Big-Bang

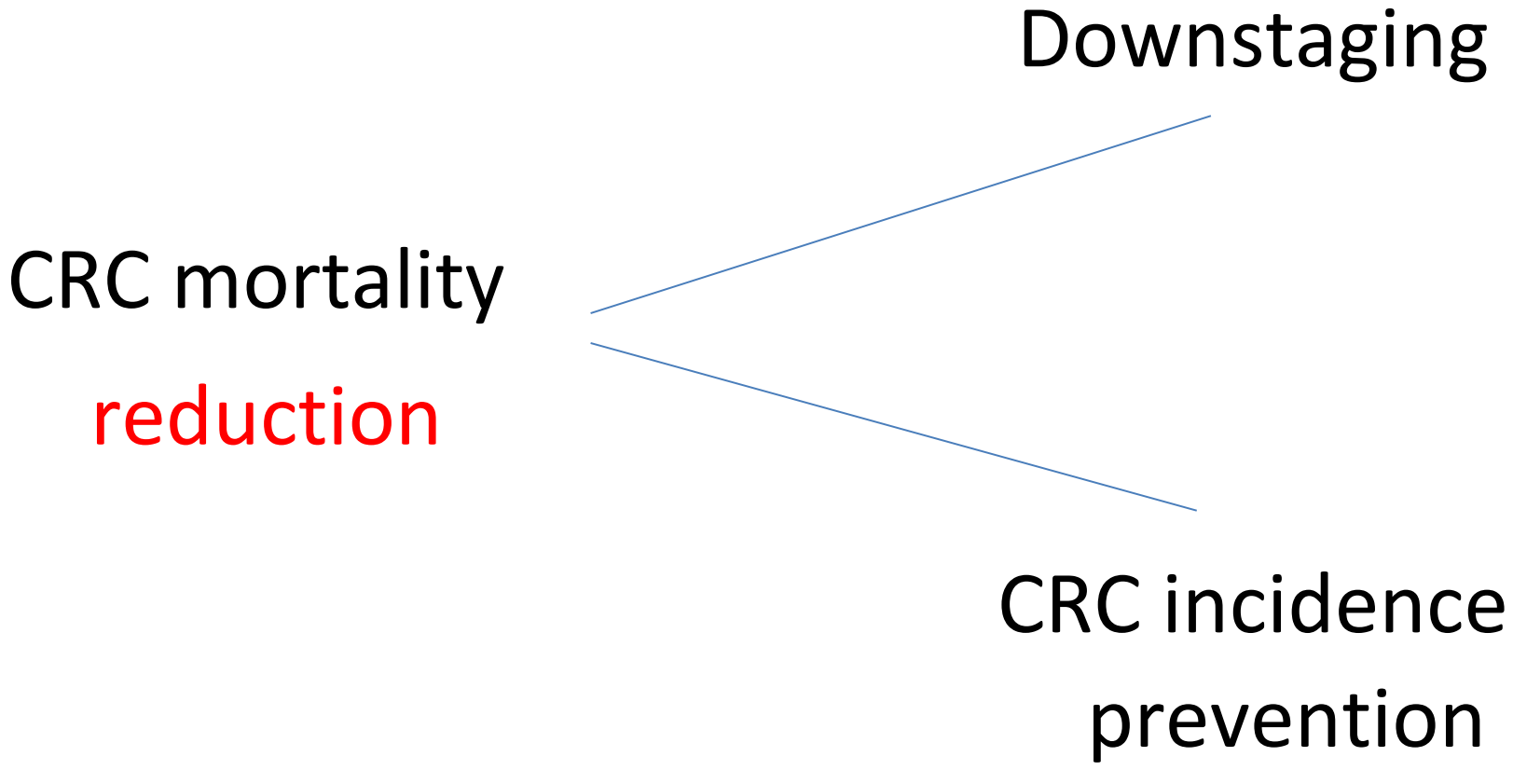
The day after

What did we learn about…?

- Downstaging vs. incidence prevention

- Comparison between Sigmoidoscopy and FIT/Colonoscopy

CRC screening efficacy



Flex. Sig. trials: Downstaging

	CRC risk	**CRC-specific mortality risk**
Control (112,939 sub.)	1.6%	29%
Screen Attendants (40,621 sub.)	1.1%	25% (Left- 21%)

Flex. Sig. trials: Downstaging

Efficacy attributable to downstaging = 1.1% x (29%-25%) = **0.05%**

NNS per 1 death prevented = **1963**

Flex. Sig. trials: CRC incidence prev.

	CRC risk	**CRC prevented**
Control (112,939 sub.)	1.6%	**0.5%**
Screen Attendants (40,621 sub.)	1.1%	

Flex. Sig. trials: CRC incid. prev.

Efficacy attributable to CRC prevention = 0.5% x 29% = **0.15%**

NNS per 1 death prevented =**657**

CRC screening efficacy

CRC mortality reduction

Downstaging **0.05%**

25%

CRC incidence prevention **0.15%**

75%

NNS per 1 death prevented =**489**

2,045 CRC-deaths prevented per 1 million attendants

What did we learn about…?

- Downstaging vs. incidence prevention

- Comparison between Sigmoidoscopy and FIT/Colonoscopy

Flex. Sig. trials: FIT

	CRC risk	CRC-specific mortality risk
Control (112,939 sub.)	1.6%	29%
Screen Attendants (40,621 sub.)	~~1.1%~~ 1.6%	~~25%~~ 21%

Flex. Sig. trials: FIT vs FS

Efficacy attributable to FIT = 1.6% x (29%-21%) = **0.1%**

Efficacy attributable to FS **0.2%**

NNS per 1 death prevented = **748**

1,336 add. CRC-deaths prevented per 1 million attendants

Flex. Sig. trials: Colonoscopy

	Proximal CRC risk	**CRC-specific mortality risk**
Screen Attendants (40,621 sub.)	0.6% (59% prevalent)	29% (estimate)

Flex. Sig. trials:
Downstaging of proximal CRC

Efficacy attributable to proximal CRC downstaging = 0.6% x (29%-21%) = **0.03%**

NNS per 1 death prevented = **3,518**

284 add. CRC-deaths prevented per 1 million attendants

Flex. Sig. trials:

Proximal CRC incidence prev.

	Proximal CRC risk	**CRC prevented**
Screen Attendants (40,621 sub.)	0.6%	**0.3%**
Assuming proximal protection by colonoscopy	0.3%	

Flex. Sig. trials:
Proximal CRC incid. prev.

Efficacy attributable to proximal CRC prevention = 0.3% x 29% = **0.08%**

NNS per 1 death prevented (including down.) = **946**

1,057 add. CRC-deaths prevented per 1 million attendants

Flex. Sig. trials: NNS per 1 death prevented

NNS FS vs no screen	**489**
NNS FS vs FIT=	**748**
NNS OC vs FS **(only downstaging)**	**3,518**
NNS OC vs FS	**946**

CONCLUSIONS

- CRC incidence prevention dominant driver of CRC-mortality reduction
- FS efficiency marginally reduced by FIT efficacy
- OC competitive only if able to prevent proximal CRC

Sigmoidoscopy

Se non ora, quando?

OPEN ISSUES

- How was it before Fles. Sig. trials?
- How should we assess Fles. Sig. trials?
- How is it after Fles. Sig. trials?

Before…

CLINICAL GUIDELINES | Annals of Internal Medicine

Screening for Colorectal Cancer: A Targeted, Updated Systematic Review for the U.S. Preventive Services Task Force

Evelyn P. Whitlock, MD, MPH; Jennifer S. Lin, MD, MCR; Elizabeth Liles, MD; Tracy L. Bell, MS; and Rongwei Fu, PhD

Population	Adults Age 50 to 75 Years*	Adults Age 76 to 85 Years*	Adults Older Than 85 Years*
Recommendation	Screen with high-sensitivity FOBT, sigmoidoscopy, or colonoscopy Grade: A	Do not screen routinely Grade: C	Do not screen Grade: D
	For all populations, evidence is insufficient to assess the benefits and harms of screening with computed tomographic colonography and fecal DNA testing. Grade: I (insufficient evidence)		

Screening Tests	High-sensitivity FOBT, sigmoidoscopy with FOBT, and colonoscopy are effective in decreasing colorectal cancer mortality. The risks and benefits of these screening methods vary. Colonoscopy and flexible sigmoidoscopy (to a lesser degree) entail possible serious complications.
Screening Test Intervals	**Intervals for recommended screening strategies:** • Annual screening with high-sensitivity FOBT • Sigmoidoscopy every 5 years, with high-sensitivity FOBT every 3 years • Screening colonoscopy every 10 years

Annals of Internal Medicine | Academia and Clinic

Update on the Methods of the U.S. Preventive Services Task Force: Estimating Certainty and Magnitude of Net Benefit

George F. Sawaya, MD; Janelle Guirguis-Blake, MD, MPH; Michael LeFevre, MD, MSPH; Russell Harris, MD, MPH; and Diana Petitti, MD, MPH, for the U.S. Preventive Services Task Force

Table 2. **Questions Considered by the U.S. Preventive Services Task Force for Evaluating Evidence Related Both to Key Questions and to the Overall Certainty of the Evidence of Net Benefit for the Preventive Service**

1. Do the studies have the appropriate research design to answer the key question(s)?
2. To what extent are the existing studies of high quality? (i.e., what is the internal validity?)
3. To what extent are the results of the studies generalizable to the general U.S. primary care population and situation? (i.e., what is the external validity?)
4. How many studies have been conducted that address the key question(s)? How large are the studies? (i.e., what is the precision of the evidence?)
5. How consistent are the results of the studies?
6. Are there additional factors that assist us in drawing conclusions (e.g., presence or absence of dose–response effects, fit within a biologic model)?

Do the studies have the appropriate research design to answer the key question(s)?

Population

All men and women aged between 55 and 64 years and registered with participating general practices were eligible to take part unless they met the following exclusion criteria: inability to provide informed consent;

age range was drawn directly from the NHS register. All individuals aged 55–64 years included in these samples (that is, resident in the study areas and listed in the NHS lists that provided their names) were mailed a questionnaire designed to assess their eligibility for and interest in screening, with an ac-

longitudinal data for epidemiological research. All residents aged 55-64 years living in the city of Oslo and Telemark County, Norway, who were registered

Keyquestion

The sample size was calculated to give 90% power to detect a 20% difference between the intervention and control groups in incidence of colorectal cancer at 10 years and mortality at 15 years since randomisation, assuming a conservative attendance rate for screening of 55%.[15]

3.5 years (25), the planned sample size and attendance rate provided 80% power to detect a statistically significant (at 5% level) reduction of 21% after 6 years of follow-up (one-sided test), or 18% after 10 years of follow-up (two-sided test), in the incidence of CRC in the intervention group. Based on the same assumptions, a statistically significant reduction in mortality was expected to be detected after 11 years of follow-up.

scopy, we regarded a 30% reduction in incidence after five years in the intention to screen population as possible to achieve and definitely worth while to detect. With a 5% significance level (two sided), we

To what extent are the existing studies of high quality? (i.e., what is the internal validitv?)

Consort

the control group. The exclusion criteria were previous open colorectal surgery, need for long term attention and nursing services (somatic or psychosocial reasons, mental retardation), ongoing cytotoxic treatment or radiotherapy for malignant disease, severe chronic cardiac or pulmonary disease (New York Heart Association III-IV), lifelong anticoagulant treatment, admission to hospital for a coronary event during the previous three months, cerebrovascular accident during the previous three months, and residence abroad.

vided. No reminder was sent to nonresponders. Responders were excluded if they reported a history of colorectal cancer, colorectal polyps, or inflammatory bowel disease had had a colorectal endoscopy within the previous 2 years; had two or more first-degree relatives with colorectal cancer; or had a medical condition that would preclude benefit from screening.

