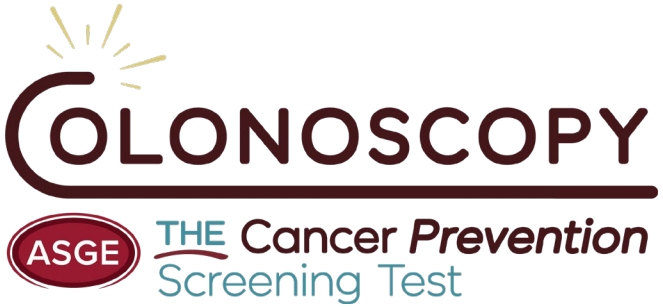
Choosing Among CRC Screening Tests



Outline

- Primer on Colorectal Cancer Screening
  - CRC: the numbers
  - CRC: the science
  - Screening and Prevention Approaches
    - Guideline based approach
    - Pros and cons
- Take home points
- Questions and discussion

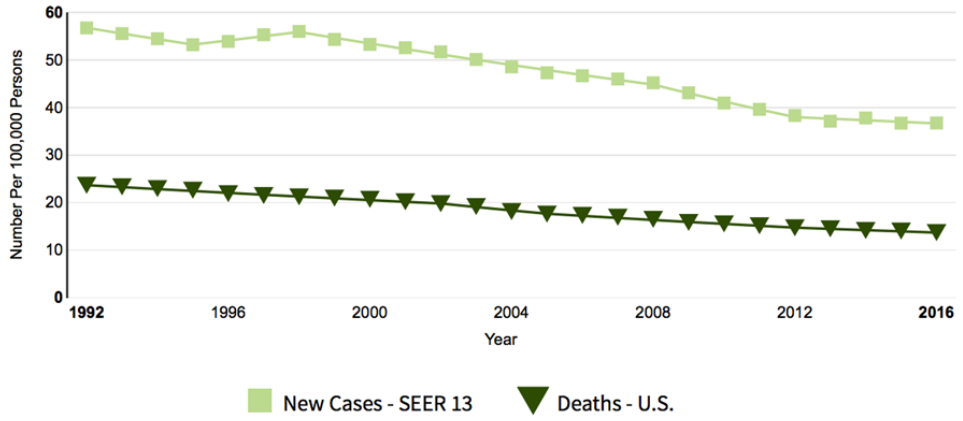
CRC: The Numbers

At a Glance

Estimated New Cases in 2019	145,600
% of All New Cancer Cases	8.3%

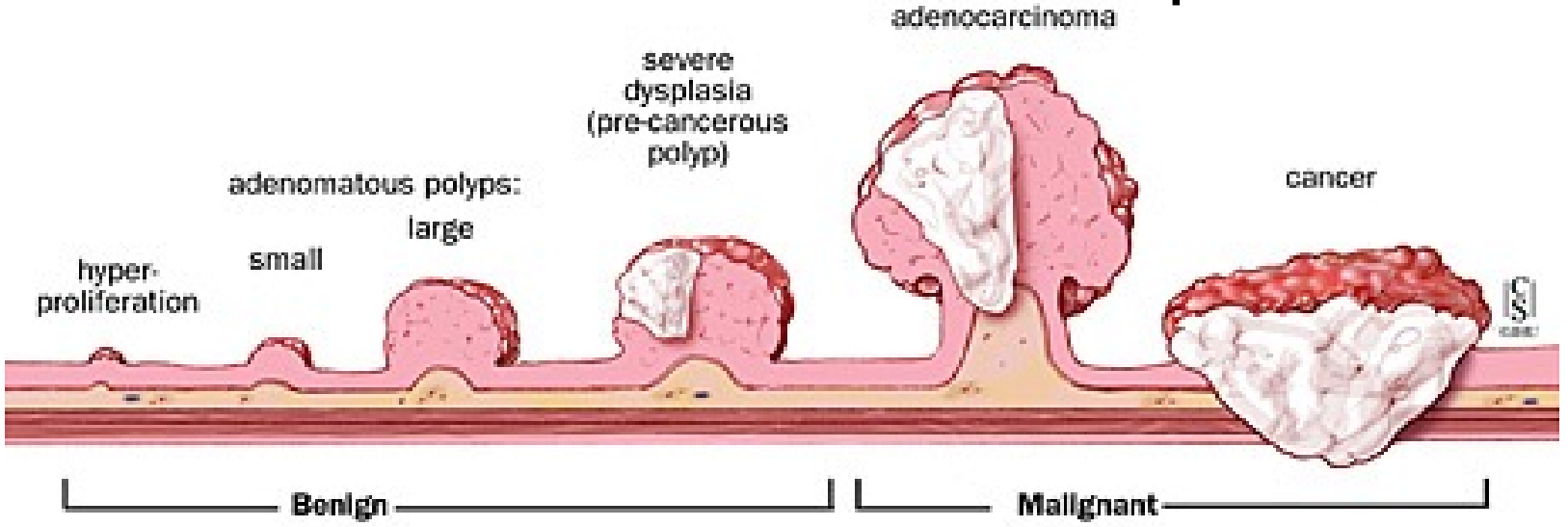
Estimated Deaths in 2019	51,020
% of All Cancer Deaths	8.4%

