



# **Comparative effectiveness studies of flexible sigmoidoscopy and other colorectal cancer screening exams**

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**Ernst J Kuipers**

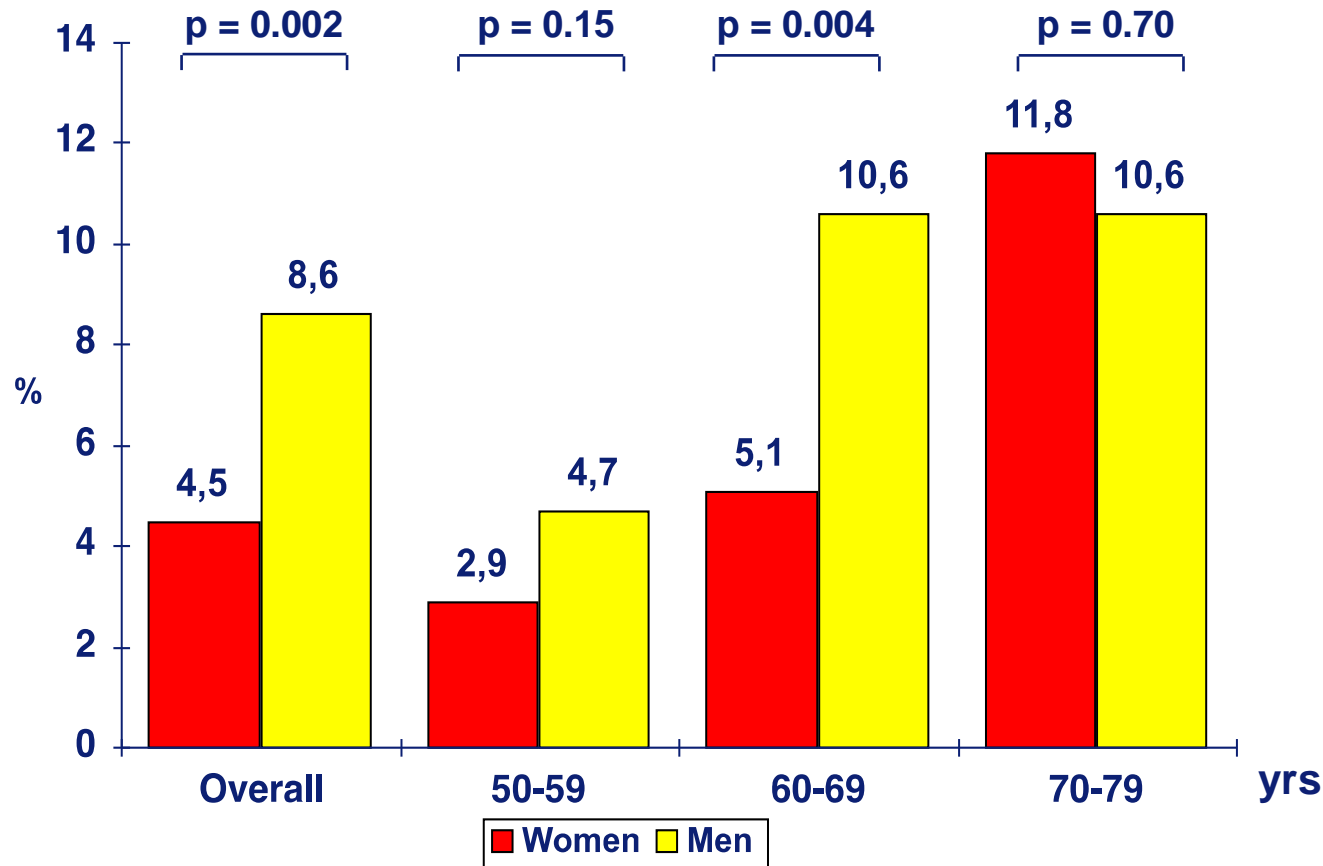
**Departments of Internal Medicine and  
Gastroenterology and Hepatology  
Erasmus University Medical Center  
Rotterdam - The Netherlands**

# Colorectal cancer screening reduces incidence and mortality; historical evidence

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- 3 randomized controlled trials of gFOBT screening
  - published 1992 - 1996
  - average 18% CRC **mortality** reduction
  - *gold standard of RCT*

# Prevalence of advanced neoplasia among men and women with a negative FOBT and no family history of colon cancer



Schoenfeld et al. NEJM 2005; 352: 2061

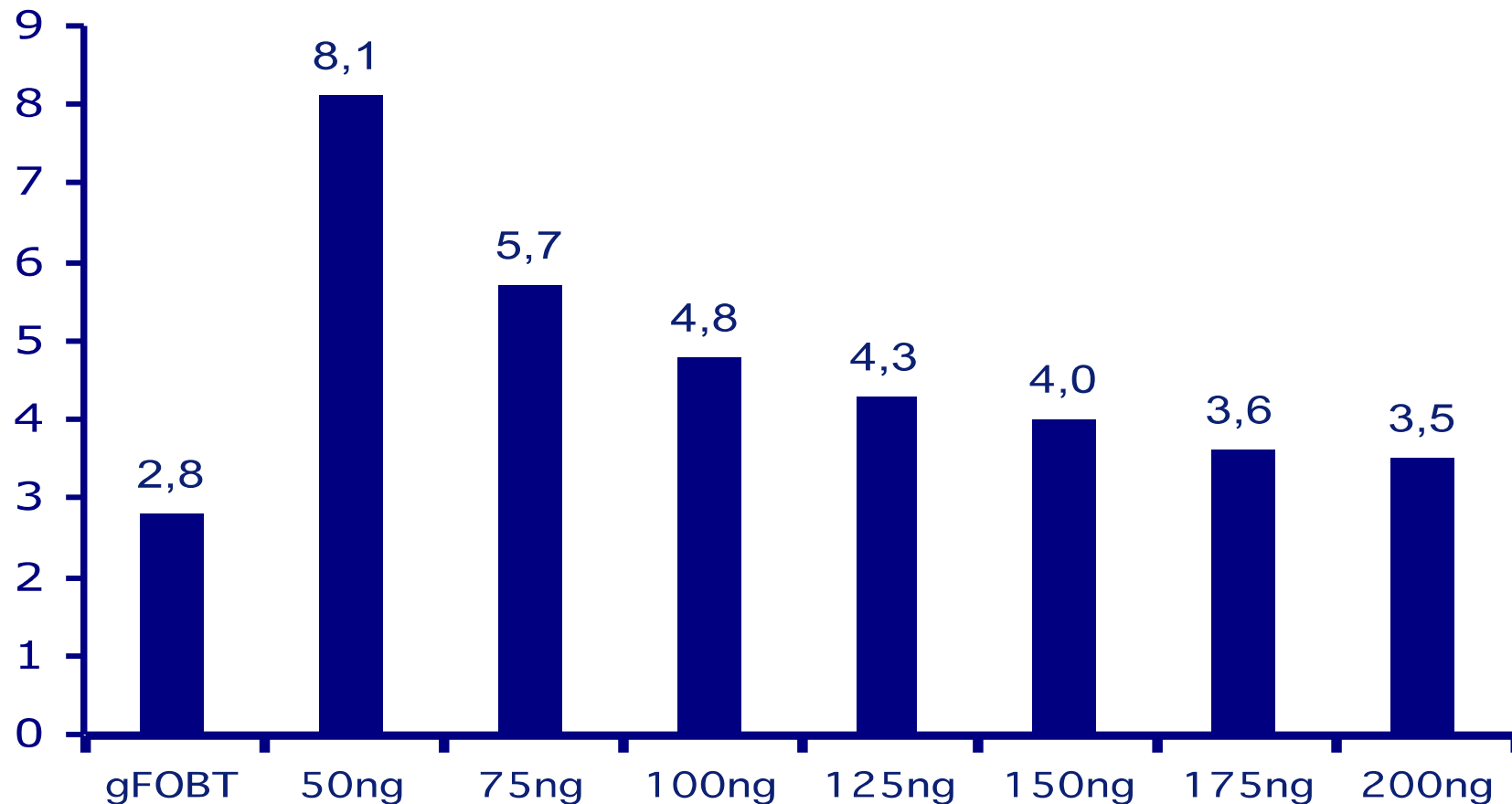
## Rotterdam screening trial in 15.013 average risk screening-naïve individuals aged 50 – 74 years

