Surveillance after polyp excision: outcomes, thresholds and comparators. A WEO position statement

Rodrigo Jover, on behalf of the ADSUR group
Hospital General Universitario de Alicante, SPAIN
Washington, 1-6-2018
PROJECT AIMS

• Explore and discuss which outcome measures (e.g. advanced adenomas or CRC incidence) are appropriate when conducting research or writing guidelines on adenoma/polyp surveillance.

• We would like to cover both:
  • outcome measures for the identification of patient cohorts at increased risk of CRC beyond baseline clearance colonoscopy
  • outcome measures for the assessment of whether a surveillance strategy has been effective in mitigating this increased CRC risk

• Discuss which thresholds are appropriate for each outcome measure. Thresholds that are sufficient to justify surveillance.

• Modified Delphi process
AN EARLY PROTOTYPE FOR GENERATING CLINICAL TRIAL OUTCOME SHORTCUTS.

BUT WHAT DOES IT ACTUALLY MEASURE?

THAT'S THE BEAUTY OF IT! NO ONE WILL EVER KNOW!
The primary aim of post-polypectomy surveillance is to reduce CRC incidence in patients found to have prior colon neoplasia, once adenoma clearance has been achieved.

Surveillance should only be offered to individuals who remain at higher risk of developing CRC, beyond the reduction seen by baseline adenoma clearance.

The secondary aim of CRC surveillance is to reduce CRC mortality. This is achieved both through the subsequent identification and resection of de novo adenomas and through the identification of CRC at an earlier stage.

The impact of surveillance in terms of CRC risk reduction should be balanced with the risks of harm (for example colonoscopy complications or psychological distress), the patient burden and the costs.

In a financially or endoscopy resource-constrained system, surveillance should also be considered in the context of other non-surveillance cohorts of patients who may benefit more from the same resource (opportunity cost).
Effectiveness of surveillance

Greuter, Ann Intern Med 2017
What outcome measures are appropriate?

• Outcome measure to assess surveillance effectiveness
• Outcome measure for the identification of patients cohort at risk of CRC
• Potential for bias
• Feasibility
What outcome measures are appropriate?

• Any adenoma at surveillance
• Non-advanced adenomas at surveillance
• Advanced adenomas at surveillance
• Advanced colorectal neoplasia at surveillance
• CRC at surveillance
• Long-term CRC incidence
• Long-term CRC mortality
• All-cause mortality
• Health-economic analysis
### RANDOMIZED COMPARISON OF SURVEILLANCE INTERVALS AFTER COLONOSCOPIC REMOVAL OF NEWLY DIAGNOSED ADENOMATOUS POLyps

**Sidney J. Winawer, M.D., Ann G. Zauber, Ph.D., Michael J. O'Brien, M.D., May Nah Ho, M.S., Leonard Gottlieb, M.D., Stephen S. Sternberg, M.D., Jerome D. Wake, M.D., John Bond, M.D., Melvin Schapiro, M.D., Edward T. Stewart, M.D., Joel Panish, M.D., Fred Ackroyd, M.D., Robert C. Kurtz, M.D., Moshe Shike, M.D., and the National Polyp Study Workgroup***

<table>
<thead>
<tr>
<th>FINDING</th>
<th>2 EXAMINATIONS (N = 338)</th>
<th>1 EXAMINATION* (N = 428)</th>
<th>RELATIVE RISK (95% CI)†</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any adenoma detected</td>
<td>141 (41.7)</td>
<td>137 (32.0)</td>
<td>1.3 (1.1–1.6)</td>
<td>0.006</td>
</tr>
<tr>
<td>Adenoma with advanced</td>
<td>11 (3.3)§</td>
<td>14 (3.3)</td>
<td>1.0 (0.5–2.2)</td>
<td>0.99</td>
</tr>
<tr>
<td>pathological features†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Long-Term Colorectal-Cancer Mortality after Adenoma Removal

Magnus Laerum, M.D., Mette Kalager, M.D., Ph.D., Øyvind Holme, M.D., Gair Hoff, M.D., Ph.D., Hans-Olav Adami, M.D., Ph.D., and Michael Bretthauer, M.D., Ph.D.
Incidence of advanced neoplasia during surveillance in high- and intermediate-risk groups of the European colorectal cancer screening guidelines

Advanced adenoma

CRC

Endoscopy 2016
Comparators and thresholds

• The optimal assessment of the effectiveness of a surveillance strategy requires an appropriate comparator group.

• Outcome measures should be reported in terms of absolute risk (as opposed to relative risk) wherever possible.

