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**OMED meeting on CRC
screening:**

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Baseline Findings of the Italian Multicenter Randomized Controlled Trial of “Once-Only Sigmoidoscopy”—SCORE

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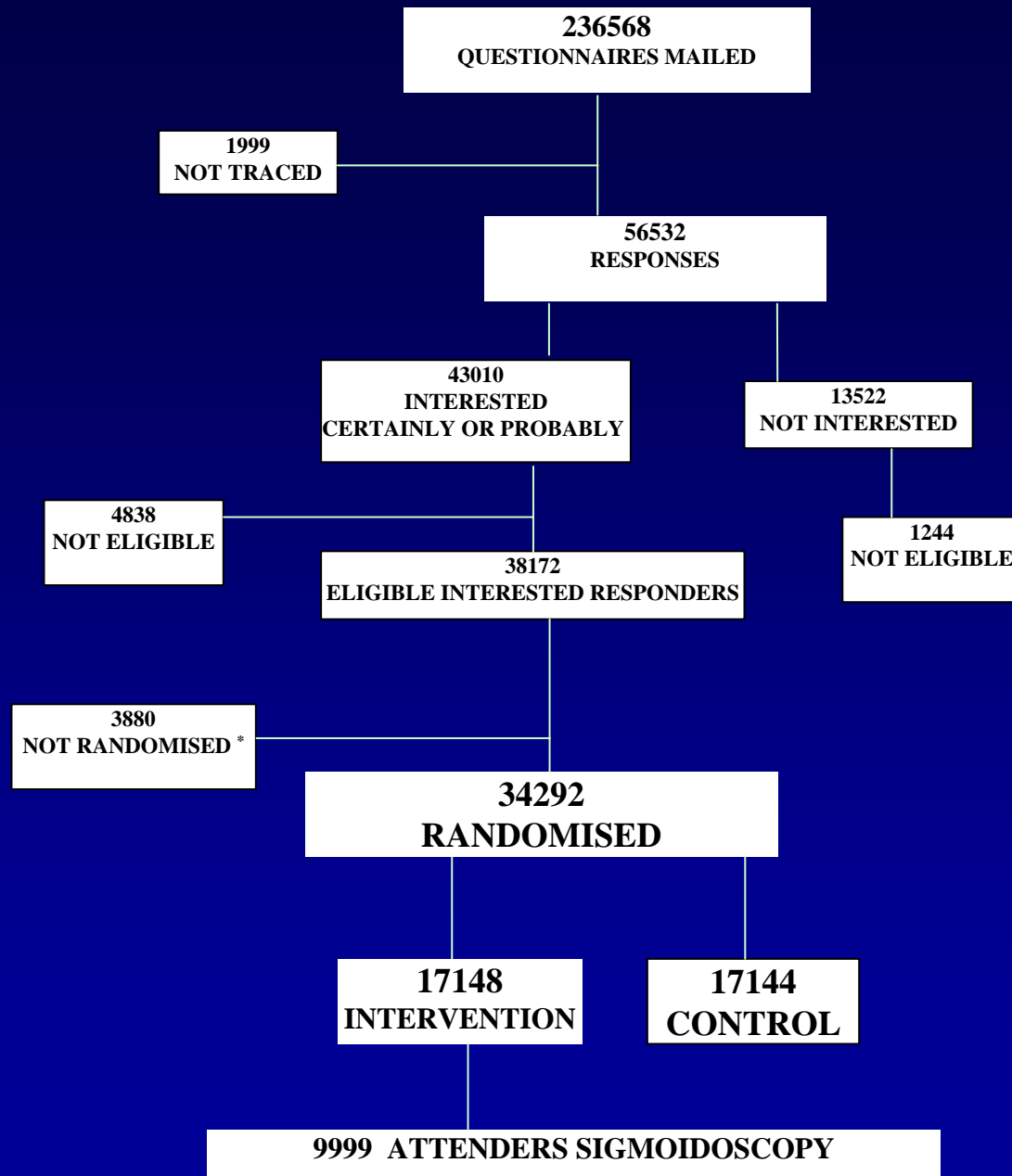
And the SCORE Working Group - Italy

