A once only colonoscopy? Surveillance does not add much: False.

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Colonoscopy is not an immunization.

• Among patients who have had normal colonoscopy or low risk adenomas, repeat colonoscopy is justified based on:
  – Increasing risk for CRC post colonoscopy
  – Limitations of currently available evidence
  – Opportunity for colonoscopy to further reduce risk
Scenario 1: Normal baseline colonoscopy
Relative risk for CRC after normal colonoscopy is low
But population screening decisions are better based on the absolute rather than relative risk of disease

• “The current guideline-recommended 10-year rescreening interval is not based on a predetermined risk threshold...an examination of absolute risk (incidence) could provide another justification for the timing for rescreening.”

Dr. Jeffery Lee

JAMA Int Med 2019
Absolute CRC incidence increases steadily after normal colonoscopy

Follow-up Years

Source: eTable 1, Lee JK JAMA Int Med 2019
CRC incidence reaches same threshold as for average risk individuals age 50 to 54 seven years post normal colonoscopy

Source: eTable 1, Lee JK JAMA Int Med 2019
CRC incidence beyond 12 years is uncertain

Source: eTables 1, Lee JK JAMA Int Med 2019
Modeling suggests a benefit to rescreening after normal colonoscopy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No repeat colonoscopy</th>
<th>Repeat colonoscopy</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC diagnosis per 1,000</td>
<td>31</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td>CRC death per 1,000</td>
<td>12</td>
<td>2</td>
<td>10</td>
</tr>
</tbody>
</table>

Lifetime cost: $3840 per person
Rescreening with other tests (e.g. FIT) also projected as beneficial

Knudsen Ann Int Med 2012
Scenario 2: Low risk adenoma

• 1-2 adenomas <10 mm in size
Low risk adenomas are associated with low risk for advanced neoplasia, and incident and fatal CRC

<table>
<thead>
<tr>
<th>Evidence</th>
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<tbody>
<tr>
<td><strong>Absolute risk for metachronous AN similar in patients with LRA vs normal colonoscopy</strong></td>
</tr>
<tr>
<td>• 4.9% vs. 3.3% Dube 2017</td>
</tr>
<tr>
<td><strong>CRC incidence lower among LRA patients compared to general population over 7 years f/u</strong></td>
</tr>
<tr>
<td>• SIR 0.68, 95% CI: 0.44-0.99 Cottet 2012</td>
</tr>
<tr>
<td><strong>CRC incidence and mortality in LRA patients similar to those who had no adenoma at up to 15 years f/u</strong></td>
</tr>
<tr>
<td>• Cumulative incidence 1.4 vs. 1.2% LRA vs normal group Click 2018</td>
</tr>
<tr>
<td><strong>Long term risk for fatal CRC lower among those with single LRA compared to general population</strong></td>
</tr>
<tr>
<td>• SMR 0.75, 95% CI, 0.63 to 0.88 Løberg 2014</td>
</tr>
</tbody>
</table>
Here is why I’m losing sleep...

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Concern</th>
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<tbody>
<tr>
<td>Absolute risk for metachronous AN similar Dube 2017</td>
<td><strong>Short (&lt; 5 year) follow up</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Surveillance may have contributed to favorable outcomes</strong></td>
</tr>
<tr>
<td>Incidence lower among LRA patients compared to general population Cottet 2012</td>
<td>47% exposed to colonoscopy</td>
</tr>
<tr>
<td></td>
<td>SIR 0.82 (0.41-1.47) without f/u colonoscopy</td>
</tr>
<tr>
<td></td>
<td>SIR 0.61 (0.17-1.57) with f/u colonoscopy</td>
</tr>
<tr>
<td>Incidence and mortality in LRA patients who had colonoscopy similar to those who had no adenoma Click 2018</td>
<td>Colonoscopy exposure 53.0% versus 36.9% at 5 years, and 78.1% versus 69.9% at 9 years follow-up for the LRA vs. no adenoma groups</td>
</tr>
<tr>
<td>Risk for fatal CRC lower among those with single LRA compared to general population: SMR 0.75 Løberg 2014</td>
<td>Can’t we do better?</td>
</tr>
</tbody>
</table>
Conclusion: repeat colonoscopy should be done

• After normal colonoscopy
  – Incidence over time reaches threshold for screening at baseline
  – Incidence beyond 12 years uncertain
  – Modeling suggests opportunity to further reduce CRC risk

• After diagnosis of 1 to 2 adenomas < 10 mm
  – Highly possible observed similar outcomes for low risk adenoma vs. normal colonoscopy patients or general population attributable to surveillance
  – Opportunity to further reduce risk
Thank you!
Rebuttals

• “hey Samir, most cancers that occur after normal colonoscopy or LRA occur within 3 years of baseline”
  – Not true. Cottet reported 15.4% of CRCs on f/u were diagnosed between 12 and 36 months
• “hey Samir, don’t you think it is overkill to try and reduce risk further – my data suggest the risk of dying is reduced by over 80%”
  – Argument does not work for individuals who did go on to develop/die of colon cancer
We start average risk screening at age 50: what is the rate of incident cancers at age 50?

Source: eTables 1 and 2, Lee JK JAMA Int Med 2019
Rate of incident cancers at age 50?

CRC incidence

CRC mortality

Source: eTables 1 and 2, Lee JK JAMA Int Med 2019
But...CRC risk after normal colonoscopy is substantial and clinically meaningful

Source: eTables 1 and 2, Lee JK JAMA Int Med 2019
But...CRC risk after normal colonoscopy is substantial and clinically meaningful

Source: eTables 1 and 2, Lee JK JAMA Int Med 2019
Left to do

• Literature search for additional papers
• Review normal colonoscopy and post polypectomy risk papers
• Find papers on proportion of cancers occurring in the early vs later phase post colonoscopy