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The voice of world endoscopy

FIT for surveillance

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Instituto de Salud Carlos III

Cofinanciado por la Unión Europea

Agenda

- The problem
- The questions
- FIT for surveillance: the evidence
- FIT for surveillance: the future

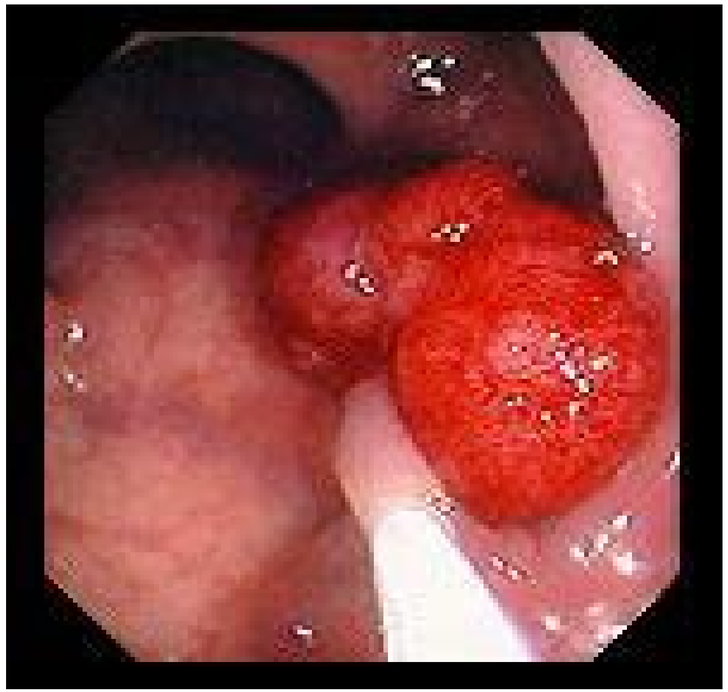
Agenda

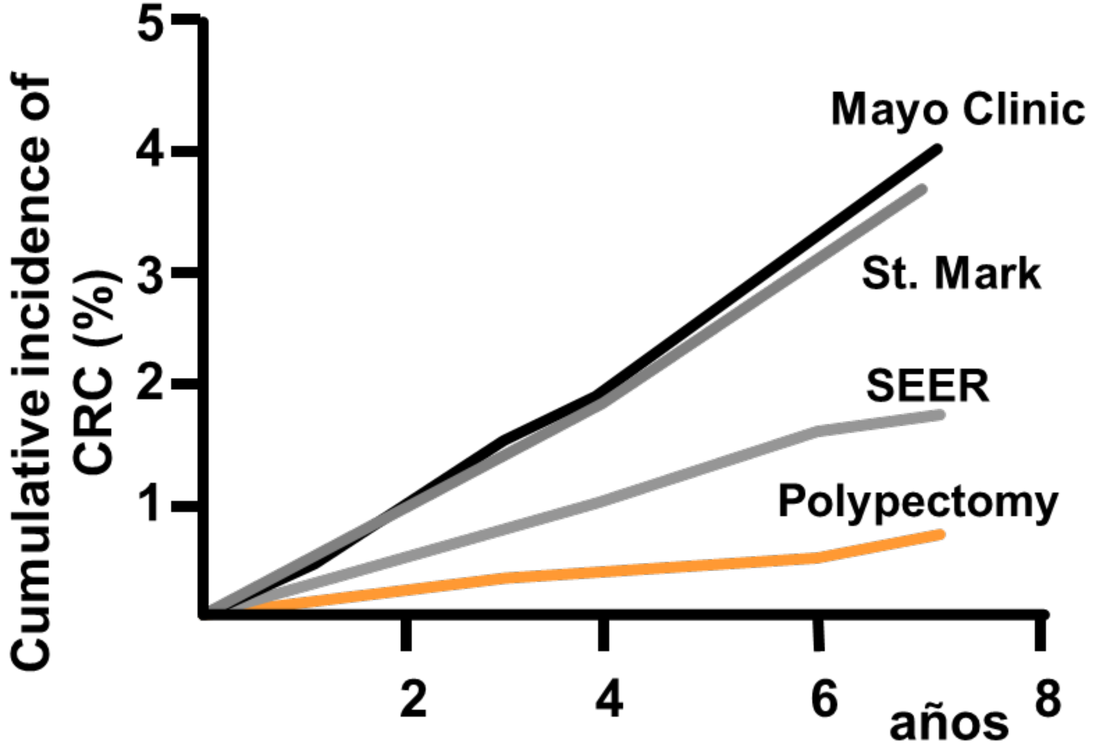
- **The problem**
- **The questions**
- **FIT for surveillance: the evidence**
- **FIT for surveillance: the future**

30 years ago....

PREVENTION OF COLORECTAL CANCER BY COLONOSCOPIC POLYPECTOMY

Sidney J. Winawer, M.D., Ann G. Zauber, Ph.D., May Nah Ho, M.S., Michael J. O'Brien, M.D., Leonard S. Gottlieb, M.D., Stephen S. Sternberg, M.D., Jerome D. Waye, M.D., Melvin Schapiro, M.D., John H. Bond, M.D., Joel F. Panish, M.D., Frederick Ackroyd, M.D., Moshe Shike, M.D., Robert C. Kurtz, M.D., Lynn Hornsby-Lewis, M.D., Hans Gerdes, M.D., Edward T. Stewart, M.D., and the National Polyp Study Workgroup*





30 years ago....

Volume 328 APRIL 1, 1993 Number 13

RANDOMIZED COMPARISON OF SURVEILLANCE INTERVALS AFTER COLONOSCOPIC REMOVAL OF NEWLY DIAGNOSED ADENOMATOUS POLYPS

Sidney J. Winawer, M.D., Ann G. Zauber, Ph.D., Michael J. O'Brien, M.D., May Nah Ho, M.S., Leonard Gottlieb, M.D., Stephen S. Sternberg, M.D., Jerome D. Waye, M.D., John Bond, M.D., Melvin Schapiro, M.D., Edward T. Stewart, M.D., Joel Panish, M.D., Fred Ackroyd, M.D., Robert C. Kurtz, M.D., Moshe Shike, M.D., and the National Polyp Study Workgroup*

Table 6. Comparison of the Findings at Both Follow-up Examinations in the Two-Examination Group with the Findings in the One-Examination Group.

Finding	2 Examinations (N = 338)	1 Examination* (N = 428)	Relative Risk (95% CI)†	P Value
	no. (%) of patients			
Any adenoma detected	141 (41.7)	137 (32.0)	1.3 (1.1–1.6)	0.006
Adenoma with advanced pathological features‡	11 (3.3)§	14 (3.3)	1.0 (0.5–2.2)	0.99

Polyp Guideline: Diagnosis, Treatment, and Surveillance for Patients with Nonfamilial Colorectal Polyps*

John H. Bond, MD, for the Practice Parameters Committee of the American College of Gastroenterology

