

THE RISK OF MISSING UPPER GASTROINTESTINAL CANCER IN FIT-POSITIVES IN A COLORECTAL CANCER SCREENING PROGRAM

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Disclosures

- No conflicts of interest



Introduction

- CRC screening programs use FOBT on assumption that AN have a tendency to bleed.
- gFOBT detects haem, whereas FIT detects intact human Hb
- However, $> \frac{1}{2}$ of FIT positives do not have AN at colonoscopy¹



Introduction

- Systematic review concluded that there is not enough evidence to recommend for/against routine EGD in FOBT positives⁴
- Some recent studies argue for EGD in FIT positives^{5,6}
- Overall, varying definitions and quality of studies

4. Allard et al, Can J Gastroenterol. 2010

5. Choi et al, Scand J Gastro 2013

6. Ng et al. Int J Colorectal Dis 2017



Aim

- Assessing the number of proximal cancers diagnosed within two years after a FIT test in FIT-positive and FIT-negative participants in a FIT-based screening program

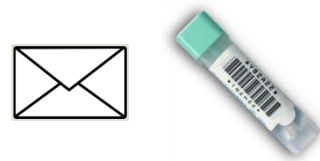


Methods

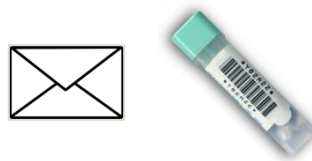
- Randomly selected asymptomatic persons aged 50-74 years
- Municipal population register
- Exclusion criteria:
 - History of IBD or CRC
 - Symptoms of CRC
 - Colonoscopy \leq 2 years
 - ASA IV or life-expectancy $<$ 5 years



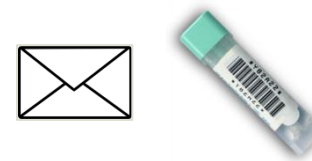
Dynamic FIT screening program



June 2006-Nov 2008



Aug 2008-nov 2010



Febr 2011-Oct 2012



Oct 2014

Cut-off FIT $\geq 10 \mu\text{g Hb/g feces}$
Linkage until 31 March 2015



Basic characteristics cohort

	Round 1	Round 2	Round 3
Invitees	14,651	18,383	19,618
Age (median, IQR)	59 (54-65)	60 (55-66)	60 (55-66)
Sex (male;%)	50	49	49



Methods

- Proximal cancers identified through linkage with the Netherlands Cancer Registry
- Definition proximal cancer: oral cavity, throat, esophageal, gastric and small bowel cancer
- All types of histopathological diagnosis
- Data: tumor type, site, follow up time since cancer diagnosis



Definitions

FIT-positives with a positive colonoscopy (AN*)

FIT-positives with a negative colonoscopy (no AN)