Selection/Blinding

assessing screening efficacy. The self-selection process associated with the low response rate to the interest-in-screening questionnaire would reduce the generalizability of results. Nevertheless, it was not as important with respect to CRC risk as it was for mortality. The

Randomisation and masking

Eligible individuals, who indicated in the questionnaire that they would take up the offer of screening if invited, were randomly allocated to the intervention (flexible sigmoidoscopy screening) or control groups in the ratio 1:2. Randomisation was stratified by trial centre,

To what extent are the results of the studies generalizable to the general primary care population and situation? (i.e., what is the external validity?)

assessing screening efficacy. The self-selection process associated with the low response rate to the interest-in-screening questionnaire would reduce the generalizability of results. Nevertheless, it was not as important with respect to CRC risk as it was for mortality. The

assessing screening efficacy. The self-selection process associated with the low response rate to the interest-in-screening questionnaire would reduce the generalizability of results. Nevertheless, it was not as important with respect to CRC risk as it was for mortality. The

Age

Health Service register. A total of 236568 men and women (47.7% men and 52.3% women), aged 55–64 years, included in these samples

longitudinal data for epidemiological research. All residents aged 55-64 years living in the city of Oslo

Previous screening

How many studies have been conducted that address the key question(s)? How large are the studies? (i.e., what is the precision of the evidence?)

	Control group (n=112 939)			Intervention group (n=57 099)						Hazard ratio (95% CI); screened vs control group*
				Not screened (n=16 478)			Screened (n=40 621)			
	Cases	Person-years	Rate (per 100 000 person-years; 95% CI)	Cases	Person-years	Rate (per 100 000 person-years; 95% CI)	Cases	Person-years	Rate (per 100 000 person-years; 95% CI)	
Incidence										
All sites	1818†	1 218 334	149 (143–156)	261†	172 260	152 (134–171)	445†‡	444 721	100 (91–110)	0·67 (0·60–0·76)
Mortality										
All-cause	13 768	1 224 523	1124 (1106–1143)	2713	173 191	1566 (1509–1627)	4062	446 854	909 (881–937)	0·95 (0·91–1·00)
Colorectal cancer¶	538	1 224 523	44 (40–48)	78	173 191	45 (36–56)	111	446 854	25 (21–30)	0·57 (0·45–0·72)

Table 2. CRC incidence and mortality among the SCORE trial subjects by per-protocol analysis*

	Control†		Intervention‡				Rate ratio (95% CI) adjusted‖
			Not screened		Screened		
	173 437 person-years§		72 832 person-years§		101 345 person-years§)		
Incidence	**No. of subjects with CRC**	**Rates per 100 000 person-years (95% CI)**	**No. of subjects with CRC**	**Rates per 100 000 person-years (95% CI)**	**No. of subjects with CRC**	**Rates per 100 000 person-years (95% CI)**	**Screened vs control group**
All sites	306	176.43 (157.73 to 197.35)	125	171.63 (144.03 to 204.51)	126	124.33 (104.41 to 148.05)	0.69 (0.56 to 0.86)
Mortality	**deaths**	**person-years (95% CI)**	**deaths**	**person-years (95% CI)**	**deaths**	**person-years (95% CI)**	**group**
All deaths among subjects diagnosed with CRC‡‡							
All sites	94	50.34 (41.12 to 61.61)	38	48.35 (35.18 to 66.44)	33	30.29 (21.53 to 42.61)	0.58 (0.38 to 0.87)

How consistent are the results of the studies?

AGE

Age (years)	CRC incidence/100,000	CRC mortality/100,000	Life-expectancy
40-44	13.3	4.6	42
45-50	27.6	9.6	37
50-54	55.1	19.0	32
55-59	97.0	34.4	28
60-64	153.4	55.4	24
65-69	226.9	85.6	19
70-74	318.6	125.9	16
75-79	412.0	171.9	12

AGE

ORIGINAL INVESTIGATION

Cost-effectiveness of a Single Colonoscopy in Screening for Colorectal Cancer

Amnon Sonnenberg, MD, MSc; Fabiola Delcò, MD, MPH

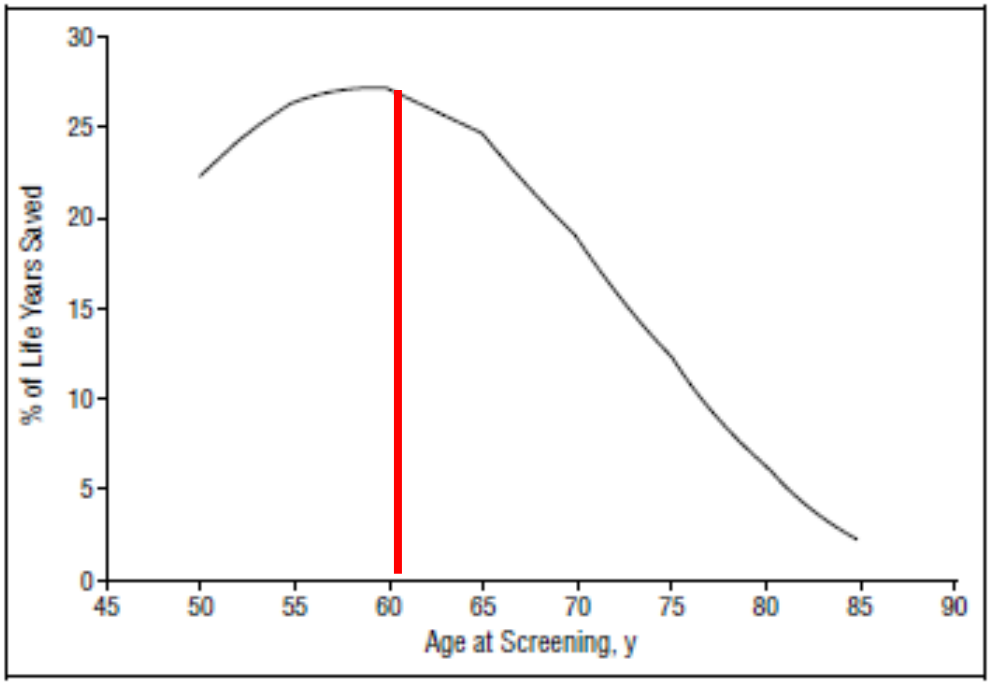


Figure 2. Influence of age at the single colonoscopy on the percentage of life years saved.

AGE

Prevention of colorectal cancer by once-only sigmoidoscopy

W. S. ATKIN J. CUZICK J. M. A. NORTHOVER D. K. WHYNES

The overall prevalence of distal adenomas as determined by flexible sigmoidoscopy screening studies has ranged between 5% and 25%, with most studies suggesting between 8% and 12%.[12,23-26] Prevalence increases strikingly after age 50 years, but appears to plateau before 60 at about 9% (table II). A single sigmoidoscopy towards the end of the sixth decade should, therefore, identify most people with distal adenomas that are likely to develop into cancer.

TABLE II—PREVALENCE BY AGE OF COLORECTAL ADENOMAS IN PERSONS UNDERGOING SCREENING BY FLEXIBLE SIGMOIDOSCOPY*

Age	Total subjects	Number *(%)* with adenomas
<40	428	18 *(4)*
40–59	843	29 *(3)*
50–59	1112	98 *(9)*
60–69	682	72 *(11)*
⩾70	327	32 *(10)*

*Combined figures from refs 23–25

CONCLUSIONS

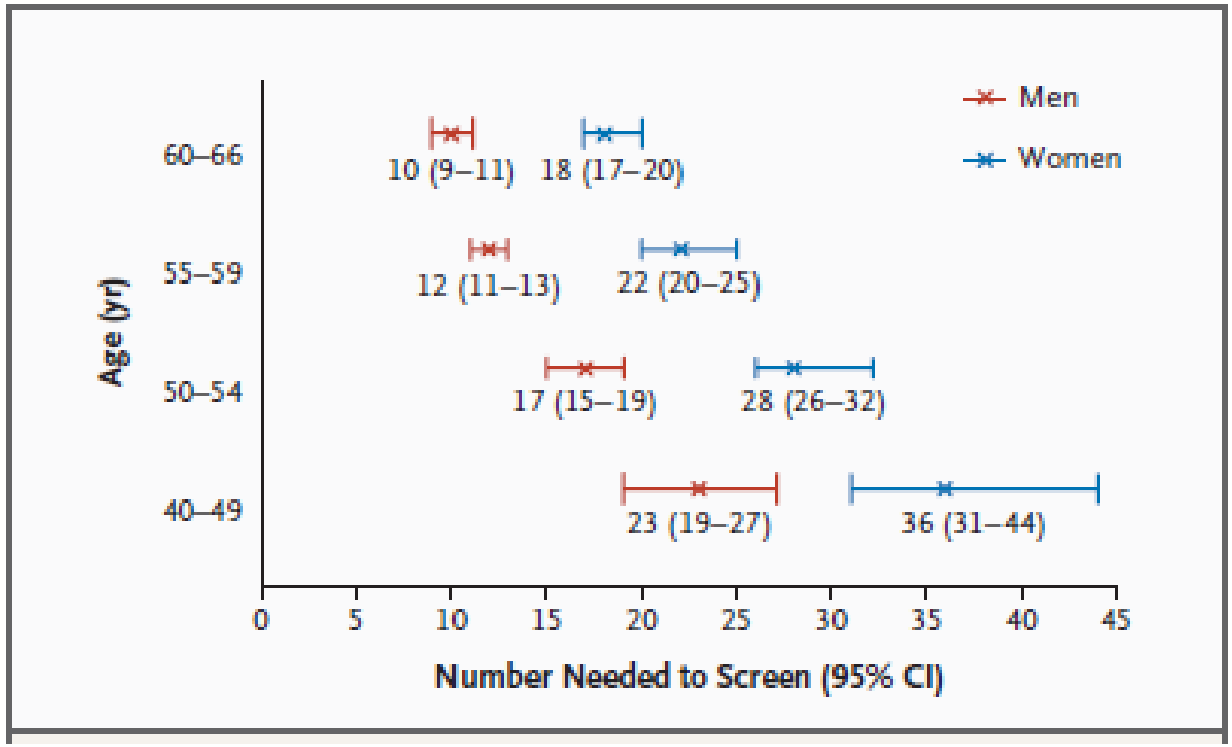
- 55-65 years as the best screening window
- g-FOBT likely to be replaced by FIT
- FS likely to be added to g-FOBT/FIT
- Colonoscopy implementation will be strictly related with its quality

SEX

ORIGINAL ARTICLE

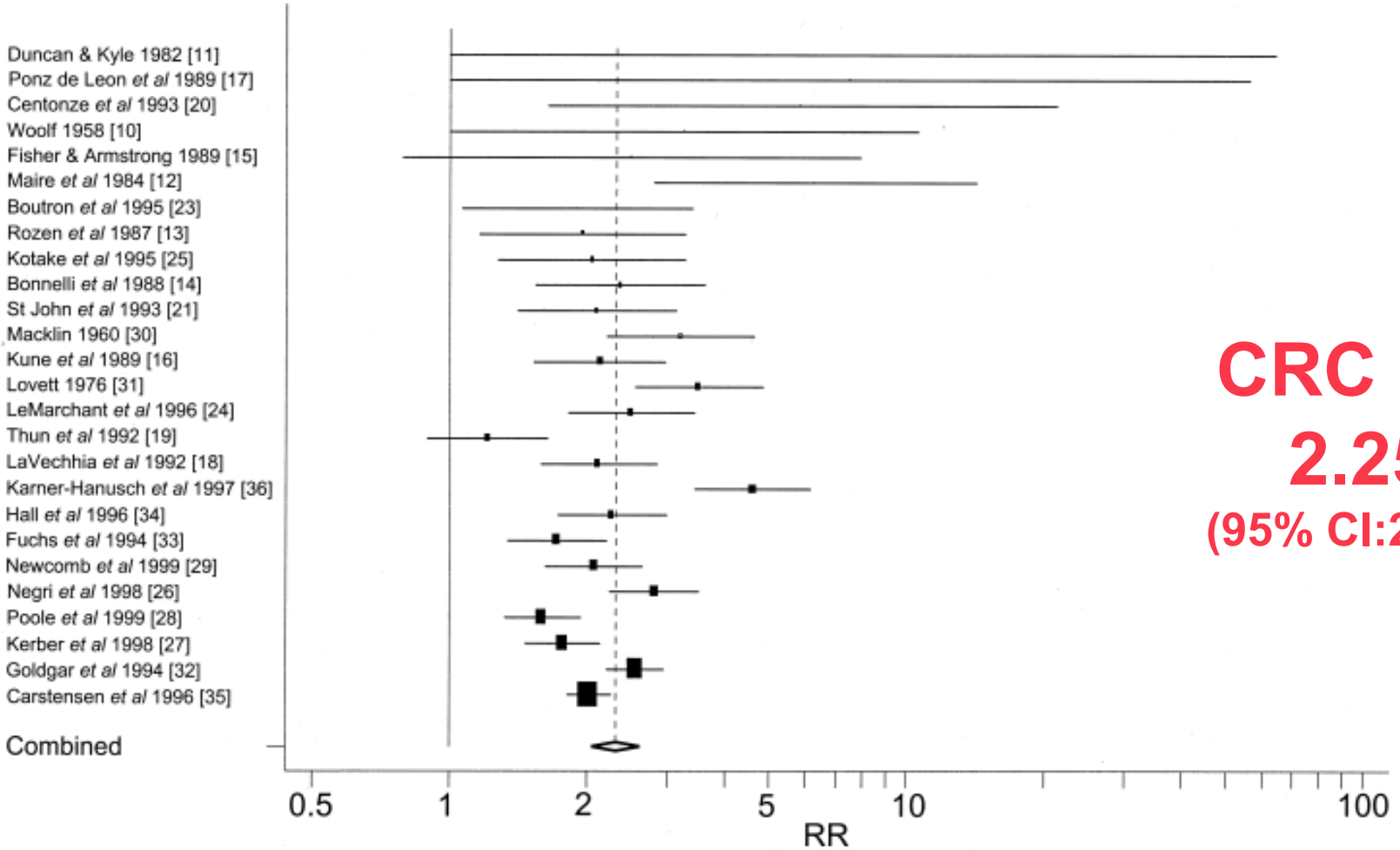
Colonoscopy in Colorectal-Cancer Screening for Detection of Advanced Neoplasia

