Le prospettive della sigmoidoscopia

GISCoR22

Carlo Senore

SSD Epidemiologia e screening - CPO

CPO

Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica in Piemonte

Il sottoscritto Carlo Senore

ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

X *che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario*

□ *che negli ultimi due anni ha avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:*

- ……
- ……
- ……

XV CONGRESSO NAZIONALE 2022

GISCoR
gruppo italiano screening colorettale

Webinar congiunto ONS – GISCoR.
Lo screening con sigmoidoscopia in Italia: risultati e prospettive

OSSERVATORIO NAZIONALE SCREENING

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Annals of Internal Medicine ORIGINAL RESEARCH

Long-Term Follow-up of the Italian Flexible Sigmoidoscopy Screening Trial

Carlo Senore, MD, MSc; Emilia Riggi, PhD; Paola Armaroli, MD, MSc; Luigina Bonelli, MD; Stefania Sciallero, MD, MPhil; Marco Zappa, MD; Arrigo Arrigoni, MD; Claudia Casella, PhD; Cristiano Crosta, MD; Fabio Falcini, MD; Franco Ferrero, MD; Mario Fracchia, MD; Orietta Giuliani, PhD; Mauro Risio, MD; Antonio G. Russo, MD, MPH; Carmen Beatriz Visioli, MD, MSc; Stefano Rosso, MD, MSc; and Nereo Segnan, MD, MPH; for the SCORE Working Group*

- **6 Centri**

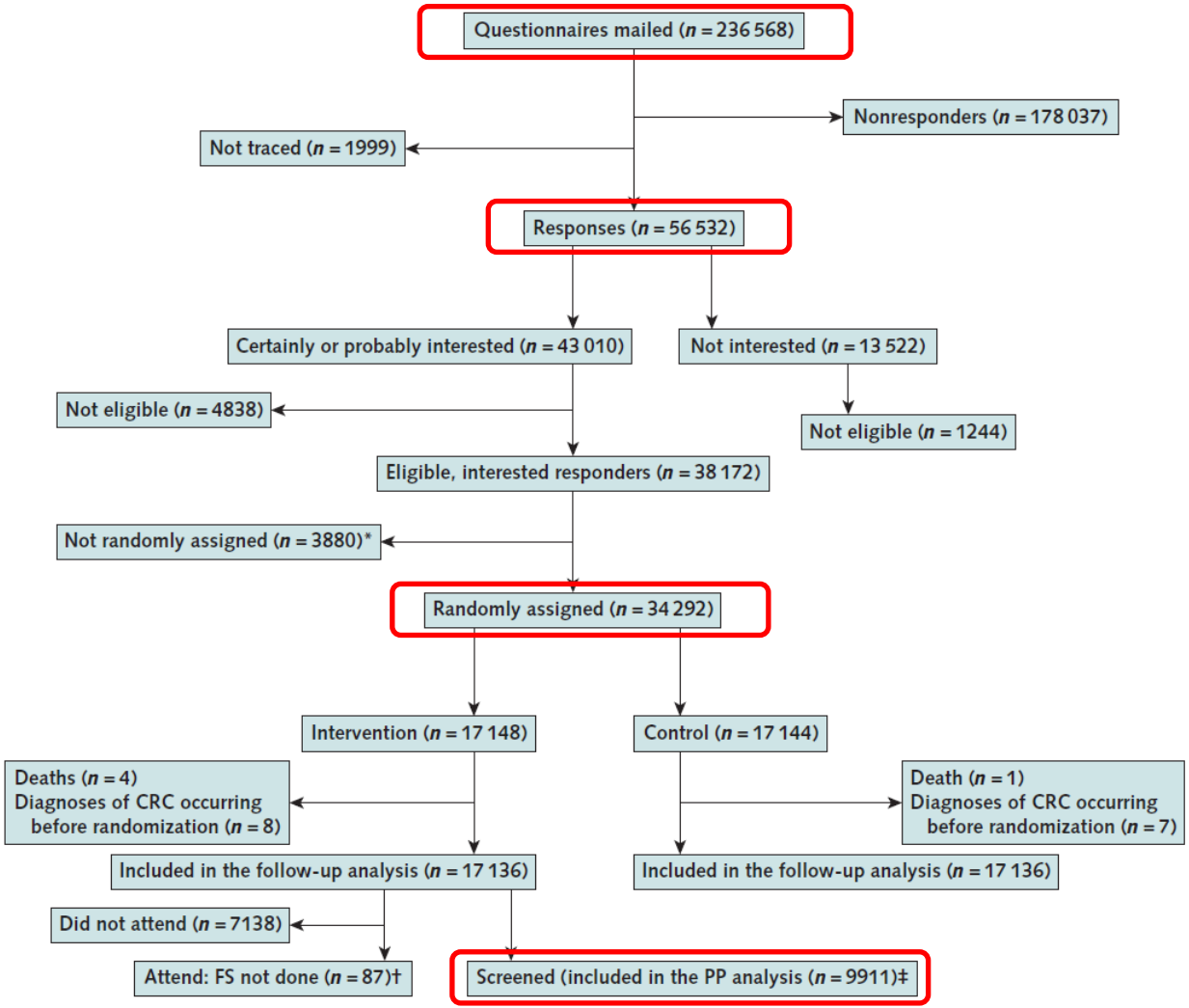
  Torino, Biella, Milano (Regione Lombardia)