Percent Surviving 5 Years
64.4%
2009-2015



Why is CRC Easier to Screen and Prevent?

Adenoma to Carcinoma Sequence



Fewer than 10% of all adenomas become cancerous. However, more than 95% of colorectal cancers develop from adenomas

Johns Hopkins Online

Figure 1. Hyperplastic polyp.

Figure 2. Tubular adenoma (pedunculated).

Figure 3. Tubular adenoma (sessile).

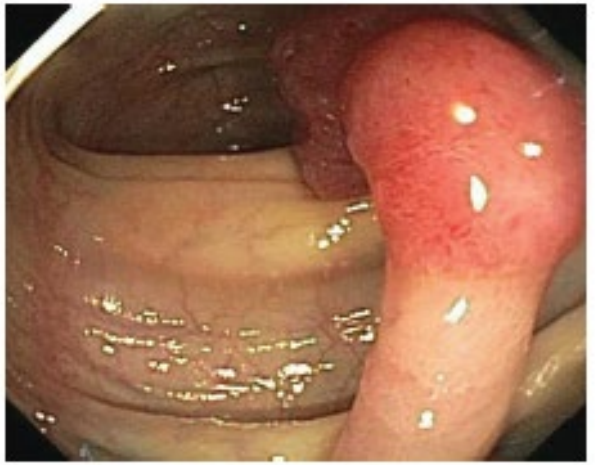
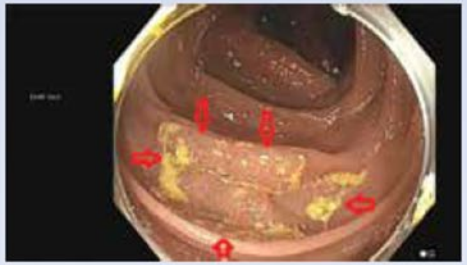


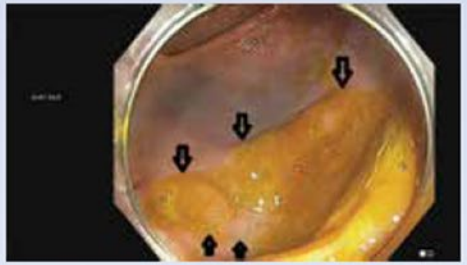
Figure 5. Tubular adenoma with high-grade dysplasia.

Villous Adenoma

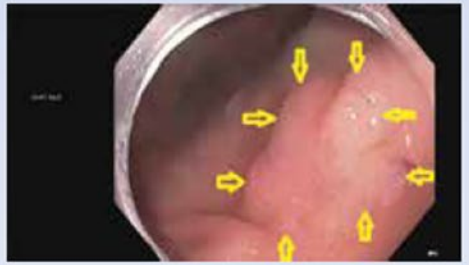
FIGURE 3. Advanced serrated lesions



A Arrows delineate the border of a sessile serrated polyp with adherent mucus over the lesion and debris around the perimeter



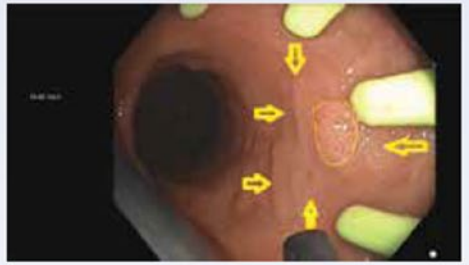
B Right colon sessile serrated polyp with thick layer of adherent mucus – arrows delineate the borders



