Modifiable Failures in the Colorectal Cancer Screening Process and Their Association With Risk of Death

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Disclosure

No conflicts of interest

Disclaimer:
I am a member of the U.S. Preventive Services Task Force (USPSTF). I author topics on colorectal cancer screening on UpToDate. The contents are my personal views and do not represent the views or policies of the USPSTF or UpToDate.
Outline

• Describe failures in the screening continuum over an extended period
• Discuss the association between screening failures and the risk of CRC death
• Describe interventions that could reduce failures of screening
Background

• Colorectal cancer (CRC) deaths are potentially avertable

• Deaths from CRC occur from:
  – Failure to screen or screen at appropriate intervals
  – Failure to follow-up on an abnormal result, or
  – Failure of the screening test itself

Data on patterns of failure can help improve the effectiveness and quality of screening or performance of screening programs.

Of particular importance are:

a. The relative proportions of screening process failure types in patients who died of CRC compared to CRC-free individuals
b. The risk of CRC death associated with screening process failures
c. How screening failures differ according to location in the colon

These questions were evaluated in a retrospective study in a large integrated health care delivery system in the United States.
Objectives of the study

• Describe the trajectories and failures in the screening continuum over an extended period

• Determine the association between screening failures and the risk of death from CRC

• Characterize the factors that are associated with screening failures
Methods

• **Design:** Retrospective cohort (2006-2012)
• **Setting:** Kaiser Permanente, Northern & Southern California
• **Patients:** People aged 55-90 who died from CRC and matched CRC-free controls
• **Data collection:** Receipt, results, indications, and follow-up for CRC testing over a 10-year lock-back period
Methods

• Data sources:
  – Electronic databases and detailed medical record audits in the 10 years prior to the reference date.
  – Covariates: Demographics, area-based socioeconomic measures, health care utilization histories, clinical histories, and facilities where care was received.
## Definition of screening failures

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>Descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Failure to screen</td>
<td>No screening during the 10-year period</td>
</tr>
<tr>
<td>2. Failure to screen at appropriate intervals</td>
<td>Received screening but had clinically important gaps</td>
</tr>
<tr>
<td>3. Failure to receive surveillance</td>
<td>Had polyp (pre-cancer), but did not receive surveillance</td>
</tr>
<tr>
<td>4. Failure to follow-up for positive screening</td>
<td>Had positive screening test but no timely follow-up</td>
</tr>
<tr>
<td>5. Up to date or failure of the screening test</td>
<td>No gaps, was up-to-date/follow-up after abnormal result</td>
</tr>
</tbody>
</table>

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Characteristics of the Patients

The sample was of 1,750 people who died of CRC and 3,486 CRC-free people:

- Mean age: 70 y
- Females: 49%
- NH white: 67%
- NH black: 12%
- Hispanics: 9%
- Asians/PI: 9%
## Characteristics by Failure Type

<table>
<thead>
<tr>
<th>Failure Type</th>
<th>Diagnosis Age dx (years)</th>
<th>Race/ethnicity</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>&lt;55</td>
<td>55-64</td>
<td>65-74</td>
<td>75-84</td>
<td>85+</td>
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<tr>
<td>Failures to screen</td>
<td>66.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Failure of surveillance</td>
<td>1.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Failure to follow-up</td>
<td>8.1</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Failure of screening</td>
<td>24.1</td>
<td>13.0</td>
<td>24.6</td>
<td>24.1</td>
<td>24.6</td>
<td>21.3</td>
</tr>
<tr>
<td></td>
<td>66.2</td>
<td>67.6</td>
<td>66.5</td>
<td>72.4</td>
<td>66.2</td>
<td>67.6</td>
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<tr>
<td></td>
<td>1.6</td>
<td>0.5</td>
<td>0.6</td>
<td>-</td>
<td>1.6</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>7.7</td>
<td>7.6</td>
<td>7.9</td>
<td>9.6</td>
<td>7.7</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>24.5</td>
<td>24.3</td>
<td>25.0</td>
<td>17.9</td>
<td>24.5</td>
<td>24.3</td>
</tr>
</tbody>
</table>
Most cancer deaths from failure to follow-up or failure of the screening test were in the right colon.