  Genova, Rimini, Arezzo

- **Follow-up**

  Incidenza : **15.4 anni** (IQR: 14.8-16.1)

  Mortalità : **18.8 anni** (IQR: 17.0-19.6)


Questionnaires mailed (n = 236 568)
Nonresponders (n = 178 037)
Not traced (n = 1999)
Responses (n = 56 532)
Certainly or probably interested (n = 43 010)
Not interested (n = 13 522)
Not eligible (n = 4838)
Not eligible (n = 1244)
Eligible, interested responders (n = 38 172)
Not randomly assigned (n = 3880)*
Randomly assigned (n = 34 292)
Intervention (n = 17 148)
Control (n = 17 144)
Deaths (n = 4)
Diagnoses of CRC occurring before randomization (n = 8)
Death (n = 1)
Diagnoses of CRC occurring before randomization (n = 7)
Included in the follow-up analysis (n = 17 136)
Included in the follow-up analysis (n = 17 136)
Did not attend (n = 7138)
Attend: FS not done (n = 87)†
Screened (included in the PP analysis (n = 9911)‡

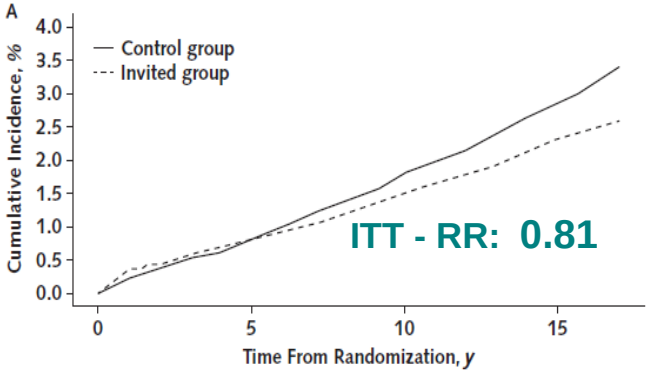
La procedura di screening

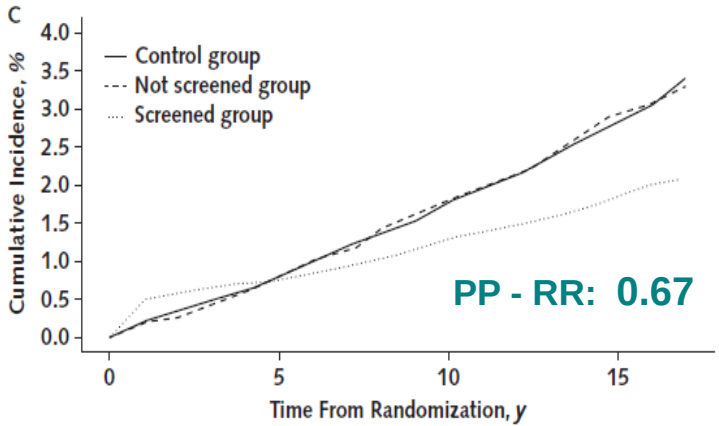
- **un clistere (133 ml sodio-fosfato) autosomministrato 2 ore prima dell'esame**

- Invio in colonscopia in caso di riscontro di
  - ✓ 1 polipo > 5 mm
  - ✓ 1 adenoma diminutivo avanzato
  - ✓ >2 adenomi LR

L'impatto dello screening sull'incidenza

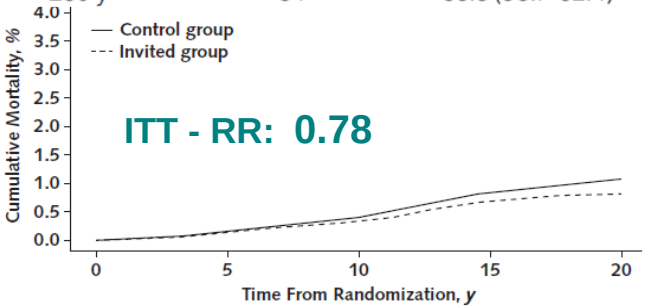
	Cases, *n*	Rate per 100 000 Person-Years (95% CI)	Cases, *n*	Rate per 100 000 Person-Years (95% CI)	Rate Ratio (95% CI)†
Incidence					
All sites	468	189.4 (173.0 to 207.4)	382	153.6 (1389.0 to 169.9)	0.81 (0.71 to 0.93)
Distal	297	120.2 (107.3 to 134.7)	209	84.1 (73.4 to 96.3)	0.70 (0.59 to 0.84)
Proximal	159	64.3 (55.1 to 75.2)	165	66.4 (57.0 to 77.3)	1.03 (0.83 to 1.28)
Sex					
Male	291	237.8 (212.0–266.8)	240	197.5 (174.0–224.1)	0.83 (0.70–0.98)
Female	177	141.9 (122.5–164.4)	142	111.7 (94.8–131.7)	0.79 (0.63–0.98)
Age§					
55–59 y	235	166.6 (146.6–189.3)	198	141.3 (122.9–162.4)	0.85 (0.70–1.02)
≥60 y	233	219.7 (193.3–249.8)	184	169.6 (146.8–196.0)	0.77 (0.64–0.94)



