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The National Centre for Screening Monitoring

Eighth Report

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Foreword

The data in this report confirm the progressive expansion of screening programmes. First and foremost, this shows the continuing positive efforts of the regional health systems. More than from the financial aspect, this effort is also characterised by great cultural and organizational commitment; the screening programmes implemented in our country represent an exemplary intervention of secondary prevention in public health.

On the other hand, however, the incomplete distribution of such interventions, considered by our legal system as Essential Levels of Care, becomes a litmus test for the crucial problems affecting regional systems, especially, but not only, in the South of Italy. In this context, activities of the central government have increased commitment with its planning.

Although at present neither the National Plan of Prevention, nor the National Cancer Plan have concluded the institutional process that will make them formalized planning instruments; both of these reaffirm their commitment to promoting the extension and improvement of cancer screening programmes. In fact, this is considered among the specific objectives of these two plans.

Regarding the first, screening programmes became models of intervention for secondary prevention mainly due to the involvement, based on solid scientific evidence, of all health system structures (hospital and area).

With regard to the Cancer Plan, aimed at putting Italy on the forefront in facing the burden of cancer, the mass-screening programmes actually involve the greatest number of people in activities against cancer.

Data collected in this report also show the need to guarantee the quality of the intervention more evenly. This effort must concentrate the resources and commitment of all the stakeholders: institutions, professionals, scientific societies, associations representing civil society, and the media. On the other hand, the evidence of things that need to be improved must not lead us to forget how seldom the quality of health interventions can be evaluated in other settings.

It is therefore with great pleasure, as well as critical awareness, that I introduce this report with the hope of seeing the gap quickly filled that sometimes separates us from fully achieving our objectives of distribution and quality, so that the work and commitment of so many workers can fully and effectively show the entire target population the benefits made possible by the health screening programmes.

Fabrizio Oleari
General Prevention Director
CCM Managing Director

Introduction
The diffusion of screening programmes in Italy: 2008

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Screening programmes in Italy are still ongoing. At a glance, almost 8,400,000 people in 2008 were invited to undergo a screening examination (3,300,000; 2,345,000 and 2,725,000 for cervical, mammographic and colorectal cancer, respectively). 3,800,000 actually complied with the invitation (1,320,000; 1,263,000 and 1,225,000 for cervical, mammographic and colorectal cancer, respectively). All Italian Regions are involved and more than 300 programmes are active. These activities resulted in identifying 5,945 breast cancers (36% of annual occurring breast cancers in Italy in the 50-69-year age group), 3,662 CIN2 or more severe cervical lesions, 2,556 colorectal cancers (16% of annual CRC cancer occurring in Italy in the 50-69-year age group) and 13,554 advanced adenomas.

Cervical cancer screening

On closer observation of this data, we see that Cervical Cancer Screening has expanded and now reaches 78% of the target population (figure 1). It is worth noting that constant expansion has been observed over time. As opposed to other screening programmes, we observe no great difference among the three macro-areas of our country. This is also because a couple of Regions in Northern Italy did not implement this sort of program across the entire Regional territory. Observing the actual extension (how many women in the target population aged 25-64 years regularly receive an invitation letter, figure 2), significant differences when comparing Northern and Central Italy to Southern Italy can be noted, even if such disparities are less evident when compared with colorectal and mammography screening.
In fact, current extension is about 60% in Northern Italy, and more than 70% in Central Italy, but only slightly higher than 50% in the South of our country.

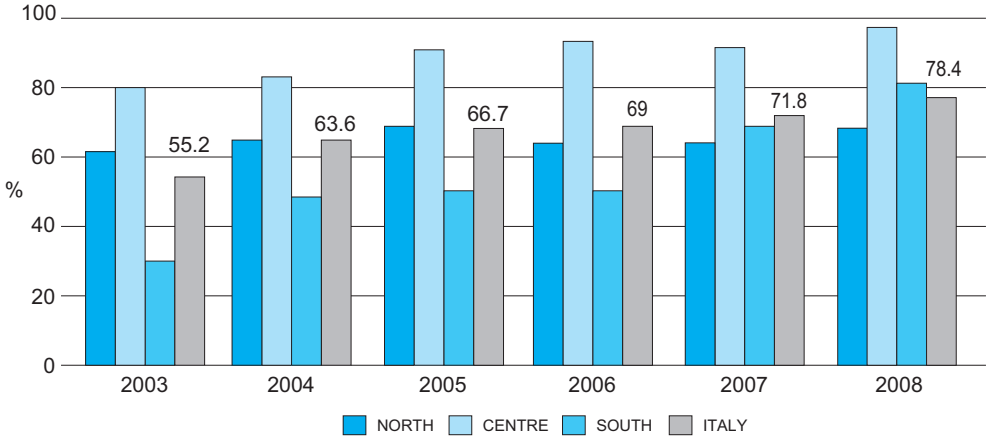

Figure 1. Theoretical extension of cervical cancer screening programmes by geographical area. ONS survey (2003-2008).

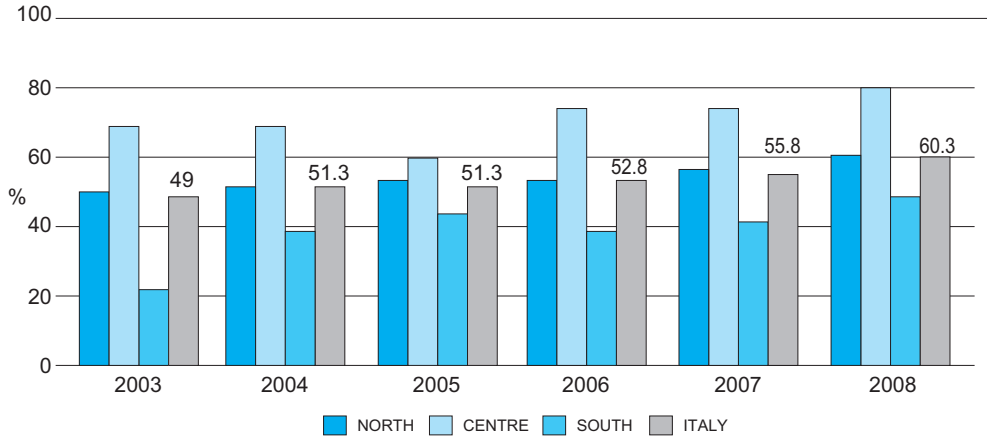

Figure 2. Actual extension of cervical cancer screening programmes by geographical area. ONS survey (2003-2008).

However, it is encouraging to note that five or six years ago actual extension was lower than 20% in Southern Italy.

Mammography screening

Regarding mammography screening (figure 3), theoretical extension (i.e., percentage of women aged 50-69 who live in areas where organised screening was implemented with respect to the entire target population) is about 90%, close to total activation, as requested by European guidelines.

Such an increase in extension must be considered a positive trend. Nevertheless, screening diffusion is still heterogeneous, with a higher distribution in Northern/Central Italy compared with Southern Italy and the Islands; theoretical extension is about 100% in the North and Centre but no higher than 70% in the South, where it was 10% five years ago.

Differences among geographical areas become more evident when we consider actual extension (i.e., how many women regularly receive an invi-

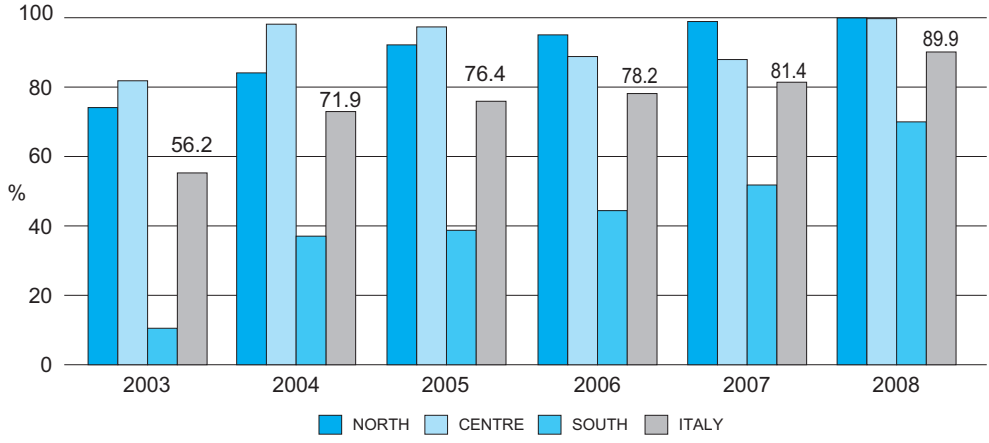

Figure 3. Theoretical extension of mammography screening programmes by geographical area. ONS survey (2003-2008).

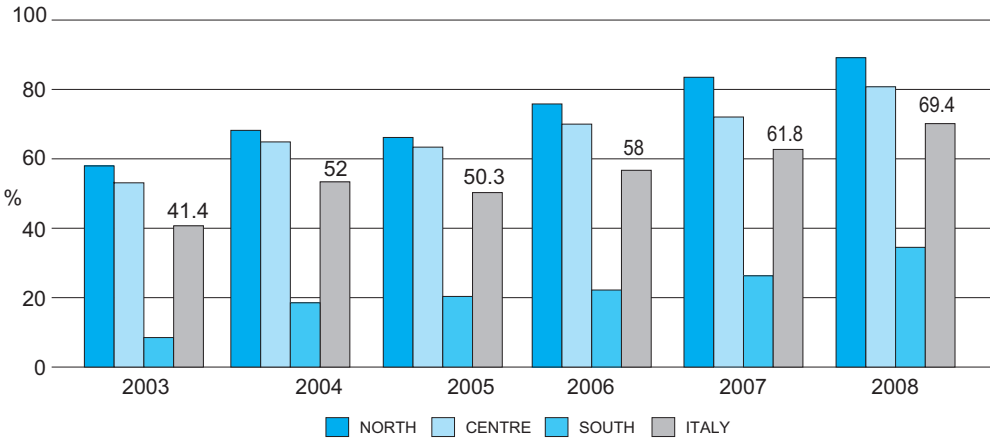

Figure 4. Actual extension of mammography screening programmes by geographical area. ONS survey (2003-2008).

tation letter, figure 4); in this case, the figures are 90% in the North, almost 80% in the Centre, and below 40% in the South, where an even more backward condition was present five years ago.

Colorectal cancer screening

In terms of colorectal cancer screening, in 2008 theoretical extension increased, rising above 50%. Such a theoretical extension represents an excellent goal, especially when compared with other European situations.

In Italy distribution of this screening remained relatively low for many years and has been implemented only recently; in fact, five years ago few pilot screening programmes were present (figure 5).

Once again, significant differences exist between the North and South of our country. Theoretical extension is higher than 70% in the North and about 60% in the Centre, but has been recorded lower than 20% in the South, though some things have changed with respect to later years.

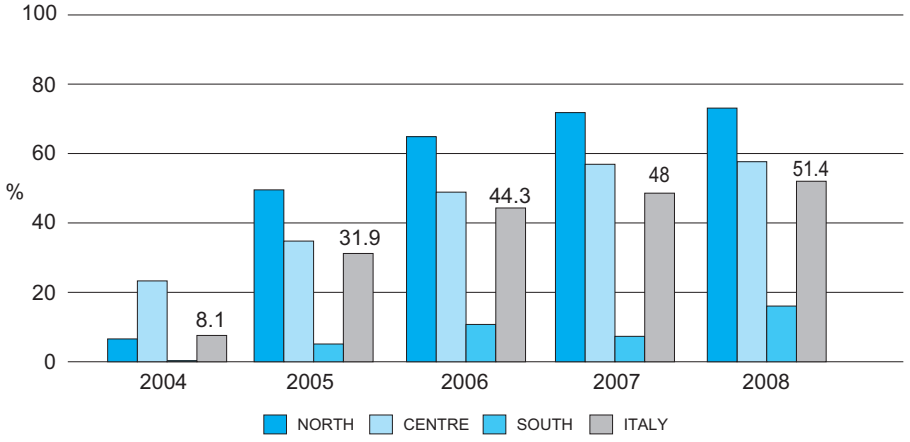

Figure 5. Theoretical extension of colorectal cancer screening programmes by geographical area. ONS survey (2004-2008).

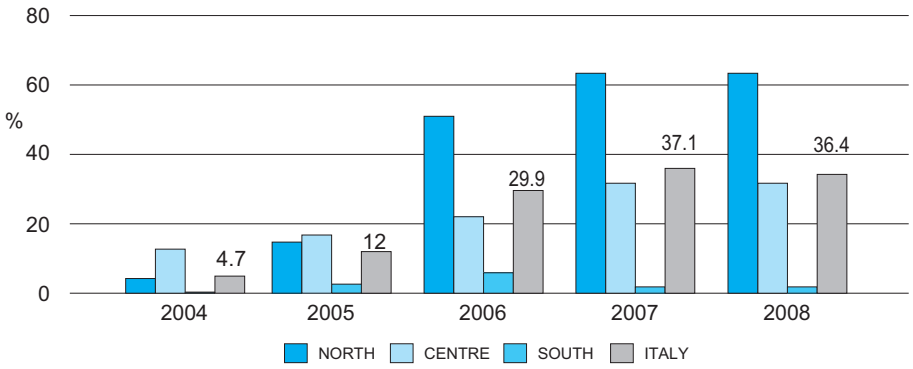

Figure 6. Actual extension of cervical cancer screening programmes (faecal occult blood test + sigmoidoscopy) by geographical area. ONS survey (2004-2008).

Differences become greater when we consider actual extension (figure 6): in fact, we recorded a 60%, 30% and 5% increase in actual extension, in the North, Centre and South, respectively.

Mammography screening in Italy: 2008 survey

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Abstract

This report is an update of similar previous papers that have been published by the ONS (Osservatorio Nazionale Screening, National Centre for Screening Monitoring) since 2002. Data for the survey come from several different programmes that may have changed over time, and may have different settings of organisation and management. During 2007, a further increase in screening activity was recorded, with the inclusion of all Northern and Central Italian Regions, and a further development in the Southern Regions and Islands, so today all Italian Regions have implemented screening programmes.

In 2008, almost 2,509,000 women aged 50-69 years were invited to have a screening mammogram, and more than 1,361,000 were screened. Theoretical extension was 89.9%, while actual extension increased from 62.3% in 2007 to 69.4% in 2008. An imbalance in coverage is still present when comparing Northern and Central Italy to Southern Italy, which only has a 69% coverage by organised screening. The Italian mean value (72.8%) of two-year extension (period 2007-2008) suggests that, at full capacity, Italian programmes are able to invite only two thirds of the target population. The percentage of women screened during 2008 accounted for 36.7% of the national target population.

During the last few years, participation rates were substantially stable around 55-57% for crude rate, and 59-61% for adjusted rate, respectively. A decreasing trend towards the South of Italy is evident for this parameter, too.

Many programmes work with low volumes of activity (below 10,000 or even 5,000 examinations per year), and only one Region surpassed the desirable level of at least 20,000 examinations for each programme.

Referral rates of 7.5% at first screening and 4.4% at repeat screening were recorded. Direct standardised detection rate was 6.2x1,000 at first test and 4.2 at repeat test, while benign to malignant ratio for first and repeat screening was 0.25 and 0.15, respectively. Detection rate of invasive cancers ≤10 mm was 1.39x1,000 at first test and 1.44 at repeat test; the proportion of in situ carcinomas was 12.5% and 14.2% for first and repeat test, respectively. Indicators by 5-year age group confirm greater diagnostic problems at younger ages, with higher referral rates, higher frequency of surgical procedures with benign outcome (B/M ratio), and a substantially lower detection rate as compared to older age groups.

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Keywords: mammography screening, breast, survey, Italy

Since the early 1990s, GISMa (Gruppo Italiano per lo Screening Mammografico, Italian Group for Mammography Screening) has carried out yearly surveys on the implementation of programmes in Italy and surveys to collect as systematically and thoroughly as possible the main process indicators for screening quality monitoring.

Starting from 2002, the results of these surveys have been published in the annual reports of the ONS (Osservatorio Nazionale Screening, National Centre for Screening Monitoring). Moreover, monitoring, comparisons and evaluation activities have led to the publication of updated operative reports of process indicators for mammography screening.[1]

In Italy, activation of mammography screening programmes is regulated by the Ministry of Health's new guidelines,[2] according to which women in the age range 50-69 years are personally invited to undergo mammography every two years, and a monitoring system and quality evaluation activity for each phase of the programme is required.

This report is an update of previous papers published by the ONS, available on ONS website (http://win.osservatorionazionalescreening.it).[3-9]

Data referring to the 2008 activity are reported stratified by Region and 5-year age groups, with the aim to provide summary data on the situation of mammography screening in Italy.

According to national[2] and European[10] screening guidelines, most programmes invite women in the 50-69 year age range. Several programmes have a marginal activity dedicated to women over 70 years of age, while in the past few years some programmes have started including women aged 45-49 years, partly as a consequence of a Ministerial Decree offering free two-year mammography to women aged 45 years or more. Commonly, screening activity for women below 50 or over 69 years is performed on demand, despite active invitation by the screening programme.

Guidelines for data interpretation

For the interpretation of the results, it must be borne in mind that these are summarised data, that may reflect different situations, both as to varying levels of experience and dissimilar settings of organisation and management.

Therefore, when evaluating results it is necessary to bear in mind some critical aspects inherent to the data: not all programmes have the possibility of differentiating between first and repeat screening tests, so for these programmes results are assigned to the round that includes the majority of the screened women; a few programmes are not yet able to provide data stratified by five-year age group, so the age-stratified results provided relate to a subset of programmes; finally, an important aspect to consider is completeness of provided information.

Table 1 shows degree of completeness of data information by Region, according to the following classification:

Region	Level of information completeness				Total no. of programmes
	0-2	3	4	5	
Abruzzo	-	-	-	1	1
Alto Adige	1	-	-	-	1
Basilicata	-	-	-	1	1
Calabria	5	-	4	-	9
Campania	4	4	4	-	12
Emilia-Romagna	-	-	2	9	11
Friuli-Venezia Giulia	-	1	-	-	1
Lazio	6	-	1	5	12
Liguria	1	-	3	1	5
Lombardia	-	-	6	9	15
Marche	2	5	2	4	13
Molise	1	-	-	-	1
Piemonte	-	-	5	4	9
Puglia	-	1	-	-	1
Sardegna	4	-	-	-	4
Sicilia	1	-	1	-	2
Toscana	-	-	4	8	12
Trentino	-	-	-	1	1
Umbria	1	2	-	1	4
Valle d'Aosta	-	-	1	-	1
Veneto	1	-	11	9	21
TOTAL	**27**	**13**	**44**	**53**	**137**

Table 1. Distribution by Region of the programmes providing data on the 2008 screening activity and level of information completeness.

