Colorectal Cancer Screening

Haleh Pazwash, M.D., FACG
Colon Cancer Incidence

- 5% lifetime incidence for patients at average risk
- Highest incidence rates in Australia, New Zealand, Europe, and North America
- 2\textsuperscript{nd} most commonly diagnosed cancer in women
- 3\textsuperscript{rd} most commonly diagnosed cancer in men
Incidence by Gender and Ethnicity

Source: Colorectal Cancer, Centers for Disease Control and Prevention, 2015
Colon Polyps

- Hyperplastic vs adenomatous
  - Biopsy typically required for distinction
  - Hyperplastic usually do not progress to cancer
  - Two-thirds of polyps are adenomatous

Source: Screening for colorectal cancer: Strategies in Patients of Average Risk, UpToDate, 2015
Adenoma-Carcinoma Sequence

• Progression ~10 years

Source: From Polyp to Cancer, Johns Hopkins Colon Cancer Center, 2015
Proximal Colon Cancer

• Common in women and with increasing age

• Gradual international shift toward right-sided (proximal) colon cancer
  – Colonoscopy effectiveness
  – Poor right-sided preps
  – Incomplete colonoscopy
  – Anatomic configurations
  – True increase?
## General Risk Factors

<table>
<thead>
<tr>
<th>Increased Risk</th>
<th>Decreased Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of physical activity</td>
<td>Multivitamins (folic acid)</td>
</tr>
<tr>
<td>Red meat consumption</td>
<td>Aspirin, NSAIDs</td>
</tr>
<tr>
<td>Obesity</td>
<td>Postmenopausal hormone use</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>Calcium supplementation</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>Selenium</td>
</tr>
<tr>
<td>Family history</td>
<td>Vegetable, fruit, fiber consumption</td>
</tr>
</tbody>
</table>
Specific Clinical Risk Factors

• Prior colorectal cancer or polyps
• Inflammatory bowel disease
• Abdominal radiation
• Endometrial cancer at young age
• Gardner and / or Turcot syndrome
Mortality

• 2\textsuperscript{nd} most deadly cancer in the United States
• Rates declining since 1980
• United States has one of the highest survival rates from CRC
  – Removal of adenomatous polyps during sigmoidoscopy/colonoscopy
Mortality

Annual U.S. cancer mortality

= $14B

Annual Treatment Costs

Screening Rates

• In the United States in 2012:
  – Only 65.1% of adults (50-75 years) in the United States up-to-date with screening
  – Colonoscopy was most commonly used screening test (nearly 62%)
Factors Affecting Screening Rates

Source: Challenges and Possible Solutions to Colorectal Cancer Screening for the Undeserved, *Journal of the National Cancer Institute*, 2014.
Tests Used for Screening

• Stool Based Tests
  – Guaiac-based fecal occult blood test (gFOBT)
  – Fecal immunochemical test (FIT)
  – Cologuard

• Endoscopic and radiologic examinations
  – Flexible sigmoidoscopy
  – Colonoscopy
  – CT colonography
## Conventional Screening Tests and Performance

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CRC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colonoscopy(^1)</td>
<td>95%</td>
<td>95%</td>
</tr>
<tr>
<td>Sigmoidoscopy(^1)</td>
<td>~50% (95% distal only)</td>
<td>~50% (95% distal only)</td>
</tr>
<tr>
<td>CT Colonography(^2-4)</td>
<td>96%</td>
<td>94%</td>
</tr>
<tr>
<td><strong>AA</strong></td>
<td></td>
<td></td>
</tr>
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</tr>
<tr>
<td><strong>Non-invasive Tests</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FIT(^1)</td>
<td>70%</td>
<td>22%</td>
</tr>
<tr>
<td>gFOBT (Hemoccult SENA)(^1)</td>
<td>70%</td>
<td>24%</td>
</tr>
<tr>
<td>gFOBT (Hemoccult II)(^1)</td>
<td>40%</td>
<td>12%</td>
</tr>
</tbody>
</table>

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Invasive Tests:
Colonoscopy
Invasive Tests: Colonoscopy

• Direct visualization of entire colonic mucosa
• Ability to biopsy or excise polyps
• Sedation required
• Possible complications
Invasive Tests: Sigmoidoscopy

• Direct visualization of sigmoid colon
• Ability to biopsy or excise polyps
• No sedation necessary
• Possible complications
Alternative: Computed Tomographic Colonography

• Multiple, thin slice CT data to construct 2D and 3D images of bowel mucosa
• No biopsy / excision ability
• No sedation required
  – Images obtained during a single 32 second breath hold
Noninvasive Tests: Guaiac Fecal Occult Blood Test

- Guaiac testing of stool – identification of hemoglobin
- Stool sample can be obtained at home
- No sedation required
- No reliable indication of polyps
- False positives (affected by diet and medications)
Noninvasive Tests: Fecal Immunochemical Test

