IL RISCHIO FAMILIARE

La sorveglianza epidemiologica dello screening dei tumori del colon-retto nella Regione Emilia-Romagna
Seminario di studio
Bologna, 15 marzo 2011

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA

CARLO SENORE

CPO
CENTRO DI RIFERIMENTO PER L'EPIDEMIOLOGIA E LA PREVENZIONE ONCOLOGICA IN PIEMONTE

RISCHI ATTRIBUIBILI

- **23%** **sesso maschile**
- **9%** **fumo**
- **4% (9%)** **familiarità**

Hoffmeister et al. 2010

- **15%** sovrappeso / attività fisica

de Vries et al. 2010

DETERMINANTI DELLA PARTECIPAZIONE ALLO SCREENING

FRAZIONE ATTIRBUIBILE

Favoriscono la partecipazione

- **36%** Consultazione del medico
- **8%** Familiarità

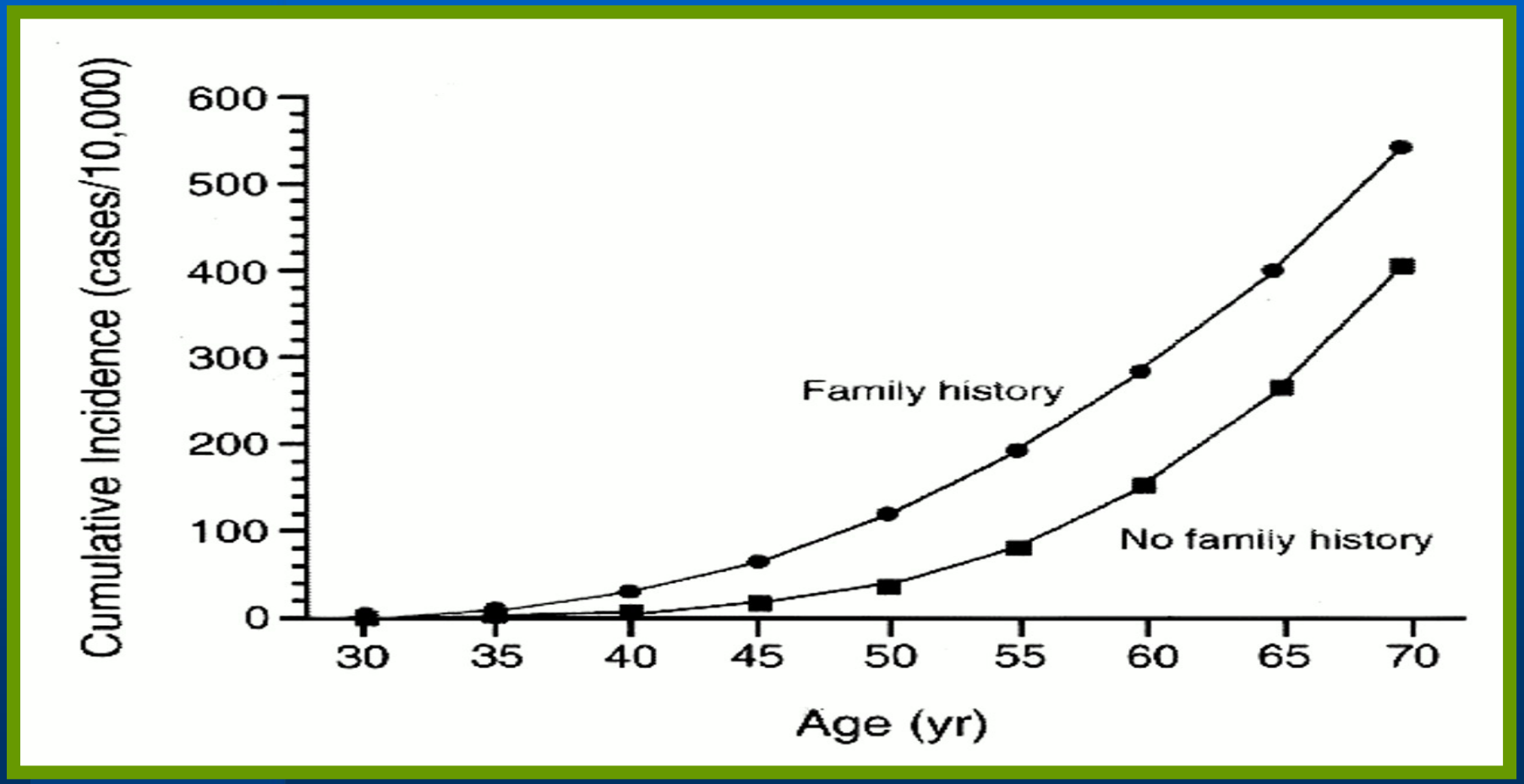
Riducono la partecipazione

- **20%** ansia
- **19%** convinzione che screening sia inutile

Senore et al. 2010

Rischio familiare: studi prospettici

120000 individui (2 coorti, NHS – 1982-1990 e HPFS -1986-1992), questionario ogni due anni su fattori di rischio, diagnosi di cancro



Fuchs, NEJM 1994

RISCHIO FAMILIARE

UPDB (2.3 milioni individui, 10556 CRC)

ETA' PROBANDO	FRR (95 % CI)
FDR < 50 aa	3.31 (2.79 – 3.89)
FDR 50 – 59 aa	2.53 (2.24 – 2.85)
FDR 60 – 69 aa	2.22 (2.04 – 2.40)
FDR > 70 aa	1.97 (1.86 – 2.08)
SDR < 50 aa	1.84 (1.61 – 2.09)

Taylor, Gastroenterology 2010

Rischio familiare di CCR

- Non ci sono evidenze significative riguardo il beneficio della sorveglianza nelle persone con una storia familiare di CCR (escluso sdr. Genetiche!!)
- Non è chiaro in chi, a che età e con che frequenza eseguire la colonscopia
- Nelle famiglie a rischio moderato il riscontro di neoplasia avanzata è raro in età < 45 aa e se non è presente alla colonscopia iniziale rimane un riscontro raro fino ai 65 aa

Dove-Edwin, BMJ 2005

Rischio familiare di CCR

Soggetti con parenti di I grado affetti – escluse sindromi genetiche

- Non ci sono evidenze di una diversa storia naturale del cancro colorettale
- Non ci sono evidenze di una differente performance diagnostica dei test di screening