Region	Theoretical extension*	Invited women in 2008	Adjusted extension	
	(%)		(%)	10th-90th percentile*
Valle d'Aosta	100.0	7,251	91.8	
Piemonte	100.0	206,914	70.7	37.0-101.6
Liguria	100.0	42,374	37.0	15.0-86.0
Lombardia	100.0	590,238	101.5	86.6-139.9
Trentino	100.0	25,984	85.5	
Alto Adige	100.0	35,639	146.9	
Veneto	100.0	224,814	82.9	76.5-114.6
Friuli-Venezia Giulia	100.0	84,008	107.3	
Emilia-Romagna	100.0	254,205	100.1	89.5-112.3
NORTH	100.0	1,471,427	88.9	63.5-114.0
Toscana	100.0	219,637	92.8	82.3-101.1
Umbria	100.0	61,665	129.3	77.4-162.4
Marche	100.0	71,249	76.5	46.0-105.9
Lazio	100.0	239,061	66.8	32.6-91.7
CENTRE	100.0	591,612	80.4	46.0-105.9
Abruzzo	67.4	34,429	43.2	
Molise	100.0	19,068	98.1	
Campania	84.1	122,322	38.2	14.1-78.0
Puglia	77.3	92,259	37.1	
Basilicata	100.0	35,249	102.5	
Calabria	100.0	63,346	56.5	0.6-94.9
Sicilia	33.1	51,730	15.7	
Sardegna	42.2	27,689	24.6	3.8-218.4
SOUTH + ISLANDS	68.9	446,092	36.0	13.6-95.5
ITALY	**89.9**	**2,509,131**	**69.4**	**37.0-111.9**

*only for Regions with more than 3 local programmes.

Table 2. Theoretical and adjusted extension of the screening programmes, age 50-69. Year 2008.

• level 0-2: programmes providing one or more of these data: target population, invited women, women who responded, women recalled for further assessments;

• level 3: programmes providing information about the number of detected cases (benign and malignant), besides data of the previous level;

• level 4: programmes providing (even if only partially) pathology data (TNM) of detected cancers, besides data of the previous level;

• level 5: programmes providing complete information on detected cases cases (a programme is considered complete when information of at least 90% of detected cases is provided).

Table 1 shows the situation at the time of data collection; it is possible that, at present, the degree of information completeness of several programmes has improved. However, data analysis highlights several critical aspects:

• 39% of the programmes were able to provide complete information about their screening activity; this could be partially due to time schedules/deadline of data collection, probably too short for several programmes to catch up with the information of all subjects referred for further diagnostic-therapeutic procedures; a difference was also recorded between programmes in the North-Centre of Italy, where about 50% of the programmes were level 5, and in the South, where only 7% of the programmes was able to provide complete data;

• some Regions persist in showing rather low degrees of data completeness, though they have been active for several years, suggesting the persistence of organisational, management, and structural problems; the improvement of programmes in Lombardia is noteworthy: all programmes show a good or high level of completeness (level 4-5).

On the whole, Regions that have been active for a longer period (such as Basilicata, Emilia-Romagna, Piemonte, Toscana, Veneto) show a higher number of programmes with complete data, suggesting that a longer experience and screening activity stability improve collection of information and data quality. It is also possible that the inclusion of screening activity in a comprehensive regional project may promote the standardisation and completeness of data collection.

Extension and attendance

We generally define extension as the percentage of women involved in a screening programme out of the total female population in the 50-69 age range resident in the area.

For a deeper understanding of screening activity and possible drawbacks, the use of two different types of extension are more appropriate:

• **theoretical extension** (or programme extension), referring to eligible women residing in areas covered by an organised screening programme;

• **actual extension** (or invitation extension), related to women who were actually sent an invitation to screening during the analysed period, based on data provided to GISMa.

In 2008 survey the calculation of actual extension has been modified in order to consider undelivered invitations: their number is subtracted from the total number of sent invitations and this extension is named «corrected extension».

In 2008, all Italian Regions were covered by screening programmes (table 2), even though theoretical extension was incomplete, and actual extension even more so, and substantial gaps were present in some Regions.

Theoretical extension showed a considerable increase in comparison with 2007, rising from 81.4% to 89.9%. This increase is mainly due to the development of programmes in the South and Islands, areas that have been lacking since years (data registered rise from 52.4% to 69.4% in 2008), and to the total coverage of Lazio Region achieved in this year. The Northern and Centre Regions are completely covered.

In comparison with 2007, a good increase in actual extension was also registered, from 62.3% to 69.4%: in 2008 two out of three women actually received an invitation to undergo screening tests.

All three major Italian areas (North, Centre, South and Islands) registered a consistent increase in actual extension of about 3-10% in comparison with 2007.

A strong imbalance in the screening offer still exists between Northern-Central and Southern Italy, despite further improvements registered in 2008 (figure 1): all the Regions in the North and Centre of Italy are almost completely covered by screening and show a good level of actual exten-

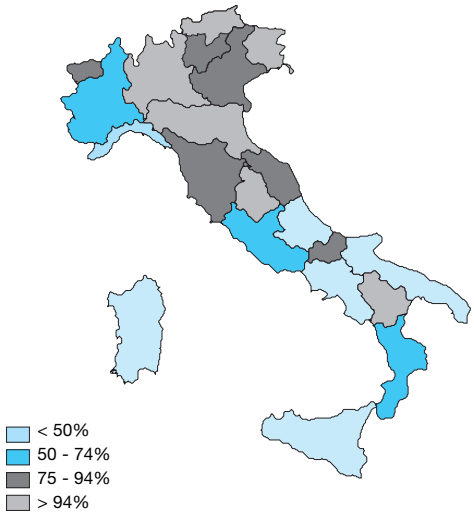


Figure 1. Actual extension (%) of mammography screening programmes. Yesar 2008.

Region	Invited women in 2007-2008	Biennal adjusted extension	
		(%)	10th - 90th percentile*
Valle d'Aosta	14,585	92.3	
Piemonte	400,516	68.6	39.0-94.6
Liguria	80,776	34.4	18.1-73.8
Lombardia	1,024,853	92.8	82.5-112.9
Trentino	48,943	80.9	
Alto Adige	na	na	
Veneto	428,254	76.7	50.1-109.6
Friuli-Venezia Giulia	155,135	98.8	
Emilia-Romagna	505,389	96.0	90.5-105.1
NORTH	2,658,451	82.0	50.1-106.8
Toscana	423,766	86.4	70.8-95.6
Umbria	193,380	89.0	77.3-105.4
Marche	141,760	74.2	50.6-106.2
Lazio	283,052	65.4	26.6-94.7
CENTRE	1,041,958	78.2	51.0-103.0
Abruzzo	60,891	56.6	
Molise	19,068	48.5	
Campania	209,264	50.0	10.0-90.0
Puglia *	97,318	25.3	
Basilicata	63,957	100.0	
Calabria	79,775	51.8	29.0-169.7
Sicilia	102,780	49.2	
Sardegna	38,237	57.2	1.9-83.1
SOUTH + ISLANDS	671,290	46.5	12.4-90.0
ITALY	**4,371,699**	**72.8**	**29.2-103.0**

na = data not available

*only for Regions with more than 3 local programmes.

Table 3. Adjusted extension of the two-year period 2007-2008 of the screening programmes, age 50-69. Year 2008.

sion. Here, only two out of three women live in areas where an organised screening programme was active in 2008, and the gap between theoretical and actual extension is much more evident than in other Italian areas, and, in the same year, about 1 woman out of 3 of the target population received an invitation to undergo mammography.

At the national level, based on a population of more than 7,420,000 women in the age range 50-69 years, the target population of active screening programmes that provided data in 2008 was of about 6,670,500 women. In the same year, almost 2,509,000 Italian women aged 50-69 years received an invitation to undergo screening mammography and more than 1,361,000 accepted. The percentage of women screened during 2008 accounted for 36.7% of the national target population.

A more detailed analysis shows that 10% of the programmes with the lower level of extension (10th percentile) invited less than 37% of the target population of the period.

A discrepancy between theoretical and actual extension, as previously noticed, is still present: 89.9% *vs* 69.4% for the total national value (the gap is more evident in the South and Island). This difference depends in some instances on organisation/management issues, so that programmes have problems in regularly inviting the whole target population every year.

In the 2008 survey, data of a two-year period ex-

tension (years 2007-2008), was also required (table 3). The Italian mean value (72.8%) suggests that, at full capacity, Italian programmes are able to invite two thirds of the target population: only 3 Regions show a two-year extension equal or more than 95%, meaning that the programme is capable of inviting all the target population within two years. A decreasing trend from North (82.0%) to South (46.5%) was present for this parameter, as well, although it must be borne in mind that in the southern area several programmes were activated during these last 2-3 years (Puglia, Sardegna, Calabria).

An indirect suggestion of non-optimal logistic-organisational conditions is deduced by the mean volume of activity of single programmes in 2008 (table 4); this aspect also has an influence on training and experience of medical and technical personnel involved in the screening.

With the exception of Lombardia, no regional mean value exceeds the desirable level of at least 20,000 examinations per programme (although several single programmes reach this value). On the contrary, many programmes work with volumes of activity that are too low (below 10,000 or even 5,000 examinations per year) to assure an appropriate level of experience of the personnel involved in the screening and good and stable performances of the activity. Sometimes, the low volume of activity is justified by the low numbers of the regional target population (Valle d'Aosta, Umbria, and Molise), but in some Regions it is probably due to management choices that should be re-evaluated.

Screening programme attendance is one of the main indicators for the impact and efficiency evaluation of mammography screening. Currently, recommended standards are: ≥50% (acceptable)

Region	Total active programmes	Invited women (age 50-69)	Perfomed tests (age 50-69)	Mean no. of tests by programme
Valle d'Aosta	1	7,300	5,600	5,600
Piemonte	9	206,900	129,300	14,400
Liguria	5	42,400	23,600	4,700
Lombardia	15	590,200	317,000	21,100
Trentino	1	26,000	19,400	19,400
Alto Adige	1	35,600	18,500	18,500
Veneto	21	224,800	148,700	7,100
Friuli-Venezia Giulia	1	84,000	51,900	51,900
Emilia-Romagna	11	254,200	167,000	15,200
NORTH	65	1,471,400	881,000	13,600
Toscana	12	219,600	142,000	11,800
Umbria	4	61,700	41,600	10,400
Marche	13	71,200	37,500	2,900
Lazio	10	211,500	94,000	9,400
CENTRE	39	564,000	315,100	8,100
Abruzzo	1	34,400	17,000	17,000
Molise	1	19,100	8,100	8,100
Campania	12	145,400	37,600	3,100
Puglia	1	92,300	27,800	27,800
Basilicata	1	35,200	17,400	17,400
Calabria	9	63,300	15,800	1,800
Sicilia	2	51,700	18,200	9,100
Sardegna	4	27,700	11,900	3,000
SOUTH + ISLANDS	31	469,100	153,800	5,000
ITALY	**135**	**2,504,500**	**1,349,900**	**10,000**

Table 4. Mean volume of activity by programme. Year 2008.

Region	Crude attendance		Adjusted attendance	
	(%)	10th-90th percentile	(%)	10th-90th percentile*
Valle d'Aosta	**77.2**		**79.0**	
Piemonte	62.6	49.1-81.2	65.6	50.5-82.0
Liguria	56.9	37.8-85.9	66.9	53.7-91.9
Lombardia	55.1	36.1-72.0	64.5	51.2-77.2
Trentino	**74.8**		**79.2**	
Alto Adige	52.0		52.5	
Veneto	66.4	50.4-80.1	77.1	62.2-88.0
Friuli-Venezia Giulia	62.6		62.6	
Emilia-Romagna	66.3	57.2-74.9	72.4	67.1-79.5
NORTH	60.8	49.3-78.9	67.9	57.1-84.3
Toscana	65.9	58.8-74.1	69.5	62.3-76.1
Umbria	68.5	64.3-72.7	73.3	68.4-78.8
Marche	53.3	33.7-78.0	54.2	36.5-78.0
Lazio	45.0	32.0-62.4	47.1	35.6-67.4
CENTRE	56.2	38.7-75.9	58.9	38.7-76.7
Abruzzo	49.9		50.5	
Molise	43.4		43.4	
Campania	31.2	20.2-52.4	35.4	22.2-52.4
Puglia	30.7		33.4	
Basilicata	49.2		49.2	
Calabria	25.8	14.3-47.5	26.2	14.3-47.5
Sicilia	39.1		41.7	
Sardegna	47.4	31.1-50.7	54.1	33.0-56.7
SOUTH + ISLANDS	35.6	20.1-49.9	38.2	20.1-52.9
ITALY	55.3	30.6-76.2	60.4	33.2-80.8

Values below minimal standards are shown in colour; values above optimal standards are in bold.
*only for Regions with more than 3 local programmes.

Table 5. Crude and adjusted attendance by Region, age 50-69. Year 2008.

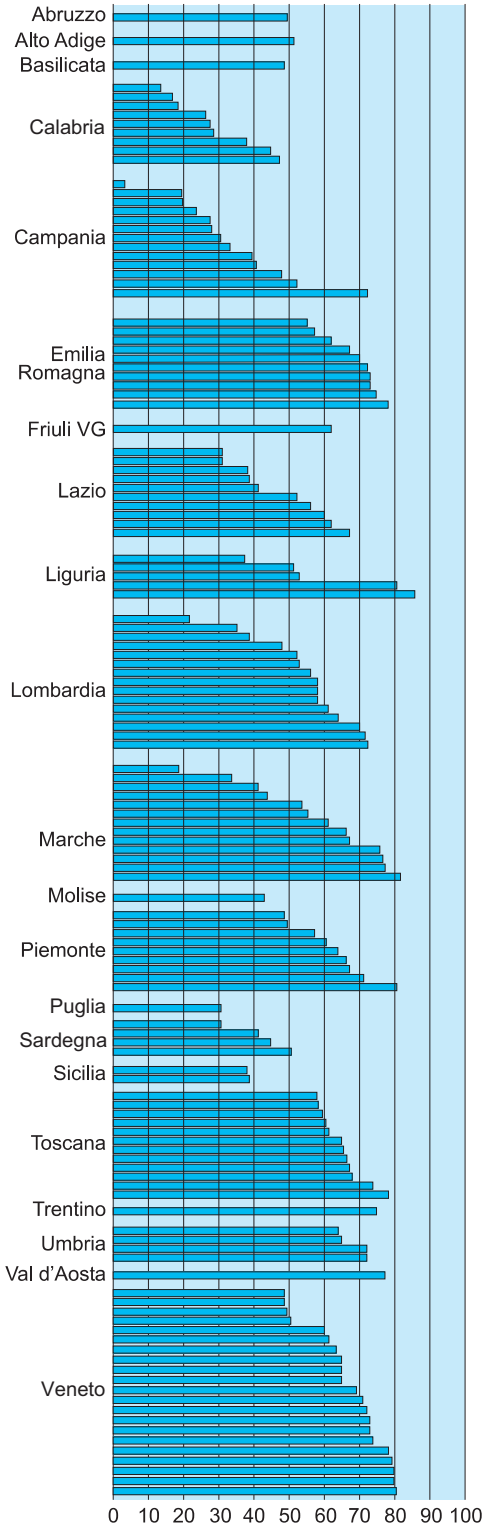
and ≥70% (desirable) for crude attendance; ≥60% and ≥75% for adjusted attendance, respectively.[1] Table 5 shows the results observed for crude and adjusted attendance for Italy and each Region. Adjusted attendance rate (where women reporting a recent mammogram outside the programme are excluded from the denominator) is more representative of real response to invitation of the target population. However, not all programmes can provide data to calculate adjusted compliance, thus the overall attendance rate is underestimated.

As already noticed in the previous years, also in 2008 participation rates were substantially stable, placing within the range of the levels registered during these last few years both for crude rate (55-57%) and for adjusted rate (59-61%). Therefore, the mean Italian value surpasses the acceptable standard for both types of attendance. A decreasing trend towards the South of Italy is evident for this parameter, as well.

Considering regional variations (table 5), with the exception of Lazio, all Regions showing attendance rates below the minimal standards are concentrated in the South and Islands areas. In 2008, 9 out of 21 Regions (43% of the total) were not yet able to reach the minimum standards for crude attendance. Only Valle d'Aosta and Trentino were above the desirable level for these parameters.

Adjusted attendance rate reveals problems of par-

Figure 2: Crude attendance rate in single programmes, by region. Year 2008.



ticipation (and of completeness of data registration) in screening programmes: only two Regions are above the optimal standard, and the number of those below the minimum standard has increased. It is important to consider that this parameter is often underestimated, as previously mentioned, since many programmes are unable to provide information about women excluded for recent mammograms.

Caution should be used when interpreting national and regional aggregated data, because they are averages of the results of single programmes, which may vary substantially even within a single Region (figure 2).

Crude attendance in single programmes in 2008 ranged from 14.3% to a maximum of 86.0%, with about one third of the programmes (34.8%) below minimal acceptable standard (50%), and 25% of them above optimal standard (70%).

The presence of figures below the minimum standard of 50% in several Regions, mainly located in the South of Italy, may only be partially correlated with the fact that most recently implemented projects, which generally require initial adjustment, are in these areas: there are Regions in which values are always below the minimum acceptable level, even though their activity started several years ago.

Attendance rates by 5-year age group (table 6) partially confirm previous Italian and international findings, that is, a higher compliance for younger women. It is interesting to note that the highest attendance is recorded among women aged 55-64 years, relatively young women who have been invited to take part in the screening for several years; consequently they are more likely to participate, being also aware of the efficiency and the quality of the diagnostic procedures within an organised screening programme.

Diagnostic indicators

Table 7 to 13 show some of the main diagnostic indicators which are representative of the quality of screening performance in 2008. Indicators are reported separately for «first test», referred to women undergoing screening for the first time, irrespective of the number of the organisational round of the programme, and «repeat test», concerning women who previously underwent screening tests (for programmes implemented during the last two years this category is not yet available).

In all tables, values below minimal standard are in colour, values above the optimal standard suggested by national guidelines are in bold.[1]

Analysed data refer to 1,345,963 tests, accounting for a total of 6,025 carcinomas detected in 2008 at first screening (1,574) or repeat screening (4,451), and 1,047 benign lesions. Screening centre databases with a too limited number of tests were excluded from this analysis.

Moreover, while analysing characteristics of detected carcinomas, information is not available for overall identified cancers and indicators are calculated in a subgroup of cases; therefore data

Age	Crude attendance (%)	Adjusted attendance (%)
50-54	52.2	58.5
55-59	58.6	64.2
60-64	59.7	64.8
65-69	55.4	60.2
TOTAL 50-69	**56.4**	**61.9**

Results refer to a subset of programmes providing age-stratified data.

Table 6. Crude and adjusted attendance by 5-year age groups. Year 2008.

