INCREASED SCREENING CUT-OFF LEVELS AND IMPACT OF A PLASMA PROTEIN ALGORITHM..??

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CONFLICTS OF INTERESTS

- Abbott Laboratories Inc., Chicago, USA
- Applied Proteomics Inc., San Diego, USA
- EDP Biotech Inc., Knoxville, USA
- VolitionRX, Isnes, Belgium

CRC SCREENING IN DENMARK

- out-reach FIT test
- results 01.04.2014 – 31.12.2015 (31.12.2016)
- invited 886,122 – (50-74 years of age)
- compliance 63.6%
- 6.8% FIT positives
- 89% accepted colonoscopy (CT-/MR colonography)
- 2,041 CRC
- 10,566 HRA / MRA (new European classification)

FIT SCREENING IN DENMARK

- additional colonoscopies due to screening
- cut-off: 100 ng/ml (OC-sensor)
- 1st round: 4 years – 2014 – 2017 (implementation)
- 18,000 colonoscopies/year
- 2nd round: 2 years – from January 2018
- 34,500 colonoscopies/year
- plus re-colonoscopies – HRA (1y) and MRA (3ys)
- sufficient capacity…???

REDUCTION OF COLONOSCOPIES ?

• The Netherlands	250 ng/ml
• Sweden	200 ng/ml – women
• Sweden	400 ng/ml – men
• Scotland	400 ng/ml
• Valencia, Spain	300 ng/ml

REDUCTION OF COLONOSCOPIES ?

- The Netherlands 250 ng/ml
- Sweden 200 ng/ml – women
- Sweden 400 ng/ml – men
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- Valencia, Spain 300 ng/ml
- miss a lot of CRC + HRA + MRA

REDUCTION OF COLONOSCOPIES ?

• The Netherlands	250 ng/ml
• Sweden	200 ng/ml – women
• Sweden	400 ng/ml – men
• Scotland	400 ng/ml
• Valencia, Spain	300 ng/ml
• other options…??	

ENDOSCOPY III, PART 1

- 01.04.14 – 31.08.16 (29 months)
- 8,415 FIT positive + colonoscopy
- 5,118 FIT negative – colonoscopy
- 8 Danish hospitals
- 16 research nurses
- 90 mls of blood
- 24 vials of serum, EDTA plasma, buffy-coats
- data from colonoscopy of every FIT+

ENDO III, PART 1 - BIOMARKERS

- proteins
- glycosylated proteins
- proteomics
- ctDNA: mutations – methylations
- nucleosomes, histone modifications
- metabolomics
- immune components – complement activity
- coagulation factors

ENDOSCOPY III, PART 1

- 8,415 FIT positives + colonoscopy
  - 100≤ FIT ≤200 ng/ml
    - 2,629 subjects – no colonoscopy (32.4%)
    - 1,481 no findings

ENDOSCOPY III, PART 1

- 8,116 FIT positives + colonoscopy
  - 100≤ FIT ≤200 ng/ml
    - 2,629 subjects – no colonoscopy (32.4%)
    - 1,481 no findings
    - 47 CRC
    - 201 HRA
    - 375 MRA
    - 525 LRA (new screening in 8 years)

ENDOSCOPY III, PART 1

- 8,116 FIT positives + colonoscopy
  - 100≤ FIT ≤200 ng/ml
    - 2,629 subjects – no colonoscopy (32.4%)
    - 1,481 no findings

Considerations…!!

Triage test…??

- 525 LRA (new screening in 8 years)

TRIAGE – HOW COME..??

1. risk of lesions correlates with age
2. risk of lesions correlates with FIT blood conc.
3. risk of lesions associated with blood biomarkers

4. Triage test: 1 + 2 + 3 = +/- colonoscopy

Phallen J, et al. Science Transl Med 2017
Wilhelmsen M, et al. Int J Cancer 2017
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   protein profiles, ctDNA, nucleosomes, metabolomes

