

The background is a light blue gradient with various medical and scientific icons. At the top, there are icons for a heart, a globe, a building, a water drop, a pill, a hospital bed, a stethoscope, and a virus. Below these are icons for a heart with a pulse line, a globe, and another globe. The overall theme is healthcare and medicine.

Colorectal Cancer (CRC) Screening: How to Maximize?

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The background of the slide features a horizontal band with various medical icons in a light blue and white color scheme. These icons include a heart with a cross, a city skyline, a microscope, a pill, a first aid kit, a stethoscope, a virus particle, and a bar chart. The icons are arranged in a row and are semi-transparent, allowing the background to show through.

Disclosure

- I am a gastroenterologist and perform colonoscopy

Learning Objective

- Average Risk CRC screening
- Why and Who we screen
- CRC Screening Modalities
 - 2021 USPSTF guidelines
 - Different Modalities and Data

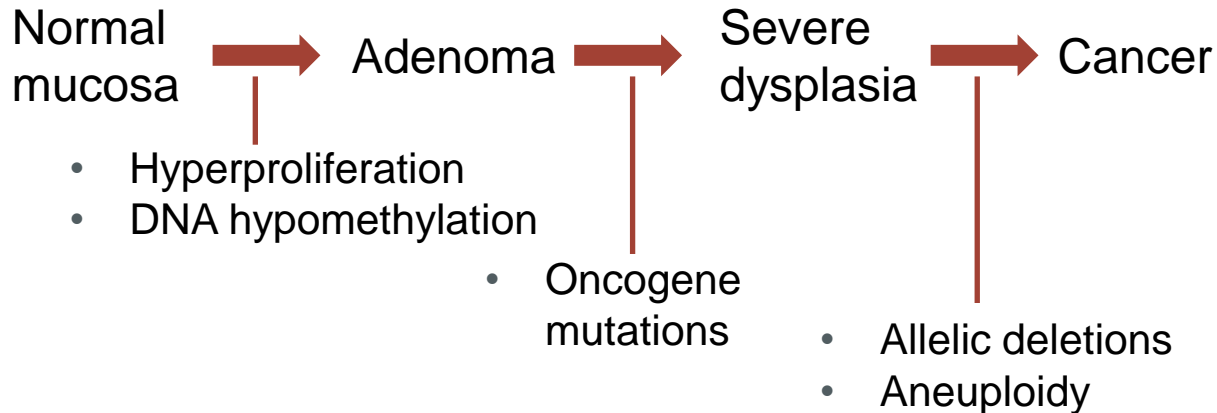
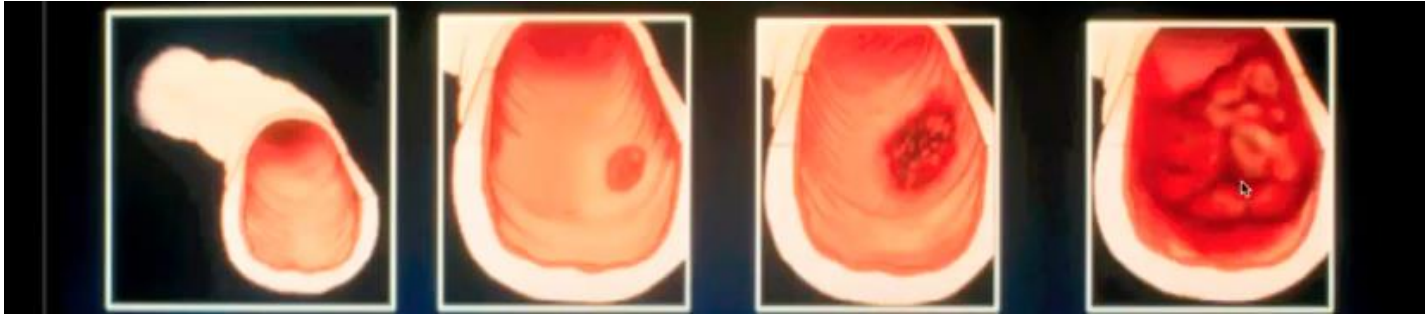
CRC: Why Screen

- Life time incidence 5%
- Majority of cases occur after age 50
- One-third of patients with CRC die from the disease
- CRC screening is cost-effective
- CRC is preventable disease