Region	Total crude referral rate (%)	10th-90th percentile* (%)	Total standardised referral rate (%)
Valle d'Aosta	11.4		11.6
Piemonte	7.6	4.5 - 14.6	7.1
Liguria	8.2	6.9 - 8.9	7.9
Lombardia	8.1	3.4 - 7.3	7.7
Trentino	6.5		6.6
Veneto	6.5	2.9 - 11.5	6.2
Friuli-Venezia Giulia	7.8		7.8
Emilia-Romagna	8.4	5.6 - 11.8	7.6
NORTH	7.8	4.3 - 11.6	7.3
Toscana	10.5	7.7 - 14.3	10.1
Umbria	**4.5**	3.0 - 13.3	**4.4**
Marche	11.4	5.0 - 31.4	11.0
Lazio	6.1	4.4 - 10.5	6.9
CENTRE	7.6	4.4 - 13.9	8.0
Abruzzo	10.9		11.8
Molise	**4.9**		5.0
Campania	7.9	4.4 - 10.3	8.3
Puglia	**3.9**		**4.3**
Basilicata	8.8		7.1
Calabria	9.6	4.2 - 15.0	13.9
Sicilia	9.7		9.3
Sardegna	5.6		5.6
SOUTH + ISLANDS	6.8	4.2 - 14.0	7.2
ITALY	7.5	4.3 - 12.8	7.4

Values below minimal standards are shown in colour; values above optimal standards are in bold.

*only for Regions with more than 3 local programmes.

Table 7. Crude and adjusted (European population) total referral rate, first screening test. Year 2008.

referring to detection rate of invasive cancers ≤1 cm and proportion of in situ carcinomas should be interpreted with additional caution.

Referral rate

Referral rate for further assessments is the main indicator of first level screening specificity. It indicates the proportion of screened women referred for diagnostic assessments. This value needs to be reasonably low, in order to limit negative psychological impact (anxiety), invasive procedures (cytology, core or surgical biopsies) which may be required, as well as costs. Recommended standards are: <7% (acceptable) and <5% (desirable) at first screening; <5% (acceptable) and <3% (desirable) at repeat screening.

Tables 7 and 8 show crude and standardised referral rate, for first and repeat screening tests. Standardised rate was calculated to take into consideration the different population setting: generally a high percentage of young women (age range 50-54) is represented in the population of programmes which have been active for several years, and this is the group of women with the highest referral rate. At the national level about 50% of screened women at first test is made up by women in the age group 50 to 54.

Considering first tests, exceeding of the maximum acceptable standard for this indicator persisted, as already observed in previous surveys. Everywhere, the slowly decreasing trend in the recall rate, which began in 2006, continued in 2008.

High values were recorded both at the national and often at the regional level: only six Regions show a value within the acceptable standard.

A more detailed analysis shows that even considering single programmes the minimum standard is often surpassed: almost two thirds of the pro-

Region	Total crude referral rate (%)	10th-90th percentile* (%)	Total standardised referral rate (%)
Valle d'Aosta	4.7		4.6
Piemonte	3.6	2.2 - 5.4	3.7
Liguria	6.5	4.0 - 15.4	6.8
Lombardia	4.3	3.4 - 7.3	4.4
Trentino	**2.2**		**2.4**
Veneto	4.3	1.3 - 8.7	4.4
Friuli-Venezia Giulia	3.1		3.2
Emilia-Romagna	3.7	2.0 - 5.0	3.9
NORTH	4.0	2.2 - 6.7	4.2
Toscana	5.2	4.2 - 6.0	5.4
Umbria	3.1	1.4 - 9.9	3.3
Marche	7.2	1.4 - 17.5	8.0
Lazio	3.6	2.7 - 10.6	3.8
CENTRE	4.8	2.6 - 10.1	5.1
Abruzzo	9.5		12.9
Molise	**2.8**		**3.0**
Campania	6.6	2.4 - 13.9	5.4
Basilicata	3.9		4.1
Calabria	8.1	4.5 - 17.8	8.2
Sicilia	7.8		8.0
SOUTH + ISLANDS	6.4	3.1 - 16.1	6.2
ITALY	4.4	2.2 - 9.6	4.5

Values below minimal standards are shown in colour; values above optimal standards are in bold.

*only for Regions with more than 3 local programmes.

Table 8. Crude and adjusted (European population) total referral rate, repeat screening test. Year 2008.

Region	Total detection rate (x 1,000 screened)	B/M ratio	Cancer ≤10 mm detection rate (x 1,000 screened)	Carcinoma in situ (%)
Valle d'Aosta	8.2	0.67	0.0	33.3
Piemonte	6.9	**0.24**	1.74	16.6
Liguria	6.4	**0.43**	3.45	6.0
Lombardia	4.7	**0.23**	1.23	8.6
Trentino	5.3	0.76	0.76	19.1
Veneto	4.6	**0.37**	1.21	13.0
Friuli-Venezia Giulia	8.7	**0.10**	na	na
Emilia-Romagna	6.5	**0.21**	1.94	17.3
NORTH	5.6	**0.25**	1.46	12.5
Toscana	5.1	**0.24**	1.25	15.2
Umbria	6.9	0.58	1.68	20.0
Marche	5.7	**0.29**	1.83	0.0
Lazio	4.1	**0.23**	1.31	9.8
CENTRE	5.0	0.30	1.34	12.6
Abruzzo	3.4	**0.20**	0.80	20.0
Campania	10.4	**0.14**	1.26	22.7
Basilicata	5.2	0.75	0.65	28.6
Calabria	5.2	**0.13**	0.80	5.7
Sicilia	6.9	**0.19**	1.81	6.0
Sardegna	na	**0.02**	na	na
SOUTH + ISLANDS	6.1	**0.21**	1.15	12.5
ITALY	5.5	**0.25**	1.39	12.5

na = data not available
Values below minimal standards are shown in colour; values above optimal standards are in bold.
Indicators for Puglia are not reported because data provided are referred to only 10% of subjects sent to surgical treatment.

Table 9. Diagnostic indicators, first screening test. Year 2008.

grammes (64.7%) register a referral rate higher than the acceptable value of 7%.

Repeat tests show better results: the national indicator is within the acceptable standard, albeit higher than the previous year (4,4% in 2008 and 4,0% in 2007); regional and single programme data show the difficulty of many Regions (almost one third of them) in complying with the limits suggested by national and European guidelines (table 8).

Total detection rate

It is one of the main indicators of a programme's diagnostic sensitivity. It indicates the proportion of detected cancers every 1,000 screened women. Detection rate should be evaluated compared to expected incidence rate in the screened population.

Benign/Malignant surgical biopsy ratio

It is an optimal indicator of the diagnostic specificity of the programme assessment phase. It is determined on women undergoing recommended surgery, and it indicates the ratio of benign to malignant (B/M) pathology outcomes. It should be as low as possible. Recommended standards in Italy are: ≤1 : 1 (acceptable) and ≤0.5 : 1 (desirable) at first screening; ≤0.5 : 1 (acceptable) and ≤0.25 : 1 (desirable) at repeat screening.

The increasing use of percutaneous core biopsy (e.g., vacuum assisted biopsy) suggests caution in interpreting this indicator, which should gradually improve.

Detection rate of cancers ≤10 mm in size

It is an important indicator of diagnostic sensitivity of the programme. It indicates the number of invasive cancers ≤10 mm detected every 1,000 screened women. It summarises the capacity of

Region	Total detection rate (x 1,000 screened)	B/M ratio	Cancer ≤10 mm detection rate (x 1,000 screened)	Carcinoma in situ (%)
Valle d'Aosta	4.4	**0.04**	1.91	8.3
Piemonte	5.1	**0.20**	1.42	15.9
Liguria	4.5	**0.20**	1.92	4.6
Lombardia	3.9	**0.14**	1.06	11.4
Trentino	5.8	**0.13**	1.94	18.2
Veneto	4.4	**0.18**	1.41	14.4
Friuli-Venezia Giulia	6.2	**0.05**	na	na
Emilia-Romagna	5.8	**0.10**	1.99	15.3
NORTH	4.7	**0.14**	1.44	13.9
Toscana	5.6	**0.07**	2.00	15.4
Umbria	4.8	0.48	1.26	20.5
Marche	3.4	**0.11**	1.26	11.4
Lazio	2.8	**0.14**	0.96	9.9
CENTRE	4.6	**0.15**	1.63	14.8
Abruzzo	3.4	**0.07**	0.49	22.2
Campania	3.3	**0.48**	0.68	6.7
Basilicata	2.1	0.53	0.57	37.9
Calabria	4.2	0.33	1.41	0.0
Sicilia	4.5	**0.07**	0.89	7.1
SOUTH + ISLANDS	3.2	0.34	0.68	17.1
ITALY	4.6	**0.15**	1.44	14.2

na = data not available.
Values below minimal standards are shown in colour; values above optimal standards are in bold.

Table 10. Diagnostic indicators, repeat screening test. Year 2008.

the programme to detect «small» cancers, most likely «early» and associated to better prognosis. Excessively low values, especially lower than 1‰ (where a low expected incidence cannot explain them), could suggest the need to re-evaluate the quality of diagnostic procedures used in the programme; on the other hand, values above 1.75-2‰ can be considered to reflect good diagnostic sensitivity of the programme.

Proportion of in situ carcinomas (Tis)

It indicates the ratio of in situ carcinomas every 100 total detected cancers with histological diagnosis. Recommended standards are 10% (acceptable) and 10-20% (desirable) at any screening round. Italian standards also provide a maximum value, since too high a proportion of in situ carcinomas might suggest overdiagnosis or inadequate use of reporting categories (overreporting) by pathologists.

European standards do not include a maximum value and suggested standards are >10% (acceptable) and >15% (desirable) at first and repeat screenings.

Though considering limitations included in the data (as previously indicated), overall the indicators recorded by Italian programmes in 2008 appear rather good and comply at a satisfactory level with recommended national standards.

Some values exceeding acceptable standards may be explained by the scantiness of cases or by the partial data registration. Further research to better evaluate data quality should be planned for the future, as well as analysis to detect any failure determinants where data seem to really be insufficient.

Table 11 shows crude and direct standardised (European population x 1,000) total detection rates for the 50-69 year age range; use of standardised rates allows for a better evaluation of detection rate, which may vary regionally not only due to the dif-

Region	First screening test		Repeat screening test	
	crude detection rate	standardised detection rate (European pop.)	crude detection rate	standardised detection rate (European pop.)
Valle d'Aosta	8.2	11.8	4.4	4.1
Piemonte	6.9	7.1	5.1	4.9
Liguria	6.4	7.9	4.5	4.1
Lombardia	4.7	5.2	3.9	3.4
Trentino	5.3	8.0	5.8	5.5
Veneto	4.6	5.4	4.4	3.9
Friuli-Venezia Giulia	8.7	8.7	6.2	4.8
Emilia-Romagna	6.5	8.1	5.8	5.3
NORTH	5.6	6.3	4.7	4.3
Toscana	5.1	6.9	5.6	5.0
Umbria	6.9	10.4	4.8	4.9
Marche	5.7	6.4	3.4	3.0
Lazio	4.1	4.3	2.8	2.7
CENTRE	5.0	5.8	4.6	4.3
Abruzzo	3.4	2.9	3.4	3.8
Campania	10.4	11.7	3.3	3.6
Basilicata	5.2	4.9	2.1	2.1
Calabria	5.2	5.6	4.2	3.1
Sicilia	6.9	7.9	4.5	4.0
SOUTH + ISLANDS	6.1	6.4	3.2	3.1
ITALY	**5.5**	**6.2**	**4.6**	**4.2**

Table 11. Crude and standardised (European population) total detection rate (x 100,000), by Region, age 50-69. First and repeat screening tests. Year 2008.

Age	Total recall rate (%)	Total detection rate (x 1,000 screened)	B/M ratio	Cancer ≤10 mm detection rate (x 1,000 screened)	Carcinoma in situ (%)
50-54	8.6	4.3	0.35	1.08	17.0
55-59	7.2	5.2	0.19	1.43	9.1
60-64	6.9	7.7	0.18	1.91	9.8
65-69	6.1	9.3	0.16	2.50	8.0
ITALY 50-69	7.7	5.6	**0.25**	1.43	12.7

Values below minimal standards are shown in colour; values above optimal standards are in bold.
Results refer to a subset of programmes providing age-stratified data.

Table 12. Diagnostic indicators by age group. First screening. Year 2008.

Age	Total recall rate (%)	Total detection rate (x 1,000 screened)	B/M ratio	Cancer ≤10 mm detection rate (x 1,000 screened)	Carcinoma in situ (%)
50-54	5.2	3.0	0.32	0.80	18.0
55-59	4.3	3.7	0.16	1.02	15.5
60-64	4.1	5.1	0.13	1.62	13.6
65-69	4.0	6.2	0.11	2.05	13.0
ITALY 50-69	4.3	4.6	**0.15**	1.43	14.3

Values above optimal standards are in bold.
Results refer to a subset of programmes providing age stratified data.

Table 13. Diagnostic indicators by age group. Repeat screening. Year 2008.

ferent underlying incidence, detection efficacy, and data recording completeness, but also the different age distribution of the examined population.

Tables 12 and 13 show diagnostic results by five-year age group, and refer to a subgroup of programmes which provided data by age group.

The 2008 data confirm the results of previous surveys in showing greater diagnostic problems at younger ages. All indicators show worse values among women aged 50-54 years, namely a higher mammography positivity rate (higher referral rates), a higher frequency of surgical procedures with benign outcome (B/M ratio) together with a substantially lower detection rate as compared to older age groups, although the latter finding is expected due to a different age-specific incidence of breast cancer.

These aspects should be borne in mind, considering the progressive increase in the number of screening programmes that include women aged 45-49, either following a standardised protocol or a request at first presentation.

Conclusions

A strong imbalance in mammography screening offer still persists in Italy between the North-Centre and the South of the country, in spite of the improvements registered in 2008. In this year, 90% of the national target population was enrolled in organised screening programmes, but while almost all the Northern and Central areas were covered, about one third of the women was not yet included in mammography screening in the South and Islands.

Results for 2008 highlight a substantial further improvement of theoretical extension in the Southern Regions and Islands. Moreover, results show a reduction in the gap between theoretical and actual extension, especially in the North and Centre. The imbalance between the two extensions points to the difficulty in maintaining a constant invitation flow over time. This difficulty surely had an influence on the ability of programmes to meet the two-year interval between two consecutive screening rounds, as recommended by the screening protocol. Data on biennal extension for the period 2007-2008 confirm the presence of this difficulty in almost all Regions.

The mean national value of attendance is quite satisfactory, although some critical situations are evident at the regional level, mainly in the Central-Southern Regions. A higher concentration in these areas of recently implemented projects (and therefore programmes generally needing longer time to reach acceptable levels for this parameter), is not sufficient to fully explain this situation, since there are long active programmes whose participation rates are always below the minimum acceptable standard. To some extent, this data may reflect a different attitude towards prevention in the North and South, as shown by other national studies, such as Istat's «Multiscopo» and «PASSI» surveys.[11]

Annual variation of attendance rates observed in the last years may indicate the interweaving of several occurrences: the introduction of new programmes and, sometimes, a variability owed to a different subset of invited populations alternatively invited during the two-year period (for example, some programmes tend to concentrate in a specific period the invitation of women who did not attend the previous screening rounds).

The real situation can be better represented considering the two-year acceptance rate: mean values registered in 2003-2004 (57.0%) and 2005-2006 (57.3%) show quite a steady participation to the invitation.[12]

Considering the same parameters for the three areas we can see a slight increase both in the North (59.9% in the first two-year period and 61.6% in the second) and in the Centre (54.5% and 56.4% respectively), while in the South a decrese is evident (41.9% *vs* 38.1%), partially due to the introduction of recent programmes.

Comparison between crude and adjusted attendance shows a substantial difference between these

two indicators, reflecting the presence of a relevant proportion of women (5%) undergoing spontaneous screening (and reporting the information to the screening project). This percentage of population is surely biased towards underestimation, both because not all women report this information, and because many Regions likely under-record this type of figures (or for lack of data transmission). This difference shows a decreasing trend going from North to South, as well.

The 2008 results show a substantial increase in the percentage of the national target population undergoing preventive mammography: from 33.3% in 2007 to 36.7% in 2008. This number, too, is surely underestimated, as GISMa surveys do not include women undergoing spontaneous screening, which in some programmes may account for a substantial proportion of the target population; adjusting for this spontaneous attendance would allow a more complete understanding of coverage by mammography screening in Italy.

Data about referral rates require a more in-depth analysis. They can be partially explained considering both the high percentage (50%) of young women (50-54 years) included in first exams, and a greater diffusion of digital mammography: 49% of the programmes indicated use of digital mammography for screening (both exclusively and together with analogic mammography).

To some extent, data on recall rates can suggest potential critical aspects for specificity in many programmes. In the near future, more opportunities for discussing observed difficulties and systematic interventions for quality assurance of the diagnostic procedures are required, especially in areas where sensitivity indicators (such as total detection rate and detection rate of invasive cancers ≤1 cm), suggest a non optimal sensitivity of the specific programmes.

Periodic monitoring of results from screening programmes is surely one of the most important procedures needed to guarantee the offer of an acceptable service quality.

Data reported in table 1 (degree of completeness of information of the Italian screening programmes) show how much still needs to be done both to evaluate, more and more adequately and closer to reality, the quality of the service provided to the population, and to bridge the gaps between North and South registered at any level of the screening programmes.

We must also take into consideration that the amount of resources and funds invested is one of the most important parameters affecting the ability of programmes to maintain a steady high level of performance, with regards to both quality and quantity.

It is worth bringing attention again to a specific aspect referred to 5-year age groups data analysis: results for 2008 confirm the findings of previous surveys, that is, greater diagnostic problems in early diagnosis procedures at younger ages. The actual progressive increase in the number of programmes including younger women (45-49 years) in the target population should be carefully considered, both in relation to this aspect and to other (sometimes conflicting) considerations:

- the difficulty encountered by many programmes, as shown by the annual surveys (and confirmed by the two-year period analisys), in regularly offering the screening test every two years to the whole target population in the age range 50-69;
- scientific suggestions of cost-efficiency analysis for mammography screening at different age ranges;
- suggestions for younger women (45-49 years) to undergo, if necessary, a mammography with a shorter screening interval (12-18 months);
- the opportunity offered by the National Health Service to women aged 45 to 69 years to undergo a free two-year mammography;
- an ever-increasing awareness of the importance of breast cancer prevention in younger women, and consequently a greater demand for mammograms at an earlier age. As reported by the last

PASSI survey,[11] 63% of the women in the pre-screening age range (40-49 years) reported having undergone preventive mammography at least once in their lifetime.

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VALLE D'AOSTA: P. Vittori, G. Furfaro
PIEMONTE: N. Segnan, L. Giordano, G. Faragli, L. Orione
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Time trends of process and impact indicators in Italian breast screening programmes: 1998-2008

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Abstract

Since its establishment in 1990, one of the main tasks of the Italian Group for Mammography Screening (GISMa) is the systematic data collection on the activity of the organised mammography screening programmes implemented in Italy. Data are collected in an aggregated way and gathered through a standardised form to calculate process and impact parameters.

Data analysis referring to the period 1998-2008 shows that crude attendance rate reached the acceptable 50% standard, presenting a higher level of participation in Northern and Central Italy compared to Southern Italy/Islands, where attendance rates are still inadequate and do not reach the acceptable standard. In areas where the centralised management is more established or complete, the participation rate was higher compared with areas without such characteristics, with differences from 5% to 22% (in 2008). The time trends of the other parameters included in the analysis showed, in 2008, a good average performance. For example, benign/malignant surgical biopsy ratio (B/M ratio) reached 0.21 at first screening and 0.11 at subsequent screening; overall detection rate, detection rate for in situ and small cancers (≤10 mm) showed a good trend, reaching 5.7‰, 1.1‰, and 1.4‰, respectively, for first screening, and 5.0‰, 0.7‰, and 1.4‰ for subsequent screening. On the contrary, excess referral rate at first screening persists over time.

