Colorectal Cancer Screening: Considerations and Controversies

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Learning Objectives

- List & describe available CRC screening tests
- List 2 advantages & disadvantages of each test
- Understand recommended guidelines for CRC screening
- Identify those individuals at high risk for CRC
- Recognize indications & intervals for surveillance
What CRC screening test and interval would you recommend for a 37-year-old male whose father was diagnosed with CRC at age 52?

A. FOBT annually
B. Flexible sigmoidoscopy q 5 years
C. Colonoscopy now, then annually
D. Colonoscopy at age 40 and q 5 years
E. Colonoscopy at age 50, then q 5-10 years
Margaret – age 60

- F/u with PMD after completing a screening colonoscopy
- PMH: HTN, Hyperlipidemia, Obesity
- FH: Mother (HTN); Father (CAD); No GI malignancy.
- Findings:  
  - Hemorrhoids (grade 1)  
  - Diverticulosis  
  - Hemi-circumferential descending colon malignancy requiring a left hemicolectomy  
- No post-operative complications

What surveillance interval will Margaret need to follow?
A. Colonoscopy annually
B. Colonoscopy at 1 yr, then 3 yrs, then 5 yrs
C. Colonoscopy every 5 years
At what age, if any, would you stop performing CRC screening?

A. 68
B. 73
C. 81
D. 83
E. 86
F. No age limit for CRC screening
Colorectal Cancer (CRC)

- In the U.S. - 149,000 cases annually; ~50,000 deaths
- Life-time cumulative incidence of ~5%
- 3rd most common cancer
- 2nd leading cause of cancer-related death (men and women)
- 90% - occur in adults > 50 years of age
- 5-year survival
  - *90% with localized disease
  - *68% with lymph node involvement
  - *10% with distant metastasis
- Only 39% are detected in early stage
- Disparities among racial and ethnic groups
- Alarm symptoms: change in bowel habit, tenesmus, change in stool caliber, hematochezia, melena, chronic bleeding, weight loss, abdominal pain.
Factors Affecting CRC Risk

Multiple factors, especially:
- Age (primary RF)
- Race
- Gender
- Family history of CRC
- Family history of adenomatous polyps
  - High-Risk Individuals
    - 1 FDR with cancer at age <50
    - 2 FDR with CRC at any age
    - FH of hereditary nonpolyposis colorectal cancer (HNPCC)
    - FH of familial adenomatous polyposis (FAP)
- Smoking
- Diet
CRC Screening Tests
CRC Screening Tests

**Early Cancer Detection**
- Fecal Occult Blood Test (FOBT)
  *Hemoccult II/ Hemoccult Sensa*
- Fecal Immunochemical Test (FIT)
- Stool DNA (sDNA)

**Early Cancer Detection and Cancer Prevention**
- Flexible Sigmoidoscopy (FS)
- Barium Enema (DCBE)
- Colonoscopy (CSPY)
- CT Colonography (CTC/virtual colonoscopy)
Fecal Occult Blood Test (FOBT)

- Detects pseudoperoxidase activity of heme as intact hgb or free heme.
- Sensitivity ~38%; Specificity ~97% (Hemoccult II)
- Sensitivity ~75%; Specificity~87% (Hemoccult Sensa)

Advantages
- Non invasive – 3 stool samples
- Inexpensive (Costs $5 - $10)
- Only test w/ evidence of efficacy (reduced mortality 16% in RCT) w/ annual testing

Disadvantages
- Low sensitivity (Hemoccult II)
- Not selective for lower GI bleeding
- Not specific for human hgb.
- Interference by plant peroxidase activity = false +
- Dietary restrictions (radishes, turnips, red meat, fish, ASA/NSAIDs)
- Antioxidants (Vitamin C) = false -
- Poor adherence - because requires annual testing
- Positive test → colonoscopy
Fecal Immunochemical Test (FIT)

- Detection of globin via specific antibodies for human hemoglobin
- Not a “guaiac” reaction (any blood)
- Sensitivity ~81%; Specificity ~97%

**Advantages**
- Globin (protein component of Hgb) degraded by digestive enzymes in UGI tract = more specific for lower GI bleed
- B/C more specific for human blood, reduces false + rate by 30%
- Non invasive
- No dietary/drug interference
- One stool sample

**Disadvantages**
- Processed in laboratory
- More expensive than FOBT ($18 - $30)
- Positive test → colonoscopy
Stool DNA

- Detects altered DNA from epithelial cells in stool shed by neoplasms

**Advantages**
- Sensitivity 91% & Specificity 93% - 1 pilot study
- Non invasive

**Disadvantages**
- Not all genetic abnormalities for CRC can be isolated
- Evolving. No test widely used. Only results from small studies
- High monetary cost
- A study found no better sensitivity than FIT
- Requires entire stool (30+ grams) – shipped with ice pack
- Positive test → colonoscopy
Flexible Sigmoidoscopy