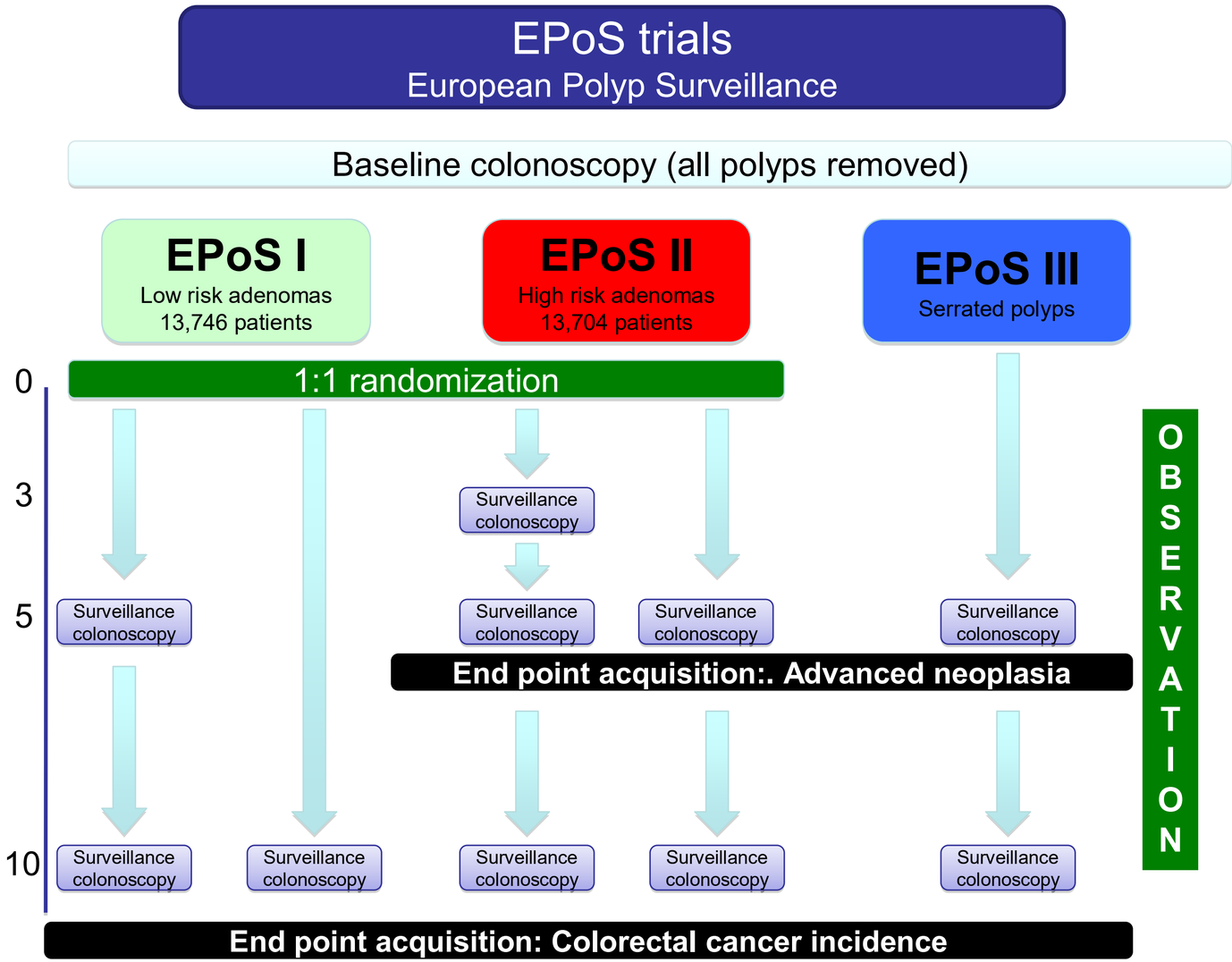
3. Postpolypectomy Surveillance
   A. Complete colonoscopy should be performed at the time of polypectomy to detect and resect all synchronous adenomas. Additional clearing examinations may be required after resection of a large sessile adenoma or of multiple adenomas to ensure complete resection.
   B. Repeated colonoscopy to check for missed synchronous and for metachronous adenomas is performed in 3 years for most patients with a single, or only a few adenomas, provided they have had a high-quality initial clearing examination.

Principles for evaluation of surveillance

	Consensus (%)
Principles	
The primary aim of postpolypectomy surveillance is to reduce CRC incidence in patients found to have prior colonic polyps, once polyp clearance has been achieved.	90
The secondary aim of CRC surveillance is to reduce CRC mortality. This is achieved both by reducing CRC incidence and through the identification of CRC at an earlier stage when CRC treatment carries a better prognosis.	81
Surveillance should only be offered to individuals who remain at higher risk of developing CRC, beyond the reduction seen by baseline polyp clearance, as compared with the general population.	80
The impact of surveillance in terms of CRC risk reduction should be balanced with the risks of harm (e.g., colonoscopy complications or psychological distress), the patient burden and the costs.	95
In a financially or endoscopy resource-constrained system, surveillance should also be considered in the context of other nonsurveillance cohorts of patients with higher positive predictive value for CRC/advanced polyps who may benefit more from the same resource (opportunity cost).	95
The findings at surveillance comprise both de novo pathology and pathology missed or incompletely excised at the prior colonoscopy. Higher quality colonoscopy will decrease the latter proportion.	95
Ideally, surveillance effectiveness should be measured after an appropriate period of postsurveillance follow-up.	90
Long-term (postsurveillance) follow-up of $\geq$5 years, preferably 10 years, is recommended.	85