C Arrows delineate edges of a sessile serrated polyp without mucus cap

D Sessile serrated polyp without mucus cap, flatter than the lesion seen in image C

E Extremely flat, subtle sessile serrated polyp without cytological dysplasia

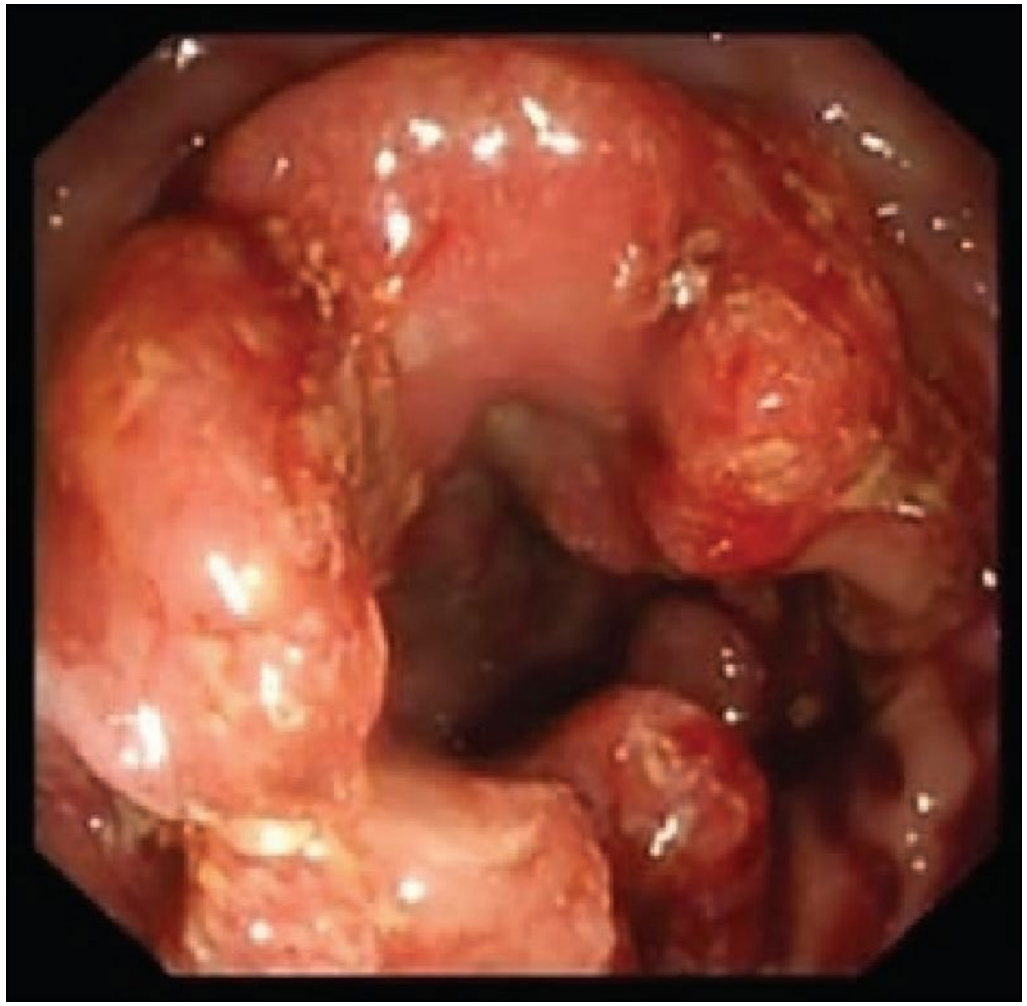


F Sessile serrated polyp with cytological dysplasia. The dysplastic portion is within the yellow line. Arrows mark the perimeter. Black object at bottom is tip of an injection catheter.

Rex, D. PRACTICAL ADVICE FOR COLORECTAL CANCER SCREENING. GI & Hepatology News 2019

Colon Cancer

Colon Cancer



CRC: The Numbers

- Rates of new colon cancer
- Down 30%!!! between 2000-2010
  - 50-80 year olds
- Parallels widespread use of colonoscopy
- Success!!