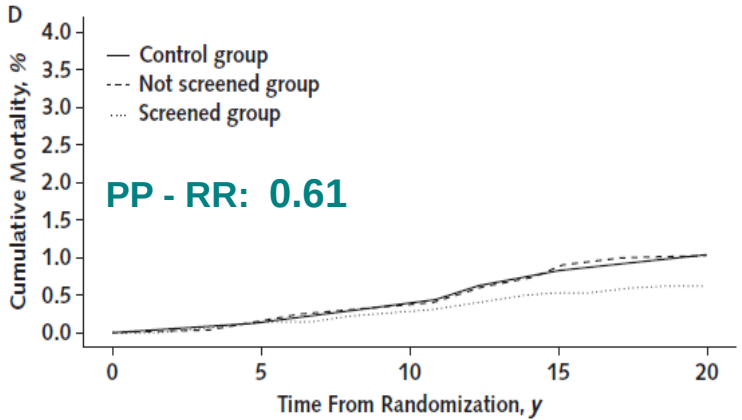


L'impatto dello screening sulla mortalità

	Deaths, *n*	Rate per 100 000 Person-Years (95% CI)	Deaths, *n*	Rate per 100 000 Person-Years (95% CI)	Rate Ratio (95% CI)†
All sites	157	53.2 (45.5 to 62.2)	122	41.1 (34.4 to 49.1)	0.78 (0.61 to 0.98)
Distal	90	30.5 (24.8 to 37.5)	62	20.9 (16.3 to 26.8)	0.69 (0.50 to 0.95)
Proximal	64	21.7 (17.0 to 27.7)	53	17.9 (13.6 to 23.4)	0.82 (0.57 to 1.19)
Sex					
Male	111	76.4 (63.4–92.0)	80	55.4 (44.5–69.0)	0.73 (0.54–0.97)
Female	46	30.7 (23.0–41.0)	42	27.6 (20.4–37.3)	0.90 (0.59–1.37)
Age§					
55–59 y	73	43.3 (34.4–54.4)	63	37.6 (29.3–48.1)	0.87 (0.62–1.22)
≥60 y	84	66.5 (53.7–82.4)	59	45.7 (35.4–59.0)	0.69 (0.49–0.96)

