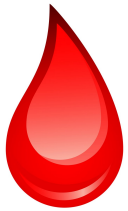
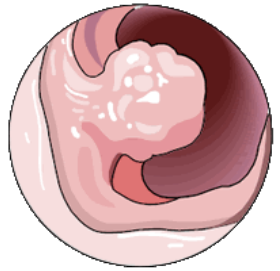
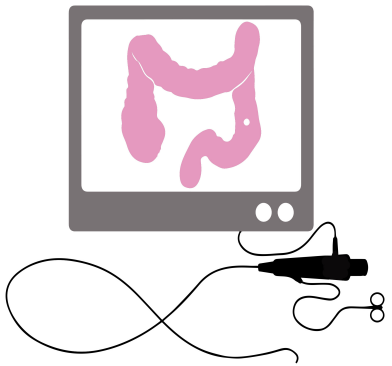
Bruk av test for blod i avføringen i klinikken og Tarmscreeningprogrammet

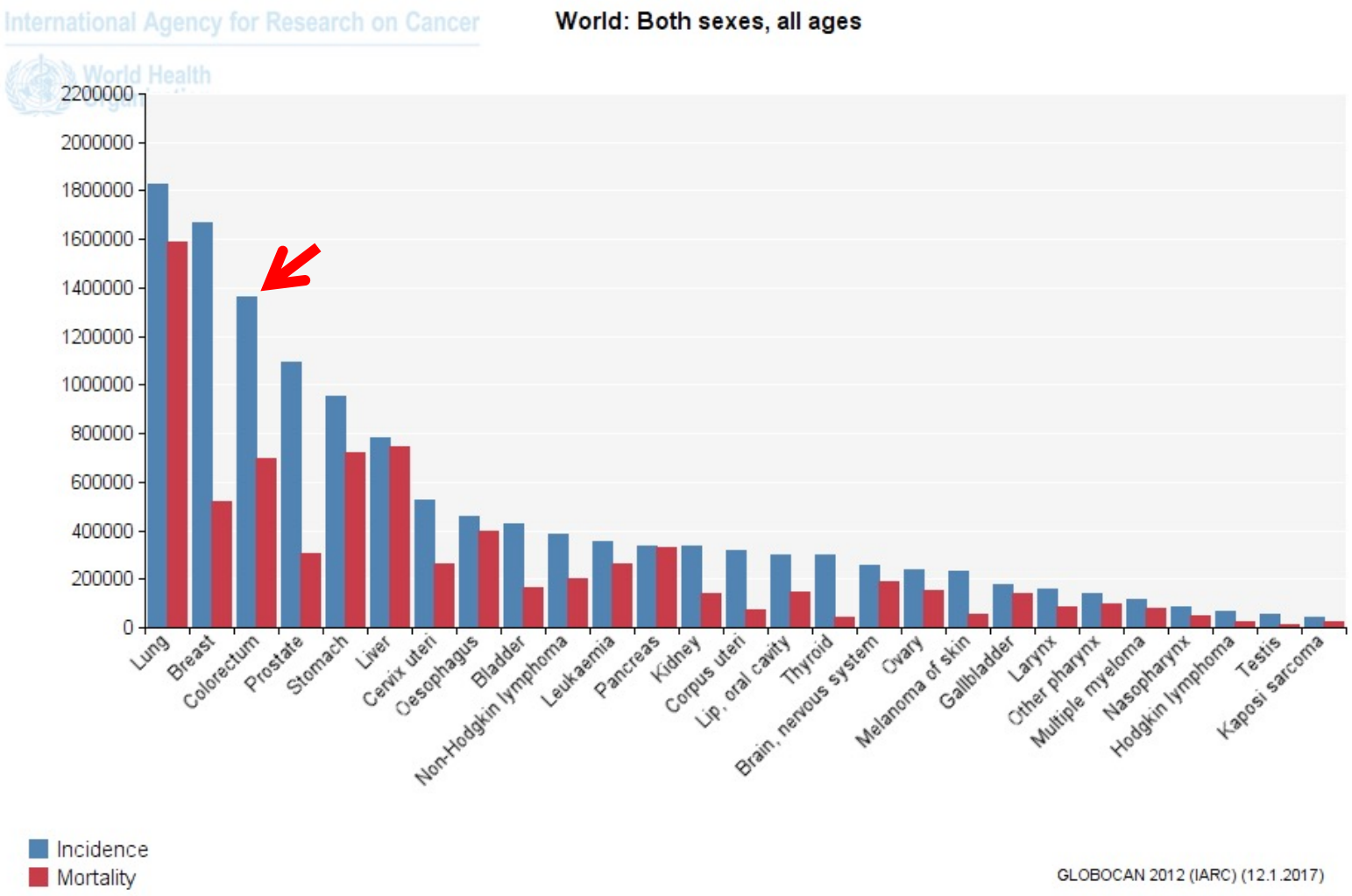
Øyvind Holme
Overlege Sørlandet Sykehus Kristiansand
Førsteamanuensis, Universitetet i Oslo
Nasjonal koordinator for Tarmscreeningprogrammet