Jaroslaw Regula, M.D., Maciej Rupinski, M.D., Ewa Kraszewska, M.Sc., Marcin Polkowski, M.D., Jacek Pachlewski, M.D., Janina Orlowska, M.D.,



FAMILY HISTORY

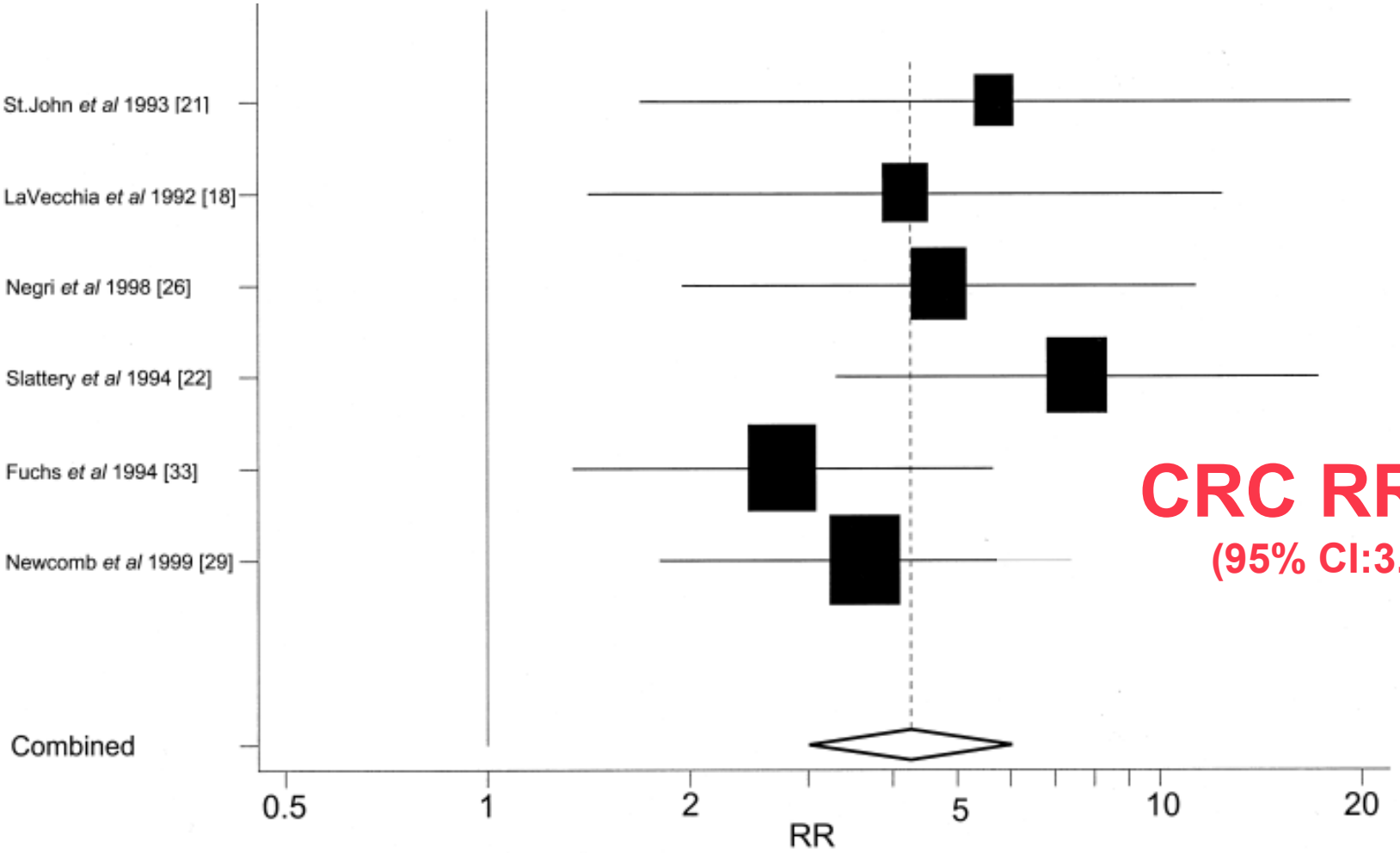
- **At least one first-degree relative with CRC**



CRC RR
2.25
(95% CI:2-2.53)

FAMILY HISTORY

- **At least two first-degree relative with CRC**
- **or one first-degree relative <45 ys**



CRC RR: 4.25

(95% CI:3.01-6.02)

EU GUIDELINES

Recommendations and conclusions[1]

1.3 Circumstantial evidence suggests that mortality reduction from gFOBT is similar in different age ranges between 45 and 80 years **(IV)**. The age range for a national screening programme should at least include 60 to 64 years in which CRC incidence and mortality are high and life-expectancy is still considerable. From there the age range could be expanded to include younger and older individuals, taking into account the balance between risk and benefit and the available resources **(VI - B).**[Sect 1.2.1.3]

1.9 There is limited evidence suggesting that the best age range for FS screening should be between 55 and 64 years **(III – C).** After age 74, average-risk FS screening should be discontinued, given the increasing co-morbidity in this age range **(V - D).**[Sect 1.3.1.3]

1.12 Indirect evidence suggests that the prevalence of neoplastic lesions in the population below 50 years of age is too low to justify colonoscopic screening, while in the elderly population (75 years and above) lack of benefit could be a major issue. The optimal age for a single colonoscopy appears to be around 55 years **(IV - C).** Average risk colonoscopy screening should not be performed before age 50 and should be discontinued after age 74 **(V - D).**[Sect 1.3.2.3]

EU GUIDELINES

Recommendations and conclusions[1]

- In the absence of hereditary syndromes people with a positive family history should not be excluded from CRC screening programmes **(III - B).**[Rec 2.5]
- Subjects belonging to families with hereditary syndromes identified at the time of screening should be referred to special surveillance programmes or family cancer clinics, if available **(III - B).**[Rec 2.6]

OPEN ISSUES

- Who should be screened?
- How should we screen?

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CLINICAL REVIEWS

Cochrane Systematic Review of Colorectal Cancer Screening Using the Fecal Occult Blood Test (Hemoccult): An Update

329,642 randomized subjects ⟶ FU 12-17 yrs.

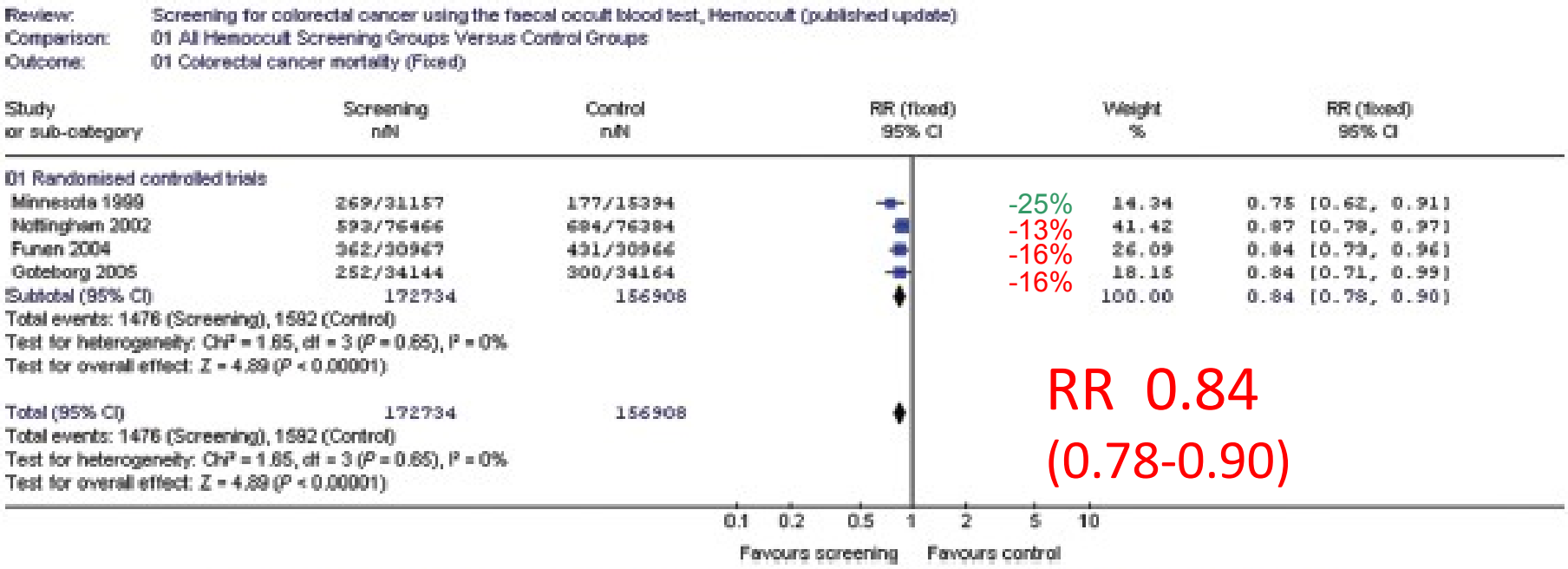

Figure 1. Effects of screening with Hemoccult on mortality from CRC (fixed effects model).

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CLINICAL REVIEWS

Cochrane Systematic Review of Colorectal Cancer Screening Using the Fecal Occult Blood Test (Hemoccult): An Update

Table 4. Number of CRC Cases and Incidence Rate of CRC Cases for the Screening and Control Groups

	No. of CRC Cases			Incidence Rate of CRC Cases	
Study	Screening Group	Control Group		Screening Group (py)	Control Group (py)
Funen	889/30,967	874/30,966	5.3%	2.06/1,000	2.02/1,000
Goteborg	252/34,144	300/34,164	6.4%	NR	NR
~~Minnesota~~	~~852/31,137~~	~~307/15,394~~	33%	32–33/1,000	39/1,000
Nottingham	1,268/76,466	1,283/76,384	2.6%	1.51/1,000	1.53/1,000

NR = not reported.

