

## Screening for colorectal cancer in Italy: 2007 survey

Manuel Zorzi,<sup>1</sup> Chiara Fedato,<sup>1</sup> Carlo Naldoni,<sup>2</sup> Romano Sassatelli,<sup>3</sup> Priscilla Sassoli de' Bianchi,<sup>2</sup> Carlo Senore,<sup>4</sup> Carmen Beatriz Visioli,<sup>5</sup> Carla Cogo<sup>1</sup>

<sup>1</sup>Registro Tumori del Veneto, Istituto Oncologico Veneto IRCCS, Padova; <sup>2</sup>Assessorato Politiche per la salute, Regione Emilia-Romagna, Bologna; <sup>3</sup>Endoscopia digestiva-AOSP Reggio Emilia; <sup>4</sup>Centro per la Prevenzione Oncologica del Piemonte, Torino; <sup>5</sup>Istituto Scientifico per la Prevenzione Oncologica, Firenze

### Abstract

*We present the main results from the fourth survey of the Italian screening programmes for colorectal cancer carried out by the National Centre for Screening Monitoring (Osservatorio Nazionale Screening, ONS) on behalf of the Ministry of Health.*

*During 2007, five new programmes were activated, but three other programmes were stopped, including the regional programme of Basilicata, and by the end of the year 46.6% of Italians aged 50-69 years were residing in areas covered by organised screening programmes (theoretical extension). Seven regions had their whole population covered. In the South of Italy and Islands only one new programme was activated in 2007, while two others were stopped, with a decline of theoretical extension from 10% to 7%.*

*The majority of programmes employ the faecal occult blood test (FOBT), while some have adopted flexible sigmoidoscopy (FS) once in a lifetime, or a combination of both.*

*Overall, about 2,600,000 subjects were invited to undergo FOBT, 79.1% of those to be invited within the year. The adjusted attendance rate was 46.3% and approximately 1,131,900 subjects were screened. Large differences in the attendance rate were observed among Regions, with 10% of programmes reporting values lower than 33%.*

*Positivity rate of FOBT programmes was 5.6% at first and 4% at repeat screening. The average attendance rate for total colonoscopy (TC) was 78.7% and in two Regions it was lower than 60%. Completion rate of TC was 91.6%.*

*Among the 914,029 subjects attending screening for the first time, the detection rate (DR) per 1,000 screened subjects was 2.7 for invasive cancer and 12.2 for advanced adenomas (AA, adenomas with a diameter  $\geq 1$  cm, with villous/tubulovillous type or with high-grade dysplasia). As expected, the corresponding figures at repeat screening were lower. The DR of cancer and adenomas increased with age and was higher among males; 25% of screen-detected cancers were in TNM stage III+.*

*Many programmes reported some difficulties in guaranteeing TC in the appropriate time frame to SOF+ subjects: in 23.9% of cases the waiting time was longer than two months.*

*Seven programmes employed FS as the screening test: 66.5% of the target population (about 50,000 subjects) were invited and 8,678 subjects were screened, with an attendance rate of 27.7%. Overall, 88% of FS were classified as complete. Overall TC referral rate was 11.1% and the DR per 1,000 screened subjects was 4.4 and 58.4 for invasive cancer and AA, respectively.*

(*Epidemiol Prev* 2009; 33(3) Suppl 2: 57-74)

**Keywords:** colorectal cancer screening programmes survey, Italy

This paper presents the data from the third survey carried out by the National Centre for Screening Monitoring (Osservatorio Nazionale Screening, ONS) on behalf of the Ministry of

Health, regarding the activities performed by Italian screening programmes for colorectal cancer during 2007. The previous surveys are available at the ONS website.<sup>1,2</sup>

Important differences prevail among colorectal cancer screening programmes in Italy. The main difference regards the type of screening test performed. While the majority of programmes employ the faecal occult blood test (FOBT), some have adopted flexible sigmoidoscopy (FS) once in a lifetime, or a combination of both (figure 1). Moreover, FOBT programmes have different targets as far as age is concerned. Invitation to attend screening starts at the age of 50 in all but one programme, however the maximum age is 69 or 70 years in most programmes, or even 74 or 75 years. Most FS programmes invite a single cohort of subjects aged 58 while two invite subjects aged 60 instead.

All FOBT programmes are set to invite their target population by mail every 2 years to undergo a 1-time immunochemical FOBT, without any dietary restriction. Quantitative haemoglobin analysis is performed by automated instruments using the 100 ng Hb/mL threshold to determine positivity (apart from two programmes that use 80 ng Hb/mL). People with a negative FOBT are notified of their results by mail and they are advised to repeat screening 2 years later. Non re-

sponders to the first invitation are mailed a reminder, usually within 6 months. Subjects with a positive screening test are contacted by phone to undergo a total colonoscopy (TC) or, when a complete colonoscopy is not possible, a double-contrast barium enema X-ray. Colonoscopies are usually performed at an endoscopic referral centre, during dedicated sessions. Patients with screen-detected neoplasms are referred to surgery or endoscopy, and then enrolled in a follow-up programme.

The GISCoR (Gruppo Italiano per lo Screening Coloretale, Italian Group for Colorectal Cancer Screening) published in 2007 an *Operative report of quality indicators* for the evaluation of colorectal cancer screening programmes.<sup>3</sup> For each indicator the reference standards (acceptable, desirable) are provided, improving the possibility to evaluate the programmes' performances. Table 1 shows the indicators and standards utilised in this paper. The *Operative report* is available at the ONS website.

### Data completeness

Only 31 of the 72 programmes that took part in the survey (43%) provided complete data. The items with the lowest level of completeness were screen-detected cancers and surgery: time to surgical treatment, stage at diagnosis, kind of treatment (endoscopic *vs* surgical). However, few programmes were unable to provide either baseline data.

### Programmes activated as of 31-12-2007

The hike in activations of new colorectal cancer screening programmes observed in 2005 and 2006 seems to have stopped in 2007. In fact, only five new programmes were launched, while three others had to cease their activity. As of 31<sup>st</sup> December 2007, 72 programmes were active in 12 Regions (table 2). In particular, programmes on a regional-scale basis were activated in Emilia-Romagna, Lombardia, Toscana, Umbria, Valle d'Aosta and Trentino. The vast majority of programmes (n=65) employ the faecal occult blood

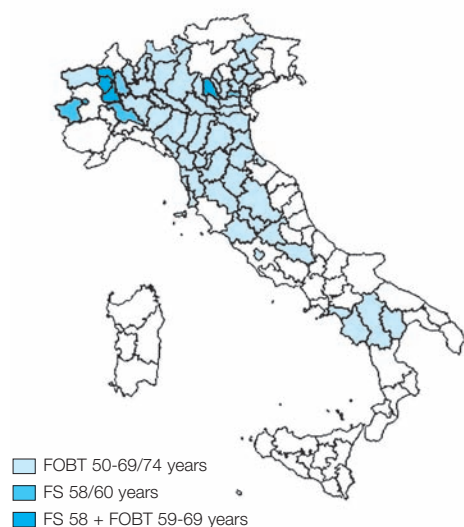


Figure 1: Colorectal cancer screening programmes: first level test and target population.