Rutter. Gastroenterology 2020

Randomized controlled trials



Jover, Endoscopy 2016

Impact on endoscopy units

WEO
World Endoscopy Organization

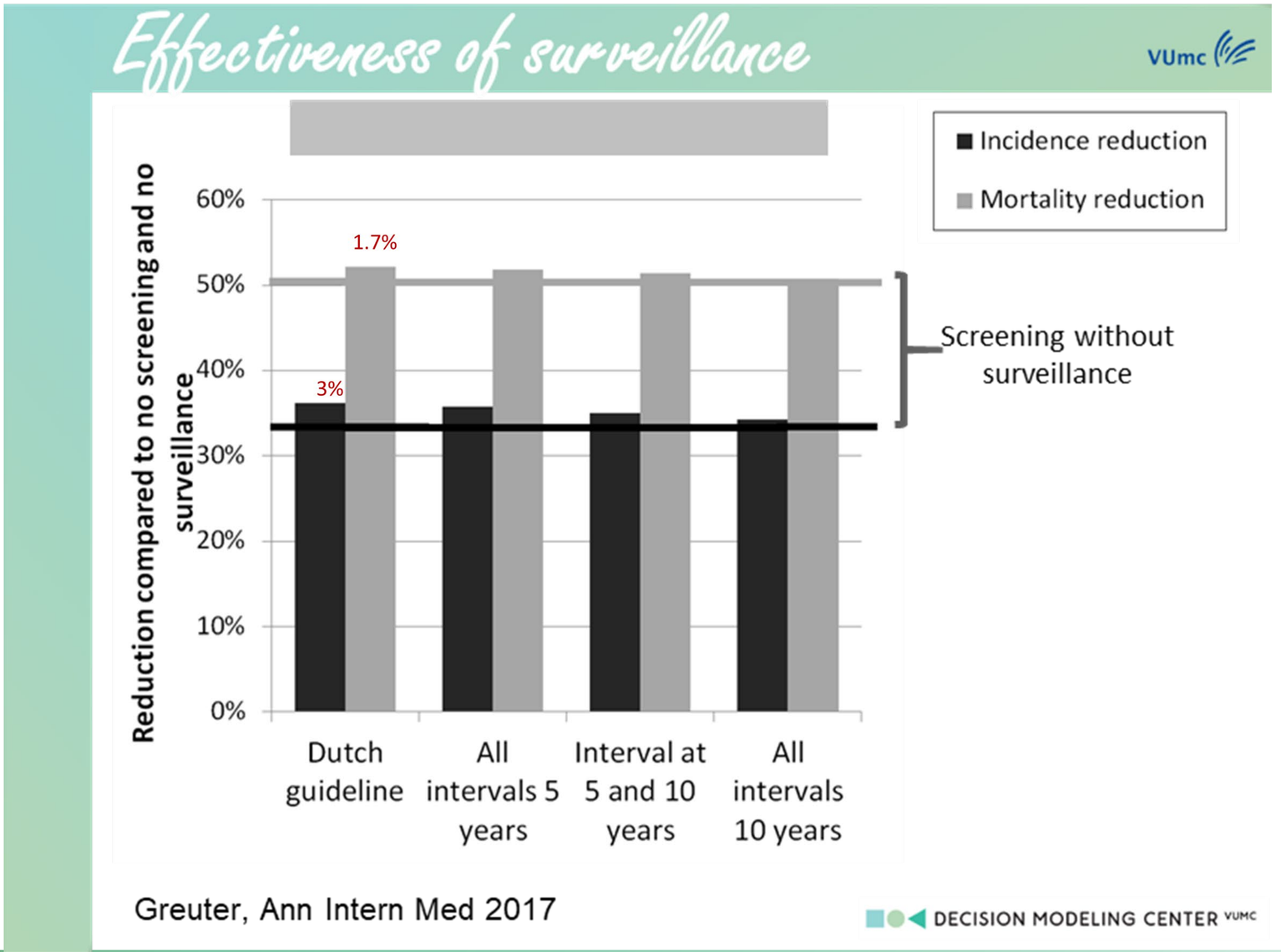
6.000.000 colonoscopies/year in Europe

Surveillance 25% of colonoscopies

1.500.000 surveillance colonoscopies/year

500.000.000 €/year

Expected impact on CRC incidence and mortality



Agenda

- The problem
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The questions

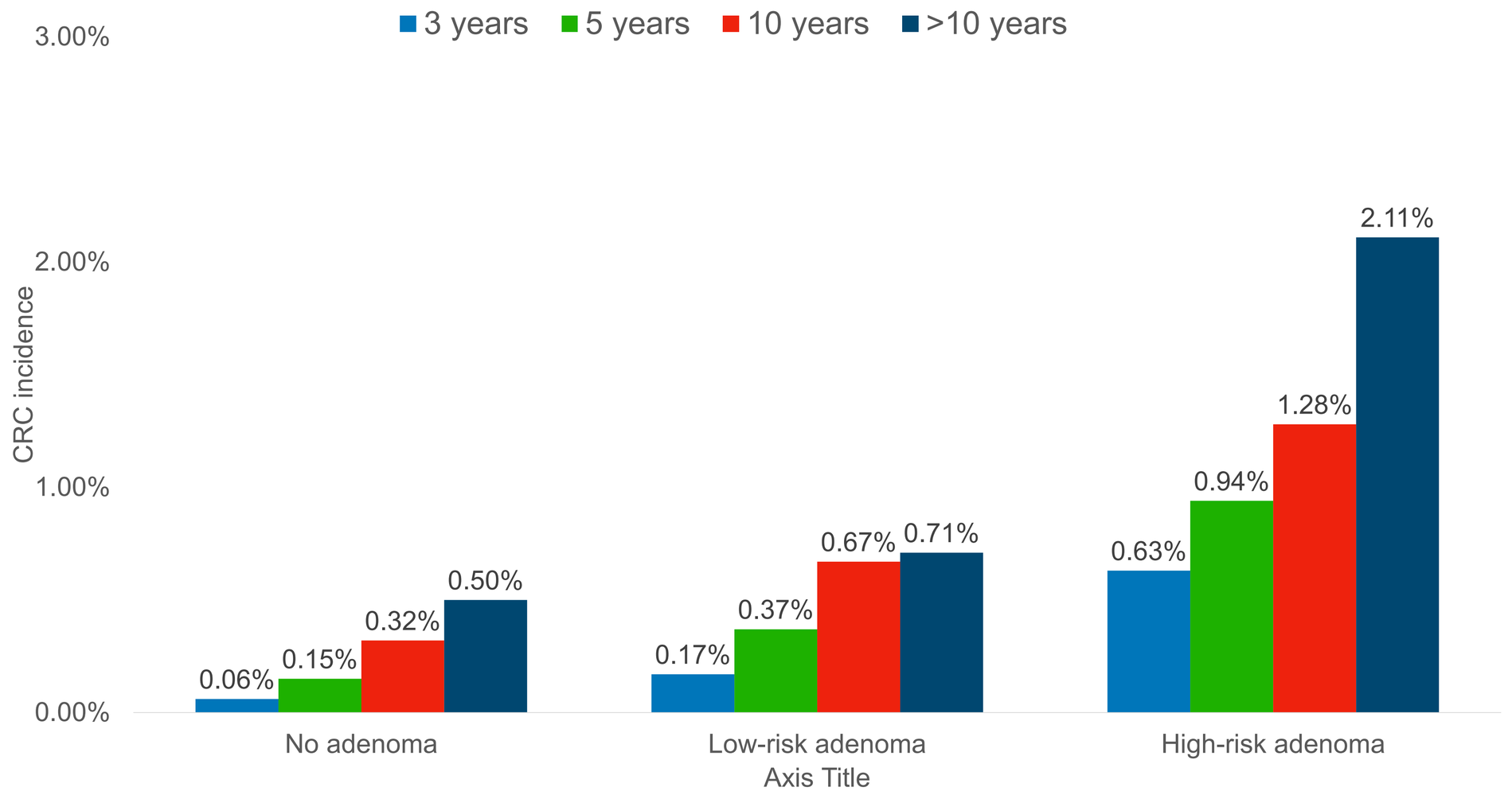
- **Has the CRC incidence changed in these 30 years?**
- **What do patients prefer?**
- **Colonoscopy or nothing? Is there any other option?**

CRC incidence: the past

	APPS (N = 837)	NPS (N = 939)	CPPS (N = 913)	PPT (N = 2024)	WBF (N = 1304)	VA (N = 871)	AFT (N = 1086)	UDCA (N = 1193)	Total (N = 9167)
Median follow-up period, mo (*range*)	49.1 (11.4–75.8)	36.9 (6.1–57.0)	48.6 (10.9–91.4)	52.1 (6.5–84.5)	39.1 (6.7–88.6)	59.0 (7.8–66.0)	36.9 (11.5–66.4)	38.0 (6.4–88.1)	47.2 (6.1–91.4)
Median number of colonoscopies (*range*)	2.0 (1.0–8.0)	1.0 (1.0–6.0)	2.0 (1.0–7.0)	2.0 (1.0–7.0)	2.0 (1.0–6.0)	1.0 (1.0–7.0)	1.0 (1.0–5.0)	1.0 (1.0–5.0)	2.0 (1.0–8.0)
Any adenoma during follow-up period, n (%)[a]	432 (51.6)	324 (34.5)	428 (46.9)	1077 (53.2)	641 (49.2)	395 (45.4)	476 (43.8)	507 (42.5)	4280 (46.7)
Large adenoma, n (%)[b]	53 (6.3)	60 (6.4)	55 (6.0)	159 (7.9)	137 (10.5)	66 (7.6)	66 (6.1)	115 (9.6)	711 (7.8)
Tubulovillous/villous histology, n (%)[c]	110 (13.1)	15 (1.6)	103 (11.3)	82 (4.1)	82 (6.3)	23 (2.6)	76 (7.0)	89 (7.5)	580 (6.3)
High-grade dysplasia, n (%)	4 (0.5)	6 (0.6)	2 (0.2)	23 (1.1)	12 (0.9)	6 (0.7)	0 (0.0)	1 (0.1)	54 (0.6)
Advanced adenoma, n (%)[d]	128 (15.3)	64 (6.8)	120 (13.1)	195 (9.6)	177 (13.6)	69 (7.9)	108 (9.9)	163 (13.7)	1024 (11.2)
Colorectal cancer, n (%)	5 (0.6)	3 (0.3)	8 (0.9)	13 (0.6)	8 (0.6)	8 (0.9)	6 (0.6)	7 (0.6)	58 (0.6)

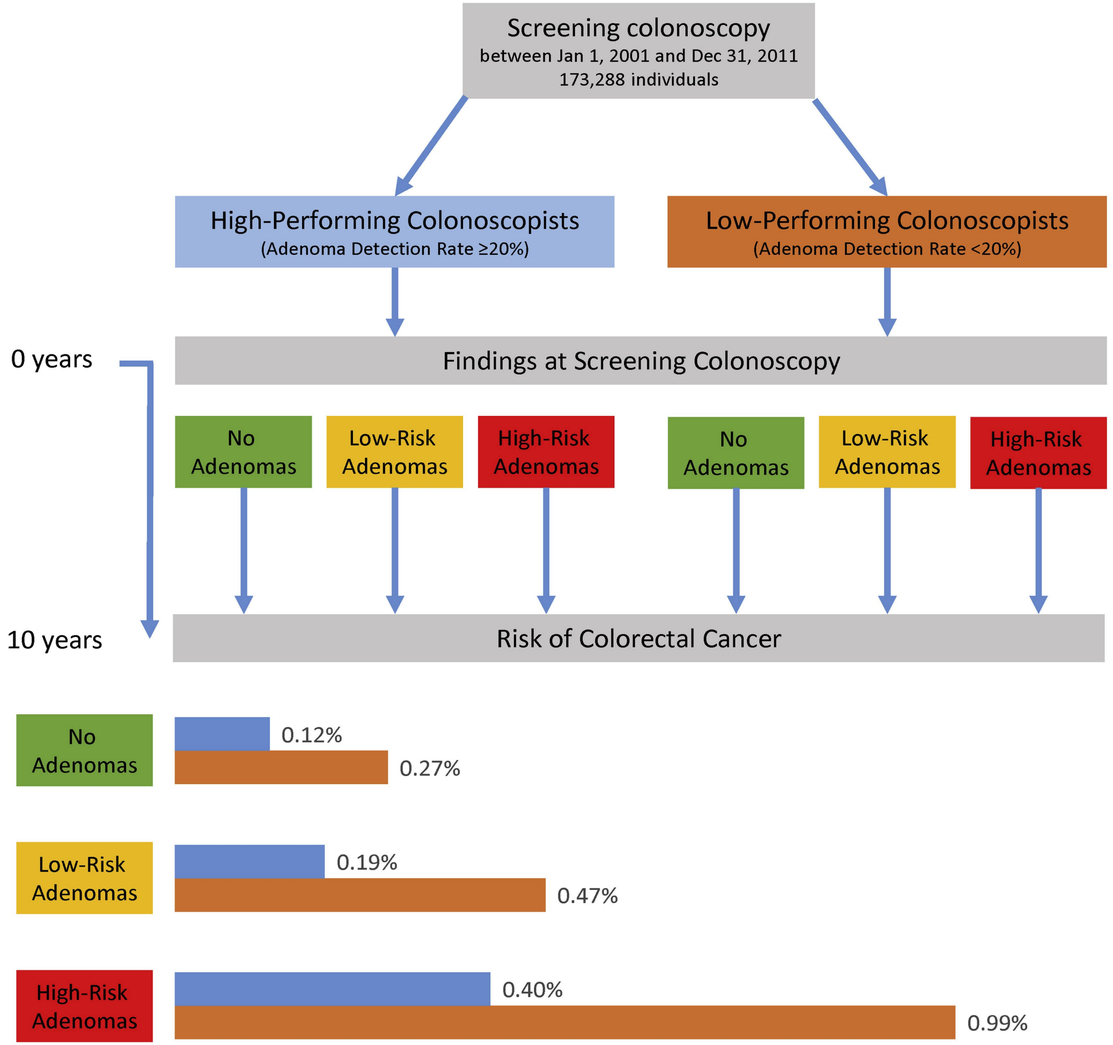
Martínez et al, Gastroenterology 2009

CRC incidence: the present??