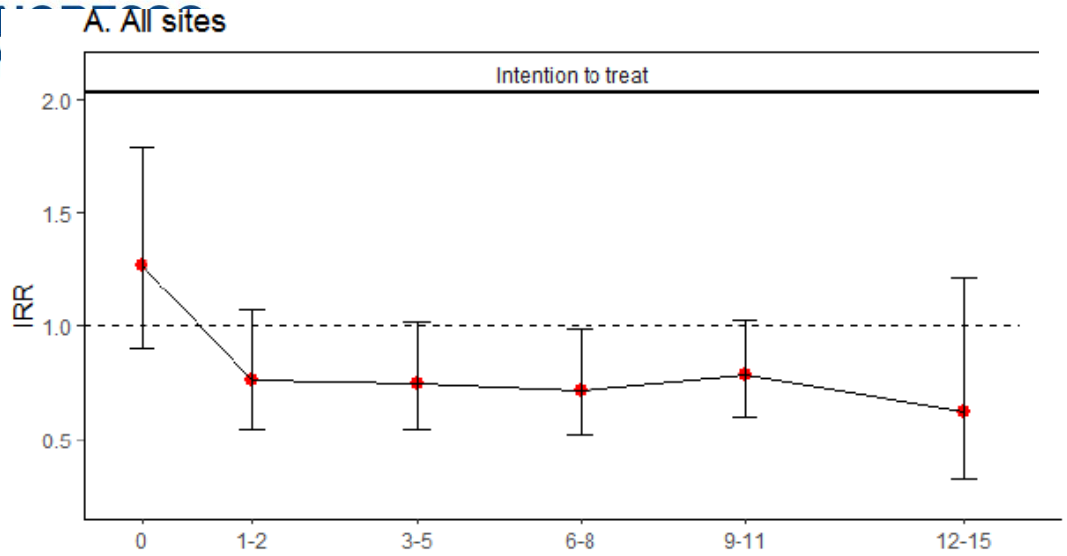


ITT - RR: 0.78



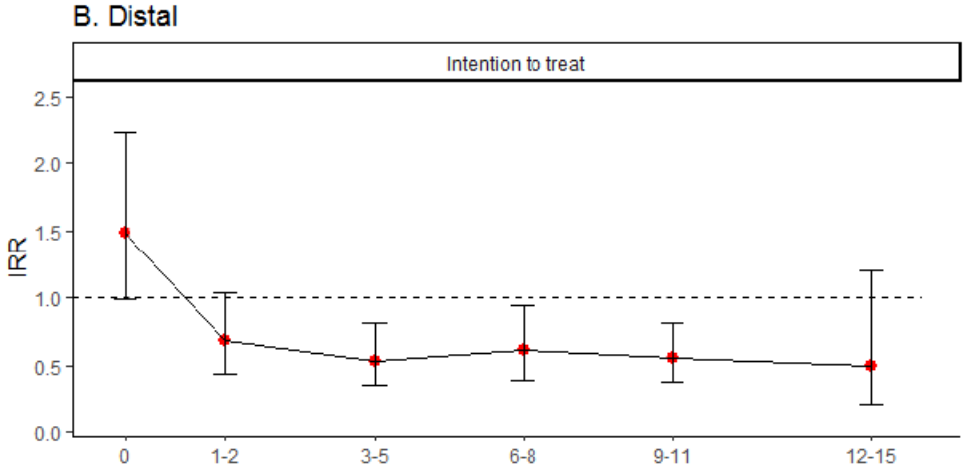
PP - RR: 0.61

Riduzione di incidenza nel tempo



NNS to prevent one CRC
180 (95% CI: 98-1134)
after 11-year f-up

115 (95% CI: 69-343)
After 15-year f-up

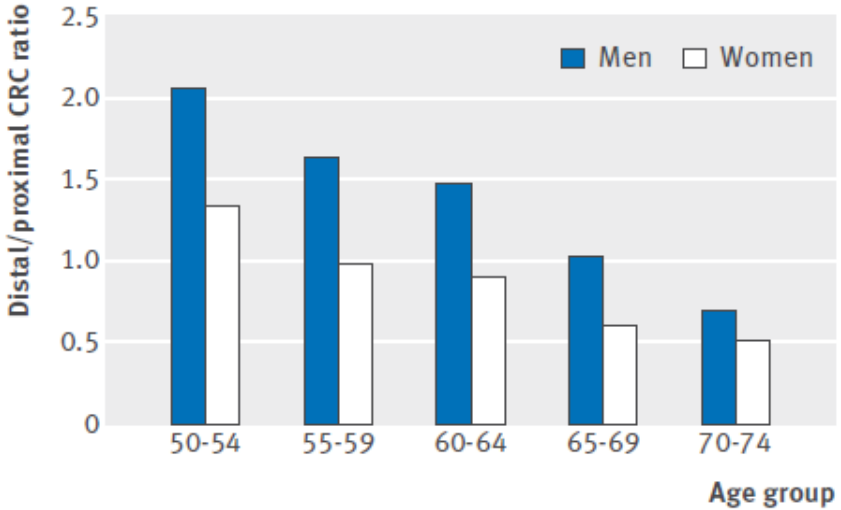


Effectiveness of flexible sigmoidoscopy screening in men and women and different age groups: pooled analysis of randomised trials

	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)	
Distal colon				
Both sexes*	0.73 (0.66 to 0.80)		0.60 (0.49 to 0.72)	
Men†	0.71 (0.63 to 0.80)		0.51 (0.40 to 0.65)	
≥60 years‡	0.72 (0.62 to 0.84)		0.48 (0.35 to 0.64)	
<60 years§	0.69 (0.56 to 0.85)	0.66	0.58 (0.38 to 0.90)	0.39
Women¶	0.76 (0.65 to 0.88)		0.79 (0.58 to 1.09)	
≥60 years‡	0.74 (0.61 to 0.91)		0.85 (0.57 to 1.27)	
<60 years§	0.78 (0.61 to 0.99)		0.71 (0.42 to 1.18)	

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

Proximal colon				
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)	



EARLY DETECTION VERSUS PREVENTION

		Intervention Group			Control Group			Averted Events			
		Total	Cancers (Ci)	Deaths (Di)	Total	Cancers (Cc)	Deaths (Dc)	Fatality Rate (FRc)	Cancers[a]	Deaths[b]	ADP[c]	ADP %[d]
		No.	No.	No.	No.	No.	No.	Percentage, (95% CI)	No.	No.	No.	Percentage, (95% CI)
ITT	PLCO 2017[6]	77,445	1008	253	77,445	1291	351	27 (25-30)	283	98		
	SCORE 2011[3]	17,136	251	65	17,136	306	83	27 (22-32)	55	18		79 (69-86)
	UK Flexible Sigmoidoscopy Screening Trial 2010[1]	57,099	706	189	112,939	1818	538	30 (27-32)	422	164		83 (59-96)
	UK Flexible Sigmoidoscopy Screening Trial 2017[2e]	57,098	1230	353	112,936	3253	996	31 (29-32)	820	298		76 (69-82)
PP	SCORE 2011[3]	9911	126	33	17,136	306	83	27 (22-32)	88	26		
	UK Flexible Sigmoidoscopy Screening Trial 2010[1]	40,621	445	111	112,939	1818	538	30 (27-32)	581	229		84 (80-88)
	UK Flexible Sigmoidoscopy Screening Trial 2017[2e]	40,621	776	215	112,936	3253	996	31 (29-32)	1096	398	335	84 (80-88)

Abbreviations: 95% CI, 95% confidence interval; ADP, averted deaths due to prevention; Cc, cancers in the control group; Ci, cancers in the intervention group; Dc, deaths in the control group; Di, deaths in the intervention group; FRc, fatality rate in the control group; ITT: intention-to-treat analysis; PLCO, Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; PP, per-protocol analysis; UK, United Kingdom.