Indicator	Standard			
	acceptable		desirable	
Actual extension	>80%		>90%	
Compliance to invitation	>45%		>65%	
Positivity rate	<b>FOBT:</b>	first test: <6% repeat tests: <4.5%	<b>FOBT:</b>	first test: <5% repeat tests: <3.5%
	<b>FS:</b>	<8%	<b>FS:</b>	<6%
Inadequate screening tests	<b>FOBT:</b>	<1%	<b>FOBT:</b>	<1%
	<b>FS:</b>	<10%	<b>FS:</b>	<5%
Attendance to further assessment	<b>FOBT:</b>	>85%	<b>FOBT:</b>	>90%
	<b>FS:</b>	>90%	<b>FS:</b>	>95%
Complete FS rate	>85%		>90%	
Complete TC rate	>85%		>90%	
Detection rate	<b>FOBT</b>		<b>FOBT</b>	
	Carcinoma	first test: >2.0% repeat tests: >1.0%	Carcinoma	first test: >2.5% repeat tests: >1.5%
	Adv. adenoma	first test: >7.5% repeat tests: >5.0%	Adv. adenoma	first test: >10% repeat tests: >7.5%
	<b>FS</b>		<b>FS</b>	
	Carcinoma	>3.0%	Carcinoma	>4.0%
	Adv. adenoma	>35%	Adv. adenoma	>40%
Detection rate of adenomas at FS	males	>10%	males	>15%
	females	>5%	females	>10%
PPV of FOBT at colonoscopy for advanced adenoma or carcinoma	first test	>25%	first test	>30%
	repeat tests	>15%	repeat tests	>20%
PPV of FS at colonoscopy for proximal advanced adenoma	>7%		>10%	
Delay between FOBT screening and negative result	>90% within 21 calendar days		>90% within 15 calendar days	
Delay between the call for assessment and the assessment procedure	>90% within 30 calendar days		>95% within 30 calendar days	
Proportion of screen-detected cancers in stage III+	<30%		<20%	

FOBT: Faecal Occult Blood Test; FS: Flexible Sigmoidoscopy; TC: Total Colonoscopy; PPV: Positive Predictive Value  
Adapted from Zorzi M et al., 2007.

Table 1: Indicators and reference standards.

test (FOBT), while some have adopted flexible sigmoidoscopy (FS) once in a lifetime, or a combination of both.

The results of FOBT programmes are reported in the following sections; data of FS programmes are presented in a specific section.

In order to describe the national situation, it is necessary to simplify the variability of the target population among the programmes, by narrowing the analysis to a homogeneous age group. Therefore, we provide the data related only to subjects aged 50-69 years, that are common to all FOBT programmes and constitute the real target population of most of them.

### Theoretical extension

Theoretical extension refers to eligible subjects residing in areas covered by organised screening programmes.

According to the National Institute of Statistics (Istat), at the beginning of 2007 approximately 14,250,000 people aged 50-69 years were living in Italy.<sup>4</sup> The number of subjects residing in areas where an organised screening programme is active was 6,634,000, with a national theoretical extension of 46.6%. This represents a small increase compared to the 44.3% observed in the previous year. Moreover important differences according to geographical area need to be pointed out (table 3).

Region	Programmes (N)	Invited subjects (N)	Actual extension*		Screened subjects (N)	Adjusted compliance**	
			(%)	10th-90th percentile		(%)	10th-90th percentile
Abruzzo	1	9,134	34.0	-	3,411	41.0	-
Campania	3	44,724	32.8	-	12,039	30.0	-
Emilia-Romagna	11***	469,786	92.8	64.9 – 104.7	217,753	47.2	37.0 – 59.6
Lazio	1	7,106	4.2	-	1,697	26.5	-
Lombardia	15***	1,308,856	104.0	80.2 – 126.4	532,868	42.7	33.4 – 57.6
Marche	1	3,742	22.9	-	1,647	44.9	-
Piemonte	5	36,329	59.7	-	11,098	30.5	-
Toscana	12***	303,878	65.7	23.6 – 88.2	126,131	48.7	34.5 – 61.3
Trentino	1***	1,191	1.7	-	410	43.4	-
Umbria	4***	117,344	100.3	89.5 – 125.9	47,745	44.0	40.6 – 46.2
Valle d'Aosta	1***	12,585	83.6	-	8,124	64.6	-
Veneto	17	270,158	62.9	31.3 – 100.2	168,977	65.0	45.2 – 76.4
<b>ITALY</b>	<b>72</b>	<b>2,584,833</b>	<b>79.1</b>	<b>23.3 – 106.4</b>	<b>1,131,900</b>	<b>46.3</b>	<b>32.6 – 65.8</b>

\* proportion of subjects who were sent an invitation to screening

\*\* subjects attending out of those invited, excluding from the denominator those reporting a recent test and those who did not receive the invitation letter

\*\*\* programmes on a regional-scale basis

Table 2: Main data of FOBT programmes by Region: 50-69 year old subjects.

Compared to the previous years, the northern and central Regions reported a further increase and their theoretical extension reached respectively 72% and 52% of their population. On the contrary, in the South of Italy and Islands only one new programme was activated (Avellino 2, in the Region of Campania) while two others had to stop their activity, including the regional programme of Basilicata, with a decrease in theoretical extension from 10% in 2006 to 7%.

### Extension of invitations

We define the extension of invitations as the proportion of half the resident population who was sent a screening invitation.

During 2007, about 2,585,000 subjects were invited to attend a screening programme, accounting for 37.1% of half the 14,250,000 people aged 50-69 years living in Italy (table 4), compared to 30% reported in 2006. Analysis by geographical macro-areas shows that most invitations were sent

	2004		2005		2006		2007	
	N	%	N	%	N	%	N	%
North	412,000	6.2	3,257,000	51.5	4,419,000	66.1	4,823,000	71.6
Centre	584,000	21.1	965,000	29.0	1,361,000	48.5	1,487,000	52.1
South-Islands	13,000	0.3	200,000	4.5	460,000	10.0	323,000	7.0
<b>ITALY</b>	<b>1,008,000</b>	<b>7.3</b>	<b>4,422,000</b>	<b>33.8</b>	<b>6,240,000</b>	<b>44.3</b>	<b>6,634,000</b>	<b>46.6</b>

Table 3: Subjects residing in areas covered by FOBT screening programmes and theoretical extension (proportion of eligible subjects residing in areas covered by organised screening programmes) by year and geographical area: 50-69 year old subjects.

	2004		2005		2006		2007	
	N	%	N	%	N	%	N	%
North	156,000	4.8	518,000	15.6	1,678,000	50.2	2,099,000	63.7
Centre	181,000	13.0	228,000	16.4	319,000	22.8	432,000	30.8
South - Islands	5,000	0.2	85,000	3.8	110,000	4.8	54,000	2.3
<b>ITALY</b>	<b>342,000</b>	<b>5.0</b>	<b>831,000</b>	<b>11.8</b>	<b>2,107,000</b>	<b>30.0</b>	<b>2,585,000</b>	<b>37.1</b>

Table 4: Subjects invited to FOBT screening and extension of invitations (proportion of half the eligible resident population who was sent an invitation to screening) by year and geographical area: 50-69 year old subjects.

in the North of Italy, where 2,614,000 subjects were invited (64% of half the resident population, compared with 50% in 2006). In 2007, extension of invitations in the Centre of Italy increased from 23 to 31%, while in the South and the Islands it decreased to 2.3%.

### Actual extension

Actual extension refers to subjects who were sent a screening invitation during 2007, based on the data provided by the national survey. In 2007, roughly 2,585,000 subjects were invited to undergo screening with FOBT, accounting for 79% of the annual target population (table 2).

This reflects the results obtained in Lombardia, where all programmes reached a very high extension of invitations, and in the Regions of Emilia-Romagna and Umbria.

A more detailed analysis shows that 10% of programmes with the lowest extension (10th percentile) invited less than 27% of their target. This is a definite improvement compared with the 10% reported in 2006, however it indicates the difficulty many programmes have in reaching and maintaining an adequate number of invitations. Overall only 54% programmes reached the GISCoR acceptable standard (>80%).

### Compliance to invitation

We report data on adjusted compliance, calculated as the proportion of subjects invited to attend screening (minus those with a wrong address and those excluded after invitation for a recent test) who underwent a screening test.

Overall about 1,131,900 people were screened with FOBT in 2007. Adjusted compliance (46.3%) slightly increased as compared to 2006 (44.6%).

In fact, this average poorly represents the huge variability among programmes, which ranged from 11% to 80%. The 10th percentile (33%) is clearly insufficient to guarantee suitable coverage of the population and, consequently, efficiency of a screening programme. Overall, 59% of pro-

grammes reached the acceptable (>45%) and only 14% the desired GISCoR standard (>65%).