CRC Screening Success!
Not So Fast

- > 20,000,000 eligible Americans are NOT screened
  - Nearly 50% of patients who should be screened
  - Access, cost, reluctance?
- “My doctor didn’t mention it!!”
  - #2 reason given by patients surveyed
  - <10% of patients eligible were told about screening
  - More than half of Medicare patients surveyed had almost 5 visits that year

1. Seeff LC et al., 2004; Shapiro JA et al., 2008; Shapiro JA et al., 2012
2. 2010 NHIS; Klabunde CN et al., submitted
3. Schenck AP et al., *Prev Chron Dis*, 2011

Screening Comparisons

- We can prevent getting colon cancer
  - 60-90% !!!
    - With colonoscopy
    - That's preventing it, not detecting it early
- Mammogram (50-69 year olds)
  - Death is 40% preventable
  - Mammograms miss 1 in 5 cancers
  - 50% of women will have a false positive over 10 years
- PSA for prostate screening
  - Decreases dying from prostate cancer by 21%

1. Am J Gastroenterol. 2016 Jan 12.
2. N Engl J Med 2015; 372:2353-2358
3. Cochrane Database Syst Rev. 2013

CRC: Younger Patients

- Incidence of colon cancer in patients <50 is rising!
- Between 2008-2011
  - **1 in 7** colon cancers
  - Presented with more advanced disease

1. Cancer. 2016 Mar 15;122(6):929-34.
2. Prev Chronic Dis. 2015 May 21;12:E80

CRC: Younger Patients

- Predictions by 2030
  - 1 in 4 >1 in 10 of all colon cancers
  - of all rectal cancers
- 20 to 34 years olds
  - Colon cancer
  - Rectal cancer
- 34 to 49 year olds
  - Colon
  - Rectum

Increase
90%
124%
28%
46%

JAMA Surg. 2015 Jan;150(1):17-22.

CRC: Younger Patients

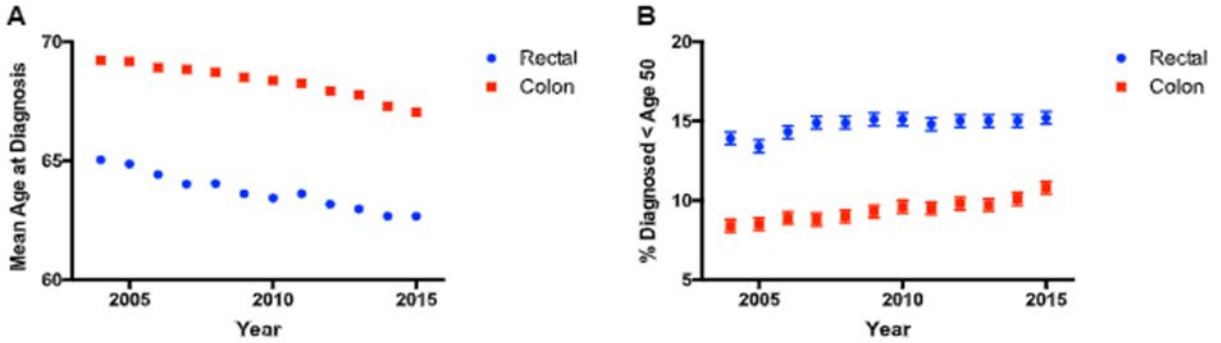


Figure 1. (A) The mean age at diagnosis of rectal and colon cancer cases in the National Cancer Data Base declined from 2004 to 2015 at a rate of 0.21 years of age per year (95% confidence interval, 0.18-0.24 years of age per year) for rectal cancer and at a rate of 0.19 years of age per year (95% confidence interval, 0.16-0.22 years of age per year) for colon cancer. (B) The proportion of both rectal and colon cancer cases diagnosed before the age of 50 years increased significantly from 2004 to 2015 ($P < .0001$). Error bars indicate the 95% confidence intervals. Note that the error bars are smaller than the points used to display some data.