	% Adherence	% positive test	% true positives*	True positives per 1000 invited
gFOBT	50	2.8	45	6
FIT <sup>50</sup>	62	8.1	42	21
Sigmoidoscopy	32	10.2	100	33

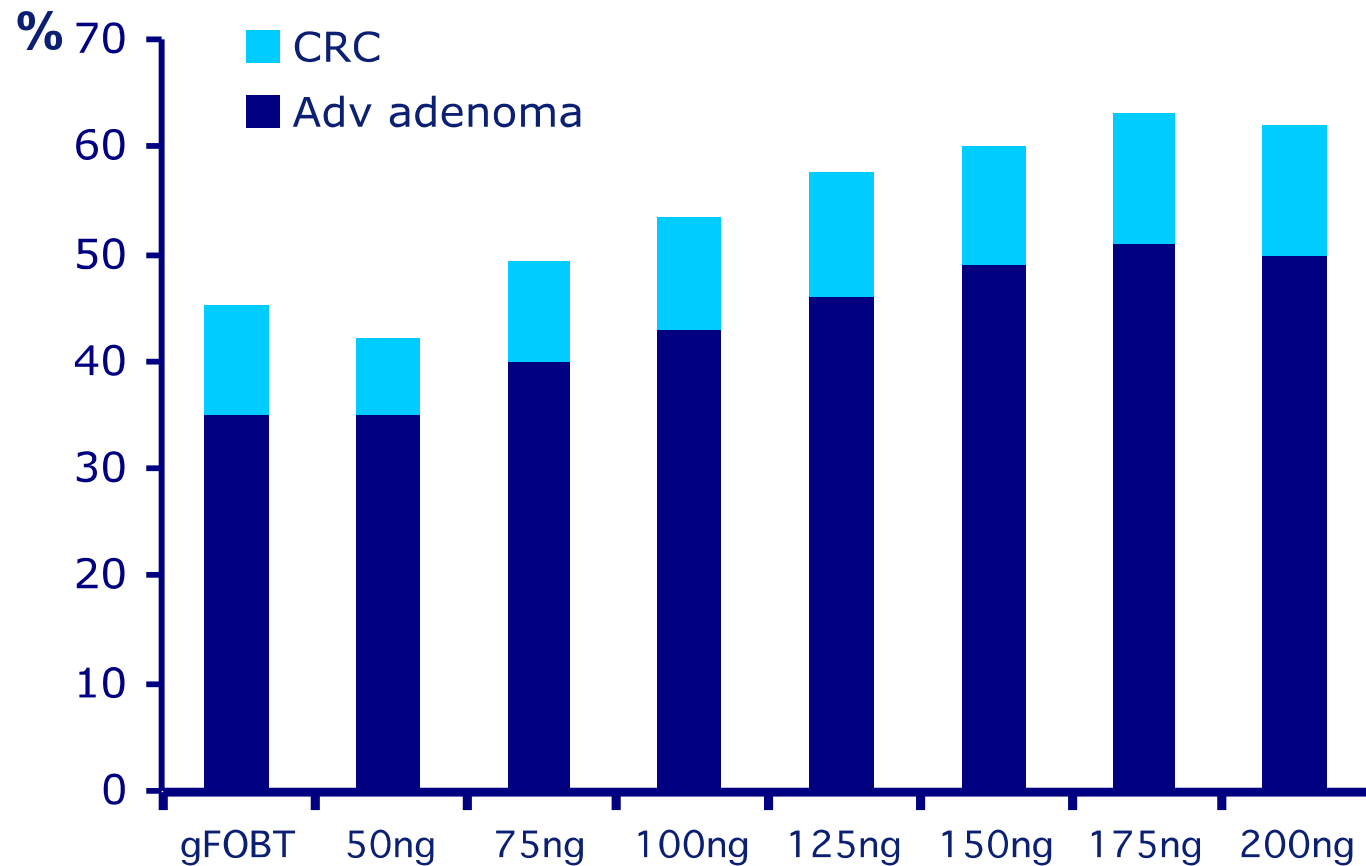
*\* of those with positive test*

Hol et al. Gut 2010

## Test positivity rate; gFOBT vs FIT at different cut-off levels



## Positive predictive value; the proportion of subjects with positive colonoscopy after positive fecal testing



## Baseline faecal occult blood concentration as a predictor of incident colorectal neoplasia: longitudinal follow-up of a Taiwanese population-based colorectal cancer screening cohort