1.7% 1.7%

EU GUIDELINES

Recommendations and conclusions[1]

Guaiac FOBT

1.1 There is good evidence that invitation to screening with FOBT using the guaiac test reduces mortality from colorectal cancer (CRC) by approximately 15% in average risk populations of appropriate age **(I)**.[Sect 1.2.1.1]

1.2 RCTs have only investigated annual and biennial screening with guaiac FOBT (gFOBT) **(II)**. To ensure effectiveness of gFOBT screening, the screening interval in a national screening programme should not exceed two years **(II - B)**.[Sect 1.2.1.2]

1.3 Circumstantial evidence suggests that mortality reduction from gFOBT is similar in different age ranges between 45 and 80 years **(IV)**. The age range for a national screening programme should at least include 60 to 64 years in which CRC incidence and mortality are high and life-expectancy is still considerable. From there the age range could be expanded to include younger and older individuals, taking into account the balance between risk and benefit and the available resources **(VI - B)**.[Sect 1.2.1.3]

OPEN ISSUES

- g-FOBT
- FIT

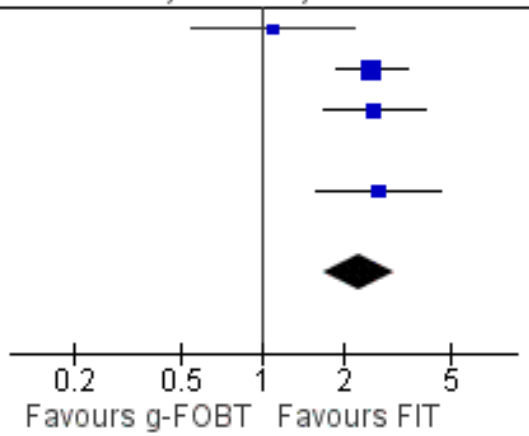
g-FOBT vs FIT

- Advanced neoplasia

Study or Subgroup	FIT Events	FIT Total	g-FOBT Events	g-FOBT Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Federici 2005	17	3716	15	3604	14.7%	1.10 [0.55, 2.20]	2005
Van Rossum 2008	145	10322	57	10301	37.1%	2.54 [1.87, 3.44]	2008
Hol 2010	73	4843	28	4798	27.0%	2.58 [1.67, 3.99]	2010
Hoffman 2010	0	0	0	0		Not estimable	2010
Levi 2011	35	4657	22	7880	21.2%	2.69 [1.58, 4.58]	2011
Total (95% CI)		**23538**		**26583**	**100.0%**	**2.28 [1.68, 3.10]**	
Total events	270		122				

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 5.29$, $df = 3$ ($P = 0.15$); $I^2 = 43\%$

Test for overall effect: $Z = 5.27$ ($P < 0.00001$)



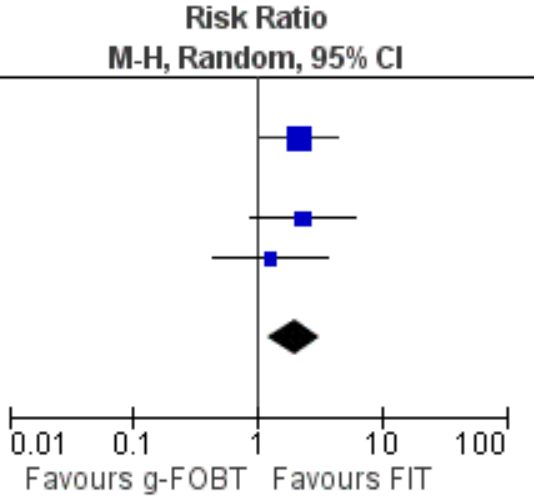
g-FOBT vs FIT

- Cancer

Study or Subgroup	FIT Events	FIT Total	g-FOBT Events	g-FOBT Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Federici 2005	0	0	0	0		Not estimable	2005
Van Rossum 2008	24	10322	11	10301	49.7%	2.18 [1.07, 4.44]	2008
Hoffman 2010	0	0	0	0		Not estimable	2010
Hol 2010	14	4843	6	4798	27.7%	2.31 [0.89, 6.01]	2010
Levi 2011	6	4657	8	7880	22.6%	1.27 [0.44, 3.66]	2011
Total (95% CI)		**19822**		**22979**	**100.0%**	**1.96 [1.19, 3.24]**	
Total events	44		25				

Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 2 (P = 0.65); I² = 0%

Test for overall effect: Z = 2.62 (P = 0.009)



CAN FIT PREVENT CRC INCIDENCE?

Effetto del test immunologico per la ricerca del sangue occulto fecale sull'incidenza del tumore al colon-retto.

Ventura L[1], Castiglione G., Grazzini G[1], Mantellini P., Romeo G[1], Buzzoni C[1], Sacchettini C[1], Rubeca T[1], Zappa M[1].
1. ISPO - Istituto per lo Studio e la Prevenzione Oncologica, Firenze

Risultati

Nella coorte degli screenati (6962 soggetti) sono stati identificati 149 cancri. Tra gli appartenenti alla coorte dei non screenati (26284 soggetti) sono stati identificati 674 cancri, con un follow-up medio di 11 anni. L'analisi di Kaplan-Maier mostra un eccesso di incidenza nei primi sei-sette anni nella coorte degli screenati rispetto ai non screenati. Successivamente a questo periodo, il trend delle due coorti si inverte, a causa dell'effetto dello screening. Successivamente a tale periodo il rischio cumulativo nella coorte degli screenati cresce in maniera significativamente inferiore che nella coorte dei non screenati. L'analisi attraverso il modello di Cox aggiustato per sesso ed età, mostra una significativa riduzione del rischio di tumore colon-rettale nella coorte degli screenati del 24% inferiore rispetto alla coorte dei non screenati (HR = 0.76, 95 CI: 0.63-0.91). Effettuando la stessa analisi suddivisa in due periodi (i primi sei anni Vs i successivi) il rischio della coorte degli screenati rispetto a quella dei non screenati risulta maggiore nei primi sei anni, statisticamente non significativo (HR = 1.11, 95 CI: 0.86-1.43) mentre successivamente il rischio risulta inferiore del 44% statisticamente significativo (HR = 0.56, 95 CI: 0.43-0.74).

EU GUIDELINES

Recommendations and conclusions[1]

Immunochemical FOBT

1.4 There is reasonable evidence from an RCT **(II)** that iFOBT screening reduces rectal cancer mortality, and from case control studies **(IV)** that it reduces overall CRC mortality.[Sect 1.2.2.1] Additional evidence indicates that iFOBT is superior to gFOBT with respect to detection rate and positive predictive value for adenomas and cancer (see also Ch. 4, Rec. 4.2) **(III).**[Sect 1.2.2.1; 4.2.5; 4.3; 4.4.2]

1.5 Given the lack of additional evidence, the interval for iFOBT screening can best be set at that of gFOBT, and should not exceed three years **(VI - C).**[Sect 1.2.2.2]

1.6 In the absence of additional evidence, the age range for a screening programme with iFOBT can be based on the limited evidence for the optimal age range in gFOBT trials (see Rec. 1.3) **(VI - C).**[Sect 1.2.2.3; 1.2.1.3]

OPEN ISSUES

- g-FOBT
- FIT
- FS

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

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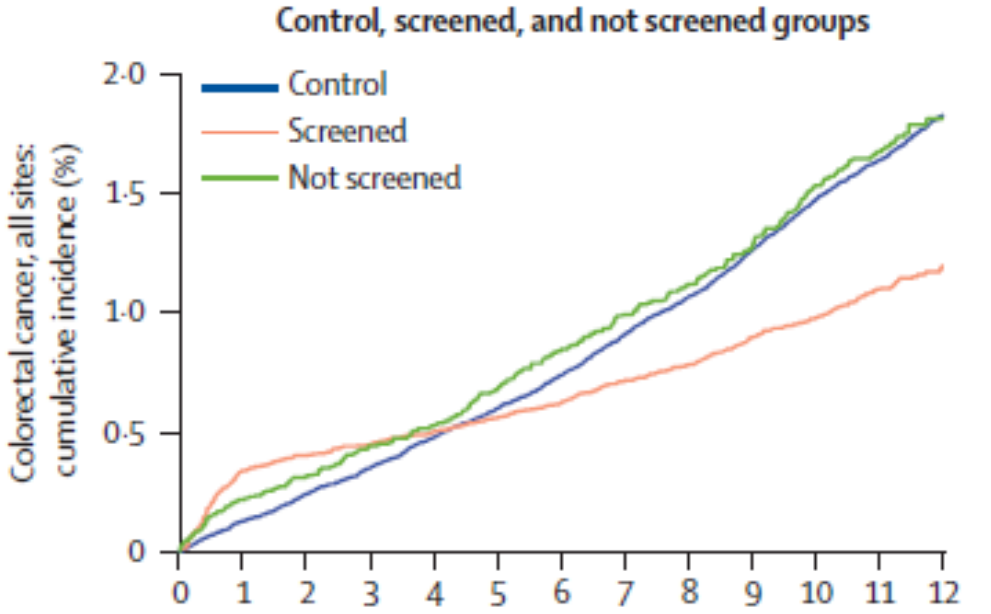


Number at risk

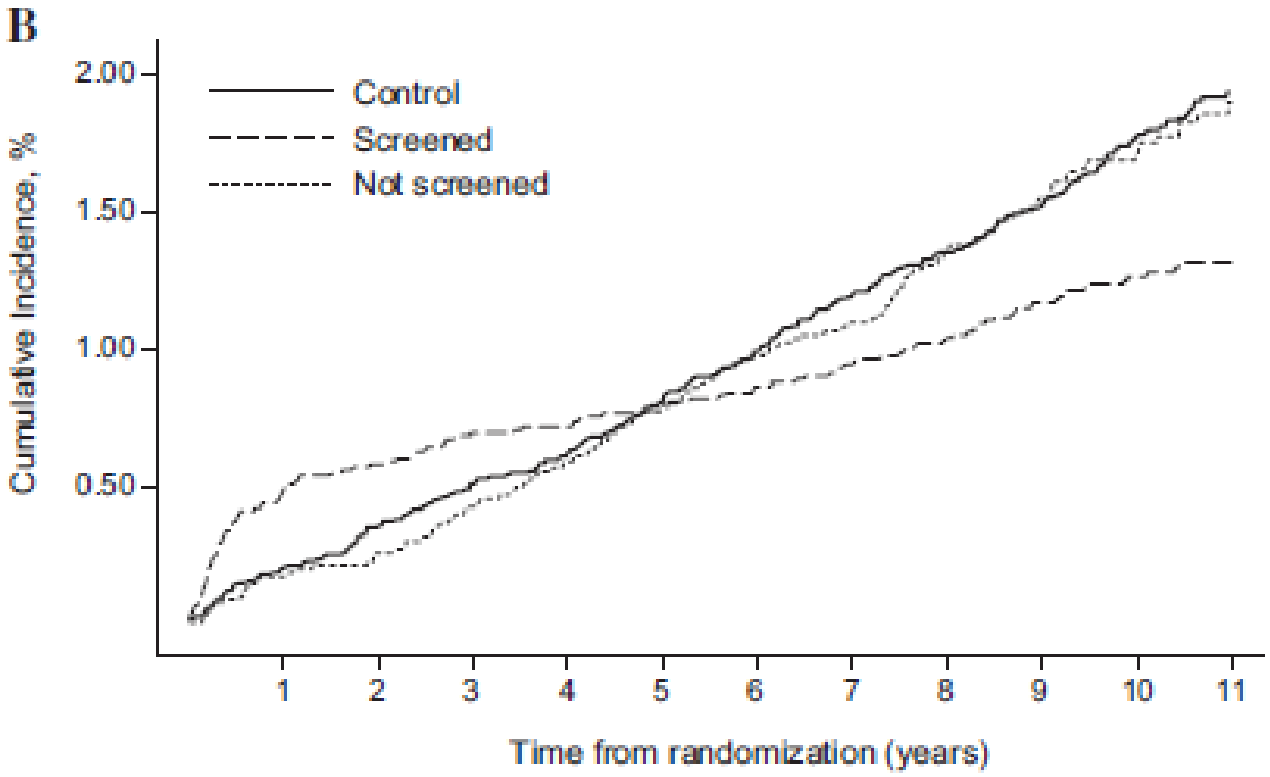
Control	112939	111113	108951	106363	103470	99629	18553
Screened	40621	40129	39547	38820	37962	36720	7131
Not screened	16478	15982	15559	15073	14539	13877	2328

CRC INCIDENCE
HR 0.67,
95% CI 0.60–0.76

-33%!