[a] Estimated as the difference between the Cc and the Ci, which was estimated assuming a control:intervention population ratio of 1:1.

[b] Estimated as the difference between the Dc and the Di, which was estimated assuming a control:intervention population ratio of 1:1.

[c] Estimated as the product of fatality rate per the averted cancers: (Cc–Ci)*(Dc/Cc).

[d] Estimated as the ratio between the prevented deaths and the averted deaths. The complete algorithm is: ADP % = ((Cc –Ci)*(Dc/Cc))/(Dc-Di).

[e] UK Flexible Sigmoidoscopy Screening Trial 2017 reports results after 17 years of follow-up versus 10.5 to 11.9 years for the other randomized controlled trials.

Segnan et al. Cancer 2017

Annals of Internal Medicine
Vol. 167 No. 8 • 17 October 2017 603

Reanalysis of All-Cause Mortality in the U.S. Preventive Services Task Force 2016 Evidence Report on Colorectal Cancer Screening

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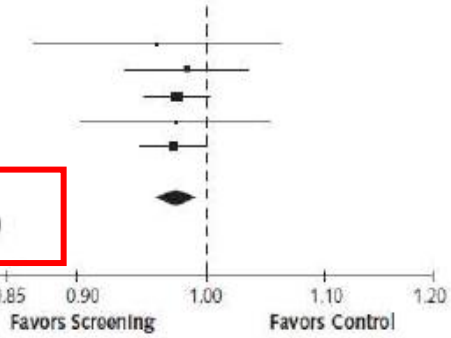
Figure 2. RR for death with screening with flexible sigmoidoscopy in randomized controlled trials.

Trial	Screening			Control			RR (95% CI)
	Deaths, *n*	Persons, *n*	Risk, %	Deaths, *n*	Persons, *n*	Risk, %	
NORCCAP							
Age 50–54 y	427	6920	6.17	2387	37 131	6.43	0.96 (0.87–1.06)
Age 55–64 y	1756	13 652	12.86	5375	41 089	13.08	0.98 (0.94–1.03)
PLCO*	9390	77 445	12.12	9627	77 455	12.43	0.98 (0.95–1.002)
SCORE	1202	17 136	7.01	1233	17 136	7.20	0.97 (0.90–1.05)
UKFSST	6775	57 099	11.87	13 768	112 939	12.19	0.97 (0.95–1.0002)
Subtotal		172 252			285 750		0.975 (0.959–0.992)
Total events	19 550			32 390			

Heterogeneity: chi-square = 0.22 ($P = 0.99$); $I^2 = 0\%$
Test for overall effect: $Z = 2.90$ ($P = 0.004$)



NORCCAP = Norwegian Colorectal Cancer Prevention; PLCO = Prostate, Lung, Colorectal, and Ovarian; RR = relative risk; SCORE = Screening for Colon Rectum; UKFSST = U.K. Flexible Sigmoidoscopy Screening Trial.
* This trial reports a modified all-cause mortality that excludes deaths from prostate, lung, and ovarian cancer because the intervention group was also screened for those types of cancer.

Complicanze e impatto sulla vita dei soggetti aderenti

(i) Impatto sulla vita quotidiana

Impegno complessivo

✓ < 3 ore per il 93% dei soggetti

(ii) Complicanze

Perforazione / sanguinamento che ha richiesto ospedalizzazione

✓ 0.03%

(inclusi approfondimenti)

Dolore

✓ Moderato - forte

10%-16%

Helsingen L, et al. BMJ 2019
Senore C et al. JMS 201

Cost-effectiveness of colorectal cancer screening programmes using sigmoidoscopy and immunochemical faecal occult blood test

J Med Screen
2019, Vol. 26(2) 76–83

Carlo Senore[1], Cesare Hassan[1,2], Daniele Regge[3,4], Eva Pagano[5], Gabriella Iussich[6], Loredana Correale[7] and Nereo Segnan[1]

Table 4. Cost, effect and net benefit for all the included strategies for a cohort of 100,000 subjects invited for screening.