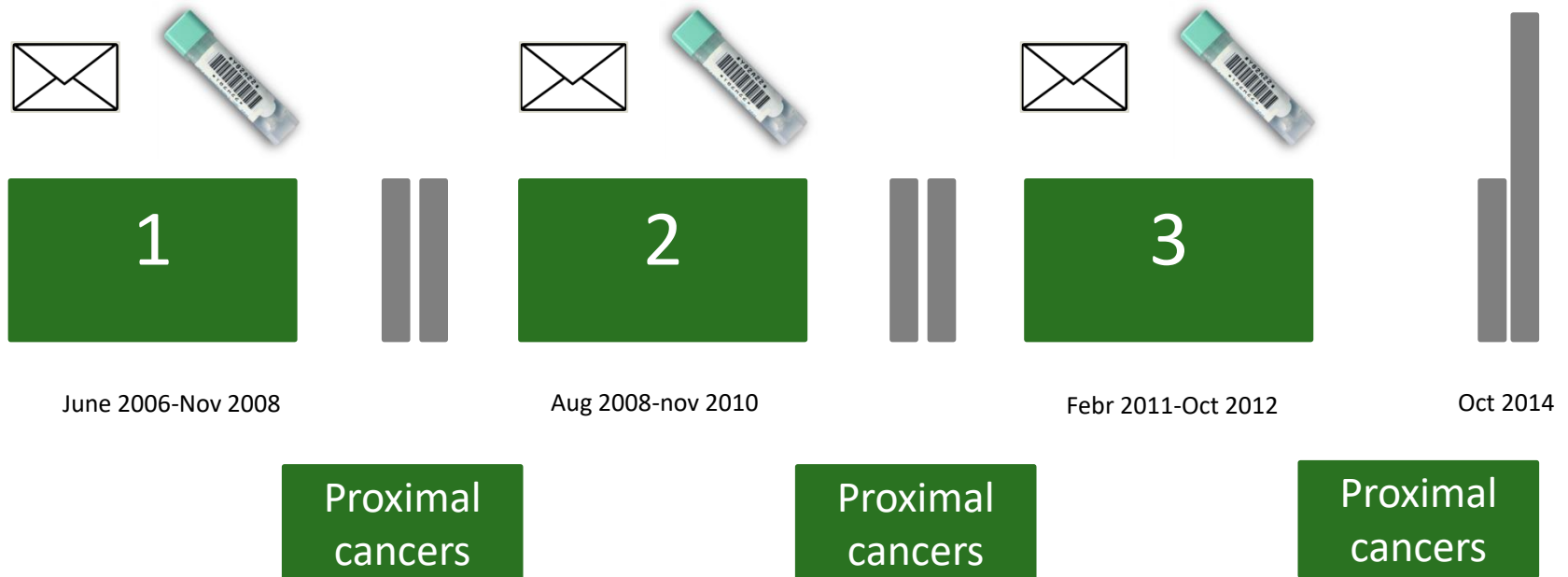
FIT-negatives

Potentially detectable cancers: tumors diagnosed < 2 years after the last performed FIT

*CRC or adenoma with a diameter ≥ 10 mm, and/or with a $\geq 25\%$ villous component, and/or high-grade dysplasia.