CRC Objective

- To reduce CRC incidence and mortality
 - Need tests that detect early stage (curable) cancers
 - Need tests that detect pre-cancerous lesions
 - Detection and treatment of pre-cancerous lesions
 - Adenomas are precursor of 70% of all CRC cancers
 - Adenoma carcinoma sequence takes 10 or > years
 - Sessile serrated polyps (SSP) precursor of 30% of all CRC cancers

Adenoma – Carcinoma Sequence

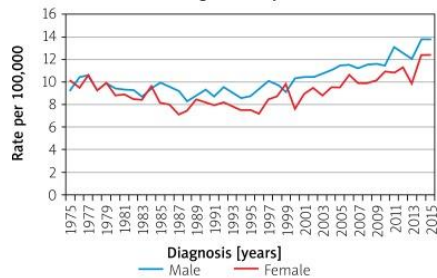


CRC Screening: Who Is at Average Risk?

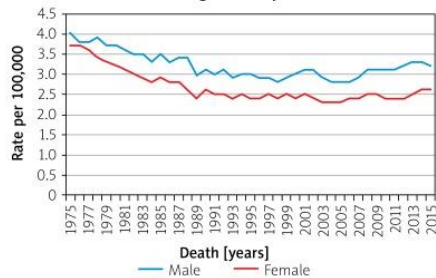
- No family or personal h/o CRC, no personal h/o colon adenoma, no IBD, no symptoms
- Age 50-75
 - 45 recommended by USPSTF, ACS, ACG, multi-society guidelines, NCCN
 - 45 year old CRC incidence increasing and = to 50 year old
 - Modeling shows screening effective, no real data
 - Adds 20-22 million American eligible for CRC screening
 - Stop at 75
 - Little data, based upon screening findings, patient preference and life expectancy 5-10 years



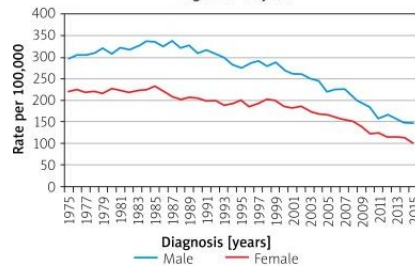
Incidence rates
Ages 20–49 years



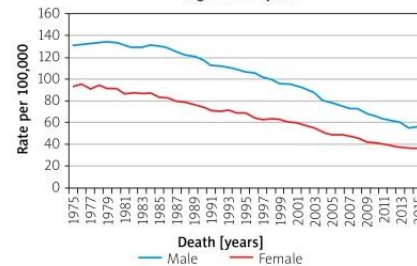
Mortality rates
Ages 20–49 years



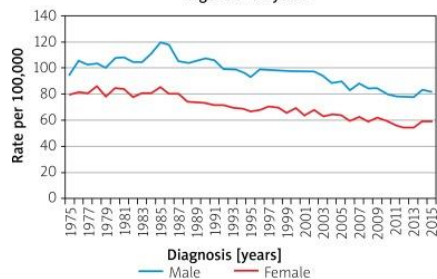
Ages 65–74 years



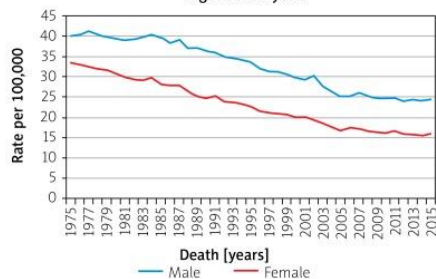
Ages 65–74 years



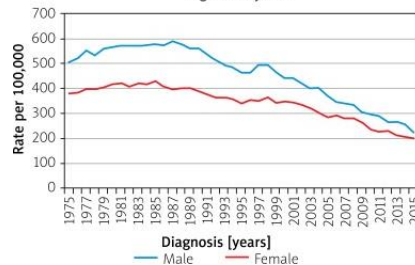
Ages 50–64 years



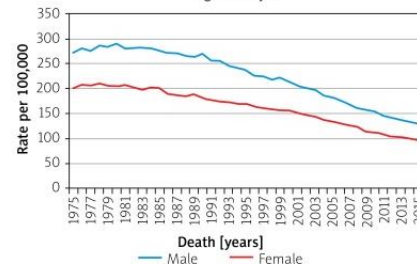
Ages 50–64 years



Ages 75+ years



Ages 75+ years



USPSTF Recommended CRC Screening Modalities in 2021

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

Fecal Occult Blood Test



- Poor sensitivity for one-time test
- Requires repeat testing
- Compliance with repeat testing poor
- Costs are deceptive