	No screening	FS	FIT	FS + FIT
CRC cases, *n*	1517	1372	1312	1264
CRC deaths, *n*	528	460	442	414
CRC prevented (%)	–	10%	14%	17%
CRC deaths prevented (%)	–	13%	16%	22%
Life-years lost, *n*	19,431	18,025	17,700	17,119
Life-years saved, *n*[a]	–	1406	1731	2312
Life-years saved discounted, *n*	–	1207	1460	1959
Sigmoidoscopy, *n*	–	28,799	–	28,799
FIT, *n*	–	–	293,333	159,514
Colonoscopy, *n*	–	2592	12,115	9180
Cost CRC care (€)[a]	44,294,628	37,097,188	38,503,258	34,781,125
Cost screening (€)[a]	–	4,607,776	6,146,373	7,893,681
Total cost (€)[a]	44,294,628	41,704,964	44,649,631	42,674,806
Total cost discounted (€)	37,884,430	36,336,360	38,400,217	37,251,655
ICER vs. no screening, € per life-year saved	–	€ 15 saving per person	353	€ 6 saving per person
MNB[b] (€)		23,990,785	34,599,573	60,687,482

CRC: colorectal cancer; FS: flexible sigmoidoscopy; FIT: faecal immunochemical test; MNB: mean net benefit; ICER: incremental cost-effectiveness ratio.
[a]Not discounted.
[b]Mean net benefit was calculated by multiplying effect by willingness to pay and subtracting cost. Willingness to pay was assumed to be €50,000 per life-year saved.

SCREENING FS

- Adenoma Detection Rate soddisfacente (sia in colonscopia che in FS)
- Diagnosi precoce di cancro in soggetti asintomatici (1 ogni 328 FS)
- Identificazione ed asportazione precoce di precursori ad alto rischio (1 ogni 21 FS)
- Trattamento endoscopico di precursori e cancri precoci

- Carico di lavoro con FS consistente (una FS ogni 15', sedute da 22 FS)
- Tempi molto stretti per svestizione-esame-vestizione
- Prolungamento per operative (peraltro previste se polipo < 1 cm)
- Usura parco strumenti (cicli di lavaggio)

Da A. Arrigoni

Adesione e DR cumulative I invito

	ROUND 1 2009-2018								
Screening	Invitati	Aderenti		Colonscopie		Detection rate			
						Adenomi avanzati		Cancri	
		n	%	n	%	n	%	n	%
FS	487559	121178	24,9	11601	9,6	5823	4,8	370	0,31
sFIT	350229	72621	20,7	3559	4,9	1148	1,6	191	0,26
Cumulativo FS e sFIT	487559	193799	39,7	15160	7,8	6971	3,6	561	0,29

Adesione indicazione TC

FS	90,0%
FIT - scambio	77,0%

1 CRC ogni **328 FS**
1 adenoma avanzato ogni **21 FS**

1 CRC ogni **380 FIT**
1 adenoma avanzato ogni **63 FIT**

Completamento FS e motivi di non completamento

	Completa	Preparazione inadeguata	Dolore	Aderenze	Altro
Donne	83,9%	5,3%	5,9%	3,1%	1,7%
Uomini	90,7%	4,4%	2,1%	1,0%	1,9%

Un FS incompleta vale comunque come screening effettuato, senza richiamo

- 20 o 30 cm possono essere considerati un «esame valido»?

- Pulizia ripetizione esame (ma il 40% non si ripresenta)
- Dolore altre metodiche (congrue al contesto, come passaggio a FIT)

Confronto FS – FIT

Coorte 1963

RS	Aderenti RS	Aderenti FIT	Invitati	Adesione RS	Adesione FIT	Totale
Donne	3052	1255	15663	19,5%	8,0%	27,5%
Uomini	3430	830	14929	23,0%	5,6%	28,5%
Totale	6482	2085	30592	21,2%	6,8%	**28,0%**

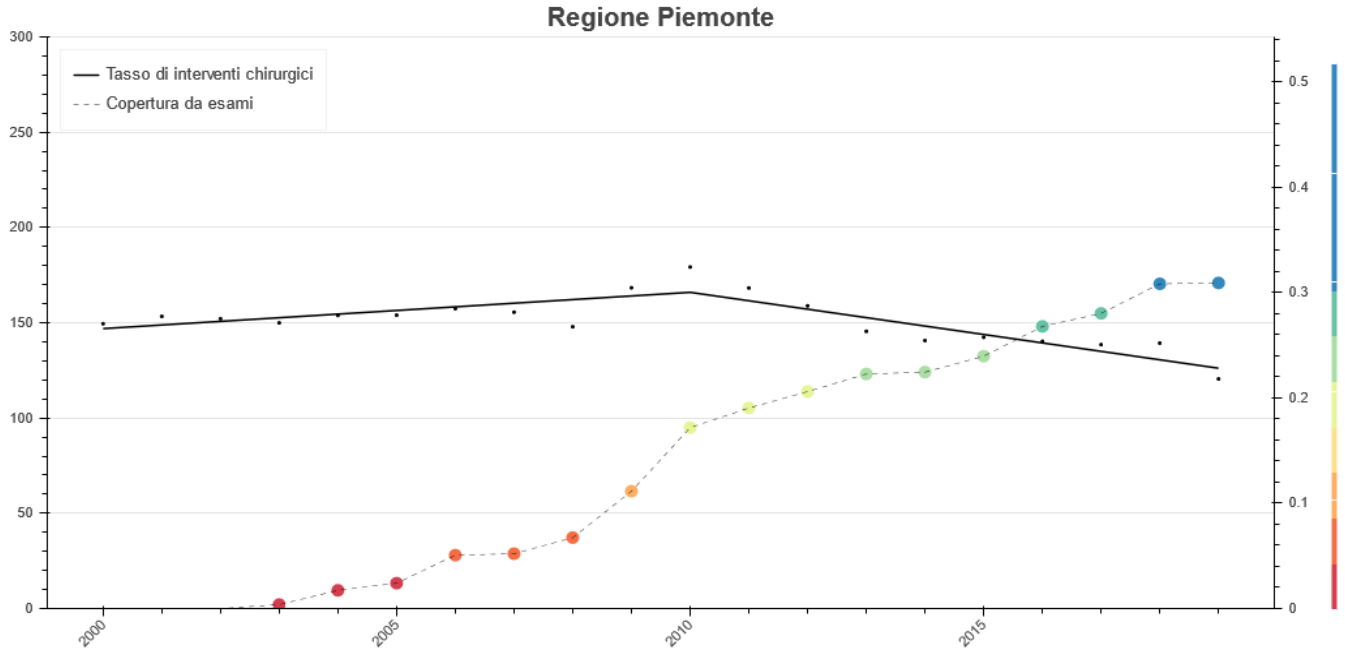
FIT		Aderenti FIT	Invitati			Totale
Donne		6159	15797			39,0%
Uomini		5230	15278			34,2%
Totale		11389	31075			**36,7%**