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 Giacomin, Orietta Giuliani, Alessandra Santarelli, Carmen Beatriz Visioli, Roberto Zanetti, Wendy S. Atkin, Carlo Senore; and the SCORE Working Group



CRC INCIDENCE
HR 0.69,
95% CI 0.56–0.86

-31%!

INCIDENCE REDUCTION IN THE DISTAL COLON

By year from randomization

UK FLEXI-SCOPE TRIAL

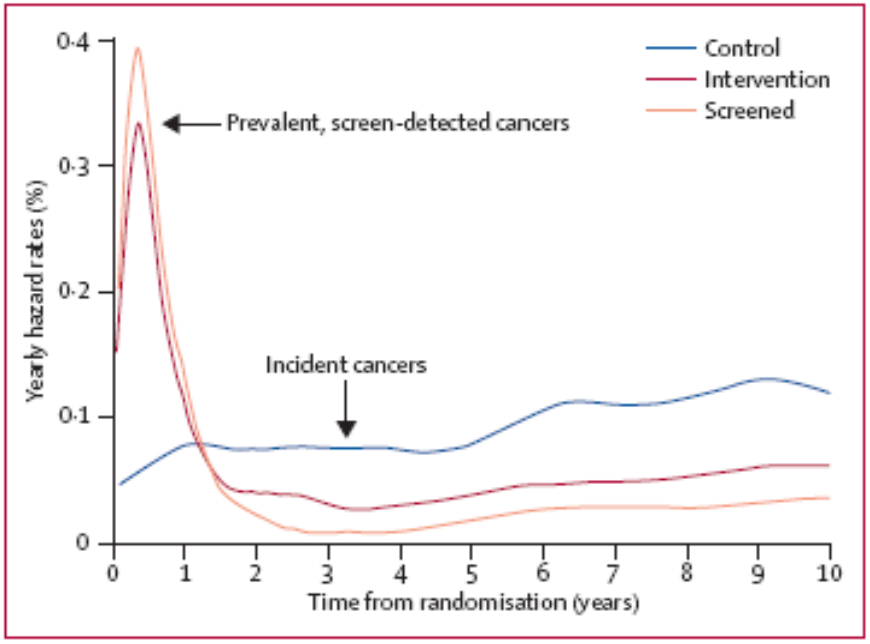


Figure 3: Smoothed yearly hazard rates for distal cancer (rectum and sigmoid colon)

SCORE TRIAL

Years from randomization†	Interval cancers at distal colon‡	
	Screened vs control	Not screened vs control
	HR (95%CI)	HR (95% CI)
All subjects§		
2	0.14 (0.04 to 0.44)	0.68 (0.35 to 1.34)
4	0.13 (0.05 to 0.31)	1.00 (0.64 to 1.55)
6	0.12 (0.06 to 0.25)	1.05 (0.75 to 1.47)
8	0.16 (0.10 to 0.28)	1.03 (0.77 to 1.38)
10	0.21(0.13 to 0.32)	0.96 (0.73 to 1.25)
Men‖		
2	0.15 (0.04 to 0.65)	0.69 (0.28 to 1.71)
4	0.17 (0.06 to 0.47)	1.44 (0.86 to 2.41)
6	0.16 (0.08 to 0.36)	1.27 (0.85 to 1.91)
8	0.21 (0.11 to 0.38)	1.28 (0.91 to 1.82)
10	0.21(0.12 to 0.35)	1.21 (0.88 to 1.67)
Women¶		
2	0.11 (0.01 to 0.84)	0.72 (0.26 to 1.99)
4	0.06 (0.01 to 0.48)	0.48 (0.20 to 1.17)
6	0.04 (0.01 to 0.31)	0.79 (0.43 to 1.45)
8	0.06 (0.01 to 0.24)	0.75 (0.44 to 1.26)
10	0.20 (0.09 to 0.44)	0.65 (0.40 to 1.07)

EU GUIDELINES

Recommendations and conclusions[1]

Sigmoidoscopy

1.7 There is reasonable evidence from one large RCT that flexible sigmoidoscopy (FS) screening reduces CRC incidence and mortality if performed in an organised screening programme with careful monitoring of the quality and systematic evaluation of the outcomes, adverse effects and costs **(II).**[Sect 1.3.1.1]

1.8 The available evidence suggests that the optimal interval for FS screening should not be less than 10 years and may even be extended to 20 years (see Rec. 1.11) **(IV - C).**[Sect 1.3.1.2; 1.3.2.2]

1.9 There is limited evidence suggesting that the best age range for FS screening should be between 55 and 64 years **(III – C).** After age 74, average-risk FS screening should be discontinued, given the increasing co-morbidity in this age range **(V - D).**[Sect 1.3.1.3]

OPEN ISSUES

- g-FOBT
- FIT
- FS
- OC

Variability in colonoscopy efficacy

Cohort studies

Author	Population	Endpoint	Person-years of follow up	Follow up duration (years)	CRC endpoint reduction
Winawer	Post-Polypectomy	Incidence	8,401	5.9	76%
Citarda	Post-Polypectomy	Incidence	14,211	10.5	66%
Rex	Screening	Incidence	10,492	14.7	67%
Robertson	Post-Polypectomy	Incidence	10,786	3.7	**5%**
Singh H	Negative colon.	Incidence	147,781	4.6	**31%**
Lakoff J	Negative colon.	Mortality	110,402§	14	**55%**
Brenner H	Negative colon.	Incidence	6,581	11.9	100%

Variability in colonoscopy efficacy

Case-control studies

Author	Population	Endpoint	CRC cases	No-CRC controls	CRC endpoint reduction
Brenner H	Colonoscopy	Incidence	1,688	1,932	77%
Brenner H	Neg. colonoscopy	Incidence	380	485	74%
Muller AD	Colonoscopy	Incidence	16,351	16,351	**45-49%**
Baxter N	Colonoscopy	Mortality	10,292	51,460	**31%**

Risk of Developing Colorectal Cancer Following a Negative Colonoscopy Examination

There were disproportionately more right-sided CRC cases in our negative colonoscopy cohort than there were in the general population during the study period. Failure of endoscopists to in-

Abbreviation: CRC, colorectal cancer.
*All the CRC cases diagnosed in the province between 1989 and 2003.

31%

Annals of Internal Medicine | ARTICLE

Association of Colonoscopy and Death From Colorectal Cancer

Nancy N. Baxter, MD, PhD; Meredith A. Goldwasser, ScD; Lawrence F. Paszat, MD, MS; Refik Saskin, MSc; David R. Urbach, MD, MSc; and Linda Rabeneck, MD, MPH

Table 3. Results of Primary Analysis: Odds Ratio for the Association Between Colonoscopy and Colorectal Cancer Death*

Table 5. Results of Analysis Stratified by Date of Exposure: Odds Ratio for the Association Between Colonoscopy and Colorectal Cancer Death*

Variable	Odds Ratio (95% CI)			
	All Cancer	Right-Sided Cancer	Left-Sided Cancer	Undefined Site of Cancer
Exposure to colonoscopy 6–24 mo before diagnosis				
No colonoscopy (referent date)	1.00	1.00	1.00	1.00
Colonoscopy (referent date)	0.84 (0.74–0.95)	1.32 (1.10–1.59)	0.46 (0.36–0.57)	1.08 (0.82–1.43)
Exposure to colonoscopy >24 mo before diagnosis				
No colonoscopy (referent date)	1.00	1.00	1.00	1.00
Colonoscopy (referent date)	0.62 (0.56–0.69)	0.92 (0.79–1.08)	0.38 (0.32–0.45)	0.80 (0.63–1.02)

* Conditional logistic regression, adjusted for Charlson Comorbidity Index score.

[illegible]

37%

OPEN ISSUES

Is the variability in efficacy

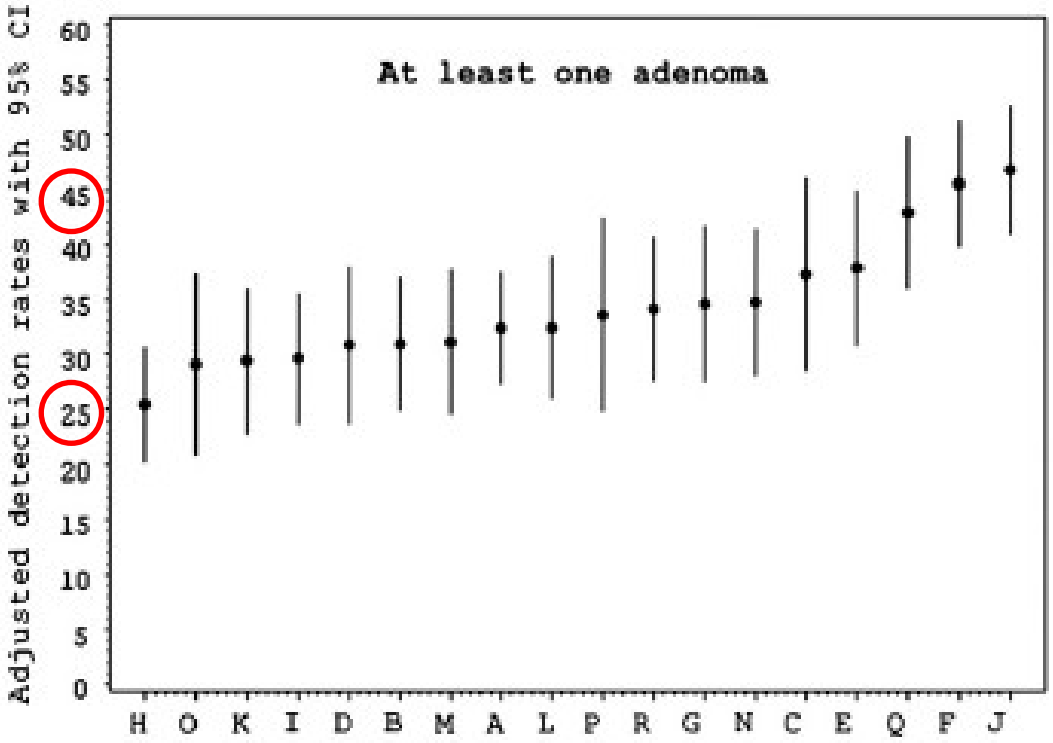
related with

the quality of colonoscopy?

Variations between endoscopists in rates of detection of colorectal neoplasia and their impact on a regional screening program based on colonoscopy after fecal occult blood testing

Jean-François Bretagne, PhD, Stéphanie Hamonic, Christine Piette, MD, Sylvain Manfredi, PhD, Emmanuelle Leray, MD, Gérard Durand, MD, Françoise Riou, PhD

18 endoscopists → 3 462 colonoscopies



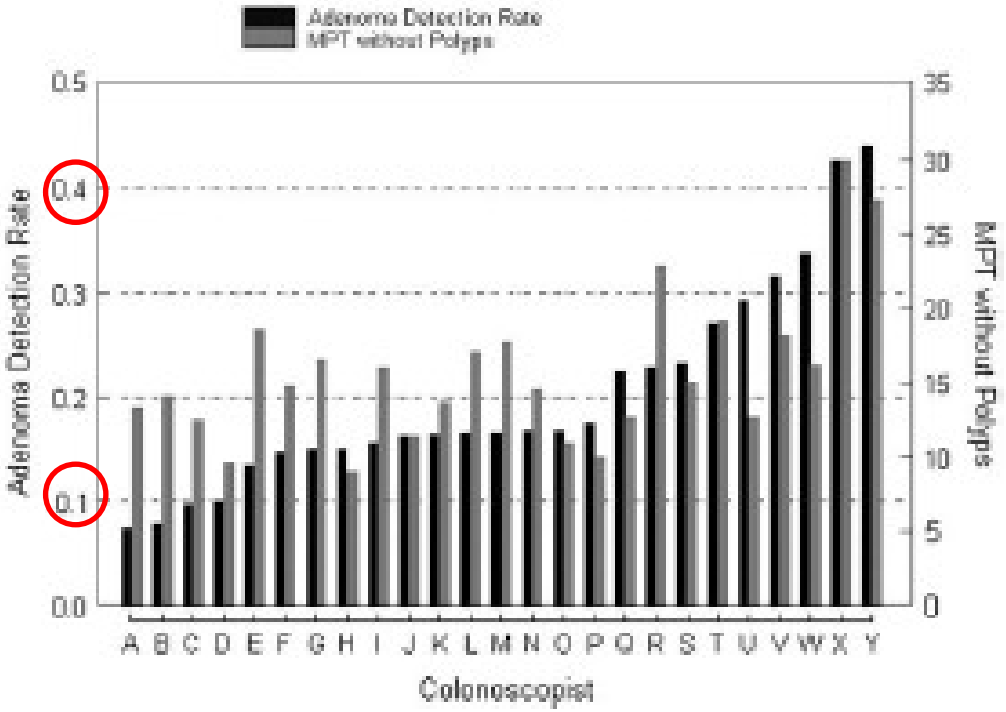
ORIGINAL ARTICLE: Clinical Endoscopy

Variation in polyp detection rates at screening colonoscopy CME

Thomas F. Imperiale, MD, Elizabeth A. Glowinski, RN, Beth E. Juliar, MS, MA, Faouzi Azzouz, MS, David F. Ransohoff, MD