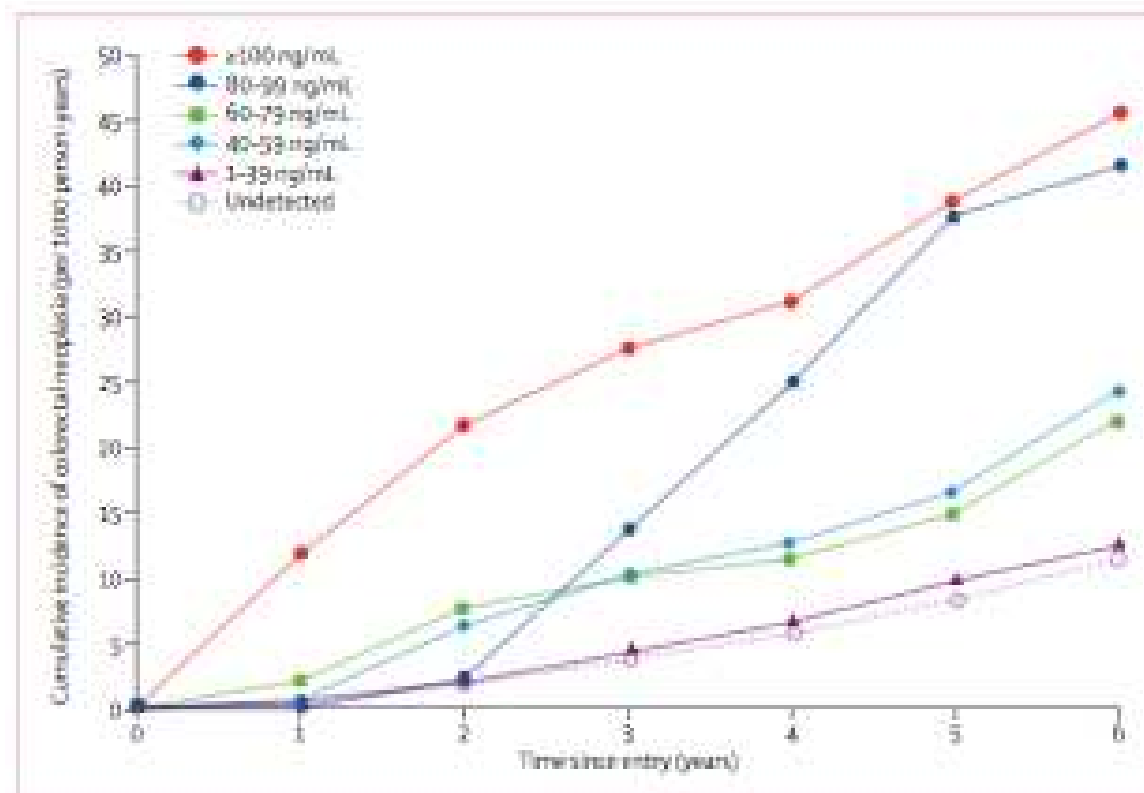
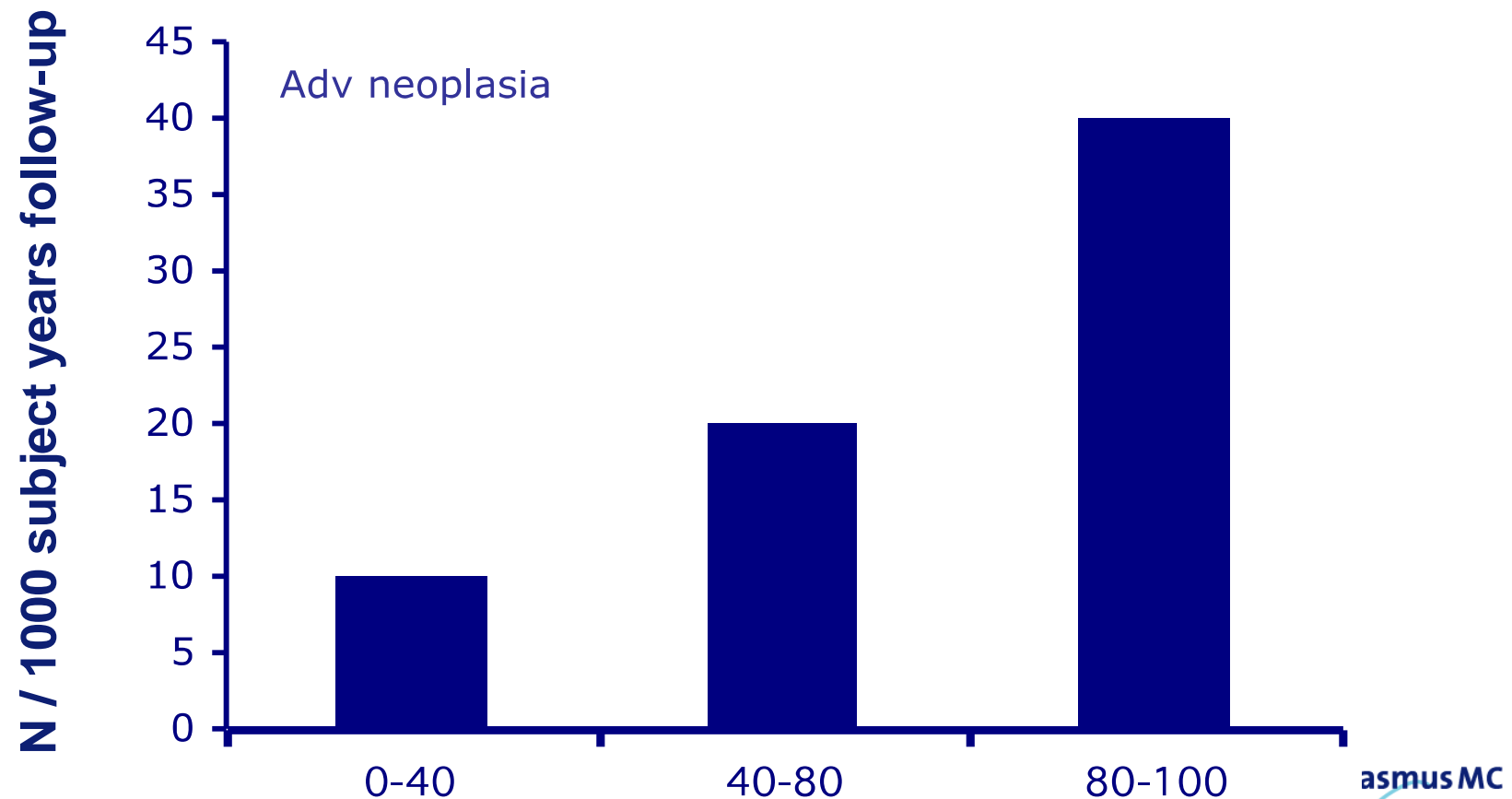


Figure 2: Cumulative incidence of adenoma and colorectal cancer, by faecal Hb concentration (Hb=haemoglobin).

# Baseline faecal occult blood concentration as a predictor of incident colorectal neoplasia: longitudinal follow-up of a Taiwanese population-based colorectal cancer screening cohort



Chen L-S et al. Lancet Oncol 2011

asmusMC

2011



## Numbers needed to screen and scope to detect one screennee with an advanced neoplastic lesion

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	NN Screen	NN Scope
<b>gFOBT</b>	<b>84</b>	<b>2.2</b>
<b>FIT<sup>50</sup></b>	<b>31</b>	<b>2.4</b>
<b>FIT<sup>75</sup></b>	<b>37</b>	<b>2.0</b>
<b>FIT<sup>100</sup></b>	<b>41</b>	<b>1.9</b>
<b>FIT<sup>125</sup></b>	<b>43</b>	<b>1.8</b>
<b>FIT<sup>150</sup></b>	<b>44</b>	<b>1.7</b>
<b>FIT<sup>175</sup></b>	<b>46</b>	<b>1.6</b>
<b>FIT<sup>200</sup></b>	<b>49</b>	<b>1.6</b>

# Trial design of 1- vs 2-FIT testing

5,690 randomly selected

1-sample  
FIT 2,493

2-samples  
FIT 3,197

Advance notification letter

*2 weeks*

Invitation + FIT

*6 weeks*

Reminder

## Attendance to 1- and 2- day FIT testing

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- Attendance of a screening-naïve population to FIT screening:
  - 1-day FIT: 61.5% (95% CI 60.1 – 62.9)
  - 2-day FIT: 61.3% (95% CI 59.6 – 63.0)

