

# ESTABLISHMENT OF AN ALGORITHM TO REDUCE THE NUMBERS OF FIT SCREENING DIRECTED COLONOSCOPIES ??

Hans Jørgen Nielsen, MD, DMSc,  
Professor of Surgical Oncology,  
Department of Surgical Gastroenterology,  
Hvidovre Hospital, University of Copenhagen,  
Hvidovre, Denmark.

[www.colorectalcancer.dk](http://www.colorectalcancer.dk)



# 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**



# FIT SCREENING IN DENMARK

- additional colonoscopies due to screening
- **cut-off: 100 ng/ml (OC-sensor)**
- **1<sup>st</sup> round: 4 years – 2014 – 2017 (implementation)**
- **18,000 colonoscopies/year**
- **2<sup>nd</sup> 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
- Scotland 400 ng/ml
- 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





# 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
  - $100 \leq \text{FIT} \leq 200$  ng/ml
    - 2,629 subjects – no colonoscopy (32.4%)
    - 1,481 no findings



# ENDOSCOPY III, PART 1

- 8,116 FIT positives + colonoscopy
  - $100 \leq \text{FIT} \leq 200$  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
  - $100 \leq \text{FIT} \leq 200$  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

Lee YC, et al. JNCI 2017

Rho JH, et al. Gut 2016

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

Phallen J, et al. Science Transl Med 2017

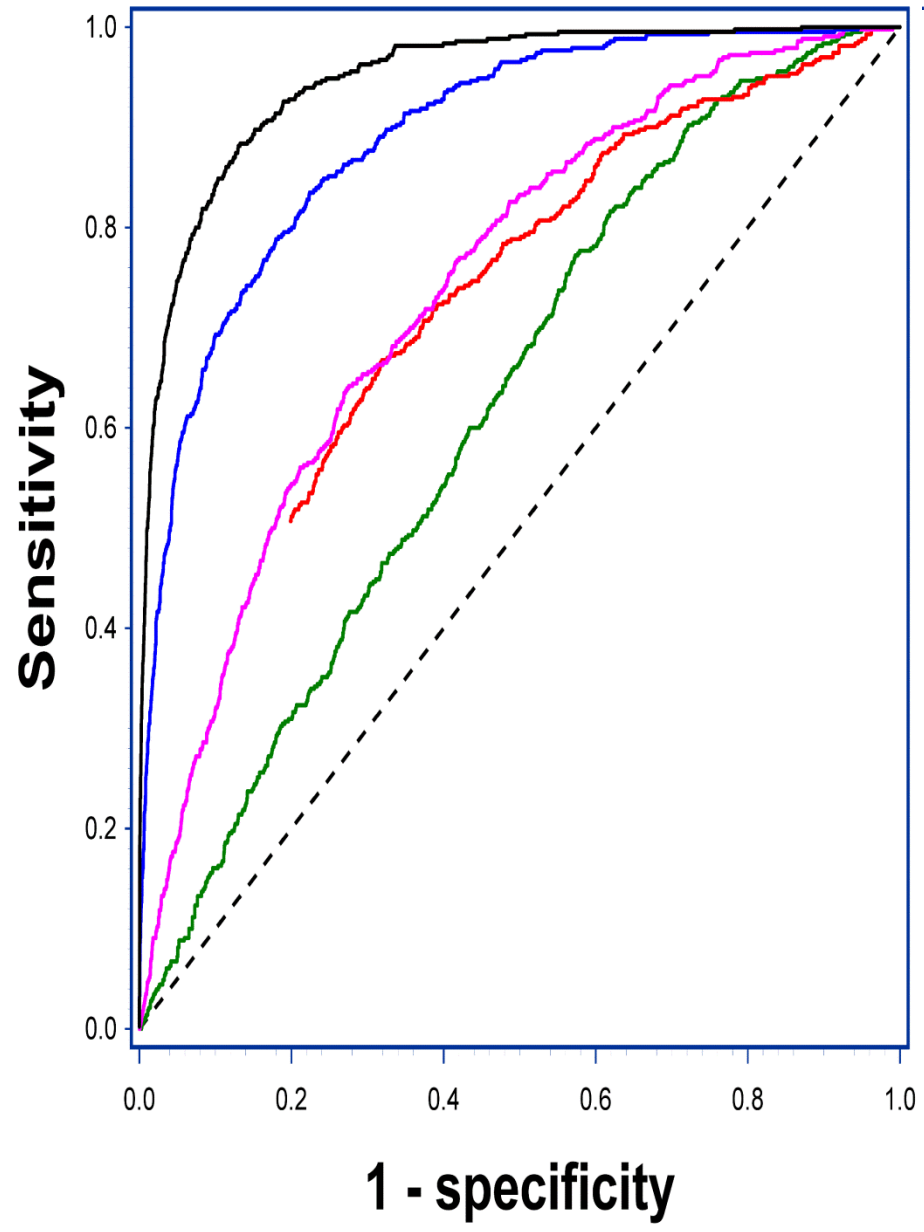
Wilhelmsen M, et al. Int J Cancer 2017

Lee YC, et al. JNCI 2017

Rho JH, et al. Gut 2016

Torre LA, et al. CA Cancer J Clin 2015





# TRIAGE – IN GENERAL

---

why triage.....requirements for colonoscopy > capacity

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





# TRIAGE – IN GENERAL

1. screening directed colonoscopy – 40% lesions
2. adenoma control colonoscopy – 25% lesions
3. diagnostic colonoscopy - 30% lesions



# TRIAGE – IN GENERAL

1. Triage protocol - 750 subjects w. pos FIT - 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)
- EDP Biotech Inc., Knoxville (Mayer)
- Exiqon A/S, Vedbaek (Mouritzen)
- Volition, Belgium (Micallef, Michel)