• The threshold for any increase in risk in the surveillance cohort should be clinically relevant, not just statistically significant.
Long-term risk of colorectal cancer after adenoma removal: a population-based cohort study

Vanessa Cottet,1,2,3 Valérie Jooste,1,2 Isabelle Fournel,1,2 Anne-Marie Bouvier,1,2,3,4,5 Jean Faivre,1,2,3 Claire Bonithon-Kopp1,2,4,5
Long-Term Colorectal-Cancer Mortality after Adenoma Removal

Magnus Leberg, M.D., Mette Kalager, M.D., Ph.D., Øyvind Holme, M.D., Geir Hoft, M.D., Ph.D., Hans-Olov Adami, M.D., Ph.D., and Michael Brettschuer, M.D., Ph.D.
Table 4. Relative Risk of Advanced Neoplasia Within 5.5 Years Based on Baseline Finding

<table>
<thead>
<tr>
<th>Baseline finding (n with examination)</th>
<th>No advanced neoplasia, n (%)</th>
<th>Advanced neoplasia, n (%)</th>
<th>RR¹</th>
<th>95% CI</th>
<th>P value</th>
<th>Cancer n (%)</th>
<th>HGD/cancer per 1000 person-y (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No neoplasia (298)</td>
<td>291 (97.6)</td>
<td>7 (2.4)</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1 (0.3)</td>
<td>0.7 (0–2.0)</td>
</tr>
<tr>
<td>Tub Ad &lt;10 mm (622)</td>
<td>584 (93.9)</td>
<td>38 (6.1)</td>
<td>2.56</td>
<td>1.16–5.67</td>
<td>.02</td>
<td>4 (0.6)</td>
<td>1.5 (0–2.9)</td>
</tr>
<tr>
<td>1 or 2 (496)</td>
<td>473 (95.4)</td>
<td>23 (4.6)</td>
<td>1.92</td>
<td>0.83–4.42</td>
<td>.13</td>
<td>3</td>
<td>1.4 (0–2.9)</td>
</tr>
<tr>
<td>&gt;3 (126)</td>
<td>111 (88.1)</td>
<td>15 (11.9)</td>
<td>5.01</td>
<td>2.10–11.96</td>
<td>&lt;.001</td>
<td>1</td>
<td>1.9 (0–5.5)</td>
</tr>
<tr>
<td>Tub Ad &gt;10 mm (123)</td>
<td>104 (84.6)</td>
<td>19 (15.5)</td>
<td>6.40</td>
<td>2.74–14.94</td>
<td>&lt;.001</td>
<td>1 (0.8)</td>
<td>6.4 (0–13.5)</td>
</tr>
<tr>
<td>Villous adenoma (81)</td>
<td>68 (83.9)</td>
<td>13 (16.1)</td>
<td>6.05</td>
<td>2.48–14.71</td>
<td>&lt;.001</td>
<td>1 (1.2)</td>
<td>6.2 (0–14.7)</td>
</tr>
<tr>
<td>HGD (46)</td>
<td>38 (82.6)</td>
<td>8 (17.4)</td>
<td>6.87</td>
<td>2.61–18.07</td>
<td>&lt;.001</td>
<td>2 (4.4)</td>
<td>26.0 (3.2–48.8)</td>
</tr>
<tr>
<td>Cancer (23)</td>
<td>15 (65.2)</td>
<td>8 (34.8)</td>
<td>13.56</td>
<td>5.54–33.18</td>
<td>&lt;.001</td>
<td>5 (21.7)</td>
<td>74.8 (14.9–134.7)</td>
</tr>
</tbody>
</table>

Number of adenomas at baseline (n)

| 1 or 2 (617) | 577 | 40 (6.5) | 7 (1.1) | 3.3 (1.2–5.5) |
| 3 or 4 (145) | 122 | 23 (15.9) | 2 (1.4) | 6.6 (0.1–13.0) |
| 5–9 (64)      | 53  | 11 (17.2) | 3 (4.7) | 13.1 (0.0–27.9) |
| 10+ (8)       | 7   | 1 (12.5)  | 0       | 0.0         |

Lieberman, Gastro 2007
What comparator is adequate in terms of longterm CRC incidence?

- General population
- Negative colonoscopy cohort
- Low-risk no surveillance cohort
- Same risk no surveillance cohort
- Local screening comparator
Which threshold of risk could be considered as clinically relevant?

• Absolute risk of CRC or advanced adenoma should be the comparator for recommending or not surveillance

• Comparison with absolute risk of CRC or advanced adenoma in the screening setting is appropriate for establish indication for surveillance

• Threshold of risk for recommending surveillance should be:
  • Long-term risk of CRC higher than in general population
  • Same risk of CRC as found in primary screening colonoscopy
  • Same risk of CRC as found in FIT + people
  • Same risk of advanced adenoma as found in FIT + people
Absolute risk of advanced adenoma and CRC after adenoma resection

- >3 adenomas
- 1 adenoma >2 cm
- 1 adenoma >1 cm
- 1-2 adenomas low risk
- Normal colonoscopy
Absolute risk of advanced adenoma and CRC

- FIT 100 ng/mL
- >3 adenomas
- 1 adenoma >2 cm
- 1 adenoma >1 cm
- 1-2 adenomas low risk
- Normal colonoscopy

CRC: colorectal cancer
Advanced adenoma
Which of these thresholds of risk could be considered as clinically relevant?

- Absolute risk of CRC at 10 years
  - Same than +ve-FIT screening
  - 3%
  - 2%
  - 1%

- Relative risk of CRC
  - 2 times general population risk
  - 1.5 times general population risk

- Absolute risk of advanced adenoma at next surveillance
  - Same than +ve-FIT screening
  - 20%
  - 15%
  - 10%

- Relative risk of advanced adenoma at next surveillance
  - 2 times general population risk
  - 1.5 times general population risk
Next steps

• Round of voting between WEO surveillance group
  • Outcomes
  • Comparator
  • Threshold

• WEO Position statement document