Background: A single sigmoidoscopy examination at around age 60 years has been proposed as a cost-effective strategy to prevent colorectal cancer. A multicenter randomized controlled trial, the SCORE trial, is in progress in Italy to estimate the impact of this strategy on colorectal cancer incidence and mortality and the duration of the protective effect. We present the baseline screening outcomes. **Methods:** A questionnaire was mailed to a random sample of 236 568 people aged 55–64 years to assess their eligibility for and

colorectal cancer incidence. [J Natl Cancer Inst 2002;94:1763–72]

Colorectal cancer is the second leading cause of cancer death in Europe (1). In Italy, mortality rates from the disease have remained fairly constant over the past decade, with approximately 17 000 deaths per year (2). Based on projections from past trends, about 40 000 new cases were expected in 2000 in Italy (3). Several observational and intervention studies have shown consistent and marked reductions in both colorectal can-

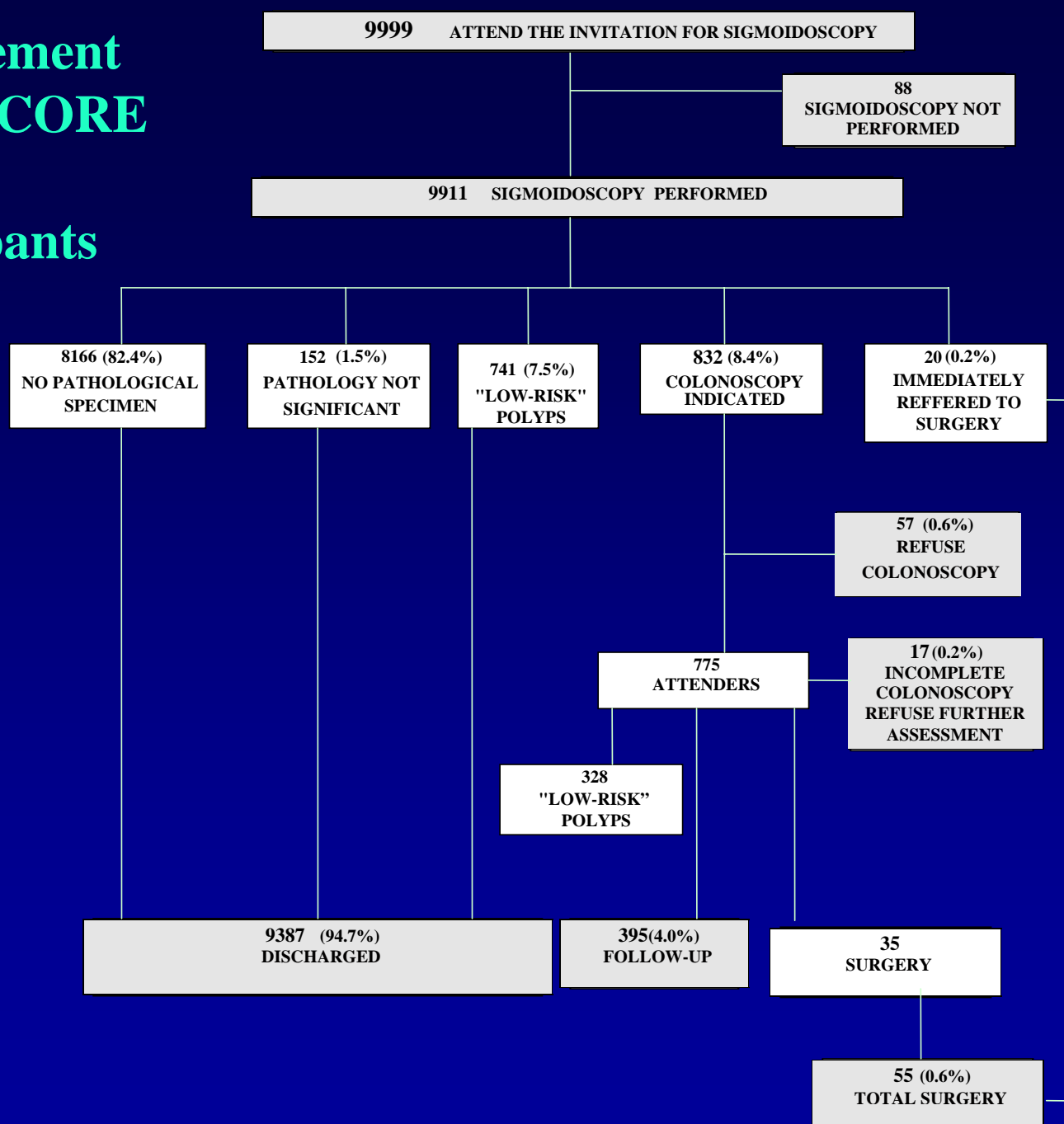
SCORE Trial Profile



RANDOMISED TRIAL OF ONCE-ONLY FLEXIBLE SIGMOIDOSCOPY SCREENING IN ITALY - SCORE

- **239,668** questionnaires sent
- **38,172 (16%)** subjects available for FS
- **17,148** invited people
- **9,999 (58%)** participants
- prevalence of polyps : **17%**
- prevalence of adenomas : **11%**
- prevalence of cancer : **0.5%**

Management of the SCORE trial participants



FU SCORE TRIAL

- In 2002 145 CRC cases in intervention arm and 141 in control arm (5yrs fu)
- end of the follow up in 2007

ARTICLES

Randomized Trial of Different Screening Strategies for Colorectal Cancer: Patient Response and Detection Rates

Nereo Segnan, Carlo Senore, Bruno Andreoni, Arrigo Arrigoni, Luigi Bisanti, Alessandro Cardelli, Guido Castiglione, Cristiano Crosta, Roberta DiPlacido, Arnaldo Ferrari, Roberto Ferraris, Franco Ferrero, Mario Fracchia, Stefano Gasperoni, Giuseppe Malfitana, Serafino Recchia, Mauro Risio, Mario Rizzetto, Giorgio Saracco, Mauro Spandre, Delio Turco, Patricia Turco, Marco Zappa, SCORE2 Working Group-Italy