Castells 2009

Rischio familiare di CCR

Il rischio è funzione dell'età di insorgenza del caso nel parente affetto

Taylor 2010

ma

per il parente sano diminuisce con l'aumentare dell'età

Sondergaard 1991

L'ESPERIENZA ITALIANA

Paziente con cancro < 60 anni o > 60 anni con almeno 1 parente di 1° grado con cancro (*Toscana, Verona*)

Paziente con cancro ogni età (*Trento, Pavia*)

Paziente SD con cancro < 70 anni (*Emilia-Romagna*)

Paziente con cancro o adenomi avanzati SD età < 60 anni (*Feltre*)

Quali familiari

Familiari di I grado

- Residenti età compresa tra 45 e 75 anni oppure 10 anni in meno del probando (*Toscana, Verona*)
- residenti nella stessa ASL di età 45-75 anni (*Toscana, Trento*)
- età compresa tra 25 e 70 anni (*Feltre*)
- età compresa tra 50 e 74 anni oppure 10 anni in meno del probando fino a 74 anni (*Emilia-Romagna*)

Quali risultati

- 3500 casi
- 3600 familiari elegibili dopo accertamento
- 1800 aderenti all'invito alla colonscopia
- DR di adenomi avanzati e cancro non molto diversa da quella riscontrata nella popolazione di screening della stessa età

PROTOCOLLI DISOMOGENEI

IMPEGNO PROBABILMENTE SPROPORZIONATO RISPETTO AI RISULTATI

IL MODELLO PIEMONTE DI SCREENING CON LA SIGMOIDOSCOPIA

PREVENZIONE SERENA

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IL PROGRAMMA PIEMONTESE

FS

INVITO
A UOMINI E DONNE DI 58 ANNI

ADERISCE:
esegue una FS

NON ADERISCE:
viene proposto lo screening con FOBT

In caso di rifiuto del FOBT riproposta della FS un anno dopo per 2 anni consecutivi

In caso di adesione: FOBT con periodicità biennale

NHS Bowel Cancer Screening Programme News

Flexible sigmoidoscopy to be introduced into the NHS Bowel Cancer Screening Programme

4th October, 2010

The Prime Minister, David Cameron, has announced that £60 million will be invested over the next four years in a new technology, flexible sigmoidoscopy, which will be used along existing techniques.