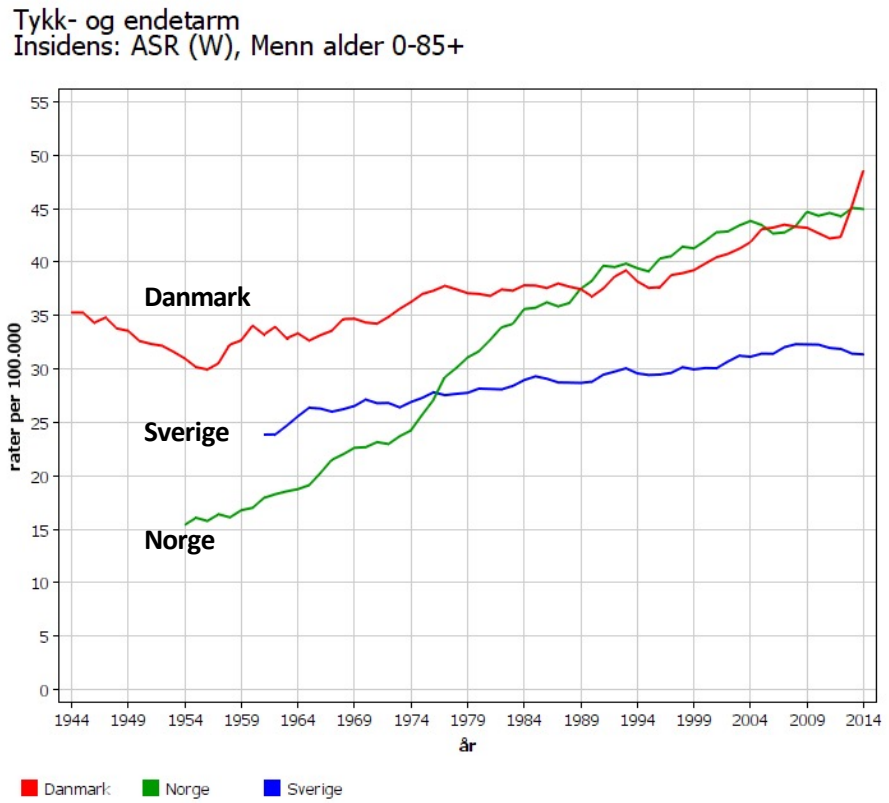




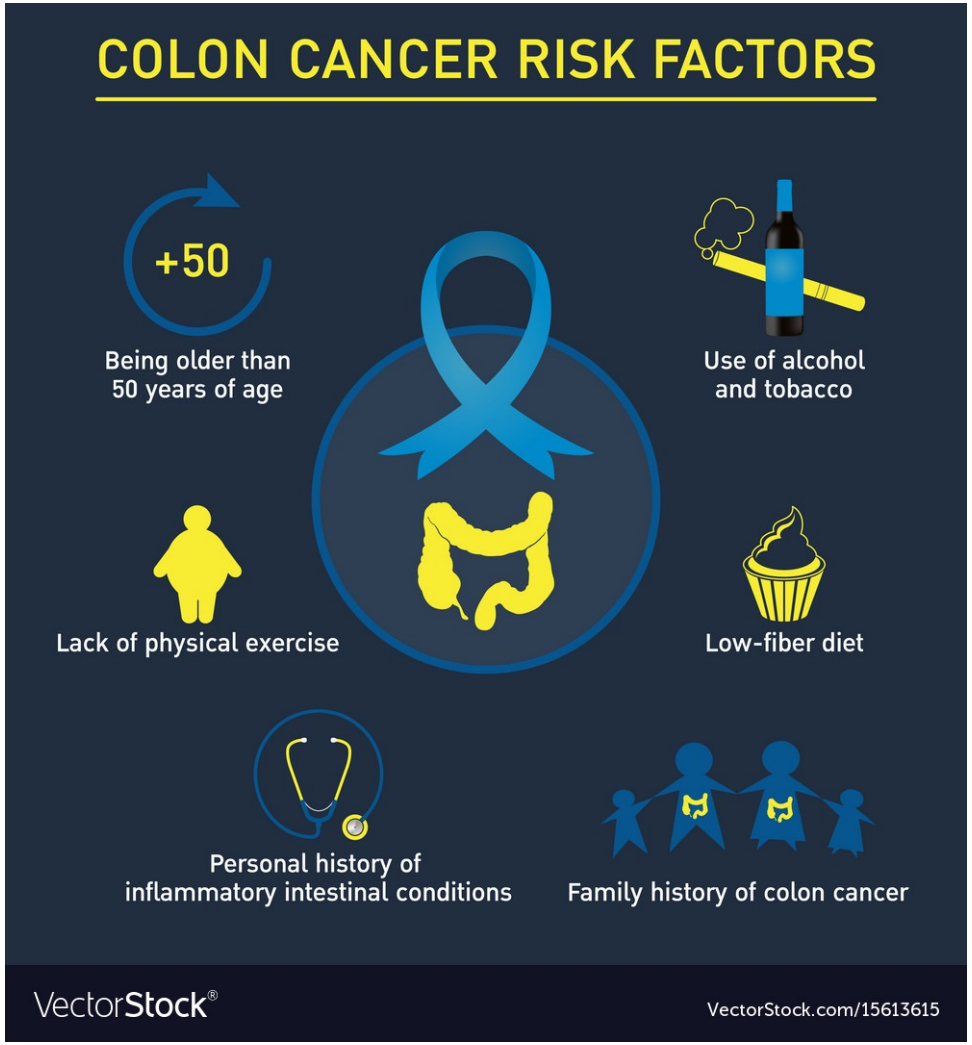
Tarmkreft i verden



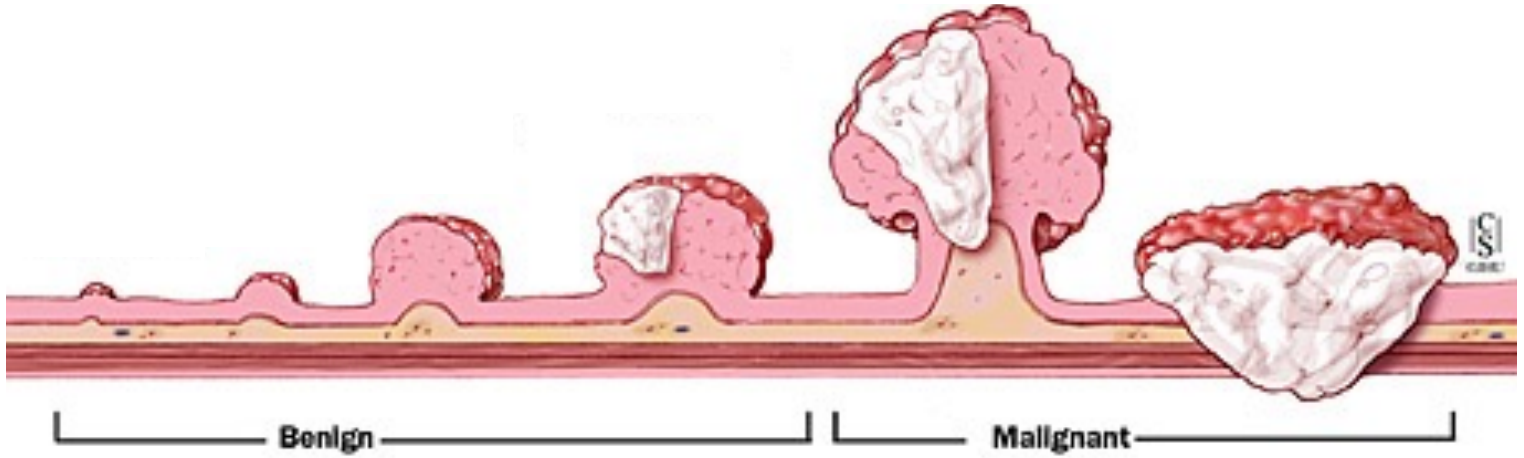
Tarmkreft i skandinavia



Risikofaktorer for tarmkreft



Tarmkreft utvikles fra polypper

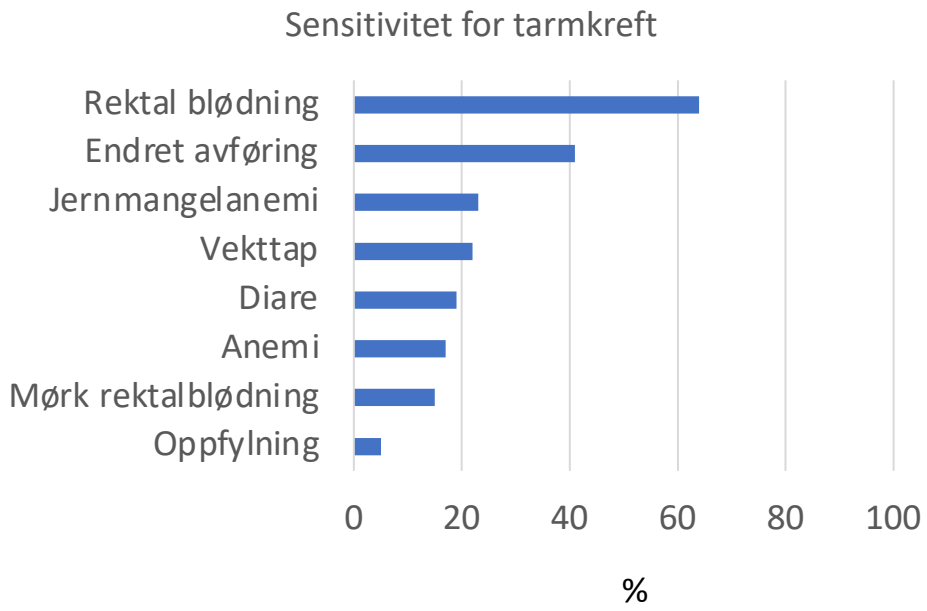


www.hopkinscoloncancercenter.org

Symptomer på tarmkreft

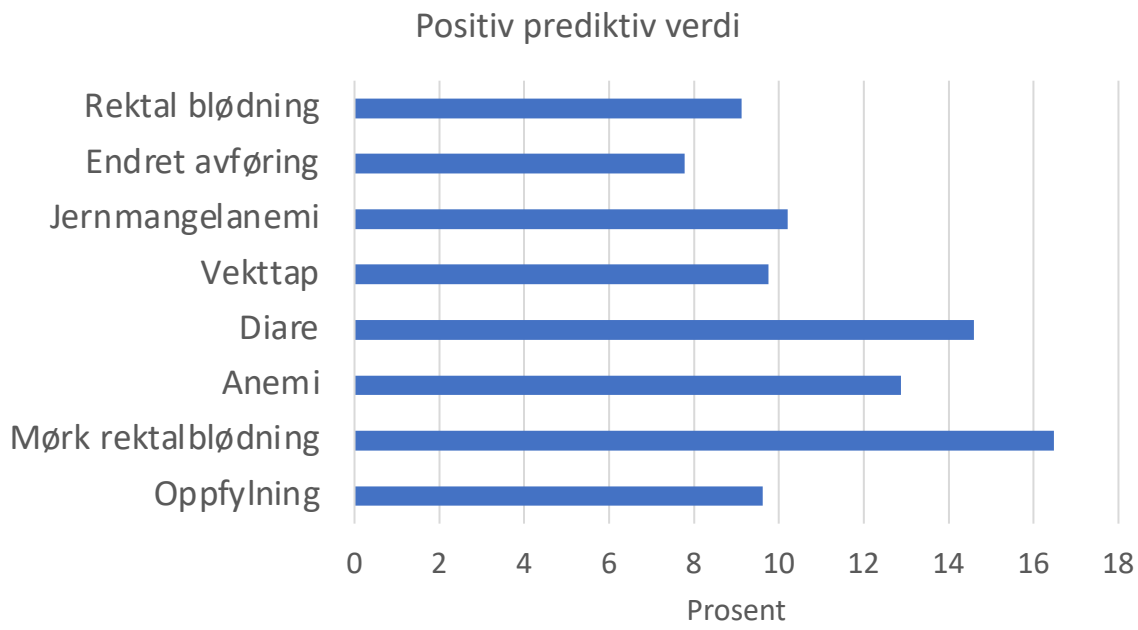
- Magesmerter
- Blod i avføringen
- Endret avføringsmønster
- Slapphet
- Vekttap