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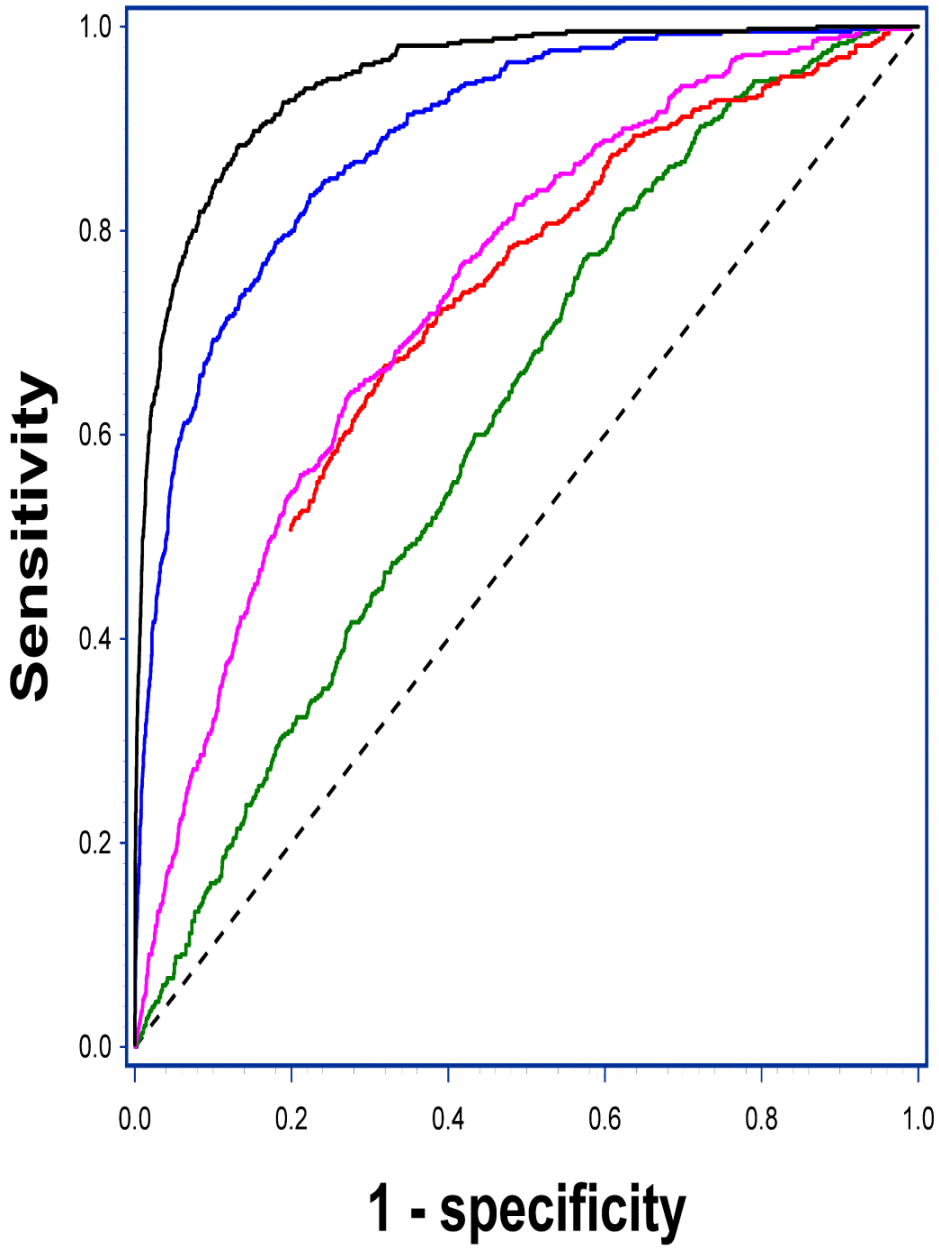
Sensitivity
1 - specificity
0.0
0.2
0.4
0.6
0.8
1.0

TRIAGE – IN GENERAL

why triage…??

requirements for colonoscopy > capacity

1. **screening directed colonoscopy**
2. **adenoma control colonoscopy**
3. **diagnostic colonoscopy**

TRIAGE – IN GENERAL

why triage…??

requirements for colonoscopy > capacity

1. **screening directed colonoscopy** **≈40% lesions**
2. **adenoma control colonoscopy** **<20% lesions**
3. **diagnostic colonoscopy** **≈30% lesions**

TRIAGE – IN GENERAL

1. Triage protocol - 750 FIT+ subjects - ongoing
2. Endoscopy IV - 5,000 adenoma control colonoscopy
3. Endoscopy V - 5,000 diagnostic colonoscopy

Overall aim: to reduce numbers of colonoscopies 30%

- benefit for the colonoscopy capacity
- benefit for the health budgets
- in particular, benefit for those who don't need colonoscopy

COLLABORATORS

- Amager, BBH, Herlev, Herning, Hillerød, Holstebro, Horsens, Hvidovre, Randers, Silkeborg, Viborg
- Screening sekretariats: Rønne (Capital Region) og Randers (Central Jutland Region)
- University of Copenhagen, Frederiksberg (Bro)
- University of Aarhus, Skejby Hospital – MoMA (Andersen)
- Herlev Hospital, Capital Region (Johansen)

- University of Ljubljana (Kos)
- VUMC, Amsterdam (Martens)
- University College London (Beck)

- MD Anderson Cancer Center, Houston, TX (Bresalier)
- University of North Carolina, Chapel Hill, NC (Ransohoff)
- EDRN - National Cancer Institute, Bethesda, MD (Lampe, Bresalier)
- Johns Hopkins Sidney Kimmel Medical School, Baltimore, MD (Velculescu)
- University of Pittsburgh, Pittsburgh, PA (Schoen)
- Fred Hutchinson Cancer Research Center, Seattle, WA (Lampe)

- Prince of Wales and St. George Hospitals, Sydney, Australia (King)

- Abbott Laboratories Inc., Chicago (Davis, Gawel)
- Applied Proteomics Inc., San Diego (Wilcox)
- ATGen Canada, Quebec (Benito)*
- EDP Biotech Inc., Knoxville (Mayer)
- Volition, Belgium (Micallef, Michel)