The analysis of compliance by Region is particularly interesting (figure 2): despite a broad intra-regional variability, important differences are observed between Regions, with average values varying from 26.5% in Lazio to 65% in Veneto. Attendance by age and gender shows higher values in females (48.4% *vs* 43.9% for males), but

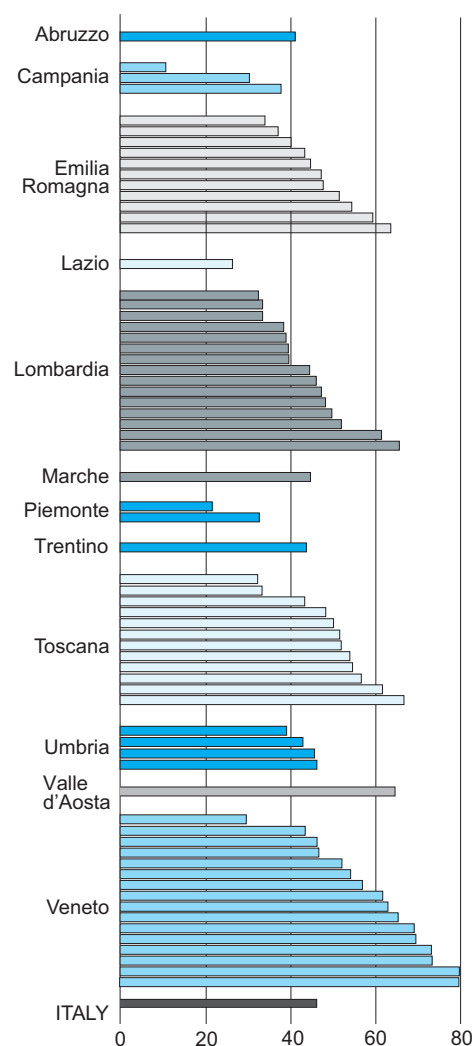


Figure 2: FOBT programmes: adjusted compliance of single programmes by Region.

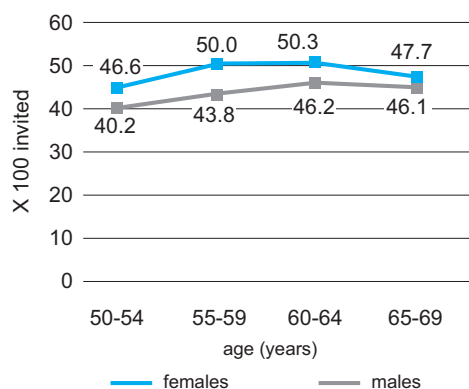


Figure 3: FOBT programmes: adjusted compliance by age and gender.

only in younger age groups (figure 3). Compliance to FOBT is highest in the central age groups and drops in the older groups. This trend was also observed in previous years and represents a warning for all screening programmes, since subjects who are more likely to refuse screening are those at greater risk of having a lesion.

It is of interest to analyse the attendance by screening history of invited subjects or, more precisely, by their history of attendance to invitation. After the prevalence round, programmes invited essentially three categories of people:

- subjects that had never been invited before (new entries to the target population: essentially 50 years old subjects and immigrants);
- subjects who had already attended a previous invitation (from which a high attendance may be expected);
- subjects that had already been invited, but never attended (who are less likely to comply).

The attendance of subjects invited for the first time was 44.5% with a trend by sex and age similar to the global one. Eighty-six percent of subjects who had already attended responded to the new invitation, without any difference by age or sex. It must be pointed out that attendance of the 10% of programmes with the worst value was lower than 76%. Finally, attendance of subjects who had never re-

sponded to previous invitations was 19.3% and decreased from the youngest (21%) to the oldest (11%) age group.

### Diagnostic indicators

The most important diagnostic indicators (positivity rates, detection rates, positive predictive values) are strongly influenced by the underlying frequency of the disease in the screened population. Colorectal cancer and pre-cancerous lesions are more frequent in males than females, and tend to increase progressively with age in both genders.<sup>5</sup> Moreover, the disease is more frequently detected in subjects at first screening test (prevalence round) than in those at repeat tests (incidence round).

Therefore, these indicators are presented separately for subjects at first and repeat screening tests, as well as by gender and five-year age groups.

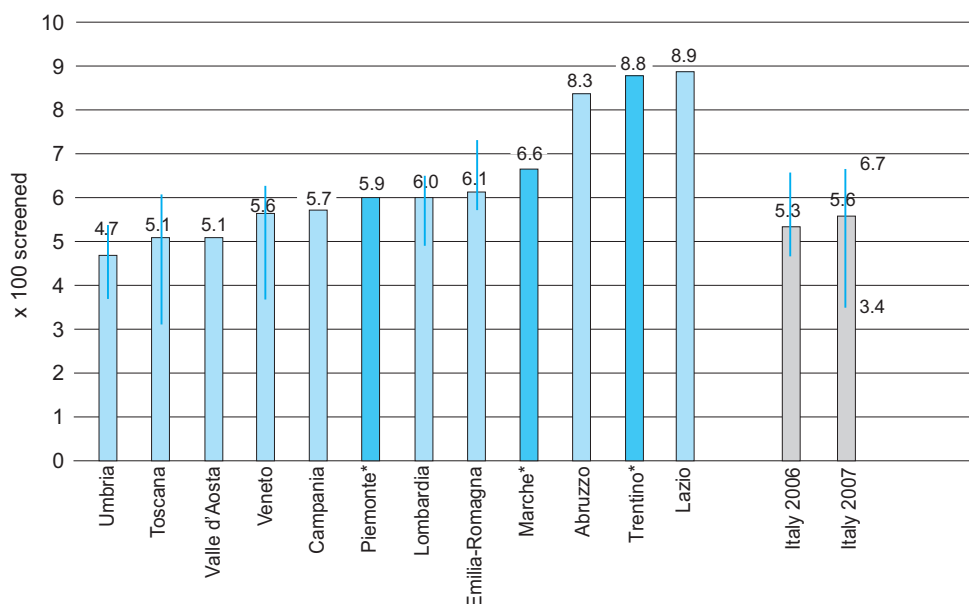
The mean values of these indicators by Region are standardised by age and gender, using the national mean as standard population. Standardisation was carried out for subjects at first screening test, since a noteworthy variability in the distribution of screened subjects according to age and gender was observed among the programmes. Such variability was essentially due to the newly activated programmes preferentially inviting subjects in older age groups. In subjects at repeat screening, we observed an elevated homogeneity among programmes and therefore we did not standardise the indicators.

We present percentiles only of Regions with more than four programmes.

The data refer to 1,143,759 subjects screened during 2007 for which data are available; of these, 914,029 (80%) underwent first screening and 229,730 (20%) subsequent examinations.

### Positivity rates

In subjects at first screening, the proportion of positive FOBT was 5.6%, with an elevated homogeneity among the mean values of Regions with a large number of screenees (figure 4). The propor-



\* not standardised: Piemonte and Trentino only screened subjects aged 60+; Marche did not provide data by age class

Figure 4: Standardised (by age and gender, utilising the national media as standard population) proportion of FOBT+ at first screening. Average, 10th and 90th percentiles by Region.

tion of FOBT+ reported by each programme ranges from 3.4% to 11.3% (10th-90th percentiles: 3.4-6.7%).

In subjects at repeat screening, the proportion of FOBT+ is 4%, with a lower variability between programmes (range: 3.0-5.9%).

Seventy-three percent of programmes met the acceptable standard at the first (<6%) exam and 68% at repeat exams (<4.5%).

As shown in figure 5, the proportions of positive results are higher in males at both first and repeat examinations, and they increase progressively with age. The reduction in FOBT+ between first and repeat exams is larger in males, and increases progressively with age.

These data are particularly useful to forecast the workload of endoscopies for programmes about to conclude their first round of screening and ready to start re-inviting subjects with a previous negative test.

