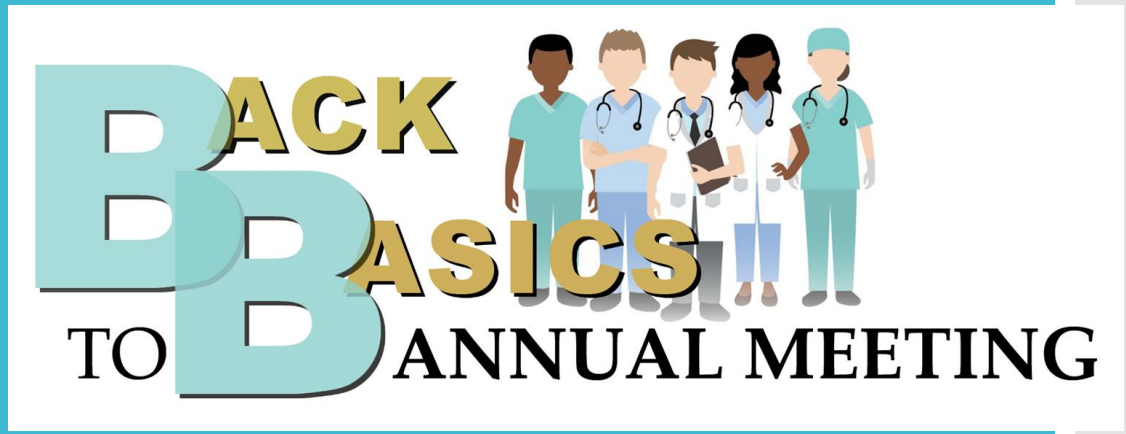
WELCOME

DELAWARE ACADEMY OF FAMILY PHYSICIANS



2022 Annual Meeting

John H. Ammon
Medical Education Center
ChristianaCare | Newark, DE

Conference Chair:
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DELAWARE ACADEMY OF FAMILY PHYSICIANS

Colorectal Cancer Screening

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BACK TO BASICS ANNUAL MEETING

Disclosure

Conflict of Interest Disclosure

- Paulina Rudy, DO and Eric Moseley, MD have no financial relationship to this presentation.

Unapproved or Off-Label Disclosures

- This presentation does not have any unapproved or off-label, experimental or investigative use of a commercial product or device.

Learning Objectives

- To define colorectal cancer (CRC).
- To explore recently published updated United States Preventive Services Task Force (USPSTF) recommendations and the evidence supporting those recommendations on colorectal cancer screening.
- To acknowledge the potential benefits and harms of colorectal cancer screening.
- To discuss the different tests and recommended screening intervals.

Colorectal Cancer (CRC)

Colorectal cancer is cancer of the colon and/or rectum.

Types of colorectal cancer:

- Adenocarcinoma (most common type) - accounts for 95% of all cases
  - Typically starts as a polyp
- Other 5 %
  - Primary colorectal lymphomas
  - Hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome
  - Gastrointestinal stromal tumors
  - Leiomyosarcomas
  - Carcinoid tumors

Colorectal Cancer

Symptoms

- Blood in the stool
- Change in bowel habits
- Unexplained weight loss

Risk Factors

- Increasing age
- IBD
- Family history
- Genetic syndromes
- Lack of physical activity
- Diet low in fruits and vegetables
- Low fiber and high fat diets
- Obesity
- Tobacco and alcohol use

Importance of Colorectal Cancer Screening

- 3rd leading cause of cancer death among men and women.
- Most frequently diagnosed among persons aged 65-74.
- Estimated that 10.5% of new CRC cases occur in persons younger than 50 years old.

Importance of Colorectal Cancer Screening

- Incidence of CRC (especially adenocarcinoma) in adults aged 40-49 has increased by nearly 15% from the early 2000s to 2014-2016.
- 25.6% of eligible adults (ages 50-75) in the US had never been screened in 2016.
- 31.2% were not up to date on screenings in 2018.
- In 2018, prevalence of 1.4M persons living with CRC.