Detection of Advanced Neoplasia with one-time test: 24%

Fecal Occult Blood Test (FOBT)

- 6 RCTs of FOBT vs. no screening
 - CRC mortality reduced by 15-31%
- FOBT intimately connected to colonoscopy
 - Mortality reduced by detection or chance leading to colonoscopy
- Data old, published in 1990s, data collected in 70s/80s
- Main problem with FOBT – nobody uses it
- DRE is not screening test

Fecal Immunochemical Test (FIT)

- Improved detection of Hb as compared to guaic based FOBT tests
 - Immunochemical testing uses antibody to human globin
 - One time use, no dietary restriction
- FIT increased sensitivity/specificity for CRC
 - Sensitivity for CRC is 73-88 percent
 - Specificity is 91-95 percent
 - Less missed cancers, less false + than FOBT
- Sensitivity for advanced adenoma is 24 to 27 percent
- FIT better at detecting CRC than FOBT
 - Is it better in reducing mortality ? We do not know

Sigmoidoscopy



Sedated/unsedated endoscopic test with prep that examines one-third of the colon

Flexible Sigmoidoscopy

- 5 RCT show sigmoidoscopy reduces overall CRC incidence and mortality 23-38 % vs. no screen
- Every + requires colonoscopy
- Problems of sigmoidoscopy
 - 52% of pts with proximal advanced adenoma missed with sigmoidoscopy
 - Sigmoidoscopy poor in women missing 65% of advanced polyps as opposed to a colonoscopy
 - Almost no one in US is using sigmoidoscopy as a screening modality

Fecal DNA Analysis

- Adenoma and carcinoma cells contain altered DNA that are shed continuously in stool
- Multi-target DNA stool assay
- Requires entire stool specimen (must be mailed)
- Multi-target stool DNA testing for CRC screening
 - Latest assay (Kras+DNA methylation+FIT)
 - 10,000 average risk screening patients randomized to stool DNA vs FIT
 - All patients then received colonoscopy as gold standard

Sensitivity of Stool DNA vs. FIT

Sensitivity of Stool DNA vs. FIT

Lesion	FIT	Stool DNA	Colonoscopy	P - value
Cancer	73.8%	92.3%	100%	P=.002
Advanced Adenoma	23.8%	42.4%	100%	P<.001
HGD polyp	46.2%	69.2%	100%	P=.004
Sessile serrated adenoma	5.1%	42.4%	100%	P<.001
Sub – cm adenoma	7.6%	17.2%	100%	P<.001

Positive Stool DNA Results: 16% of All Tests

- Advanced adenoma 19.9 percent
- False positive 76.4%
- Colorectal cancer 3.7%
- Insufficient evidence on the appropriate FU of positive findings on a negative colonoscopy
 - May lead to overly intense surveillance due to concerns over the DNA component

Multi-Targeted Stool DNA (FIT-DNA)

- Approved by FDA and CMS in 2014
- Advantages
 - Non invasive, no bowel prep needed
 - Home based
 - Significantly better test than FIT
- Disadvantages
 - A cancer detection test, NOT a prevention test
 - Limited advanced adenoma detection
 - No ability to detect subcm adenoma
 - Cost/insurance cover subsequent colonoscopy?
 - Not a therapeutic test, need colonoscopy