These results continue to be consistent with those achieved by other European programmes and reassuring for all Italian mammography screening professionals.

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Keywords: mammography screening, breast, trend survey, Italy

Since its establishment in 1990, one of the main tasks the Italian Group for Mammography Screening (GISMa) is the systematic data collection on the activity of the organised mammography screening programmes implemented in Italy. This routine investigation has allowed screening staff not only to compare outcomes from different programmes but also to assess the protocols, the organisational features and the evaluation difficulties of each centre. GISMa data collection has improved over time, reaching a higher level of standardisation and completeness, with the favourable effect of improving the magnitude and quality of national and international data comparison. Census and annual monitoring of the activity of new breast screening programmes represent a very important instrument of exchange and an incentive to improve local prevention policies.

As already highlighted in previous reports, the creation of the ONS (Osservatorio Nazionale Screening, National Centre for Screening Monitoring) in 2002, the inclusion of cancer screening programmes in the Basic Healthcare Parameters (LEA) and the regional configuration of screening activities have greatly improved scope and methodology of this data collection.[1-3] Furthermore, the involvement of different professionals has worked as a stimulus in reducing the heterogeneity among the Italian areas involved in mammography screening. Differences in starting dates and level of implementation, organisation and management, and levels of awareness of the target populations have been overcome thanks to common efforts by screening operators and on-

going multidisciplinary exchange of information. Data are collected in an aggregated way and gathered through a standardised form to calculate process and impact parameters which have been agreed on at a national level and recently updated by the group.[4] Thanks to the collaborative efforts of the group, every year the GISMa surveys provide a good, complete picture of the implementation and progress of the Italian organised mammography screening programmes. Table 1 lists the indicators used for the analysis, providing for each one the definition and the correlated standard which has been recommended both at national and European level. This document is an update of a previous report, published in the 2009 edition of the official annual ONS Report.[5] It describes and compares data from the Italian breast screening programmes active in the decade 1998-2008.

Attendance rate

It is well known that compliance of women with screening invitation is a key indicator of the impact and efficacy of a screening programme in reducing breast cancer mortality. Crude attendance (i.e., women attending out of those invited) over the years has been above the acceptable 50% standard (figure 1, table 1). This indicator was calculated considering all programmes adhering to the GISMa survey since 1998, when monitoring reached good levels of standardisation and completeness. As already specified in previous reports, a higher prevalence of newly implemented programmes during 1999-2001 could partially explain a substantial reduction in attendance rate in that period. The evaluation of attendance rates by geographical areas confirms, in 2008, a higher level of participation in Northern and Central Italy compared to Southern Italy/Islands, where the rates are still inadequate and do not reach the acceptable standard (figure 2).
Figure 3 compares the 2004-2008 crude attendance rates between areas where a regional centralisation is established with areas where further improvements are needed. In the former context the participation rates are higher compared with the latter. in 2008, differences range from 5% to 22%. In 2008, differences range from 5% to 22%. This higher difference observed is due to the increasing number of centralised programmes active in North/Central Italy while the decentralised scenarios are mainly represented by programmes of South Italy/Islands where participation rates are generally lower.
Since 1999, indicators are also available with stratification by 5-year age classes. Table 2 shows adjusted attendance (excluding from the denominator women reporting a recent mammography outside the programme) by age class during 2000-2008. Younger women have a higher attendance rate over the whole study period, with the exception of the age class 50-54, where compliance was lower in the last five years (2004-2008). This result must be cautiously interpreted because of the incompleteness of data collection. The presence of a

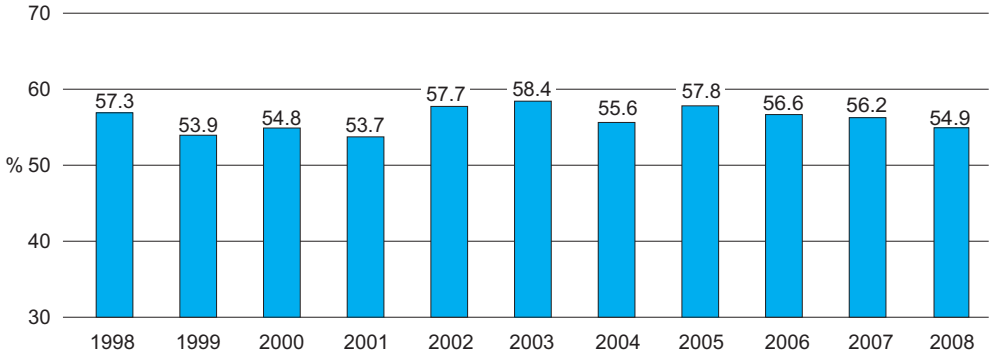

Figure 1. Overall crude attendance: 1998-2008.

Indicator	Standard	
Definition	**Acceptable**	**Desirable**
Participation Rate Number of women invited that attend to screening. We can distinguish **Crude attendance:** women that attend screening on the total population invited excluding women that didn't receive the invitation letter (if the programme could recognize them); **Correct attendance:** women that attend screening excluding women that didn't receive the invitation letter (if the programme could recognize them) and women with recent examination (executed in the last twelve months).	**GISMa** At first screening and at repeat screening Crude attendance: ≥50% Correct attendance: ≥60% **European guidelines 2006** At first and repeat screening: >70%	**GISMa** At first screening and at repeat screening Crude attendance: ≥70% Correct attendance: ≥75% **European guidelines 2006** At first and repeat screening: >75%
Recall rate - Further assessment rate Proportion of women undergoing further assessments on women that attend screening	**GISMa** First screening: <7% Repeat screening: <5% **European guidelines 2006** First screening: <7% Repeat screening: <5%	**GISMa** First screening: <5% Repeat screening: <3% **European guidelines 2006** First screening: <5% Repeat screening: <3%
Benign to malignant open surgical biopsy ratio Ratio between benign and malignant cancers in women that undergo to core biopsy or intervention	**GISMa** First screening: ≤1:1 Repeat screening: ≤0,5:1 **European guidelines 2006** At first and repeat screening: ≤1:2	**GISMa** First screening: ≤0,5:1 Repeat screening: ≤0,25:1 **European guidelines 2006** At first and repeat screening: ≤1:4
Breast cancer detection rate - DR Ratio between invasive screen-detected cancers and women that attend screening	**GISMa** There is no reference standard since it's expression of the expected incidence **European guidelines 2006** Indication only for prevalence/incidence Ratio	**GISMa** There is no reference standard since it's expression of the expected incidence **European guidelines 2006** Indication only for prevalence/incidence Ratio
Invasive screen-detected cancers ≤10 mm detection rate Ratio between the number of women with screen-detected invasive cancer ≤10 mm and women that attend screening	**GISMa** No standard, suggestion for how to calculate the rate **European guidelines 2006** Not considered	**GISMa** No standard, suggestion for how to calculate the rate **European guidelines 2006** Not considered
Proportion of invasive screen-detected cancers ≤10 mm Proportion of invasive screen-detected cancers ≤10 mm on the total of women with screen-detected invasive cancers	**GISMa** First screening: ≥20% Repeat screening: ≥25% **European guidelines 2006** First screening: not applicabile Repeat screening: ≥25%	**GISMa** First screening: ≥25% Repeat screening: ≥30% **European guidelines 2006** First screening: ≥25% Repeat screening: ≥30%
Screen-detected DCIS detection rate Ratio between screen-detected cancers with a DCIS diagnosis and women that attend screening	**GISMa** No standard, suggestion for how to calculate the rate **European guidelines 2006** Not considered	**GISMa** No standard, suggestion for how to calculate the rate **European guidelines 2006** Not considered
Proportion of DCIS screen-detected cancers Proportion of DCIS screen-detected cancers and women with screen-detected invasive cancers	**GISMa** First and repeat screening: 10% **European guidelines 2006** First and repeat screening: 10%	**GISMa** First and repeat screening: 10-20% **European guidelines 2006** First and repeat screening: >15%
From: Giordano L et al, 2006		

Table 1. Indicators and reference standards.

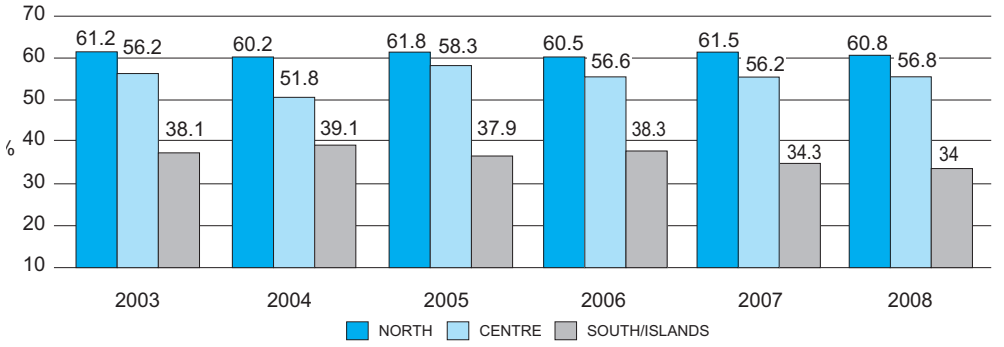

Figure 2. Total crude attendance in Northern, Central and Southern Italy: 2003-2008.

widespread opportunistic screening activity throughout the country can partially explain these outcomes and should be further investigated.

2000-2008 activity

Time trends of overall referral rates, Benign/Malignant biopsy ratio, overall detection rate, detection rate of cancers ≤10 mm and detection rate of in situ carcinomas

As in the past, analysis of time trends of some processes and early impact indicators was carried out in 2008. Figures 4-8 describe the time trends of these indicators at first and subsequent screening for all the programmes providing data for the whole period: Basilicata, Belluno, Bologna, Cesena, Ferrara, Firenze, Livorno, Milano, Modena, Padova, Perugia, Pisa, Pistoia, Ravenna, Reggio Emilia, Rimini, Roma H, Siena, Torino, Valle d'Aosta, Verona.

Table 1 summarises the most important performance indicators and their reference standards, the latter being discussed and agreed by GISMa through a continuous exchange between programmes and other European screening groups.[4]

Women referred for further assessments (referral rate)

The proportion of screened women referred for further assessments at first screening continued to follow a negative trend. Good performance for this indicator was achieved at subsequent screening (acceptable GISMa standard is <7% or <5% at first or subsequent screening, respectively), although the warning threshold is getting closer (figure 4).

Excess referral rate at first screening persisted over time while the number of women referred for further assessments should be reasonably low, in order to limit the negative psychological impact (anxiety) and the invasive procedures (cytology, core or surgical biopsies) which may be required, as well as

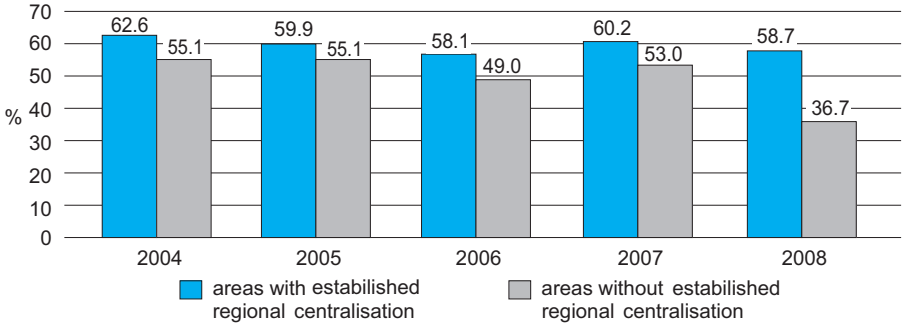

Figure 3. Crude attendance rates: comparison between areas with and without established regional centralisation: 2004-2008.

Age class	2000	2001	2002	2003	2004	2005	2006	2007	2008
50-54	62.8	63.4	62.7	62.0	58.6	56.4	59.6	58.4	58.5
55-59	61.8	65.2	64.1	67.0	62.6	62.5	65.7	64.9	64.2
60-64	60.7	64.1	63.0	66.2	61.8	63.0	65.7	64.7	64.8
65-69	54.6	57.6	55.2	59.0	57.5	59.1	61.4	60.6	60.2
TOTAL	**60.6**	**60.2**	**60.8**	**62.4**	**62.7**	**60.2**	**63.1**	**61.0**	**61.9**

Table 2. Adjusted (the adjustment was obtained by excluding from the denominator women reporting a recent mammography outside the programme) attendance rate (%) by 5-year age classes: 2000-2008.

costs. For these reasons it will be necessary to plan further analyses of this indicator within each programme, correlating its performance with other process indicators such as the positive predictive value and the detection rate.

Benign/Malignant surgical biopsy ratio

The benign to malignant surgical biopsy ratio (B/M) maintained a good performance over the years, although this time trend needs to be cautiously interpreted (figure 5).

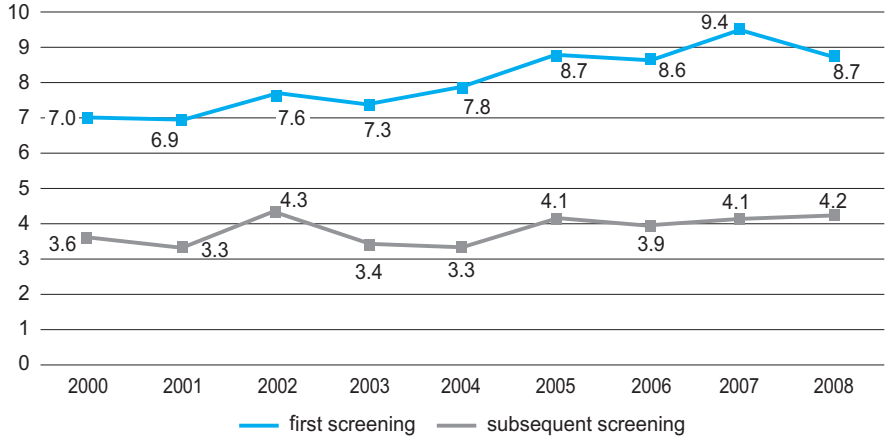

Figure 4. Time trend of referral rates: 2000-2008.

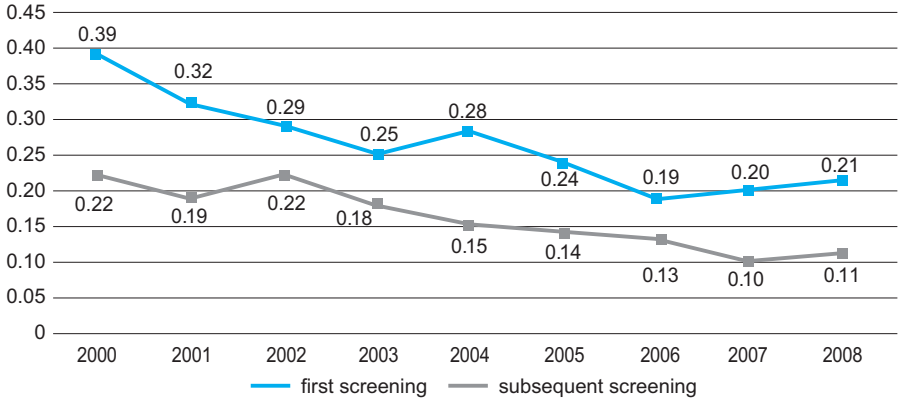

Figure 5. Time trend of B/M biopsy ratio: 2000-2008.

B/M ratio, even though decreasing over time, is strongly influenced by the increasing use of new micro-invasive diagnostic techniques, such as classic or vacuum-assisted percutaneous core biopsy, which might deserve a specific evaluation. In the past few years, the GISMa group carried out more detailed analyses on these aspects. Similar considerations have been made within the European Group for Breast Cancer and a further reduction of the acceptable standard for B/M (acceptable ≤1:2; desirable ≤1:4) has been included in the new edition of the *European guidelines for quality assurance in breast cancer screening and diagnosis*.[6]

Overall detection rate, detection rate of cancers ≤10 mm and in situ carcinomas

These parameters indicate the proportion of detected cancers (total, with a diameter ≤10 mm, or in situ carcinomas) every 1,000 screened women. They are the main indicators of the diagnostic sensitivity of the programmes. In particular, the detection rate of lesions smaller than 1 cm summarises the ability of the programmes to detect «small» cancers, most likely «early» and associated to a better prognosis. Even including the 2008 activity, the time trends of these three parameters confirmed the results obtained in the past, that is a good general performance and stability over time (figures 6-8). The representation of these indicators, despite proving useful in providing a general picture and suggesting new supplemental investigations, needs to be carefully interpreted because of limits due to the different cancer incidence in the Italian geographical areas, the different stratification by age of the target population, and the lack of uniformity in the level of completeness of the data collected.

Conclusions

This document has been drawn up to offer to all the Italian professionals involved in organised mammography screening the opportunity to evaluate and compare the effectiveness and the quality of their activity over time. Time trends analysis allows screening staff to discuss and consider not only positive outcomes of screening but also critical issues and difficulties persisting over the years. Despite some limitations such as the type of data collected (aggregated data), the variability in data completeness and the heterogeneity of areas involved in the investigations, thanks to the work of several operators GISMa surveys have become an important instrument for evaluating quality assurance of breast cancer screening programmes in Italy. Adding 2008 activity data allows us to draw the following conclusions.

Participation

Participation rate confirmed a good, constant time trend, reaching and exceeding the acceptable standard (50%). Nevertheless, even including the 2008 data, a great variability among programmes still persists even within individual Regions.

Among various determinants affecting attendance rate, the communication strategies (especially those addressed to specific sub-groups of the target population such as elderly women or immigrant women) and the opportunistic screening activity can play an important role. An appropriate communication approach can influence breast screening participation, favouring a better understanding of benefits, risks, and limitations of screening procedures, creating a mutual trust relationship with the users. Screening operators should involve women in the informed decision-making process, meeting their information needs, disproving myths and bad information and trying to understand the reasons for rejection.

At the same time, the presence of a conspicuous opportunistic screening activity, quite relevant in some Italian settings, can explain the wide heterogeneity in participation rates within the same Region, the lower participation of younger women (particularly in the last period) and the difficulty in reaching the entire target population.

