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
- 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)
- 1\textsuperscript{st} round: 4 years – 2014 – 2017 (implementation)
- 18,000 colonoscopies/year
- 2\textsuperscript{nd} round: 2 years – from January 2018
- 34,500 colonoscopies/year
- plus re-colonoscopies – HRA (1y) and MRA (3ys)
- sufficient capacity...???

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### REDUCTION OF COLONOSCOPY?

<table>
<thead>
<tr>
<th>Location</th>
<th>Recommended Level</th>
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</thead>
<tbody>
<tr>
<td>The Netherlands</td>
<td>250 ng/ml</td>
</tr>
<tr>
<td>Sweden</td>
<td>200 ng/ml – women</td>
</tr>
<tr>
<td>Sweden</td>
<td>400 ng/ml – men</td>
</tr>
<tr>
<td>Scotland</td>
<td>400 ng/ml</td>
</tr>
<tr>
<td>Valencia, Spain</td>
<td>300 ng/ml</td>
</tr>
</tbody>
</table>

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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
- *miss a lot of CRC + HRA + MRA*
REDUCTION OF COLONOSCOPY?

- 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...??

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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
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    - 1,481 no findings
    - 47 CRC
    - 201 HRA
    - 375 MRA
    - 525 LRA (new screening in 8 years)

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Considerations...!!

Triage test...??

- 525 LRA (new screening in 8 years)
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

Lee YC, et al. JNCI 2017
Torre LA, et al. CA Cancer J Clin 2015
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
   protein profiles, ctDNA, nucleosomes, metabolomes

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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)