Rationale for USPSTF Update

- Recent changes in epidemiology - increasing incidence and prevalence in those <50
- CISNET Colorectal Cancer Modeling studies

Past USPSTF guidelines

2016 guideline

- Recommended screening for colorectal cancer starting at age 50 years and continuing until age 75 years.
- The decision to screen for colorectal cancer in adults aged 76 to 85 years should be an individual one, taking into account the patient's overall health and prior screening history.
- Screening should be discontinued after age 85 years.

Current USPSTF guidelines

2021 guideline

- Continues to recommend colorectal cancer screening in adults aged 50 to 75 years.
- Now recommend offering screening starting age 45.
- Continues to conclude that screening in adults aged 76 to 85 years should be an individual decision.
- Screening should be discontinued after age 85 years.

Screening Tests

- **Stool based Tests**
  - High sensitivity guaiac fecal occult blood test (gFOBT)
  - Fecal immunochemical test (FIT)
  - Stool DNA test (sDNA-FIT)
- **Direct Visualization Tests**
  - Colonoscopy
  - CT colonography
  - Flexible sigmoidoscopy
  - Flexible sigmoidoscopy with FIT

Stool based test: gFOBT

- **What is it?**
  - High-sensitivity guaiac fecal occult blood test (gFOBT) utilizes a chemical detection of blood in the stool.
- **Frequency of test:** every year.
- **Evidence of efficacy:**
  - RCTs show that it reduces CRC mortality.
- **Other considerations:**
  - Harms from screening with gFOBT arise from colonoscopy to follow up abnormal gFOBT results.
  - Requires dietary restrictions and 3 stool samples.
  - Requires good adherence over multiple rounds of testing.
  - Does not require bowel prep, anesthesia or sedation, or transportation to and from screening exam.

Stool based test: FIT

- **What is it?**
  - Fecal immunochemical test (FIT) utilizes antibody detection of blood in the stool.
- **Frequency of test:** every year.
- **Evidence of efficacy:**
  - One large cohort study showed that screening with FIT reduces CRC mortality.
  - Certain FIT tests have improved accuracy compared to gFOBT and HSgFOBT.
- **Other considerations:**
  - Harms arise from from colonoscopy to follow up abnormal FIT results.
  - Can be done with single stool sample.
  - Requires no dietary restrictions prior to screening.
  - Requires good adherence over multiple rounds of testing.
  - Does not require bowel prep, anesthesia or sedation, or transportation to and from screening exam.

Stool based test: sDNA-FIT

- **What is it?**
  - Stool DNA (sDNA) tests detect DNA biomarkers for cancer cells shed from the lining of the colon and rectum into stool.
  - Currently the only sDNA test approved by the FDA is a multitarget stool DNA test that also includes a FIT component, referred to as sDNA-FIT.
- **Frequency of test:** every 1 to 3 years
- **Evidence of efficacy:**
  - Improved sensitivity compared with FIT.
  - Specificity is lower than that of FIT, resulting in more false positive results, more follow up colonoscopies, and more associated adverse events as compared to FIT test.
  - Modeling studies suggest that screening every 3 years does not provide a favorable balance of benefits and harms compared with other stool based screening options (annual FIT or sDNA-FIT every 1-2 years).
  - No direct evidence evaluating the effect of sDNA-FIT on CRC mortality.

Stool based test: sDNA-FIT

- **Other considerations:**
  - Harms arise from colonoscopy to follow up abnormal sDNA-FIT results.
  - Can be done with single stool sample, but involves collecting an entire bowel movement.
  - Requires good adherence over multiple rounds of testing.
  - Does not require bowel prep, anesthesia or sedation, or transportation to and from screening exam.

Direct visualization test: Colonoscopy

- **What is it?**
  - Endoscopic examination of the entire colon and rectum via camera visualization.
- **Frequency of test:** every 10 years.
- **Evidence of efficacy:**
  - Several cohort studies prove that colonoscopy reduces CRC mortality.
- **Other considerations:**
  - Screening and diagnostic follow up allowed in same visit.
  - Requires less frequent screening.
  - Bowel prep, anesthesia or sedation, and transportation.