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Screening trajectories, classifications, and outcomes

- **Screening eligible patients**
  - Screening initiated later than recommended
    - Test was negative, but did not rescreen as recommended
    - Positive or incomplete test
      - No follow-up
    - Screening up to date/rescreened
      - Negative
      - Adenomas or malignant lesions
        - Timely diagnostic work-up
        - Normal
        - No follow-up
        - Timely follow-up
  - Did not receive screening
  - Screening initiated on time
    - No screening in the 10-year period
      - No follow-up
      - No gaps and was up-to-date/follow-up for abnormal result
      - Adenomas or malignant lesions
        - Timely diagnostic work-up
        - Normal
        - No follow-up
        - Timely follow-up
    - Received screening but had clinically important gap
      - Had abnormal result, no timely follow-up
      - Had polyp (pre-cancer), but did not receive surveillance
      - Failure to receive surveillance
    - Failure to screen at appropriate intervals
      - Failure to screen
    - Failure to receive surveillance
      - Failure of follow-up on abnormal result

10-year period of screening history

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Screening trajectories, classifications, and outcomes

<table>
<thead>
<tr>
<th>Screening eligible patients</th>
<th>Failure to screen</th>
<th>Failure to screen at appropriate intervals</th>
<th>Failure of follow-up on abnormal result</th>
<th>Failure to receive surveillance</th>
<th>Up to date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not receive screening</td>
<td>33.8 %</td>
<td>32.8 %</td>
<td>8.1 %</td>
<td>1.3 %</td>
<td>24.1 %</td>
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<tr>
<td>Screening initiated later than recommended</td>
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<tr>
<td>Test was negative, but did not rescreen as recommended</td>
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<tr>
<td>No follow-up</td>
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<td>Positive or incomplete test</td>
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<td>Screening initiated on time</td>
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<td>Screening up to date/rescreened</td>
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<tr>
<td>Negative</td>
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</tr>
<tr>
<td>Failure to receive surveillance</td>
<td>1.3 %</td>
<td>2.2 %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
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<td>Timely follow-up</td>
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<tr>
<td>Timely diagnostic work-up</td>
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<td>Adenomas or malignant lesions</td>
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<tr>
<td>Failure to receive surveillance</td>
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<td>2.2 %</td>
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<tr>
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<td>Timely follow-up</td>
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<tr>
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<td>1.3 %</td>
<td>2.2 %</td>
<td></td>
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<tr>
<td>Normal</td>
<td></td>
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<tr>
<td>Timely follow-up</td>
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<td>Timely diagnostic work-up</td>
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<tr>
<td>Adenomas or malignant lesions</td>
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<td></td>
</tr>
<tr>
<td>10-year period of screening history</td>
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</table>

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Screening trajectories, classifications, and outcomes

<table>
<thead>
<tr>
<th>Classification</th>
<th>Cases %</th>
<th>Controls %</th>
<th>OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure to screen</td>
<td>33.8</td>
<td>25.4</td>
<td>2.46 (2.08-2.91)*</td>
</tr>
<tr>
<td>Failure to screen at appropriate intervals</td>
<td>32.8</td>
<td>26.6</td>
<td>2.36 (2.00-2.78)*</td>
</tr>
<tr>
<td>Failure of follow-up on abnormal result</td>
<td>8.1</td>
<td>1.2</td>
<td>7.26 (5.26-10.03)*</td>
</tr>
<tr>
<td>Failure to receive surveillance</td>
<td>1.3</td>
<td>2.2</td>
<td>2.15 (1.24-3.73)*</td>
</tr>
<tr>
<td>Up to date</td>
<td>24.1</td>
<td>44.6</td>
<td>0.38 (0.33-0.44)**</td>
</tr>
</tbody>
</table>

*Relative to being up to date; **Relative to all other groups combined

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## What Factors are associated with failures of screening (OR)

<table>
<thead>
<tr>
<th></th>
<th>Overall, not up to date</th>
<th>Individual Failures to...</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Ever Screen</td>
<td>Screen Adequately</td>
</tr>
<tr>
<td>Age 75-84 vs. 65-74</td>
<td>1.39</td>
<td>1.79</td>
<td>1.20</td>
</tr>
<tr>
<td>Men</td>
<td>1.17</td>
<td>1.26</td>
<td>1.22</td>
</tr>
<tr>
<td>NH black vs. NHW</td>
<td>1.17&lt;sup&gt;NS&lt;/sup&gt;</td>
<td>1.12&lt;sup&gt;NS&lt;/sup&gt;</td>
<td>1.21&lt;sup&gt;NS&lt;/sup&gt;</td>
</tr>
<tr>
<td>% &lt;HS education (ref=Q1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.16</td>
<td>1.14</td>
<td>1.18</td>
</tr>
<tr>
<td>3</td>
<td>1.32</td>
<td>1.36</td>
<td>1.33</td>
</tr>
<tr>
<td>4</td>
<td>1.35</td>
<td>1.38</td>
<td>1.29</td>
</tr>
<tr>
<td>PCP Visits (&lt;3)</td>
<td>3.02</td>
<td>3.45</td>
<td>2.49</td>
</tr>
<tr>
<td>Charlson (ref=0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1.17</td>
<td>1.11</td>
<td>1.19&lt;sup&gt;NS&lt;/sup&gt;</td>
</tr>
<tr>
<td>2+</td>
<td>1.76</td>
<td>1.89</td>
<td>1.61</td>
</tr>
</tbody>
</table>