Symptomer og tarmkreft



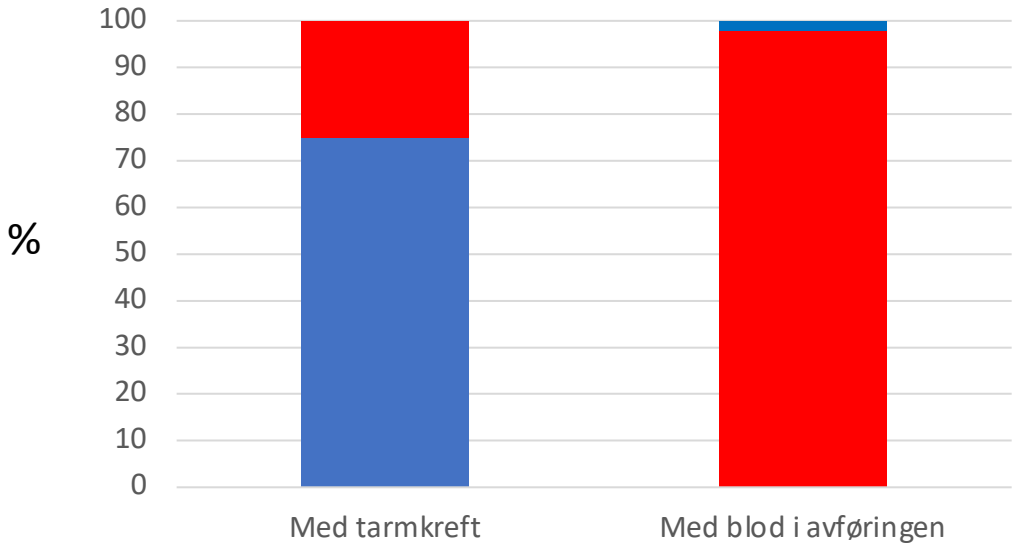
Ford et al. Gut 2008

Positiv prediktiv verdi av symptomer



Ford et al. Gut 2008

Erfaring fra pilotprosjektet (tarmscreening)



Personer med synlig blod i avføringen

Pakkeforløp hos 9822 pasienter (England): De fleste har ingen funn!

Table 2 Frequency of pathology findings at colonoscopy in symptomatic patients referred via 2WW pathways

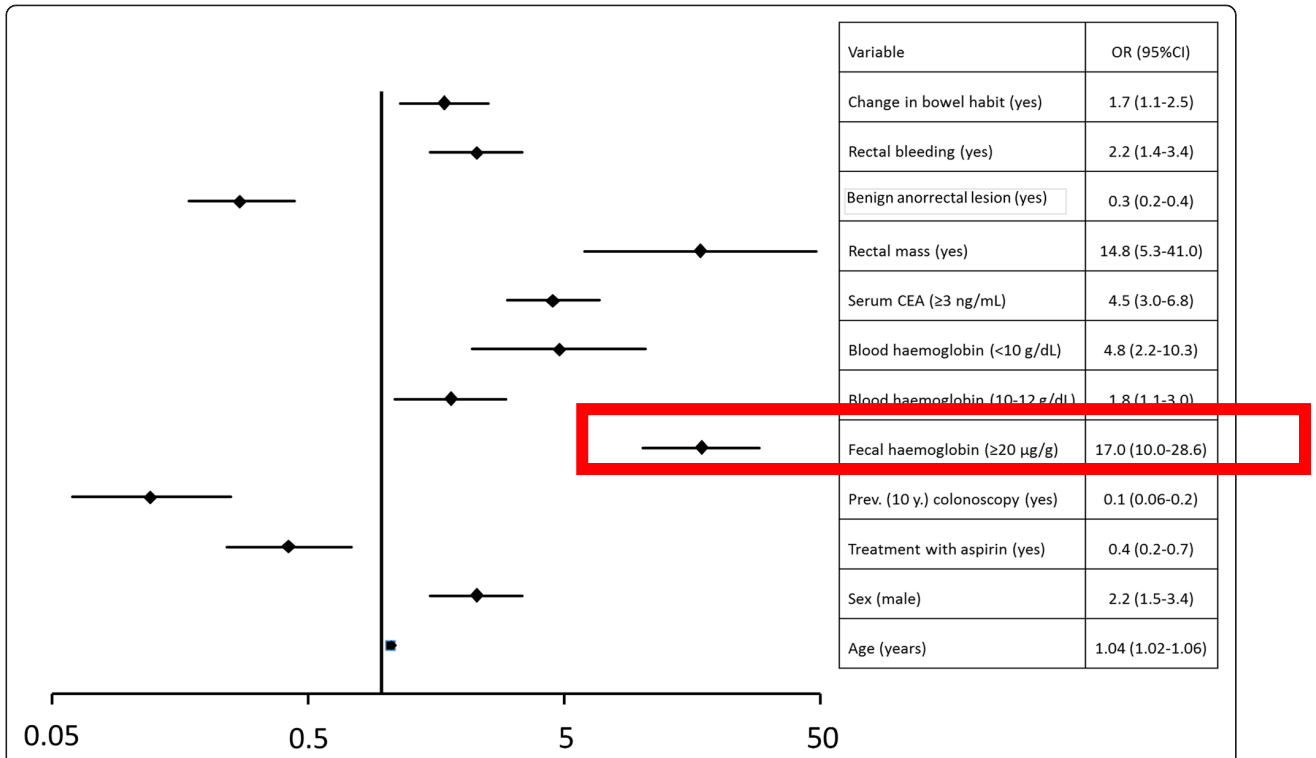
Diagnosis	N	%
Normal	3079	31.3
Low risk adenoma	2321	23.6
Diverticular disease	2294	23.4
Perianal disease*	723	7.4
Inflammatory bowel disease	427	4.3
High-risk adenoma	421	4.3
Colorectal cancer	329	3.3
Microscopic colitis	152	1.5
Other†	53	0.5
Angiodysplasia	23	0.2

D'Souza N, *et al*. *Gut* 2021;**70**:1130–1138.

Kan test for blod i avføringen hjelpe oss?

- Kan F-Hb hjelpe fastlegene i diagnostisk utredning og henvisning?
- Kan F-Hb hjelpe sykehuslegene til å prioritere?

F-Hb bedre enn det meste annet!