## 1- vs 2-day FIT screening

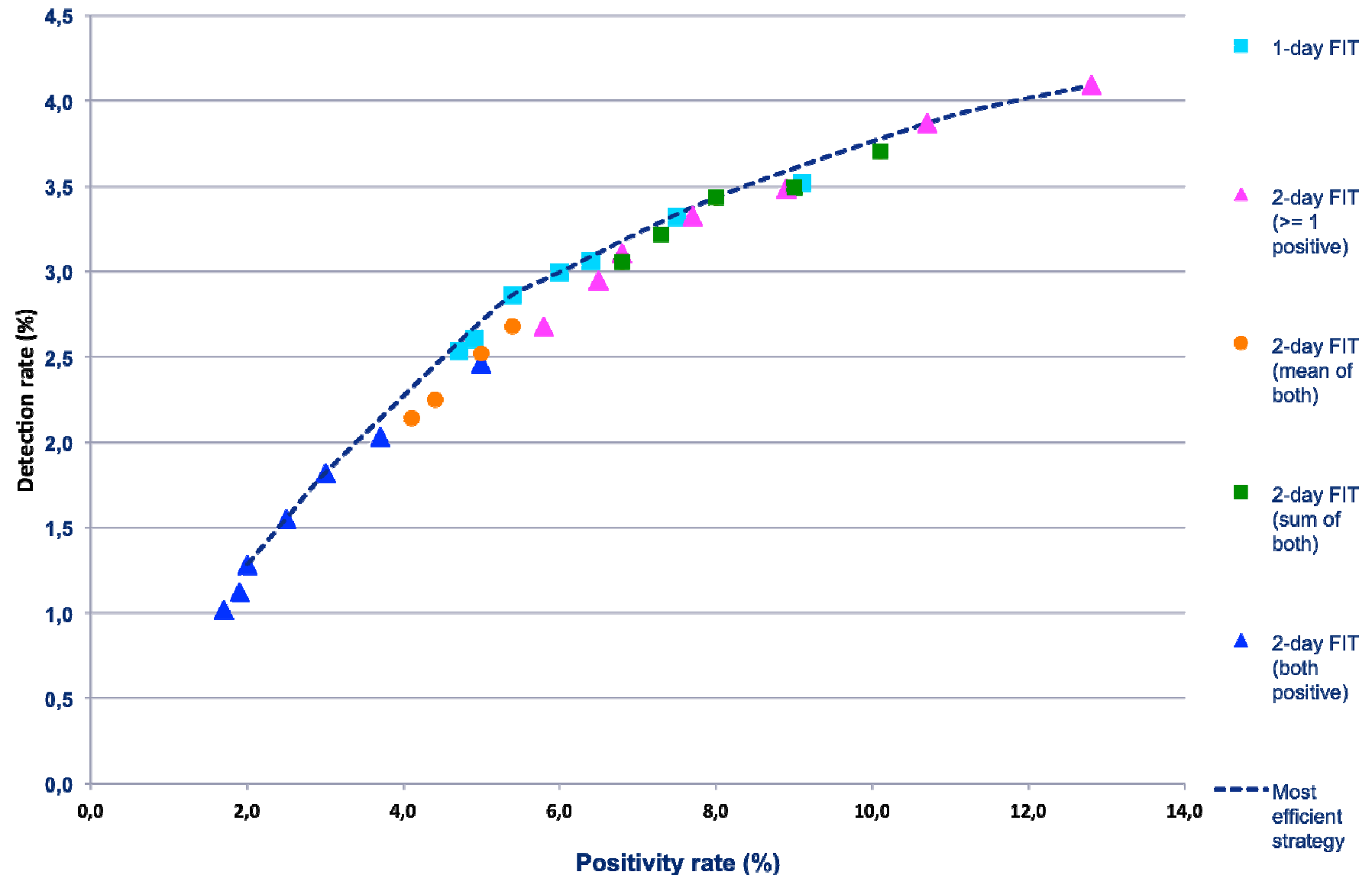
	% positive test	% true positives*	True positives per 1000 invited
1-day FIT <sup>50</sup>	8.1	41	20
2-day FIT <sup>50</sup> 1-2 pos tests	12.8	34	27
2-day FIT <sup>50</sup> mean pos	10.1	39	24
2-day FIT <sup>50</sup> 2 pos tests	5.0	53	16

*\* of those with positive test*

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# Positivity rate versus detection rate of 1- and 2-day FIT<sup>50</sup> screening

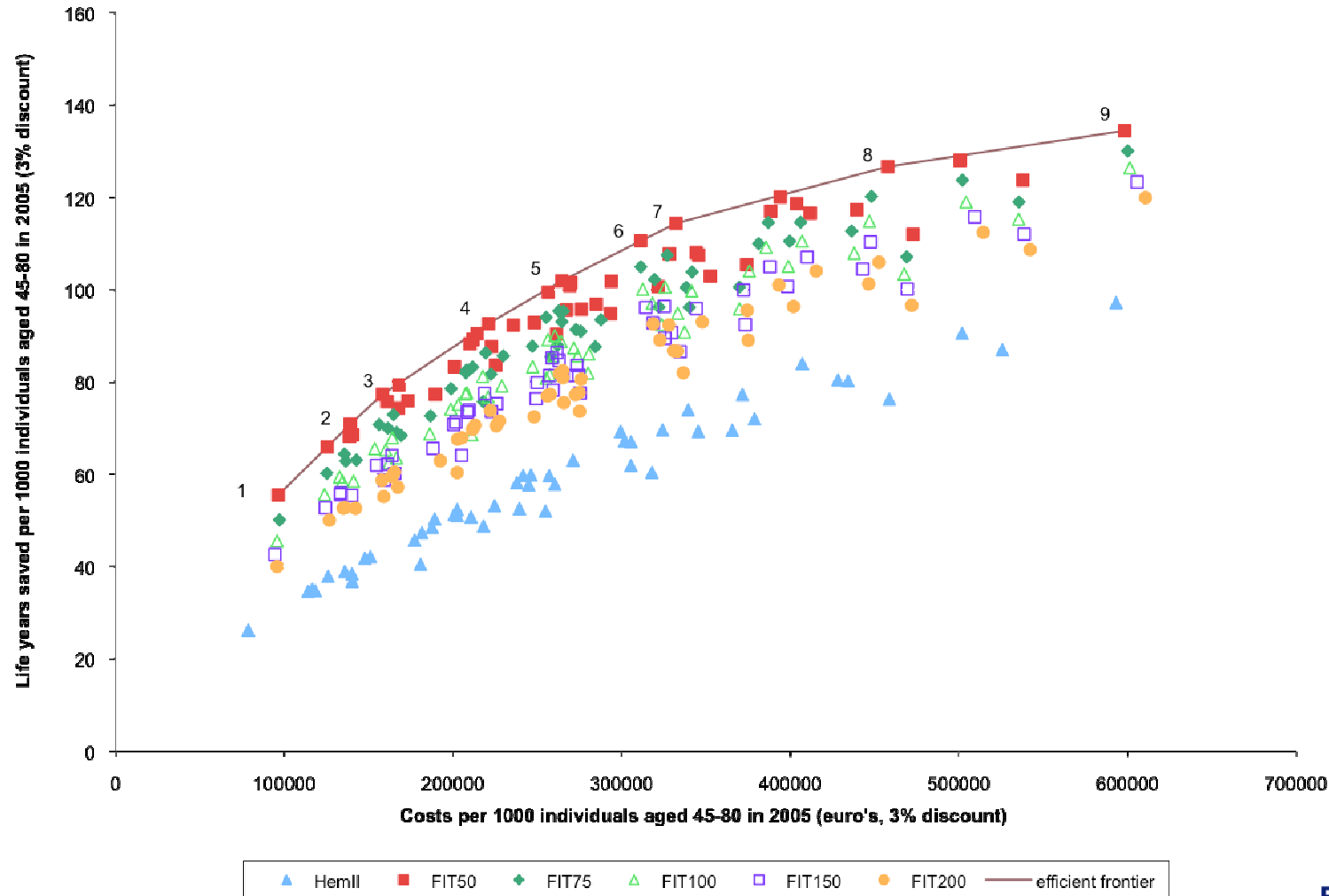


## Rotterdam Screening trial; 1st vs 2nd round FIT<sup>50</sup> screening

	% Adherence	% positive test	% true positives*	True positives per 1000 invited
1st round	62	8.1	42	21
2nd round	63	5.8	46	17
3rd round	65			

