Blood-based and Imaging-based Options for CRC Screening

Aasma Shaukat MD MPH Director GI Outcomes Research
Robert M. and Mary H. Glickman Professor of Medicine
Professor of Population Health
NYU Grossman School of Medicine
Objectives

• Review recent trends in Colorectal cancer (CRC) Incidence in the US
• Updates on recent evidence on CRC Screening
• Improving adherence to CRC screening
• Current and future options for CRC screening
• Take home points
CRC Mortality Over Time

CRC Incidence

When Should Screening Start For CRC?

American College of Gastroenterology
- Recommended in all adults 50 to 75 years of age
- Suggest in all average risk adults 45 to 49 years of age
- Recommend decision to screen after 75 be individualized

US Preventive Services Task Force
- Recommended in all adults 50 to 75 years of age
- Recommended in adults 45 to 49 years of age
- Recommended that clinicians selectively offer screening in adults 76-85 years of age

US Multi Society Task Force
- Suggested to all average-risk adults ages 45 to 49
- For adults ages 76 to 85, the decision to start or continue screening should be individualized and based on prior screening history, life expectancy, CRC risk, and personal preference
- Screening is not recommended after age 85

2020: Percentage of Adults 50–75 Years fully meeting USPSTF recommendation for CRC Screening, by State

Behavioral Risk Factor Surveillance System, United States, 2020

Overall screening rates are 68%

Screening rates by Race:
- Whites 71%
- AA 70%
- Asian 64%
- Hispanics

Screening rates by Health Insurance:
- Yes 71%
- No 40%

Screening rates by Regular HCP:
- Yes 73%
- No 36%

21 million adults 45-49 yrs

What do we need to Build?
And who will come?

Newly Eligible + Overdue+ never screened
Endoscopic capacity+ Access
Ensuring Health Equity

What got us here may not be enough to get us there

80% in every Community
<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity CRC</th>
<th>Sensitivity AA</th>
<th>Specificity</th>
<th>Invasive</th>
<th>USPSTF</th>
<th>Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colonoscopy</td>
<td>96%</td>
<td>95%</td>
<td>90%</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>FIT</td>
<td>74%</td>
<td>24%</td>
<td>96%</td>
<td>N</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>mtsDNA stool</td>
<td>92%</td>
<td>42%</td>
<td>87%</td>
<td>N</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Septin-9</td>
<td>48%</td>
<td>-</td>
<td>91%</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Liquid Biopsy</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>N</td>
<td>TBD</td>
<td>TBD</td>
</tr>
</tbody>
</table>
Approach to Colon Cancer Screening

1 Step Tests

2 Step tests

*Blood based*

Stool Based

Imaging based:
  CTC
  Colon Capsule

Cancer Detection

Cancer Prevention
### Preferred CRC Screening Tests Among 1,000 Unscreened Americans

<table>
<thead>
<tr>
<th></th>
<th>US MSTF Five Recommended Tests</th>
<th>US MSTF Tier 1 Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Multitarget stool DNA test</td>
<td>Fit every year</td>
</tr>
<tr>
<td></td>
<td>Colon video capsule every 5</td>
<td>Colonoscopy every 10</td>
</tr>
<tr>
<td></td>
<td>years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Colonoscopy every 10 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>FIT every year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Colon CT scan every 5 years</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Multitarget stool DNA test</th>
<th>Colon Video Capsule</th>
<th>Colonoscopy</th>
<th>FIT</th>
<th>Colon CT Scan</th>
<th>Colonoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49 yo</td>
<td>34.6%</td>
<td>28.2%</td>
<td>13.7%</td>
<td>12.2%</td>
<td>11.3%</td>
<td></td>
</tr>
<tr>
<td>≥50 yo</td>
<td>37.3%</td>
<td>22.9%</td>
<td>13.6%</td>
<td>18.7%</td>
<td>7.6%</td>
<td></td>
</tr>
</tbody>
</table>

68.9%     31.1%

77.4%     22.6%

Future Trends
Blood Based CRC screening tests
<table>
<thead>
<tr>
<th>Test</th>
<th>Details of Technology</th>
<th>Special Considerations</th>
<th>Completion</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stool and blood based</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical genomics</td>
<td>Stool and blood-based biomarker (NCT00843375) for CRC and AN</td>
<td>Study plans to recruit 1800 average risk individuals 18 years+</td>
<td>♦ 2022</td>
<td></td>
</tr>
<tr>
<td><strong>Blood-Based</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Freenome</td>
<td>Cell free DNA plus artificial intelligence for CRC and AN (NCT04369053)</td>
<td>Aims to recruit 25,000 average risk individuals between 45-85</td>
<td>♦ 2022</td>
<td></td>
</tr>
<tr>
<td>Guardant</td>
<td>ctDNA LUNAR test to detect cell free tumor DNA in blood (NCT04136002)</td>
<td>Aims to recruit 10,000 average risk individuals between 45-84 years</td>
<td>♦ 2022</td>
<td>87% sensitive, 90% specific for CRC; 12% sensitive for Adv adenoma</td>
</tr>
<tr>
<td>CancerSEEK</td>
<td>Multi-cancer detection test for 8 common cancers, including CRC Detects circulating proteins and mutations in circulating tDNA (NCT04213326) has enrolled 6399 cancer free as well as individuals with cancer, ages 50 and older since 2019</td>
<td>♦ 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GRAIL</td>
<td>♦ Multi-cancer early detection test (breast, colorectal, pancreatic, lung and hematologic malignancies)</td>
<td>♦ In validation study, specificity 99.5%, sensitivity for cancer 51.5% ♦ Ongoing prospective validation study with 6,600</td>
<td>♦ 2022</td>
<td>Available for $949. Not covered by insurance</td>
</tr>
</tbody>
</table>

Setting the Bar: CMS National Coverage Decision

Screening for Colorectal Cancer - Blood-Based Biomarker Tests

CAG-00454N

Decision Summary

The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is sufficient to cover a blood-based biomarker test as an appropriate colorectal cancer screening test once every 3 years for Medicare beneficiaries when performed in a Clinical Laboratory Improvement Act (CLIA)-certified laboratory, when ordered by a treating physician and when all of the following requirements are met:

- Sensitivity for CRC: 74%
- Specificity for CRC: 90%
- FDA approval: ✔️
Practical questions

- How ordered? → Information required
- How completed? → Navigation or not
- How collected? → Clinic, commercial lab, mobile phlebotomy, home
- How processed? → Commercial lab, central lab, regional labs
- Turn around time? → 2 days to 14 days
- Require interpretation? → Clinician or staff?
- How is follow up colonoscopy ensured?
Adherence to Blood based tests
413 randomized adults

Blood Test Arm
99.5% (CI95: 97.3%-100%)
completed test

FIT Arm
88.1% (CI95: 83.0%-91.8%)
completed test

= a difference of 11.4% (CI95: 6.9%-15.9%, p<.001)

Liles EG et al. Uptake of a colorectal cancer screening blood test is higher than of a fecal test offered in clinic: A randomized trial. 2017 Cancer Treatment and Research Communications;10: 27-31
Summary

Summary

- Screening for CRC is effective, current rates at 70%
- Programmatic approaches are needed to identify unscreened
- Adherence is key
- New blood and imaging based options under development
Thank you!