- Examines only distal colon. Must reach 40 cm to be acceptable for screening
- Sensitivity ~70%
- 2 Case-control studies evaluated use in screening
  *59% reduction in CRC mortality within reach of scope

**Advantages**
- Simple bowel prep (Mag Citrate/Fleet’s enema)
- No sedation. Mild discomfort.
- Relatively quick exam (5-10 minutes); No recovery
- Performed in diverse settings (PCP office; rural clinics)

**Disadvantages**
- Requires well trained endoscopist
- Cannot detect lesions beyond length of sigmoidoscope (60cm)
- Complications: perforation (1 in 20,000), bleeding, infection
- Low reimbursement rates
- Polyps detected → colonoscopy
Double Contrast Barium Enema

- Radiologic exam uses barium and air to evaluate the entire colon
- No randomized, controlled trials evaluating efficacy as primary screening
- Sensitivity ~80%; Specificity ~92%
- Being replaced by other screening tests, i.e. CT colonography; colonoscopy

**Advantages**
- Examines entire colon. Detects most polyps/cancers.
- Performed when incomplete/failed colonoscopy
- No sedation/rapid exam (20-40 mins)/return to work

**Disadvantages**
- Requires well-trained radiologist
- Questionable polyp vs. stool → colonoscopy
- Radiation exposure - multiple radiographs
- Bowel prep – dietary and laxative. Suboptimal prep reduce sensitivity/specificity
- Uncomfortable: Rectal tube for air/contrast
- Complications: perforation (1 in 25,000)
- Positive exam (polyp/mass) → colonoscopy
Double Contrast Barium Enema
Colonoscopy

- Insertion of a flexible camera to view entire colon (160 cm)
- Sensitivity ~97.5%
- Studies - incidence of CRC reduced by 76% - 90%
  - 59% reduction in mortality w/ therapeutic interventions

**Advantages**
- Greatest advantage = direct inspection and therapeutic intervention
- Can detect flat polyps
- Regarded as the “gold standard” for diagnosis of polyps/CRC
Disadvantages
- Invasive procedure. Expensive.
- Dietary and bowel cleansing (considered most unpleasant)
- Sedation and chaperone home
- Skilled endoscopist. No quality assurance programs exist.
- Carries most risks/complications: post-polypectomy bleeding (most common), perforation (1:1000), cardiopulmonary, infection, missed lesions (polyps = 6%–15%; cancer ~5%).
- Possible incomplete polypectomy
  * A factor in up to 25% of interval cancers.

Not perfect, but still the best test for cancer prevention
Colon Polyyps/Mass

Colon mass (Adenocarcinoma)

Pedunculated

Sessile

Flat
**Colonoscopy for Surveillance**

- Surveillance interval is based on:
  - A. Number
  - B. Size
  - C. Histology

<table>
<thead>
<tr>
<th>Post-polypectomy</th>
<th>Interval/Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperplastic</td>
<td>10 years</td>
</tr>
<tr>
<td>1-2 tubular adenomas &lt;1 cm</td>
<td>5-10 years</td>
</tr>
<tr>
<td>3-10 adenomas; villous features; ≥1cm; HGD</td>
<td>3 years</td>
</tr>
<tr>
<td>&gt;10 adenomas</td>
<td>&lt; 3 years</td>
</tr>
<tr>
<td>Large sessile adenoma removed piecemeal</td>
<td>2-6 months</td>
</tr>
<tr>
<td>Post surgical resection of colorectal cancer</td>
<td>1/3/5 years post resection</td>
</tr>
</tbody>
</table>
Larry – age 51

- Screening colonoscopy last year
- Findings: 4 polyps
  - 5mm, 7mm, 3mm, 4mm
  - Histology: Tubular adenoma (all)

When is Larry due for his next colonoscopy?

A. 1 year
B. 3 years
C. 5 years
D. 10 years
CT Colonography
(CTC/Virtual Colonoscopy)
CT Colonography

- A low radiation dose CT used to detect colon mass/polyps

**Advantages**
- Imaging of entire colon with 2D & 3D display
- Used for incomplete colonoscopy (10%)
- Rapid exam (~10 minutes); Minimally invasive
- No sedation; no recovery
- Detects polyps >1 cm/CA with high sensitivity
  - 70% - 90% (adenomas); 95% (cancer)
**Disadvantages**

- Reimbursement for screening limited
- No RCT to demonstrate efficacy in reducing mortality from CRC
- Imaging only; not therapeutic
- Bowel prep. Dietary restrictions (clear) + full cathartic
- Discomfort (rectal tube, air insufflation); Risk of perforation
- Controversy - radiation exposure; Pregnant women
- Incidental findings & false + lead to work-up = increased cost
- Difficult detecting flat polyps & those <6 mm
- Consensus that 1 or more polyps >1 cm; 3 or more >6 mm → CSPY
  *With <3 polyps <6 mm = controversial re: colonoscopy
- Positive findings (polyps/mass) → colonoscopy
Oh, please. The IRS perfected that years ago.
## CRC Screening for Average-Risk