Background: Although there is general consensus concerning the efficacy of colorectal cancer screening, there is a lack of agreement about which routine screening strategy should be adopted. We compared the participation and detection rates achievable through different strategies of colorectal cancer screening. **Methods:** From November 1999 through June 2001 we conducted a multicenter, randomized trial in Italy among a sample of 55–64 year olds in the general population who had an average risk of colorectal cancer. People with previous colorectal cancer, adenomas, inflammatory bowel disease, a recent (≤ 2 years) colorectal endoscopy or fecal occult blood test (FOBT), or two first-degree relatives with colorectal cancer were excluded. Eligible subjects were

method. Screening strategies using a fecal occult blood test (FOBT) and sigmoidoscopy are currently being evaluated for implementation in population-based screening programs in several European countries (i.e., the United Kingdom, Norway, and Finland) and in Australia (5–9). In Italy, the National Board for Oncology has issued guidelines recommending the implementation of pilot projects involving sigmoidoscopy and an FOBT for colorectal cancer screening (10). Although colonoscopy is the most complete endoscopic procedure available for colorectal cancer screening (11,12), direct evidence about its effectiveness, its complications, and its acceptability among individuals at average risk of the disease is still not sufficient to justify its use for routine screening (13). Comparative data about neoplasia detection rates, participation rates, economic costs, and the side effects of the different screening strategies are needed to estimate the effectiveness and the balance between ben-

