In post-polypectomy surveillance, are we asking questions that are ‘overly-cautious’?

David F. Ransohoff
Michael Bretthauer
Hans-Olov Adami
Background

EPoS is only the 2nd RCT of surveillance intervals.
The 1st RCT (NPS; NEJM 1993) asked, in retrospect, an ‘overly-cautious’ question (q1 and q3yr f/u vs q3yr)
Will EPoS ask an overly-cautious question, too?

Challenge in 2016
Can we anticipate ‘next’ questions, less ‘overly-cautious,’ that EU/EPoS might address?

Comment
The most-important questions likely cannot be answered in US, because of intense pressure to be ‘overly-cautious’.
'Overly-cautious question’
What is it, and why important?

Definition/Importance
• When surveillance intervals studied are too short (e.g., in 2016 for low-risk group with 1-2 small (<1cm) adenomas), then we can’t tell if longer intervals work, like happened in NPS 1993.
• If guidelines and behavior get ‘set’ based on ‘overly-cautious’ question, then it becomes impossible to even study longer intervals.
‘Overly-cautious question’
What is it, and why important?

Status in 2016

• Some evidence suggests that a ‘low-risk’ group can have follow-up surveillance in 10 yrs:
  - Atkin (NEJM 1992)
  - Loberg (NEJM 2014)
  - Wieszczy (submitted, 2016)

• But, in USA, guidelines for ‘low risk’ are 5-10 yrs; practice behavior is more aggressive than guidelines. In USA, it is hard to study ‘longer’ intervals.
Practice (in USA) for “low risk” persons is aggressive

**Approach:** Colonoscopy reports were examined, in doctors’ offices, to learn, for persons with first-time screening colonoscopy, how surveillance interval relates to #/size/histology.
In USA, even single tiny adenoma (<5mm), good prep, may get aggressive follow-up.
'Overly-cautious question’
What is it, and why important?

Status in 2016

• While EPoS studies a ‘low-risk’ group getting q10yr follow-up, some new ‘forces’ may make studying this group irrelevant overly-cautious, like NPS (NEJM 1993).

• So when EPoS is done, will we regret having been overly-cautious?
**EPoS**

**I** Low-risk adenomas
13,746 patients

**EPoS II** High-risk adenomas
13,704 patients

**EPoS III** Serrated polyps

1:1 randomization

Surveillance colonoscopy

10 years

Final colonoscopy
New forces in 2016 may make EPoS’ question overly-cautious: *Upstaging*

Upstaging of ‘low-risk’ persons (1-2 small adenomas) happens when new and more-intensive diagnostic approaches (like focus on ADRs, better scopes) cause ‘reclassification’ of persons previously with ‘low-risk’.

---

**THE WILL ROGERS PHENOMENON**

Stage Migration and New Diagnostic Techniques as a Source of Misleading Statistics for Survival in Cancer

Alvan R. Feinstein, M.D., Daniel M. Sosin, M.D., and Carolyn K. Wells, M.P.H.

Abstract  We found that a cohort of patients with lung cancer first treated in 1977 had higher six-month survival rates for the total group and for subgroups in each of the three main TNM stages (tumor, nodes, and metastases) than a cohort treated between 1953 and 1964 at the same institutions. The more recent cohort, however, had undergone many new diagnostic imaging procedures. According to the “old” diagnostic data for both cohorts, the recent cohort had a prognostically favorable “zero-time shift.” In addition, by demonstrating metastases that had formerly been silent and unidentified, the new technological data resulted in a stage migration. Many patients who previously would have been classified in a “good” stage were assigned to a “bad” stage. Because the prognosis of those who migrated, although worse than that for other members of the good-stage group, was better than that for other members of the bad-stage group, survival rates rose in each group without any change in individual outcomes. When classified according to symptom stages that would be unaltered by changes in diagnostic techniques, the two cohorts had similar survival rates. (N Engl J Med 1985; 312:1604-8.)
New forces: how upstaging could occur in EPoS
(‘black arrow’ shows reclassification/upstaging caused by better technology and focus on ADRs)

Net result: Both ‘low-risk’ and ‘high-risk’ groups contain lower risk persons; for persons now called ‘high-risk’ we lose opportunity to study long interval.
New forces: how upstaging could occur in EPoS
(‘black arrow’ shows reclassification/upstaging caused by better technology and focus on ADRs)

Net result: Both ‘low-risk’ and ‘high-risk’ groups contain lower risk persons; for persons now called ‘high-risk’ we lose opportunity to study long interval.
One way to deal with upstaging:
Take some out of the ‘high-risk’ group and classify as ‘low-risk’, getting q10 yr exam (not feasible in 2016).

**Challenges: Which persons? Are we at equipoise?**
Beyond 2016: What is needed to set the stage about importance, feasibility?

• What questions do we really want to ask (if we could not be overly-cautious)?
  Pretend we are king or queen of the world.

• Can we formulate question/design of ‘next’ study now
  ... using EPoS infrastructure, instead of waiting 25yr for the ‘next’ RCT, like the 25yr from NPS to EPoS?

• Challenges
  - Are we really at equipoise?
  - Will docs, patients, funders participate? (USA: doubtful)
  - Are we really prepared to propose this?