Odds ratio for advanced adenomas by screening arm, gender and age

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

	OR[a]	95% CI
Distal neoplasms		
55–59 y		
FS, n = 1100	1	
FIT, n = 1090	0.14	0.07–0.29
TC, n = 899	0.78	0.52–1.16
Women, n = 1544	1	
Men, n = 1545	2.09	1.39–3.12
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
Distal neoplasms		
60–64 y		
FS, n = 822	1	
FIT, n = 875	0.24	0.12–0.51
TC, n = 697	1.39	0.87–2.22
Women, n = 1239	1	
Men, n = 1155	1.69	1.08–2.65
All neoplasms		
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
All neoplasms		
All subjects		
FS, n = 1922	1	
FIT, n = 1965	0.22	0.14–0.35
TC, n = 1596	1.42	1.08–1.88
55–59 y, n = 3089	1	
60–64 y, n = 2394	1.04	0.78–1.38
Women, n =2783	1	
Men, n = 2700	2.04	1.55–2.70

NOTE. Multivariable ORs, 95% CI.
[a]ORs adjusted for screening center and for all other variables in the table.

Segnan et al. Gastroeneterology 2007

INCIDENZA CUMULATIVA – Studio SCORE2

STADIO UICC		% su invitati
I	20	0,12%
II	**8**	**0,05%**
III	**15**	**0,09%**

FOBT – 3 round

CCR	Adenoma ≥ 10 mm	Esami	INVITI
47	169	13822	17344
0,27%	0,97%		

STADIO UICC		% su invitati
I	23	0,09%
II	**2**	**0,01%**
III	**4**	**0,02%**

FS – un solo esame

CCR	Adenoma ≥ 10 mm	Esami	INVITI
29	354	6966	25394
0,12%	1,39%		

I TRIAL DI VALUTAZIONE DELLO SCREENING CON FS

Table 6. Summary of randomized controlled trials testing the effectiveness of screening flexible sigmoidoscopy*

Variable	UKFSST	SCORE	NORCCAP	PLCO
Citation	7	8	9	
Location	United Kingdom (14 centers)	Northern Italy (6 centers)	Norway (Oslo/Telemark)	United States (10 centers)
Recruitment period	1996–1999	1995–1999	1995–1999	1993–2001
Age eligibility (y)	55–64	55–64	50–64	55–74
Exclusion based on recent LGI†	within 3 years	within 2 years	none	within 3 years
No. assigned to screened group	57 254	17 148	20 003	77 465
No. screened	40 674	9911	12 960	64 658
Compliance with sigmoidoscopy (%)	71.0	57.8	64.8	83.5
Sex, % male‡	50.4	50.0	48.6	51.1
Age ≥60 years, %‡	43.8	44.2	26.0	66.4
Definition of positive screen	Biopsy at screen or referral for colonoscopy or surgery	Biopsy at screen or referral for colonoscopy or surgery	Referral for colonoscopy	Polyp or mass at screen
Positive screen, %§	27.7	17.6	20.4	23.4
Criteria for colonoscopy	≥1.0 cm polyp, 3 or more adenomas, tubulovillous or villous change, severe dysplasia, malignancy	≥0.5 cm polyp, 3 or more adenomas, tubulovillous or villous change, severe dysplasia, malignancy	≥1.0 cm polyp, any adenoma, or malignancy	Contingent on personal physician and medical care
Colonoscopy follow-up, %§‖	5.0	7.8	19.5	16.2
Yields from initial sigmoidoscopy				
Any distal adenoma, %¶	12.1	10.8		7.2
Advanced distal lesions, %¶#**	4.7	3.4		2.7
Any proximal adenoma, %††‡‡	0.9	1.2		3.1
Advanced proximal adenoma, %**††‡‡	0.3	0.4		0.8
Any adenoma, no cancer, %			17.0	8.8
Any advanced adenoma, no cancer, %††			4.2	3.3
Cancer, per 1000 screened	3.4	5.4	3.2	2.9