- Incidence of colon cancer in patients <50 is rising!
- Between 2004-2015, 12% of all CRC occurred in < 50 year olds

John Virostko, Anna Capasso, Thomas E. Yankeelov, Boone Goodgame. *Cancer*, 2019

CRC: Younger Patients

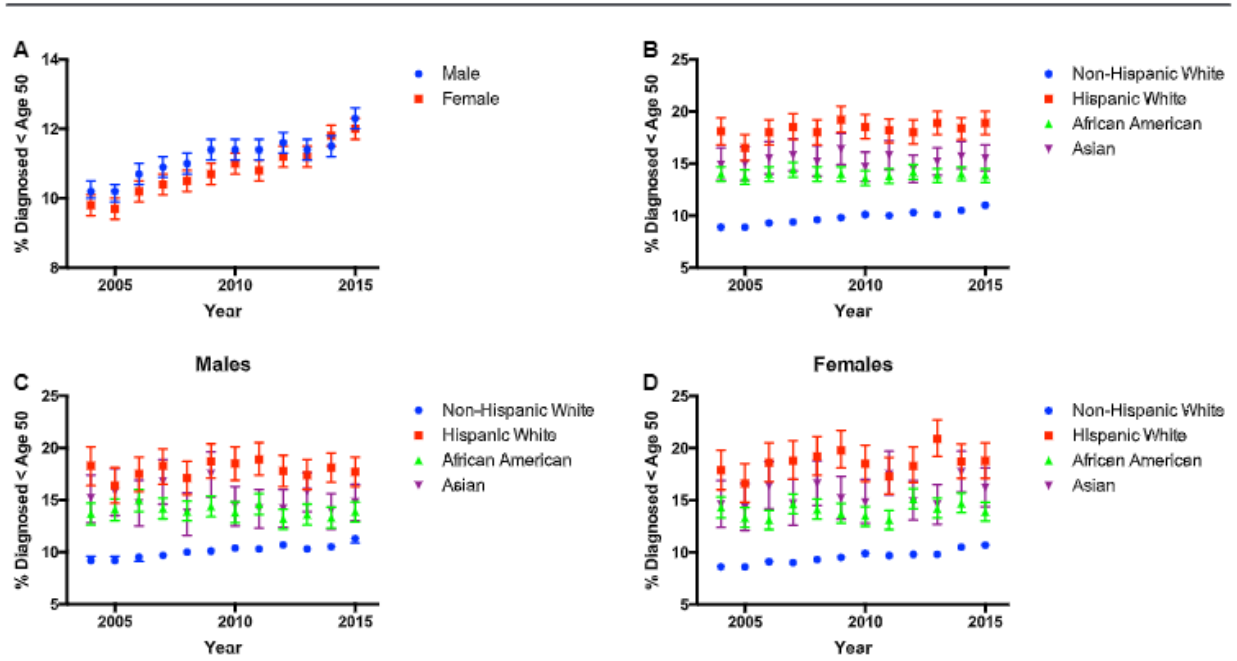


Figure 2. (A) The proportion of cases of colorectal cancer in the National Cancer Data Base diagnosed before the age of 50 years increased from 2004 to 2015 in both men and women (P for both groups <.0001). (B) Across men and women, the proportion of cases of colorectal cancer diagnosed before the age of 50 years increased from 2004 to 2015 in Hispanic whites ($P < .05$) and non-Hispanic whites ($P < .001$). (C) Among men, the proportion of cases of colorectal cancer diagnosed before the age of 50 years increased only in non-Hispanic whites ($P < .0001$). (D) Among women, the proportion of cases of colorectal cancer diagnosed before the age of 50 years increased in Hispanic whites ($P < .05$) and non-Hispanic whites ($P < .001$). Error bars indicate the 95% confidence intervals. Note that the error bars are smaller than the points used to display some data.

John Virostko, Anna Capasso, Thomas E. Yankeelov, Boone Goodgame. *Cancer*, 2019

CRC: Younger Patients

- Reason for increased rates
  - Obesity epidemic
  - Ethnic differences (California database)
    - Higher risk in African Americans
    - Lowest overall rate in Hispanics
      - But greatest acceleration in incidence
- Undiagnosed hereditary colon cancer syndromes
  - 5-8% of patients
  - 92% of patients would not have a family history
- Environmental exposures
- Antibiotic use?