*\* of those with positive test*

# Cost – performance modelling of gFOBt and FIT



Van Wilschut JA, van Ballegooijen M, et al. Gastroenterology 2011; in press

## Does FIT sensitivity differ for left and right-sided lesions?

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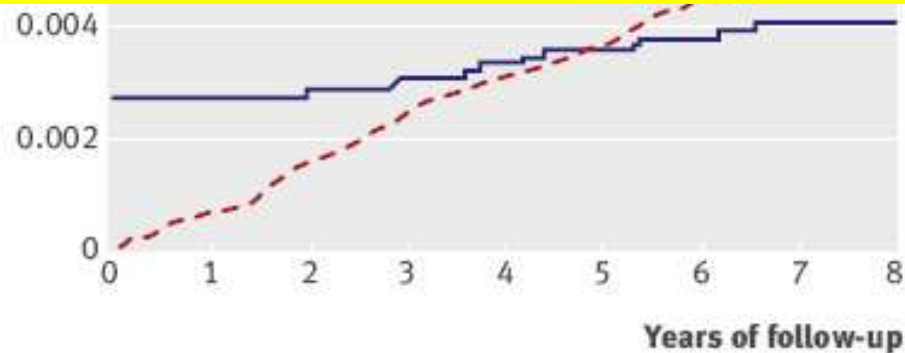
- Haug U et al. Br J Cancer 2011
  - 2310 subjects undergoing screening colonoscopy
  - 228 with advanced neoplasia
  - Left and right-sided FIT sensitivity 33% (26-41) vs 20% (11-31);  $p=0.04$
- De Wijkerslooth T et al. DDW 2011
  - 1256 subjects undergoing screening colonoscopy
  - 119 with advanced neoplasia
  - Left and right-sided FIT sensitivity 38% (29-47) vs 37% (28-46);  $p=0.99$



## Risk of colorectal cancer seven years after flexible sigmoidoscopy screening: randomised controlled trial

Geir Hoff, professor,<sup>1,2</sup> Tom Grotmol, professor,<sup>1</sup> Eva Skovlund, professor,<sup>3</sup> Michael Bretthauer, physician and researcher,<sup>1,4</sup> for the Norwegian Colorectal Cancer Prevention Study Group for the Norwegian Colorectal Cancer Prevention Study Group

For attenders compared with controls, a statistically significant reduction in mortality was apparent for both total colorectal cancer (HR 0.41, 0.21 to 0.82,  $p=0.011$ ) and rectosigmoidal cancer (0.24, 0.08 to 0.76,  $p=0.016$ )



**Fig 3** | Cumulative hazard for rectosigmoidal cancer among attenders compared with control group

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# Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

Wendy S Atkin, Rob Edwards, Ines Kralj-Hans, Kate Wooldrage, Andrew R Hart, John M A Northover, D Max Parkin, Jane Wardle, Stephen W Duffy, Jack Cuzick, UK Flexible Sigmoidoscopy Trial Investigators

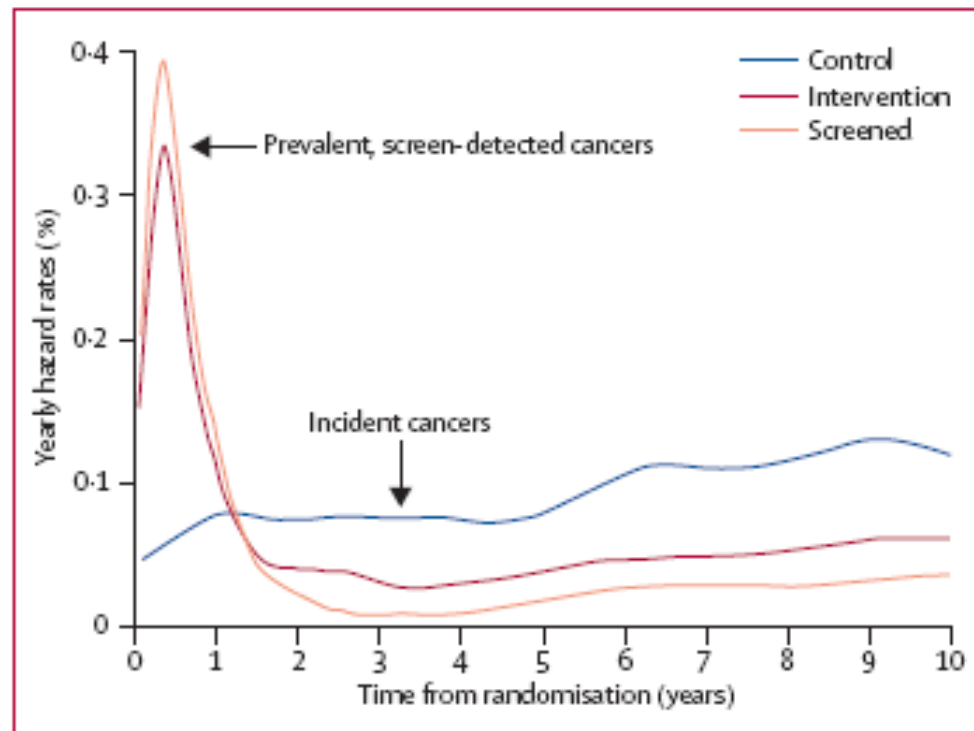
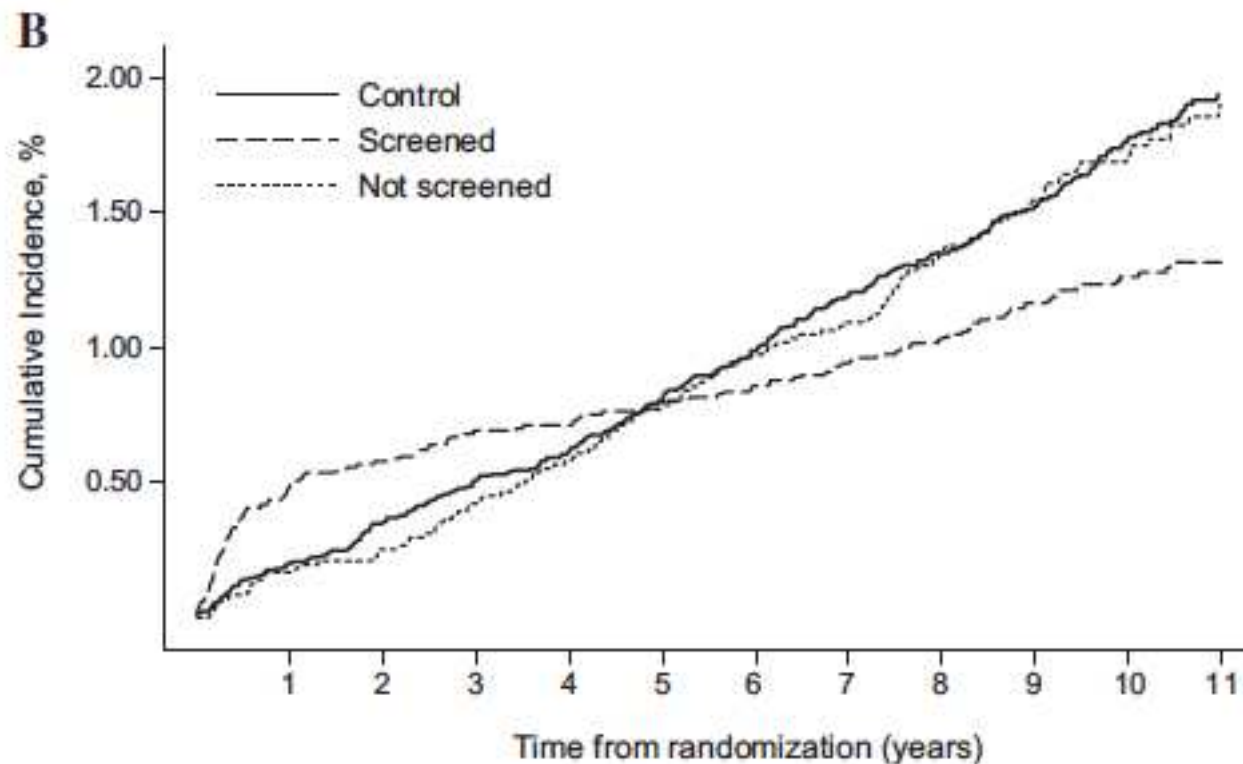


Figure 3: Smoothed yearly hazard rates for distal cancer (rectum and sigmoid colon)

Curves are truncated at 10 years of follow-up because of incomplete ascertainment of cancers in the final calendar year of the study.

