Screening Start Age in Light of New ACS Guidelines

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CRC Screening for Average-Risk Adults: 2018 Guideline Update from the American Cancer Society

• Adults aged 45 years and older with an average risk of CRC should undergo screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability.

  Qualified Recommendation

• Qualified: Clear evidence of benefit, but less certainty about the balance of benefits and harms.

On attendait Grouchy, ce fut Blücher

Victor Hugo, Les Misérables

(The expected did not occur, but the unexpected did)
Epidemiologic Evidence

- CRC incidence has declined for ≥ 50 yo
- 22% relative incidence increase in 40-49 yo between 2000-2013 (mostly left and rectal)
- Absolute risk/100,000 person-years: 5.9 to 7.2 between 2000 and 2013
- Current age-specific incidence/100,000:
  - 17.6 in 40-44 yo
  - 31.4 in 45-49 yo
  - 58.4 in 50-54 yo

Compared to a reference group of persons born in 1949, subsequent cohorts of 45-49 yo have increasing CRC incidence rate ratios.

Adults born around 1990: twice the risk of colon cancer and 4 times the risk of rectal cancer compared to those born around 1950.

Siegel et al. JNCI 2017; 109(8): djw322.
Epidemiologic Evidence

- Recent convergence in incidence rates in 50-54 yo and 55-59 yo
- Proportion of colon cancer in adults < 55 yo increased from 11.6% in 1989-90 to 16.6% in 2012-13 (rectal: 14.6% to 29.2%)
- Reasons unclear—diet/obesity?
- ACS states “not likely due to detection bias...because negligible screening and case finding occur in the youngest cohorts”

### Modeling Analyses

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<tr>
<th>SCREENING TEST</th>
<th>LYG</th>
<th>NO. OF CSY</th>
<th>MODEL RECOMMENDABLE</th>
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<td>CSY every 10 y, 45-75</td>
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<td>mt-sDNA every 3 y, 50-75</td>
<td>350</td>
<td>2331</td>
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</table>

- Updated Microsimulation models based on new epidemiologic data
- Assessed “efficiency ratios” (Δ colonoscopies/ Δ LYG)
- Colonoscopy Q 10 years from 45 to 75 yo had highest LYG with ER <45
- 50 to 45: 810 additional colonoscopies to prevent 3 additional CRC cases and 1 CRC death, per 1000 adults

Direct Evidence

• No direct empirical evidence in average-risk 45-49 yo

• FOBT RCTs did enroll younger patients but numbers small and subgroup analyses not done/published.
Epidemiologic Trends: Real or Increased Screening?

- Colonoscopy use in adults < 50 yo increased by 30% between 2001 and 2009, parallel to CRC incidence
- Consistent trend across ages, sex, geographic regions
- 40-49 yo: 1 in 30 had colonoscopy
- Reasons unclear—”spillover” effect, screening of persons with family hx, diagnostic colonoscopies

Murphy et al. Gastroenterology 2017; 152: 1809-12.
Epidemiologic Trends: Lead Time Bias?

Increase in incidence not correlated with mortality, suggesting lead-time bias

Epidemiologic Trends: Real or Increased Screening?

- Wide CIs: Uncertainty about long-term trends
- Reference group has lowest CRC rate ratio since 1890


- Average-risk screening already recommended in certain young and vulnerable populations (USMSTF: 45 yo in African-Americans).
Model Limitations

- Metric used (efficiency ratio) is not intuitive
- Surrogate measure of resources required for a unit of health benefit, but difficult to interpret clinically
- Traditional CE analysis metrics not included
- **Model assumes 100% adherence to screening**, which is unrealistic especially in younger patients (likely < 60% observed in ≥ 50 yo)
- Model does not provide “clear evidence of benefit“ as direct clinical data
  - Vaccine to 22 Million people analogy
  - Screening 22 M people to prevent 7000 new CRC cases and 1800 CRC deaths
  - Cost about $ 6 M per death averted

Potential Intended Consequences

- CRC prevention in 45-49 year age group
- CRC prevention in high-risk minority groups
- Increase in screening rates in ≥50 year age group

Potential Unintended Consequences

- Diversion of resources to lower-risk population
- Increase in screening disparities
- Substantial cost
- Lost opportunity to study screening effectiveness in younger adults
- Actual benefits may fall short of predictions

What’s next?

- USMSTF and USPSTF responses have been lukewarm
- Tailoring the new recommendation based on patient risk may help its translation and improve the balance of benefit and burden
- 45-49 year olds with additional risk factors (male, high BMI, smoking) could be targeted in risk-stratified approach
- Risk score calculators adapted for 45-49 yo in the West could help
- Consideration for less invasive screening (fecal tests, sigmoidoscopy)
- ...Insurance coverage?