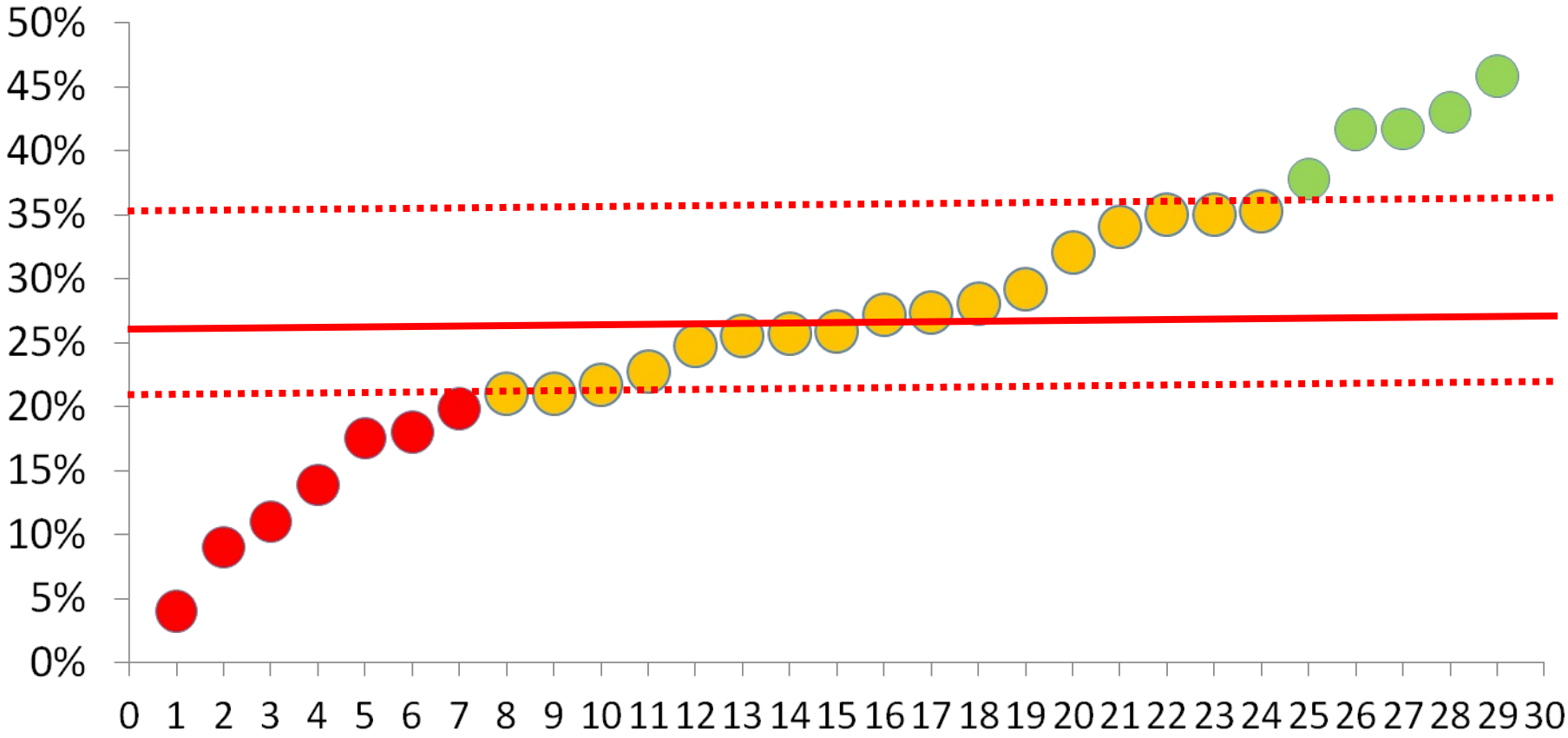
Indianapolis, Indiana, USA

25 endoscopists → 2 664 colonoscopies



30 centres
(144 endoscopists)

3 150 colonoscopies



Analysis of Administrative Data Finds Endoscopist Quality Measures Associated With Postcolonoscopy Colorectal Cancer

Table 3. Multivariate Model Generalized Estimating Equation Logistic Predicting PCCRC

	Proximal cancers		Distal cancers	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (for every 10-year increase)	1.05 (0.98–1.13)	.17	1.18 (1.08–1.28)	.0001
Sex				
Female	1.00 (referent)	.83	1.00 (referent)	.005
Male	1.02 (0.86–1.20)		0.79 (0.66–0.93)	
Charlson score				
0	1.00 (referent)	.004	1.00 (referent)	<.0001
1	1.27 (0.98–1.65)		1.88 (1.44–2.46)	
2	1.60 (1.09–2.34)		2.29 (1.58–3.31)	
3+	2.02 (1.34–3.03)		2.78 (1.78–4.35)	
Log (endoscopist volume)	1.00 (0.89–1.13)	1.00	0.94 (0.84–1.05)	.28
% Completeness for endoscopist				
<80%	1.00 (referent)	.002	1.00 (referent)	.03
80%–84%	1.16 (0.86–1.56)		0.90 (0.65–1.25)	
85%–89%	0.69 (0.51–0.93)		0.65 (0.47–0.89)	
90%–94%	0.66 (0.50–0.87)		0.71 (0.54–0.93)	
95%+	0.72 (0.53–0.97)		0.73 (0.54–0.97)	
% Polypectomy for endoscopist				
<10%	1.00 (referent)	.0001	1.00 (referent)	.39
10%–14%	1.11 (0.81–1.53)		0.99 (0.73–1.35)	
15%–19%	0.75 (0.54–1.04)		0.78 (0.57–1.06)	
20%–24%	0.75 (0.52–1.07)		0.82 (0.58–1.16)	
25%–29%	0.52 (0.35–0.79)		0.87 (0.61–1.24)	
30%+	0.61 (0.42–0.89)		0.79 (0.54–1.14)	
Specialty of endoscopist				
Gastroenterologist	1.00 (referent)	.006	1.00 (referent)	.001
Surgeon	1.23 (0.96–1.57)		0.96 (0.73–1.25)	
Other	1.87 (1.34–2.60)		1.67 (1.13–2.46)	
Setting of colonoscopy				
Academic hospital	1.00 (referent)	.05	1.00 (referent)	.05
Community hospital	1.11 (0.83–1.50)		0.96 (0.73–1.25)	
Nonhospital	1.88 (1.2–2.92)		1.67 (1.13–2.46)	

Prevalence and Predictors of Interval Colorectal Cancers in Medicare Beneficiaries

Gregory S. Cooper, MD[1,2]; Fang Xu, MS[1,3]; Jill S. Barnholtz Sloan, PhD[2,3]; Mark D. Schluchter, PhD[2,3]; and Siran M. Koroukian, PhD[2,3]

Characteristic	Adjusted OR (95% CI)	*P*
Facility type		
Inpatient	1.00 (Ref)	—
Outpatient	1.43 (1.32-1.56)	<.001
Ambulatory surgical center	1.58 (1.34-1.86)	<.001
Other	1.64 (1.33-2.01)	<.001
Physician specialty		
Gastroenterology	1.00 (Ref)	—
Colorectal surgery	1.16 (1.00-1.35)	.05
General surgery	1.38 (1.17-1.63)	<.001
Family practice	1.45 (1.16-1.83)	.001
Internal medicine	1.42 (1.24-1.62)	<.001
Other	1.22 (0.94-1.59)	.14
Unknown	1.66 (1.43-1.94)	<.001
Polypectomy rate by physician from noncancer sample. %		
0-0.24	1.00 (Ref)	—
0.24-0.33	0.84 (0.76-0.93)	.001
0.33-0.43	0.80 (0.72-0.89)	<.001
≥0.43	0.70 (0.63-0.78)	<.001
Colonoscopy volume by physician from noncancer sample		
1-48	1.00 (Ref)	—
49-85	1.10 (0.99-1.22)	.07
86-140	1.17 (1.04-1.31)	.01
≥141	1.27 (1.13-1.43)	<.001

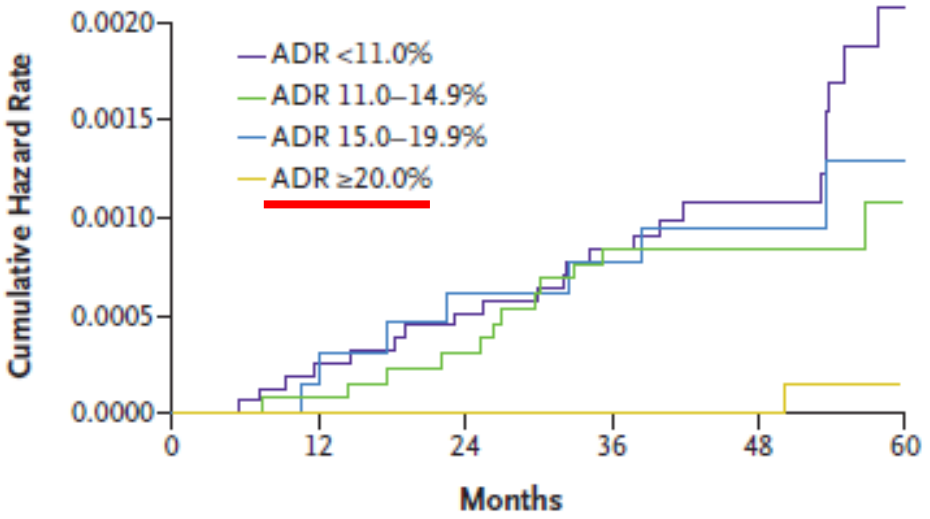
Abbreviations: CI, confidence interval; OR, odds ratio; Ref, reference categoroy; SEER 9, Surveillance, Epidemiology, and End Results 9 registries.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Quality Indicators for Colonoscopy and the Risk of Interval Cancer

Michal F. Kaminski, M.D., Jaroslaw Regula, M.D., Ewa Kraszewska, M.Sc., Marcin Polkowski, M.D., Urszula Wojciechowska, M.D., Joanna Didkowska, M.D., Maria Zwierko, M.D., Maciej Rupinski, M.D., Marek P. Nowacki, M.D., and Eugeniusz Butruk, M.D.



No. at Risk						
ADR <11.0%	15,883	15,805	15,744	15,669	9355	4717
ADR 11.0–14.9%	13,281	13,223	13,182	13,120	7571	4003
ADR 15.0–19.9%	6,607	6,582	6,562	6,539	4022	2529
ADR ≥20.0%	9,255	9,235	9,202	9,166	7155	5548

The NEW ENGLAND JOURNAL of MEDICINE

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Table 2. Characteristics of 186 Endoscopists, According to the Adenoma Detection Rate.*

Characteristic	Adenoma Detection Rate				
	<11.0%	11.0 to 14.9%	15.0 to 19.9%	≥20.0%	Total
Colonoscopists — no. (%)	80 (43.0)	46 (24.7)	34 (18.3)	26 (14.0)	186 (100.0)
No. of colonoscopies included in study					
Median (interquartile range)	130 (54–230)	161 (98–304)	125 (98–194)	178 (112–654)	145 (80–262)
Range	30–1824	34–1848	35–1589	32–1737	30–1848
No. of interval cancers/100,000 person-yr of follow-up	33.6	22.1	25.5	2.4	22.3

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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Michal F. Kaminski, M.D., Jaroslaw Regula, M.D., Ewa Kraszewska, M.Sc., Marcin Polkowski, M.D., Urszula Wojciechowska, M.D., Joanna Didkowska, M.D., Maria Zwierko, M.D., Maciej Rupinski, M.D., Marek P. Nowacki, M.D., and Eugeniusz Butruk, M.D.

hazard ratios for a rate below 11% (hazard ratio, 10.94; 95% confidence interval [CI], 1.37 to 87.01), 11.0 to 14.9% (hazard ratio, 10.75; 95% CI, 1.36 to 85.06), and 15.0 to 19.9% (hazard ratio, 12.50; 95% CI, 1.51 to 103.43) (P=0.02 for all comparisons). The results of the secondary analysis are

Pick up the small (adenoma)

not to miss the BIG (cancer)!