Zhang et al, Exp Rev Gast Hep 2022

CRC incidence: the endoscopist



Wieszczy et al, Gastroenterology 2021

Will Rogers phenomenon??

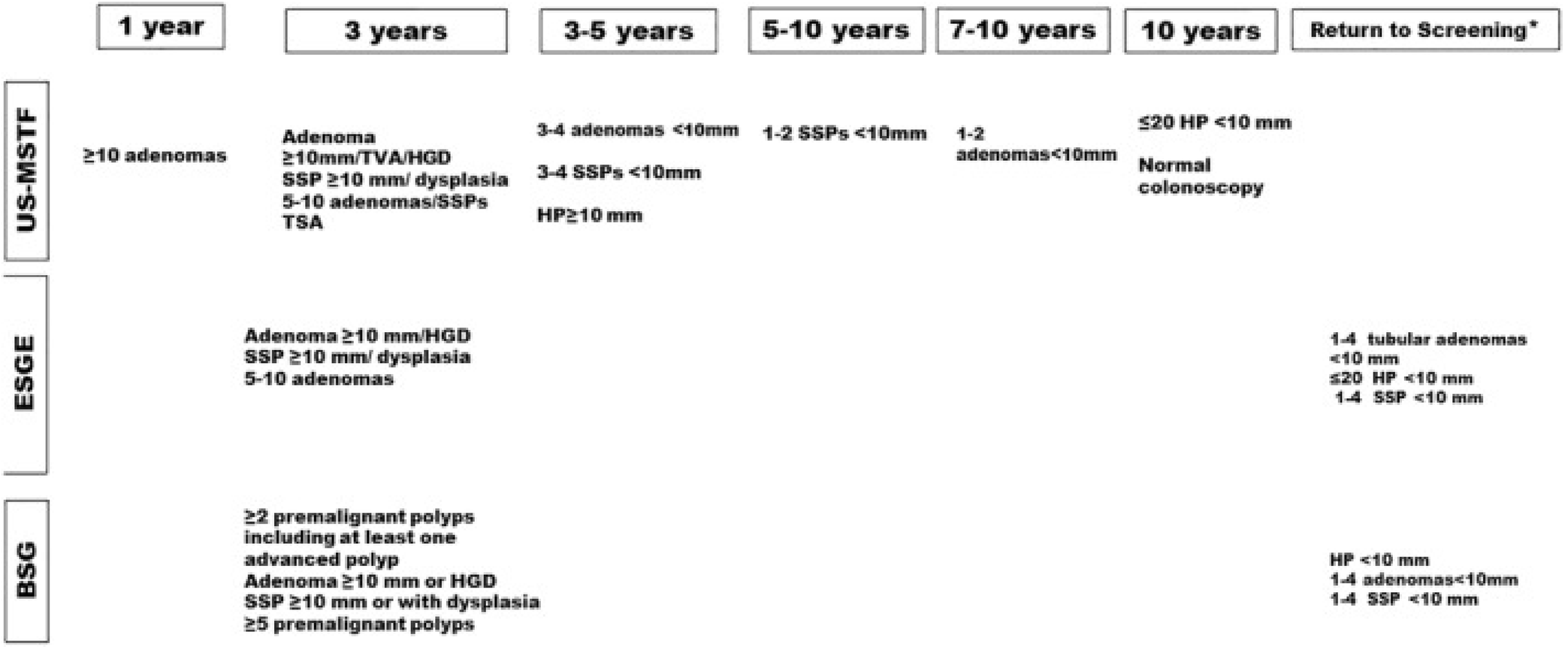


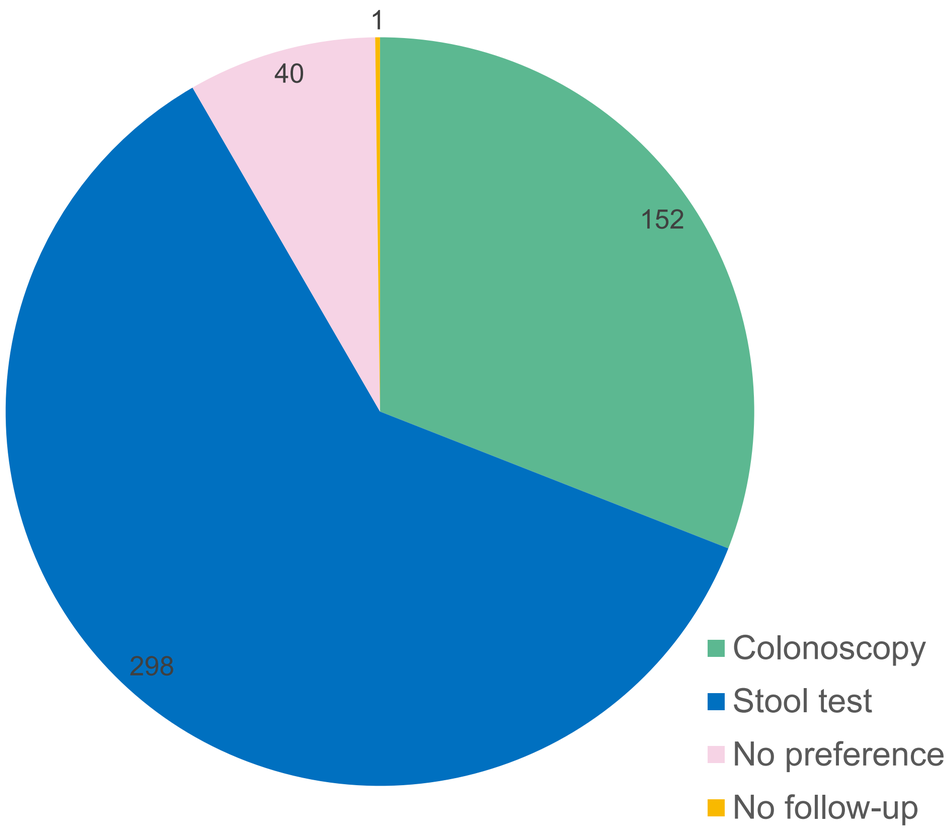
Figure 1: Main recommendations of the three guidelines