<table>
<thead>
<tr>
<th>Screening Test</th>
<th>ACS-USMSTF-ACR</th>
<th>USPSTF</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitive guaiac fecal occult blood test</td>
<td>Recommended if &gt;50% sensitivity for CRC</td>
<td>Recommended</td>
<td>1 year</td>
</tr>
<tr>
<td>Fecal immunochemical test</td>
<td>Recommended if &gt;50% sensitivity for CRC</td>
<td>Recommended, only if high sensitivity test used</td>
<td>1 year</td>
</tr>
<tr>
<td>Stool DNA test</td>
<td>Recommended if &gt;50% sensitivity for CRC</td>
<td>Not recommended due to insufficient evidence to assess sensitivity and specificity of fecal DNA</td>
<td>Uncertain</td>
</tr>
<tr>
<td>Flexible Sigmoidoscopy</td>
<td>Recommended if sigmoidoscope is inserted to 40 cm or to the splenic flexure</td>
<td>Recommended with guaiac fecal occult blood test every 3 yrs</td>
<td>5 year</td>
</tr>
<tr>
<td>Barium Enema</td>
<td>Recommended, but only if other tests are not available</td>
<td>Not recommended</td>
<td>5 year</td>
</tr>
<tr>
<td>CT Colonography</td>
<td>Recommended, with referral for colonoscopy if polyps &gt;6 mm are detected</td>
<td>Not recommended</td>
<td>5 year</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>Recommended</td>
<td>Recommended</td>
<td>10 year</td>
</tr>
</tbody>
</table>


ACS: American Cancer Society  
USMSTF: US Multi-Society Task Force on CRC  
ACR: American College of Radiology  
USPSTF: US Preventative Services Task Force
Societal Consensus

Agree

- Sensitive FOBT (Hemoccult Sensa) q 1 year
- FIT q 1 year
- Flex Sig (to 40cm or splenic flexure); q 5 years
- Colonoscopy q 10 years

Disagree

- Stool DNA
- Barium enema
- CT Colonography
Question

Which methods of CRC screening are recommended by all Societal guidelines?

A. Only colonoscopy and FOBT/FIT
B. Colonoscopy, flexible sigmoidoscopy, FOBT/FIT
C. Colonoscopy, flexible sigmoidoscopy, FOBT/FIT, fecal DNA
CRC Screening Rates are Improving, but...

~40% ≥ 50 years of age are not being screened

2006 Behavioral Risk Factor Surveillance System (BRFSS) Survey:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>2002 (%)</th>
<th>2006 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥50 years who received FOBT within the past yr and/or FS/Colon within the past 10 yrs</td>
<td>53.9</td>
<td>60.8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>43.9</td>
<td>47.2</td>
</tr>
<tr>
<td>Education less than a High School Diploma</td>
<td>41.0</td>
<td>45.5</td>
</tr>
<tr>
<td>$15,000 - $35,000 household income</td>
<td>49.1</td>
<td>53.9</td>
</tr>
<tr>
<td>Health Insurance</td>
<td>55.9</td>
<td>63.0</td>
</tr>
<tr>
<td>Lack of health insurance</td>
<td>33.1</td>
<td>36.7</td>
</tr>
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</table>

CDC. MMWR. 2008; 57:253-258.
The single most effective method to increase CRC screening remains the recommendation for screening by the patient’s primary care provider.
Clinicin Barriers to Recommending CRC Screening

- Not familiar with screening guidelines
- Differences in guidelines
- Perceived patient anxiety regarding testing
- Unfamiliarity with cost/insurance coverage
- Lack of reminders and/or available tracking systems
- Time

Age to Stop Routine CRC Screening

Purpose of screening = detect early CRC & extend life years
If life expectancy <10 years, no utility in screening.
Studies: screening debilitated, terminally ill = little benefit.

U.S. Preventative Services Task Force
- 50 – 75 yrs: CRC screening recommended
- 76 – 85 yrs: Do not routinely screen
- 86+: Do not screen

Only recommendations, use clinical judgment.
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• CRC screening reduces cancer incidence & mortality & saves lives.

• Decreased incidence & mortality attributed to screening & improved treatment; however, the majority are not screened.

• Every year, CRC claims ~50,000 lives; many preventable through early detection & trmt..

• Clinician barriers or patients fears (lack of understanding/embarrassment) surrounding the tests, the key is to raise awareness of CRC & get patients screened.
There are several CRC screening tests available, each with its considerations and controversies and no Societal consensus on one “best” test. Despite this, we can all agree, the “best” test is the one the patient understands, agrees with, and completes.
Questions and Answers