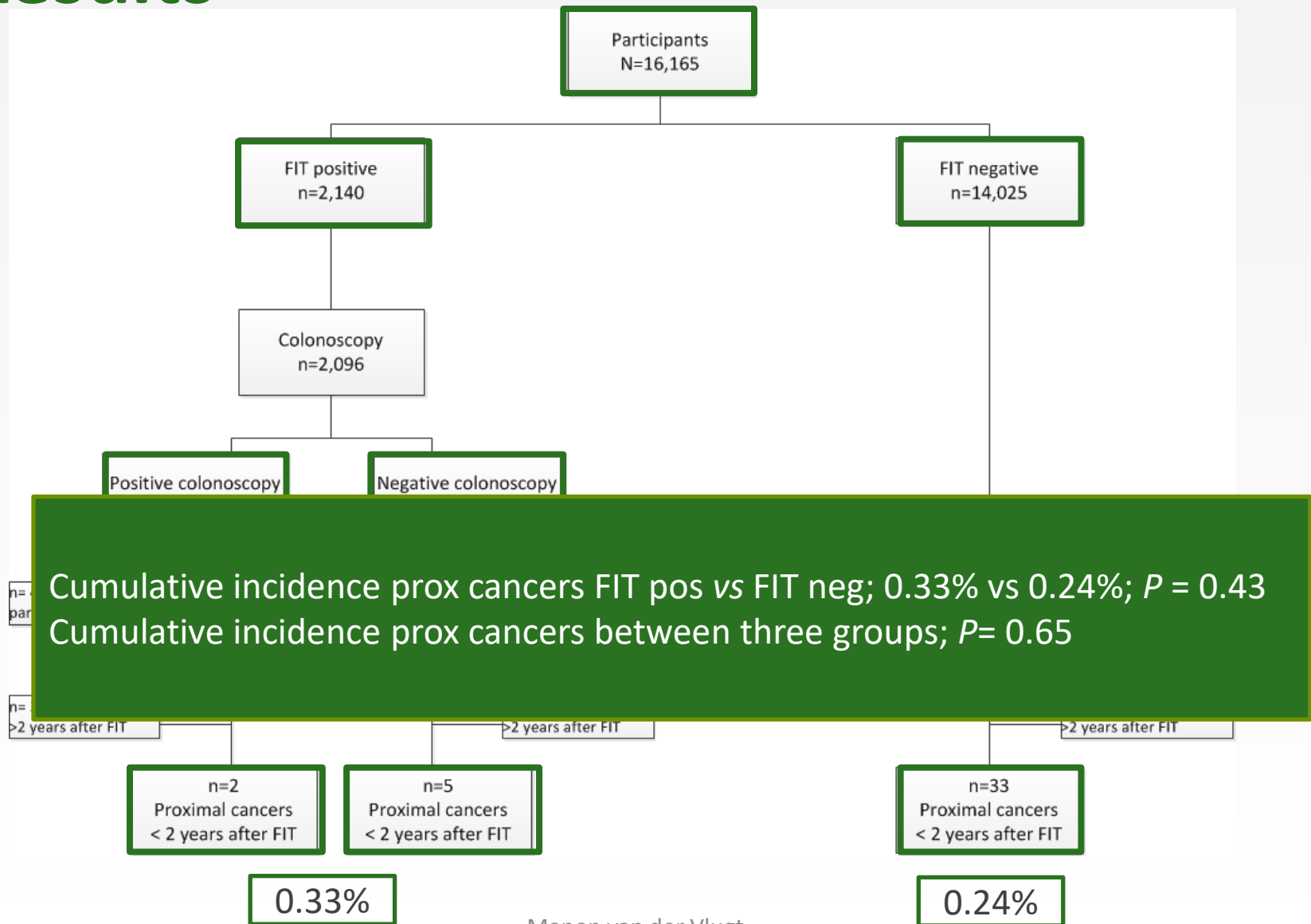
Linkage to FIT screening program



Cut-off FIT $\geq 10 \mu\text{g Hb/g feces}$
Linkage until 31 March 2015



Results



Histopathology and location

	Positive FIT, negative colonoscopy	Positive FIT, positive colonoscopy	Negative FIT
Total number of persons at risk	1367	729	14,027
Oral/Throat*			
-carcinoma unspecified	0	0	1
-squamous cancer	2	1	10
Esophagus			
-squamous cancer	0	1	4
-adenocarcinoma	1	0	11
Gastric			
-adenocarcinoma	0	0	5
-linitis plastica	0	0	1
-GIST	0	0	1
Small bowel			
-adenocarcinoma			
-carcinoid			
-GIST			
Total number of cancers			

No difference when comparing FIT positives (n=2) and FIT negatives (n=22) for only esophagus/gastric $P= 0.48$



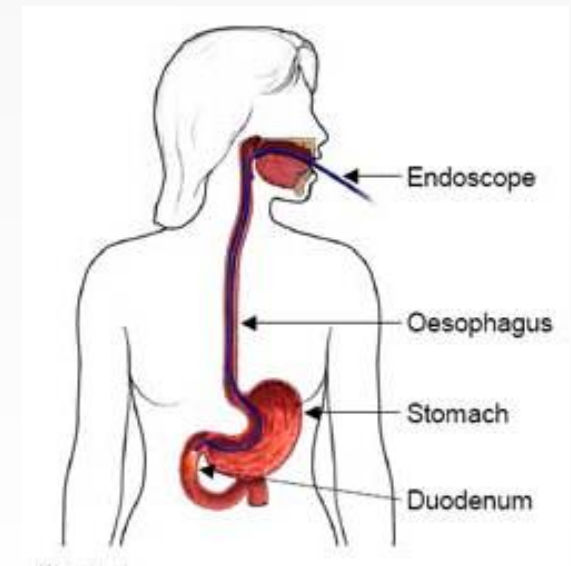
Patient characteristics with proximal cancers < 2 years after FIT

	Positive FIT, negative colonoscopy	Positive FIT, positive colonoscopy	Negative FIT	P-value
Total number of cancers	5	2	33	.645
Age at diagnosis, median (IQR)	68 (59-73)	61	65 (58-73)	.864
Sex (male, n (%))	4 (80%)	1 (50%)	22 (67%)	.918
Type of cancer (n)				But very small numbers!!
-Oral/Throat	2 (40%)	1 (50%)	11 (33%)	
-Esophagus/gastric	1 (20%)	1 (50%)	22 (67%)	
-Small bowel	2 (40%)	0 (0%)	0 (0%)	
Time between test and diagnosis cancer (mean, ±SD, yr)	1.11 (0.51)	0.6 (0.01)	1.2 (0.6)	.237



Number needed to scope (NNSc)

- The NNSc to detect 1 gastric/esophageal cancer in FIT + with negative colonoscopy=1,367



Conclusion

- Similar & very low risk for prox cancers between FIT positives and FIT negatives < 2 years after FIT testing
- Hypothetical NNSc in FIT + with – colo = 1367
- So.... EGD is not recommended in (asymptomatic) persons participating FIT screening