Direct visualization test: CT colonography

- **What is it?**
  - CT of colon.
- **Frequency of test:** every 5 years.
- **Evidence of efficacy:**
  - Reasonable accuracy to detect CRC and adenomas.
  - No direct evidence on CRC mortality.
  - Limited evidence on benefits vs harms and treatment of extracolonic findings (1.3% to 11.4% of exams; <3% required medical or surgical treatment).
- **Other considerations:**
  - Potential harms from follow up colonoscopy.
  - Bowel prep.
  - No anesthesia or transportation to and from screening exam.

Direct visualization test: Flexible sigmoidoscopy

- **What is it?**
  - Endoscopic examination of the sigmoid colon.
- **Frequency of test**: every 5 years.
- **Evidence of efficacy:**
  - RCTs suggest reduction in CRC mortality.
  - Less risk of bleeding and perforation in comparison to colonoscopy.
  - Modeling suggests that it provides fewer life-years gained alone than when combined with FIT or in comparison to other testing strategies.
- **Other considerations:**
  - Additional harms from follow up colonoscopy.
  - Declining test availability.

Direct visualization test: Flexible Sigmoidoscopy with FIT

- **What is it?**
  - Sigmoidoscopy with FIT.
- **Frequency of test:** Sigmoidoscopy every 10 years and FIT every year.
- **Evidence of efficacy:**
  - RCTs suggest reduction in CRC mortality.
  - Modeling suggests combination testing provides similar benefits to those of colonoscopy with fewer complications such as bleeding or perforation.
- **Other considerations:**
  - Potential harms due to follow up colonoscopy.
  - Declining availability.
  - FIT screening requires good adherence over multiple years of testing.

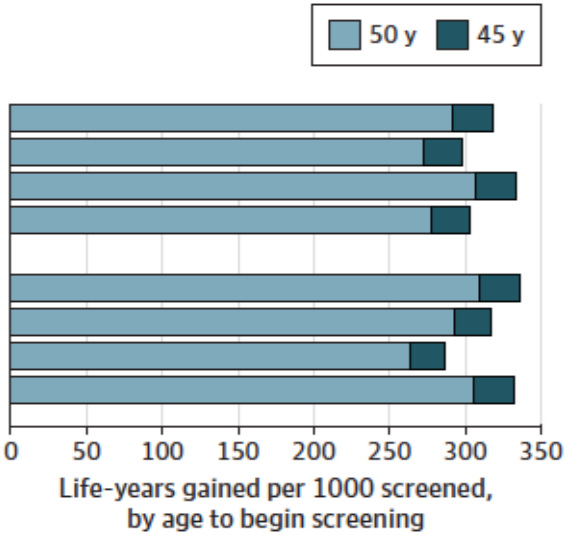
Benefits and harms of colorectal cancer screening for adults aged 45-49 years old

- USPSTF found evidence that screening for CRC in adults aged 45-49 years provides a moderate benefit in reducing CRC mortality and increasing life years gained.
- The majority of harms result from the use of colonoscopy (bleeding and perforation); however, risk is low, and some studies suggest risk may be lower at younger ages.

Summary of rationale to updates:

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

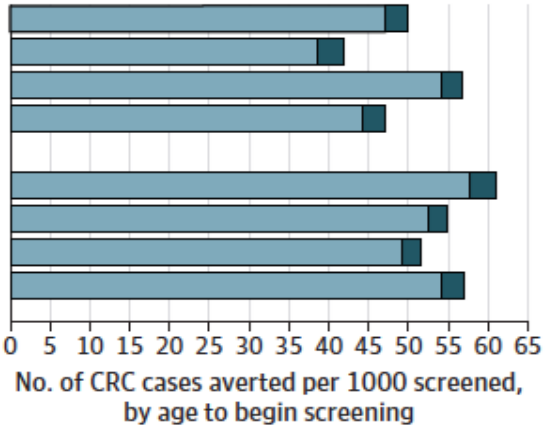
Screening modality and frequency	Mean life-years gained if start screening[b]		Additional life years gained if start screening at age 45 y
	At age 50 y	At age 45 y	
Stool tests			
FIT every year	292	318	26
HSgFOBT every year[c,d]	272	298	26
sDNA-FIT every year	307	333	26
sDNA-FIT every 3 y[d]	278	303	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