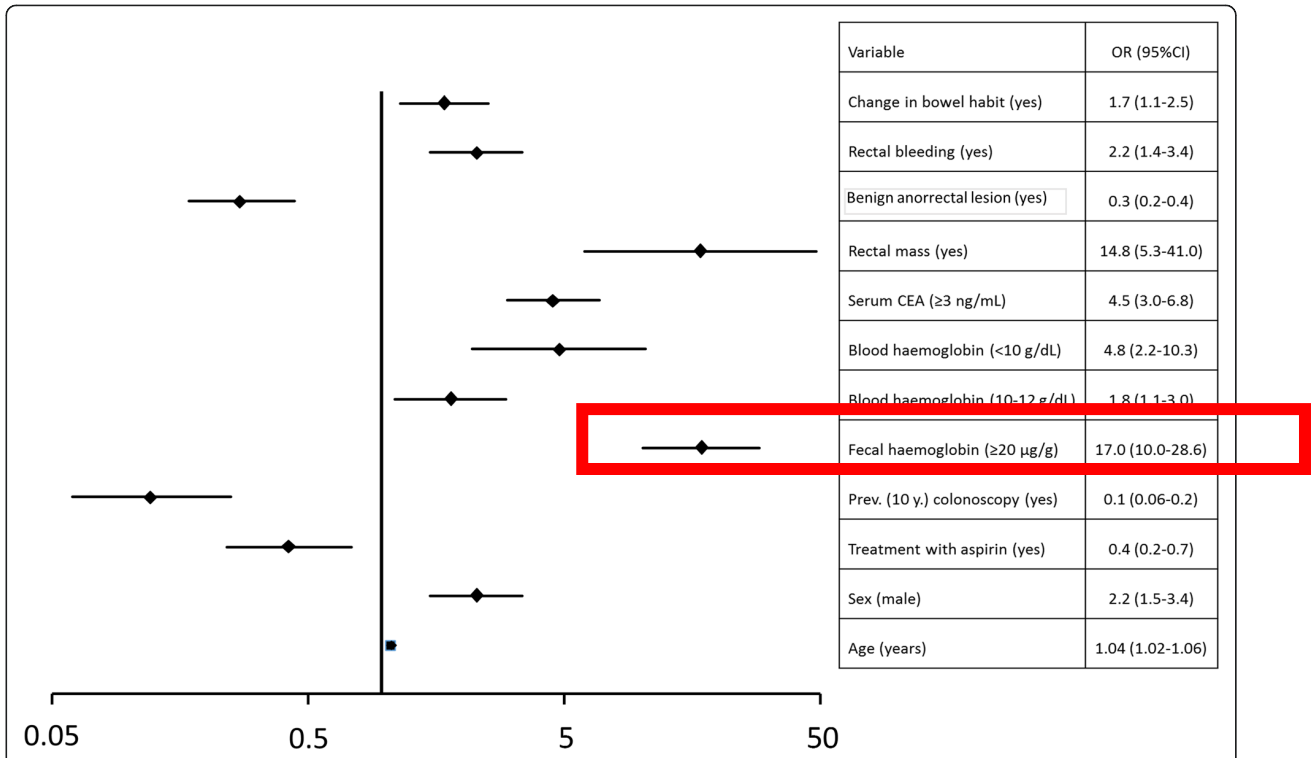


Variable	OR (95%CI)
Change in bowel habit (yes)	1.7 (1.1-2.5)
Rectal bleeding (yes)	2.2 (1.4-3.4)
Benign anorrectal lesion (yes)	0.3 (0.2-0.4)
Rectal mass (yes)	14.8 (5.3-41.0)
Serum CEA (≥3 ng/mL)	4.5 (3.0-6.8)
Blood haemoglobin (<10 g/dL)	4.8 (2.2-10.3)
Blood haemoglobin (10-12 g/dL)	1.8 (1.1-3.0)
Fecal haemoglobin (≥20 μg/g)	17.0 (10.0-28.6)
Prev. (10 y.) colonoscopy (yes)	0.1 (0.06-0.2)
Treatment with aspirin (yes)	0.4 (0.2-0.7)
Sex (male)	2.2 (1.5-3.4)
Age (years)	1.04 (1.02-1.06)

Fig. 2 Variables included in the COLONPREDICT model. The relationship with colorectal cancer risk in the multivariate logistic regression model is expressed as the odds ratio (*OR*) and its 95 % confidence interval (*CI*). *CEA* carcinoembryonic antigen; *Prev* previous

Cubiella *et al. BMC Medicine* (2016) 14:128

F-Hb bedre enn det meste annet!



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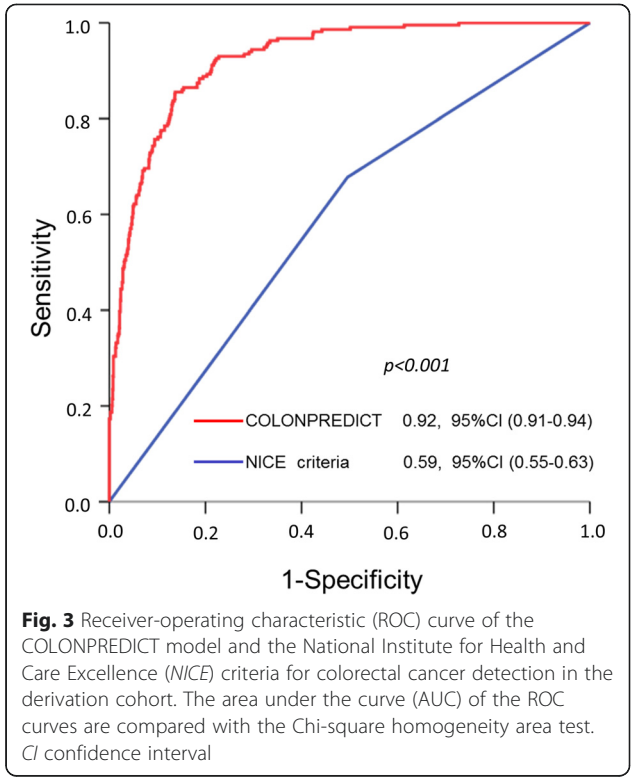


Fig. 3 Receiver-operating characteristic (ROC) curve of the COLONPREDICT model and the National Institute for Health and Care Excellence (*NICE*) criteria for colorectal cancer detection in the derivation cohort. The area under the curve (AUC) of the ROC curves are compared with the Chi-square homogeneity area test. *CI* confidence interval

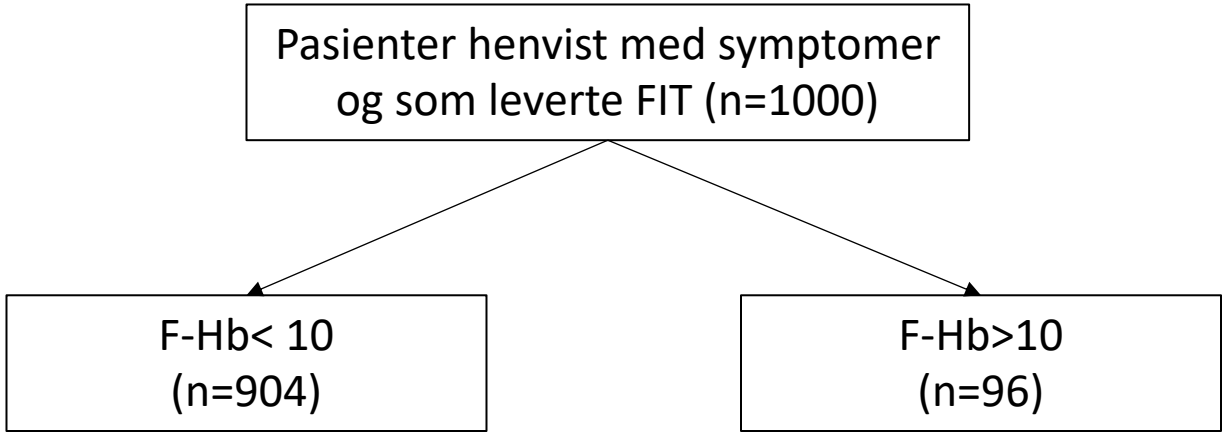
Meta-analyse fra primærhelsetjenesten

- 22 studier: 69 000 pasienter med mageplager

Terskelverdi	Tarmkreft	
mcg Hb/g feces	Sensitivitet	Spesifisitet
> 10	0,87 (0,81-0,92)	0,84 (0,79-0,88)
> 20	0,84 (0,79-0,88)	0,87 (0,76-0,93)
> 150	0,64 (0,58-0,70)	0,95 (0,91-0,97)

Pin-Vieito N, *et al*. *Gut* 2021;0:1–11.

Kan f-Hb brukes til risiko-stratifisering?



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DOI: 10.1111/apt.15969

Alimentary Pharmacology & Therapeutics WILEY

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[1]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK
[2]Department of Clinical Biochemistry, John Radcliffe Hospital, Oxford University Hospitals Trust, Oxford, UK
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Funding information
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Summary

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Results: In 9896 adult patients with at least 6-month follow-up, a FIT result ≥10 μg Hb/g faeces had a sensitivity for colorectal cancer of 90.5% (95% CI 84.9%-96.1%), specificity 91.3% (90.8%-91.9%), positive predictive value (PPV) 10.1% (8.15%-12.0%) and negative predictive value (NPV) 99.9% (99.8%-100.0%). The PPV and specificity for serious colorectal disease were higher and the sensitivity and NPV lower than for colorectal cancer alone. The area under the curve for all adults did not change substantially by gender or by increasing the minimum age of testing. Using ≥10 μg Hb/g faeces, 10% of adults would be investigated to detect 91% of cancers, a number needed to scope of ten to detect one cancer. Using ≥7, ≥50 and ≥150 μg Hb/g faeces, 11%, 4% and 3% of adults would be investigated, and 91%, 74% and 54% cancers detected, respectively.

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Mowat C, *et al. BMJ Open Gastro* 2019;**6**:e000293.