Da Weissfeld JL, et al JNCI 2005

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

	Control group (n=112 939)			Intervention group (n=57 099)			Hazard ratio (95% CI); intervention *vs* control group	p value
	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)	706*†	616 981	114 (106–123)	0·77 (0·70–0·84)	<0·0001
Distal: rectum and sigmoid colon	1192‡	1 220 175	98 (92–103)	386†‡	618 053	62 (57–69)	0·64 (0·57–0·72)	<0·0001
Proximal	628‡	1 222 639	51 (48–56)	311†‡	618 962	50 (45–56)	0·98 (0·85–1·12)	0·75
Mortality								
All-cause	13 768	1 224 523	1124 (1106–1143)	6775	620 045	1093 (1067–1119)	0·97 (0·94–1·00)	0·0519
Colorectal cancer§	538	1 224 523	44 (40–48)	189	620 045	30 (26–35)	0·69 (0·59–0·82)	<0·0001
Non-colorectal cancer causes§	13 230	1 224 523	1080 (1062–1099)	6586	620 045	1062 (1037–1088)	0·98 (0·95–1·01)	0·25
Colorectal cancer (verified¶)	637	1 224 523	52 (48–56)	221	620 045	36 (31–41)	0·68 (0·59–0·80)	<0·0001
Non-colorectal cancer causes (verified¶)	13 131	1 224 523	1072 (1054–1091)	6554	620 045	1057 (1032–1083)	0·99 (0·96–1·02)	0·33

*41 cancers with site not specified were included, 29 in control group and 12 in the intervention group. Only the earliest cancer was counted for patients with more than one cancer. †140 patients had cancers detected at baseline screening (126 distal cancers and 14 proximal cancers). ‡34 patients had both a distal and a proximal cancer (19 synchronous and 15 metachronous): 31 patients in control group and three in the intervention group. §Deaths certified by the Office for National Statistics as colorectal cancer as underlying cause of death by automatic coding. ¶Assignment of colorectal cancer as underlying cause of death by independent expert coder.

Table 1: **Colorectal cancer incidence and mortality in control and intervention groups**

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	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†	1218 334	149 (143–156)	261†	172 260	152 (134–171)	445†‡	444 721	100 (91–110)	0·67 (0·60–0·76)
Distal: rectum and sigmoid colon	1192§	1220 175	98 (92–103)	171§	172 565	99 (85–115)	215‡§	445 488	48 (42–55)	0·50 (0·42–0·59)
Proximal	628§	1222 639	51 (48–56)	87§	172 879	50 (41–62)	224‡§	446 084	50 (44–57)	0·97 (0·80–1·17)
Mortality										
All-cause	13768	1224 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	1224 523	44 (40–48)	78	173 191	45 (36–56)	111	446 854	25 (21–30)	0·57 (0·45–0·72)
Non-colorectal cancer causes¶	13 230	1224 523	1080 (1062–1099)	2635	173 191	1521 (1461–1581)	3951	446 854	884 (857–912)	0·97 (0·93–1·02)
Colorectal cancer (verified‖)	637	1224 523	52 (48–56)	94	173 191	54 (44–66)	127	446 854	28 (24–34)	0·56 (0·45–0·69)
Non-colorectal cancer causes (verified‖)	13 131	1224 523	1072 (1054–1091)	2619	173 191	1512 (1455–1571)	3935	446 854	881 (854–909)	0·98 (0·93–1·03)

*Adjusted for non-compliance with screening. †41 cancers with site not specified were included, 29 in control group and 12 in the intervention group (four not screened and eight screened). Only the earliest cancer was counted for patients with more than one cancer. ‡140 patients had cancers detected at baseline screening (126 distal cancers and 14 proximal cancers). §34 patients had both a distal and a proximal cancer (19 synchronous and 15 metachronous): 31 patients in the control and three in the intervention group (one not screened and two screened). ¶Deaths certified by the Office for National Statistics as colorectal cancer as underlying cause of death by automatic coding. ‖Assignment of colorectal cancer as underlying cause of death by independent expert coder.

Table 2: **Colorectal cancer incidence and mortality by randomisation and compliance with screening**

Once-only flexible sigmoidoscopy screening in prevention of colorectal cancer: a multicentre randomised controlled trial