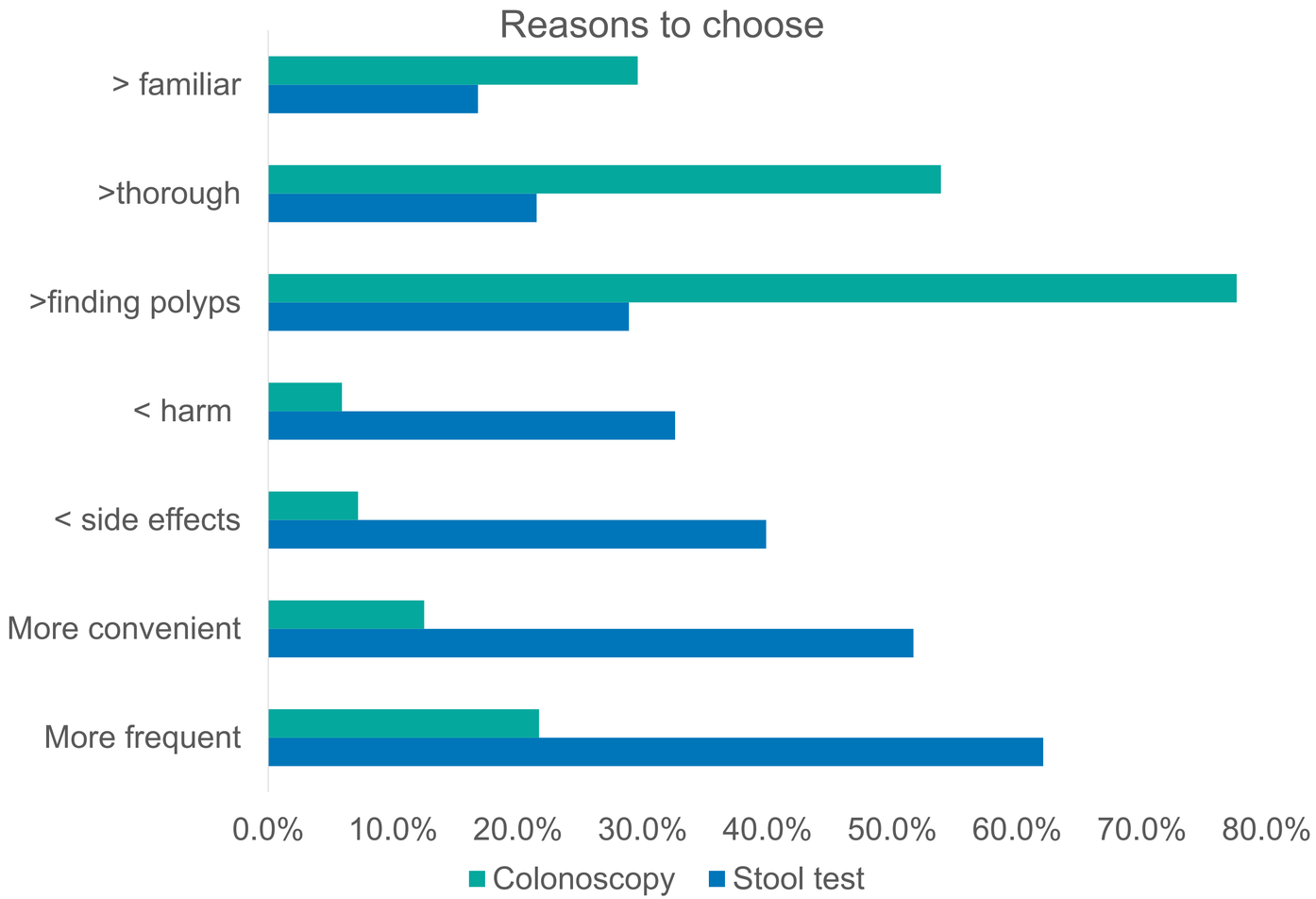
- Return to local screening recommendations (FIT) when invited (BSG)
- Return to local screening recommendation (FIT) or colonoscopy after 10 years if organized CRC screening program is not available (ESGE)

TVA=Tubulovillous adenoma, HGD=High-grade Dysplasia, SSP= Sessile serrated polyp, TSA=Traditional Serrated adenoma, HP= Hyperplastic polyp

Abu-Freha et al,
UEG Journal 2021

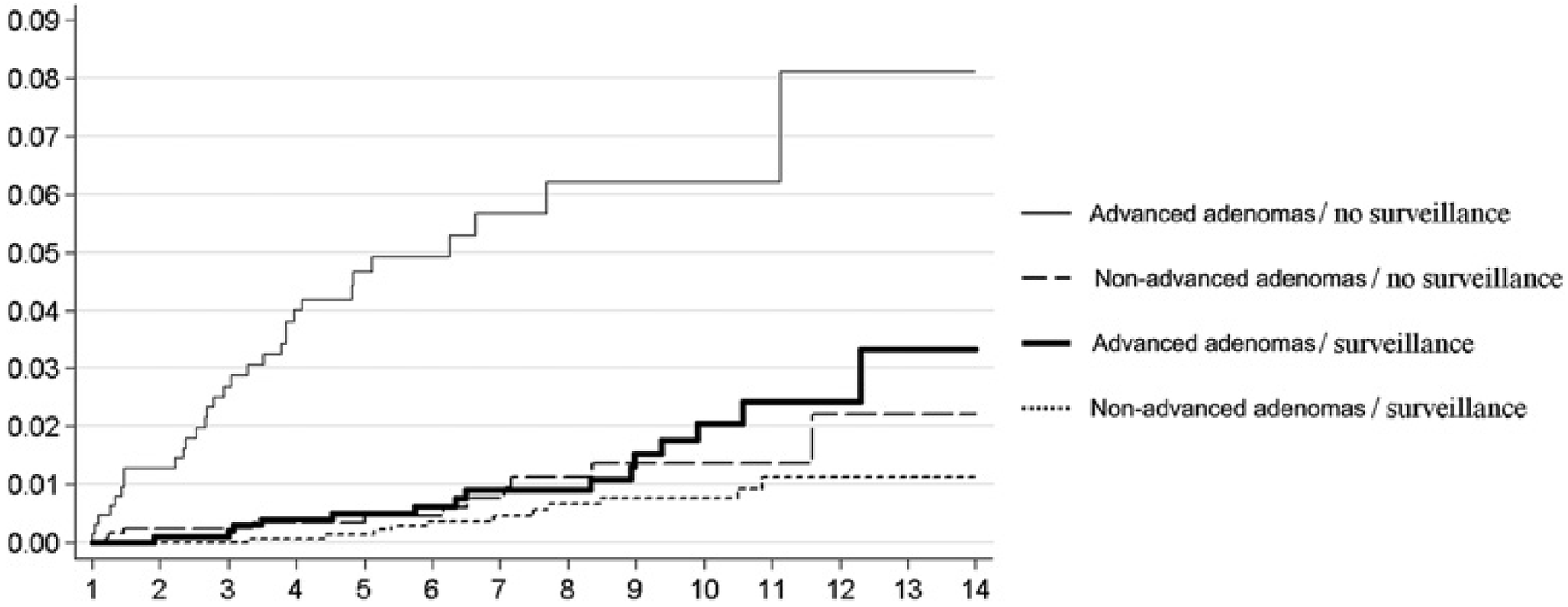
Patient perspective





Bonello BMC Gast 2016

Colonoscopy or nothing?