- Antibodies specific to human globin – respond to colorectal bleeding
- Stool sample can be obtained at home
- No sedation required
- No reliable indication of polyps
- Fewer false positives
## Noninvasive Tests
### FIT vs gFOBT

<table>
<thead>
<tr>
<th>Feature</th>
<th>Auto-FIT</th>
<th>Guaiac Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary Restrictions</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>Restriction on Medications</td>
<td>None</td>
<td>Yes</td>
</tr>
<tr>
<td>Number of Samples Required</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Number of Days Required for Sample Collection</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Specificity</td>
<td>99%</td>
<td>98%*</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>100%</td>
<td>50%</td>
</tr>
<tr>
<td>Patient Compliance</td>
<td>91%**</td>
<td>23%</td>
</tr>
<tr>
<td>Methodology</td>
<td>Automated</td>
<td>Manual</td>
</tr>
<tr>
<td>Specimen Container</td>
<td>Completely Closed System</td>
<td>Open System, Risk of Exposure</td>
</tr>
<tr>
<td>Collection of Sample</td>
<td>Easy, one step</td>
<td>Subject to Patient Error</td>
</tr>
</tbody>
</table>

*Denotes strict adherence to sample collection regarding diet and medications
** European J of Cancer Prevention 2006; 15: 384-390
Exact Sciences and Cologuard

A Solution for Colorectal Cancer Screening

**SENSITIVE**
92% sensitive for colorectal cancer, more sensitive than a leading FIT test* (74%)

**EASY TO USE**
Noninvasive sample collection in the privacy of the patient’s home

**24/7 Support**
Multilingual support for patients and customers

**CLINICALLY PROVEN**
Prospective, head-to-head, 90-site, point-in-time, pivotal study of 10,000 patients

**RECOMMENDED**
Covered by Medicare and included in American Cancer Society guidelines

**COMPLIANCE DRIVEN**
World-class support center dedicated to patient compliance

*Note: FIT* has a higher specificity than Cologuard (95% vs. 87%)

*OC FIT-CHEK, Polymedco, Inc.
Cologuard is intended for the qualitative detection of colorectal neoplasia associated DNA markers and for the presence of occult hemoglobin in human stool. A positive result may indicate the presence of colorectal cancer (CRC) or advanced adenoma (AA) and should be followed by diagnostic colonoscopy. Cologuard is indicated to screen adults of either sex, 50 years or older, who are at typical average-risk for CRC. Cologuard is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high risk individuals.

Cologuard is intended for use with patients, age 50 years and older, at average risk who are typical candidates for CRC screening. Cologuard was not clinically evaluated for the following types of patients:

- Patients with a history of colorectal cancer, adenomas, or other related cancers.
- Patients who have had a positive result from another colorectal cancer screening method within the last 6 months.
- Patients who have been diagnosed with a condition that is associated with high risk for colorectal cancer. These include but are not limited to: Inflammatory Bowel Disease (IBD), Chronic ulcerative colitis (CUC), Crohn’s disease, Familial adenomatous polyposis (FAP), family history of colorectal cancer, as well as patient’s diagnosed with a relevant familial (hereditary) cancer syndrome (see Cologuard labeling for more details).
Cologuard FDA Labeling

Warnings and Precautions

The performance of Cologuard has been established in a cross sectional study (i.e., single point in time). Programmatic performance of Cologuard (i.e., benefits and risks with repeated testing over an established period of time) has not been studied. Performance has not been evaluated in adults who have been previously tested with Cologuard. Non-inferiority or superiority of Cologuard programmatic sensitivity as compared to other recommended screening methods for CRC and AA has not been established.

- CRC screening guideline recommendations vary for persons over the age of 75. The decision to screen persons over the age of 75 should be made on an individualized basis in consultation with a healthcare provider. Cologuard test results should be interpreted with caution in older patients as the rate of false positive results increases with age.
- A negative Cologuard test result does not guarantee absence of cancer or advanced adenoma. Patients with a negative Cologuard test result should be advised to continue participating in a colorectal cancer screening program with another recommended screening method. The screening interval for this follow-up has not been established.
- Cologuard may produce false negative or false positive results. A false positive result occurs when Cologuard produces a positive result, even though a colonoscopy will not find cancer or precancerous polyps. A false negative result occurs when Cologuard does not detect a precancerous polyp or colorectal cancer even when a colonoscopy identifies the positive result.