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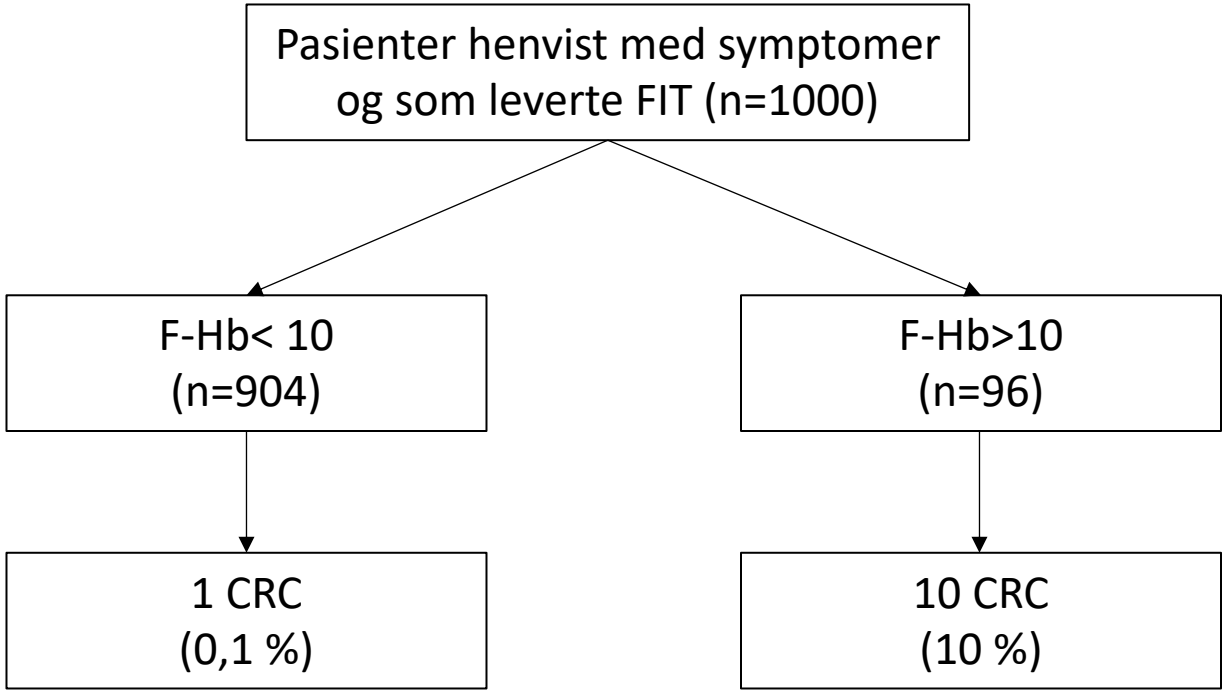

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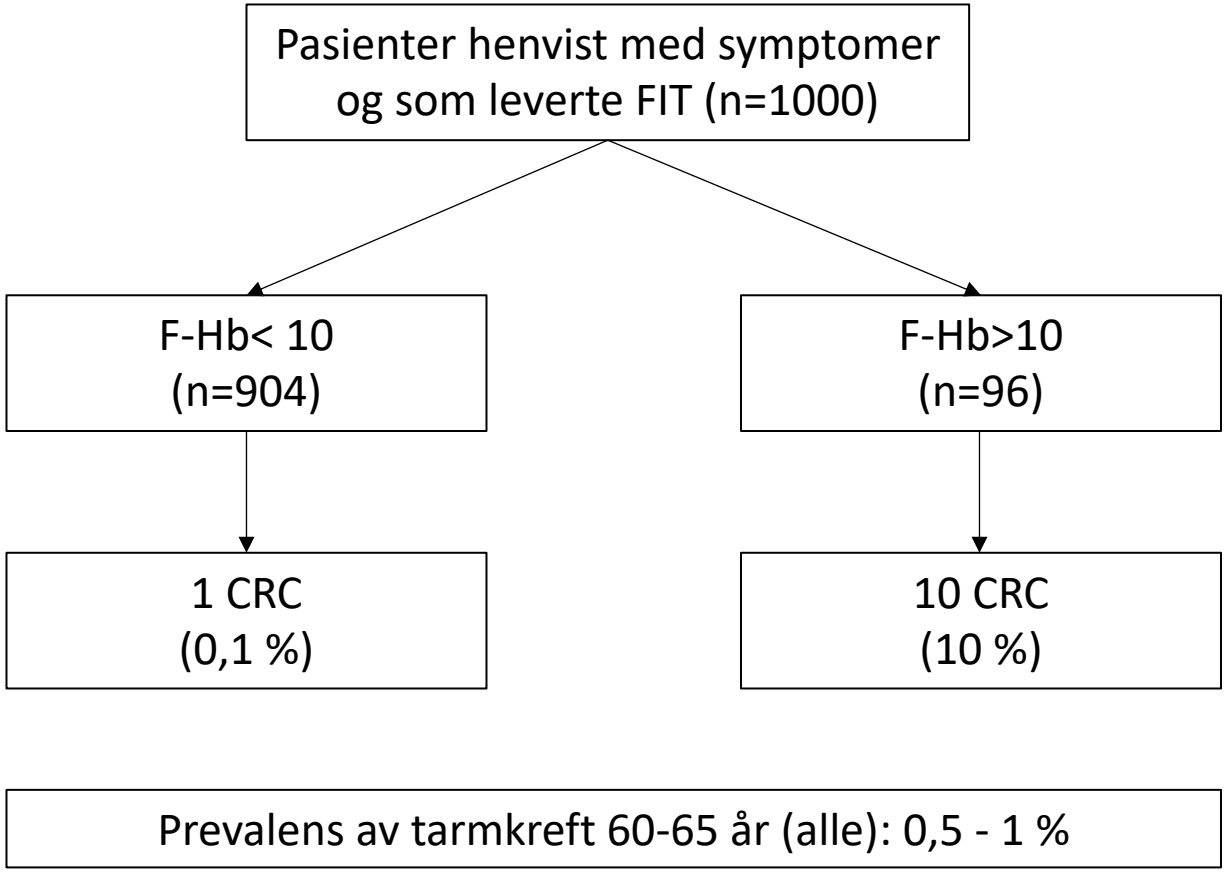

Prevalens av tarmkreft 60-65 år (alle): 0,5 - 1 %

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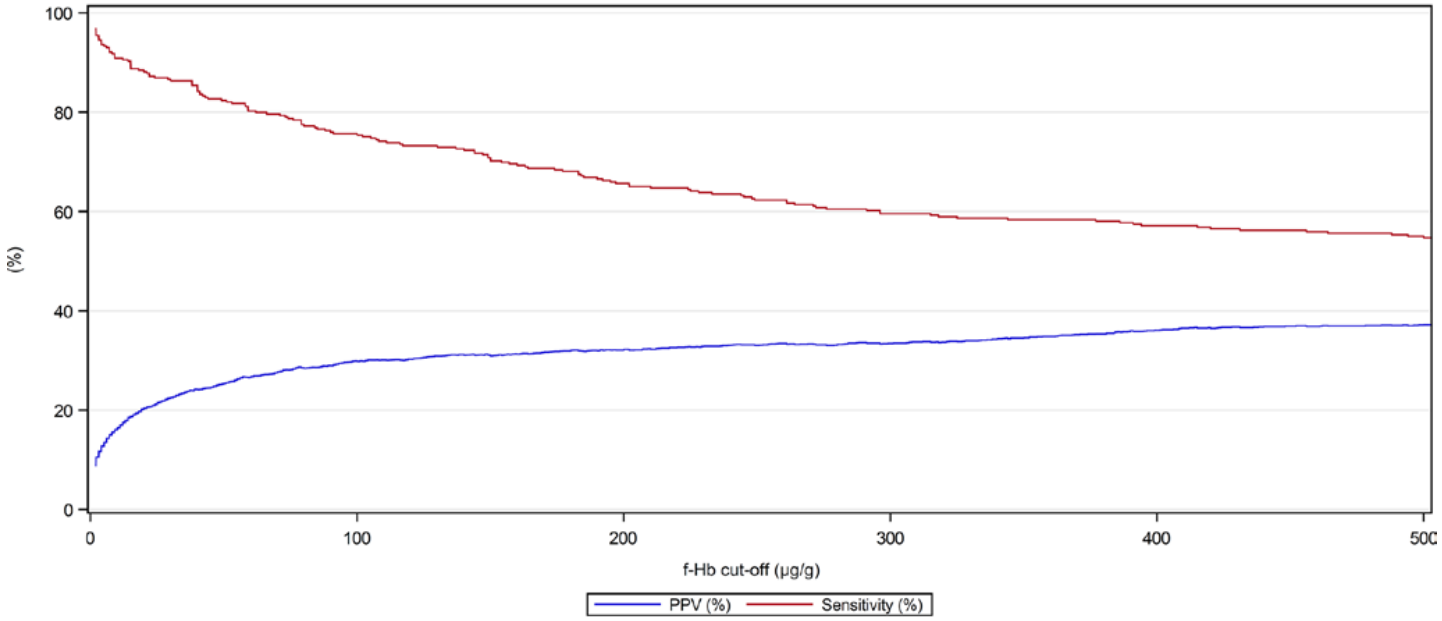
Positiv prediktiv verdi for tarmkreft og F-Hb



D'Souza N, *et al*. *Gut* 2021;**70**:1130–1138.

F-Hb har stor innvirkning på henvisning

Table 1 Influence of faecal haemoglobin concentration (f-Hb) on clinical decision-making in patients (n, (%)) with new bowel symptoms (n=5372)

	Total n	f-Hb <10 µg/g n (%)	f-Hb ≥10 µg/g n (%)	P value†
Patients with valid f-Hb result	5372	4197 (78.1)	1175 (21.9)	
Not referred by GP	2521	2403 (95.3)	118 (4.7)	<0.001

43 % henvist

90 % henvist

Mowat C, *et al. BMJ Open Gastro* 2019;**6**:e000293. doi:10.1136/bmjgast-2019-000293

Hvilken grense skal vi sette?