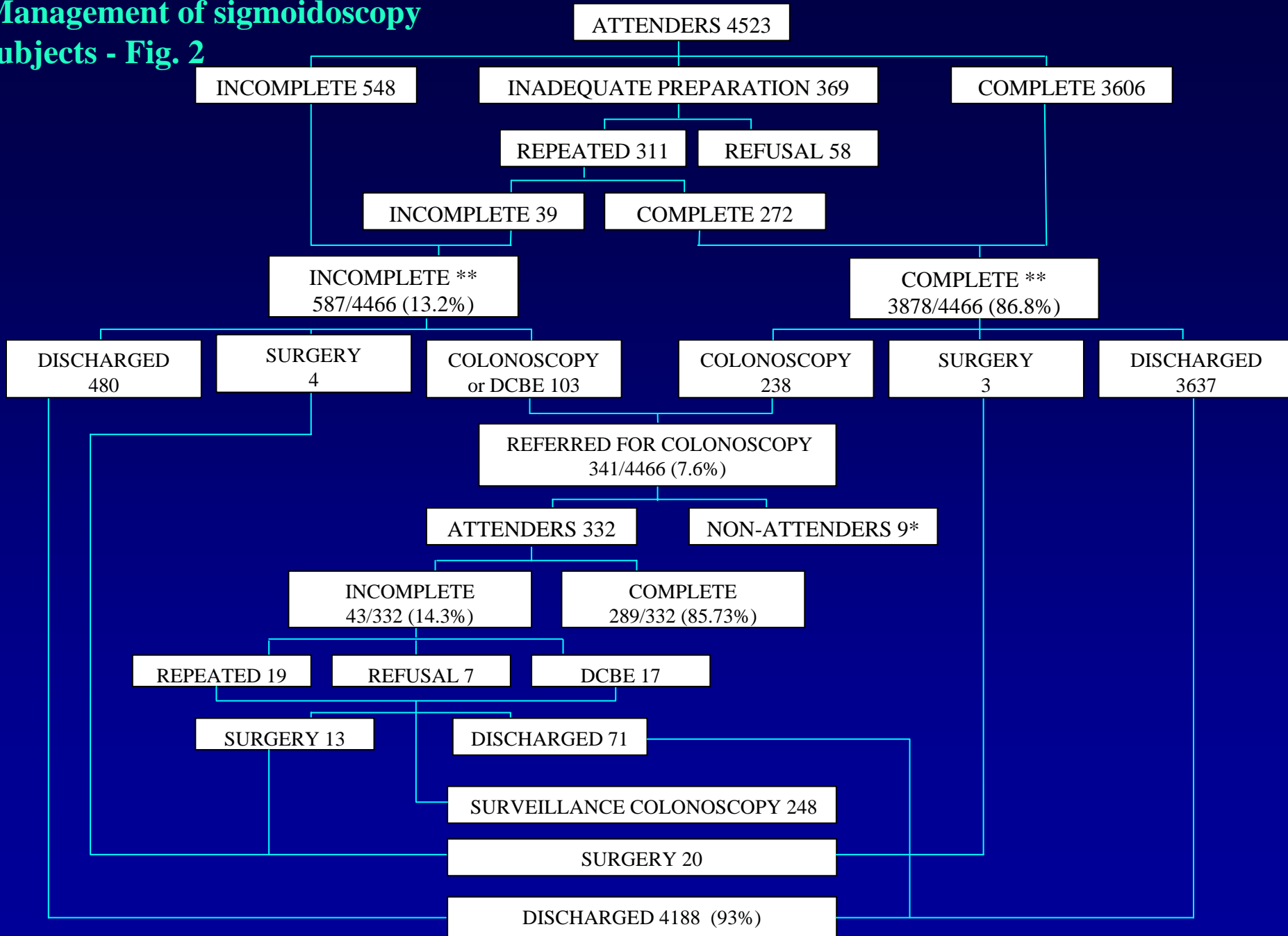
Size of randomized groups by sex and age - Table 1

	MEN [n (%)]		WOMEN [n (%)]		
SCREENING ARM	55-59 yrs	60-64 yrs	55-59 yrs	60-64 yrs	TOTAL (n)
FOBT by mail	524 (22.5)	550 (23.6)	628 (27.0)	624 (26.8)	2326
FOBT by GP or screening facility	1476 (24.7)	1408 (23.5)	1569 (26.2)	1532 (25.6)	5985
Patient's choice	872 (24.0)	842 (23.2)	966 (26.6)	951 (26.2)	3631
Once-only sigmoidoscopy	917 (24.8)	825 (22.3)	963 (26.1)	990 (26.8)	3695
Sigmoidoscopy + biennial FOBT	2611 (23.6)	2484 (22.5)	2893 (26.2)	3057 (27.2)	11045
TOTAL	6400 (24.0)	6109 (22.9)	7019 (26.3)	7154 (26.8)	26682

