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La sorveglianza epidemiologica
dello screening dei tumori del colon-retto
nella Regione Emilia-Romagna

Seminario di studio

Bologna, 5 aprile 2018

L'impatto del programma di screening sulle lesioni del colon destro: le evidenze disponibili

Carlo Senore

Epidemiologia

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology

journal homepage: https://ees.elsevier.com/ybega/default.asp

Distribution of colorectal polyps: Implications for screening

Available evidence is supporting the hypothesis of an increase in the proportion of right-sided adenomas (and CRCs) with age, while a similar trend was not observed for SSA/Ps, among subjects aged 50 or older.

The reported trend toward a proximalization of colorectal adenomas over time likely results from improved diagnostic performance and/or population ageing.

Anatomic distribution of cancers and colorectal adenomas according to age and sex and relationship between proximal and distal neoplasms in an i-FOBT-positive average-risk Italian screening cohort

F. Parente · S. Bargiggia · C. Boemo · C. Vailati · E. Bonoldi · A. Ardizzoia · A. Ilardo · F. Tortorella · S. Gallus

Int J Colorectal Dis (2014) 29:57–64

Table 2 Distribution of 2,281 i-FOBT-positive subjects, who underwent colonoscopy, according to total proximal neoplasms (adenomas+colorectal cancers) and advanced proximal neoplasms (advanced adenomas+colorectal cancers), by sex, age and distal neoplasms. Corresponding OR and 95 % CI

	Total of subjects		Subjects with 1 or more proximal neoplasms			Subjects with 1 or more advanced proximal neoplasms		
			N	%	OR[a] (95 % CI) of ≥1 vs. 0 proximal neoplasms	*N*	%	OR[a] (95 % CI) of ≥1 vs. 0 proximal neoplasms
Sex								
Women	929	40.7	174	30.4	1[b]	76	28.5	1[b]
Men	1,352	59.3	398	69.6	1.81 (1.47–2.21)	191	71.5	1.84 (1.39–2.43)
Age (years)								
50–59	936	41.0	189	33.0	1[b]	89	33.3	1[b]
60–70	1,345	59.0	383	67.0	1.57 (1.28–1.92)	178	66.7	1.44 (1.10–1.89)
Distal adenomas (advanced)								
0	1,564	68.6	360	62.9	1[b]	153	57.3	1[b]
≥1	717	31.4	212	37.1	1.31 (1.07–1.60)	114	42.7	1.63 (1.25–2.12)

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

RIDUZIONE DI INCIDENZA NEL COLON DISTALE

UK FLEXI-SCOPE TRIAL

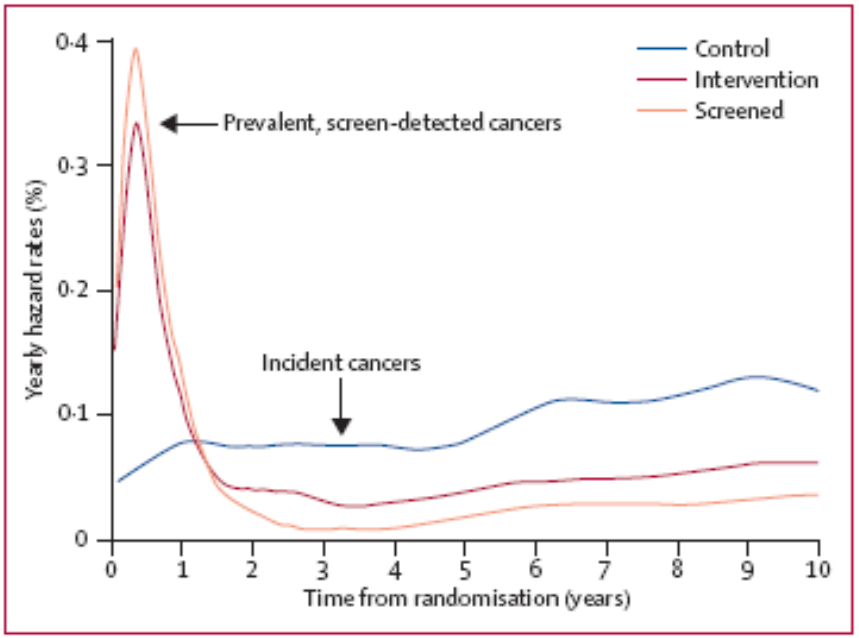


Figure 3: Smoothed early hazard rates for distal cancer (rectum and sigmoid colon)

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)

UN PLATEAU PER GLI ADENOMI PROSSIMALI?

Comparing Attendance and Detection Rate of Colonoscopy With Sigmoidoscopy and FIT for Colorectal Cancer Screening

NEREO SEGNAN,* CARLO SENORE,* BRUNO ANDREONI,‡ ALBERTO AZZONI,§ LUIGI BISANTI,‖ ALESSANDRO CARDELLI,¶ GUIDO CASTIGLIONE,# CRISTIANO CROSTA,** ANDREA EDERLE,‡‡ ALBERTO FANTIN,‡‡ ARNALDO FERRARI,§§ MARIO FRACCHIA,‖‖ FRANCO FERRERO,‖ STEFANO GASPERONI,¶ SERAFINO RECCHIA,¶¶ MAURO RISIO,## TIZIANA RUBECA,*** GIORGIO SARACCO,‡‡‡ MARCO ZAPPA,§§§ and the SCORE3 Working Group—Italy

GASTROENTEROLOGY 2007;132:2304–2312

Table 4. Age-Specific Prevalence of Distal and Proximal Adenomas Among People Attending TC Screening

Age, y	All distal adenomas (%)[a]	Advanced distal adenomas (%)	All proximal adenomas (%)[b]	Advanced proximal adenomas (%)
55–56	11.0	6.3	4.6	2.4
57–58	9.6	2.8	7.5	2.0
59–60	12.7	3.7	7.2	1.7
61–62	13.2	5.3	10.8	3.7
63+	13.1	5.3	16.2	2.8

NOTE. Distal refers to adenomas detected in the rectum or sigmoid colon.

[a] χ^2 For linear trend, 1.73; $P = .18$.

[b] χ^2 For linear trend, 26.97; $P = .000$.

Advanced proximal neoplasia of the colon in average-risk adults

Linda Rabeneck, MD, MPH,[1,2,3,4,5] Lawrence F. Paszat, MD, MS,[1,4,5,6] Robert J. Hilsden, MD, PhD,[7] S. Elizabeth McGregor, PhD,[8] Eugene Hsieh, MDCM,[9] Jill M. Tinmouth, MD, PhD,[1,3,6] Nancy N. Baxter, MD, PhD,[1,4,10,11] Refik Saskin, MSc,[1] Arlinda Ruco, MPH,[6] David Stock, MSc[6]