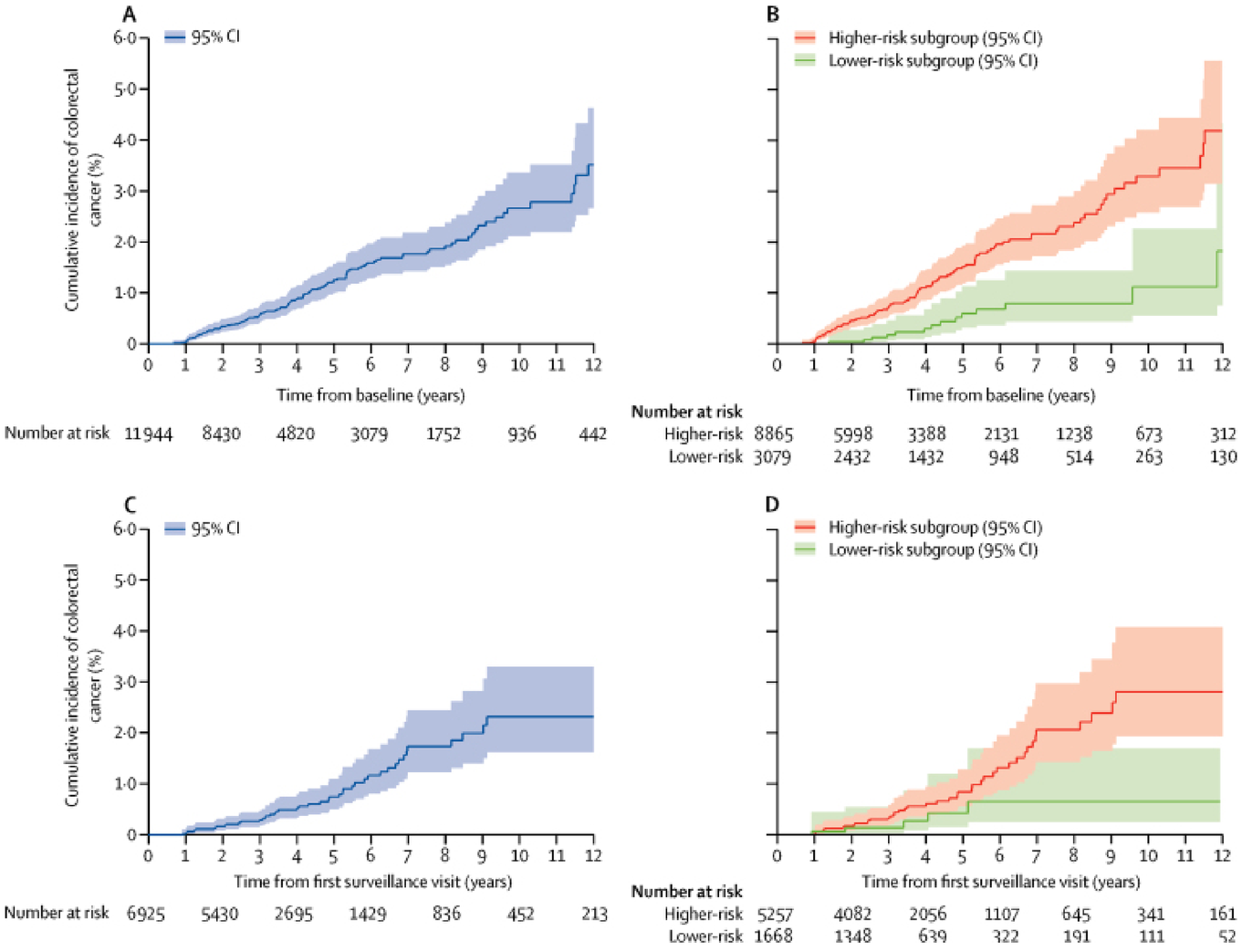


Cottet et al. Gut 2012

Non-AA
Number need to prevent a CRC: 555

AA
Number need to prevent a CRC: 29

Colonoscopy or nothing?



Atkin, Lancet Oncol 2017

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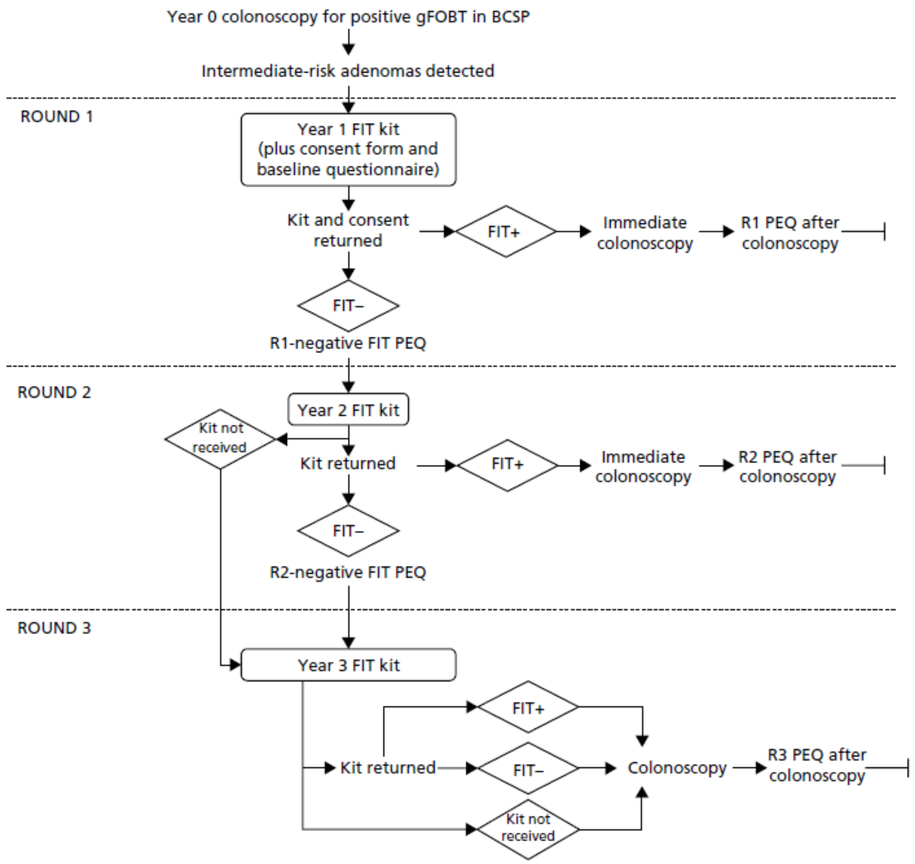
FIT Dx accuracy in surveillance

	Adenoma Surveillance (n = 292)	Genetics surveillance (n = 147)	Other family history (n = 80)	CRC follow up (n = 69)
CRC (*n*)	1	1	0	2
HRA (*n*)	23	8	3	3
CRC + HRA (*n*)	24	9	3	5
FIT test positive at LoD (%)	45.4	33.6	47.8	27.5
Missed pathology				
CRC	0	0	0	2
HRA	4	3	1	0
PPV				
CRC	0.8 (0.7–0.9)	1.1 (1.0–1.2)	N/A	0.0
HRA	14.4 (11.8–17.5)	5.3 (3.1–8.9)	9.1 (4.0–19.5)	9.1 (7.1–11.5)
CRC plus HRA	15.2 (12.4–18.3)	6.4 (4.1–9.9)	9.1 (4.0–19.5)	9.1 (4.5–17.6)
NPV				
CRC	100	100	N/A	94.4 (93.1–95.6)
HRA	97.6 (94.3–99.0)	93.6 (85.3–97.4)	98.3 (92.0–99.7)	100
CRC plus HRA	97.6 (94.3–99.0)	93.6 (85.3–97.4)	98.3 (92.0–99.7)	94.4 (85.0–98.1)
Sensitivity				
CRC	100 (2.5–100)	100 (2.5–100)	N/A	0.0 (0.0–84.2)
HRA	82.6 (61.2–95.1)	62.5 (24.5–91.5)	66.7 (9.4–99.2)	100
CRC plus HRA	83.3 (62.6–95.3)	66.7 (29.9–92.5)	66.7 (9.4–99.2)	60.0 (14.7–94.7)
Specificity				
CRC	55.9 (50.0–61.6)	33.6 (25.8–42.0)	N/A	50.7 (38.2–63.2)
HRA	58.9 (52.8–64.8)	33.1 (24.5–41.7)	74.0 (62.8–83.4)	54.5 (41.8–66.9)
CRC plus HRA	59.1 (53.1–65.0)	33.1 (25.4–42.1)	74.0 (62.8–83.4)	53.1 (40.2–65.7)