In this context, the role of general practitioners (GPs) should be carefully reconsidered. Only a

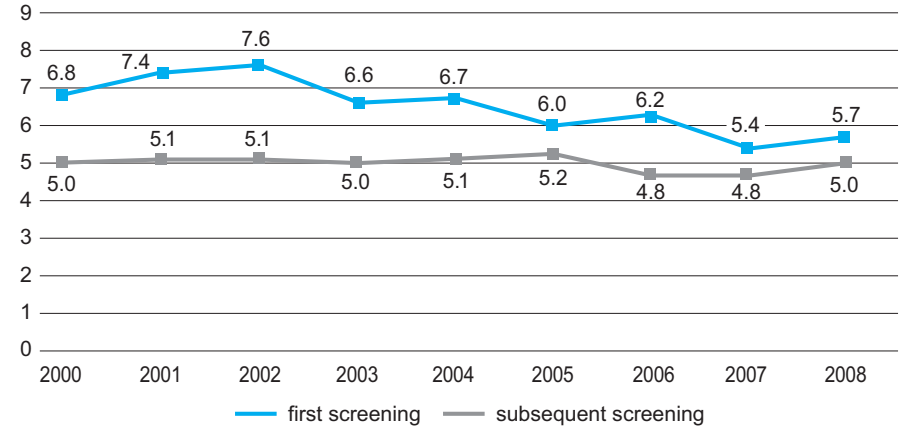

Figure 6. Time trend of overall detection rate: 2000-2008.

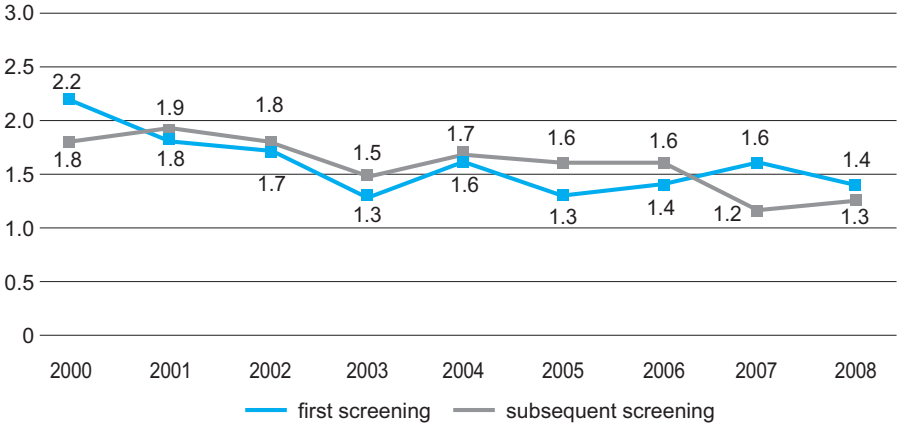

Figure 7. Time trend of detection rate of cancer ≤1 cm (‰): 2000-2008.

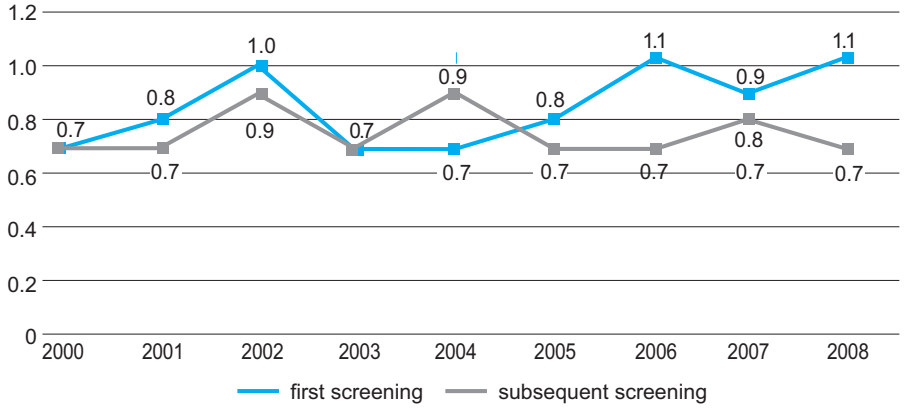

Figure 8. Time trend of detection rate of in situ cancers (‰): 2000-2008.

public health programme with a major involvement of GPs in all the screening phases, but especially in the recruitment step, can ensure a wider and more conscious access to screening for those women who usually refuse health services.
Furthermore, a centralised organisation can stimulate useful synergies among the different screening phases, resulting in a wider and more successful involvement of the target population. GISMa resources and efforts, together with those of the colorectal and cervical screening workgroups, should continue to move in this direction to assess and solve the common problems related to participation.

Diagnostic indicators

Italian mammography screening programmes show good quality activity in general and over time. In 2008, the assessment of diagnostic indicators confirms the trend observed in the previous years. The only exception is the referral rate: it exceeds the maximum standard at first screening and shows a small decrease at subsequent screening. Further analysis will be needed in the future. This value, referred to programmes that have already been running for several years, cannot be ascribed to the «learning curve effect», typical of newly implemented programmes. To better assess this trend, it will be useful to evaluate the referral rate by single screening units and radiologists. Multidisciplinary sessions on screen-detected lesions, collective revision of atypical outcomes and reinforcement of the training procedures can be some practical approaches to improve the performance of the programmes.
Overall, the results here described, although derived from aggregated data, continue to be reassuring and reward the great effort undertaken by all the screening operators over time. This effort is mainly aimed at finding opportunities to compare and discuss outcomes, questioning activity and trying to define and evaluate new strategies for further improvement.
As matters stand, it is important to stress the concept of «equity» in accessing health services in order to reduce, in screening, too, the gap between Northern Italy and Southern Italy/Islands; to continue to work together to increase the integration between different health services and professionals; to collaborate to favour a common direction and a more optimal use of the available resources; to improve data monitoring so that the results achieved may represent an incentive for all members of the screening staff to improve the quality of their work, putting to good use even negative outcomes by analysing their underlying reasons to promote improvement.

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Extension of organised cervical cancer screening programmes in Italy and their process indicators: 2008 activity

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Abstract

Italian national guidelines recommend to Regions the implementation of organised screening programmes for cervical cancer. As in previous years since 1998, we collected from Italian organised cervical screening programmes aggregated tables of data in order to centrally compute process indicators.

Data on women invited during 2008 and screened up to April 2009 were considered. In 2008, the target population of Italian organised screening programmes included 13,094,025 women, corresponding to 78.4% of Italian women aged 25-64 years. Compliance to invitation was 39.7%, with a strong North-South decreasing trend. However, it should be considered that many women are screened outside the organised programmes. Of the women screened, 5.2% were referred for repeat cytology and 63.0% of them complied; 2.4% of screened women were referred to colposcopy. Compliance with colposcopy referral was 85.1% among women referred because of ASCUS or more severe cytology and 89.3% among those referred because of HSIL or more severe cytology. The positive predictive value (PPV) of referral because of ASCUS or more severe cytology for CIN2 or more severe histology was 16.0%. The unadjusted detection rate of CIN2 or more severe histology was 3.1 per 1,000 screened women (3.0 standardised on the Italian population, truncated 25-64).

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Keywords: cervical cancer screening programmes, Italy

The Italian health system is managed by Italy's 20 Regions. Since 1996, Italian national guidelines have recommended to Regions the implementation of organised screening programmes for cervical cancer.[1-3] These recommendations, largely based on European guidelines,[4,5] include personal invitations to women aged 25 to 64 years for a Pap smear every three years, a monitoring system and quality assurance for each phase of the programme.

Indeed, one of the reasons for the introduction of organised programmes was to allow monitoring and evaluation, in order to improve the quality of each phase of the screening process, to maximise its effectiveness and to minimise its undesired effects. Surveys designed to assess the level of implementation of organised programmes in Italy and to collect process indicators have been conducted by GISCi (Italian Group for Cervical Screening) since 1997. Their results have been published by the ONS (Osservatorio Nazionale Screening, National Centre for Screening Monitoring) since 2002.[6-12]

These surveys have made it possible to collect data in a standardised format from most active cervical screening programmes, enabling computation of national statistics and programme comparison. We believe these data play an essential role for correct management of screening programmes, as they provide the information needed for actions targeted to improvement and, if needed, changes.

Methods

As in previous years, a survey on organised cervical screening programmes active in Italy in 2008 was conducted by the ONS on behalf of the Italian Ministry of Health. A programme was considered active if at least 1,000 women were invited during 2008. The survey conducted in 2009, reported here, includes women invited during 2008 and screened within the first 4 months of 2009.

Given the different approaches to integration of invitations and spontaneous activity, some programmes reported data only on women screened after invitation and others on all screened women, independently of invitation. In the latter case data on spontaneous activity included women screened during 2008.

We collected data using a standard questionnaire, based on tables dealing with some fundamental steps of the screening process, following those recommended by the European guidelines.[5] In general, these tables were nested, so that each table was the denominator of the next. They were used to centrally compute process indicators (most of those recommended by Italian[2,3] and European[5] guidelines) and to study their distribution. This approach was judged to guarantee better standardisation and comparability than asking each centre to directly compute and provide indicators. Data were checked for completeness and consistency. Each Region appointed a person to provide data and finally verify them. We interacted, sometimes repeatedly, with providers, to obtain clarifications and integrations, if needed.

For each indicator we computed the national overall mean, i.e., the value obtained by pooling all the population for which all data needed for computation were available. In addition, we analysed the distribution of indicators between Regions and between local programmes within each Region.

«Programme» is defined as each entity for which we obtained aggregated data. In general, according to national guidelines,[1-3] this corresponds to an organisational unit that manages and co-ordinates the different steps of screening, from invitation to diagnostic assessment and treatment. These units are generally well defined, but sometimes they undergo re-organisation (e.g., aggregation of smaller programmes). Furthermore, their size is highly variable. For example, in some Regions there is a single programme (e.g., Basilicata and Friuli) while others have many local programmes with regional co-ordination and evaluation (e.g., Piemonte, Veneto, Emilia-Romagna, Toscana).

We report (table 3) the mean national value of some indicators and their 10th and 90th percentile. The values of the last survey and of the two previous ones are reported. The year denotes the period of screening activity considered (therefore the year before the conduction of the survey).

In addition, for the survey conducted in 2009 we present graphs where each bar corresponds to a Region and a line represents the 10th and 90th percentile of the distribution of programmes within the Region itself.

Results

Extension of organised cervical screening programmes and compliance with invitation

For the first part of the survey on the 2008 activity we obtained questionnaires from 120 programmes. Target population of active organised programmes in the last and in previous surveys is reported in table 1. Target populations are also expressed as the percentage of women aged 25 to 64 years resident in the same area.

In 2008, active programmes in Italy had a target population of 13,094,025 women, representing 78.4% of the Italian female population aged 25-64 *vs* 71.8% in 2007. The increase was observed mainly in Southern Italy, thanks to the extension of the programmes in the Regions Puglia, Calabria and Sardegna.

In 2008, active programmes included in their target population the entire female population aged 25 to 64 years in 13 Regions (Valle d'Aosta, Piemonte, Veneto, Trentino, Alto Adige, Friuli-

	2008	2007	2006	End 2005	End 2004	End 2003	End 2002
Women 25-64 yrs included in the target population of organised programmes	13,094,025*	11,872,810	11,362,580*	10,969,571**	10,206,741**	8,910,772	8,415,285
Population 25-64 yrs	16,693,052	16,543,059	16,463,948	16,435,228	16,311,937	16,151,206	
Nominal extension[a]	78.44	71.77	69.01	66.74	62.57	55.19	52.12
Actual extension[b]	59,85 (3,330,289/ 5,564,350)	54.80 (3,021,734/ 5,514,353)	52.91 (2,873,202/ 5,487,982)	50.74 (2,779,570/ 5,478,409)	51.30 (2,789,346/ 5,347,312)	40.83 (2,197,952/ 5,383,735)	23.06
Compliance with invitation (%)[c]	39.69 (1,332,376/ 3,356,931)	39.83 (1,217,000/ 3,055,353)	38.49 (1,116,006/ 2,899,817)	36.71 (1,032,127/ 2,811,707)	37.67 (1,066,910/ 2,831,961)		
NORTHERN ITALY							
Women 25-64 yrs included in the target population of organised programmes	5,210,405*	4,942,788*	4,911,641*	5,187,239**	4,967,193	4,742,729	4,691,582
Population 25-64 yrs	7,615,828	7,555,407	7,545,425	7,536,067	7,476,970	7,408,484	
Nominal extension[a]	68.42	65.42	65,09	68.83	66.43	64.04	63.33
Actual extension[b]	55.38 (1,525,113/ 2,538,609)	55.38 (1,394,613/ 2,518,469)	52.91 (1,330,768/ 2,515,141)	52.56 (1,320,224/ 2,512,022)	52.80 (1,315,936/ 2,492,323)	51.08 (1,261,438/ 2,469,494)	
Compliance with invitation (%)[c]	47.67 (734,577/ 1,541,010)	46.93 (664,344/ 1,415,361)	45.62 (612,069/ 1,341,812)	46.65 (623,302/ 1,335,998)	46.25 (614,197/ 1,327,862)		
CENTRAL ITALY							
Women 25-64 yrs included in the target population of organised programmes	3,252,167*	3,008,931*	3,029,340*	2,933,326**	2,634,497	2,577,038	2,188,737
Population 25-64 yrs	3,315,532	3,275,594	3,224,341	3,215,573	3,188,862	3,149,126	
Nominal extension[a]	98.09	91.86	93.95	91.22	82.61	81.02	68.81
Actual extension[b]	80.51 (889,801/ 1,105,177)	74.54 (813,887/ 1,091,865)	75.05 (806,609/ 1,074,780)	62.59 (670,880/ 1,071,857)	69.61 (739,974/ 1,062,954)	60.94 (639,690/ 1,049,708)	
Compliance with invitation (%)[c]	40.17 (357,846/ 890,868)	40.23 (330,925/ 822,548)	35.70 (290,632/ 814,208)	35.61 (241,063/ 677,036)	36.00 (267,345/ 742,660)		
SOUTHERN ITALY AND ISLANDS							
Women 25-64 yrs included in the target population of organised programmes	4,631,453*	3,921,091*	3,421,599*	2,849,006**	2,775,255	1,642,152	1,534,966
Population 25-64 yrs	5,761,692	5,712,058	5,694,182	5,683,588	5,646,105	5,593,596	
Nominal extension[a]	80.38	68.65	65,63	50.17	49.15	29.54	27.61
Actual extension[b]	47.66 (915,375/ 1,920,564)	42.71 (813,234/ 1,904,019)	38.77 (735,825/ 1,898,060)	41.62 (788,466/ 1,894,529)	40.03 (753,471/ 1,882,035)	15.92 (296,824/ 1,864532)	
Compliance with invitation (%)[c]	27.73 (239,953/ 925,053)	27.12 (221,731/ 817,444)	28.68 (213,305/ 743,797)	21.01 (167,762/ 798,673)	24.34 (185,368/ 761,439)		

[a] percentage of the resident population aged 24-64 that is included in the target population of active organised programmes.
[b] numerator: population invited in the relevant year; denominator: 1/3 of the resident population aged 25-64.
[c] denominator: number of women invited; numerator: number of women who showed up for screening among them (within the first 4 months of the following year).
* data were collected in February 2009.
** data include only women aged 25-64. Some programmes also invite women out of this range.

Table 1. Target population of active organised screening programmes in Italy, population invited and compliance to invitation.

Region		
Valle d'Aosta	**Single regional programme**	
Piemonte	**Regional programme. Fully active**[a] Città di Torino, Cuneo, Alessandria, Moncalieri, Rivoli, Ivrea, Biella-Vercelli, Novara, Asti	
Lombardia	ASL Lodi, ASL Mantova, ASL Pavia, ASL Cremona, ASL Brescia, ASL Valle Camonica-Sebino	
Self-governing province of Trento	**Single regional programme**	
Self-governing province of Bolzano	**Single regional programme**	
Veneto	**Single regional programme. Fully active**[a] Ulss-1 Belluno, Ulss-2 Feltre, Ulss-3 Bassano del Grappa, Ulss-4 Alto Vicentino, Ulss-5 Ovest Vicentino, Ulss-6 Vicenza, Ulss-7 Pieve di Soligo, Ulss-8 Asolo, Ulss-9 Treviso, Ulss-10 Veneto orientale, Ulss-12 Veneziana, Ulss-13 Mirano, Ulss-15 Alta Padovana, Ulss16 Padova, Ulss-17 Este, Ulss-18 Rovigo, Ulss-19 Adria, Ulss-20 Verona, Ulss-21 Legnago, Ulss-22 Bussolengo	
Friuli-Venezia Giulia	**Single regional programme**	
Emilia-Romagna	**Single regional programme. Fully active**[a] Bologna, Cesena, Ferrara, Forlì, Imola, Modena, Parma, Piacenza, Ravenna, Reggio Emilia, Rimini	
Toscana	**Regional programme. Fully active**[a] Arezzo, Empoli, Firenze, Grosseto, Livorno, Lucca, Massa Carrara, Pisa, Pistoia, Prato, Siena, Viareggio	
Umbria	**Regional programme. Fully active**[a] Perugia, Terni, Foligno, Città di Castello	
Marche	**Regional programme. Fully active**[a] Ancona, Ascoli Piceno, Camerino, Civitanova, Fano, Fermo, Fabriano, Jesi, Macerata, Pesaro, San Benedetto del Tronto, Senigallia, Urbino	
Molise	**Single regional programme**	
Lazio	**Regional programme.** The following programmes were active: Latina, Rieti, Roma A, Roma B, Roma C, Roma D, Roma E, Roma G, Viterbo	
Abruzzo	**Single regional programme. Fully active**[a]	
Campania	Avellino 1, Avellino 2, Benevento, Caserta 1, Caserta 2, Napoli 1, Napoli 2, Napoli 3, Napoli 4, Napoli 5, Salerno 1, Salerno 2, Salerno 3	
Basilicata	**Single regional programme**	
Calabria	AS 1-Paola; AS 2-Castrovillari, AS 3-Rossano, AS 4-Cosenza, AS 5-Crotone, AS 6-Lamezia Terme, AS 7 Catanzaro, AS 8-Vibo Valentia, AS 9-Locri, AS 10-Palmi	
Sicilia	Caltanissetta, Catania, Ragusa, Siracusa, Trapani, Messina	
Sardegna	Cagliari	
Puglia	**Single regional programme**	

[a] Fully active means that all the regional female population aged 25-64 is included in the target population of active. cervical screening programmes.

Table 2. Active organised cervical screening programmes and target population (age 25-64) by Region.

Venezia Giulia, Emilia-Romagna, Toscana, Umbria, Marche, Abruzzo, Molise, Basilicata) and over 90% in four other (Lazio, Campania, Calabria and Puglia, table 2 and figure 1).