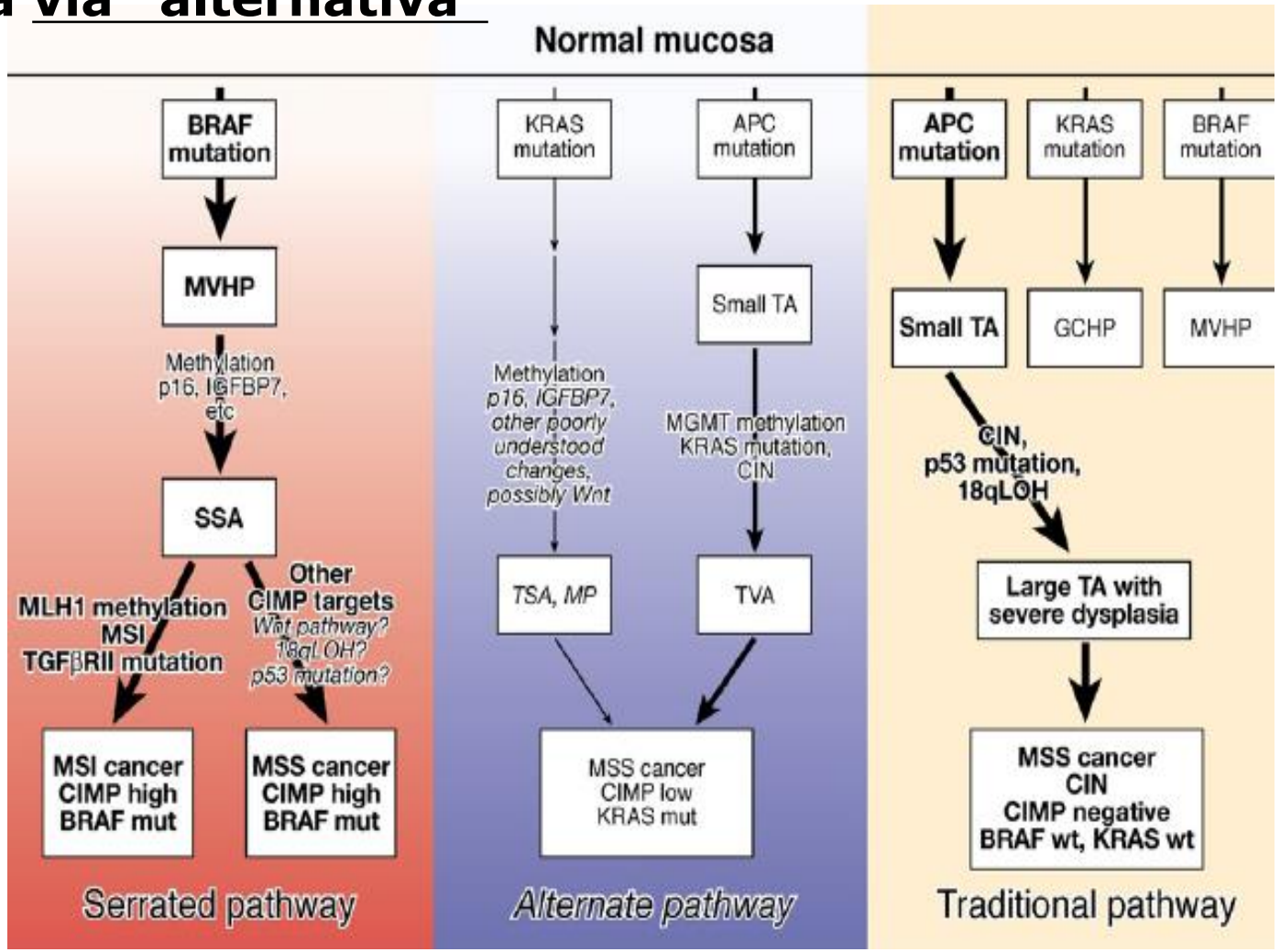
Età 50 - 74 anni (54.4% donne)

TABLE 1. Characteristics of the study cohort among those with and without APN

		APN (n = 142)	Total (N = 4651)	OR*(95% CI)
Age, no. (%), y				
50-54	2.3%	36 (25.4)	1577 (33.9)	1.00
55-59	2.8%	35 (24.6)	1265 (27.2)	1.19 (0.74-1.91)
60-64	3.6%	35 (24.6)	961 (20.7)	1.62 (1.01-2.60)
65-69	4.2%	23 (16.2)	547 (11.8)	1.89 (1.11-3.21)
70-74	4.3%	13 (9.2)	301 (6.5)	1.94 (1.02-3.71)

- In persons at average risk for colorectal cancer, the prevalence of advanced proximal neoplasia (APN) and isolated APN is low (3.1% and 1.8%, respectively).

Dal punto di vista molecolare c'è evidenza che parte (12-15%) dei CCR sporadici prossimali rappresentino una entità distinta e che possano derivare per lo più dalla via "alternativa"



Jass JR, Crit Rev Oncog 2006
Laggett B, Gastroenterology 2010

Caratteristiche molecolari dei CCR intervallari

CIMP Status of Interval Colon Cancers: Another Piece to the Puzzle

Mustafa A. Arain, MD[1], Mandeep Sawhney, MD[2], Shehla Sheikh, MD[1], Ruth Anway, BA[1], Bharat Thyagarajan, MD, PhD[3], John H. Bond, MD[1] and Aasma Shaukat, MD, MPH[1,4]

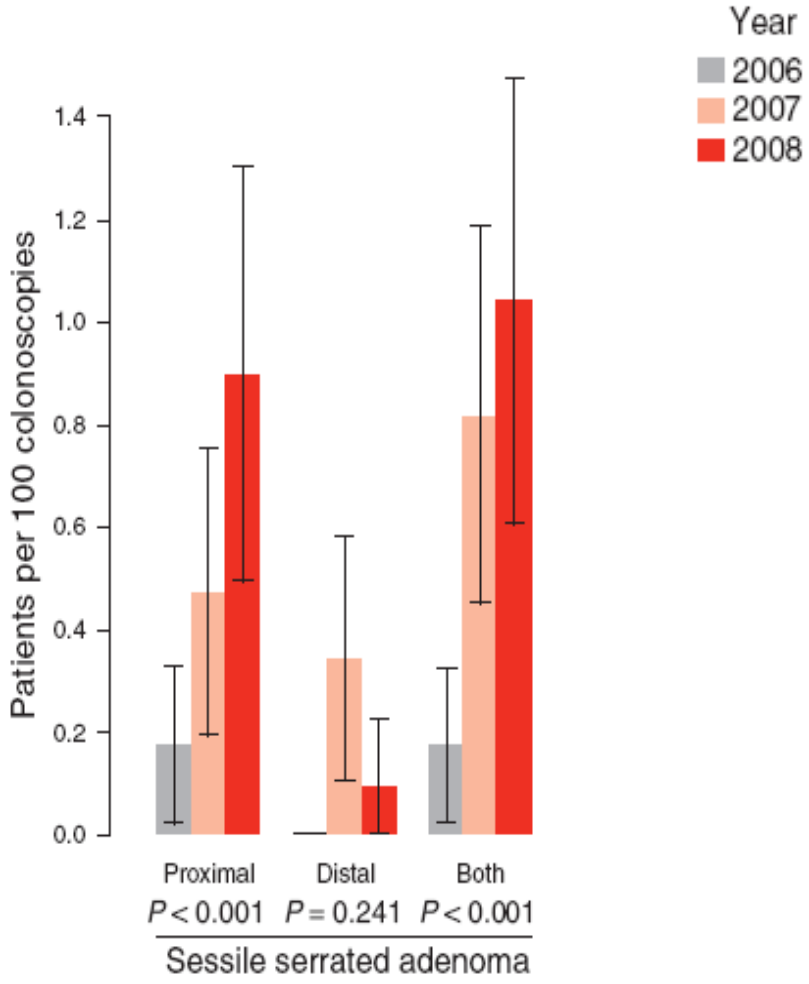
Table 2. Molecular characteristics of interval vs. non-interval cancers

	Interval	Non-interval	*P* value
CIMP[a]			
Positive	31 (57%)	33 (33%)	0.004
Negative	23 (43%)	75 (66%)	
MSI[b]			
MSI	16 (29%)	12 (11%)	0.004
MSS	39 (71%)	95 (89%)	

CIMP, CpG island methylator phenotype; MSI, microsatellite instability; MSS, microsatellite stable.
[a]*n*=167.
[b]*n*=162.
All values expressed as number and % with respect to interval/non-interval status.

