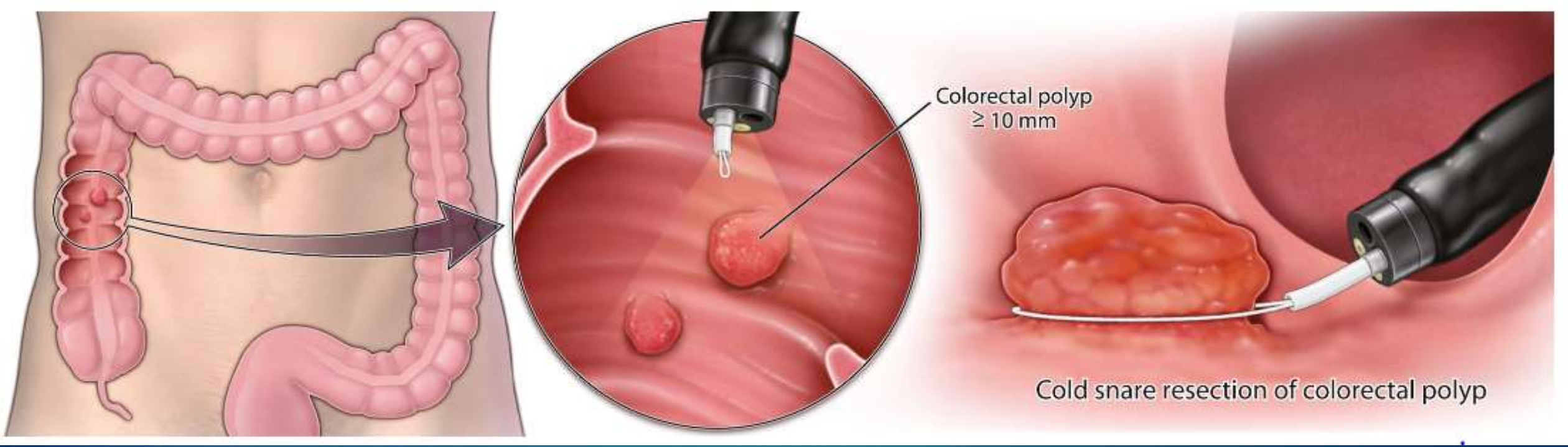
Colon Cancer



Cold snare polypectomy

Lift and cut polypectomy.

Snare electrocautery



Take home messages for colonoscopy and colorectal cancer screening.

- Colon cancer is the second most common cause of cancer death and third most common cancer overall.
- Colon cancer is a nearly ideal model for screening.
- Colon cancer is a preventable disease, by colon cancer screening.
- Early stage colon cancer and polyps rarely cause symptoms.
- Colonoscopy is safe and accurate.
- Colonoscopy prep has improved over the years.

The Best Colon Cancer Screening Test

- Whatever is acceptable and gets done.
- Any test is better than no test.
  - All currently available tests are effective to varying degrees

Q&A

- Thank you for your attention.

ENS-CNS GUT-BRAIN Connection

- CNS function ↔ gut function
  - Pre-prandial phase of digestion
  - Emotion induced GI reactions, stress related digestive issues (IBS).
- 100 million neurons in two layers of the GI tract running from esophagus to rectum
- All neurotransmitters found in the brain have also been found in the gut. Serotonin.
- Psychoactive medications are useful in GI conditions
- Interplay between nerve signals, gut hormones and the microbiome.

Bidirectional nature of BGA is likely mediated by microbiome.

From gut microbiota to brain:
Production, expression and turnover of neurotrasmitters (i.e. serotonin, GABA) and neurotrophic factor (BDNF)
Protection of intestinal barrier and tight junction integrity
Modulation of enteric sensory afferents
Bacterial metabolites
Mucosal immune regulation
From brain to gut microbiota:
Alteration in mucus and biofilm production
Alteration in motility
Alteration of intestinal permeability
Alteration in immune function

GERD

- GER is normal.
- Refluxate is gastric acid, bile, pancreatic secretion, food

- Physiology becomes pathology
  - Oropharynx (decreased saliva)
  - Esophagus (altered motility)
  - LES (decreased tone) HH.
  - Stomach emptying issues, motility issues.

GERD: symptoms

- Typical 70%
  - Heartburn
  - Regurgitation
- Atypical symptoms 30%
  - Chest pain (#1 cause of NCCP)
  - Water brash/hypersalivation
  - Globus
  - Dysphagia
  - Odynophagia
  - Nausea
  - Asthma
  - Sinusitis/laryngitis/recurrent otitis
  - Dental erosion
  - Chronic cough
  - Chronic lung disease (aspiration)

GERD: Epidemiology

- 25-40% of healthy adult Americans experience GERD symptoms at least monthly. 7-10% daily symptoms.
- GERD: M=F
  - Reflux esophagitis 2-3:1
  - Barrett's esophagus 10:1
- GERD prevalence: unaffected by age
  - EE and BE increase after age 50

Pathophysiology

- TLESR
  - Normal
  - Disease state increase frequency and or duration.
- Causes of TLESR
  - Belching
  - Food: coffee, alcohol, chocolate, fatty meals
  - Medications: nitrates, CCB, anticholinergics.
  - Hormones: progesterone.
  - Sleep/sedation
- Hypotensive LES

Pathophysiology

- Gastric
  - Delayed emptying (DM, idiopathic, post viral)
  - Invasive/infiltrative conditions.
  - Medications: opiates, antipsychotics.
- Increased acid secretion
  - Gastritis
  - ZES

Pathophysiology

- Hiatal hernia multiple effects.
  - LES migration proximally

    Impairs LES control
- Residual gastric contents in hernia
  - Re-reflux
- Widening of DH
  - Loss of LES augmentation