# Once-Only Sigmoidoscopy in Colorectal Cancer Screening: Follow-up Findings of the Italian Randomized Controlled Trial—SCORE

Nereo Segnan, Paola Armaroli, Luigina Bonelli, Mauro Risio, Stefania Sciallero, Marco Zappa, Bruno Andreoni, Arrigo Arrigoni, Luigi Bisanti, Claudia Casella, Cristiano Crosta, Fabio Falcini, Franco Ferrero, Adriano Giacomini, Orietta Giuliani, Alessandra Santarelli, Carmen Beatriz Visioli, Roberto Zanetti, Wendy S. Atkin, Carlo Senore; and the SCORE Working Group



## Yield of sigmoidoscopy versus colonoscopy

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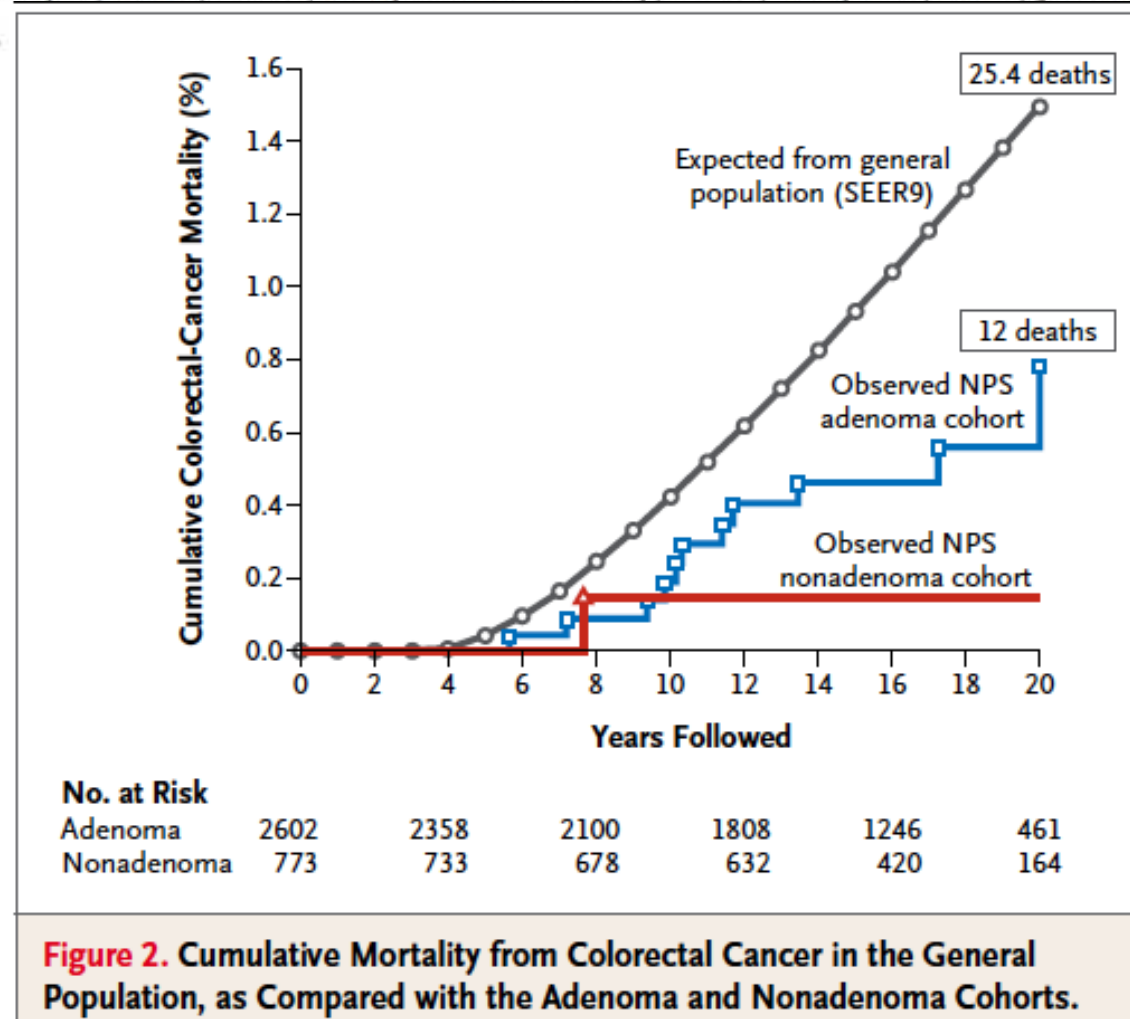
- Advanced lesions in men:
  - 60% located distal to the splenic flexure
  - 20% located proximal, together with distal adenomas
  - 20% located proximal without distal adenomas
- Advanced lesions in women:
  - 55% located proximal without distal adenomas
- Sigmoidoscopy to the splenic flexure followed by colonoscopy in subjects with distal adenomas detects:
  - 80% of advanced lesions in men \*
  - 45% of advanced lesions in women \*\*

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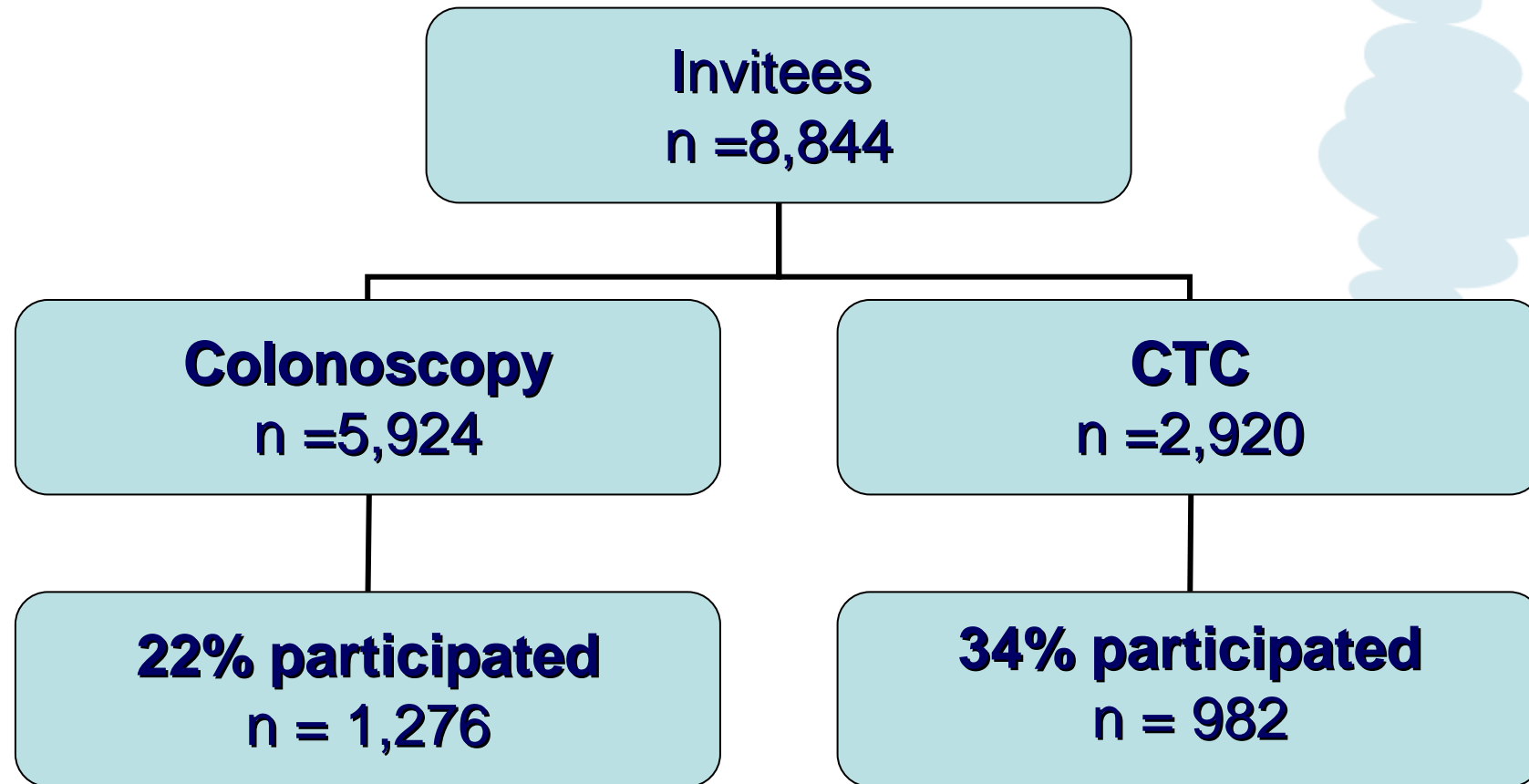
\* Lieberman, et al. NEJM 2000; 343: 162-8, \*\*Schoenfeld et al. NEJM 2005; 352: 2061-8