Arain M, Am J Gastroenterol 2009

DETECTION RATE DI LESIONI SERRATE NEGLI ANNI



Hetzel et al. 2011

Sessile Serrated Polyps at Screening Colonoscopy: Have They Been Under Diagnosed?

Jill Tinmouth, MD, PhD[1–3], Pauline Henry, MD, PhD[3,4], Eugene Hsieh, MDCM[3,4], Nancy N. Baxter, MD, PhD[1,5–7], Robert J. Hilsden, MD, PhD[8], S. Elizabeth McGregor, PhD[8,9], Lawrence F. Paszat, MD, MS[1,3,7,10,11], Arlinda Ruco, MPH[3], Refik Saskin, MSc[1], Andrew J. Schell, MD[12,13], Emina E. Torlakovic, MD, PhD[4,14] and Linda Rabeneck, MD, MPH[1,2,7,10,11]

We enrolled 2,527 persons who underwent colonoscopy in whom 111 had HPs >5 mm. Thirty-two of the 111 participants (28.8%) with HPs >5 mm had their polyps reclassified as SSA/Ps. There were no significant differences in patient characteristics between those with reclassified SSA/Ps and those who had HPs >5 mm. SSA/Ps were more likely to be proximal ($P<0.001$) and larger ($P<0.007$) than the HPs. In all, 48.3% of those with high-risk adenomas received appropriate follow-up compared with 26.1% of those with high-risk SSA/Ps.

Sensibilità dei test di screening

Sensibilità del FIT

Gli studi di accuratezza diagnostica che hanno valutato la performance del FIT in soggetti sottopsti a colonscopia mostrano una minore sensibilità del test per le lesioni prossimali rispetto a quelle del colon distale

(Haug et al 2011; Hirai et al. 2016; Brenner et al 2017)

La sensiblità non era migliorata
riducendo il cut-off (Kim et al. 2016)
utilizzando più campioni (Wong et al. 2015)

Sensitivity of immunochemical faecal occult blood testing for detecting left- *vs* right-sided colorectal neoplasia

U Haug*[,1], KM Kuntz[2], AB Knudsen[3], S Hundt[1] and H Brenner[1]
British Journal of Cancer (2011) 104, 1779 – 1785

Higher f-Hb levels in subjects with pedunculated polyps

Logistic regression analyses adjusted for site showed a statistically significant association of pedunculated shape with test sensitivity.

Similar findings reported in a recent analysis of the COLONPREV cohort

Cubiella et al 2014

Sensitivity of immunochemical faecal occult blood testing for detecting left- *vs* right-sided colorectal neoplasia

U Haug*,[1], KM Kuntz[2], AB Knudsen[3], S Hundt[1] and H Brenner[1] British Journal of Cancer (2011) 104, 1779 – 1785

The higher proportion of pedunculated adenomas in the left colon is consistent with autopsy studies that reported on the shape of adenomas according to anatomical site

Blatt, 1961;
Eide and Stalsberg, 1978;
Rickert et al, 1979;
Williams et al, 1982.

Difference in diagnostic performance according to anatomical site occurred only for lower positivity cut-off

Interval cancers in a FOBT-based colorectal cancer population screening programme: implications for stage, gender and tumour site

R J C Steele,[1,2] P McClements,[3] C Watling,[3] G Libby,[2] D Weller,[4] D H Brewster,[3] R Black,[3] F A Carey,[5] C G Fraser[2]

Table 4 Anatomical site distribution of screen-detected, interval and non-screened cancers in all three rounds

Site	Screen-detected, % (n)	Interval, % (n)	Non-screened, % (n)
Right colon	21.2 (136)	32.3 (201)	25.4 (1704)
Left colon	53.3 (342)	35.6 (222)	43.6 (2925)
Rectum	25.5 (164)	32.1 (200)	31.0 (2077)

High sensitivity of five colorectal screening programmes with faecal immunochemical test in the Veneto Region, Italy

Manuel Zorzi,[1] Chiara Fedato,[1] Grazia Grazzini,[2] Fiorella Carmen Stocco,[1] Flavio Banovich,[3] Antonio Bortoli,[4] Luigi Cazzola,[5] Adriana Montaguti,[6] Tina Moretto,[7] Marco Zappa,[2] Marcello Vettorazzi[1]

Table 3 Person-years, observed interval cancers, expected cancers and screening sensitivity by time since last test, age, gender, history of screening and anatomic site and by screening programme according to 2 years of follow-up after a negative screening episode

	Person-years	Observed interval cancers	Expected cancers	2 years sensitivity (1 − O/E)%	95% CI
Time since last test (months)					
0–11	267 021	50	326	84.7	79.8 to 88.6
12–23	201 285	76	245	69.0	61.3 to 75.6
Age (years)					
50–54	120 782	20	72	72.2	57.0 to 83.0
55–59	130 370	26	129	79.8	70.4 to 86.8
60–64	119 939	25	174	85.6	78.7 to 90.7
65–70	97 215	55	197	72.1	63.7 to 79.0
50–59	251 152	46	201	77.1	69.4 to 83.2
60–70	217 154	80	371	78.4	73.2 to 82.9
Gender					
Males	222 682	69	347	80.1	74.8 to 84.5
Females	245 605	57	226	74.8	67.3 to 80.9
History of screening					
First test	326 489	89	388	77.1	71.8 to 81.6
Subsequent test	141 817	37	183	79.8	72.2 to 85.8
Anatomical site					
Colon	468 306	90	391	77.0	71.7 to 81.5
Proximal	468 306	46	145	68.3	57.7 to 76.8
Distal	468 306	44	246	82.1	76.0 to 87.0
Rectum	468 306	36	182	80.2	72.6 to 86.1

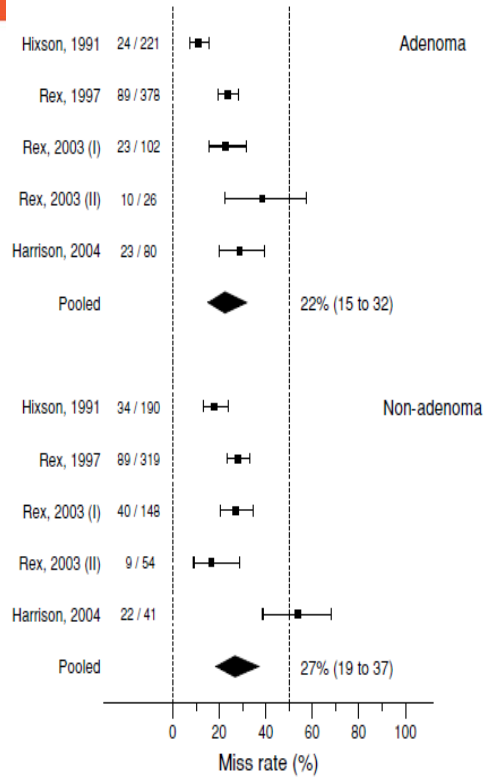


Figure 3. Polyp miss rate by type.