J Adolesc Young Adult Oncol 3:176-184, 2014.
John Virostko, Anna Capasso, Thomas E. Yankeelov, Boone Goodgame. Cancer, 2019

What Can't Be Changed

- Age
- Racial & ethnic background
- Personal history of Colon Cancer/Polyps
- Personal history of Ulcerative Colitis or Crohn's disease of the colon
- Family history of Colon Cancer/Polyps
- Inherited syndromes
  - Familial Adenomatous Polyposis (FAP)
  - Lynch Syndrome (HNPCC)

Source: American Cancer Society

What Can Be Changed

- Diet
  - Limit/avoid red meat & processed meat (deli meats)
  - Increase daily vegetables and fiber
- Increased Physical Activity
- Weight loss through proper diet & exercise
- Control Type II Diabetes
- Quit Smoking
- Limit alcohol use
- Get screened for colon cancer

Source: American Cancer Society

Average Risk Screenimg

- Start at age 45

Systematic review of colorectal cancer screening guidelines for average-risk adults: Summarizing the current global recommendations. World Journal of Gastroenterology 2018 Jan 7;24(1):124-13

High Risk Screening

Table 2. Colonoscopy Screening Recommendations Based on Risk Factors

Risk factor	*Age to initiate screening*	*Interval if normal (years)*
Single first-degree relative with colorectal cancer or an advanced adenoma diagnosed at ≥ 60 years of age	50 years (may start at 45 years in blacks)	10
Single first-degree relative with colorectal cancer or an advanced adenoma diagnosed at < 60 years of age	40 years or 10 years younger than affected relative's age when diagnosed, whichever is earlier	5
Two first-degree relatives with colorectal cancer or an advanced adenoma diagnosed at any age	40 years or 10 years younger than the youngest affected relative's age when diagnosed, whichever is earlier	5

NOTE: *An advanced adenoma is defined as an adenoma that is 10 mm or larger, has villous elements, or has high-grade dysplasia.*

Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: recommendations for physicians and patients from the US Multi-Society Task force on Colorectal Cancer. *Gastroenterology*. 2017;153(1):307-323.

CRC Screening Options

TABLE 1. Colorectal cancer screening strategies considered appropriate by the US Preventive Services Task Force[1]

Test	Recommended Frequency
Stool-based	
Guaiac fecal occult blood test	Annually
FIT	Annually
FIT-fecal DNA stool test	Annually or every 3 years
Direct Visualization	
Colonoscopy	Every 10 years
Computed tomography colonography	Every 5 years
Flexible sigmoidoscopy	Every 5 years
Flexible sigmoidoscopy with FIT	Flexible sigmoidoscopy every 10 years plus FIT annually

Abbreviation: FIT, fecal immunochemical test.

US Preventive Services Task Force, Bibbins- Domingo K, Grossman DC, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *JAMA*. 2016;315(23):2564-2575.

CRC Screening Options

TABLE 2. Ranking of screening tests by the US Multi-Society Task Force on Colorectal Cancer[2]

Tier 1
Colonoscopy every 10 years
FIT annually
Tier 2
FIT-fecal DNA stool test every 3 years
~~Computed tomography colonography every 5 years~~
~~Flexible sigmoidoscopy every 5-10 years~~
Tier 3
~~Capsule colonoscopy every 5 years~~

Abbreviation: FIT, fecal immunochemical test.

Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: recommendations for physicians and patients from the US Multi-Society Task force on Colorectal Cancer. *Gastroenterology*. 2017;153(1):307-323.

Colonoscopy – The GOLD Standard

- Colonoscopy detects:
  - 3x more advanced lesions than FIT
  - 2x more advanced lesions than FIT-fecal DNA

TABLE 4. Why colonoscopy dominates colorectal cancer screening in the United States

Most effective colorectal cancer *prevention* test
Sensitivity for polyp detection far exceeds that of all other tests
Allows single-session diagnosis and resection of precancerous lesions
Only test with sufficient sensitivity to be performed at a 10-year interval

Rex, D. PRACTICAL ADVICE FOR COLORECTAL CANCER SCREENING. GI & Hepatology News 2019

Reasons Patients Delay Colonoscopy

- Invasive
- Concern for intolerance of prep
- Concern for safety of procedures
- Self-conscious of body image
- Logistics
  - Day off work plus driver
- Costs
  - High deductible or co-pays