CT Colonography/Virtual Colonoscopy

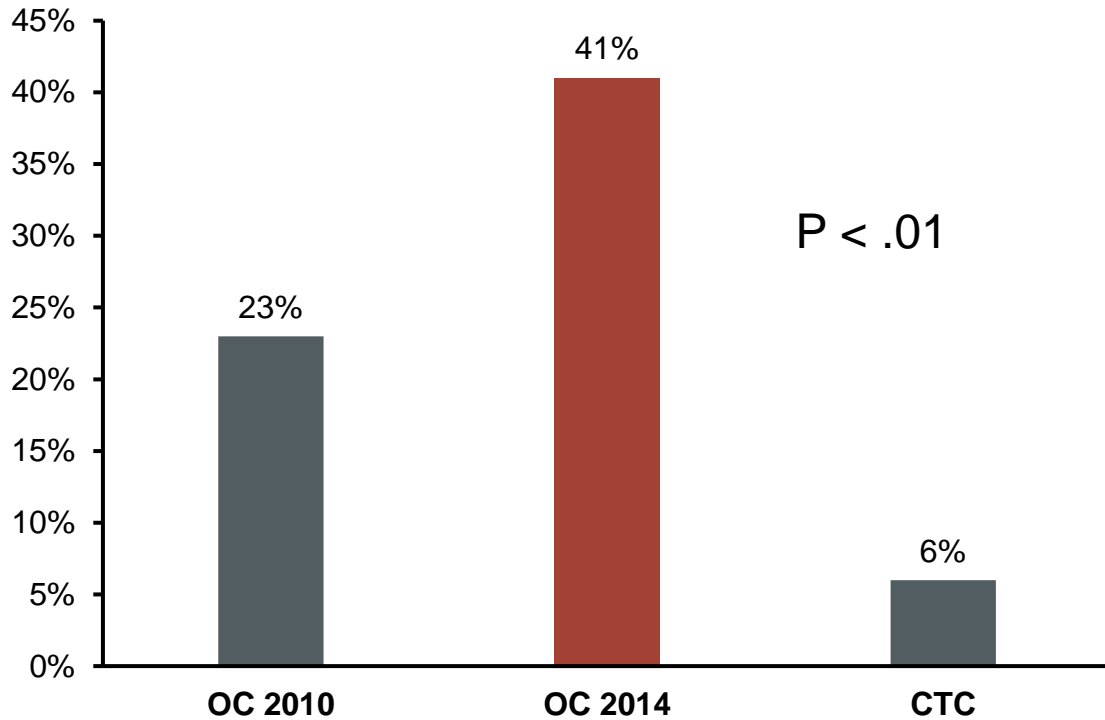
- CT procedure that uses helical, multiple thin section images along with a specialized computer programming to provide 3-D and 2-D images of the colon
- REQUIRE bowel prep
- Diagnostic NOT therapeutic test
- Covered for screening by some insurers
- Not covered for screening by medicare

National CT Colonography Trial

- 2351 patients in 15 centers – compared to colonoscopy
 - 84% per polyp sensitivity for advanced adenoma
 - 70% per polyp sensitivity for adenoma 6 mm or >
- USPSTF – 67-94% sensitivity of adenomas 10 mm or >



% of pts
screened with
an adenoma
detected



CT Colonography: Extra-Colonic Findings

- 40-70%
- Additional work-up in 5-37%
- Significant diagnoses in 2-3%
- Unsuspected cancer in 1:300 adults
- Other screening possibilities:
 - AAA
 - Osteoporosis
 - Liver disease (steatosis, hemochromatosis), etc

CT Colonography or Virtual Colonoscopy

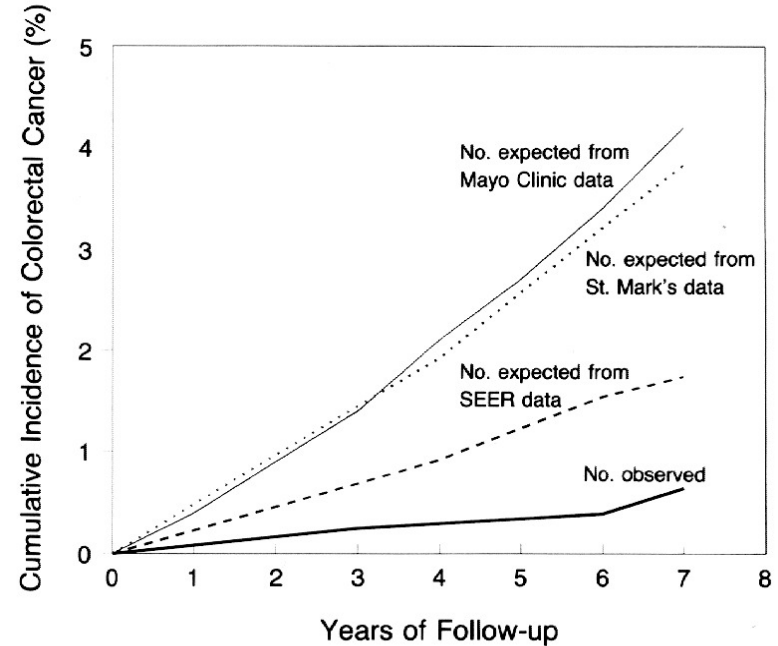
- Advantages
 - CRC prevention test
 - Closest test to colonoscopy for polyp detection
 - Minimally invasive: no sedation needed
 - Extra-colonic findings
- Disadvantages
 - NOT a therapeutic test, need colonoscopy
 - Need bowel prep
 - Extrac-olonic findings
 - Radiation ?, sessile serrated polyps?
 - Has not gained popularity in US