Table 3 Diagnostic accuracy of FIT for CRC at different cut-offs

Cut-off (µg/g)	Positivity (%)	NNS	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	TP	FN	FP	TN
2	37.2	11.5	97.0 (94.5 to 98.5)	64.9 (63.9 to 65.8)	8.7 (7.8 to 9.7)	99.8 (99.7 to 99.9)	319	10	3336	6157
10	19.0	6.2	90.9 (87.2 to 93.8)	83.5 (82.8 to 84.3)	16.1 (14.4 to 17.8)	99.6 (99.5 to 99.7)	299	30	1563	7930
150	7.6	3.2	70.8 (65.6 to 75.7)	94.6 (94.1 to 95.0)	31.1 (27.8 to 34.6)	98.9 (98.7 to 99.1)	233	96	516	8977
<2	62.8	616.7	3 (1.5 to 5.5)	35.1 (34.2 to 36.1)	0.2 (0.1 to 0.3)	91.3 (90.3 to 92.2)	10	319	6157	3336

95% CIs within brackets.

CRC, colorectal cancer; FIT, faecal immunochemical test; FN, false negatives; FP, false positives; NNS, number needed to scope; NPV, negative predictive value; PPV, positive predictive value; TN, true negatives; TP, true positives.

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Kanskje bedre med 0 som grense?

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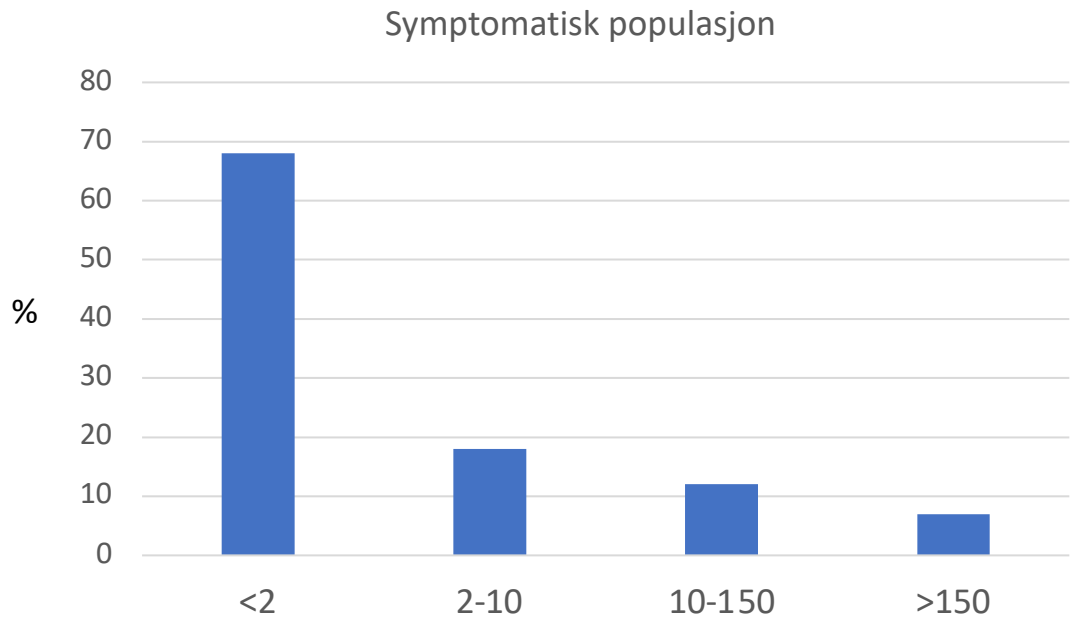
D'Souza N, *et al*. *Gut* 2021;**70**:1130–1138.

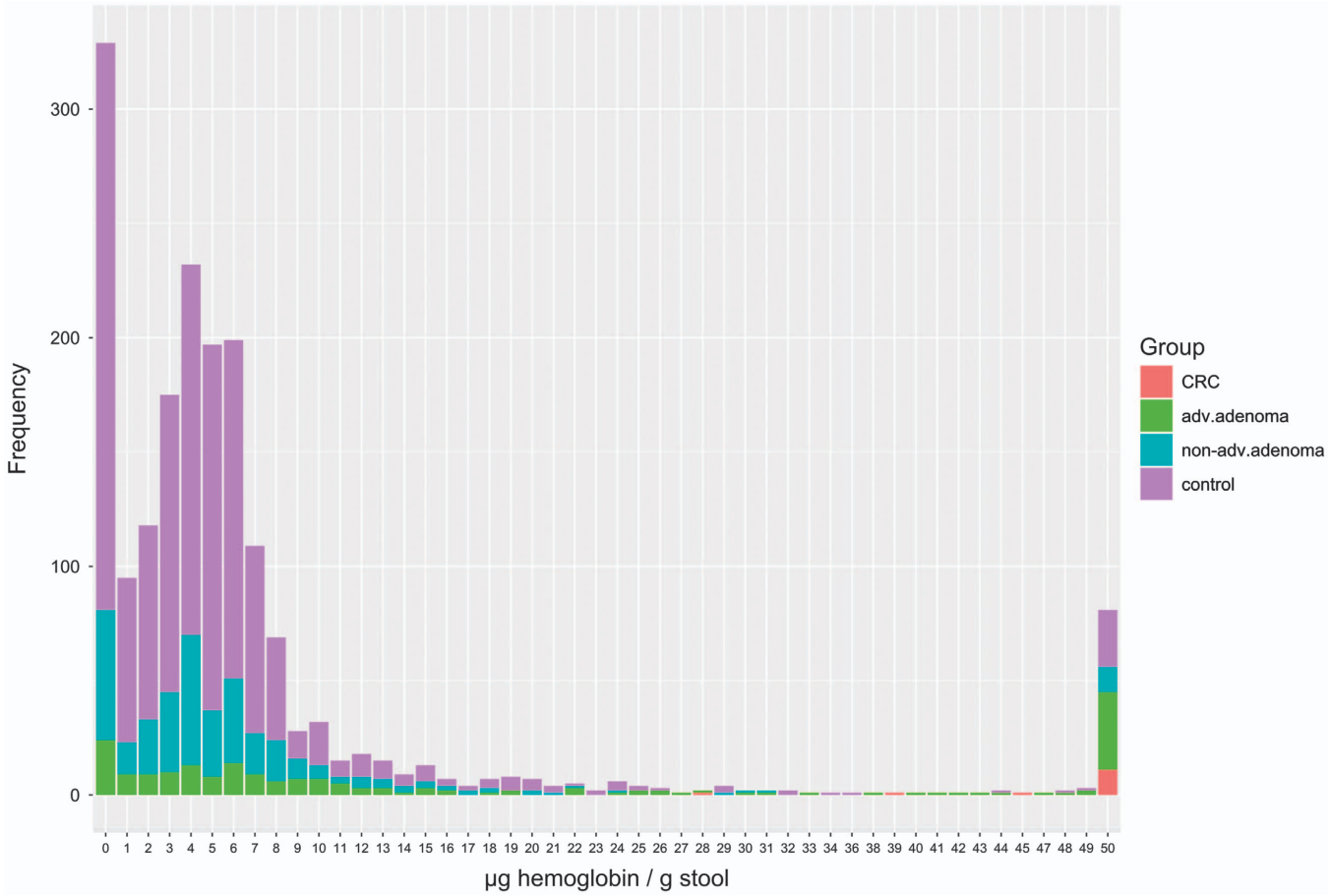
Det vanligste er å ikke ha blod i avføringen!



Fordeling av F-Hb verdier i symptomatisk populasjon

D'Souza N, *et al*. *Gut* 2021;**70**:1130–1138.