A complete set of Warnings and Precautions are available at www.CologuardTest.com
Cologuard: The Science of Early Detection

- **Cologuard**
  - Detects *altered* DNA and hemoglobin
  - DNA biomarkers are *continuously* shed into stool
  - 11 biomarkers

- **Fecal Blood Test**
  - Only detects *blood* in stool
  - Cancer and precancer may *bleed intermittently*¹
  - 1 biomarker

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*OC FIT-CHEK, Polymedco, Inc.
Source: 1. Ahlgren DA et al., Cancer (1989)
Cologuard Uses 11 Biomarkers to Detect Cancer and Precancer

- 7 DNA mutation markers ($\text{KRAS}$)
- 2 DNA methylation markers ($\text{NDRG4, BMP3}$)
- 1 Hemoglobin marker
- 1 Beta-actin*

*Beta-actin serves as an internal control
Major Clinical Study Establishes Cologuard as 92% Sensitive for Colorectal Cancer

DeeP-C Clinical Study¹

- 10,000 patients
- 90 sites*

- Prospective, head-to-head, point-in-time, pivotal study
- Colonoscopy performed as the reference method for all patients
- Published in the New England Journal of Medicine
- *All sites in US except 1 in Canada

92% Cancer sensitivity (all stages)

94% Early stage cancer sensitivity (stages I-II)

87% Specificity (excludes cancer and advanced adenoma)

Head-to-head superiority for cancer and precancer detection vs. a leading fecal blood test (FIT*)

Note: FIT* has a higher specificity than Cologuard (95% vs. 87%)

**Cologuard Performance Summary**

**Pivotal Study Sensitivity Results**

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Cologuard</th>
<th>FIT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer Sensitivity</td>
<td>92.3%</td>
<td>73.8%</td>
</tr>
<tr>
<td>High Grade Dysplasia Sensitivity</td>
<td>69.2%</td>
<td>46.2%</td>
</tr>
<tr>
<td>Advanced Adenoma Sensitivity</td>
<td>42.4%</td>
<td>23.8%</td>
</tr>
<tr>
<td>Specificity</td>
<td>86.6%</td>
<td>94.9%</td>
</tr>
</tbody>
</table>

*Polymedco OC-CHEK FIT.
Collection Kit Ships Directly to Patient’s Home
### Sample Collection Process

<table>
<thead>
<tr>
<th>Step</th>
<th>Action 1</th>
<th>Action 2</th>
<th>Action 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SIT</td>
<td>Place container into bracket under toilet seat</td>
<td>Collect bowel movement</td>
</tr>
<tr>
<td>2</td>
<td>SCRAPE</td>
<td>Remove probe from tube</td>
<td>Scrape surface of stool with probe</td>
</tr>
<tr>
<td>3</td>
<td>SOAK</td>
<td>Open liquid preservative</td>
<td>Pour all liquid into container; close tightly</td>
</tr>
<tr>
<td>4</td>
<td>SHIP</td>
<td>Pack, label, and seal components in box</td>
<td>Ship to lab via prepaid UPS overnight</td>
</tr>
</tbody>
</table>
Two Convenient Ways to Order Cologuard

- SECURE FAX
- WEB PORTAL
1. **USE** a paper requisition form
   (Forms are in your Office Starter Pack. Additional requisition forms can be obtained online at CologuardTest.com)

2. **COMPLETE** the entire form, including the physician’s signature

3. **FAX** the completed form to 1-844-870-8875
How to Interpret Results

**POSITIVE:** A positive result means the test detected altered DNA and/or blood that could be caused by cancer or precancer in the colon or rectum. Any positive result should be followed by a diagnostic colonoscopy.*

**NEGATIVE:** A negative result means the test did not detect elevated levels of altered DNA and/or hemoglobin that could be caused by cancer or precancer in the colon or rectum.* It does not guarantee absence of cancer or advanced adenoma. Patients should be advised to continue participating in a colorectal cancer screening program with a recommended screening method. The screening interval for this follow-up has not been established.

*If a result cannot be obtained due to insufficient sample size, low DNA capture, etc., the lab will automatically request a second sample.*
Exact Sciences Handles All Billing and Reimbursement

**Medicare**
- Cologuard is covered by Medicare. Traditional Medicare (Part B) patients will not have any co-pays or deductible amounts.
- Medicare Advantage patients may be subject to laboratory co-pays, co-insurance or deductibles as determined by their plan.

**Private Insurance**
- Exact Sciences is seeking to have Cologuard included in private insurance coverage as soon as possible, in the meantime, we encourage patients to call their insurance company directly to answer questions about their specific benefits.
- Billed under code: **G0464**

Source: 1. National Coverage Decision released on October 9, 2014
Noninvasive Tests: Cologuard
Non-invasive Screening Options
Increase Screening Rates

![Compliance Rate Graph](image)

## Early Detection and Prevention

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonoscopy</td>
<td>Every 10 years</td>
</tr>
<tr>
<td>Computed tomographic colonography</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>Flexible sigmoidoscopy</td>
<td>Every 5 years</td>
</tr>
<tr>
<td>Fecal occult blood testing</td>
<td>Every year</td>
</tr>
<tr>
<td>Fecal immunochemical-based testing</td>
<td>Every year</td>
</tr>
</tbody>
</table>
Discontinuing Screening

- Life expectancy less than 10 years
- Adults 76-85 years without individual considerations
- Patients over 85 years
I need courage. I need a heart. I need a brain. I'm over 50. I need a colorectal exam.