Colonoscopy and CRC Screening

- Advantages
 - Highest sensitivity for cancer and all pre-cancerous lesions
 - Single session for diagnosis and treatment
 - Long interval (10 yr) between exam
- Disadvantages
 - Require bowel prep
 - Complications
 - Perforation .5 per 1000
 - Bleeding 2.6 per 1000
 - Sedation, off from work, transportation

Why Colonoscopy Screening Works

- Cohort study of populations who did and didn't have polyps removed



Colonoscopy Screening and Mortality

- 9 case control or cohort studies show colonoscopy decreases CRC mortality
 - 40-80% reduction in CRC incidence and mortality
- Case control solely in screening patients
 - 67% reduction in CRC cancer mortality
- Long-term CRC incidence and mortality after lower endoscopy
 - Multi hazard ratio for CRC incidence 0.44
 - Hazard ratio of 0.32 for CRC mortality
- Colonoscopy polypectomy and long-term prevention of CRC deaths
 - 2600 patients followed for 15 years
 - 53% reduction in CRC mortality with colonoscopic polypectomy

Colonoscopy Screening and Mortality

- Adenoma detection rate (ADR) and risk of CRC and death
- 315,000 patients undergoing colonoscopy
- Endoscopist with high vs. lower ADR
 - 5 ADR quintiles from 16.6%
 - Lower CRC incidence: HR 0.52
 - Lower CRC mortality HR 0.38
 - Each 1% increase in ADR, 3% decrease in CRC

CRC Screening: Cancer Detection Tests

- **FOBT/FIT: CRC detection test**
 - FOBT – 15-31% reduction in CRC mortality in 6 RCTs
 - FIT – No data on reduction in CRC incidence or mortality
 - 949 studies in the literature
- **Fecal DNA: CRC detection test**
 - No data on reduction of CRC incidence and mortality
 - 169 studies in literature

CRC Screening: Cancer Prevention Tests

- Sigmoidoscopy – CRC prevention test
 - 5 RCTs: 23-38% reduction in CRC mortality
 - 1552 studies in the literature
- CT colonography – CRC prevention test
 - No data on CRC incidence and mortality
 - 1063 studies in literature
- Colonoscopy – CRC prevention test
 - 9 case /control /cohort studies, 40% to 80% reduction in CRC mortality
 - 9007 studies in the literature

CRC Screening: Adherence Rates

- U.S. Adherence Rates
 - Breast Cancer 73%
 - Cervical Cancer 81%
 - CRC 69%

Implementation problems with FOBT

- FOBT not offered as a good option for screening average-risk patients
- Patient preferences for FOBT not taken into account
- Use of tests that are no longer recommended
- Use of in-office tests
- Abnormal tests not followed up with colonoscopy
- FOBT tests not repeated annually

Implementations Problems With Colonoscopy

- Polyps are missed
- The cecum is not reached
- Bowel prep is sub-optimal
- The colonoscopy report is missing important elements
- Recommendations for screening and surveillance intervals are not consistent with guidelines
- Endoscopists do not monitor their performance, so they are not aware when they are not meeting quality standard

COVID and CRC Screening

- EPIC data: 86% reduction in CRC screening nationally
 - Impact in underserved communities
- 50% reduction in new CRC diagnosis
- “getting a screening colonoscopy safer than going to grocery store”

CRC Screening: Conclusion

- CRC screening reduces CRC incidence, mortality and is cost effective
- Screening modalities
 - No data to support one modality more effective than others
 - Know data on modalities when counseling patients
- USPSTF
 - Recommended – colonoscopy, FIT, Sigmoidoscopy, HS gFOBT, stool DNA, CT colonography
 - New in 2021: screen 45 and above

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Answer to Question

E. Fecal Occult Blood Test (FOBT)