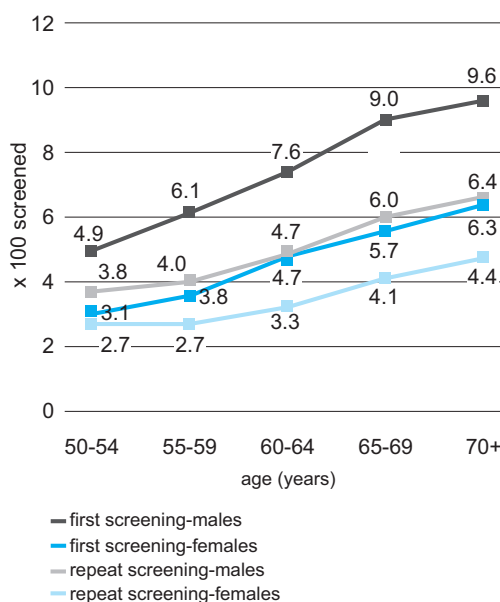


Figure 5: Proportion of FOBT+ by age and gender.



### Inadequate tests

Inadequate tests are essentially due to an incorrect sampling by the subject. During 2007, 90% programmes reported a proportion of inadequate FOBT lower than 1%, while only two programmes reported a result exceeding 2%. Overall, the national mean value was 0.3%. Some programmes reported inadequate tests due to a mismatch of the specimen with the subject.

### Attendance to colonoscopy assessment

Attendance to colonoscopy assessment is essential for screening programmes to achieve colorectal cancer mortality reduction. Overall, 78.7% of FOBT+ subjects attended colonoscopy in 2007. This result is lower than that observed in 2005 and 2006 (81.9% and 81.2%, respectively). Only 22% of programmes met the desired standard (>90%).

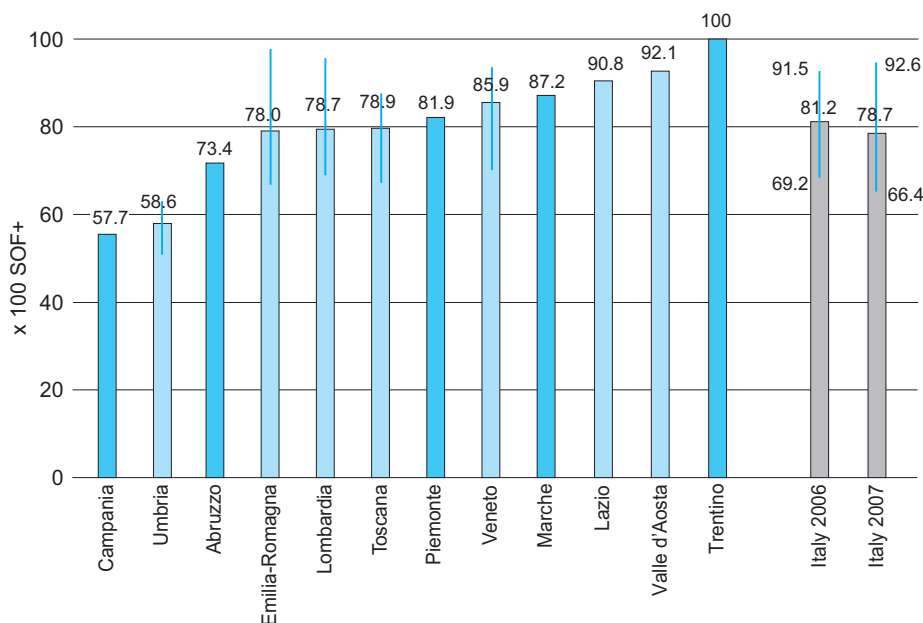
Attendance was higher in males (80%) than in females (77.4%). This has been described in the lit-

erature.<sup>6</sup> Some studies explored the reasons for non-attendance also in screening settings. One of the most important reasons is a feeling of shame. Women, as a matter of fact, reported some concern about the gender of the endoscopist, who is usually a man.<sup>7,8</sup>

The Regions of the Centre and South of Italy (Campania, Umbria, Abruzzo) reported the lowest values, the Regions of Trentino, Valle d'Aosta and Lazio the highest (figure 6). Some programmes could not specify what proportion of non-attendees received a colonoscopy in non-screening centres. The value might be underestimated due to a delay in colonoscopy data collection or in data flow towards the information technology screening systems.

### Complete colonoscopies

Besides compliance to colonoscopy, a cornerstone element in measuring the effectiveness of a screening programme is the completeness of the endo-



Note. Deep orange columns refer to Regions whose indicators are based on a limited number of cases.

Figure 6: FOBT programmes. Compliance to colonoscopy: average, 10th and 90th percentiles by Region.



scopic examination. Overall, 91.6% of the colonoscopies carried out in 2007 were classified as complete, a highly satisfactory result. Eighty-nine percent of programmes met the acceptable (>85%) and 76% the desired standard (>90%). The high variability among Regions reported in the previous years was much reduced, with mean regional values ranging from 87.2% in Lazio and 100% in Campania and Abruzzo (in the latter two Regions the number of exams performed was quite low). The values of single programmes ranged from 64.7% to 100% and the lowest values were due to few outliers (10th percentile: 84.8%).

All programmes reported higher proportions of complete exams in males compared to females (overall 92.5% *vs* 90.4%, respectively), as reported in the literature.<sup>9</sup>

Fifty-two programmes reported data about further assessments in case of an incomplete TC, which took place in 69.1% of cases. Fifty-nine percent of cases underwent a further colonoscopy, 41% a barium enema or a computed tomographic colonoscopy.

### Complications at colonoscopy

Forty programmes reported the data about complications at TC, relative to 34,624 examinations overall. Complications reported included 190 cases of bleeding (0.55%, 10th-90th percentiles 0-1.4%), as well as 27 perforations (0.08%, 10th-90th percentiles 0-0.18%).

These results meet the GISCOR standard (<0.5% for non-operative and <2.5% for operative TCs for all kinds of complications). However, a high variability in recording criteria was observed. Most programmes do not provide a systematic data collection at a fixed interval after the examination (e.g., 30 days), possibly resulting in an underestimation of complications, including the most serious ones. On the other hand, the data about bleeding might refer to self-limiting episodes that did not require any intervention such as hospitalisation, blood transfusion, or endoscopic interventions. In that case the indicator would be overestimated.

### Detection rates

We describe the detection rates (DR) of invasive carcinomas, advanced adenomas (i.e., adenomas with a diameter  $\geq 1$  cm, with villous/tubulo-villous type, or with high-grade dysplasia), and non-advanced adenomas (smaller in size, tubular type, and low grade dysplasia). DRs are defined as the number of histologically-confirmed lesions detected per 1,000 screened subjects.

Overall, in subjects screened for the first time 2,449 carcinomas, 11,280 advanced adenomas, and 7,067 non-advanced adenomas were detected. Therefore the DR was 2.7‰ for carcinoma, 12.2‰ for advanced adenomas, and 7.7‰ for non-advanced adenomas (figure 7). Seventy-four percent of programmes reached the acceptable standard for carcinoma (>2‰), and 79% for advanced adenoma (>7.5‰).

However, the ratio between the DRs of advanced and non-advanced adenomas does not reflect the underlying prevalence of the two groups of lesions in the screened population, the frequency of non-advanced adenomas being higher than that of advanced adenomas. The DR of advanced adenomas is higher since FOBT appears to be highly selective for these lesions that tend to bleed more

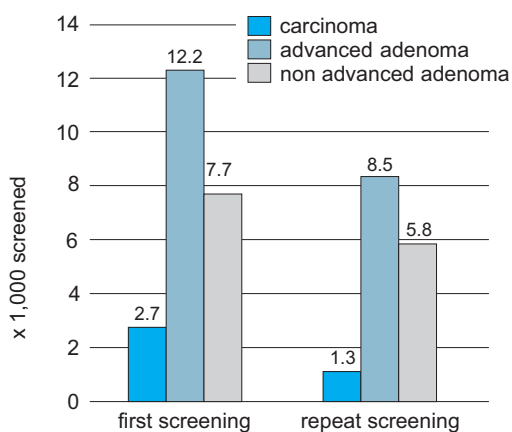


Figure 7. FOBT programmes. Detection rates of carcinoma, advanced adenoma and non-advanced adenoma at first and repeat screening.