The values above consider the entire target population from the moment the programme was active, regardless of the number of women actually invited. It is obviously relevant that active programmes invite women at a rate sufficient to reach the entire target population in a 3-year round. As

	Target population aged 25-64 years	Nominal extension (%)	Target population invited in last year* (%)	Target population invited in last 3 years* (%)	Adjusted target population invited in last 3 years** (%)
	35,299	100.0	26.7	86.7	86.7
	1,231,674	100.0	31.8	87.9	87.9
	772,415	28.3	25.7	65.1	70.6
	141,304	100.0	29.8	77.7	77.7
	131,581	100.0	24.2	43.4	-
	1,338,977	100.0	25.7	72.1	84.0
	342,179	100.0	29.4	81.1	93.1
	1,226,976	100.0	33.4	90.1	97.2
	1,032,986	100.0	29.9	88.9	96.8
	248,362	100.0	31.5	84.3	89.1
	425,491	100.0	33.4	96.9	99.2
	102,715	100.0	21.5	54.2	54.2
	1,545,328	95.8	23.3	57.7	71.0
	373,696	100.0	23.8	75.2	-
	1,516,253	94.7	18.5	40.3	44.3
	169,541	100.0	-	83.0	83.0
	493,622	90.1	23.8	70.5	84.0
	628,997	45.7	21.2	33.1	41.6
	283,055	58.4	26.4	39.6	76.3
	1,063,574	93.5	9.9	<3 yrs	<3 yrs

* only women aged 25-64 years considered both in numerator and denominator.
** numerator: women aged 25-64 years invited in the last 3 years; denominator: target population aged 25-64 years minus women excluded before invitation because already invited or other reason.

a rule, in a fully active programme, about one third of the target population is expected to be invited per year. In order to take this problem into account, table 1 also reports the «actual extension» of screening programmes, computed as the ratio between the number of women invited during each year and the number that should have been invited in case of full implementation, i.e., 1/3 of the resident population aged 25-64 years. In 2008, actual extension was 60% at national level.

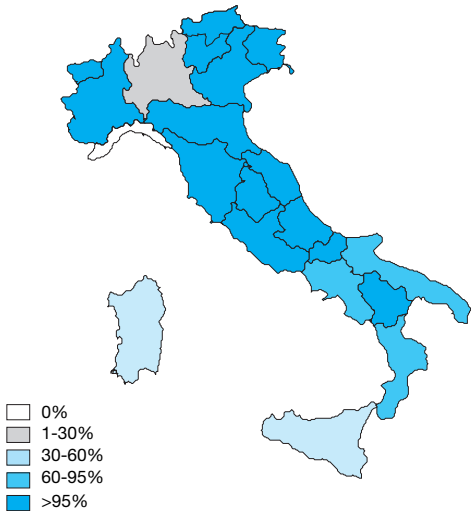


Figure 1. Percentage of women aged 25-64 in the target population of organised screening programmes.

However, variations from year to year can result from local criteria of organisation. In addition, it must be kept in mind that some programmes only invited women who had not been tested spontaneously in the last 3 years. For this reason, the percentage of women in the target population invited in the last 3 years is reported in table 2. Table 2 also reports the same percentage computed excluding from the denominator the women not invited because of recent testing or for other specified reasons (adjusted %). There is a clear North-South gradient in completeness of invitation.

During 2008, 39.7% of invited women were screened, *vs* 39.8% in the previous year (table 1). A clear decreasing trend in compliance with invitation from Northern (47.7%) to Central (40.2%) and to Southern (27.7%) Italy was present, as previously observed. Compliance was over 30% in 15 Regions, and over 50% in Valle d'Aosta, Umbria, Friuli-Venezia Giulia, and Emilia Romagna (figure 2). In each macro-area compliance was similar to, or slightly better, than that observed in the previous year. Therefore, after a reduction in compliance, that had started in 2003 and continued until 2005 (and was mainly due to the new entry of Southern Regions), 2008 confirmed the trend to increase which had begun in 2006.

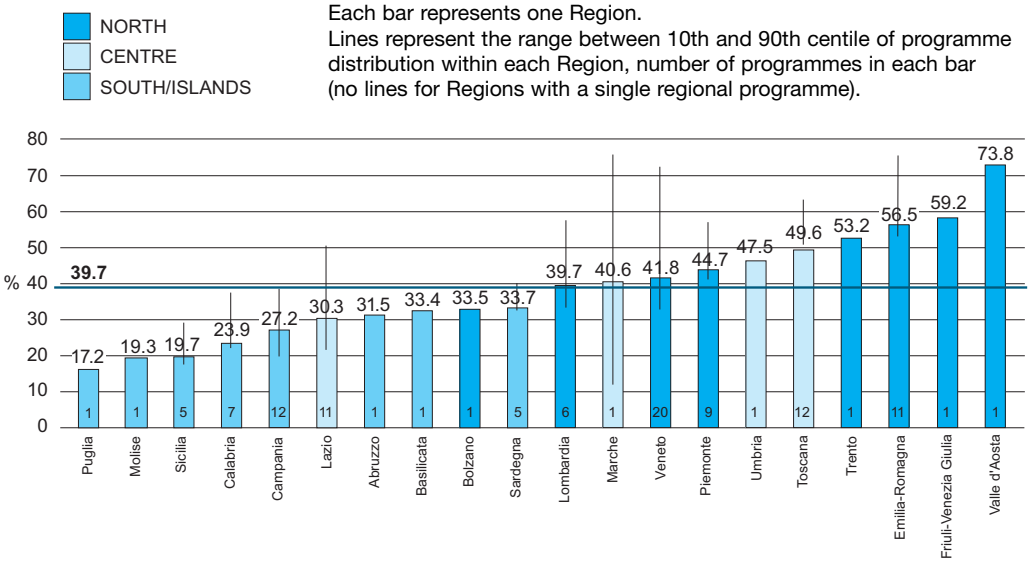


Figure 2. Percent compliance to invitation, by Region. Survey of 2008 activity.

Process indicators in organised programmes

In 2008, the 116 programmes that provided data on part two of the survey screened 1,556,373 women. Some programmes reported data only on women screened after invitation. This figure cannot be related to the number of invited women reported in the section on extension and compliance with invitation, partly because they are based on different programmes. Table 3 reports for each indicator the number of programmes for which the indicator itself could be computed.

In 2008, some 5.2% of screened women were recommended to repeat cytology *vs* 5.0% in 2007, 5.9% in 2006, and values between 6% an 7% in the previous three years. This proportion is not very high, but it shows some variability (figure 3). In five Regions cytology repeat was recommended to more than 8% of screened women. In three of these Regions many repeats were due to «other reasons», likely reactive changes, that represent the main source of variability. Repeats for unsatisfactory smears were over 6% in Molise and Sardegna. A non-negligible proportion of women was recommended to repeat after ASCUS citology (and in some cases, AGC and LSIL, as well) in some Regions. Among women who were recommended to repeat the smear, 63% actually had a new smear (60% in 2007, 62% in 2006). Three Regions were below 50% and two above 80% (figure 4). These values do not take into account that some women should have repeated cytology after a time interval that had not ended when data were collected.

In 2008, the referral rate to colposcopy was 2.4%, as in 2007, *vs* 2.3% both in 2006 and 2005 (table 3) after a constant trend to reduction. Two Regions, Abruzzo and Sicilia, referred to colposcopy more than 4% of screened women. There was a high variability within some Regions.

Out of 113 programmes with relevant data 75 (66.4%) referred to colposcopy less than 3% of screened women and 100 (88.5%) less than 4%.

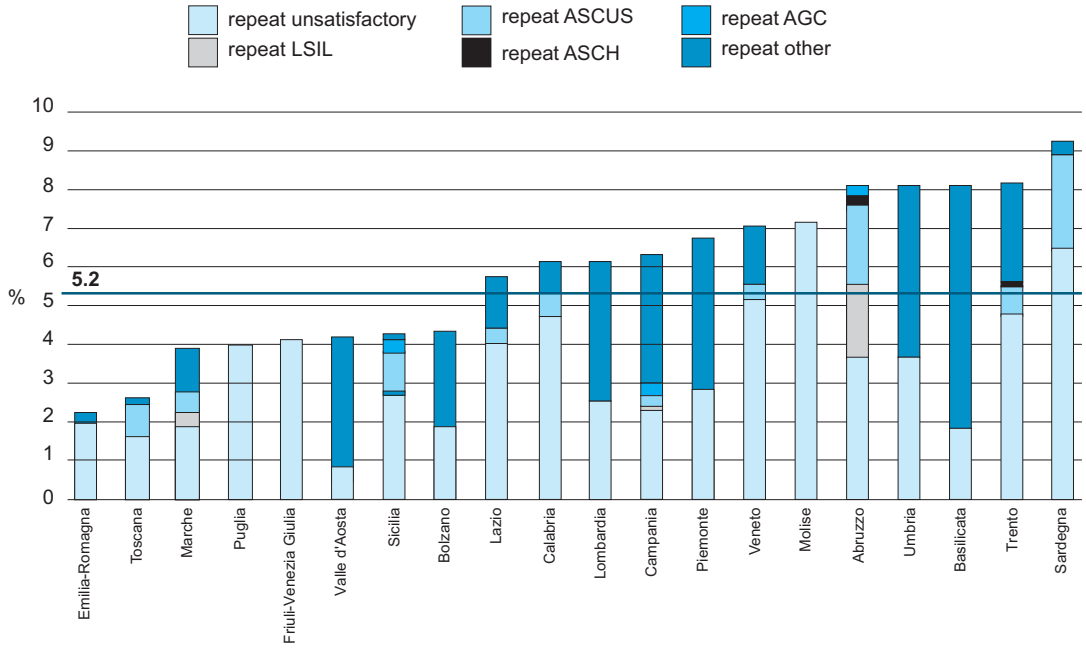


Figure 3. Percentage of screened women referred for repeat cytology, by Region. Survey of 2008 activity.

Year of activity[a]	2006				2007				2008			
	N	Mean (num/den)	centile (%) 10th	90th	N	Mean (num/den)	centile (%) 10th	90th	N	Mean (num/den)	centile (%) 10th	90th
Population screened[b]	118	1,356,391			117	1,390,454			116	1,556,373		
Recommendation to repeat cytology[c]	105	5.9% (77,693/ 1,299,932)	0.7	11.3	106	5.0% (66,001/ 1,329,783)	1.0	11.0	107	5.2 (78,086/ 1,505,559)	1.2	12.1
Compliance with recommendation to repeat cytology[d]	78	61.6% (35,561/ 57,708)	37.3	85.3	85	60.4% (30,354/ 50,290)	41.2	87.7	87	63.0 (32,874/ 52,154)	46.4	83.8
Referral rate[e]	115	2.3% (30,461/ 1,297,772)	1.0	3.9	116	2.4% (32,430/ 1,335,960)	1.0	4.4	113	2.4 (36,268/ 1,474,737)	1.0	4.4
Compliance with colposcopy referral for ASCUS+[f]	111	81.6% (22,880/ 28,034)	53.6	100	109	82.3% (24,190/ 29,407)	65.1	100	110	85.1 (28,661/ 33,681)	63.9	100
Compliance with colposcopy referral for HSIL+[g]	106	87.1% (2,324/ 2,668)	58.3	100	105	89.5% (2,632/ 2,940)	71.0	100	107	89.3 (3,084/ 3,453)	73.9	100
VPP of referral to colposcopy because of ASCUS+cytology for histologically confirmed CIN2+[h]	103	16.1% (3,423/ 21,217)	5.4	32.4	103	16.0% (3,662/ 23,102)	6.0	29.4	107	16.0 (4,514/ 27,986)	5.9	32.5
DR CIN2 + unadjusted[i]	100	2.8 (3,399/ 1,214,761)	0.7	4.8	103	2.9 (3,662/ 1,263,887)	1.0	4.8	106	3.1 (4,425/ 1,416,564)	0.6	5.2
DR CIN2 + standard Italy[j]	91	2.6	0.5	5.2	85	3.1	1.3	5.1	89	3.0	0.4	5.7

[a] year before the conduction of the survey; in each survey women invited during the previous year and screening within the first 4 months of the current year are included (see text).
[b] in some programmes it includes only women screened after invitation, in others all screened women, independently of invitation (see text).
[c] denominator: number of screened women; numerator: number of women recommended to repeat cytology.
[d] denominator: total number of women recommended to repeat cytology; numerator: women who repeated within 15 April 2009.
[e] denominator: number of screened women; numerator: number of them referred for colposcopy (any reason).
[f] denominator: number of women referred for colposcopy because of cytology ASCUS or more severe; numerator: number of them who underwent colposcopy.
[g] denominator: number of women referred for colposcopy because of cytology HSIL or more severe; numerator: number of them who underwent colposcopy.
[h] denominator: number of women who underwent colposcopy because of cytology ASCUS or more severe; numerator: number of them who had had a CIN2 or more severe lesion detected (histologically confirmed – most severe lesion within six months from cytology considered).
[i] denominator: number of screened women; numerator: number of them who had a CIN2+ detected (histologically confirmed – most severe lesion within six months from cytology considered); cases per 1,000 screened women.
[j] see (i); adjusted for age in 5-year groups on the Italian population (census 1991, truncated 25-64); the national mean was directly computed for the pool of all programmes with valid required data; percentiles were obtained after computing the standardised DR for each programme with valid required data.

Table 3. Value of some process indicators (national mean, 10th and 90th percentile) in the last three surveys.

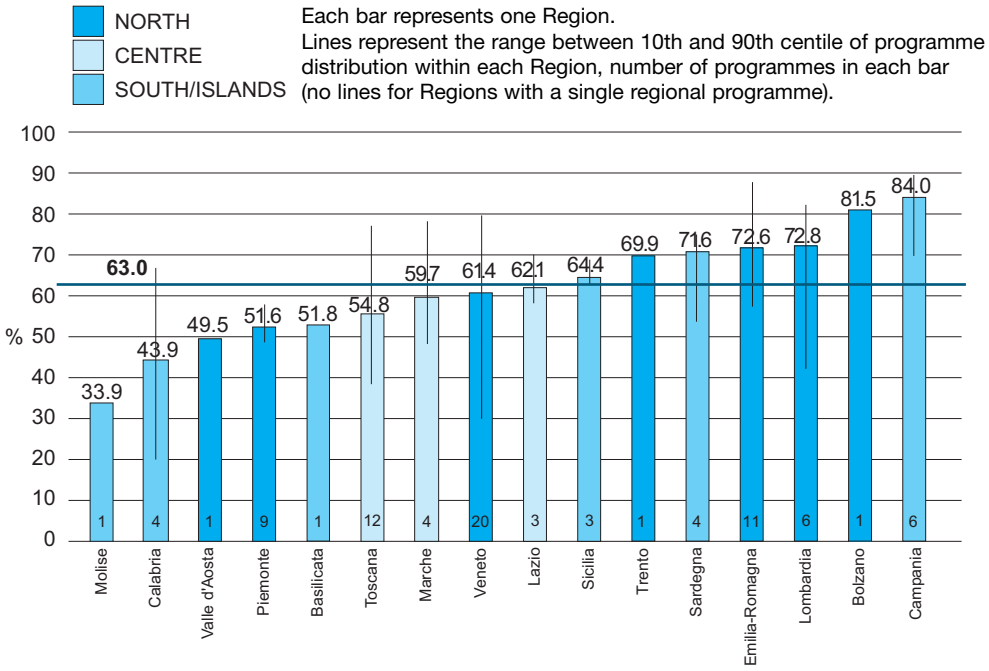


Figure 4. Compliance with repeat cytology. Women who repeated cytology by April 15 2009 out of all those referred for repeat cytology. Survey of 2008 activity.

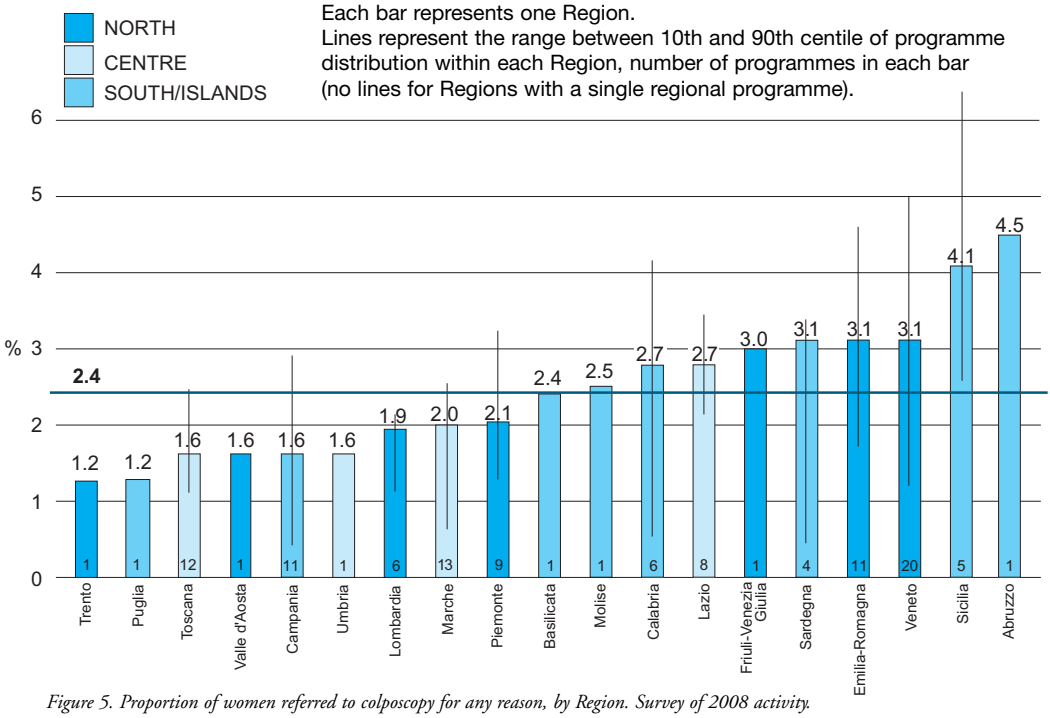


Figure 5. Proportion of women referred to colposcopy for any reason, by Region. Survey of 2008 activity.

However, in six programmes the referral rate was >5% and in two of them >9% (figure 6). With respect to the reason for referral (figure 7), the most frequent, and the largest source of variability, was ASCUS cytology.

Positive predictive value (PPV) was computed as the proportion of women with cervical intraepithelial neoplasia grade 2 (CIN2) or more severe histology among those who had a colposcopy because of an ASCUS or more severe cytology. We considered histological diagnoses of at least CIN2 because these lesions are usually treated. At a national level, the value of this indicator in 2008 was 16.0%, as in 2007, slightly lower than in 2006 (16.1%) and 2005 (16.8%). Previously there had been a trend to increase from 2001 (when PPV was 13.6%) after a decrease from 1997 (18.3%) to 2000 (11.4%). Figure 8 shows the distribution of PPV in Italian Regions during 2008. There is a relevant variability between Regions, with mean values <10% in four Regions (Basilicata, Molise, Puglia, Sicilia) and >20% in other four Regions (Lombardia, Toscana, Trentino, Umbria). Three of the latter refer to colposcopy no or very few women at the first diagnosis of ASCUS, as a result of the implementation of triage systems for this cytological category. Figure 6 presents together PPV and referral rate (for ASCUS+ cytology). The two parameters show an overall inverse relation.

