Endpoints for Surveillance studies

Prof. Michael Bretthauer MD, PhD
Oslo University Hospital and University of Oslo
Frontier Science, Boston
Screening and what comes with it

• Screening programmes introduced «everywhere»
• Colonoscopy rates up
• More and more individuals diagnosed with polyps (and cancer)
• Need for surveillance
General Themes for Controversies in Surveillance

1. Who needs it
   - Who is at higher risk
   - What is the benefit-harm ratio

2. Best surveillance for those who need it
   - What tests
   - Which interval

3. How to measure it
   - Number of detected lesions (adenomas, cancer)
   - Recurrence (curative intent)
   - CRC-specific survival
   - All-cause survival, mortality
Some general issues to be aware of

• Lead time
• Length time
• Overdiagnosis
Lead time and overdiagnosis bias

• Overdiagnosis: detection of lesions which would not have been detected (patient died from) in remaining lifetime
  – Adenomas: big numbers, small harm
  – CRC: smaller numbers (?), more harm

• Lead time bias and survival
  – Two volunteers
Length-time bias

Size at which cancer causes death

Size at which cancer causes symptoms

Abnormal cell

Time

Screening

Length-time

Death from other causes

Very Slow

Non-progressive

Slow

Fast

Overdiagnostikk
Endpoints in Surveillance studies

• Polyps
• Advanced polyps
• Advanced lesions (polyps and cancer)
• Recurrences
• Cancer incidence
• Cancer mortality
• All-cause death/survival

• Compared to what, when?
  – Valid control groups

• Study design (Cesare)
Evaluation of effect: valid control groups

Challenge:
• Valid control groups
  • Risko factors
  • Treatment
  • Awareness
  \[ \text{Changes over time} \]
In an observational setting: four-group comparison

Mortality from breast cancer women aged 50-69 years in the four groups

Endpoints in Surveillance studies

- Polyps
  - Overdiagnosis, risk for progression, time
- Advanced polyps
  - Overdiagnosis, risk for progression, time, n
- Advanced lesions (polyps and cancer)
  - Just don’t! (I know it is tempting)
- Recurrence
  - Of the above and more harm at tx, does it matter?
- Cancer incidence
  - Good, but make sure time is similar vs. Last intervention; n
- Cancer mortality
  - no lead time, overdiagnosis bias, but N, and surveillance is about incidence, isn’t it?
- All-cause
One more thing

- If you want to count cancer stage
  - Do it right (overdiagnosis)
  - More early cancer, less late cancer
  - More early cancer, equal late cancer
EPoS
European Polyp Surveillance Trial
EPoS trials
European Polyp Surveillance

EPoS I
Low risk adenomas
13,746 patients

EPoS II
High risk adenomas
13,704 patients

EPoS III
Serrated polyps
observation

1:1 randomization

0 years

3 years

Surveillance colonoscopy
Surveillance colonoscopy
Surveillance colonoscopy
Surveillance colonoscopy

5 years

10 years final colonoscopy

10 years