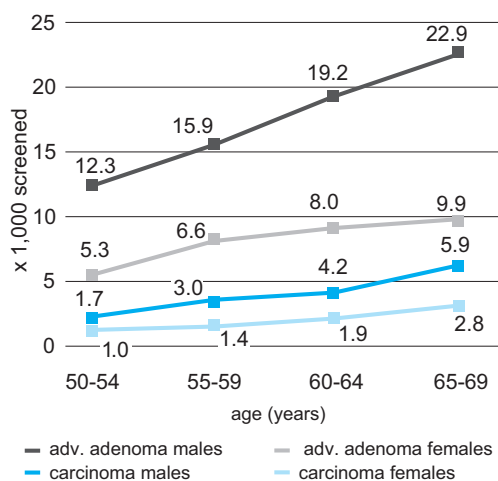


Figure 8. FOBT programmes. Detection rates of carcinoma and advanced adenoma by age and sex at first screening.

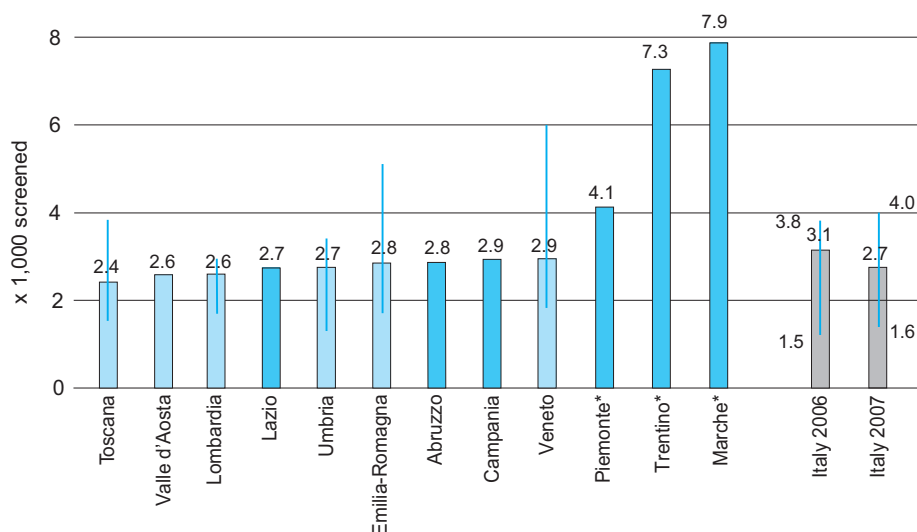
easily than non-advanced adenomas, as described in the literature.<sup>10</sup>

In subjects undergoing repeat testing, 295 carcinomas, 1,824 advanced adenomas and 1,334

non-advanced adenomas were detected. As expected, the DRs were lower than the corresponding figure at first testing (DR of carcinoma 1.3‰, advanced adenomas 8.5‰ and non-advanced adenomas 5.8‰, figure 7). Seventy-seven percent of programmes reached the acceptable standard for carcinoma (>1‰), and 83% for advanced adenoma (>5‰).

As expected on the basis of underlying epidemiological figures, the DRs of the different lesions are higher in males and progressively increase with age in both genders (figure 8). This trend may be observed both in subjects screened for the first time and in those at repeat screening, even if with lower values (data not shown).

With the exception of Regions with unstable data due to the limited number of screened subjects, we observed little difference between the mean regional values of DRs of carcinoma (from 2.4‰ in Toscana to 2.9‰ in Veneto, figure 9), while those of advanced adenomas showed a



\* not standardised: Piemonte and Trentino only screened subjects aged 60+; Marche did not provide data by age class

Note. Deep orange columns refer to Regions whose indicators are based on a limited number of cases.

Figure 9. FOBT programmes: standardised (by age and gender, utilising the national media as standard population) detection rates of carcinoma at first screening. Average, 10th and 90th percentiles by Region.

higher variability (Umbria 8.3‰, Valle d'Aosta 15.5‰, [figure 10](#)).

### Positive predictive value

Positive predictive value (PPV) of FOBT+ at colonoscopy is defined as the number of subjects with a diagnosis of carcinoma or advanced adenoma, as a proportion of FOBT+ subjects that underwent colonoscopy.

In 2007, the FOBT showed a noteworthy capability of selecting subjects with a high risk of invasive carcinoma or advanced adenoma, as already reported in the previous years. In fact, among the 39,864 subjects at first screening round who underwent a colonoscopy after a FOBT+, a diagnosis of carcinoma was formulated in 6.1% and an advanced adenoma in a further 29.9% ([figure 11](#)). Among the 7,765 subjects at repeat screening, the corresponding values were respectively 3.9% for carcinoma and 25.5% for advanced adenoma. Eighty-one percent of programmes reached the acceptable standard for subjects at first screening

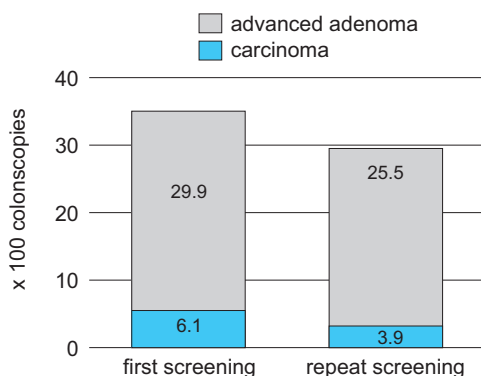
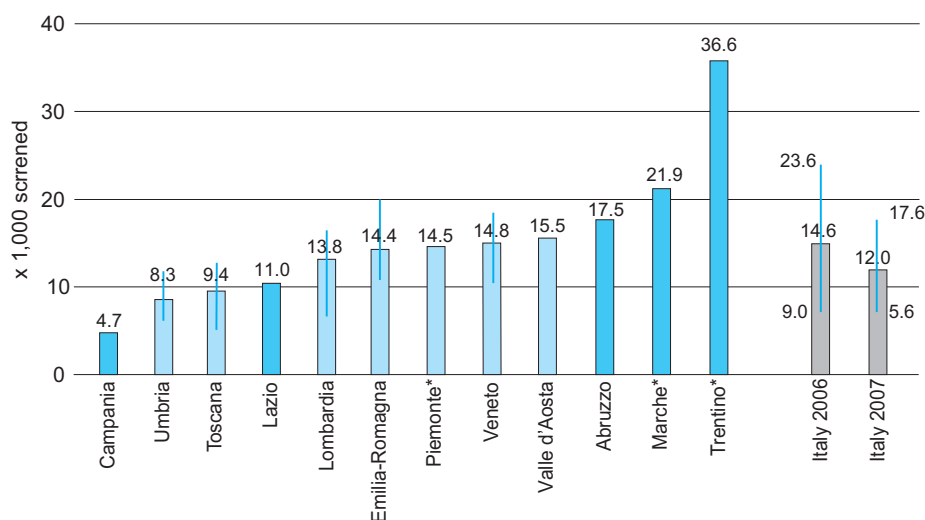


Figure 11: FOBT programmes: positive predictive value (PPV) of FOBT+ at colonoscopy for carcinoma and advanced adenoma at first and repeat screening.

(>25%) and 90% for repeat screening (>15%). Similar values had also been observed in the previous years.

Once again, males showed consistently higher values than females and an increasing PPV trend was observed with age, but only for carcinoma ([figure 12](#)).



\* not standardised: Piemonte and Trentino only screened subjects aged 60+; Marche did not provide data by age class

Note. Deep orange columns refer to Regions whose indicators are based on a limited number of cases.

Figure 10. FOBT programmes: standardised (by age and gender, utilising the national media as standard population) detection rates of advanced adenoma at first screening. Average, 10th and 90th percentiles by Region.