American Journal of Gastroenterology
© 2006 by Am. Coll. of Gastroenterology
Published by Blackwell Publishing
ISSN 0002-9270
doi: 10.1111/j.1572-0241.2006.00390.x

CME

Polyp Miss Rate Determined by Tandem Colonoscopy: A Systematic Review

Jeroen C. van Rijn, M.D.,[1] Johannes B. Reitsma, M.D., Ph.D.,[1] Jaap Stoker, M.D., Ph.D.,[2]
Patrick M. Bossuyt, Ph.D.,[1] Sander J. van Deventer, M.D., Ph.D.,[3] and Evelien Dekker, M.D., Ph.D.[3]

Precursori neoplastici possono NON essere diagnosticati

(lesioni perse)

Quelli ***"non polipoidi"*** (neoplastici e <u>non neoplastici</u> tra cui le lesioni serrate) sono quelli ragionevolmente si "perdono" più facilmente

→ Lesioni NPL e SSA sono più prevalenti nel **colon prossimale**

CANCRI INTERVALLO DOPO COLONSCOPIA

CCR diagnosticati entro 3-5 anni da una colonoscopia completa negativa

si considera il mean sojourn time stimato per le lesioni invasive asintomatiche

CCR diagnosticati entro 10 anni da una colonscopia completa negativa

si considera l'intervallo raccomandato per la ripetizione.

Valutazione dell'effetto protettivo

Risk of Developing Colorectal Cancer Following a Negative Colonoscopy Examination

Evidence for a 10-Year Interval Between Colonoscopies

Harminder Singh, MD
Donna Turner, PhD
Lin Xue, MSc
Laura E. Targownik, MD, MSHS
Charles N. Bernstein, MD

Table 6. Colorectal Cancer Proximal to Splenic Flexure by Time of Diagnosis After the Index Colonoscopy

	No. (%) of CRC Cases Proximal to the Splenic Flexure		
	Negative Colonoscopy Cohort	All CRC Cases*	*P* Value
Overall	84 (51)	3450 (34)	<.001
Diagnosed, y			
0.5-2.0	37 (63)	3450 (34)	<.001
>2.0-5.0	26 (49)	3450 (34)	.01
>5	21 (42)	3450 (34)	.20

Abbreviation: CRC, colorectal cancer.
*All the CRC cases diagnosed in the province between 1969 and 2003.

Table 5. Univariate and Multivariate Logistic Regression Analysis for the Characteristics of Patients, Procedures, Physicians, and Settings Associated with New or Missed Cancer After Colonoscopy Among Men in Ontario April 1, 1997 to March 31, 2002

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)
Age (in yearly increments)	1.05[a] (1.04–1.07)	1.04[a] (1.02–1.05)
History of abdominal or pelvic surgery		
No	1	1
Yes	1.46[b] (1.03–2.05)	0.99 (0.69–1.43)
History of diverticular disease		
No	1	1
Yes	8.70[a] (6.44–11.76)	6.88[a] (5.00–9.47)
CRC site		
Rectal or sigmoid	1	1
Splenic flexure/descending	1.19 (0.57–2.47)	1.16 (0.55–2.44)
Transverse	2.40[b] (1.43–4.03)	1.98[b] (1.16–3.41)
Right	3.12[a] (2.31–4.21)	2.52[a] (1.84–3.45)
Excision of polyp		
No	1	1
Yes	0.64[a] (0.47–0.88)	0.66[b] (0.47–0.92)
Fulguration of polyp		
No	1	1
Yes	0.86 (0.50–1.49)	0.91 (0.51–1.62)
Physician specialty		
Gastroenterology	1	1
General surgery	1.15 (0.82–1.62)	1.16 (0.82–1.66)
Internal medicine or family practice	1.72[a] (1.13–2.63)	1.77[b] (1.14–2.74)
Other	0.82 (0.41–1.63)	0.85 (0.42–1.71)
Colonoscopy setting		
Hospital	1	1
Office	2.32[a] (1.57–3.44)	3.07[a] (2.02–4.66)

Bressler B,

Gastroenterology 2007

12487 pts con diagnosi di CCR

→ 430 (3.4%) pts con CCR dopo colonscopia 6-36 mesi prima

% di **CCR intervallari**

prossimali: 6%

distali: 2%

Table 2. Patient, Geographic, Facility, and Procedure Predictors of Interval Colorectal Cancers

Characteristic	Adjusted OR (95% CI)	*P*
Age group, y		
69-74	1.00 (Ref)	—
75-79	1.02 (0.93-1.11)	.73
80-84	0.93 (0.85-1.03)	.16
≥85	0.84 (0.76-0.94)	<.001
Sex		
Women	1.00 (Ref)	—
Men	1.07 (0.99-1.16)	.07
Cancer location		
Proximal colon	1.00 (Ref)	—
Distal colon	0.42 (0.39-0.46)	<.001
Rectum	0.47 (0.42-0.53)	<.001
Unspecified	0.93 (0.73-1.17)	.53
Comorbidity score		
0	1.00 (Ref)	—
1	1.21 (1.11-1.31)	<.001
2	1.43 (1.28-1.60)	<.001
≥3	1.89 (1.68-2.14)	<.001
Diverticulosis		
No	1.00 (Ref)	—
Yes	6.00 (5.57-6.46)	<.001

Table 2. (Continued)

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 cate-

Cooper G, Cancer 2011

57839 pts con diagnosi di CCR →

4192 (7.2%) con CCR dopo colonscopia 6-36 mesi prima

CCR intervallari **prossimali:** 9.9% **distali:** 4.6%

Post-colonoscopy colorectal cancer (PCCRC) rates vary considerably depending on the method used to calculate them: a retrospective observational population-based study of PCCRC in the English National Health Service

Eva J A Morris,[1] Matthew D Rutter,[2,3,4] Paul J Finan,[3,5] James D Thomas,[6] Roland Valori[7]

Table 4 Odds of the development of a PCCRC within 3 years of a colonoscopy

Characteristic	OR	Lower 95% CI	Upper 95% CI	p Value
Year of colonoscopy	0.94	0.93	0.95	<0.01
Sex				
Male	1.00			
Female	1.13	1.06	1.20	<0.01
Age (per year)	1.00	0.99	1.00	<0.01
IMD income category				
Most affluent	1.00			
2	1.01	0.92	1.11	0.76
3	0.92	0.84	1.01	0.09
4	0.99	0.90	1.09	0.90
Most deprived	1.01	0.92	1.12	0.79
Previous hospital admission for Crohn's disease				
No	1.00			
Yes	2.54	2.11	3.06	<0.01
Previous hospital admission for ulcerative colitis				
No	1.00			
Yes	5.82	5.17	6.54	<0.01
Previous hospital admission for diverticular disease				
No	1.00			
Yes	1.86	1.75	1.98	<0.01
Site of tumour				
Rectum/sigmoid colon	1.00			
Splenic flexure/descending colon	0.98	0.84	1.15	0.82
Transverse colon	1.17	1.02	1.35	0.02
Right colon	1.42	1.32	1.52	<0.01
Colon NOS	2.34	2.13	2.58	<0.01
Number of colonoscopies in PCCRC/detected category (per colonoscopy)	2.93	2.71	3.15	<0.01

IMD, Index of Multiple Deprivation; PCCRC, post-colonoscopy colorectal cancer; NOS, not otherwise specified.

Fattori predittivi

- **Specializzazione dell'operatore**
- **Indicatori di performance (numero di polipectomie, ADR)**
- **Setting**
- **Sede della lesione**
- **Diverticolosi**

Numerosi studi hanno evidenziato come la colonscopia sia efficace nel ridurre incidenza e mortalità dei tumori del colon, indicando allo stesso tempo come l'effetto protettivo sia di entità sostanzialmente diversa per i tumori ad insorgenza nel colon destro rispetto a quelli ad insorgenza distale

l'efficacia reale della colonoscopia nell'evidenziare e nel ridurre l'incidenza di lesioni neoplastiche del **colon prossimale** è "limitata"

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

	All Cancer	Right-Sided Cancer	Left-Sided Cancer
Complete TC	0.63 (0.57–0.69)	0.99 (0.86–1.14)	0.33 (0.28–0.39)

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.