**Participation rate by sex, age, and screening arm
(undelivered invitations are excluded from the denominator) (2) - Table 2**

	TOTAL	
	55-59 yrs	
SCREENING ARM	invited	attended (%)
FOBT by mail	2266	682 (30.1)
FOBT by GP or screening facility	5893	1654 (28.1)
Once-only sigmoidoscopy	3650	1026 (28.1)
Sigmoidoscopy + biennial FOBT	10867	3049 (28.1)
Patient's choice	3579	
FOBT		522 (14.6)
Sigmoidoscopy		448 (12.5)
Total		970 (27.1)
TOTAL	26255	7381 (28.1)

Management of sigmoidoscopy subjects - Fig. 2



Odds ratio for participation rate by age, sex, and screening arm in the FOBT and sigmoidoscopy arms and in whole study population (1) - Table 3

	n	OR* (95% CI)
FOBT ARMS		
FOBT by GP or screening facility	5893	1.00 (referent)
FOBT by mail	2266	1.11 (0.99-1.23)
55-59 yrs	3530	1.00 (referent)
66-64 yrs	4629	1.01 (0.92-1.11)
Women	4297	1.00 (referent)
Men	3862	0.82 (0.74-0.90)
SIGMOIDOSCOPY ARMS		
Sigmoidoscopy + biennial FOBT	10867	1.00 (referent)
Once-only sigmoidoscopy	3650	1.00 (0.92-1.09)
55-59 yrs	6433	1.00 (referent)
66-64 yrs	8084	0.89 (0.82-0.95)
Women	7794	1.00 (referent)
Men	6723	1.22 (1.14-1.32)

* Multivariable ORs adjusted for screening center and for all the other variables in the table

Odds ratio for advanced adenomas in FOBT and sigmoidoscopy arms by age and sex and among all patients examined, excluding those in the patient's choice arm, by age, sex, and screening test (2) - Table 5

	n	OR* (95% CI)
ALL PATIENTS EXAMINED (excluding those in patient's choice arm)		
FOBT arms	2336	1.00 (referent)
Sigmoidoscopy arms	4025	3.58 (2.49-5.14)
55-59 yrs	2578	1.00 (referent)
66-64 yrs	3783	1.32 (1.01-1.72)
Women	3316	1.00 (referent)
Men	3045	1.61 (1.24-2.090)

* Multivariable ORs adjusted for screening center and for all the other variables in the table

Side effects

- FS (n=4466): 5 self limited bleedings, 16 mild vagal reactions, 1 discharged within 24 hours for severe vagal reaction with cardiac arrest
- TC (n=332): 8 self limited bleeding after polypectomy, 5 mild vagal reactions, 1 severe hemorrhage

Side effects of FS subjects (n=4466)

- Mild pain : 62,3%
- less painful than expected: 25.4%
- hoping not repeat: 11.1%
- most severe pain ever experienced: 1.2%

- OR women vs men 2.32 (95%CI: 1.9 -2.83)
for “most severe pain and hope to not
repeat”

Predictors of patients participation - SCORE 2: ORs(95% CI)

- Consulting GP: 4.4 (3.3-5.9)
- CRC in 1st degree relative: 3.3 (1.9-5.8)
- regular physical activity: 2.0 (1.5-2.8)
- screening ineffective: 0.15 (0.1-0.2)
- higher education: 2.6 (1.0-6.5)
- anxiety:0.35 (0.2-0.5)

SCORE 3 COMPLIANCE

- **FOBT** 31.9% (1936/6077)
- **FS** 28.7% (1732/6039)
- **CT** 23.0% (1390/6038)

- **RR (FOBT vs FS)** 1.11 (1.05-1.17)
- **RR (FOBT vs CT)** 1.38 (1.30-1.47)
- **RR (FS vs CT)** 1.25 (1.17-1.32)