	Positività	Adesione CT	CT Complete	DR CRC	DR AAD
FIT	6,0%	79,8%	96,1%	0,2%	1,2%
RS	11,5%	78,8% *	96,9%	0,2%	4,2%

* 88% tra persone con polipi distali a rischio

** Su 809 persone aderenti a FIT dopo rifiuto FS sono stati diagnosticati : 3 CRCs e 8 AAd

Trend dei tassi di interventi chirurgici per CCR



Conclusioni

Lo screening con sigmoidoscopia

- mostra un effetto protettivo che si mantiene oltre 15 -18 anni
  - riduzione di incidenza 21% ITT; 33% PP
  - riduzione di mortalità 20% ITT; 40% PP

- La riduzione di mortalità è in larga parte attribuibile alla riduzione di incidenza
  - riduzione dei costi per il SSN
  - riduzione del carico di malattia per i soggetti invitati

Conclusioni

- L'effetto protettivo sembra inferiore per le donne rispetto agli uomini, in particolare per la fascia di età 60-64 anni, ma la riduzione del carico di malattia associato al CCR è importante

- il rischio di complicanze è molto ridotto e l'impatto dello screening sulla vita dei soggetti aderenti è molto limitato

Questa strategia rappresenta quindi un opzione efficace e sostenibile che permette di ampliare l'offerta di screening

Grazie

Members of the SCORE

Working Group

Members of the SCORE Working Group who contributed to this work but did not author it:

Arezzo: A. Carnevali (Pathology Unit, San Donato Hospital, Azienda USL Toscana Sud-Est), A. Agnolucci and P. Ceccatelli (Endoscopy Unit, Azienda USL Toscana Sud-Est), F. Mirri (Screening Unit, Azienda USL Toscana Sud-Est); **Biella**: A. Penna (ASL Vercelli), G. Genta (EE Tempia Foundation), A. Marutti (EE Tempia Foundation); **Genoa**: A. Guelfi (Screening Unit, IRCCS Ospedale Policlinico San Martino), B. Gatteschi (Unit of Pathology, IRCCS Ospedale Policlinico San Martino); **Milan**: G. Fiori (Endoscopy Unit, IRCCS European Institute of Oncology); **Rimini**: G. Fabbretti (Pathology Unit, Infermi Hospital, AUSL Rimini), S. Gasperoni (Gastroenterology Unit, S Maria delle Croci Hospital, Ravenna); **Turin**: A. Bertone, M. Pennazio, M. Spandre (Gastroenterology Unit, University Hospital Città della Salute e della Scienza di Torino), Marco Silvani (CPO Piemonte), M. Demaria (ARPA Piemonte).