De fleste personer med polypper har F-Hb < 10



Clinical and Translational Gastroenterology (2017) **8,** e111

Det er også andre ting i tarmen

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Det er også andre ting i tarmen

Table 2 Frequency of pathology findings at colonoscopy in symptomatic patients referred via 2WW pathways

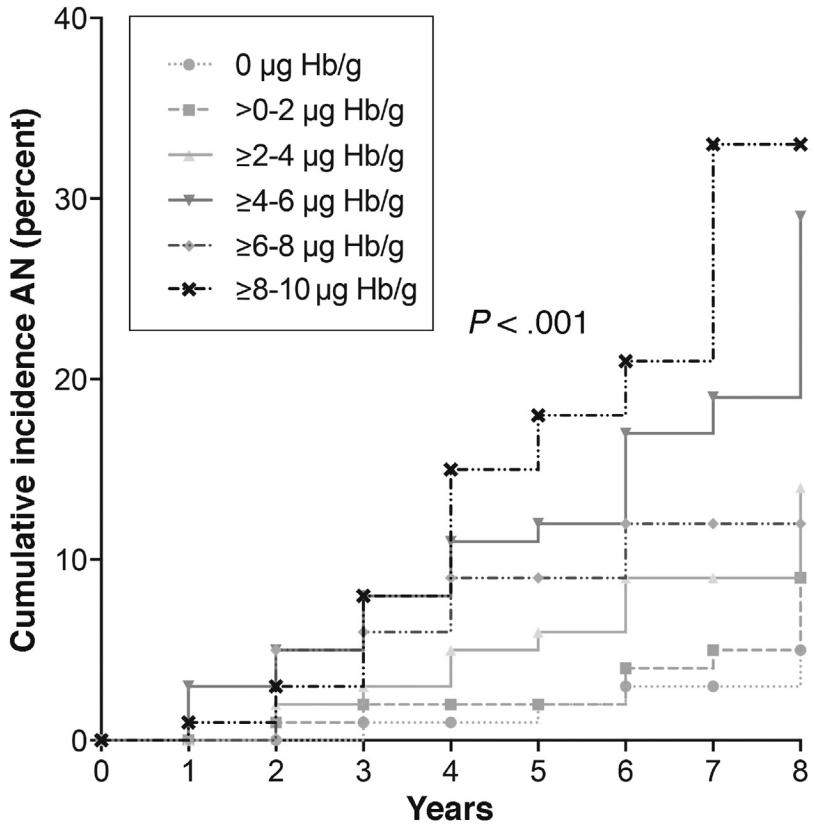
Diagnosis	N	%
Normal	3079	31.3
Low risk adenoma	2321	23.6
Diverticular disease	2294	23.4
Perianal disease*	723	7.4
Inflammatory bowel disease	427	4.3
High-risk adenoma	421	4.3
Colorectal cancer	329	3.3
Microscopic colitis	152	1.5
Other†	53	0.5
Angiodysplasia	23	0.2

Table 4 Diagnostic accuracy of FIT for CRC and SBD at different cut-offs

Risk category	FIT positivity	Cut-off (µg/g)	Sensitivity	Specificity	PPV	NPV
≥2	37.2	CRC	97.0 (94.5 to 98.5)	64.9 (63.9 to 65.8)	8.7 (7.8 to 9.7)	99.8 (99.7 to 99.9)
		HRA	65.8 (61.0 to 70.3)	64.1 (63.1 to 65.0)	7.6 (6.7 to 8.5)	97.7 (97.3 to 98.0)
		IBD	73.1 (68.6 to 77.2)	64.4 (63.4 to 65.4)	8.5 (7.7 to 9.5)	98.1 (97.8 to 98.5)
		SBD	77.1 (74.6 to 79.5)	68.2 (67.2 to 69.2)	24.8 (23.4 to 26.3)	95.6 (95.1 to 96.1)
≥10	19.0	CRC	90.9 (87.2 to 93.8)	83.5 (82.8 to 84.3)	16.1 (14.4 to 17.8)	99.6 (99.5 to 99.7)
		HRA	45.4 (40.5 to 50.3)	82.2 (81.4 to 83.0)	10.3 (8.9 to 11.7)	97.1 (96.7 to 97.5)
		IBD	[illegible]	82.8 (82.0 to 83.6)	13.3 (11.8 to 14.9)	97.7 (97.4 to 98.1)
		SBD	62.6 (59.8 to 65.4)	87.0 (86.3 to 87.7)	39.6 (37.4 to 41.8)	94.5 (93.9 to 95.0)
≥150	7.6	CRC	[illegible]	94.6 (94.1 to 95.0)	31.1 (27.8 to 34.6)	98.9 (98.7 to 99.1)
		HRA	22.1 (18.2 to 26.4)	93.0 (92.5 to 93.5)	12.4 (10.1 to 15.0)	96.4 (96.0 to 96.8)
		IBD	36.8 (32.2 to 41.5)	93.7 (93.2 to 94.2)	21.0 (18.1 to 24.1)	97.0 (96.7 to 97.4)
		SBD	41.0 (38.2 to 43.9)	96.9 (96.5 to 97.3)	64.5 (60.9 to 67.9)	92.4 (91.8 to 92.9)

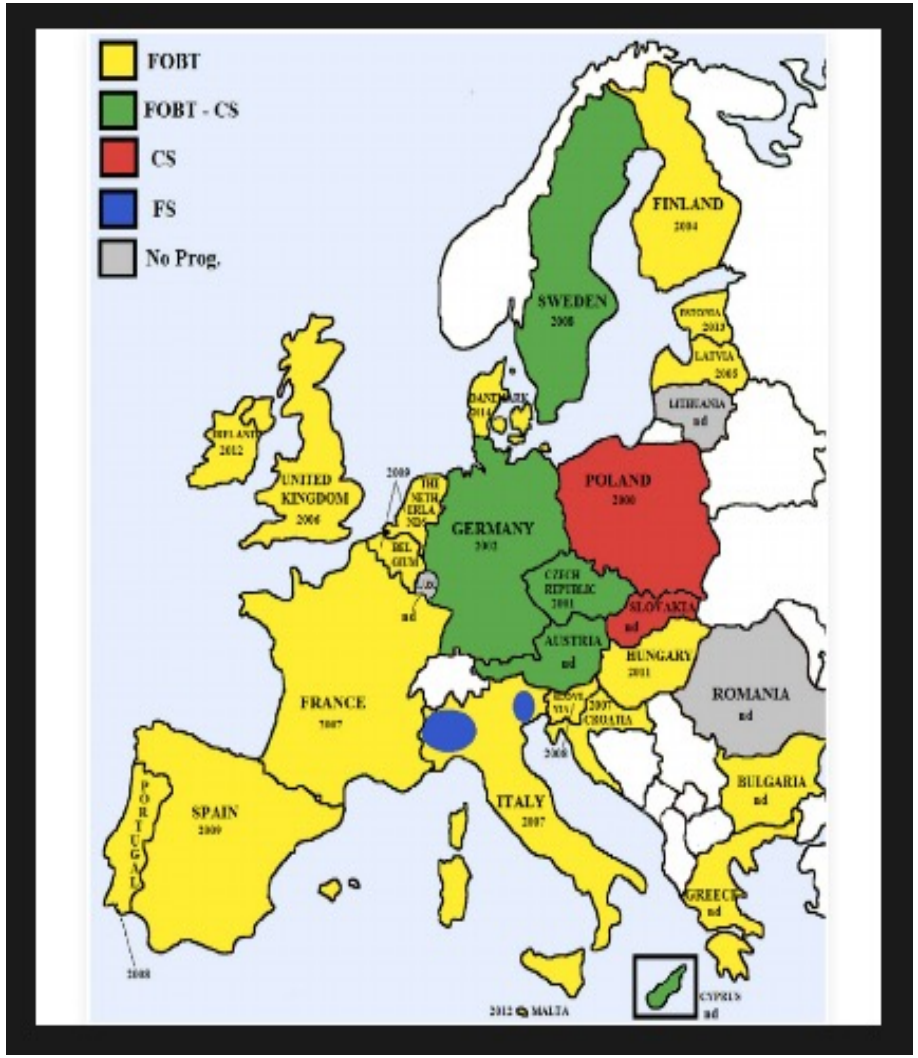
D'Souza N, *et al*. *Gut* 2021;**70**:1130–1138.

Hva skjer i tiden etter hos personer med F-Hb< 10?