ADR = -Miss Rate Ad. = -Miss Rate CRC

EU GUIDELINES

Recommendations and conclusions[1]

Colonoscopy

1.10 Limited evidence exists on the efficacy of colonoscopy screening in reducing CRC incidence and mortality **(III)**. However, recent studies suggest that colonoscopy screening might not be as effective in the right colon as in other segments of the colorectum **(IV).** Sect 1.3.2.1

1.11 Limited available evidence suggests that the optimal interval for colonoscopy screening should not be less than 10 years and may even extend up to 20 years **(III - C).** Sect 1.3.2.2

1.12 Indirect evidence suggests that the prevalence of neoplastic lesions in the population below 50 years of age is too low to justify colonoscopic screening, while in the elderly population (75 years and above) lack of benefit could be a major issue. The optimal age for a single colonoscopy appears to be around 55 years **(IV - C).** Average risk colonoscopy screening should not be performed before age 50 and should be discontinued after age 74 **(V - D).** Sect 1.3.2.3

OPEN ISSUES

- Is there a variability in colonoscopy-related CRC prevention rate?
- If any, is such variability related with ADR?

OPEN ISSUES

- Are low-risk patients the same as average-risk?

Recommendations

- In the absence of hereditary syndromes people with a positive family history should not be excluded from CRC screening programmes **(III - B).**[Rec 2.5]
- Subjects belonging to families with hereditary syndromes identified at the time of screening should be referred to special surveillance programmes or family cancer clinics, if available **(III - B).**[Rec 2.6]

Low-risk as average-risk?

Five-Year Colon Surveillance After Screening Colonoscopy

DAVID A. LIEBERMAN,* DAVID G. WEISS,‡ WILLIAM V. HARFORD,§ DENNIS J. AHNEN,‖ DAWN PROVENZALE,¶

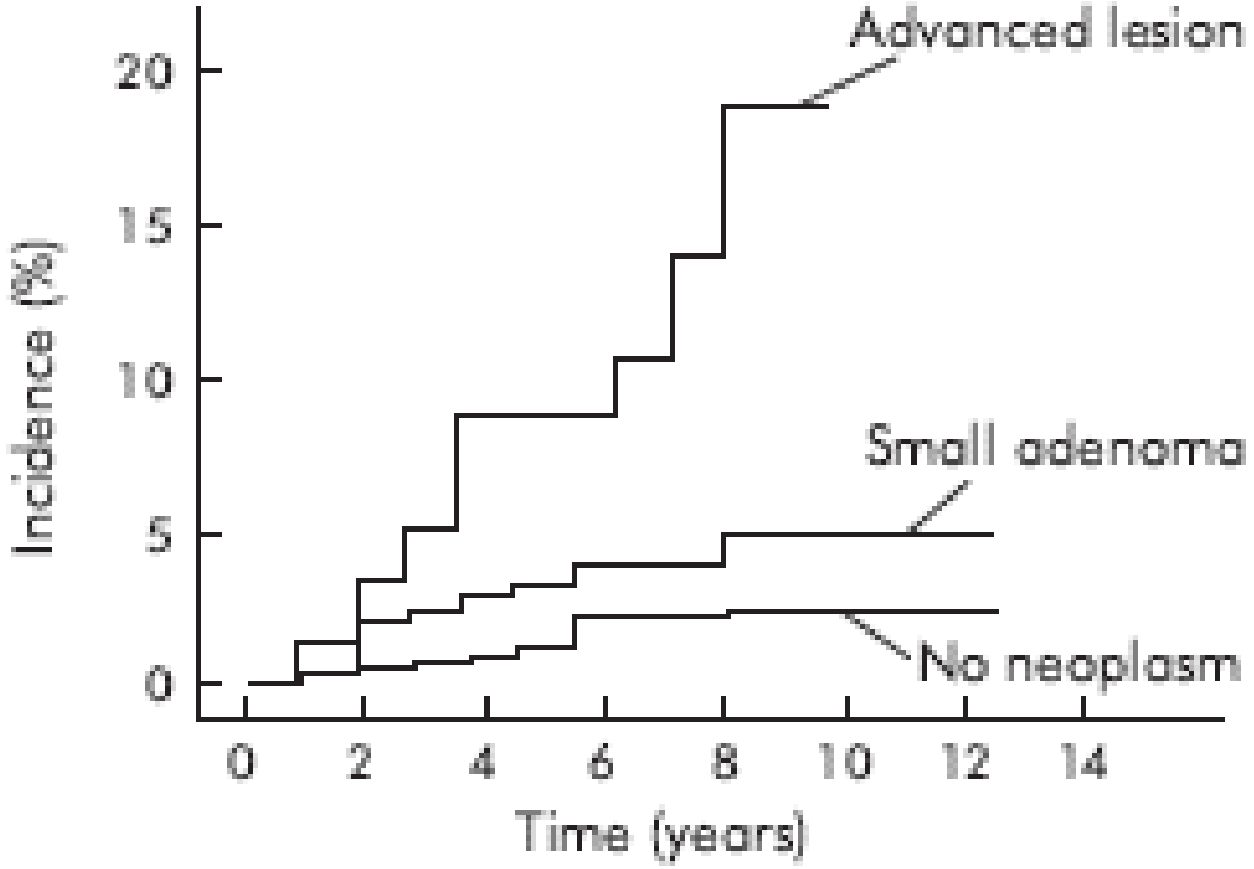
Table 4. Relative Risk of Advanced Neoplasia Within 5.5 Years Based on Baseline Finding

Baseline finding (n with examination)	No advanced neoplasia, n (%)	Advanced neoplasia, n (%)	RR[a]	95% CI	*P* value
No neoplasia (298)	291 (97.6)	7 (2.4)	1.00		
Tub Ad <10 mm (622)	584 (93.9)	38 (6.1)	2.56	1.16–5.67	.02
1 or 2 (496)	473 (95.4)	23 (4.6)	1.92	0.83–4.42	.13
>3 (126)	111 (88.1)	15 (11.9)[b]	5.01	2.10–11.96	< .001
Tub Ad >10 mm (123)	104 (84.6)	19 (15.5)	6.40	(2.74–14.94)	< .001
Villous adenoma (81)	68 (83.9)	13 (16.1)	6.05	(2.48–14.71)	< .001
HGD (46)	38 (82.6)	8 (17.4)	6.87	(2.61–18.07)	< .001
Cancer (23)	15 (65.2)	8 (34.8)	13.56	(5.54–33.18)	< .001
Number of adenomas[c] at baseline (n)					
1 or 2 (617)	577	40 (6.5)			
3 or 4 (145)	122	23 (15.9)			
5–9 (64)	53	11 (17.2)			
10+ (8)	7	1 (12.5)			

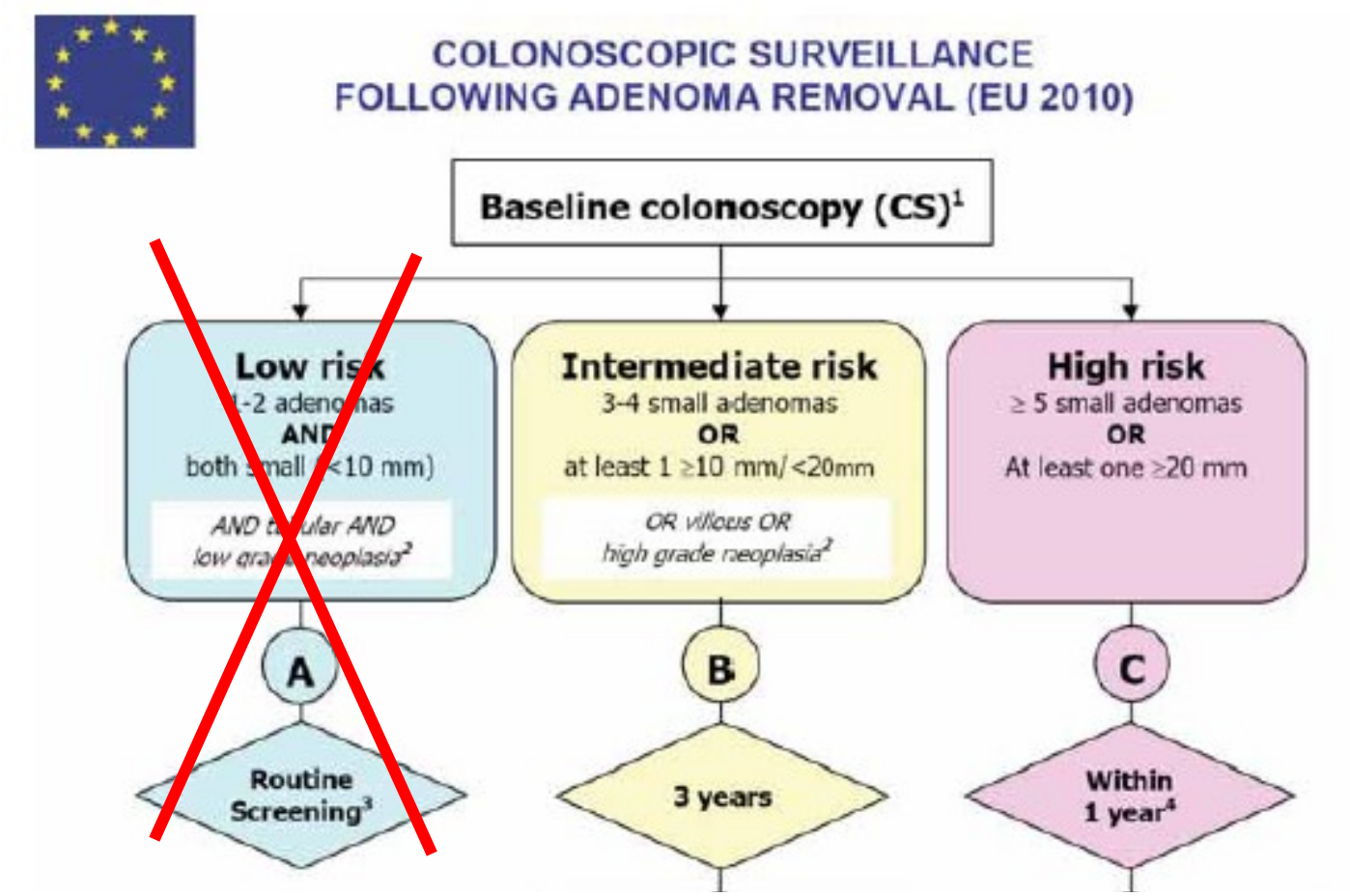
Low-risk as average-risk?

COLORECTAL CANCER

Incidence and recurrence rates of colorectal adenomas



Low-risk as average-risk?



Low-risk = FP

Low-risk as average-risk?