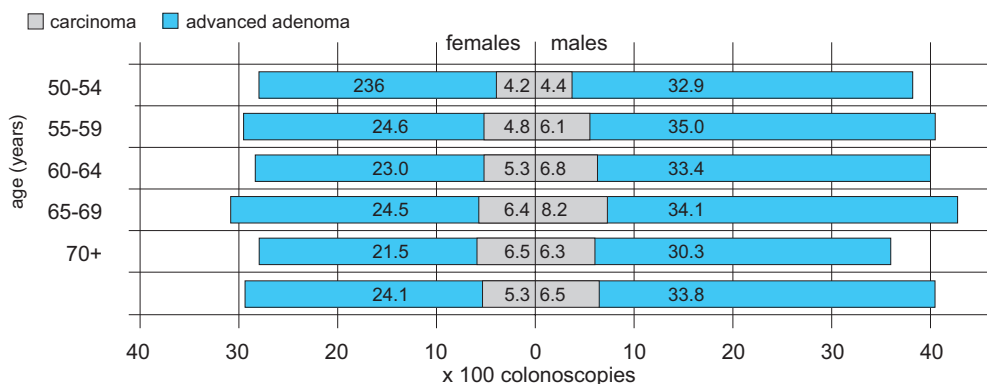


Figure 12. FOBT programmes: positive predictive value (PPV) of FOBT+ at colonoscopy for carcinoma and advanced adenoma by age and gender at first exams.

### Waiting times

In order to reduce the anxiety of screened subjects, the delay between the test and the mailing of a negative result or the carrying out of a further assessment for those positive must be kept as short as possible. Since FOBT is a laboratory test, it can be carried out quite quickly (as compared to the reading of mammograms and Pap smears), therefore the delay between the test and the mailing of a negative result is generally short. In fact, almost 90% of letters after a negative result were mailed within 21 days.

On the contrary, we recorded serious difficulties in guaranteeing a colonoscopy to FOBT+ subjects within a short period of time. Overall, colonoscopy was carried out within 30 days after FOBT only in 41% of cases (56% in 2006) and only 13% programmes met the acceptable standard (>90% within 30 days). Fifteen percent of subjects had to wait more than two months. The situation was particularly problematic in Lombardia, Veneto and Umbria, where 28.5%, 26.7%, and 22%, respectively, of subjects had to wait for more than two months.

### FS screening programmes

FS is proposed as a first level test by 5 programmes in Piemonte and 2 in Veneto. Three of these programmes also offer FOBT to subjects refusing FS

screening and to those up to 69 years of age. The principal data are presented in table 6. Overall, during 2007, the 7 programmes invited 32,159 subjects, corresponding to a 66.5% actual extension over their target population ( $n = 48,450$ ). Three programmes showed values equal to 100% (Alessandria, Novara, and Verona), while another two (Collegno-Pinerolo and Padova) had very low levels (22% and 25%, respectively).

Taking all programmes together, 8,678 subjects were screened with FS. Compliance to invitation was 27.7% (range 17.6%-38.1%), slightly lower than that reported in 2006 (29.2%). In all programmes, compliance was higher for males in comparison to females (overall: 29.4% *vs* 26.1%), as currently reported in the literature.

Compliance to FS screening was lower than for FOBT. However, the comparison is related to different geographical areas. Some programmes offer FOBT to subjects refusing FS screening. This strategy makes it possible to increase the overall coverage and to reduce gender differences. In Torino the proportion of subjects who underwent at least one test was 37% in both sexes.

Since FS is performed on a "once in a lifetime" basis, the proportion of complete exams should be as high as possible. On the other hand, caution must be taken to avoid perforations, bleeding, or other complications. Overall, 88% of FSs were

classified as complete, with a considerably high variability between programmes (range: 75-93%). The proportion of complete exams was higher in males (90%) than in females (82%).

Generally, the programmes referred 14.3% of screened males and 7.3% of females, respectively, to colonoscopy assessment. Only in less than half the cases was the reason prompting colonoscopy an advanced adenoma, which, according to the literature, is associated with an increased probability of neoplasia in the proximal colon.

The overall attendance rate of the assessment (90%) was higher than that observed for the FOBT screening, probably due to a greater motivation of the subject to undergo further assessment following a diagnosis of advanced adenoma. Colonoscopy completeness rate was 92.7%, and all centres reached high levels (range 88.8-100%). Among the subjects referred to colonoscopy, the prevalence of proximal advanced lesions (advanced adenomas plus cancers) ranged between 2% and 8%.

Overall, FS programmes detected 38 carcinomas, of which 35 in the distal tract of the colon, and 483 advanced adenomas, with a DR of 4.4‰ and 58.4‰, respectively. In accordance with the risk

of disease, a higher prevalence of colorectal cancer, advanced and non-advanced adenomas is evident in males than in females.

When comparing the DRs of FS and FOBT programmes, we observed a higher sensitivity of FS for adenomas (the DRs are more than 10 times higher for non-advanced adenomas and almost 5 times higher for advanced adenomas), while the difference is much lower for carcinoma. However, the interpretation of these data is limited by the different age of screened subjects.

### Stage at diagnosis

Overall, 2,449 cancers were detected in subjects at first screening and 295 at repeat screening. Sixty programmes reported the information about cancerised adenomas, which represented 24.8% of cancers at first screening and 30.4% at repeat screening. FS programmes detected 38 cancers, 7 of which were cancerised adenomas.

As already observed in the previous years, many programmes did not collect any data about stage at diagnosis, while information provided by others is incomplete. Therefore, stage is available only for 1,788 cases (65.2% of the total). The incompleteness of this information is one of the

	Males	Females	Total
Screened (n)	4,489	4,189	8,678
Reason prompting colonoscopy (%)			
advanced adenoma*	7.6	3.2	5.4
other**	6.7	4.4	5.7
Detection rate (‰)***			
carcinoma	6.2	2.4	4.4
advanced adenoma	74.0	36.0	58.4
non advanced adenoma	104.0	70.7	92.2
PPV (%)****			
carcinoma	0.5	0.0	0.3
advanced adenoma	7.1	1.5	4.1
* at least one advanced adenoma (with a diameter $\geq 1$ cm, with villous/tubulo-villous type or with high-grade dysplasia); 3 or more adenomas with diameter $< 10$ mm, with tubular type and low grade dysplasia; carcinoma			
** all centres: inadequate preparation with adenoma; Verona: at least one adenoma or polyp $\geq 5$ mm			
*** estimates			
**** proximal colon			

Table 6: Main results of FS programmes.

most critical issues of Italian programmes encountered during 2007.

**Table 7** shows the distribution by stage at diagnosis of cases screen-detected by FOBT and FS programmes. Overall the results are very similar, except for a higher proportion of cancerised adenomas at repeat FOBT. That difference comes to naught when excluding the programmes that do not have any cases at repeat screening.

Overall, 25% of cases were in stage III+ at diagnosis, in accordance with the acceptable standard (<30%).

In particular, no differences were reported between cases at first and repeat screening. This could be due to the cases that are not detected by FOBT at the first screening round.

Stage distribution is distinctly better than a clinical series observed in the absence of organised programmes, 40 to 50% of which were in stage III+ at diagnosis.

## Discussion

During 2007, the theoretical extension of colorectal cancer screening showed a very small increase as compared to 2006. After the activation of numerous programmes starting from 2004, only five new programmes started during 2007 and three others had to stop their activity, including the regional-scale programme of Basilicata. The delays that are taking place in the South of Italy and the Islands should be pointed out: no programmes

were active in five Regions of this area as of the end of 2007.

Compared to 2006, actual extension further increased to almost 80% of the target population to be invited within the year. In some Regions, all programmes reached the desired level of extension. This shows that adequate planning and resource raising are possible, in order to achieve the desired volumes of activity.

However, the huge variability in extension between programmes underpins a chronic difficulty of many programmes started in previous years in reaching and maintaining the biennial invitation rate. This determines a lengthening of the inter-screening interval with possible effects on a programme's efficacy.

Uptake of invitation increased to 46.3%, compared to that observed in 2006. However, the very low values that affect many programmes, particularly when associated with a limited extension of invitations, are of particular concern, as in some cases the combined effect of these two elements makes the proportion of the target population that has been effectively screened marginal.

Intra-regional attendance showed high levels of variability, which suggests the possibility of increasing the performance of many programmes.

