Evidence on the effectiveness of surveillance: What is known, evidence gaps, future research

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Outline

• UK 2002 adenoma surveillance guidelines: Lessons learned

• UK 2020 post-polypectomy surveillance guidelines
  - Updates
  - Application of the new guidelines to existing data – do they work?

• Future directions
# 2002 UK Adenoma Surveillance Guidelines

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Baseline characteristics</th>
<th>Surveillance recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk</td>
<td>1 or 2 small (&lt;1cm) adenomas</td>
<td>No surveillance, or 5 yearly</td>
</tr>
<tr>
<td>Intermediate-risk</td>
<td>3 or 4 small adenomas or 1 or 2 adenomas with at least 1 ≥1cm</td>
<td>3 yearly</td>
</tr>
<tr>
<td>High-risk</td>
<td>5+ adenomas, or 3+ adenomas with at least 1 ≥1cm</td>
<td>1 year and then 3 yearly</td>
</tr>
</tbody>
</table>

Atkin & Saunders, Gut 2002
Problems with the UK 2002 Surveillance Guidelines

- Hadn't been updated since 2002
- Lack of evidence on surveillance needs based on colorectal cancer (CRC) risk
- Colonoscopy standards have greatly improved since 2002
- Lack of evidence to inform the optimum frequency of surveillance

Any evidence that justifies fewer surveillance colonoscopies benefits patients and reduces the burden on overstretched endoscopy resources
All Adenomas Study: Aims

Aim: To assess surveillance requirements based on long-term CRC risk

Research Questions:

• What is the long-term CRC risk in patients with no surveillance?
• Does surveillance reduce CRC risk?
• Are some patients at such low risk that surveillance is not warranted?
• Does risk vary within the three risk groups?
• Do some patients require less surveillance than recommended?
• What are the cost-savings of alternative surveillance strategies?
All Adenomas Study: Methods

- Retrospective cohort study: ~250,000 patients, 17 UK NHS hospitals
- 33,000 patients diagnosed with adenomas at baseline colonoscopy
- Data extracted from electronic hospital endoscopy and pathology databases
- Follow-up data on CRC diagnoses through 2016
All Adenomas Study: Study Population

33,011 Patients with adenomas in cohort

- 4,039* Patients excluded
- 28,972 Patients available for analysis

14,401 (50%) Patients classified as low-risk
11,852 (41%) Patients classified as intermediate-risk
2,719 (9%) Patients classified as high-risk

* CRCs, resections, IBD, high-risk conditions, no adenomas, missing exam dates, risk not classifiable, lost to follow-up
### Characteristics of Each Risk Group

<table>
<thead>
<tr>
<th></th>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
</tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>14,401</td>
<td>11,852</td>
<td>2,719</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64</td>
<td>66</td>
<td>67</td>
</tr>
<tr>
<td>% female</td>
<td>44</td>
<td>44</td>
<td>29</td>
</tr>
<tr>
<td>% attended ≥1 surveillance</td>
<td>50</td>
<td>60</td>
<td>66</td>
</tr>
<tr>
<td>Years from baseline to 1st surveillance</td>
<td>3.2</td>
<td>3.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Follow-up time (years)</td>
<td>9.6</td>
<td>9.1</td>
<td>8.4</td>
</tr>
<tr>
<td>CRCs diagnosed</td>
<td>195</td>
<td>246</td>
<td>84</td>
</tr>
<tr>
<td>CRC incidence rate/100,000 person years</td>
<td>140</td>
<td>221</td>
<td>366</td>
</tr>
</tbody>
</table>
Patients at Highest Risk Within Each Group

<table>
<thead>
<tr>
<th>Baseline Risk Factors</th>
<th>Low Risk (n=14,401)</th>
<th>Intermediate Risk (n=11,852)</th>
<th>High Risk (n=2,719)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete colonoscopy</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Adenoma w/ villous growth pattern</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal polyps</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Adenoma with high-grade dysplasia</td>
<td></td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Patients at highest risk within each group</td>
<td>9,166 (64%)</td>
<td>7,114 (60%)</td>
<td>902 (33%)</td>
</tr>
</tbody>
</table>
Cumulative CRC Incidence (censored at 1st surveillance)

**Low-Risk**

- Higher-risk: 2.1% (incomplete, villous, prox)
- Lower-risk: 1.2% at 10yrs

**Intermediate-Risk**

- Higher-risk: 3.7% (incomplete, prox, HGD)
- Lower-risk: 1.3% at 10yrs

**High-Risk**

- Higher-risk: 9.9% (incomplete; HGD)
- Lower-risk: 3.8% at 10yrs

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Cross et al., Long-term colorectal cancer incidence after adenoma removal & the effects of surveillance on incidence: a multicentre, retrospective, cohort study. Gut, 2020
Low-Risk Group: Results

**WHOLE LOW-RISK GROUP**

1 surveillance visit: 45% reduction in CRC risk

No surveillance: CRC risk similar to gen pop: SIR=0.86 (0.73-1.02)

**LOWER-RISK SUBGROUP**

1 surveillance visit: Surveillance did not significantly affect CRC risk

No surveillance: CRC risk half that of general pop: SIR=0.51 (0.35-0.73)

**HIGHER-RISK SUBGROUP**

1 surveillance visit: 48% reduction in CRC risk

No surveillance: CRC risk similar to general pop: SIR=1.07 (0.88-1.28)

Cross et al., Long-term colorectal cancer incidence after adenoma removal & the effects of surveillance on incidence: a multicentre, retrospective, cohort study. Gut, 2020
Intermediate-Risk Group: Results