The associations varied across the healthcare facilities

Estimates are simultaneously adjusted for each variable in the table as well as length of enrollment in health plan, index year, number of health care visits during a 5-year period, and medical facility. Standard errors were from robust variance estimation based on CRC death.
Summary

• Most (76%) of the patients dying from CRC were not up to date on screening or did not receive timely follow up

• There are socio-demographic, clinical, and healthcare facility* variations in lack of screening, rescreening, and follow-up
  – Patients who traditionally have difficulties with access have higher odds of failures in the screening process

• The predominant failures and associated factors may vary across settings because of differences in screening context

*Estimates were not shown
Summary

• Being up to date on screening was associated with a 62% lower risk of dying from CRC compared to not being up to date on screening.

• Compared with patients up to date on screening, the risk of CRC death was:
  – >2-fold higher in those who did not screen/screen at appropriate interval
  – ~7-fold higher in patients who did not receive follow-up

• Most deaths from failure of the screening test were of right colon cancers.
Conclusions

• There are potential but underemphasized opportunities to further decrease avoidable CRC deaths

• Screening programs should address not just screening initiation, but also rescreening and follow-up

• Measuring and tracking screening process metrics and identifying populations with failures is critical for increasing population impact
Screening eligible patients

Screening initiated on time

- Screening initiated later than recommended
  - Test was negative, but did not rescreen as recommended
  - Positive or incomplete test
    - Had timely diagnostic work-up
      - Adenomas or malignant lesions
        - No follow-up
          - No follow-up
            - Normal
              - Failure to receive surveillance
                - Failure to screen at appropriate intervals
                  - Failure of follow-up on abnormal result
                    - Failure to screen
                      - Health Outcomes: Death from CRC

Screening up to date/rescreened

- Negative
  - No follow-up
    - Failure to receive surveillance
      - Up to date
        - Health Outcomes: Death from CRC

Classification:
- Failure to screen
  - Failure to screen at appropriate intervals
    - Failure of follow-up on abnormal result
      - Failure to receive surveillance
        - Health Outcomes: Death from CRC

Health Outcomes:
- Death from CRC: 2.46 (2.08-2.91)*
- Failure to screen at appropriate intervals: 2.36 (2.00-2.78)*
- Failure of follow-up on abnormal result: 7.26 (5.26-10.03)*
- Failure to receive surveillance: 2.15 (1.24-3.73)*
- Up to date: 0.38 (0.33-0.44)**

*Relative to being up to date; **Relative to all other groups combined

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Screening eligible patients

- Did not receive screening
- Screening initiated later than recommended
- Test was negative, but did not rescreen as recommended
- Positive or incomplete test
- No follow-up
- Adenomas or malignant lesions
- No follow-up
- Timely diagnostic work-up
- Normal
- Timely follow-up
- Negative
- Screening up to date/rescreened

Classifications

- Failure to screen
- Failure to screen at appropriate intervals
- Failure of follow-up on abnormal result
- Failure to receive surveillance
- Up to date

Health Outcomes

- Death from CRC

Measure and track performance separately for each screening failure in populations with attention to the left and right sides of the colon

Population

Screening trajectories

Classifications

Health Outcomes

Accurately identify screening eligible people

Timely initiation of screening

Regular rescreening to remain up-to-date

Quality of screening

Timely follow-up for positive/incomplete test or symptoms

Quality of treatment

Timely receipt of surveillance

Accuracy of screening

Screening process failures
Next steps…

• A failure of the screening test assumes adequate quality of the test
• There is a need to fully characterize failures of the screening test (WEO expert group classification is a starting point):
  – Missed lesions because of:
    • Operator error (lesion not visualized or perceived as not clinically important), or
      – Not visualized
      – Lesion was not resected
      – Lesion was incompletely resected
    • An inadequate exam
      – True interval cancers
• Molecularly characterize lesions that represent true interval cancers to understand the biology of those cancers
Many thanks to:

<table>
<thead>
<tr>
<th>Douglas A. Corley</th>
<th>Virginia P. Quinn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theodore R. Levin</td>
<td>Nirupa Ghai</td>
</tr>
<tr>
<td>Christopher D. Jensen</td>
<td>Ann G. Zauber</td>
</tr>
<tr>
<td>Joanne Schottinger</td>
<td>Robert H. Fletcher</td>
</tr>
</tbody>
</table>

and many more, including the patients...