Colonoscopy Risks

- Major complications for average risk screening
- Cardiopulmonary
  - < 1%
- Perforation (0.3-0.07%)
  - 1 in 2,000 is considered standard of care (0.05%)

Source: ASGE Guidelines 2011

Colonoscopy Risks

- Major Bleeding After a Polyp is Removed
  - Standard of care: 1 in 100 (1%)
  - ASGE: 2 in 1,000 (0.5%)

- Death directly attributable to colonoscopy
  - 19 in 284,000, or 0.007%

Source: ASGE Guidelines 2011

Colonoscopy Summary

- Safe & well tolerated
- By far the most sensitive test
- The only test that ***prevents*** colon cancer
- Should be the ***first test*** offered to average risk patients
- The ***only test*** recommended for high risk patients
- Should be done by high performing GI

Fecal Immunochemical Test (FIT)

- Stool test that checks for
  - Hemoglobin
- Assumes cancers will bleed
- Once a year
- Requires stool sample be obtained

FIT Testing

- Threshold for detection of hemoglobin
  - 20 µg/gram feces
- Advantages
  - Done at home
  - Low cost - $22
  - Better adherence in organized settings (Kaiser)
- If threshold for hemoglobin 10 µg/gram feces
  - Sensitivity for cancer 91%
  - Specificity for cancer 90%

FIT Testing - Take Home Points

- Low cost
- Easy to use
- Good (but not great) sensitivity for CRC
  - Much improved if decreased for hemoglobin threshold
- Colonoscopy is needed if test is positive
- Only prevents cancer when it results in colonoscopy

FIT-Fecal DNA

- Combination of FIT-fecal DNA
  - Fecal DNA
    - Methylation Markers
- Intended for:
  - Average risk colon cancer screening (ages 45-85)
- Cologuard is NOT recommended if:
  - Adenomas on prior colonoscopies
  - Family history of colon cancer or advanced polyps

FIT-Fecal DNA

- If FIT-fecal DNA is negative (normal)
  - Needs to be repeated every 3 years
- Advantages over colonoscopy:
  - Done at home
  - No preparation needed
  - No days off work
  - No driver needed
- Colonoscopy is needed if test is positive

CRC Screening Comparisons

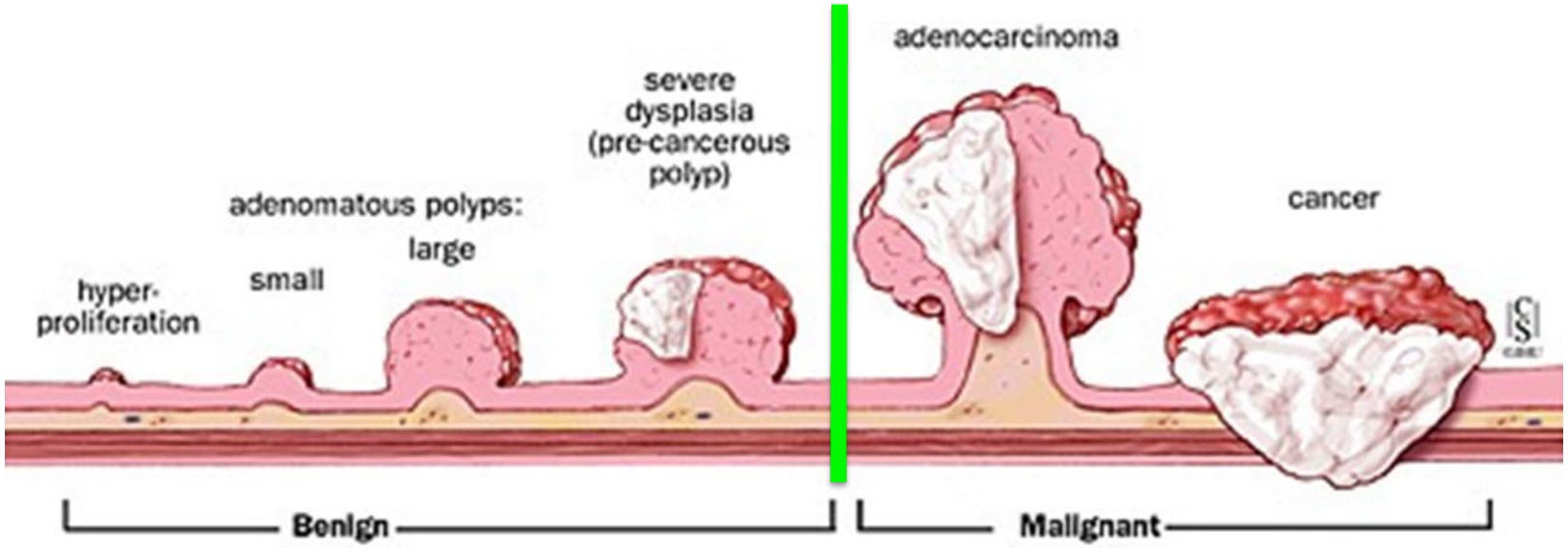
Test	Finds Colon Cancer	Finds High Risk Polyps (>10mm)	False Positives	False Negatives (Cancer Miss Rate)
FIT-fecal DNA	92%	42%	12%	Misses 1 in 13 Cancers
Fit Testing	75-80%	30%-40%	<4%	Misses 1 in 5 Cancers
Colonoscopy	95%	>95%	--	0-6%** Interval Cancers