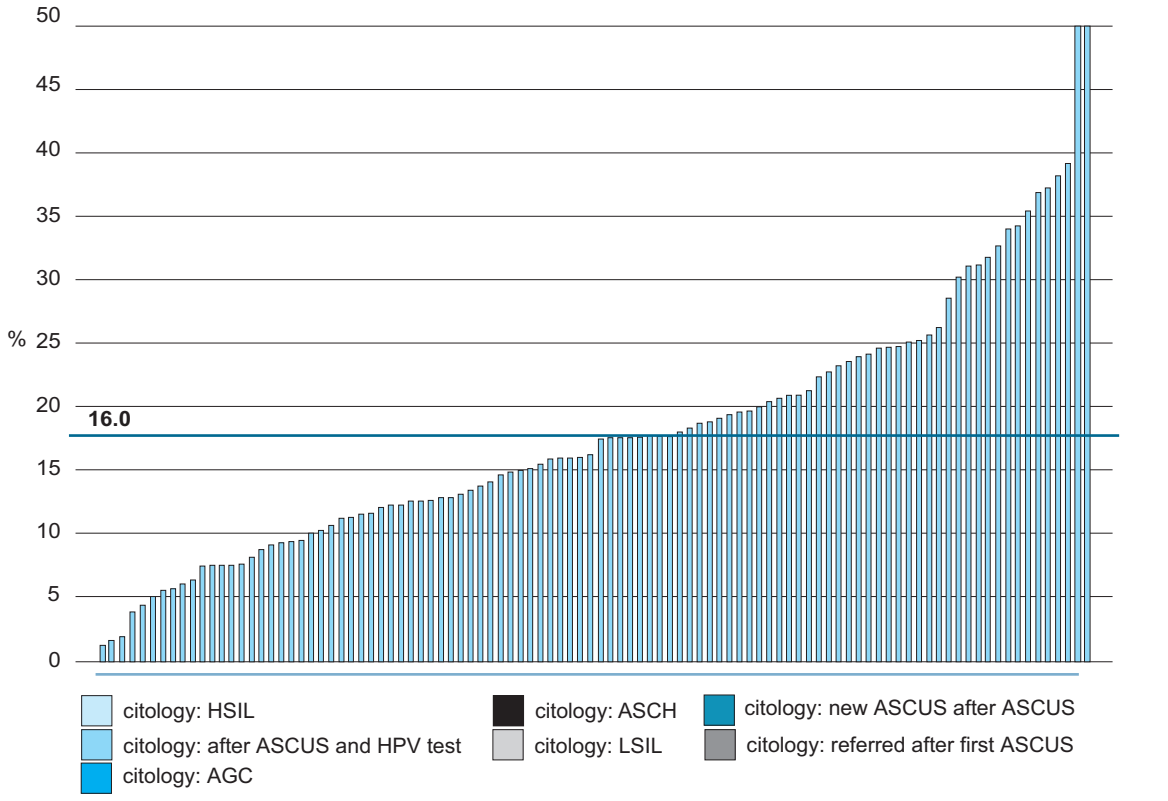
Among women referred to colposcopy with an ASCUS or more severe cytology during 2008, 85.1% actually had one. The percentage of programmes that reached acceptable (≥80%) and desirable (90%) levels of compliance was 70.0% and 50.9%, respectively (figure 9). Among women referred to colposcopy with a HSIL or more severe cytology, compliance was 89.3%. The percentage of programmes that reached acceptable (≥90%) and desirable (≥95%) levels of compliance was 67.3% and 55.1%, respectively (figure 10). When considering women referred to colposcopy with ASCUS or more severe cytology, 9/110 programmes registered a compliance <60% and 7 others between 60% and 70%. When considering women referred to colposcopy with HSIL or more severe cytology, compliance was below 60% in 4/107 programmes and between 60% and 70% in 5 other programmes.

Figure 11 shows the detection rate (DR) of histologically confirmed CIN2 or more severe lesions during the 2008 activity. At a national level the crude DR was 3.1 lesions detected per 1,000 screened women (*vs* 2.9 in 2007, 2.8 in 2006 and 2.7 both in 2004 and 2005) and the standardised (on the Italian population truncated 25-64) DR was 3.0 *vs* 3.1 in 2007 and 2.6 in the two previous years. Overall, there was a decreasing trend from North to South, and, to a lower extent, from North-East to North-West. However, high DR was observed in Sardegna (where the start of new programmes in the absence of previous intensive spontaneous activity likely led to the detection of a high number of prevalent lesions) and Abruzzo.

Discussion

During 2007 there was a further relevant increase of the extension of organised cervical screening programmes, which now include almost 80% of the national population in target age group. The increase was mainly in Southern Italy, which is relevant, given the low spontaneous coverage in this area. The 20% of the Italian population not included in organised programmes is partly the result of a still incomplete implementation in a few Regions in Southern Italy (Sicilia and Sardegna) but mostly of a very poor or completely absent implementation in a few Regions in Northern Italy (Lombardia and Liguria).

Strengthening screening programmes is essential nationwide. However, the programmes active in Northern and Central Italy were able to increase invitation rates in the last years, and now frequently reach complete or almost complete invitational coverage. In Southern Italy, on the other hand, where programmes started more recently, the invitation rate is sometimes much lower than need-



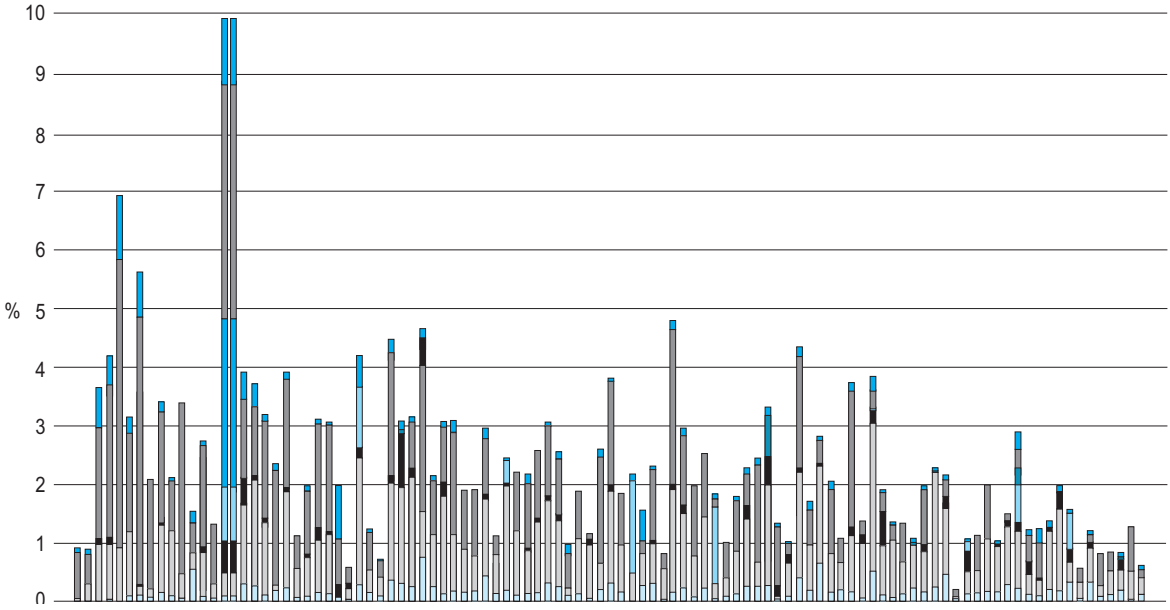


Figure 6. Positive predictive value (above) and referral rate (for ASCUS+, below) by programme. Survey of 2008 activity.

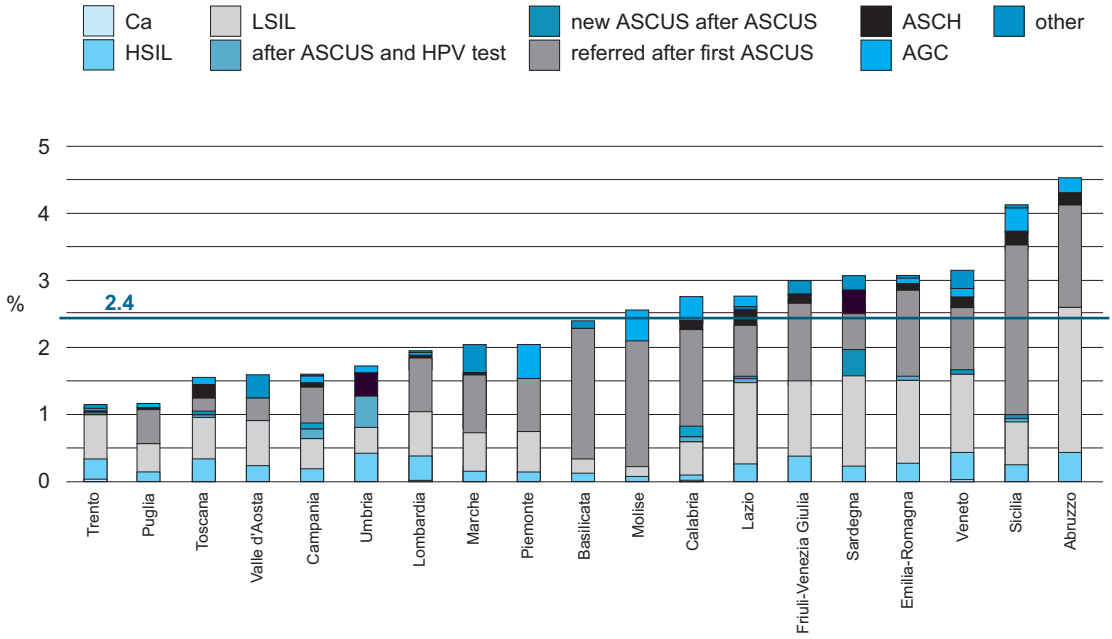


Figure 7. Proportion of women referred to colposcopy by Region and reason. Survey of 2008 activity.

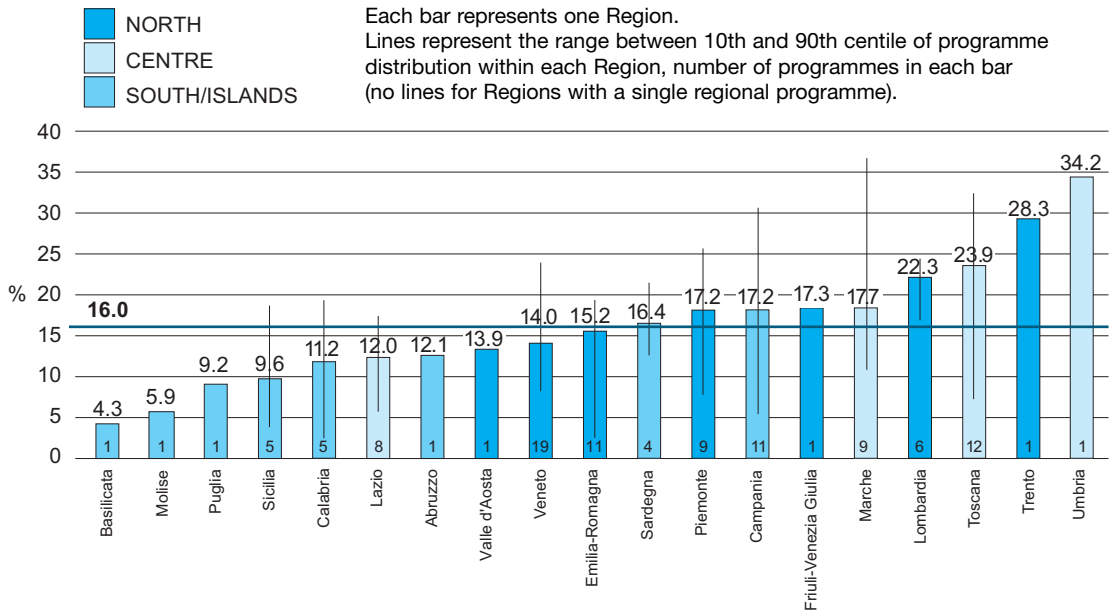


Figure 8. Positive predictive value by Region. Survey of 2008 activity.

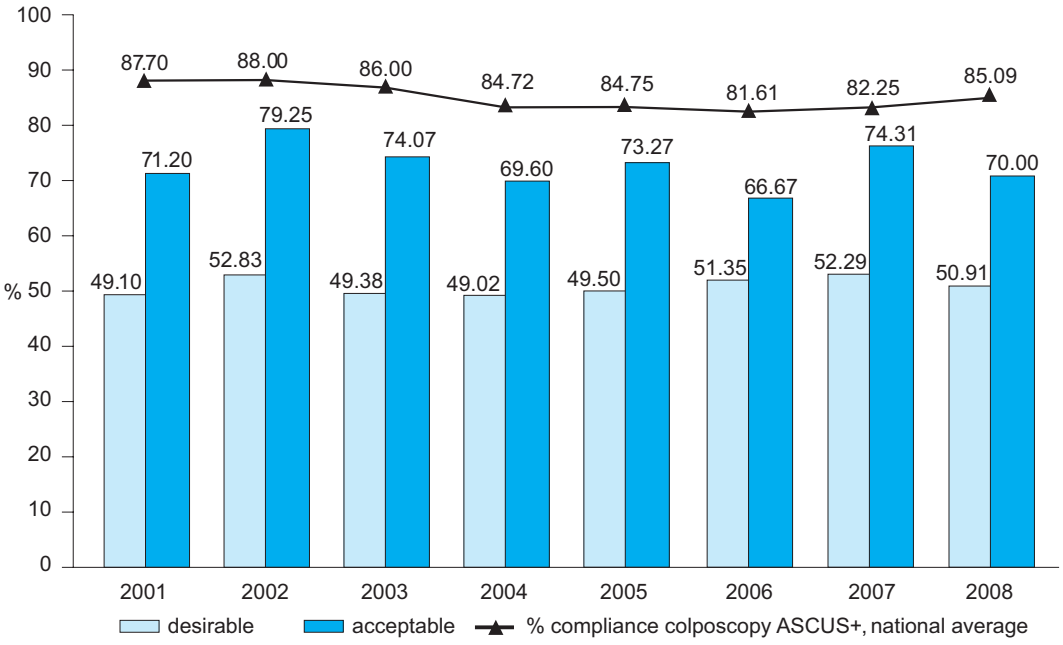


Figure 9. Compliance with colposcopy (referral because of ASCUS or more severe cytology result). Percentage of programmes that reach «acceptable» and «desirable» values by year of activity.

ed. In addition, a relevant gap in invitation uptake (which must be interpreted taking into account that a relevant proportion of women are screened outside organised programmes) is still present between Southern Regions and the others. An evaluation of the effect of organised programmes on the overall screening coverage would be particularly useful in these areas.

In interpreting time trends of performance indicators it must be taken into account that the population examined has partly changed over time, mainly because of the increased extension of organised programmes. Furthermore, the detection rate of high-grade CIN is expected to be higher in newly activated programmes than in screening programmes that are already at subsequent screening rounds. Finally, data suggests North-South geographical differences in baseline risk. Therefore care is needed also in comparing programmes.

The trend towards an increasing PPV, in the presence of a substantially stable detection rate, observed in previous years and substantially maintained in the last 3 years, can likely be attributable to the adoption of more specific criteria of interpretation and of more conservative protocols, including cytology repeat or triaging by papillomavirus testing in case of ASCUS cytology. PPV is however substantially lower in Italy than in other European countries where more conservative protocols for the management of ASCUS are extensively applied.[13]

A relevant variability in criteria of interpretation of cytology persists both within and between Regions. On one hand, data continue to show a cluster of programmes that apply too broad criteria of interpretation of cytology and are resistant to change. On the other hand, it is remarkable that the Regions with the lowest PPVs are from Southern Italy, where organised programmes started their activity more recently. The very low CIN2+ detection rate observed in a few Regions that just

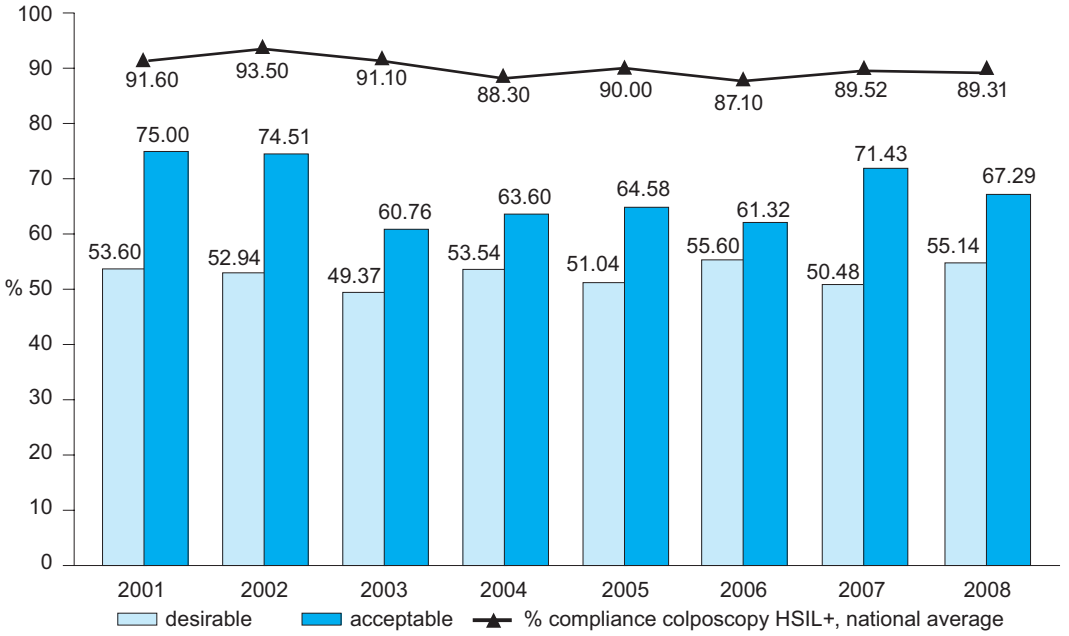


Figure 10. Compliance with colposcopy (referral because of HSIL or more severe cytology result). Percentage of programmes that reach «acceptable» and «desirable» values by year of activity.

started organised screening could reflect low sensitivity of cytology and/or histology.

Overall, data suggest that most of the programmes that have been active for many years reached a good quality, likely as a result of the widespread use of ongoing monitoring and of an intensive activity of quality assurance, promoted in particular by GISCi. On the other hand, the newly started programmes in Southern Italy need strong support to improve quality.

An active offer, free of charge, of the prophylactic vaccination against *human papillomavirus* types 16 and 18 to adolescents aged 12 (and to a few older cohorts in some Regions) started in Italy during 2008. This is bound to cause remarkable changes in the epidemiology of cervical cancers and of intraepithelial lesions, with an obvious impact on cervical screening. Randomised trials conducted in Sweden,[14] the Netherlands[15] and the UK[16] showed that screening based on HPV testing allows earlier detection of clinically relevant precancerous lesions compared to cytology-based screening. A large Italian RCT confirmed these results and directly showed increased protection from invasive cervical cancer with HPV-based screening, suggesting a shift to cervical screening based on HPV testing as primary screening test.[17]

This change will make the presence of organised programmes even more important, in order to guarantee high coverage, high quality, and close comprehensive monitoring. There is indeed the risk that new technologies, although of potential benefit, may result, if improperly employed, in an increase of false positive tests, in overdiagnosis and in overtreatment. Therefore, we need to ensure that adequate protocols are applied, and that adequate quality assurance systems, which are already emerging from research projects,[18] are implemented. Indicators and computerised databases suited to the new situation also need to be developed.