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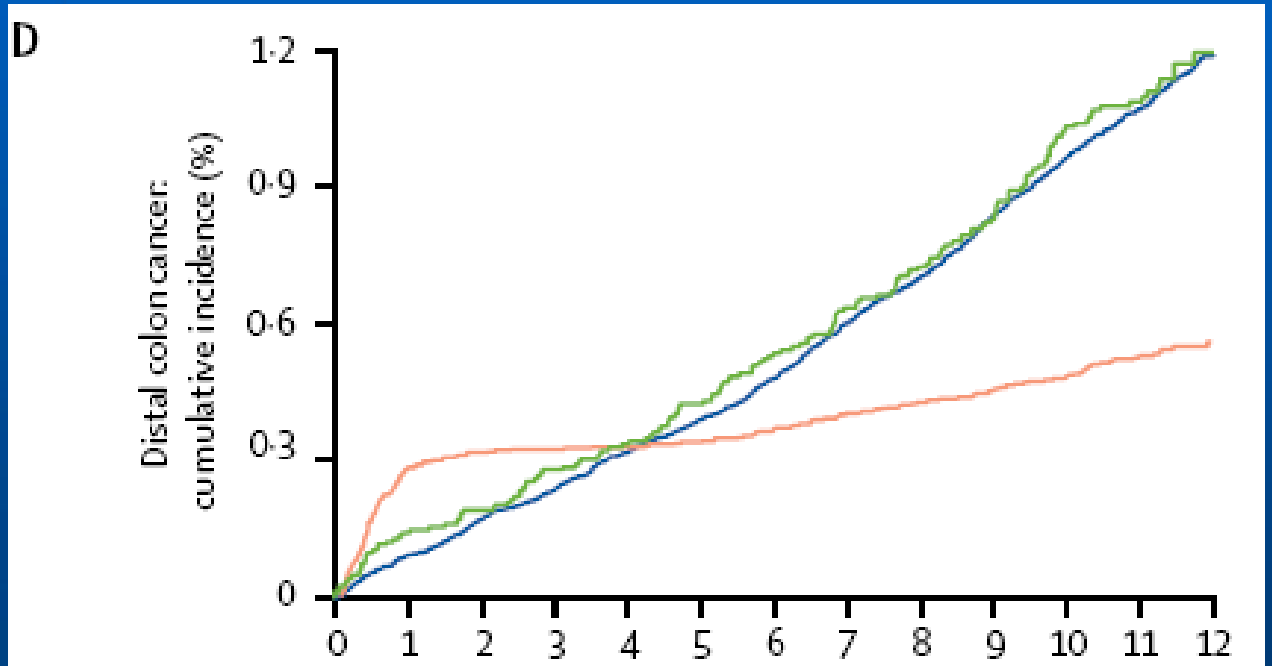

Number at risk

Control	112 939	111 165	109 053	106 529	103 693	99 926	18 619
Screened	40 621	40 156	39 595	38 885	38 043	36 827	7157
Not screened	16 478	15 997	15 577	15 100	14 571	13 917	2335

Trial multicentrico italiano di valutazione della sigmoidoscopia once-only – SCORE trial

Sottomesso per la pubblicazione

Presentazione al DDW (Chicago 7 Maggio)

Risultati consistenti con quelli del trial inglese

Riduzione significativa di incidenza

↓ stadi avanzati (UICC III e IV)

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

GASTROENTEROLOGY 2007;132:2304–2312

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

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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; $P = .000$.

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

Annals of Internal Medicine 2009

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

	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)

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-Sided Cancer
Prevalence ratio	0.52 (0.37–0.73)	1.05 (0.63–1.76)	0.33 (0.21–0.53)