Robertson DJ, Lee JK, Boland CR, et al. *Gastrointest Endosc*. 2017;85(1):2-21.e3.

Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. N Engl J Med. 2014;370(14):1287-1297.

FIT-Fecal DNA Misses Polyps and Cancer

More than 30% of polyps that will soon become cancer



Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. *N Engl J Med*. 2014;370(14):1287-1297.

TABLE 5. Advantages and limitations of the FIT-fecal DNA stool test for colorectal cancer screening

Advantages
Noninvasive
High (92%) sensitivity for cancer
Recommended at 3-year intervals (compared to 1 year for FIT)
Limitations
Less sensitive for cancer than high-quality colonoscopy
Less sensitive for adenomas and serrated lesions than colonoscopy
High (12%) false-positive rate
False-positive rate increases with patient age
Expensive ($500) compared to FIT ($22)
Most of the sensitivity derives from the FIT, which itself is inexpensive
Dominated by FIT in cost models: FIT is more effective and cost-effective than the FIT-fecal DNA test
No evidence to support use outside of screening
Basis for positive results (FIT or DNA stool tests, or both) is not reported
Colonoscopy for a positive FIT-fecal DNA test is considered part of the continuum of care for colon cancer screening. There is no out-of-pocket cost for the colonoscopy.

Abbreviation: FIT, fecal immunochemical test.

Rex, D. PRACTICAL ADVICE FOR COLORECTAL CANCER SCREENING. GI & Hepatology News 2019

FIT-Fecal DNA Take Home Points

- Easier than a colonoscopy
- Misses in 1 in 13 colon cancers
- Misses > 30% of polyps that will become cancer
- Misses almost 60% of polyps that could turn into cancer
- Only prevents colon cancer if it results in colonoscopy and polyp removal

Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. *N Engl J Med*. 2014;370(14):1287-1297.

FIT-Fecal DNA Take Home Points

- Easier than a colonoscopy
- Misses in 1 in 13 colon cancers
- Misses > 30% of polyps that will become cancer
- Misses almost 60% of polyps that could turn into cancer
- Only **prevents** colon cancer **if** it results in colonoscopy and polyp removal

Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. *N Engl J Med*. 2014;370(14):1287-1297.

Take Home Points

- Colon cancer is common and deadly
- Colon cancer rates are rising for younger patients
- Colon cancer and death is nearly entirely **preventable**
- But 50% of eligible patients are not screened
- ANY SCREENING IS BETTER THAN NO SCREENING…but

Take Home Points

- Colonoscopy remains the only test that **prevents** cancer of entire colon.
  - Start at age 45
  - Family history of colon cancer/advanced polyps
  - Colonoscopy age 40 or 10 years before diagnosis
    - Whichever is younger
- For patients who refuse colonoscopy
  - FIT testing every year is the next recommendation

Then…

- FIT-Fecal DNA
  - Important alternative test with important limitations

COLONOSCOPY

ASGE THE Cancer Prevention Screening Test

Content developed by Ilche Nonevski, MD and Joseph Vicari, MD, MBA, FASGE at Rockford Gastroenterology Associates