COMPLETION RATE OF THE EXAMS

	FS COMPLETED	TC COMPLETED	
	%	%	% TC WITH SEDATION
BIELLA	86,6	87,5	66,0
FIRENZE	90,3	86,7	13,3
MILANO	84,8	85,5	80,7
RIMINI	90,7	89,4	13
TORINO	90,2	84,4	26,4
VERONA	91,1	85,6	21,3
TOTAL	89,7	86,2	32,1

FOBT RESULTS

- TESTS PERFORMED 1920
 - % positive 4.5% (N= 86)
 - VPP (74 TCs performed) 31, 1%
- 1 CRC, 22 advanced adenomas

DETECTION RATE

distal advanced lesions

• **FS** (n= 1708)

4.5%

(67 adenomas; 10 CRC)

• **TC** (n=1380)

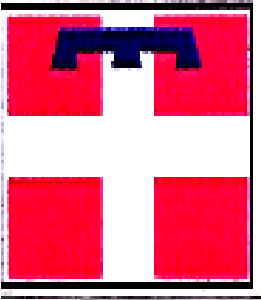
4.6%

(60 adenomas 4 CRC)

DETECTION RATE

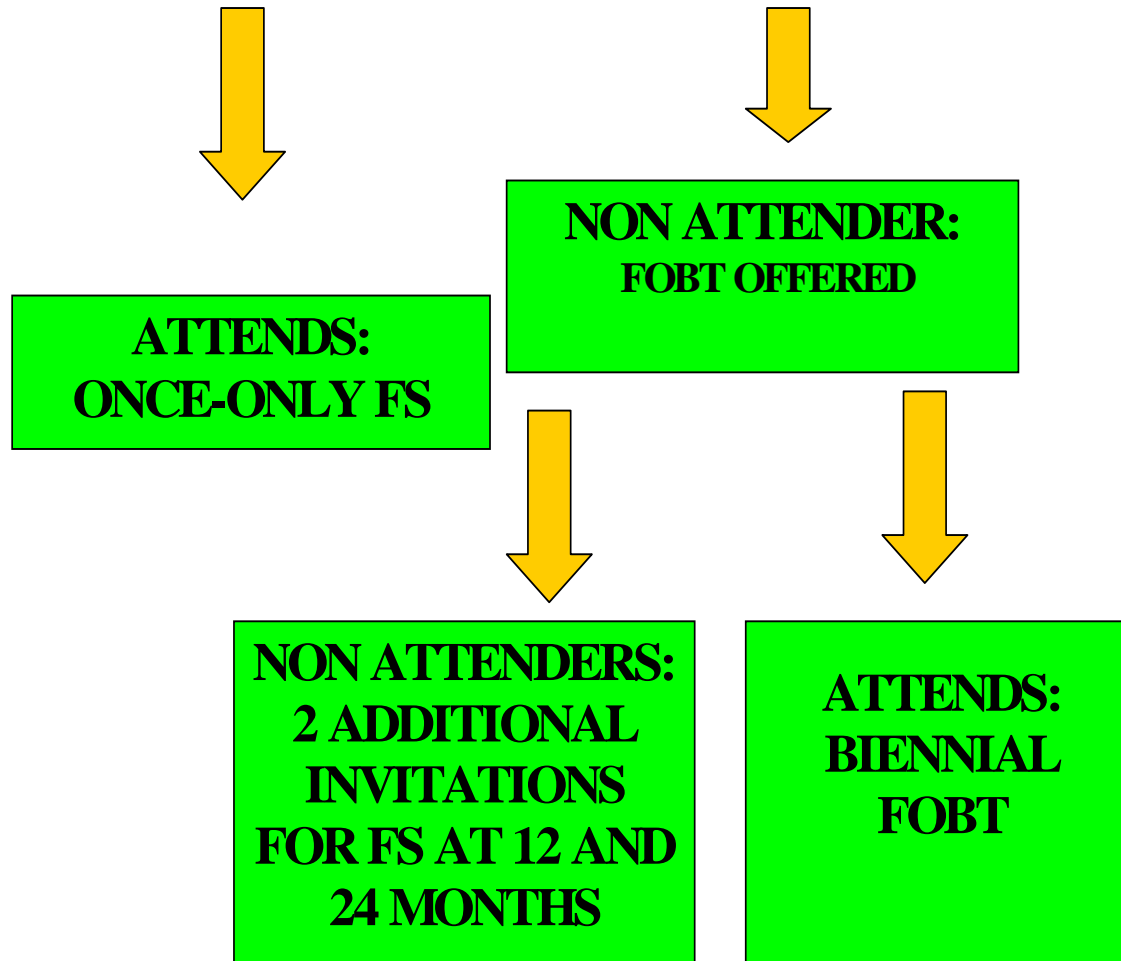
proximal advanced lesions

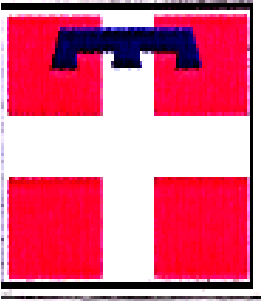
- TC (n=1390) 2.5%
(32 adenomas; 3 Crc)
74.3% with distal
negative finding or
with distal low-
risk polyps