The analysis of attendance by the history of compliance to previous invitations allows a deeper insight into this indicator. The average value depends on the specific attendance of subjects that had never been invited before, of subjects who had already attended a previous invitation, and of those that had already been invited, but never attended, and on the relative weight of these three groups.

During 2007, about half of the programmes had already activated a new round and reported separate data.

In a biennial FOBT screening, a salient issue is whether or not the attendance of invited people can be sustained over time. Data from randomised trials showed that uptake tends to decline round

Stage	FOBT programmes		FS programmes (n=33)
	first screening (n=1517)	repeat screening (n=238)	
I	40.8	36.6	33.3
I*	13.4	20.6	15.2
II	21.1	17.6	24.2
III-IV	24.8	25.2	27.3
Stage I: T1 or T2, N0, M0			
Stage I*: T1 NX			
Stage II: T3 or T4, N0, M0			
Stage III-IV: lymphnode involvement or distant metastases			

Table 7. Stage distribution of screen detected cancers (%). Cases with known stage.

by round.<sup>11</sup> Overall, 13% of the subjects that attended a screening episode did not respond to the subsequent invitation.

We did not observe any differences by age or gender: this suggests that the experience of the previous screening episode becomes the main driver for subsequent attendance, so that the effect of other factors, which influence the attendance to the first invitation, ceases.

The low attendance (19%), recorded by subjects that had already been invited but never attended, reflects both the possibility to enrol higher risk subjects (because they had never been screened) and the presence of a group of people wayward to screening. Programmes should evaluate whether to deal with this problem by introducing *ad hoc* invitation strategies, given the scarce efficacy of the traditional invitation by mail.

The proportion of FOBT+ is quite homogeneous among programmes (apart from those with a low volume of activity), particularly at repeat screening. The variability observed in the first screening round can be partly attributed to a possible self-selection of symptomatic subjects, especially where attendance rates are low.

Particular attention should be given to attendance to colonoscopy that decreased from 81.2% in 2006 to 78.7% in 2007. Probably the real proportion of FOBT+ subjects that did not undergo any further assessment is lower, since many programmes did not collect data about assessments performed in non-screening devoted structures. However, it must be stressed that it is precisely the duty of screening programmes not only to reach high levels of attendance to colonoscopy, but also to make sure that FOBT+ subjects have undergone assessment, even if outside the programme. The data reported in 2007 suggest that many programmes did not deal with this aspect.

A further aspect to analyse in future surveys will be the relationship between attendance to colonoscopy and the use of sedation.

Attendance to colonoscopy may also be negative-

ly affected by a long waiting time for the performance of examinations. In 2007, we observed a generalised difficulty for endoscopic services to deal with the excess workload deriving from the screening positives.

Compared with 2006, we observed a reduction in the DR of carcinoma (2.7‰ vs 3.1‰) and advanced adenoma (12.2‰ vs 14.6‰) at first screening. This is not worrisome, since the number of programmes that have ended the first round is progressively increasing. At subsequent rounds, a high proportion of the population that undergoes the screening test for the first time is represented by fifty-year-old subjects, which are at lower risk of disease.

The fluctuations in DRs observed between programmes suggest the presence of other factors responsible for this aspect other than the diagnostic sensitivity of the screening programme.

Since DRs are calculated dividing the diagnosed lesions by the screened population, they are inversely associated to the loss of attendance to colonoscopy. Different criteria to classify adenomas as advanced or non-advanced are used by programmes. Finally, some programmes suffer from a weakness in the link between the clinical component (pathologists and endoscopists) and data managers, who sometimes have to classify and register the lesions without any medical advice.

Analysis of the PPV of FOBT+ at colonoscopy confirms the high values reported in the previous years.

According to these findings, it is essential that screening programmes adopt strategies in order to maximise colonoscopy attendance, or to be sure that subjects with a positive FOBT undergo further diagnostic assessment in non-screening devoted structures.

Concerning FOBT screening, the performance of the diagnostic phase was consistent with other international experiences. Nevertheless, comparing Italian results with data emerging from the first round of the UK Pilot study (see [table 8](#)), impor-



tant differences were evident.<sup>12</sup> Positivity rates were much higher in Italian programmes but, on the other hand, detection rates for cancer and for adenoma in the UK study were lower than those observed in Italy. In addition, although the Italian positivity rate was higher, the positive predictive values for cancer of a positive test result were similar to those registered in the UK study, given the large number of lesions detected by a more sensitive test.

### Final considerations

The present survey still provides insufficient information regarding colonoscopy and surgical treatment. Many programmes provided largely incomplete data for the second assessment level and surgery, therefore the related indicators were not calculated. Second level assessment and therapy are integral parts of screening and their monitoring is necessary to ensure high screening quality, but many of these programmes fail to control them.

Moreover, many screening programmes are conducted without the use of adequate statistical software modules.

Another aspect to be considered is the short delay between the end of the period of interest in

the survey and the deadline for sending the data. In colorectal cancer screening the diagnostic and therapeutic process may be very long, due to the waiting time for assessment, repetition of the exam in some cases, and the waiting time for the pathological diagnosis and surgery. This may determine a selective loss of the cases with more advanced lesions that on average require longer diagnosis and treatment processes. Thus, some important indicators may be underestimated.

Collection of interval cancers and evaluation of the follow-up of advanced adenomas are two further important aspects in the assessment of colorectal cancer screening programmes; both require *ad hoc* surveillance systems that are beyond the objectives of the present survey.

### Data for colorectal survey for the year 2007 were provided by:

ABRUZZO: A. Sedici (Avezzano Sulmona)

CAMPANIA: A. Chianca

EMILIA-ROMAGNA: C. Naldoni. P. Sassoli de' Bianchi

LAZIO: A. Barca, D. Baiocchi, F. Quadri

LOMBARDIA: B. Pesenti (Bergamo);

C. Scotti (Brescia); M. Gramegna (Como);

M. Dal Soldà (Cremona); V. Gabriele (Lecco);

G. Marazza (Lodi); M. Arvati (Mantova); E. Tidone,

N. Leonardo (Milano città); M. Bersani (Milano 1);

L. Fantini (Milano 2); M. Ignone (Milano 3);

G. Magenes (Pavia); L. Cecconami (Sondrio);

F. Sambo (Varese); L. Pasquale (Vallecampa)

MARCHE: C. Mancini

PIEMONTE: C. Senore

TOSCANA: P. Mila, G. Tornabene (Massa e

Carrara); S. Coccioli, D. Giorgi (Lucca); M. Rapanà,

L. Ieri (Pistoia); F. Cipriani, L. Abdelghani,

C. Epifani (Prato); M. Perco (Pisa); P. Lopane,

C. Maffei (Livorno); R. Turillazzi (Siena); F. Mirri

(Arezzo); R. Rosati (Grosseto); G. Grazzini,

C. Visioli, P. Falini (Firenze); L. Rossi,

D. Marovelli (Empoli); C. Ciabattini (Viareggio),

	UK Pilot study	Italy 2007
Test	guaiac	immunochemical
Participation (%)	56.8	44.5
Positivity rate (%)	1.9	5.6
Detection rate (%) cancer neoplasia*	1.6 6.9	2.7 22.6
PPV (%) cancer neoplasia*	10 46	6 53
Compliance to colonoscopy (%)	82.2	78.7
* carcinoma or advanced adenoma or non-advanced adenoma		

Table 8: UK Pilot study (first round) and Italian FOBT screening programmes (first exams): comparison of the main results.