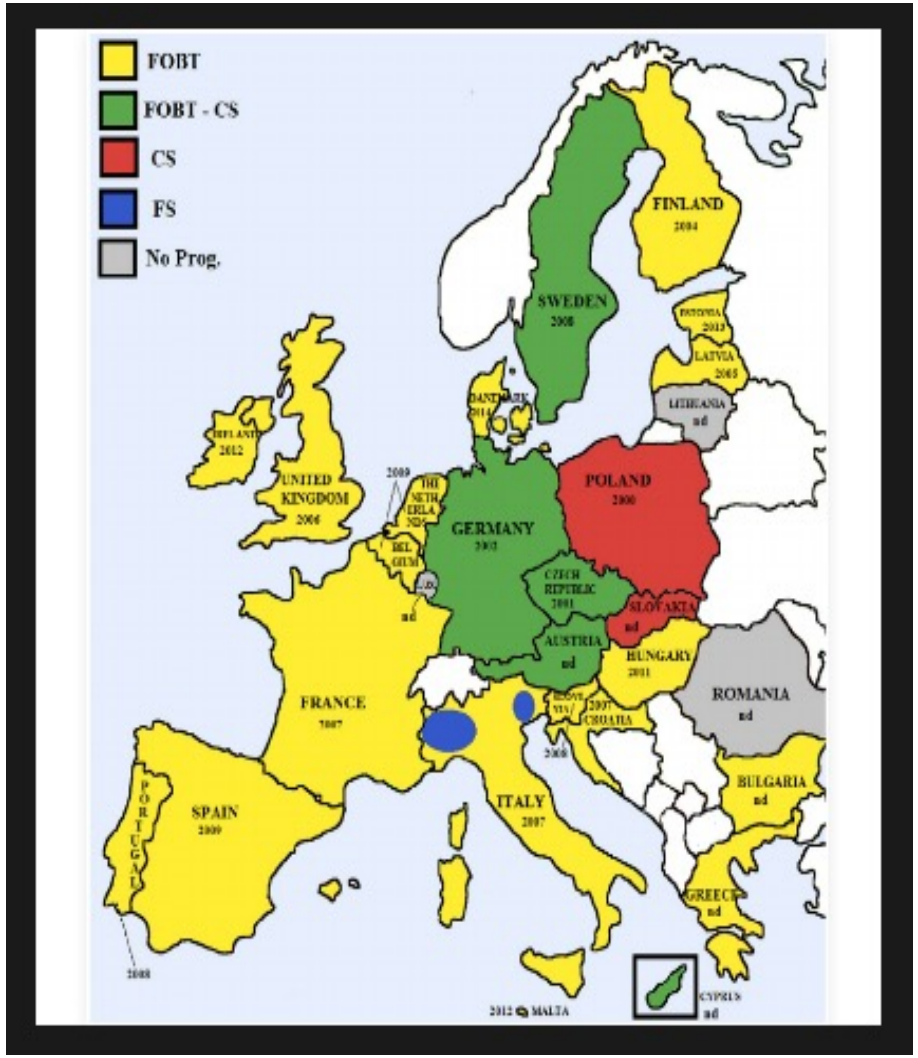


Gastroenterology 2017;153:1251–1259

F-Hb og screening for tarmkreft



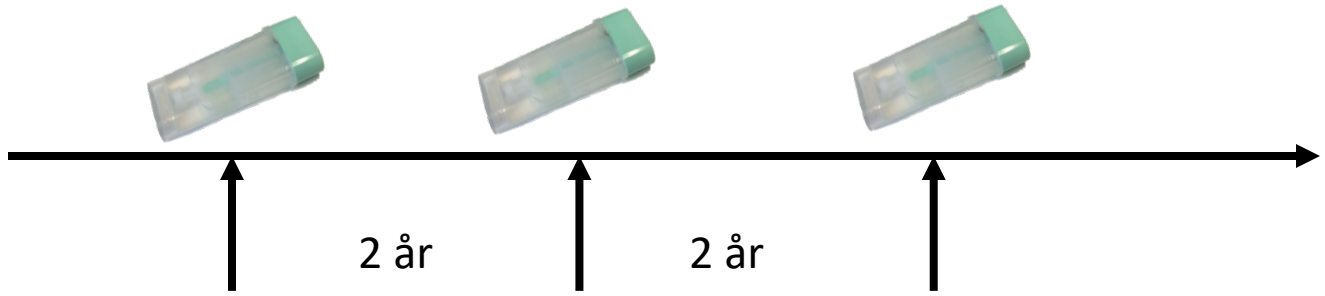
F-Hb og screening for tarmkreft



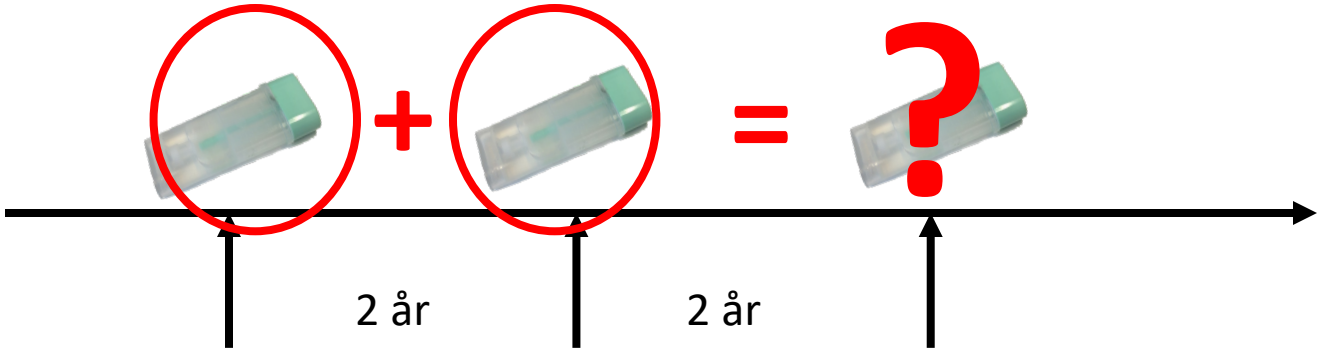
Tarmscreening i Norge:

- F-Hb
- Terskelverdi: 15 mcg/g
- Starter våren 2022
- 55 år
- 2.hvert år

F-Hb for persontilpasset screening?



F-Hb for persontilpasset screening?



F-Hb for persontilpasset screening?

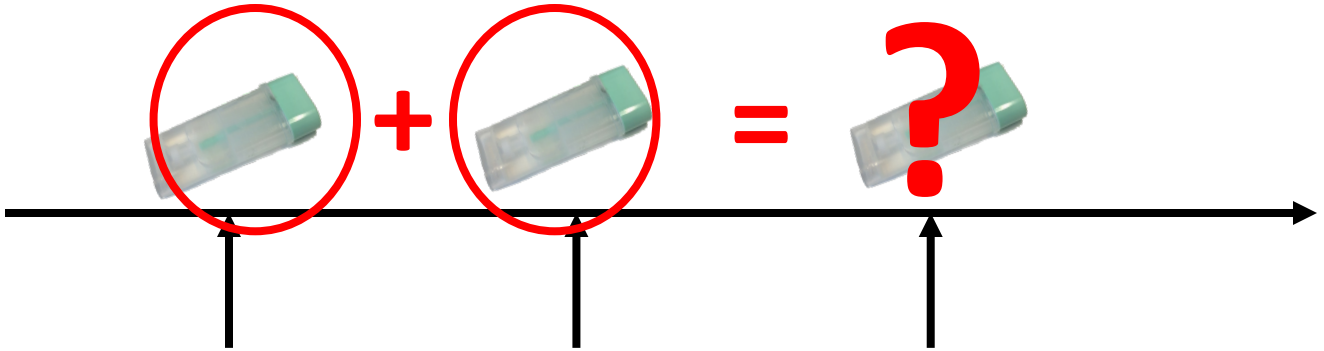


Table 2 Predictors of the DR of CRC, advanced adenoma and AN at the third FIT

		CRC	
		OR	95% CI
Cumulative f-Hb level at previous 2 FIT tests (FIT1 + FIT2) µg Hb/g faeces	**0**	1	
	0.1–3.9	2.26	1.47 to 3.46
	4–9.9	4.01	2.51 to 6.39
	10–14.9	10.11	6.04 to 16.93
	15–19.9	11.63	6.42 to 21.07
	≥20	38.92	22.50 to 67.31

Senore C, *et al*. *Gut* 2019;**0**:1–8.

Hvorfor test for blod i avføringen

- Kan F-Hb hjelpe fastlegene i diagnostisk utredning og henvisning?
- Kan F-Hb hjelpe sykehuslegene til å prioritere

Hvorfor test for blod i avføringen

- Kan F-Hb hjelpe fastlegene i diagnostisk utredning og henvisning?
  - Ja

Hvorfor test for blod i avføringen

- Kan F-Hb hjelpe fastlegene i diagnostisk utredning og henvisning?
  - Ja, men:
    - Er ikke en diagnostisk test
    - Kan skille ut de som har lav risiko for tarmkreft og som ikke trenger henvisning
      - Kun Australia, UK og Spania anbefaler dette
      - Hvilken terskelverdi er den riktige?
      - Samvalg – hvilken risiko for alvorlig sykdom er akseptabel? Ressursbruk?

Hvorfor test for blod i avføringen

- Kan F-Hb hjelpe sykehuslegene til å prioritere?
  - Ja!

Oppsummering

- F-Hb er den beste biomarkøren vi har for tarmkreft
- Kliniker har behov for et kvantitativt svar
- Nyttig verktøy, men ikke som diagnostisk test

Hvorfor test for blod i avføringen

- Kan F-Hb hjelpe fastlegene i diagnostisk utredning og henvisning?
  - Er et hjelpemiddel i utredning
  - Er ikke en diagnostisk test
  - Kan skille ut de som har lav risiko for tarmkreft og som ikke trenger henvisning
    - Kun Australia, UK og Spania anbefaler dette
    - Hvilken terskelverdi er den riktige?
    - Samvalg – hvilken risiko for alvorlig sykdom er akseptabel?