Protection From Right- and Left-Sided Colorectal Neoplasms After Colonoscopy: Population-Based Study

Hermann Brenner, Michael Hoffmeister, Volker Arndt, Christa Stegmaier, Lutz Altenhofen, Ulrike Haug

J Natl Cancer Inst 2010;102:89–95

Table 2 . Associations of previous colonoscopy with prevalence of advanced colorectal neoplasia (cancer or advanced adenoma) detected at screening colonoscopy, overall and by anatomical sites

	All Cancer	Right-Sided cancer	Left-SidedCancer
Prevalence ratio	0.52 (0.37–0.73)	1.05 (0.63–1.76)	0.33 (0.21–0.53)

L'effetto protettivo osservato si mantiene per almeno 15 anni

Protection From Colorectal Cancer After Colonoscopy

A Population-Based, Case–Control Study

Hermann Brenner, MD, MPH; Jenny Chang-Claude, PhD; Christoph M. Seiler, MD, MSc; Alexander Rickert, MD; and Michael Hoffmeister, PhD

Table 4. Association Between Previous Colonoscopy and Risk for Right-Sided and Left-Sided CRC in Various Subgroups

Group	Control Participants		Patients With Right-Sided CRC			Patients With Left-Sided CRC		
	Total Participants, *n*	Colonoscopy 1–10 y Before, *n* (%)	Total Patients, *n*	Colonoscopy 1–10 y Before, *n* (%)	Adjusted Odds Ratio (95% CI)*	Total Patients, *n*	Colonoscopy 1–10 y Before, *n* (%)	Adjusted Odds Ratio (95% CI)*
Women	825	320 (38.8)	259	56 (21.6)	0.45 (0.32–0.65)	407	36 (8.9)	0.15 (0.10–0.22)
Men	1107	473 (42.7)	278	69 (24.8)	0.43 (0.31–0.58)	653	65 (10.0)	0.16 (0.12–0.22)
Age								
50–59 y	293	79 (27.0)	62	14 (22.6)	0.74 (0.37–1.46)	184	9 (4.9)	0.13 (0.06–0.29)
60–69 y	596	256 (43.0)	171	47 (27.5)	0.52 (0.35–0.78)	400	34 (8.5)	0.13 (0.09–0.20)
70–79 y	655	305 (46.6)	180	40 (22.2)	0.32 (0.21–0.49)	343	45 (12.9)	0.17 (0.12–0.25)
≥80 y	388	153 (39.4)	124	24 (19.4)	0.37 (0.21–0.63)	133	13 (9.8)	0.15 (0.08–0.29)
Family history†								
No	1668	665 (39.9)	448	101 (22.5)	0.44 (0.34–0.57)	871	80 (9.2)	0.16 (0.12–0.20)
Yes	211	111 (52.6)	72	21 (29.2)	0.41 (0.22–0.76)	153	19 (12.4)	0.14 (0.08–0.26)
Year of recruitment								
2003–2004	469	143 (30.5)	274	54 (19.7)	0.63 (0.42–0.94)	490	48 (9.8)	0.27 (0.18–0.39)
2005	415	163 (39.3)	96	26 (27.1)	0.51 (0.30–0.86)	219	21 (9.6)	0.17 (0.10–0.29)
2006–2007	1022	470 (46.0)	167	45 (27.0)	0.38 (0.25–0.57)	350	31 (8.9)	0.11 (0.07–0.17)

CRC = colorectal cancer.

* Adjusted for age and sex in addition to education level, participation in general health screening examination, family history of CRC, smoking status, body mass index, ever regular use of nonsteroidal anti-inflammatory drugs, and ever regular use of hormone replacement therapy.

† History of CRC in a first-degree relative.

Long-Term Colorectal-Cancer Incidence and Mortality after Lower Endoscopy

Reiko Nishihara, Ph.D., Kana Wu, M.D., Ph.D., Paul Lochhead, M.B., Ch.B., Teppei Morikawa, M.D., Ph.D., Xiaoyun Liao, M.D., Ph.D., Zhi Rong Qian, M.D., Ph.D., Kentaro Inamura, M.D., Ph.D., Sun A. Kim, M.D., Ph.D., Aya Kuchiba, Ph.D., Mai Yamauchi, Ph.D., Yu Imamura, M.D., Ph.D., Walter C. Willett, M.D., Dr.P.H., Bernard A. Rosner, Ph.D., Charles S. Fuchs, M.D., M.P.H., Edward Giovannucci, M.D., Sc.D., M.P.H., Shuji Ogino, M.D., Ph.D., and Andrew T. Chan, M.D., M.P.H.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 19, 2013 VOL. 369 NO. 12

Table 4. Colorectal-Cancer Mortality after Screening Lower Endoscopy.

Variable	No Screening Lower Endoscopy	Screening Sigmoidoscopy	Screening Colonoscopy*
All participants			
All deaths from colorectal cancer			
No. of person-yr	1,182,248	302,330	357,008
No. of deaths	349	73	52
Age-adjusted hazard ratio (95% CI)	1.00	0.57 (0.44–0.73)	0.32 (0.24–0.44)
Multivariate hazard ratio (95% CI)†	1.00	0.59 (0.45–0.76)	0.32 (0.24–0.45)
Deaths from proximal colon cancer‡			
No. of deaths	121	46	25
Age-adjusted hazard ratio (95% CI)	1.00	1.04 (0.73–1.47)	0.49 (0.31–0.79)
Multivariate hazard ratio (95% CI)†	1.00	1.04 (0.73–1.48)	0.47 (0.29–0.76)
Deaths from distal colorectal cancer‡			
No. of deaths	195	21	16
Age-adjusted hazard ratio (95% CI)	1.00	0.29 (0.19–0.46)	0.18 (0.10–0.30)
Multivariate hazard ratio (95% CI)†	1.00	0.31 (0.20–0.49)	0.18 (0.10–0.31)

Data suggest added value of colonoscopy versus sigmoidoscopy, especially for prevention of deaths from cancer of the proximal colon, which should be elaborated in further research and weighed against the higher costs, complexity, discomfort, complication rates, and high quality capacities and quality assurance needed,[64-67] as well as possible differences in compliance.

Brenner BMJ 2014

Rate of Detection of Advanced Neoplasms in Proximal Colon by Simulated Sigmoidoscopy vs Fecal Immunochemical Tests

Antoni Castells,[*,a] Enrique Quintero,[‡,a] Cristina Álvarez,[§] Luis Bujanda,[‖] Joaquín Cubiella,[¶] **et al.**

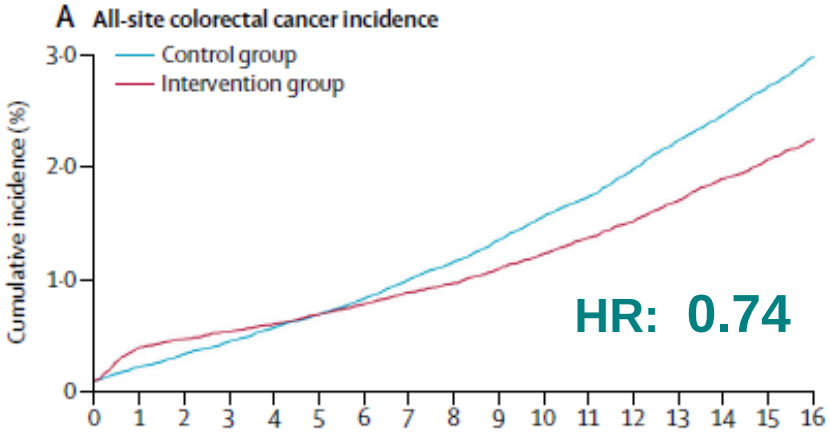
Clinical Gastroenterology and Hepatology 2014;12:1708–1716