**WHOLE INTERMEDIATE-RISK GROUP**

1 surveillance visit: 42% reduction in CRC risk

No surveillance: CRC risk similar to gen pop: SIR=1.16 (0.97-1.37)

**LOWER-RISK SUBGROUP**

1 surveillance visit: Surveillance did not significantly affect CRC risk

No surveillance: CRC risk 30% lower than gen pop: SIR=0.70 (0.48-0.99)

**HIGHER-RISK SUBGROUP**

1 surveillance visit: 47% reduction in CRC risk

No surveillance: CRC risk 1.5 times higher than gen pop: SIR=1.46 (1.19-1.78)

Cross et al., Long-term colorectal cancer incidence after adenoma removal & the effects of surveillance on incidence: a multicentre, retrospective, cohort study. Gut, 2020
High-Risk Group: Results

**WHOLE HIGH-RISK GROUP**

**1 surveillance visit:**
49% reduction in CRC risk

**No surveillance:**
CRC risk 1.9 x higher than gen pop: SIR=1.91 (1.39-2.56)

**LOWER-RISK SUBGROUP**

**1 surveillance visit:**
Surveillance did not significantly affect CRC risk

**No surveillance:**
CRC risk similar to that of gen pop: SIR=1.10 (0.64-1.76)

**HIGHER-RISK SUBGROUP**

**1 surveillance visit:**
59% reduction in CRC risk

**No surveillance:**
CRC risk 3.6 times higher than gen pop: SIR=3.55 (2.34-5.17)

Cross et al., Long-term colorectal cancer incidence after adenoma removal & the effects of surveillance on incidence: a multicentre, retrospective, cohort study. Gut, 2020
All Adenomas Study: Findings

• Colonoscopy surveillance benefits most patients with adenomas

• However, a large proportion do not remain at increased CRC risk post-polypectomy, including:
  - The low-risk group
  - Intermediate-risk patients with a complete baseline colonoscopy and no adenomas with HGD or proximal polyps

  **Surveillance is probably not necessary for these patients**

• Risk of CRC remains elevated post-polypectomy among:
  - The high-risk group
  - Intermediate-risk patients with an incomplete baseline colonoscopy, adenomas with HGD, or proximal polyps

  **Surveillance is warranted for these patients**

Cross et al., Long-term colorectal cancer incidence after adenoma removal & the effects of surveillance on incidence: a multicentre, retrospective, cohort study. Gut, 2020
2020 UK Post-Polypectomy Surveillance Guidelines

High-risk findings
- ≥2 premalignant polyps, of which ≥1 is large (≥1cm) or has high-grade dysplasia
- ≥5 premalignant polyps
- 1 large (≥20mm) non-pedunculated polyp

Colonoscopy

High-risk findings?

NO
- No surveillance. Participate in screening

YES
- Surveillance colonoscopy after 3 years
Study Population

- **33,011** Patients with adenomas in cohort
- **11,693*** Patients excluded
- **21,318** Patients available for analysis
- **15,079 (71%)** Patients classified as low-risk
- **6,239 (29%)** Patients classified as high-risk

*CRCs, resections, IBD, high-risk conditions, no adenomas, missing exam dates, risk not classifiable, lost to follow-up (all as before)
PLUS: Incomplete baseline colonoscopy, poor bowel prep
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Cumulative CRC Incidence (censored at 1st surveillance)

**Effect of surveillance on CRC risk**

- **High-risk:**
  - HR for 1 surveillance: 0.73 (0.51-1.05)
  - HR for ≥2 surveillance: 0.42 (0.27-0.66)

- **Low-risk:**
  - HR for 1 surveillance: 0.57 (0.40-0.81)
  - HR for ≥2 surveillance: 0.48 (0.30-0.75)

**SIR: compared to general population**

- **High-risk:**
  - After baseline, no surv: 1.30 (1.03-1.62)
  - After 1st surv: 1.22 (0.91-1.60)

- **Low-risk:**
  - After baseline, no surv: 0.75 (0.63-0.88)
  - After 1st surv: 0.54 (0.42-0.68)

HR, hazard ratio; SIR, standardised incidence ratio

Cross et al., Colorectal cancer risk following polypectomy in a multicentre, retrospective, cohort study: an evaluation of the 2020 UK post-polypectomy surveillance guidelines. Gut, 2021
Surveillance Colonoscopy is not Perfect

- Not 100% sensitive
- Expensive
- Increased demand with bowel cancer screening programme
- Complications associated with 1-2% of procedures
- Invasive, inconvenient (patients’ perspective)
- Advanced adenomas and cancer in small proportion of exams
- Suggested that >50% of CRCs detected after colonoscopy are the result of missed lesions

- BUT CURRENTLY THERE ARE NO VIALBLE ALTERNATIVES

Future

- Little data on on-going surveillance and CRC incidence
  - Who needs ongoing surveillance?
  - How much benefit is conferred by ongoing surveillance?
  - Should surveillance continue until 1 or 2 consecutive negative colonoscopies?
  - Should recommendations for 2nd surveillance (SV2) be based on SV1 findings only?
  - The effect of interval between surveillance exams
- Understanding barriers & facilitators to adherence to surveillance guidelines (patients/clinicians)
- Age – those below screening entry and when to discontinue in the older age groups
Take home messages

Surveillance reduces CRC risk

Unnecessary in some post-polypectomy patients

Consider CRC risk relative to gen pop

Intervals?

Ongoing surveillance?

Adherence?

Age?
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All 17 hospitals and patients