Digby, UEG Journal 2020

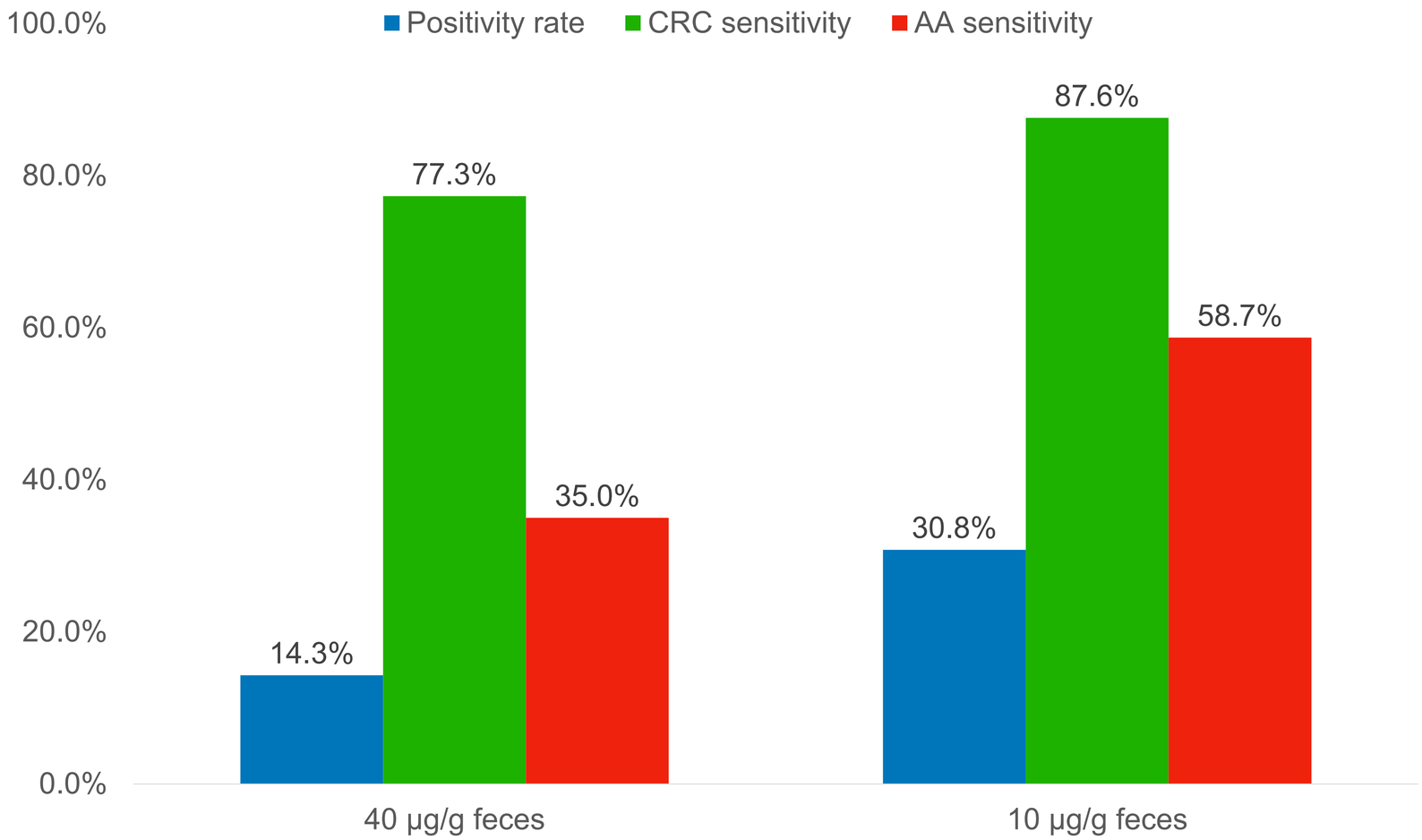
FIT for Follow-up study



	Uptake			Positivity rate		Diagnostic yield*			
	Invited	Completed FIT test†		Tested positive‡		Colorectal cancer		Advanced adenomas**	
Year	n	n	(%)	n	(%)	n	(%)	n	(%)
1	8009	5938	(74.1)	346††	(5.8)	8	(2.5)	78	(24.4)
2	5479	5329	(97.3)	236	(4.4)	7	(3.2)	37	(17.1)
3	5179	5022	(97.0)	204	(4.1)	2	(1.1)	36	(19.0)
Cumulative	8009	5938	(74.1)	786‡‡	(13.2)	17	(2.3)	151	(20.8)
Routine year 3 colonic exam						12	(0.3)	295	(6.6)
Entire study findings						29	(0.6)	446	(8.5)

Cross Gut 2019

FIT for Follow-up study



Cross Gut 2019

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Polyprev (NCT04967183)

- **Hypothesis:**

After the resection of high risk adenomas detected within CRC screening program, the 10 year CRC incidence in patients participating in **CRC screening programs** (FIT) **is not superior** to patients undergoing endoscopic surveillance

- **Objectives:**

  - **10 year CRC incidence**

  - Diagnostic performance for CRC and advanced adenomas at a 3 year interval

  - Mortality (global and associated with CRC), colonic lesion detection, participation and adverse effect

Regueiro, Diagnostics 2021

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Polyprev (NCT04967183)

XUNTA DE GALICIA | CONSELLERÍA DE SANIDADE

GENERALITAT VALENCIANA
Conselleria de Sanitat Universal i Salut Pública

Osakidetza

Región de Murcia
Consejería de Salud

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Polyprev (NCT04967183)

- **Inclusion criteria:** Individuals aged 50 to 65 years with at least one advanced adenoma/serrated lesion, and / or at least three non-advanced adenomas detected and resected completely within the population-based CRC screening program.

- **Exclusion criteria:** Personal history of CRC, colonic lesion ≥10mm resected without histological diagnosis, more than 10 adenomas in baseline colonoscopy, serrated polyposis syndrome, two or more first-degree relatives with CRC, hereditary predisposition to CRC: Lynch syndrome, pathogenic mutation associated with polyposic syndromes, relevant comorbidity with life expectancy inferior to 5 years, colonoscopy with incomplete mucosal examination (no cecal intubation, Boston Score <6 or <2 in any of the sections), incomplete resection of baseline lesions, non-acceptance after reading the informed consent

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Polyprev (NCT04967183)

- **Sample size:**

CRC incidence: 1.24%

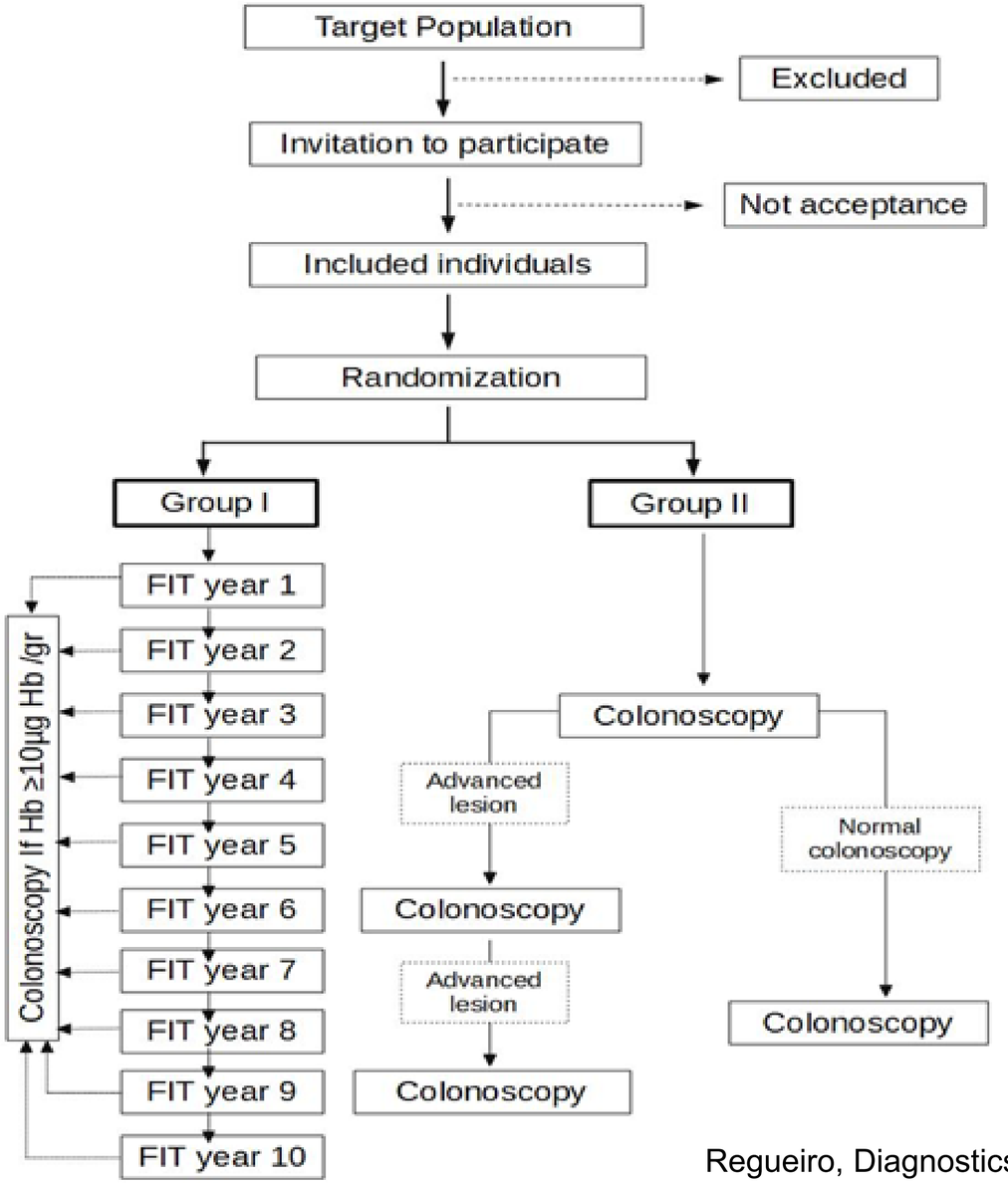
Non superiority limit 1.00%

Ratio 1:1

B= 0.2, α=0.05

Dropout: 20%

1894 subjects in each group.