	Screening group	Expected ADN prevalence,[b] n (%)	Detected ADN, n (%)	Estimated ADN detection rate[c] (%)	Expected APN prevalence,[b] n (%)	Detected APN, n (%)	Estimated APN detection rate[c] (%)
Overall	Sigmoidoscopy[d] (n = 5059)	365 (7.2)	317 (6.3)	86.8	204 (4.0)	39 (0.8)	19.1
	FIT (n = 10,507)	758 (7.2)	254 (2.4)	33.5	424 (4.0)	63 (0.6)	14.9
Men, 50–59 y old	Sigmoidoscopy[d] (n = 1349)	104 (7.7)	89 (6.6)	85.7	66 (4.9)	15 (1.1)	22.7
	FIT (n = 2406)	185 (7.7)	66 (2.7)	35.6	118 (4.9)	18 (0.7)	15.3
Men, 60–69 y old	Sigmoidoscopy[d] (n = 1109)	142 (12.8)	124 (11.2)	87.4	79 (7.1)	19 (1.7)	24.1
	FIT (n = 2279)	292 (12.8)	101 (4.4)	34.6	162 (7.1)	26 (1.1)	16.1
Women, 50–59 y old	Sigmoidoscopy[d] (n = 1407)	55 (3.9)	48 (3.4)	87.5	31 (2.2)	1 (0.1)	3.2
	FIT (n = 2981)	116 (3.9)	34 (1.1)	29.3	65.6 (2.2)	8 (0.3)	12.2
Women, 60–69 y old	Sigmoidoscopy[d] (n = 1194)	64 (5.4)	56 (4.7)	86.9	27 (2.3)	4 (0.3)	14.6
	FIT (n = 2841)	153 (5.4)	53 (1.9)	34.6	65 (2.3)	11 (0.4)	16.8

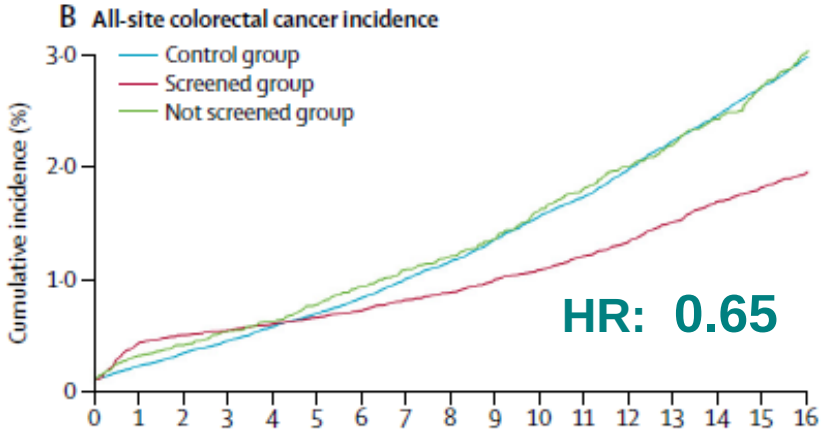
Long-term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK Flexible Sigmoidoscopy Screening randomised controlled trial

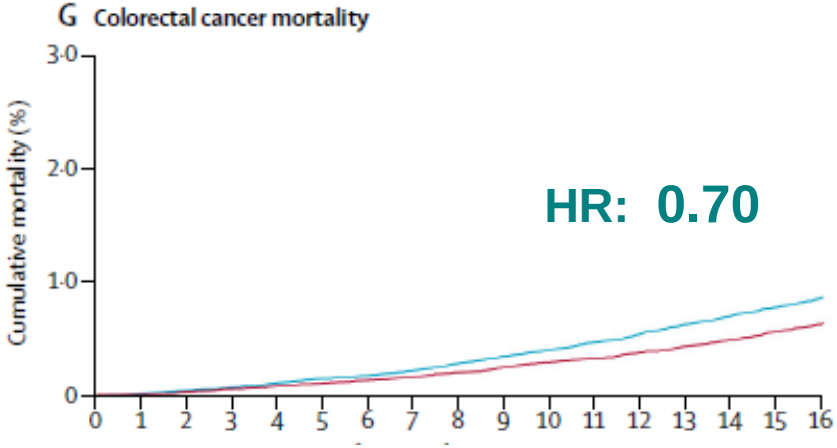
Wendy Atkin, Kate Wooldrage, D Maxwell Parkin, Ines Kralj-Hans, Eilidh MacRae, Urvi Shah, Stephen Duffy, Amanda J Cross

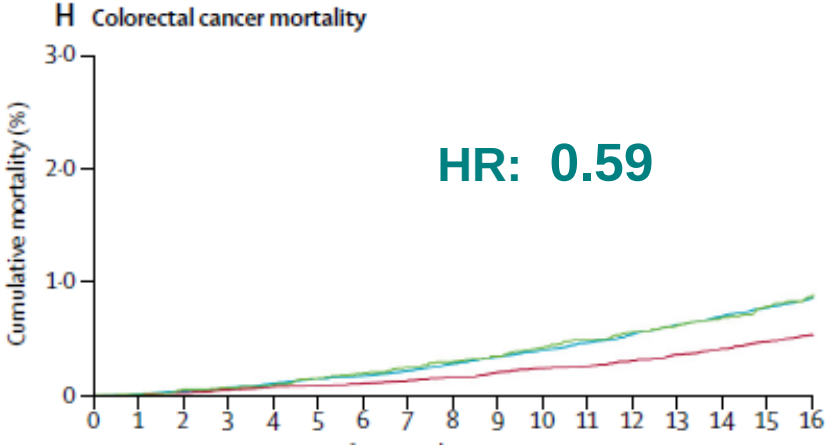
Invited to screening and control groups



Screened, not screened, and control groups







Effectiveness of flexible sigmoidoscopy screening in men and women and different age groups: pooled analysis of randomised trials

Øyvind Holme,[1,2] Robert E Schoen,[3] Carlo Senore,[4] Nereo Segnan,[4] Geir Hoff,[5,6] Magnus Løberg,[2,8] Michael Bretthauer,[1,2,7,8] Hans-Olov Adami,[2,7,9] Mette Kalager[2,7,8]

	Screening group *v* control group			
	Colorectal cancer incidence (relative risk (95% CI))	P for interaction	Colorectal cancer mortality (relative risk (95% CI))	P for interaction
Colon and rectum				
Both sexes*	0.79 (0.74 to 0.84)		0.73 (0.64 to 0.83)	
Men†	0.76 (0.70 to 0.83)		0.67 (0.57 to 0.80)	
≥60 years‡	0.76 (0.68 to 0.84)		0.67 (0.55 to 0.82)	
<60 years§	0.76 (0.65 to 0.88)	0.12	0.67 (0.49 to 0.91)	0.55
Women¶	0.83 (0.75 to 0.92)		0.82 (0.67 to 1.00)	
≥60 years‡	0.90 (0.80 to 1.02)		0.88 (0.69 to 1.12)	
<60 years§	0.71 (0.59 to 0.84)		0.73 (0.53 to 1.02)	

Effectiveness of flexible sigmoidoscopy screening in men and women and different age groups: pooled analysis of randomised trials

