Colorectal Cancer Screening

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CRC Epidemiology

- 4th most common malignancy in US (136,000 cases/yr)
- 2nd most common cause of cancer death (50,000 cases/yr)
- Cumulative lifetime risk of CRC is 6%
- Slight male predominance
- Average age of diagnosis: 65 yo
- 80% of cases occur in people without identifiable risk factors
- Prognosis is directly related to stage of disease
Colon cancer arises from a defined precursor lesion.

- Tubular adenoma
- Tubulovillous Adenoma
- High grade dysplasia (Carcinoma-in-situ)
- Invasive cancer

Time: 7-10 yrs
Colorectal cancer (CRC) screening

1. Who to screen?
   - Average risk 75%
   - Moderate risk 20%
   - High risk 5%

2. How and how often to screen?
   - FOBT/FIT
   - Flexible sigmoidoscopy
   - Colonoscopy
   - Virtual colonoscopy
   - Molecular/genetic testing
Stool based screening tests for colon cancer

- Blood
  - Hemoccult (guaiac)
  - FIT

- Sloughed tumor cells
  - Stool DNA
    - "Cologuard"

Colon cancer

Colon polyp
Prospective evaluation of fecal DNA testing

N = 9989 subjects referred for screening colonoscopy

<table>
<thead>
<tr>
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<th>Sensitivity (CRC)</th>
<th>Sensitivity (Advanced Adenoma)</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Fecal DNA</td>
<td>92.3%</td>
<td>42.4%</td>
<td>86.6%</td>
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<tr>
<td>FIT</td>
<td>73.8%</td>
<td>23.8%</td>
<td>94.9%</td>
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from Imperiale, NEJM, 2014
Stool tests for CRC screening

• **PROS:**
  – Cheaper
  – Easy to perform
  – FOBT can decrease risk of cancer death by 23%

• **CONS:**
  – Unpleasant to handle stool
  – Positive tests require colonoscopy
  – Potentially greater benefit from other screening tests
Colonoscopy vs. sigmoidoscopy
National Polyp Study: *polypectomy reduces incidence of CRC 76-90%*  

Winawer, NEJM, 1993
PLCO Trial (U.S.)

- 154,900 men and women randomized to screening flexible sigmoidoscopy or usual care
- Follow-up: 11.9 years
- Results: 21% reduction in CRC incidence
  26% reduction in CRC mortality

R. Schoen, NEJM, 2012
Virtual colonoscopy
## Virtual colonoscopy: performance characteristics

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<tr>
<td>&gt; 10 mm</td>
<td>94%</td>
<td>55%</td>
<td>59%</td>
<td>91%</td>
</tr>
<tr>
<td>&gt; 6 mm</td>
<td>89-94%</td>
<td>39%</td>
<td>51%</td>
<td>59%</td>
</tr>
<tr>
<td>(No. subjects)</td>
<td>(1233)</td>
<td>(600)</td>
<td>(614)</td>
<td>(605)</td>
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*Laxative free exams
CT Colonography: limitations

- No therapeutic capabilities
- Detection rate of small, flat polyps is low
- Discomfort from air insufflation
- Pre-procedure laxative preparation required
- Not reimbursed by insurance
CRC Screening: Average risk patient

- Men and women over age 50
- No symptoms (bleeding)
- No risk factors for CRC (Family history)

Tests that detect polyps and cancer (** preferred)
- Flex Sig every 5 yrs
- Colonoscopy every 10 yrs
- Virtual colonoscopy every 5 yrs

Tests that primarily detect cancer
- Stool occult blood or FIT annually
- Stool DNA every 3 years

RISK OF COLON CANCER: ROLE OF FAMILY HISTORY

Relative risk of CRC:

- Control: 1
- One Relative: 1.72, 1.8
- ≥ Two Relatives: 2.75, 5.7, 5.37, 3.7
- Age < 45: 5.37, 3.7

Graph comparison of Fuchs, 1994 and St. John, 1993 data.
CRC Screening: Moderate Risk Patient

Family History of CRC/polyps

- CRC or polyps in 1st degree relative < 60 or two 1st degree relatives of any age:
  
  \[
  \text{Colonoscopy at age 40, or 10 yrs before youngest case. Then every 5 years.}
  \]

- CRC or polyps in 1st degree relative ≥ 60 or two 2nd degree relatives of any age:
  
  \[
  \text{Average risk recommendations, but start screening at age 40}
  \]
“Hereditary Colon Cancer”

- Those with a very strong family history may have a condition known as “Hereditary Colon Cancer”

- Very high risk of colon cancer (up to 80%)

- Increased risk of other tumors (up to 50%)
  - Uterus, Stomach, Small intestine

- Increased risk of cancer in family members
When to suspect Hereditary Colon Cancer

- Colon cancer in 2 or more family members
- Colon cancer before age 50, polyp before age 45
- More than 10 cumulative polyps
- Colon cancer in conjunction with other cancers: uterine

- Genetic testing can be used to diagnose “Hereditary Colon Cancer”
CRC incidence and mortality are falling in the US

- CRC incidence rate
- CRC mortality rate

SEER data
Participation with CRC screening guidelines

Overall rate of participation: 65%
Everyone requires colon cancer screening
– There are many options for CRC screening
– Accurate risk stratification is key, and this depends upon a careful family history
– High-risk families should have a genetic evaluation