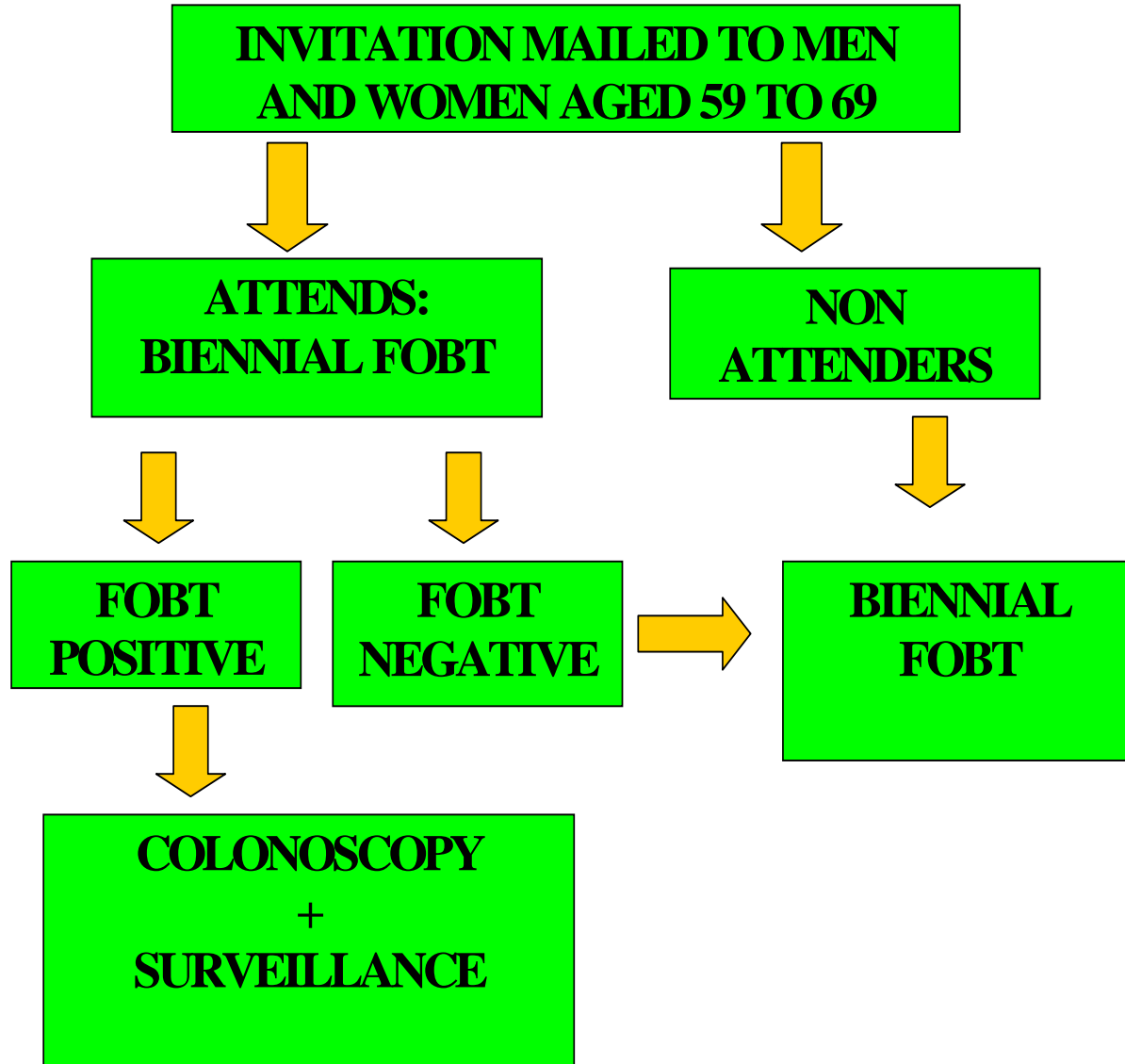
THE PIEDMONT PROGRAMME

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THE PIEDMONT PROGRAMME



Number of patients with colorectal cancer according to method of treatment, Dukes' stage and TNM* status - SCORE Trial

Treatment	Total		T status			N status				M status		
	n	%	T1	T2	T3	N0	N1	N2	Nx	M0/Mx	M1	
Endoscopic excision	11	(20.4)	11						11	11		
Local excision	1	(1.9)	1						1	1		
Open abdominal surgery												
Dukes' A	17	(31.5)	13	4		13			4‡	17		
Dukes' B	9	(16.7)			9	9				9		
Dukes' C	14	(25.9)	1		13		10	2	2§	14		
Dukes' D	2	(3.7)			2			2			2	
Total	n	54	(100)	26	4	24	22	10	4	18	52	2

Segnan et al. Journal of the National Cancer Institute 2002; 94(23)

Most advanced lesions (distal or proximal) identified through screening by sex, age, and screening arm (4) - Table 4

	55-59 yrs		66-64 yrs		TOTAL	
SCREENING ARM	n	%	n	%	n	%
Sigmoidoscopy (once-only sigm. or sigm. + FOBT)						
Patients screened	1661	100	2364 ***	100	4025	100
No findings	1360	81.9	1917	81.1	3277	81.4
Non-neplastic polyps **	102	6.1	140	5.9	242	6.0
Low-risk adenomas	112	6.7	166	7.0	279	6.9
Advanced adenomas	83	5.0	130	5.5	213	5.3