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Proximal colon	Incidence		Mortality	
Both sexes*	0.86 (0.79 to 0.93)		0.87 (0.73 to 1.04)	
Men†	0.83 (0.73 to 0.94)		0.89 (0.70 to 1.13)	
≥60 years‡	0.82 (0.71 to 0.95)		0.96 (0.73 to 1.28)	
<60 years§	0.84 (0.66 to 1.07)	0.04	0.71 (0.44 to 1.14)	0.61
Women¶	0.91 (0.79 to 1.03)		0.85 (0.66 to 1.10)	
≥60 years‡	1.03 (0.88 to 1.20)		0.89 (0.65 to 1.21)	
<60 years§	0.65 (0.50 to 0.84)		0.79 (0.51 to 1.23)	

DETECTION RATE DI NEOPLASIA PROSSIMALE AVANZATA

CONFRONTO COLONSCOPIA - FS – PER ETA'

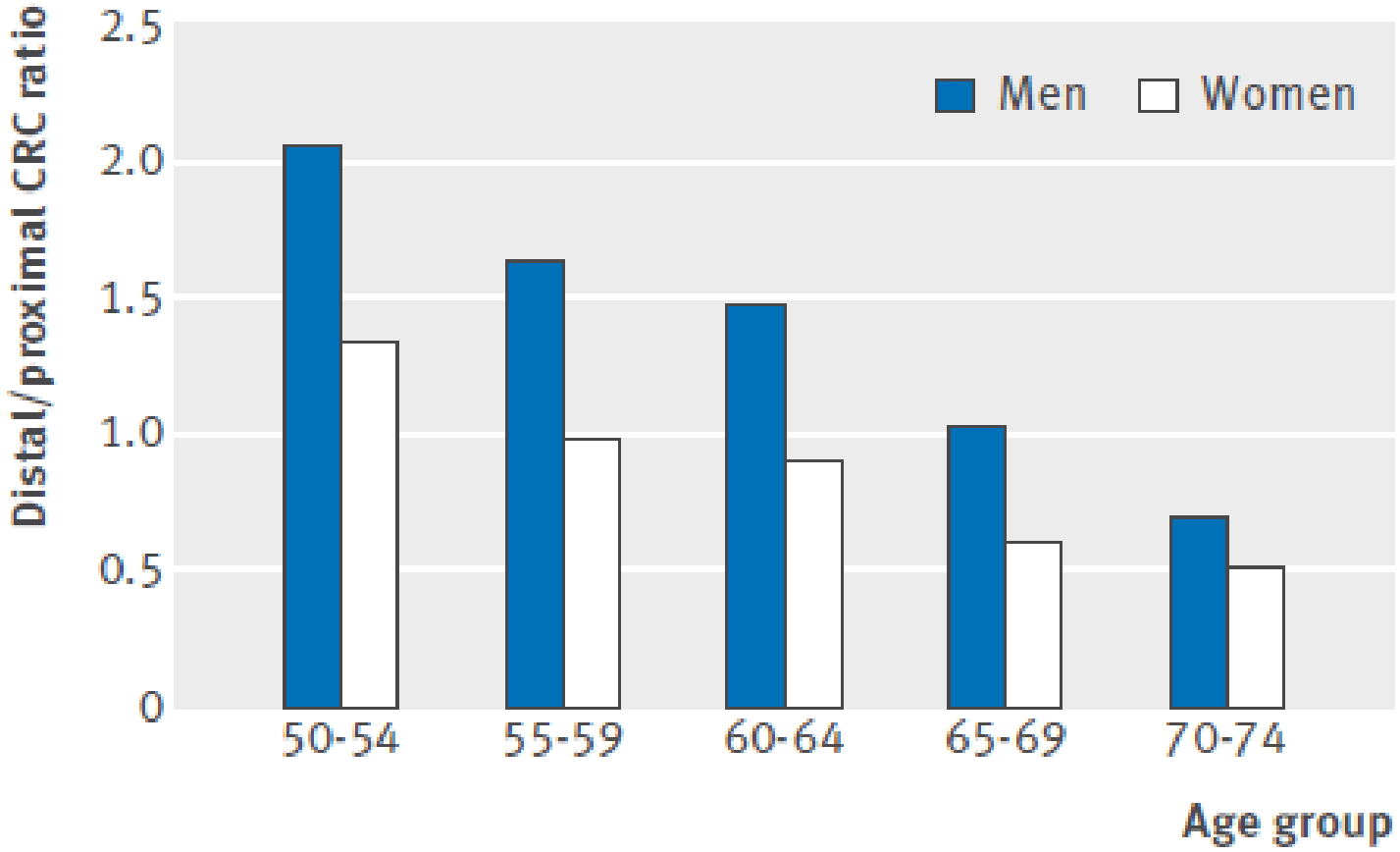
Table 5. Prevalence ORs of Advanced Adenomas and CRC by Screening Strategies

	OR[a]	95% CI
All neoplasms		
55–59 y		
FS, n = 1100	1	
FIT, n = 1090	0.20	0.11–0.37
TC, n = 899	1.08	0.74–1.57
Women, n = 1544	1	
Men, n = 1545	2.45	1.67–3.60
60–64 y		
FS, n = 822	1	
FIT, n = 875	0.27	0.13–0.54
TC, n = 697	2.00	1.30–3.09
Women, n = 1239	1	
Men, n = 1155	1.65	1.10–2.48

Segnan et al. 2007 - modified

Effectiveness of flexible sigmoidoscopy screening in men and women and different age groups: pooled analysis of randomised trials

Øyvind Holme,[1,2] Robert E Schoen,[3] Carlo Senore,[4] Nereo Segnan,[4] Geir Hoff,[5,6] Magnus Løberg,[2,8] Michael Bretthauer,[1,2,7,8] Hans-Olov Adami,[2,7,9] Mette Kalager[2,7,8]



CONCLUSIONI 1

La prevalenza di lesioni prossimali aumenta con l'età

I test di screening mostrano una sensibilità sub-ottimale per queste lesioni

POTENZIALITA' DI MIGLIORAMENTO DELLA SENSIBILITA'

Tecnica dell'esame endoscopico
(incluse preparazione e polipectomia)

Retraining e collaborazione multidisciplinare

Migliore caratterizzazione del rischio

Combinazione di test

Il problema delle lesioni prossimali: quale impatto sull'efficacia dello screening?

Long-Term Impact of the Dutch Colorectal Cancer Screening Program on Cancer Incidence and Mortality—Model-Based Exploration of the Serrated Pathway

Marjolein J.E. Greuter[1], Erhan Demirel[1], Jie-Bin Lew[2,3], Johannes Berkhof[1], Xiang-Ming Xu[2,3], Karen Canfell[2,3], Evelien Dekker[4], Gerrit A. Meijer[5], and Veerle M.H. Coupé[1]

This study predicts that without screening, colorectal cancer incidence will increase by 42% in the next 30 years. The Dutch colorectal cancer screening program combined with surveillance guidelines will decrease colorectal cancer incidence by 35% and 31% for a contribution of 0% and 30% of the serrated pathway to colorectal cancer, respectively. For colorectal cancer mortality, reductions are 47% and 45%.