Summary of rationale to updates:

B Benefit: Estimated No. of CRC cases averted per 1000 individuals screened[a]

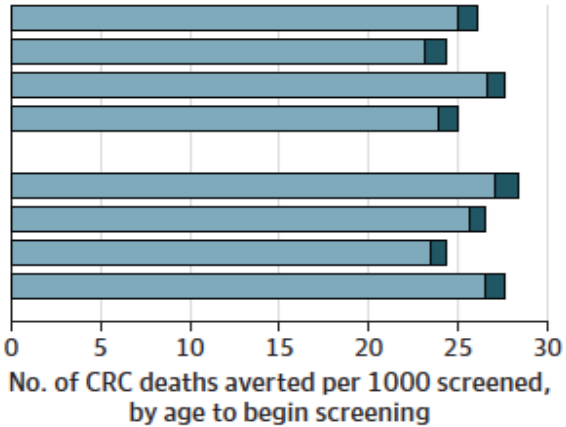
Screening modality and frequency	Mean CRC cases averted if start screening[b] At age 50 y	At age 45 y	Additional CRC cases averted if start screening at age 45 y
Stool tests			
FIT every year	47	50	3
HSgFOBT every year[c,d]	39	42	3
sDNA-FIT every year	54	57	3
sDNA-FIT every 3 y[d]	44	47	3
Direct visualization tests			
COL every 10 y	58	61	3
CT colonography every 5 y	53	55	2
Flexible SIG every 5 y	49	51	2
Flexible SIG every 10 y plus FIT every year	54	57	3



Summary of rationale to updates:

C Benefit: Estimated No. of CRC deaths averted per 1000 individuals screened[a]

Screening modality and frequency	Mean CRC deaths averted if start screening[b] At age 50 y	At age 45 y	Additional CRC deaths averted if start screening at age 45 y
Stool tests			
FIT every year	25	26	1
HSgFOBT every year[c,d]	23	24	1
sDNA-FIT every year	27	28	1
sDNA-FIT every 3 y[d]	24	25	1
Direct visualization tests			
COL every 10 y	27	28	1
CT colonography every 5 y	26	26	0.9
Flexible SIG every 5 y	23	24	0.9
Flexible SIG every 10 y plus FIT every year	26	28	1



Recommendations of other societies

- General consensus across other societies is that average-risk adults aged 50-75 years be screened and that screening should be individualized in older adults aged 76-85 years with clear consensus that screening should stop after age 85 years.
- In 2018, American Cancer Society recommended screening begin at age 45 years in all adults.
- AAFP states insufficient evidence to begin screening before age 50 years.
- In 2021, American College of Gastroenterology suggested screening in average-risk persons aged 45-49.

Research Needs and Gaps

- Need for randomized control studies comparing the effectiveness of different screening modalities including hybrid strategies which switch between modalities over time.
- Research on adherence to screening modalities and the effect adherence has on the overall benefits of a screening program.
- More research on accuracy and effectiveness of emerging screening tests such as urine and serum based as well as capsule endoscopy to potentially improve acceptance and adherence to CRC screening.

Conclusions

- Modeling studies suggest that CRC screening may lead to sizable reductions in the lifetime risks of developing and dying from colorectal cancer.
- Many screening strategies are estimated to provide an efficient balance of the burden and benefit of screening; these strategies encompass a range of screening modalities, intervals, and ages.
- Starting screening at age 45 was generally estimated to result in more life years gained and fewer colorectal cancer cases and deaths than similar strategies with screening starting at age 50 or age 55, albeit with a higher lifetime burden of both colonoscopy and non-colonoscopy testing and slightly higher lifetime risks of complications.