FATTIBILITA' E COSTI

FOBT SCREENING - TORINO

120,000 PERSONE DI ETA' 50 - 69

PARTECIPAZIONE 50%

POSITIVITA' 5%

CARICO DI LAVORO ENDOSCOPICO

3000 CT ≈ (9000 FS)

FS SCREENING - TORINO

12,000 PERSONE DI 58 ANNI

PARTECIPAZIONE 50%

INVII IN TC 7.5%

CARICO DI LAVORO ENDOSCOPICO

6000 FS + 450 CT

COSTO PER PERSONA ESAMINATA: 1 FS ≈ 4 FOBT

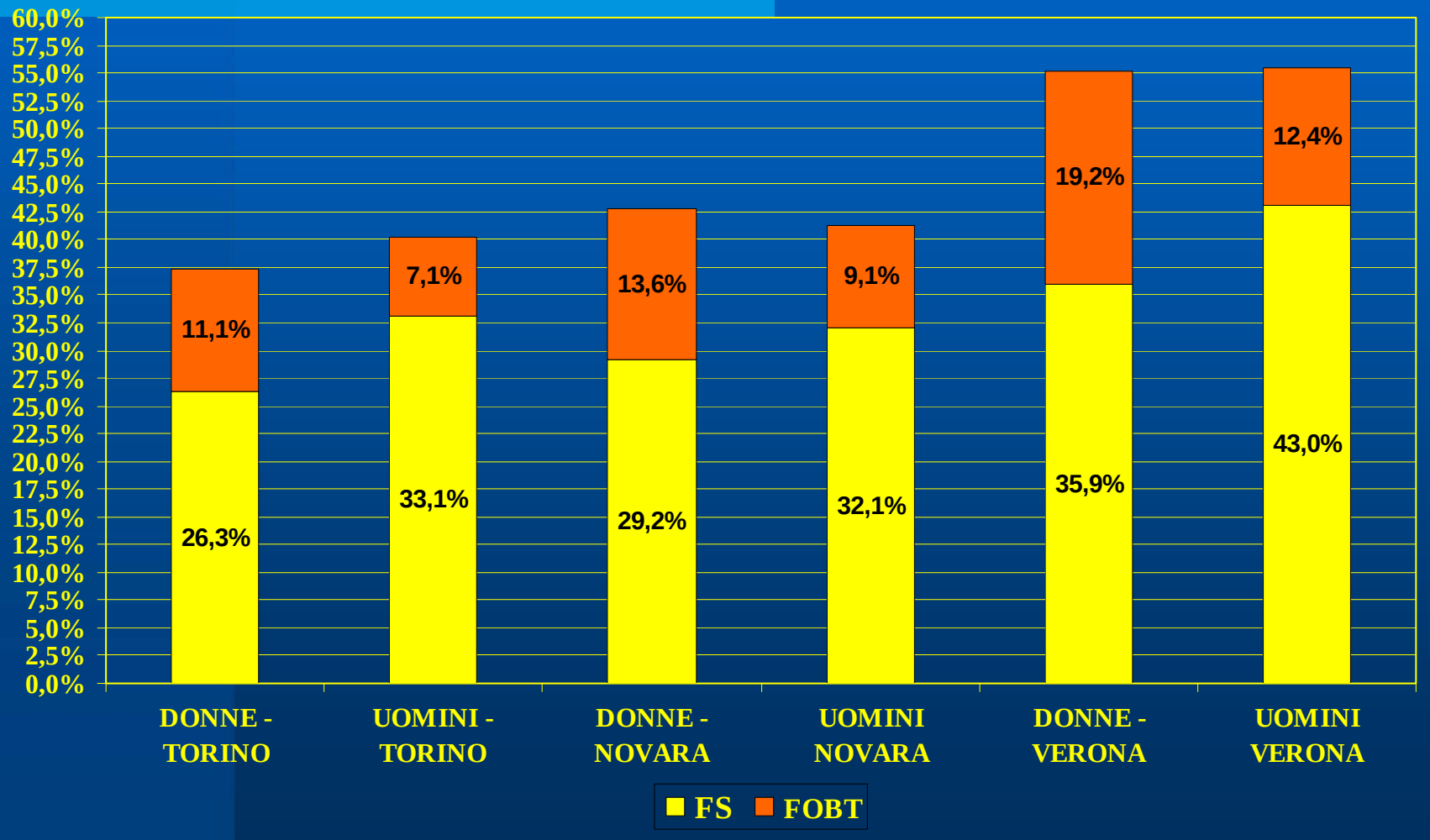
PIEMONTE Adesione 25%	N. test / anno	Costo(€) / anno	Morti evitate	Casi prevenuti
FOBT 50-69 aa ogni 2 anni	137819 + CT: 3673	3.445.486	329 + 186	372
FS “once only” 58 aa	14617 + CT: 1023	1.607.870	58 + 575	1150
+ FOBT 59-69	39440 (73274-6414) + CT: 974 (1815-158)	1.218.696 (2.264.167-198.193)	158 + 78	157