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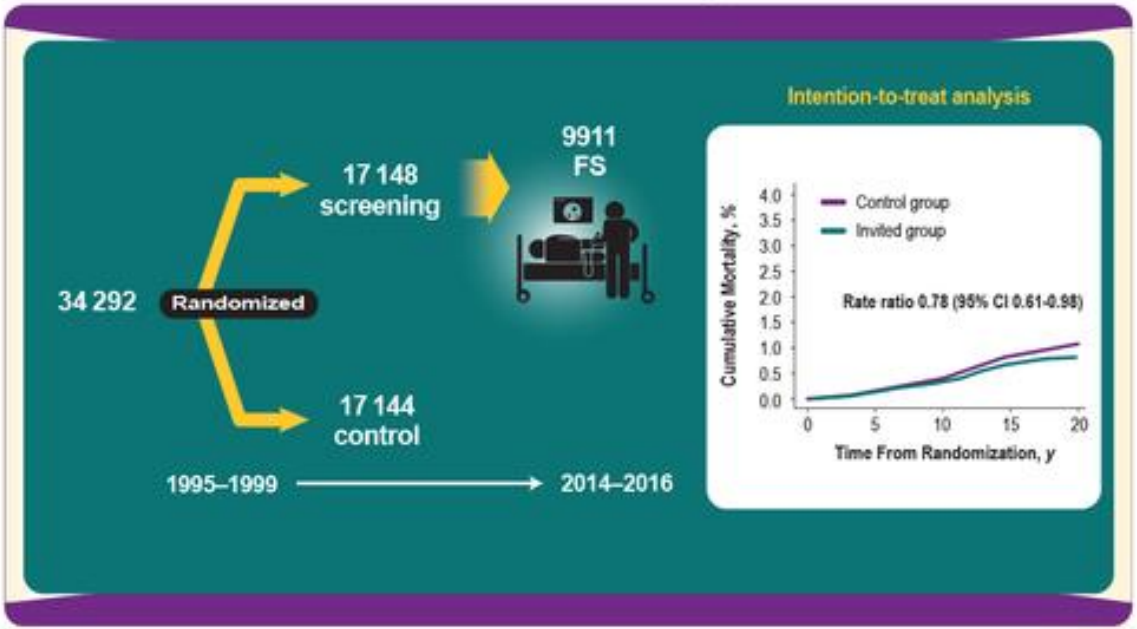
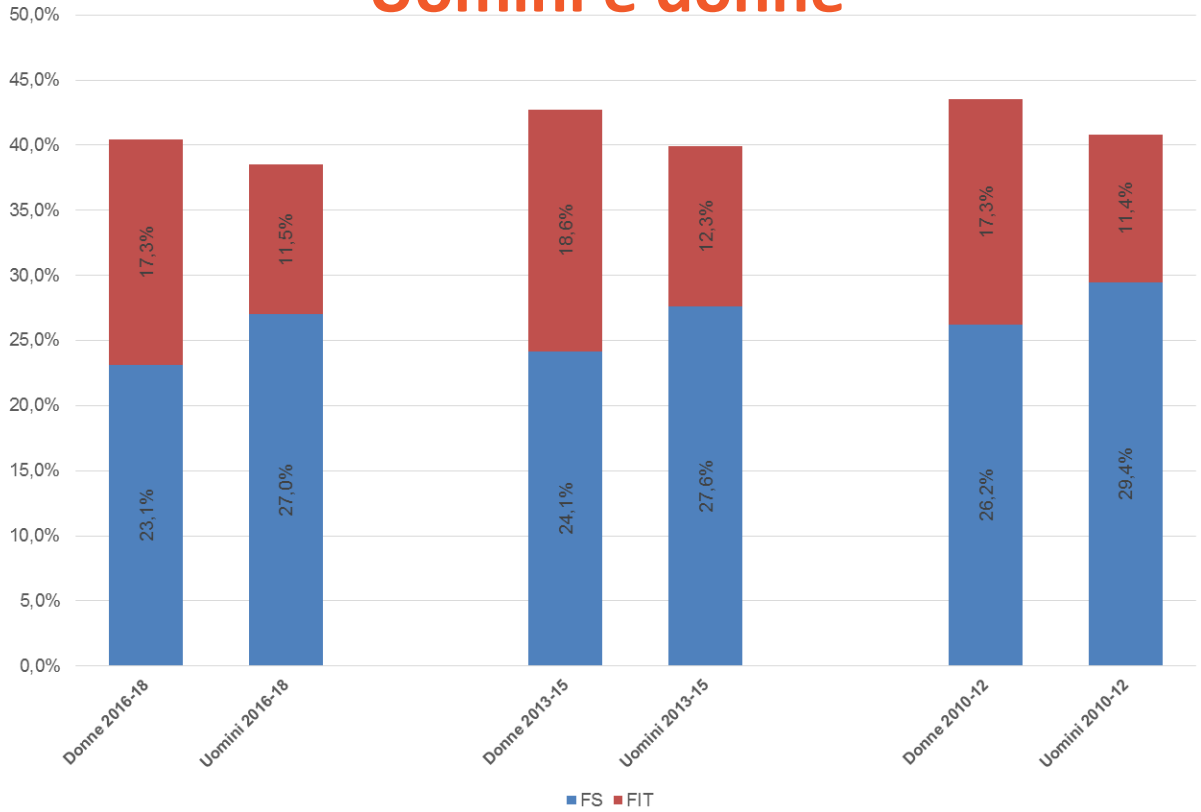
GISCoR
Gruppo Italiano Screening ColoRettale


34 292
Randomized
17 148
screening
9911
FS
17 144
control
1995–1999
2014–2016
Intention-to-treat analysis
Control group
Invited group
Rate ratio 0.78 (95% CI 0.61-0.98)
Cumulative Mortality, %
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
5
10
15
20
Time From Randomization, y

Andamento del tempo dell'adesione al I invito (sequenziale) – Piemonte

Uomini e donne



Adesione

Tra le persone che aderiscono al primo invito al FIT in alternativa alla FS,

- il 73% di quelli invitati 3 volte esegue 3 esami (81% 2 esami su 3)
- il 67% di quelli invitati 4 volte esegue 4 esami (76% 3 esami su 4)

487559	97512		
	3900	39005	
350229	52534		
	2101	16811	31971