# Colonoscopic Polypectomy and Long-Term Prevention of Colorectal-Cancer Deaths

Ann G. Zauber, Ph.D., Sidney J. Winawer, M.D., Michael J. O'Brien, M.D., M.P.H., Iris Lansdorp-Vogelaar, Ph.D., Marjolein van Ballegooijen, M.D., Ph.D., Benjamin F. Hankey, Sc.D., Weiji Shi, M.S., John H. Bond, M.D., Melvin Schapiro, M.D., M.D.



# Primary screening with colonoscopy vs CT colonography; a randomized trial



**RR 1.56**

(1.46-1.68;  $p < 0.001$ )

# Diagnostic yield CTC vs Colo

(number of subjects with advanced neoplasia)

	CC	CTC	P-value	RR (95%CI)
n/100 participants	8.7	6.1	0.02	1.46 (1.06-2.03)
n/100 invitees	1.9	2.1	0.56	0.91 (0.66-2.03)

# Colonoscopy versus Fecal Immunochemical Testing in Colorectal-Cancer Screening

- Randomized trial comparing 1<sup>st</sup> round FIT and colonoscopy:
  - Uptake 34.2 vs 24.6%
  - CRC detection 33 (0.1%) vs 30 (0.1%)
  - Advanced adenoma detection 231 (0.9%) vs 514 (1.9%); OR 2.30 (1.97-2.69)