CONFRONTO FS – FOBT

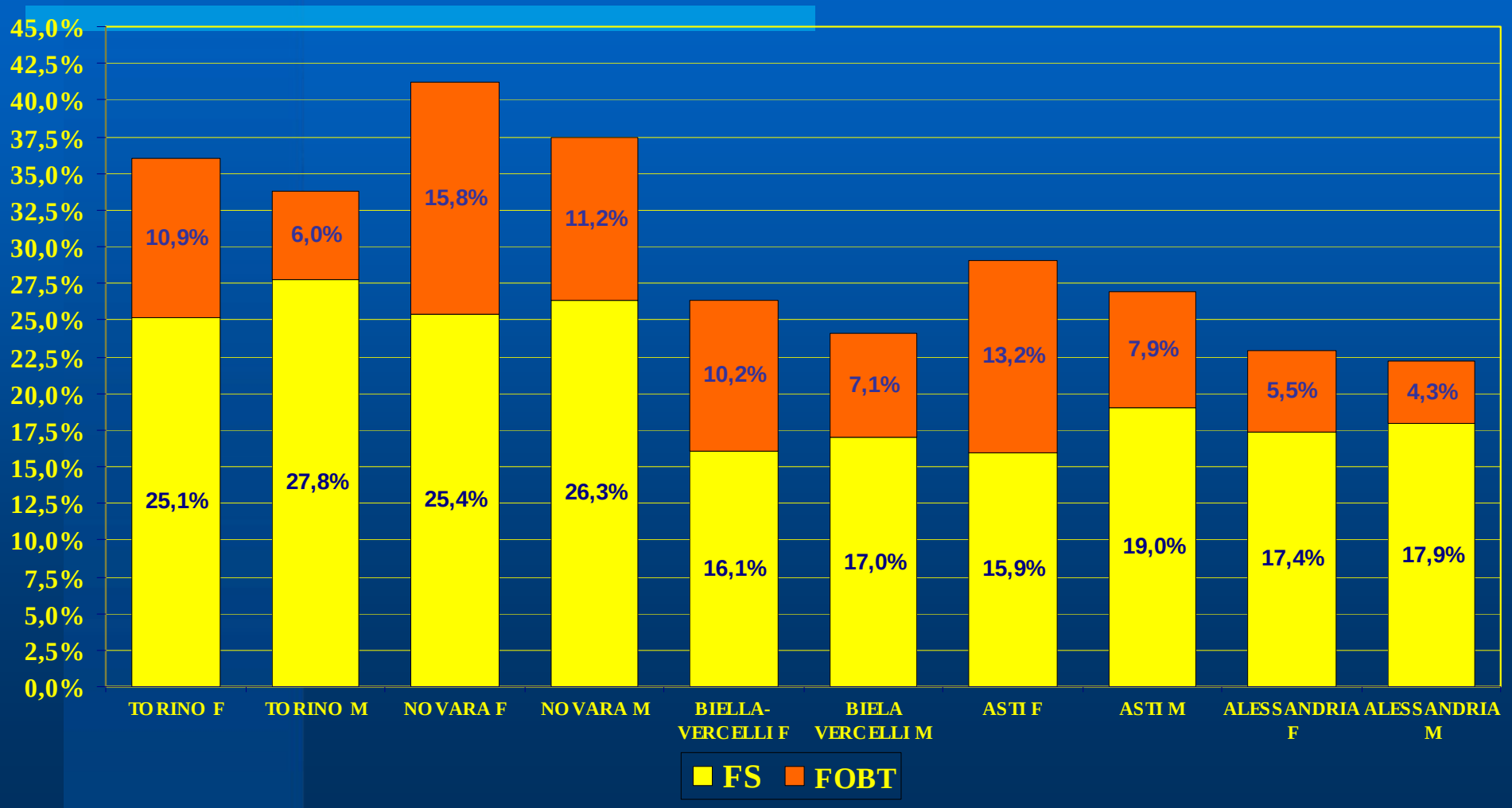
SU 4 ROUND 67% DEGLI ADERENTI AL I PASSAGGIO ESEGUE 4 TEST

		I ROUND	7 ANNI / 4 ROUND
FS	VERONA	39.3%	39.3%
	TORINO	29.6%	29.6%
FS – SCAMBIO	VERONA	55.2%	49.9%
	TORINO	38.8%	35.7%
FOBT	EMILIA-ROMAGNA	59.5%	39.9%
	ITALIA	50.0%	33.5%

COPERTURA RAGGIUNTA CON L'OFFERTA DEL FOBT AI NON ADERENTI ALLA FS



Risultati RS Piemonte

- Copertura da inviti (2010) : 88.1% (49634/56537)
- Adesione (2009): 31.7%
- Invii in colonscopia (2009): 10.2%
- DR di adenomi avanzati (2009): 5.0%
- DR di cancro (2009): 0.4%

COPERTURA RAGGIUNTA CON L'OFFERTA DEL FOBT AI NON ADERENTI ALLA FS 2009