“For my part I know nothing with any certainty, but the sight of the stars makes me dream”
- Vincent Van Gogh

Risk of Dying from Colorectal Cancer (CRC)

62% Lower risk of dying from CRC in patients who were up to date on screening

Distribution of screening failures in CRC deaths and CRC-free people

>2-fold higher risk of CRC death in those who were not up to date

<table>
<thead>
<tr>
<th>Category</th>
<th>CRC deaths</th>
<th>CRC-free people</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not up to date, overall</td>
<td>2.6</td>
<td>55.4</td>
</tr>
<tr>
<td>Failure to screen</td>
<td>2.5</td>
<td>25.4</td>
</tr>
<tr>
<td>... screen at appropriate intervals</td>
<td>2.4</td>
<td>26.8</td>
</tr>
<tr>
<td>Failure of surveillance</td>
<td>2.1</td>
<td>1.3</td>
</tr>
<tr>
<td>Failure of follow-up</td>
<td>7.3</td>
<td>8.1</td>
</tr>
</tbody>
</table>

*Reference group is those up to date on screening – numbers shown are the point estimates.

76% of people dying of CRC were not up to date on screening
### Association between screening patterns and CRC death, KPNC/KPSC 2006-2012

<table>
<thead>
<tr>
<th>Models and screening histories analyzed</th>
<th>Cases, n</th>
<th>Controls, n</th>
<th>OR, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model on up-to-date status:</td>
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<td></td>
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</tr>
<tr>
<td>Not up-to-date</td>
<td>1,328</td>
<td>1930</td>
<td>1.0 (Ref)</td>
</tr>
<tr>
<td>Up-to-date</td>
<td>422</td>
<td>1556</td>
<td>0.38 (0.33-0.44)</td>
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<tr>
<td>Model 3:</td>
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<tr>
<td>Up to date on screening</td>
<td>422</td>
<td>1556</td>
<td>1.0 (Ref)</td>
</tr>
<tr>
<td>Failure to ever screen</td>
<td>591</td>
<td>884</td>
<td>2.46 (2.08-2.91)</td>
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<tr>
<td>Failure to screen at appropriate intervals</td>
<td>574</td>
<td>929</td>
<td>2.36 (2.00-2.78)</td>
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<tr>
<td>Failure to receive surveillance</td>
<td>22</td>
<td>41</td>
<td>2.15 (1.24-3.73)</td>
</tr>
<tr>
<td>Failure to follow-up for abnormal test</td>
<td>141</td>
<td>76</td>
<td>7.26 (5.26-10.03)</td>
</tr>
</tbody>
</table>

Estimates from separate conditional logistic models of screening histories on risk of CRC death adjusted for race-ethnicity, SES, Charlson score, and primary care visits. Not up-to-date included failures to screen and failure to follow-up on abnormal result.

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Crude associations between failures of follow-up and CRC death in those at-risk for failure of follow-up or surveillance

<table>
<thead>
<tr>
<th>Failure type</th>
<th>Cases</th>
<th>Controls</th>
<th>OR and CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surveillance Failure</strong></td>
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</tr>
<tr>
<td>Yes</td>
<td>22</td>
<td>41</td>
<td>Ref</td>
</tr>
<tr>
<td>No</td>
<td>13</td>
<td>77</td>
<td>3.17 (1.41–7.14)</td>
</tr>
<tr>
<td><strong>Positive FOBT</strong></td>
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<tr>
<td>Yes</td>
<td>103</td>
<td>42</td>
<td>Ref</td>
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<tr>
<td>No</td>
<td>29</td>
<td>77</td>
<td>6.51 (3.50–12.10)</td>
</tr>
<tr>
<td><strong>Any abnormal or positive</strong></td>
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</tr>
<tr>
<td>Yes</td>
<td>141</td>
<td>76</td>
<td>Ref</td>
</tr>
<tr>
<td>No*</td>
<td>41*</td>
<td>156*</td>
<td>7.06 (4.30–11.58)</td>
</tr>
<tr>
<td><strong>Any abnormal or positive</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>141</td>
<td>76</td>
<td>Ref</td>
</tr>
<tr>
<td>No**</td>
<td>36</td>
<td>121</td>
<td>6.70 (4.90–9.19)</td>
</tr>
<tr>
<td><strong>Failure of follow-up or surveillance†</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>163</td>
<td>117</td>
<td>Ref</td>
</tr>
<tr>
<td>No</td>
<td>49</td>
<td>198</td>
<td>5.63 (3.67–8.63)</td>
</tr>
</tbody>
</table>

The crude or unadjusted odds ratios and 95% confidence intervals from the respective 2 X 2 contingency table cells using the STATA `tabodds`.

*This analysis included patients who were up-to-date and were at-risk for failure of both diagnostic testing and surveillance (n=40; 5 case patients and 35 control patients).

**This analysis excluded patients who were at-risk for failure both of diagnostic testing and surveillance, were up-to-date at the diagnosis date.

†Analysis included all patients flagged for follow-up or surveillance testing and included those who were also at-risk for diagnostic testing.