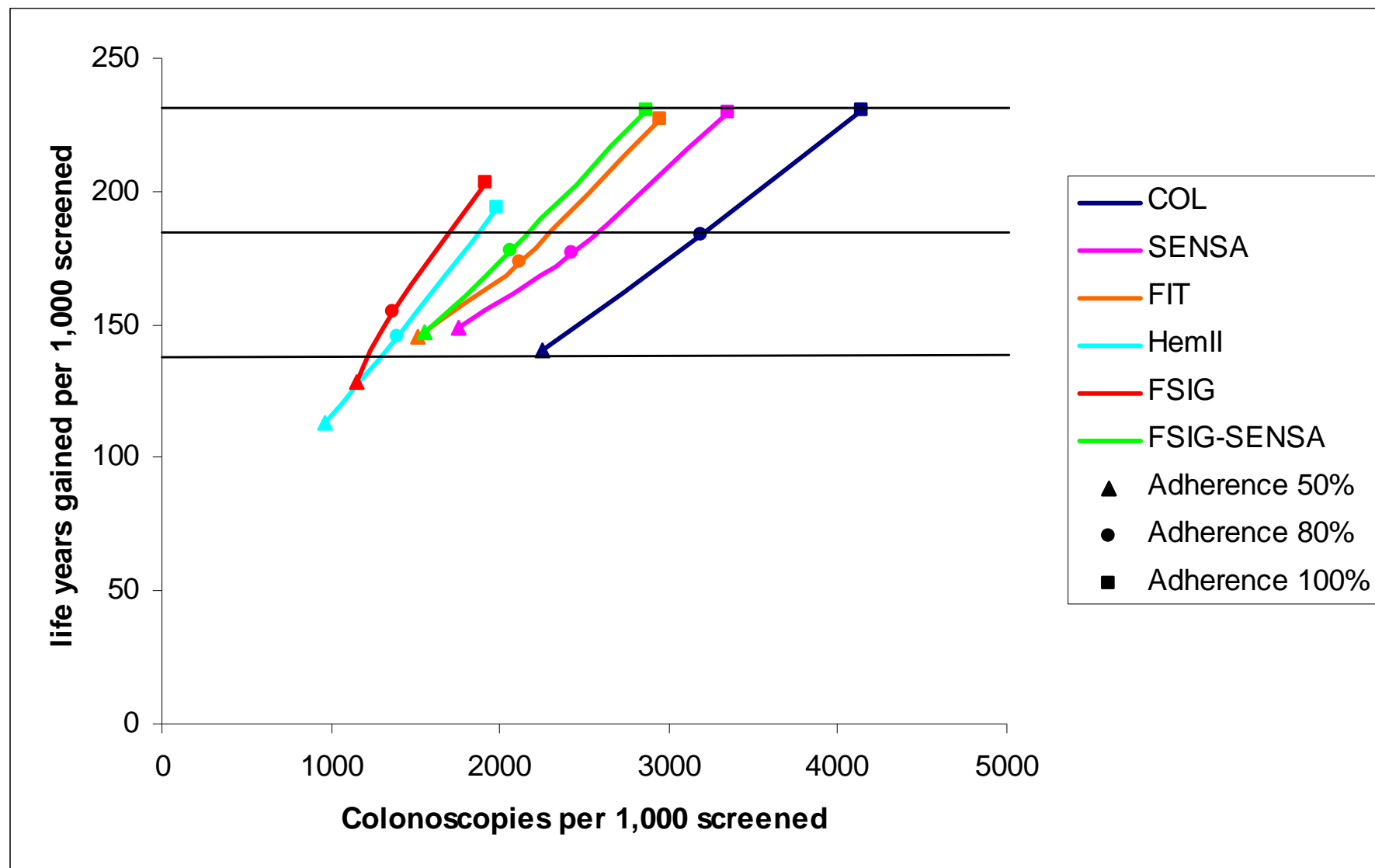


## Sensitivity of FIT50 for CRC and advanced neoplasia

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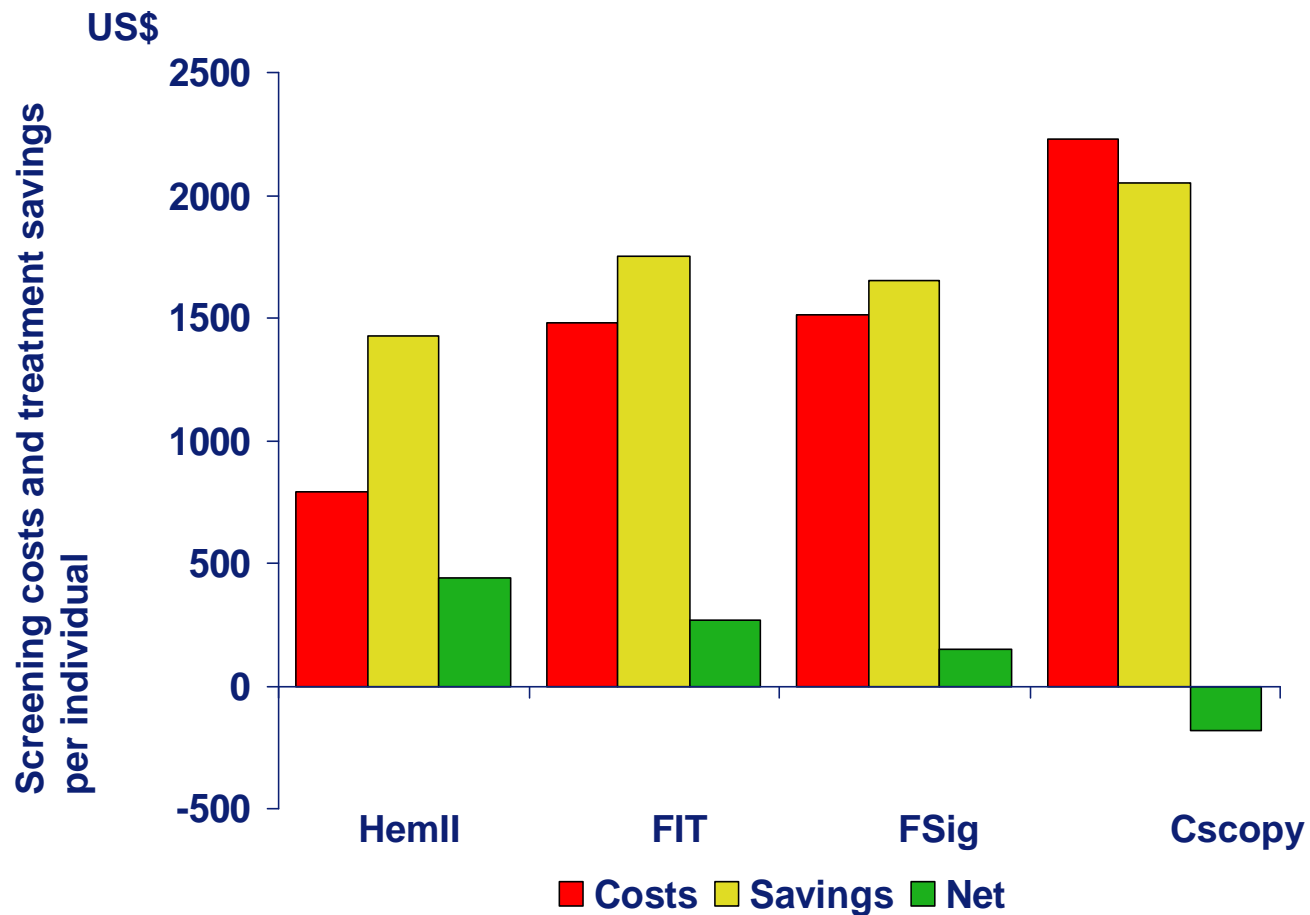
FIT50	Sens (CI)	Spec (CI)	PPV (CI)	NPV (CI)
CRC	88 (47-99)	91 (89-92)	6 (3-12)	100 (99-100)
Advanced neoplasia	38 (29-47)	93 (92-95)	37 (29-46)	93 (92-95)

# MISCAN Model Adherence Plot



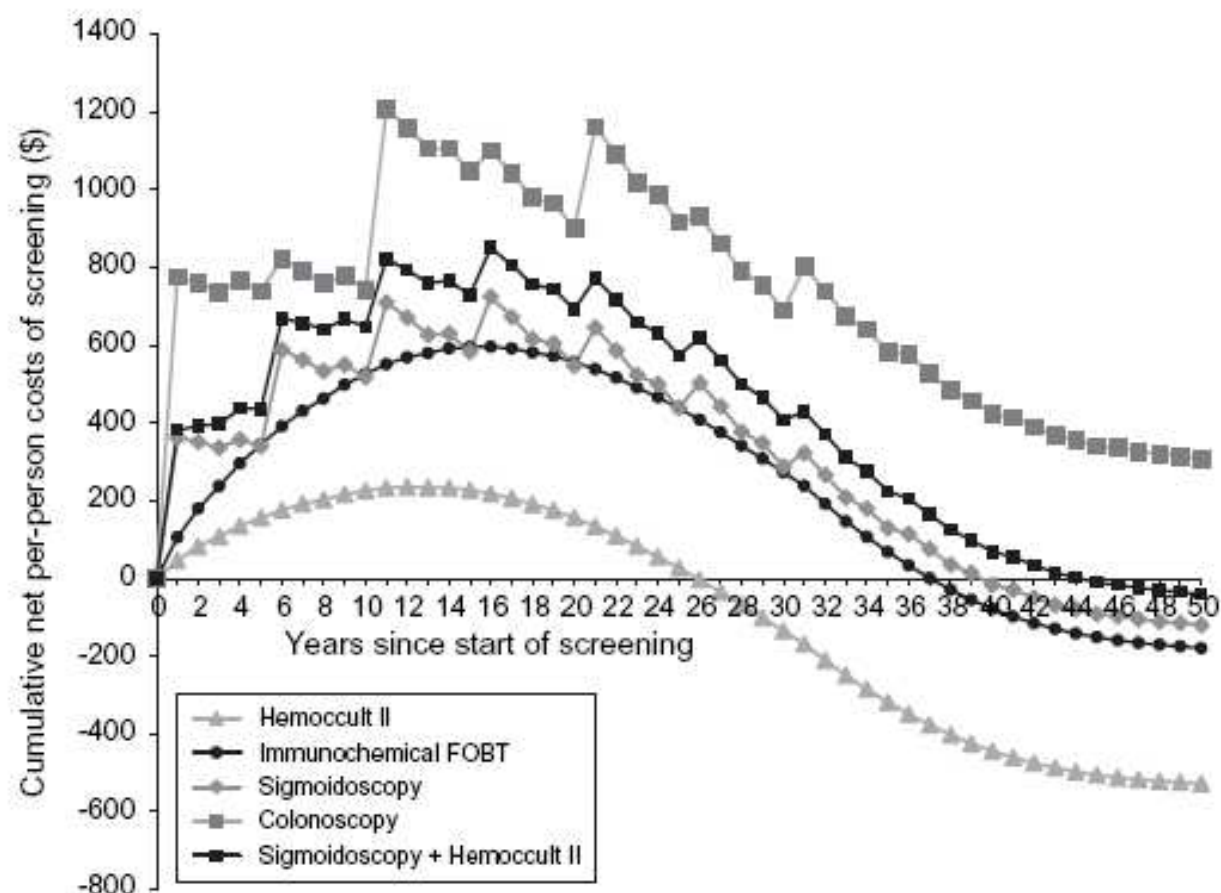
# Effect of Rising Chemotherapy Costs on the Cost Savings of Colorectal Cancer Screening

Iris Lansdorp-Vogelaar, Marjolein van Ballegooijen, Ann G. Zauber, J. Dik F. Habbema, Ernst J. Kuipers



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Sigmoidoscopy	32	10.2	100	33
2-step: Sigmo + FIT <sup>50</sup>	57	16.8		43

*\* of those with positive test*

Hol L, et al. Gut 2010, **Int J Cancer 2011; in press**

## Colorectal Cancer Screening; Conclusions

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- A range of CRC screening methods are available.
- There major difference lies in immediate detection rates, and thus the interval of screening
- The ultimate of a screening program with a given method is strongly determined by participation rates