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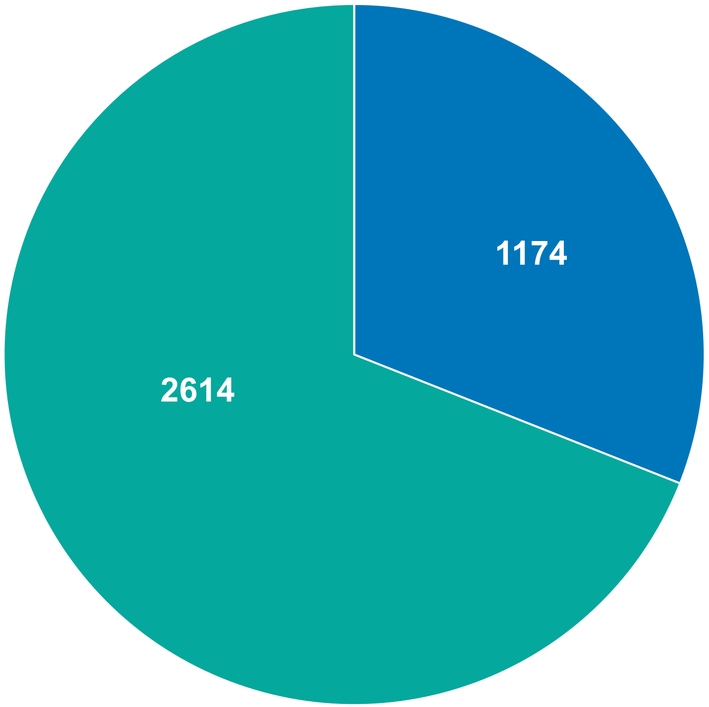

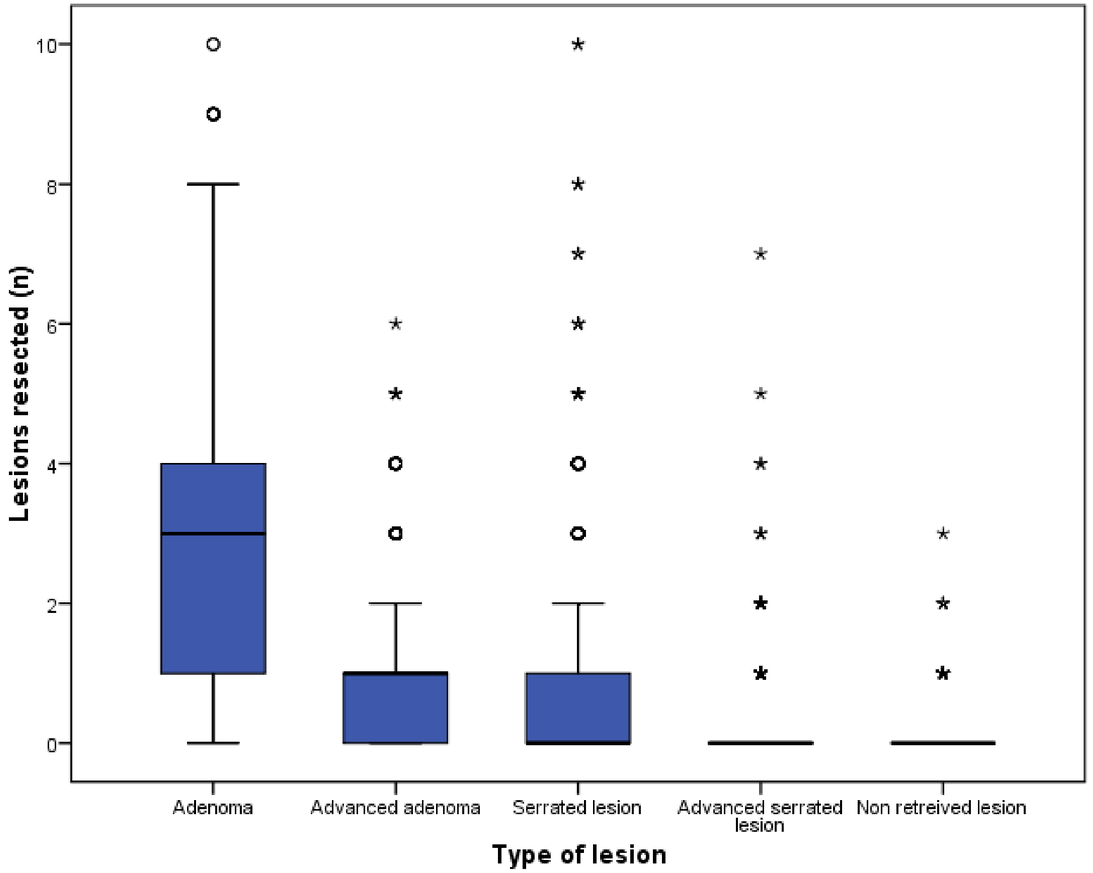

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Ongoing trials

FIT2RUN Study (NCT05396560)

Observation study (Diagnostic accuracy)

Advanced colorectal neoplasia

FIT for purpose (ANZCTR 1261900174315

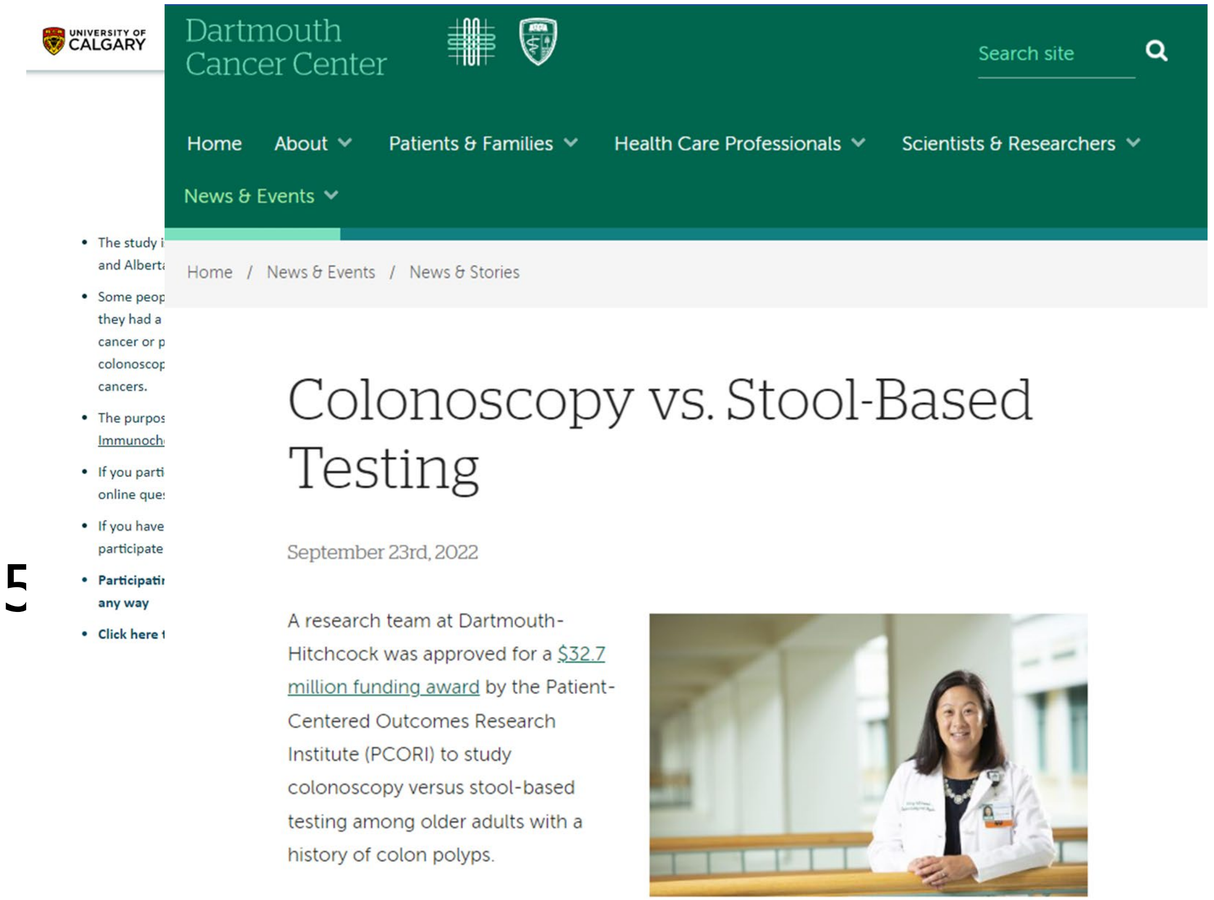
RCT (surveillance vs delayed colonoscopy-FIT result)

Advanced colorectal neoplasia

Colonoscopy vs Stool Testing for Older Adults With Colon Polyps (NCT05612347)

RCT (annual FIT vs colonoscopy)

Advanced colorectal neoplasia



Conclusions

- **FIT could be an alternative to endoscopic surveillance in high quality colonoscopy controlled CRC screening programs**
- **We need more research in:**
    - **Patient preferences**
    - **Diagnostic accuracy**
    - **Long-term impact on CRC incidence and mortality**

Muchas gracias

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