9.3.1 Low risk group

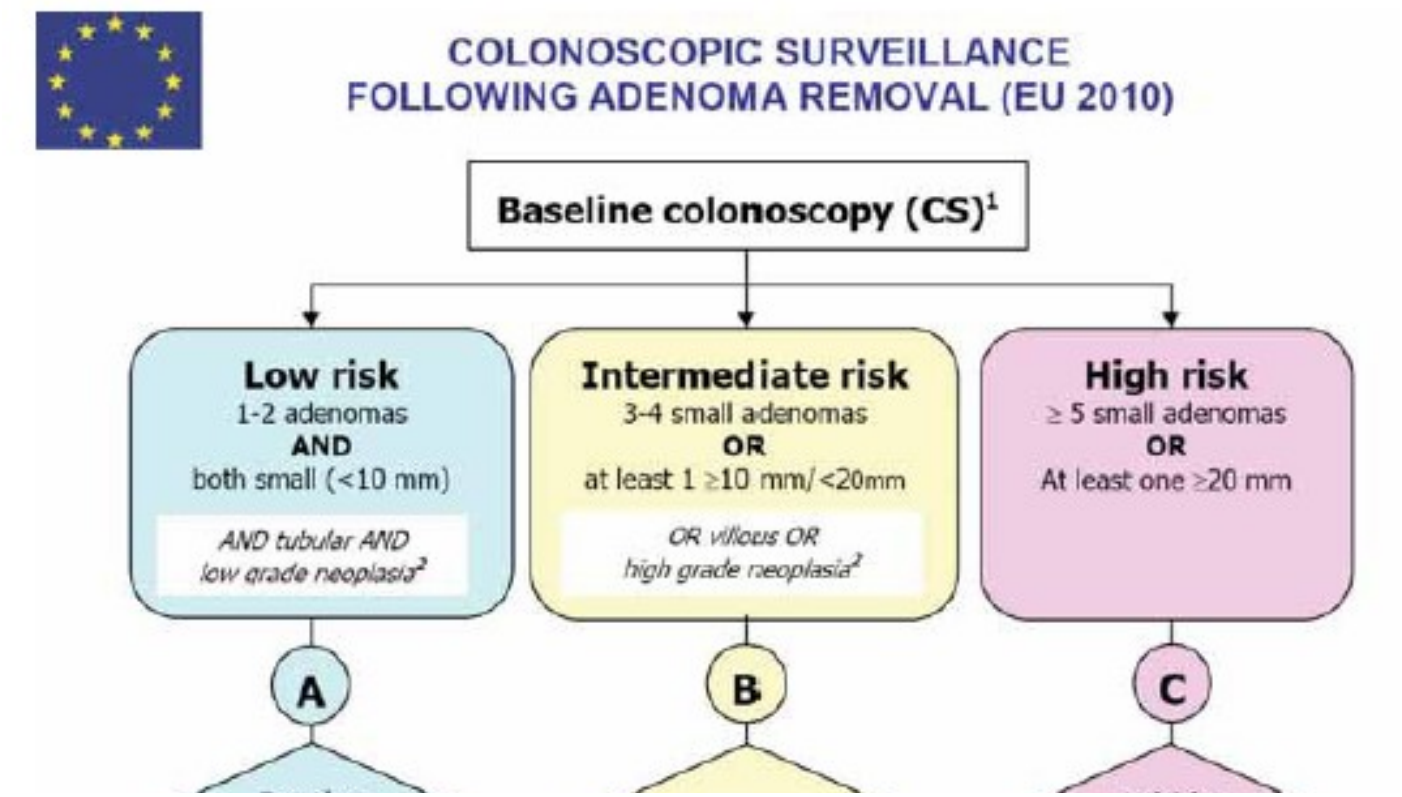
The longer term risk of developing colorectal cancer has been examined for patients from whom adenomas were removed from the distal sigmoid colon and rectum by sigmoidoscopy. No increased incidence of cancer was observed in comparison with the general population in 751 residents of Rochester, Minnesota, following removal of small (≤10 mm) colorectal polyps (Spencer et al. 1984), most of which were unexamined histologically. A similar study from St Mark's Hospital (Atkin, Morson & Cuzick 1992), in which all removed lesions were examined histologically, found that patients from whom only small (<10 mm) tubular adenomas were removed from the distal sigmoid colon or rectum had no long-term increased risk of developing colon cancer in comparison with the general population.

Low-risk as average-risk?

	Risk reduction
TP = >10 mm polypectomy	-60/80%
True FP = negative colonoscopy	-30/70%
TP = <10 mm polypectomy	-0%

OPEN ISSUES

- Are low-risk patients the same as average-risk?
- Should we preclude a 1-year examination to intermediate risk subjects



9.3.3 High risk group

Thus, although not entirely consistent, the data suggest that an additional clearing colonoscopy at 12 months may be warranted in people found at a single colonoscopy to have 5 or more adenomas or an adenoma of size 20 mm or larger. These patients require careful surveillance colonoscopy because of the substantial risk of missing adenomas with high malignant potential **(III - B).**[Rec 9.5]

Why 3-years in intermediate risk?

GASTROENTEROLOGY 2009;136:832–841

A Pooled Analysis of Advanced Colorectal Neoplasia Diagnoses After Colonoscopic Polypectomy

MARÍA ELENA MARTÍNEZ,[*,‡] JOHN A. BARON,[§] DAVID A. LIEBERMAN,[‖] ARTHUR SCHATZKIN,[¶] ELAINE LANZA,[#] SIDNEY J. WINAWER,[**] ANN G. ZAUBER,[‡‡] RUIYUN JIANG,[*,‡] DENNIS J. AHNEN,[§§] JOHN H. BOND,[‖‖] TIMOTHY R. CHURCH,[¶¶] DOUGLAS J. ROBERTSON,[##] STEPHANIE A. SMITH–WARNER,[***] ELIZABETH T. JACOBS,[*,‡] DAVID S. ALBERTS,[*,‡,‡‡‡] and E. ROBERT GREENBERG[§,§§§]

Table 5. Pooled Odds Ratios of Colorectal Neoplasia for Baseline Patient and Adenoma Characteristics

	Crude OR (95% CI)		Adjusted OR[a] (95% CI)	
Characteristic	Nonadvanced	Advanced	Nonadvanced	Advanced
Adenoma number				
1	1.00	1.00	1.00	1.00
2	1.58 (1.42–1.77)	1.81 (1.54–2.14)	1.46 (1.30–1.64)	1.39 (1.17–1.66)
3	2.38 (2.04–2.79)	2.85 (2.30–3.54)	2.05 (1.73–2.42)	1.85 (1.46–2.34)
4	2.70 (2.09–3.48)	4.11 (2.99–5.63)	2.23 (1.71–2.92)	→ 2.41 (1.71–3.40)
5+	4.30 (3.33–5.56)	6.94 (5.12–9.40)	3.63 (2.76–4.78)	→ 3.87 (2.76–5.42)
			P trend < .0001	*P* trend < .0001
Adenoma location[f]				
Distal colorectum	1.00	1.00	1.00	1.00
Any proximal	1.78 (1.62–1.95)	2.27 (1.98–2.60)	1.29 (1.16–1.44)	1.68 (1.43–1.98)
Size of largest adenoma, mm				
<5	1.00	1.00	1.00	1.00
5 to <10	1.03 (0.92–1.16)	1.15 (0.95–1.39)	1.01 (0.90–1.14)	1.17 (0.95–1.42)
10 to <20	0.92 (0.82–1.04)	2.18 (1.82–2.62)	0.94 (0.82–1.08)	→ 2.27 (1.84–2.78)
20+	1.02 (0.84–1.23)	2.92 (2.28–3.73)	1.00 (0.80–1.25)	→ 2.99 (2.24–4.00)
			P trend = .4944	*P* trend < .0001

Guidelines for Colonoscopy Surveillance After Cancer Resection: A Consensus Update by the American Cancer Society and the US Multi-Society Task Force on Colorectal Cancer

DOUGLAS K. REX,* CHARLES J. KAHI,* BERNARD LEVIN,† ROBERT A. SMITH,§ JOHN H. BOND,‖

CRC risk 0.7%

Table …scopy

2. Pat…al cancer sho…n (or 1 yea…was per…This colonoscopy at 1 year is in addition to the perioperative colonoscopy for synchronous tumors.

Why 3-years in intermediate risk?

GASTROENTEROLOGY 2009;136:832–841

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Table 4. Risk of New Neoplasia at Follow-Up Evaluation, According to Baseline Patient and Adenoma Characteristics

Characteristic	Number (%)	Nonadvanced adenoma, % (95% CI)	Advanced adenoma, % (95% CI)	Cancer, % (95% CI)
Adenoma number[a]				
1	5465 (60.0)	30.2 (29.0–31.4)	8.6 (7.8–9.3)	0.5 (0.4–0.7)
2	2054 (22.5)	38.3 (36.2–40.4)	12.7 (11.3–14.1)	0.5 (0.2–0.9)
3	890 (9.8)	45.4 (42.1–48.7)	15.3 (12.9–17.6)	1.1 (0.4–1.8)
4	326 (3.6)	45.4 (40.0–50.8)	19.6 (15.3–23.9)	1.2 (0.0–2.4)
5+	377 (4.1)	51.2 (46.1–56.2)	24.1 (19.8–28.5)	0.8 (0.0–1.7)
Adenoma location				
Distal colorectum	4434 (48.4)	30.4 (29.1–31.8)	8.5 (7.7–9.3)	0.4 (0.2–0.6)
Proximal only	2620 (28.6)	37.3 (35.4–39.1)	11.8 (10.6–13.1)	0.8 (0.5–1.2)
Proximal and distal	1754 (19.1)	44.2 (41.9–46.6)	17.5 (15.7–19.3)	1.0 (0.6–1.5)
Unknown	359 (3.9)	26.7 (22.2–31.3)	8.1 (5.3–10.9)	0.0
Adenoma size (mm)[a]				
<5	2540 (28.8)	36.4 (34.5–38.3)	7.7 (6.6–8.7)	0.5 (0.2–0.8)
5 to <10	3115 (35.3)	36.8 (35.1–38.5)	8.7 (7.7–9.7)	0.5 (0.2–0.7)
10 to <20	2487 (28.2)	31.4 (29.6–33.3)	15.9 (14.5–17.4)	0.8 (0.5–1.2)
20+	672 (7.6)	31.8 (28.3–35.4)	19.3 (16.4–22.3)	1.2 (0.4–2.0)

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Table 3. Patient Summary End Points During Surveillance Follow-Up Evaluation

	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									2.0 (1.0–8.0)
Any adenoma duri									30 (46.7)
n (%)[a]									
Large adenoma, n									11 (7.8)
Tubulovillous/villou									30 (6.3)
High-grade dysplas									54 (0.6)
Advanced adenom									24 (11.2)
Colorectal cancer,									58 (0.6)

moderate degree of discrimination. Compared with patients who could be categorized as low risk, those deemed high risk were more often diagnosed with both advanced adenoma (15.5% vs 6.9%) and colorectal cancer (0.8% vs 0.5%). There was essentially no difference in the occurrence of nonadvanced neoplasms.

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Table 1. Description of Studies Included in the Pooled Analyses

	APPS	NPS	CPPS	PPT	WBF	VA	AFT	UDCA
Number enrolled	864	1418	930	2079	1429	3121/895[a]	1121	1285
Study design	4-arm trial	2-arm endoscopy study	2-arm trial	2-arm trial	2-arm trial	2-arm endoscopy study	3-arm trial	2-arm trial
Entry criteria	Any recent adenoma	First adenoma found at screening	Any recent adenoma	Any recent adenoma	Any recent adenoma	First adenoma found at screening	Any recent adenoma	Any recent adenoma
Recruitment period	1984–1988	1980–1990	1991–1998	1991–1998	1990–1998	1994–1997	1994–1998	1995–1999
Age range (*y*)	25–79	22–88	27–80	35–89	40–80	50–75	29–79	40–80
Number of centers	6	7	7	8	1	13	9	2
Follow-up colonoscopy schedule	Years 1 and 4	Years 1 and 3 or year 3	Years 1 and 4	Years 1 and 4	Years 1 and 3 for 889 patients;	Years 2 and 5 for patients with large adenomas;	Year 3	Year 3

CCE-2 vs FIT

- 6% of subjects will result FIT+
- FIT PPV ⟶ <30%
- CCE-2 as triage in FIT+

SEX

	50	60	70	80	90	95+
45 Male	0.149%	0.869%	2.373%	**4.387%**	5.717%	6.021%
45 Fem.	0.130%	0.663%	1.752%	3.434%	**4.983%**	5.429%

CCE-2 vs FS

- 10-20% of subjects will result positive at FS
- FS PPV ⟶ <20%
- CCE-2 as triage in FS+