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QUESTIONS?

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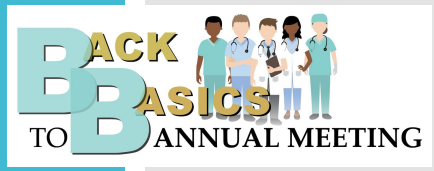

Table 2. Key Question 2: Summary of Test Accuracy Results for Direct Visualization Screening Tests[a]

Screening test group	No. of studies	No. of participants	CRC	Adenomas ≥10 mm		Adenomas ≥6 mm	
			Sensitivity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Flexible sigmoidoscopy	0	NA	NA	NA	NA	NA	NA
CT colonography[b]	7	5328	0.86-1.0 (0.21-1.0)	0.89 (0.83-0.96)	0.94 (0.89-1.0)	0.86 (0.78-0.95)	0.88 (0.83-0.95)
Colonoscopy	4	4821	0.18-1.0 (0.01-1.0)	0.89-0.95 (0.70-0.99)	0.89 (0.86-0.91)[c]	0.75-0.93 (0.63-0.96)	0.94 (0.92-0.96)[c]

Abbreviations: CRC, colorectal cancer; CT, computed tomography; NA, not available.

[a] Pooled estimates from meta-analysis when available; otherwise, range of values and range of the 95% CI reported.

[b] Test accuracy shown for CT colonography with bowel preparation only. Two additional studies without bowel preparation are not represented in this table.

[c] Only 1 study reported specificity.

Table 3. Key Question 2: Summary of Test Accuracy Results From Studies With Colonoscopy Follow-up for Stool and Serum Screening Tests[a]

Screening test group	No. of studies	No. of participants	CRC		Advanced neoplasia		Advanced adenoma	
			Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
High-sensitivity gFOBT: Hemoccult Sensa	2[b]	3503	0.50-0.75 (0.09-1.0)	0.96-0.98 (0.95-0.99)	0.07-0.21 (0.02-0.27)	0.96-0.99 (0.96-0.99)	0.06-0.17 (0.02-0.23)	0.96-0.99 (0.96-0.99)
FIT								
OC-Sensor	13[b,c]	44 887	0.74 (0.64-0.83)	0.94 (0.93-0.96)	0.25 (0.21-0.31)	0.96 (0.95-0.97)	0.23 (0.20-0.25)	0.96 (0.95-0.97)
OC-Light	4[b]	32 424	0.81 (0.70-0.91)	0.93 (0.91-0.96)	0.27 (0.16-0.38)	0.95 (0.92-0.98)	0.28 (0.19-0.37)	0.94 (0.91-0.97)
Other	12[b,c]	53 527	0.50-0.97 (0.09-1.00)	0.83-0.97 (0.82-0.97)	0.02-0.66 (0.01-0.99)	0.60-0.99 (0.58-1.0)	0.18-0.50 (0.13-0.56)	0.85-0.98 (0.84-0.98)
mtsDNA-FIT: Cologuard	4[b]	12 424	0.93 (0.87-1.0)	0.85 (0.84-0.86)	0.47 (0.44-0.50)	0.89 (0.87-0.92)	0.43 (0.40-0.46)	0.89 (0.86-0.92)
Serum: Epi proColon	1	6857	0.68 (0.53-0.80)	0.79 (0.77-0.81)	0.25 (0.22-0.28)	0.79 (0.76-0.82)	0.22 (0.18-0.24)	0.79 (0.76-0.82)

Abbreviations: CRC, colorectal cancer; FIT, fecal immunochemical test; gFOBT, guaiac fecal occult blood test; mtsDNA, multitargeted stool-based DNA.

[a] Pooled estimates and 95% CI from meta-analysis when available; otherwise, range of values and range of the 95% CIs reported.

[b] Includes newly identified studies.

[c] One nested case-control study[104] (n = 516) is not represented in this table.