Tailoring Colorectal Cancer Screening by Considering Risk of Advanced Proximal Neoplasia

Thomas F. Imperiale, MD,[a,b,c] Elizabeth A. Glowinski, RN,[d] Ching Lin-Cooper, BS,[a] David F. Ransohoff, MD[e]

Table 4 Absolute Risk of Advanced Proximal Neoplasia by Age, Sex, and Distal Findings

	No. With Advanced Proximal Neoplasia/Total N (%)		
Group	Age 50-59 y	Age 60-69 y	Age ≥ 70 y
All men	1.75% (70/3999)	3.42% (49/1433)	8.82% (21/238)
Men, no distal neoplasia	1.38% (47/3413)	2.85% (34/1194)	7.61% (14/184)
All women	1.11% (36/3221)	1.08% (11/1019)	4.21% (9/214)
Women, no distal neoplasia	0.85% (25/2942)	0.88% (8/909)	3.06% (6/196)

CONCLUSIONS: Risk of advanced proximal neoplasia is a function of age and gender. Women aged less than 60 to 70 years have a very low risk, particularly those with no distal adenoma. Sigmoidoscopy with or without occult blood testing may be sufficient and even preferable for screening these subgroups.

 • *The American Journal of Medicine (2012) 125, 1181-1187*

Il problema delle lesioni prossimali: quali ricadute?

Mercato per tecnologie endoscopiche innovative

Miglioramento della qualità dell'endoscopia

Migliore comprensione della storia naturale

Giustificazione per trial di valutazione della colonscopia

Come comunicare i dati di efficacia dei protocolli di screening? Il trial PROTEUS

AN detection was 5.1% for CTC vs. 4.8% for FS

[**RR: 1.1; 0.9-1.4**]

	Flexible Sigmoidoscopy	**CT Colonography**	**Relative Risk^{++} [95% CI]**
Rectosigmoid Women Men **Total**	2.8 (36) 5.3 (73) **4.1 (109)**	1.8 (23) 3.9 (53) **2.9 (76)**	**0.72 [0.54-0.96]**
Proximal Colon^{+} Women Men Total	1.0 (13) 1.7 (21) **1.3 (34)** $^{+}$	1.7 (21) 3.6 (48) **2.7 (69)**$^{+}$	**2.06 [1.37-3.10]**

Numbers in brackets are the actual number of individuals. $^{+}$Proximal is defined as descending colon, transverse colon, ascending colon, or caecum. $^{+}$Including 16 (47.1%) FS patients and 12 (17.3%) CTC patients who had synchronous advanced neoplasia in the rectum-sigmoid colon. $^{++}$Relative Risk, experimental (CTC) vs. control (FS) group.

Regge et al. Gut 2016

CONCLUSIONI 2

Il miglioramento della sensibilità non risolve le incertezze relative al protocollo di screening.

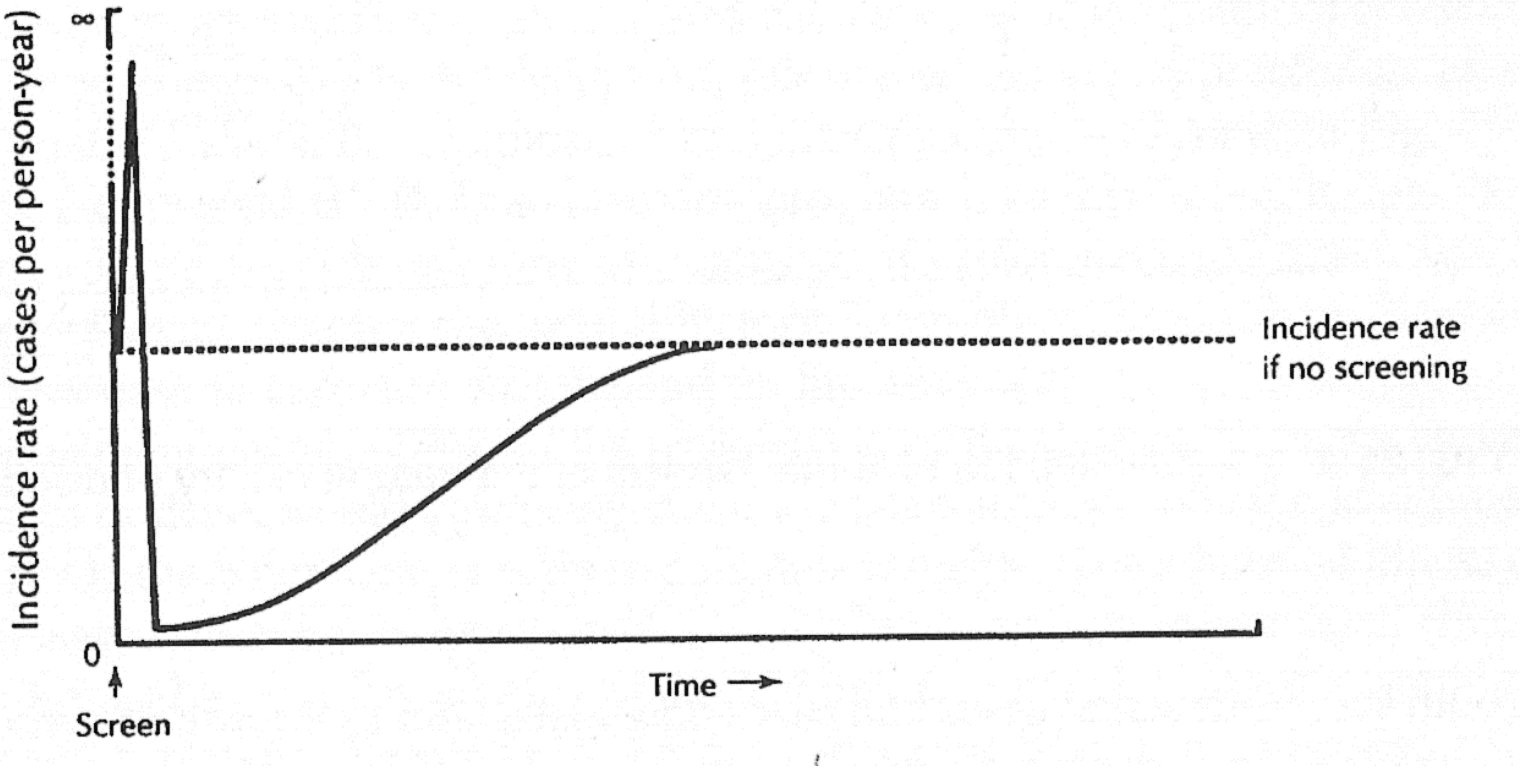
E’ ipotizzabile che si arrivi a definire un protocollo di screening che garantisca una effetto protettivo ancora superiore

L’impatto sul rischio di cancro delle strategie che abbiamo a disposizione è comunque importante

Grazie per l’attenzione!

carlo.senore@cpo.it

IMPATTO DELLO SCREENING SULL'INCIDENZA DEL CANCRO



L'efficacia (mortalità/morbidità) dipende dal **rapporto tra cancri screen-detected e** quelli diagnosticati clinicamente in seguito alla comparsa di sintomi dopo un test negativo: **cancri intervallo**

Fattori che influenzano la proporzione di CCR screen-detected

- Intervallo di screening

- Mean sojourn time

  (durata media della fase pre-clinica diagnosticabile)

- Sensibilità del test

Colorectal Cancer Incidence Trends in the United States and United Kingdom: Evidence of Right- to Left-Sided Biological Gradients with Implications for Screening

Rafael Meza, Jihyoun Jeon, Andrew G. Renehan, et al.

Cancer Res 2010;70:5419-5429. Published OnlineFirst June 8, 2010.

Modello matematico applicato ai dati di incidenza del SEER e dei Registri Tumori Inglesi

Progressione più rapida delle lesioni pre-neoplastiche nel colon sinistro rispetto a quelle del colon destro, che avrebbero un sojourn time più lungo (di oltre 10 anni)

Maggiore frequenza di eventi inizianti nel colon destro