Colorectal cancer	4	0.2	10	0.4	14	0.3
Sigmoidoscopy (patient's choice)						
Patients screened	183	100	258	100	441	100
No findings	157	85.8	202	78.3	359	81.4
Non-neplastic polyps **	12	6.6	23	8.9	35	7.9
Low-risk adenomas	9	4.9	18	7.0	27	6.1
Advanced adenomas	4	2.2	12	4.7	16	3.6
Colorectal cancer	1	0.5	3	1.2	4	0.9

*** Hyperplastic polyps, normal or inflammatory mucosa, inadequate samples, and missed polyps are included in this category

**** One patient refused to undergo colonoscopy, and therefore his polyp was not excised

REASONS FOR STOPPING

	FS COMPLETED	TC COMPLETED
	%	%
INADEQUATE PREPARATION	53,1	16,0
PATIENT'S PAIN	21,7	43,0
ADHESIONS	14,3	32,0

RESPONSE RATE BY CENTER

	FOBT		FS		CT	
	INVITED	COMPLIERS	INVITED	COMPLIERS	INVITED	COMPLIERS
BIELLA	1030	260	1013	219	1005	145
		25,2%		21,6%		14,4%
FIRENZE	971	307	932	261	947	227
		31,6%		28,0%		24,0%
MILANO	1014	228	1053	224	1052	167
		22,5%		21,3%		15,9%
RIMINI	801	249	822	222	808	168
		31,1%		27,0%		20,8%
TORINO	1262	329	1215	310	1205	232
		26,1%		25,5%		19,3%
VERONA	999	563	1004	496	1021	451
		56,4%		49,4%		44,2%
TOTAL	6077	1936	6039	1732	6038	1390
		31,9%		28,7%		23,0%