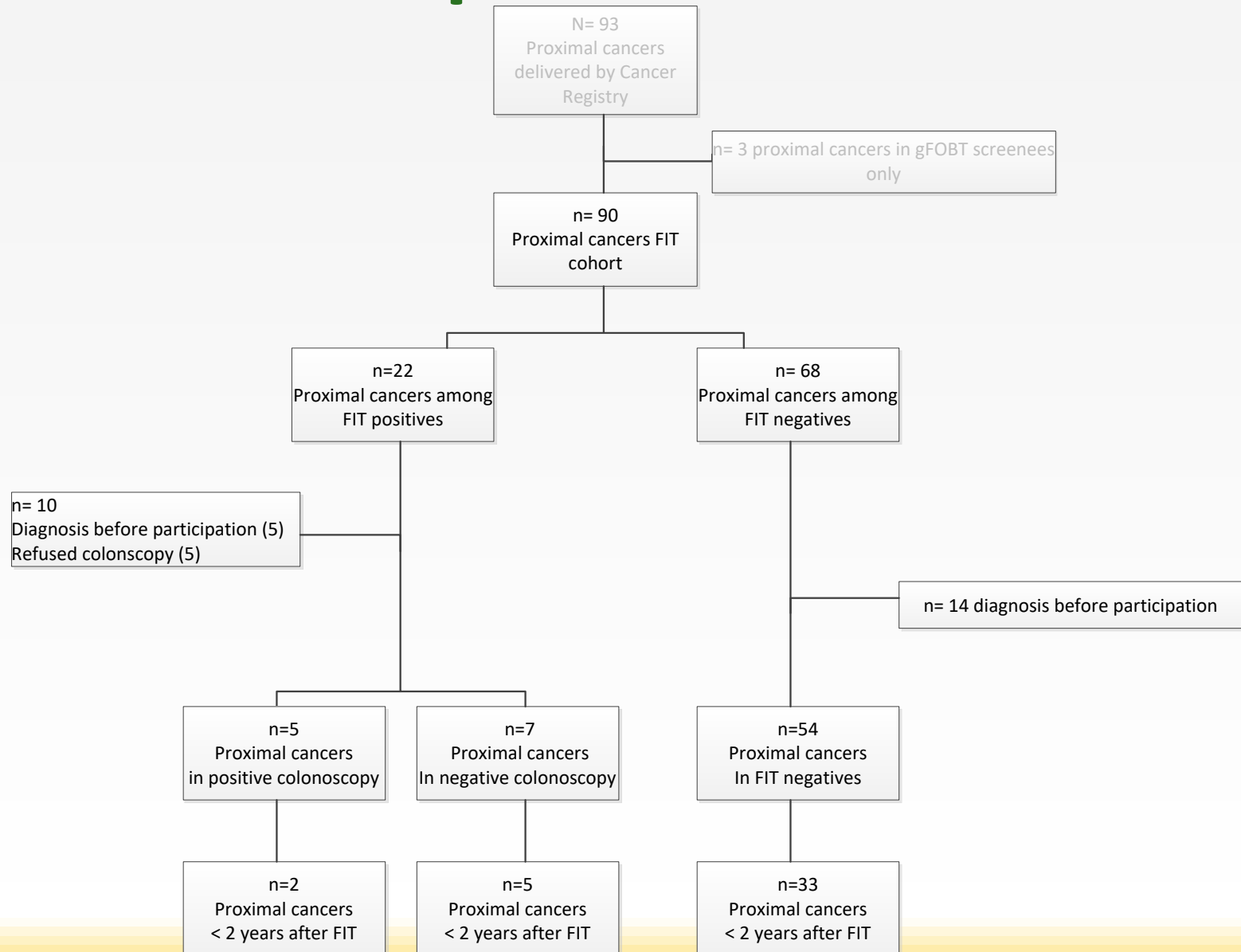


Acknowledgements

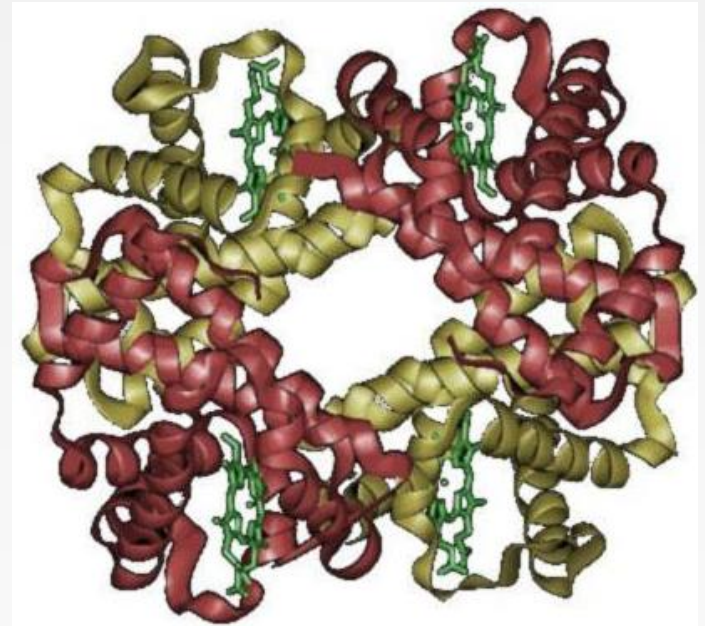
- Foundation of Population Screening Mid-West Netherlands, Amsterdam, The Netherlands (BoMW)
- Foundation of Population Screening South-West Netherlands, Rotterdam, The Netherlands (BoZW)
- Netherlands Comprehensive Cancer Organisation (IKNL)
- Netherlands Organization for Health Research and Development of the Dutch Ministry of Health (ZonMW)



All identified proximal cancers



Hemoglobin



- Hb contains 4 types of subunits of which **haem** is one (green image)
- gFOBT: hydrogen peroxide oxidizes alpha guaiacolic acid to blue colored quinone and **haem** catalyzes this reaction
- FIT uses antibodies directed against **intact human Hemoglobin**