TRENTINO: E. Barberi

UMBRIA: G. Vinti (Città di Castello); D. Antonini (Foligno); M. Malaspina (Perugia); R. Corvetti (Terni)

VALLE D'AOSTA: S. Crotta

VENETO: D. Dal Santo, S. Saccon (Alto Vicentino);

G. Diacono (Asolo); S. Di Camillo, R. Mel (Belluno);

A. Ganassini, C. Fedato (Bussolengo); S. Callegaro (Camposampiero Cittadella); M.L. Polo (Chioggia);

A. Montaguti (Dolo); M. Gennaro, F. Talpo (Este Monselice); C. Fedato (Feltre); S. Soffritti (Legnago);

G. Caldonazzo, V. Mecenero (Ovest Vicentino);

F. Sambo (Padova); T. Moretto (Pieve di Soligo);

A. Stomeo (Rovigo); M. Bovo (Treviso); A. Favaretto

(Veneto Orientale); M.C. Chioffi, L. Benazzato

(Verona); A. Dal Zotto (Vicenza)

## References

1. Zorzi M, Falcini F, Fedato C et al. Screening for colorectal cancer in Italy: 2006 survey. *Epidemiol Prev* 2008; 32(2) Suppl 1: 55-68. Available at [http://www.osservatorionazionale screening.it/ons/pubblicazioni/altre\\_ons.htm](http://www.osservatorionazionale screening.it/ons/pubblicazioni/altre_ons.htm)
2. Zorzi M, Barca A, Falcini F et al. Screening for colorectal cancer in Italy: 2005 survey. *Epidemiol Prev* 2007; 31(2-3) Suppl 2: 49-60. Available at [http://www.osservatorionazionale screening.it/ons/pubblicazioni/altre\\_ons.htm](http://www.osservatorionazionale screening.it/ons/pubblicazioni/altre_ons.htm)
3. Zorzi M, Sassoli de' Bianchi P, Grazzini G, Senore C e Gruppo di lavoro GISCoR sugli indicatori. Quality indicators for the evaluation of colorectal cancer screening programmes. *Epidemiol Prev* 2007; 31(6) Suppl 1: 6-56. Available at [http://www.osservatorionazionale screening.it/ons/pubblicazioni/altre\\_ons.htm](http://www.osservatorionazionale screening.it/ons/pubblicazioni/altre_ons.htm)
4. <http://demo.istat.it/pop2007/index.html>
5. AIRT Working Group. Italian cancer figures – Report 2006. Incidence, mortality and estimates. *Epidemiol Prev* 2006; 30(1) Suppl 2: 38-41.
6. Wardle J, Miles A, Atkin W. Gender differences in utilization of colorectal cancer screening. *J Med Screen* 2005; 12: 20-22.
7. Farraye FA, Wong M, Hurwitz S et al. Barriers to endoscopic colorectal cancer screening: are women different from men? *Am J Gastroenterol* 2004; 99: 341-49.
8. Brotherstone H, Vance M, Edwards R et al. Uptake of population based flexible sigmoidoscopy screening: a nurse-led feasibility study. *J Med Screen* 2007; 14: 76-80.
9. Segnan N, Senore C, Andreoni B et al, SCORE2 Working Group-Italy. Randomized trial of different screening strategies for colorectal cancer: patient response and detection rates. *J Natl Cancer Inst* 2005; 97(5): 347-57.
10. Ciatto S, Martinelli F, Castiglione G et al. Association of FOBT-assessed faecal Hb content with colonic lesions detected in the Florence screening programme. *Br J Cancer* 2007; 96(2): 218-21.
11. Hewitson P, Glasziou P, Watson E et al. Cochrane systematic review of colorectal cancer screening using the fecal occult blood test (hemoccult): an update. *Am J Gastroenterol* 2008; 103(6): 1541-49.
12. UK Colorectal cancer screening pilot group. Results of the first round of a demonstration pilot of screening for colorectal cancer in the United Kingdom. *BMJ* 2004; 329; 133-35.

## Programmes participating in the survey

Programme	Head of the programme
<b>Abruzzo</b>	
Avezzano Sulmona	A. Sedici
<b>Campania</b>	
Avellino 2	V. Landolfi
Salerno 1	V. Gallo, A. Caiazzo, G. Storti
Salerno 2	A. Rossi, M.G. Panico
<b>Emilia-Romagna</b>	
AUSL Piacenza	F. Fornari, E. Borciani, G. Gatti
AUSL Parma	C. Zurlini
AOSP Parma	A. Franzè, M. Zatelli, F. Maradini
AUSL Reggio Emilia	L. Paterlini, C. Campari
AOSP Reggio Emilia	R. Sassatelli, C. Campari
AUSL Modena	R. Corradini, C. Goldoni
AUSL Bologna	N. Collina, M. Manfredi, N. D'Imperio, V. Eusebi
AOSP Bologna	F. Bazzoli
AUSL Imola	R. Nannini, L. Caprara
AUSL Ferrara	G. Zoli, M.C. Carpanelli, O. Buriani
AOSP Ferrara	V. Matarese
AUSL Ravenna	O. Triossi, M. Serafini, B. Vitali
AUSL Forlì	F. Falcini, B. Piantini, O. Giuliani
AUSL Cesena	P. Pazzi, M. Palazzi, C. Imolesi
AUSL Rimini	M. Giovanardi, D. Canuti, C. Casale, C. Fava
<b>Lazio</b>	
Policlinico Universitario	
Campus Biomedico	F. Bartolozzi
Istituti Fisioterapici	
Ospitalieri-Regina Elena	V. Stigliano
Roma D	P. Grammatico
AO San Camillo	
- Forlanini	R. Mangiarotti
AO San Filippo Neri	L. Capurso
Viterbo	M. Anti, S. Brezzi
Rieti	G. Baldi, F. Barberani
Latina	P. Bellardini, F. Gagliardi, A. Sgrò
Frosinone	M. Di Cicco, L. Martufi, G. Paliani
<b>Lombardia</b>	
Bergamo	R. Paginoni, G. Rocca, L.
Tessandri	
Brescia	C. Scotti
Como	M. Gramegna
Cremona	L. Boldori
Lecco	N. Devecchi
Lodi	A. Belloni
Mantova	E. Anghinoni
Milano città	L. Bisanti
Provincia Milano 1	ME. Pirola, P. Ceresa
Provincia Milano 2	L. Fantini
Provincia Milano 3	M. Ignone
Pavia	L. Campana, G. Magenes
Sondrio	L. Ceconami
Vallecarnonica	L. Pasquale
Varese	F. Sambo

Programme	Head of the programme
<b>Marche</b>	
Fano	M. Agostini
<b>Piemonte</b>	
Alessandria	G. Faragli
Biella Vercelli	N. Lorenzini
Collegno Pinerolo	M. Sartori
Novara	P. Bestagini, G. Pretti
Torino	C. Senore
<b>Toscana</b>	
Arezzo	F. Mirri, P. Ceccatelli
Empoli	L. Rossi, M. Biagini
Firenze	G. Grazzini, C. Visioli, F. Franceschini
Grosseto	R. Rosati, S. Quaranta, A. Rechichi
Livorno	P. Lopane, C. Maffei, G. Niccoli
Lucca	G. Finucci, S. Cocciolo, G. Gujana
Massa Carrara	U. Bola, M. Panichi, F. Pincione
Pisa	G. Venturini, M. Perco, V. Calvaruso
Pistoia	A. Natali, M. Rapanà
Prato	A. Battaglia, F. Cipriani, A. Candidi Tommasi
Siena	R. Turillazzi, P. Galgani, A. Ciarrocchi
Viareggio	C. Ciabattoni, U. Ferro
<b>Trentino</b>	S. Piffer
<b>Umbria</b>	
Città di Castello	D. Felicioni
Foligno	A. Di Marco
Perugia	B. Passamonti, M. Malaspina
Terni	R. Corvetti
<b>Valle d'Aosta</b>	S. Crotta
<b>Veneto</b>	
Alto Vicentino	F. Banovich
Aso	O. Bertipaglia
Belluno	R. Mel
Bussolengo	A. Bortoli
Chioggia	ML. Polo
Dolo Mirano	A. Montaguti
Este Monselice	M. Penon
Feltre	L. Cazzola
Legnago	S. Soffritti
Ovest Vicentino	V. Mecenero
Padova	F. De Lazzari
Pieve di Soligo	S. Cinquetti
Rovigo	L. Gallo
Treviso	M. Pieno
Veneto Orientale	A. Favaretto
Verona	P. Costa, A. Ederle
Vicenza	P. Costa