Data providers for the 2008 survey

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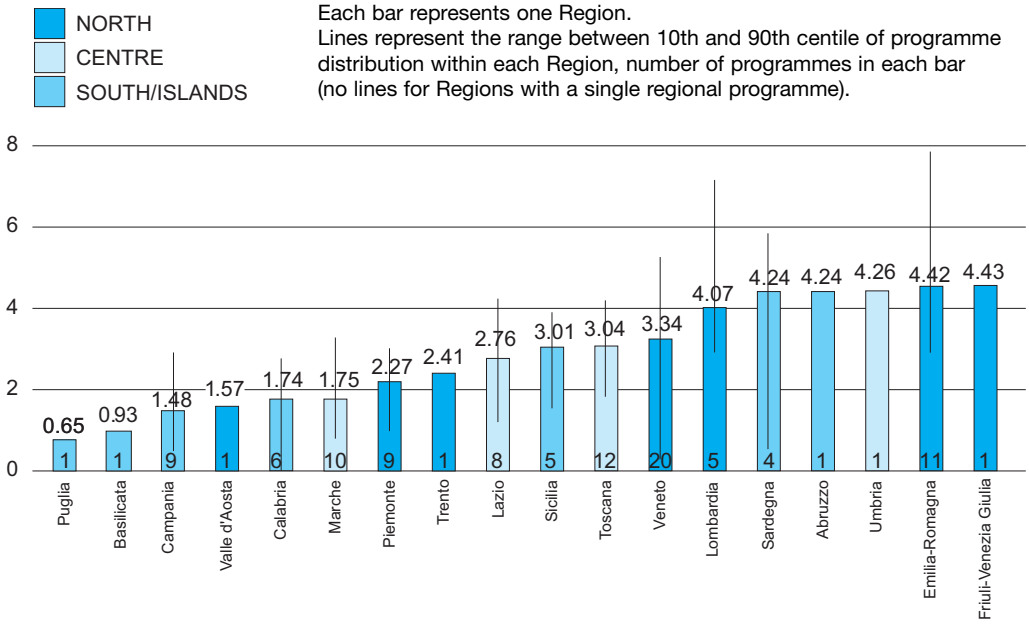

Figure 11. Unadjusted detection rate (per 1,000 women) of histologically confirmed CIN2+, by Region. Survey of 2008 activity.

L. Rossi, D. Marovelli (Empoli); S. Coccioli, D. Giorgi (Lucca); M. Rapanà, P. Marini (Pistoia); P. Vivani, C. Nicolai, G. Tornabene ((Massa Carrara); R. Turillazzi, E. Monti (Siena); A. Scarfantoni (Viareggio); M. Perco (Pisa); C. Maffei, P. Lopane (Livorno); R. Rosati (Grosseto); C. Epifani, L. Abdelghani (Prato); F. Mirri (Arezzo)

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ABRUZZO: C. Angeloni, A. Lattanzi

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CALABRIA: L. Rizzo, P. Petrucci (AS 1 Paola); L. Postorivo (AS 2 Castrovillari); N. D'Angelo (AS 3 Rossano); A. Giorno (AS 4 Cosenza); C. Spadafora (AS 5 Crotone); M.P. Montesi (AS 6 Lamezia Terme); C. Amodei (AS 8 Vibo Valentia); M.A. Bova (AS 9 Locri); O. Arfuso (AS 10 Palmi)

PUGLIA: V. Pomo, Murgolo (ARES); F. Longo, M. De Palma (Regione Puglia); C. Germinario (OER Puglia); V. Giordano, S. Aquilone, R. Gagliardo, M. Chiazza, G. Gragnaniello (ASL BA); V. Colucci (ASL BR); A. Marra, M.L. De Blasi (ASL LE)

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Screening for colorectal cancer in Italy: 2008 survey

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Abstract

We present the main results from the fifth 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. By the end of 2008, 87 programmes were active (14 had been activated during the year), and 52,9% of Italians aged 50-69 years were residing in areas covered by organised screening programmes (theoretical extension). Ten Regions had their whole population covered. In the South of Italy and Islands, 12 new programmes were activated in 2008, including those of Abruzzo and Molise Regions, with an increase of theoretical extension from 7% to 21%. 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 2,593,000 subjects were invited to undergo FOBT, 71% of those to be invited within the year. The adjusted attendance rate was 47.5% and approximately 1,171,000 subjects were screened. Large differences in the attendance rate were observed among Regions, with 10% of programmes reporting values lower than 30%. Positivity rate of FOBT programmes was 5.9% at first screening (range 2.0-11%) and 4% at repeat screening (range 2.9-6.5%). The average attendance rate for total colonoscopy (TC) was 81.3% and in three Regions it was lower than 70%. Completion rate of TC was 92.2%. Among the 665,264 subjects attending screening for the first time, the detection rate (DR) per 1,000 screened subjects was 2.7 for invasive cancer and 13.1 for advanced adenomas (AA, adenomas with a diameter ≥1 cm, with villous/tubulo-villous type or with high-grade dysplasia). As expected, the corresponding figures in the 552,391 subjects at repeat screening were lower (1.3‰ and 8.3‰ for invasive cancer and AA, respectively). The DR of cancer and adenomas increased with age and was higher among males. Many programmes reported some difficulties in guaranteeing TC in the appropriate time frame to FOBT+ subjects: in 16.0% of cases the waiting time was longer than two months.

Seven programmes employed FS as the screening test: 58.8% of the target population (about 50,000 subjects) were invited and 8,135 subjects were screened, with an attendance rate of 27.2%. Overall, 83% of FS were classified as complete. Overall TC referral rate was 13.5% and the DR per 1,000 screened subjects was 4.7 and 47.5 for invasive cancer and AA, respectively.

(*Epidemiol Prev* 2010; 4 (5-6) Suppl 4: 53-72)
Keywords: colorectal cancer screening programmes survey, Italy

This paper presents the data from the 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 2008. The previous surveys are available at the ONS website.[1]

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 em-

ploy 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 one programme 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 responders 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.

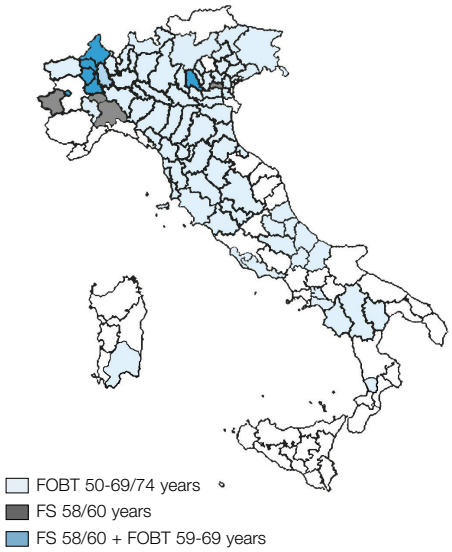


Figure 1. Colorectal cancer screening programmes: first level test and target population.

The GISCoR (Gruppo Italiano per lo Screening Colorettale, Italian Group for Colorectal Cancer Screening) published in 2007 an *Operative report of quality indicators* for the evaluation of colorectal cancer screening programmes.[2] For each indicator the reference standards (acceptable, desirable) are provided. Table 1 shows the indicators and standards utilised in this paper. The *Operative report* is available at the ONS website.

Data completeness

Only 48 of the 87 programmes that took part in the survey (57%) provided complete data. The items with the lowest level of completeness were screen-detected lesions and surgery: time to surgical treatment, stage at diagnosis, kind of treatment (endoscopic *vs* surgical). However, some programmes were unable to provide baseline data, either.

Programmes activated as of 31-12-2008

In Italy, colorectal cancer screening programmes were mainly activated in 2005 and 2006. After a pause observed in 2007, 14 new programmes were launched during 2008, 12 of which in the South of Italy and Islands, including those of Abruzzo and Molise (figure 2). As of 31st December 2008, 87 programmes were active in 12 Regions (table 2). In particular, programmes on a regional-scale basis were activated in Abruzzo, Basilicata, Emilia-Romagna, Friuli-Venezia Giulia, Lombardia, Molise, Toscana, Umbria, Valle d'Aosta and Trentino. The vast majority of programmes (n=80) employ the faecal occult blood test (FOBT), while three have adopted flexible sigmoidoscopy (FS)

Indicator	Standard	
	acceptable	desirable
Actual extension	>80%	>90%
Compliance to invitation	>45%	>65%
Positivity rate	**FOBT:** first test: <6% repeat tests: <4.5% **FS:** <8%	**FOBT:** first test: <5% repeat tests: <3.5% **FS:** <6%
Inadequate screening tests	**FOBT:** <1% **FS:** <10%	**FS:** <5%
Attendance to further assessment	**FOBT:** >85% **FS:** >90%	**FOBT:** >90% **FS:** >95%
Complete FS rate	>85%	>90%
Complete TC rate	>85%	>90%
Detection rate	**FOBT** Carcinoma first test: >2.0‰ repeat tests: >1.0‰ Adv. adenoma first test: >7.5‰ repeat tests: >5.0‰ **FS** Carcinoma >3.0‰ Adv. adenoma > 35‰	**FOBT** Carcinoma first test: >2.5‰ repeat tests: >1.5‰ Adv. adenoma first test: >10‰ repeat tests: >7.5‰ **FS** Carcinoma >4.0‰ Adv. adenoma >40‰
Detection rate of adenomas at FS	males >10% females >5%	males >15% females >10%
PPV of FOBT at colonoscopy for advanced adenoma or carcinoma	first test >25% repeat tests >15%	first test >30% 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.

once in a lifetime, and four 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 2008 approximately 14,381,000 people aged 50-69 years were living in Italy.[3] The number of subjects residing in areas where an organised screening programme is active was 7,605,000, with a national theoretical extension of 52.9%, six points higher than that observed in 2007 (46.6%) (table 2).

Region	Programmes	Total resident subjects (N)[1]	Subjects residing in areas covered by a programme (N)	Theoretical extension (%)[2]
Abruzzo	6	326,673	326,673	100.0
Basilicata	1*	132,952	132,952	100.0
Calabria	1	451,498	28,471	6.3
Campania	4	1,245,926	314,155	25.2
Emilia-Romagna	11*	1,067,933	1,067,933	100.0
Friuli-Venezia Giulia	1*	325,180	325,180	100.0
Lazio	4	1,355,068	457,057	33.7
Lombardia	15*	2,381,977	2,381,977	100.0
Molise	1*	74,122	74,122	100.0
Piemonte°	6	672,515	179,726	26.7
Sardegna	1	417,825	133,525	32.0
Toscana	12*	940,341	940,341	100.0
Trentino	1*	122,618	122,618	100.0
Umbria	4*	231,456	231,456	100.0
Valle d'Aosta	1*	30,109	30,109	100.0
Veneto	18	1,171,715	858,479	73.3
Other Regions	0	3,463,696	0	0.0
ITALY	**87**	**14,381,381**	**7,604,774**	**52.9**

[1] residents 50-69 years old at 01.01.2008 (source: Istat).

[2] proportion of eligible subjects residing in areas covered by organised screening programmes.

* regional-based programmes.

° In the Region Piemonte, programmes screen only subjects aged 59-69 years.

Table 2. Main data of FOBT programmes by Region in 2008: 50-69 year old subjects.

Compared to the previous years, the Northern and Central Regions reported a small increase, while in the South of Italy and Islands the theoretical extension increased from 7 to 21% thanks to the activation of many new programmes and of the reopening of the regional programme of Basilicata (table 3).

Extension of invitations

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

During 2008, about 2,593,000 subjects were invited to attend a screening programme, accounting for 71.3% of the target population to be invited in the year (table 4). Particularly significant results were reached by Emilia-Romagna and Lombardia, which confirmed the full capacity reached in the previous years, and Molise, which reached an extension of 87%. The low levels reported in other Regions are due either to the recent activation of many programmes or to the chronic difficulty of many programmes in ensuring the necessary number of invitations.

	2006		2007		2008	
	N	%	N	%	N	%
North	4,420,000	66.1	4,823,000	71.6	4,966,022	73.3
Centre	1,361,000	48.5	1,487,000	52.1	1,628,854	56.3
South - Islands	460,000	10.0	323,000	7.0	1,009,898	21.4
ITALY	**6,240,000**	**44.3**	**6,634,000**	**46.6**	**7,604,774**	**52.9**

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.

Region	Invited subjects (N)	Extension of invitation[1]		Screened subjects (N)	Adjusted compliance[2]	
		(%)	10° - 90° percentile		(%)	10° - 90° percentile
Abruzzo	21,850	13.3	3.5 - 29.7	9,644	45.8	40.4 - 70.1
Basilicata	9,734	33.4	–	3,065	33.1	–
Calabria	8,269	55.1	–	2,336	29.9	–
Campania	41,247	53.6	28.2 - 94.2	21,361	53.9	33.3 - 58.9
Emilia-Romagna	518,433	99.8	71.8 - 110.3	271,664	53.7	49.2 - 58.8
Friuli-Venezia Giulia	32,564	24.4	–	11,831	36.8	–
Lazio	35,132	14.9	4.1 - 28.0	11,331	33.3	22.6 - 38.2
Lombardia	1,139,599	93.8	63.1 - 125.3	440,836	42.0	31.9 - 61.3
Molise	32,392	87.1	–	10,847	33.6	–
Piemonte°	57,269	63.9	–	16,803	29.3	–
Sardegna	600	0.9	–	144	24.7	–
Toscana	332,884	69.8	18.3 - 95.1	163,885	50.8	33.5 - 58.4
Trentino	17,831	28.8	–	9,255	53.6	–
Umbria	69,538	59.4	38.7 - 80.5	25,660	37.9	35.0 - 43.7
Valle d'Aosta	10,276	68.5	–	6,792	66.1	–
Veneto	265,793	69.0	20.3 - 106.2	165,304	63.7	43.1 - 74.6
ITALY	**2,593,411**	**71.3**	**9.5 - 108.2**	**1,170,578**	**47.5**	**29.8 - 65.7**

[1] proportion of the annual target population that was actually invited.

[2] subjects attending out of those invited, excluding from denominator those reporting a recent test and those who did not receive the invitation letter.

° In the Region Piemonte, programmes screen only subjects aged 59-69 years.

Tabella 4. FOBT programmes: extension of invitations and adjusted compliance by Region: 50-69 year old subjects.

This interpretation is confirmed if we exclude the newly-activated programmes from the analysis: the average extension is 83.7%, however 10% of programmes with the lowest extension (10th percentile) invited less than 30% of the annual target. Overall, in 2008 the 10th percentile was lower than 10% and only 47% of programmes reached the GISCoR acceptable standard (>80%) (54% in 2007).

Intra-regional variability, illustrated in table 4 through the percentiles for the Regions with at least four programmes, is high in all but Emilia-Romagna and Lombardia, where all programmes reached high levels.

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.

Figure 2. Colorectal cancer screening programmes by year of start.

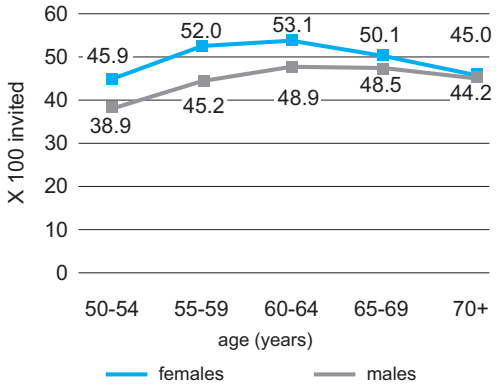


Figure 3. FOBT programmes: adjusted compliance by age and gender.

Overall, about 1,170,578 people were screened with FOBT in 2008. Adjusted compliance (47.5%) slightly increased as compared to 2007 and 2006 (46.3% and 44.6%, respectively) (table 4).

The analysis of compliance by Region shows a high inter-regional variability, with values ranging from 24.7% in Sardegna to 66.1% in Valle d'Aosta (table 4). Moreover, a high intra-regional variability in almost all Regions must be highlighted. The compliance obtained by single programmes ranged from 21% to 79%. The 10th percentile (30%) is clearly insufficient to guarantee suitable coverage of the population and, consequently, efficiency of a screening programme. Overall, 57% of programmes reached the acceptable (>45%) and only 11% the desired GISCoR standard (>65%).

Attendance by age and gender shows higher values in females (49.7% *vs* 44.8% for males), but only in younger age groups (figure 3). Compliance to FOBT is highest in the central age groups. 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 who had already been invited, but never attended (who are less likely to comply).

The attendance of subjects invited for the first time was 41.4% with a trend by sex and age similar to the global one. Eighty-one percent of subjects who had already responded attended the new invitation, with lower values in males, particularly at younger ages. It must be pointed out that attendance of the 10% of programmes with the worst value was lower than 66%.

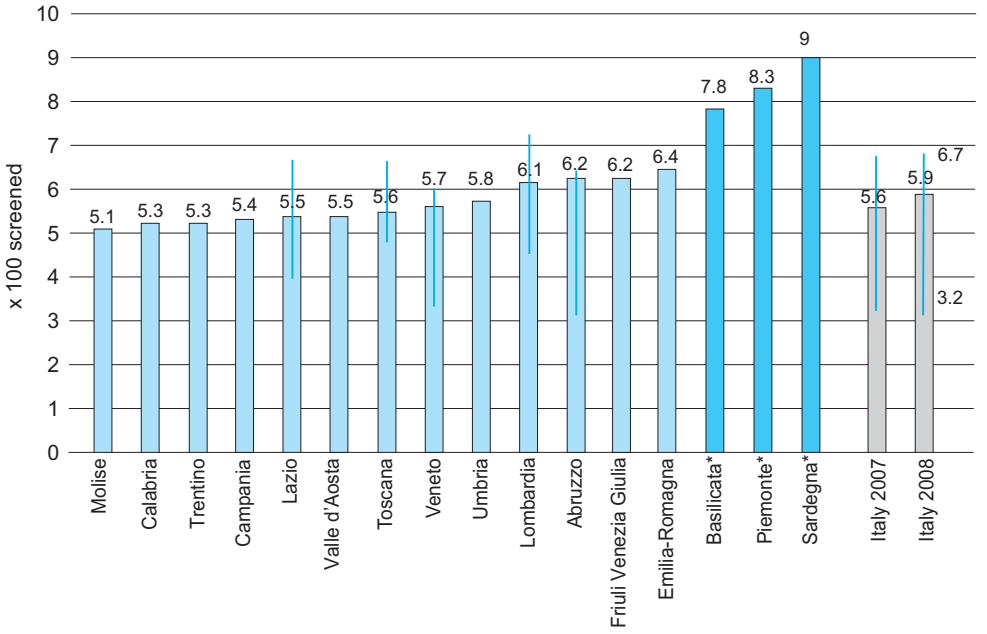
Finally, attendance of subjects who had never responded to previous invitations was 19.6% and decreased from the youngest (21%) to the oldest (14%) age group.

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.[4] 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



* not standardised (screenee aged 60+ only).

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

observed an elevated homogeneity among programmes and therefore we did not standardise the indicators. The data refer to 1,217,655 subjects screened during 2008 for which data are available; of these, 665,264 (55%) underwent first screening and 552,391 (45%) subsequent examinations.

Positivity rates

In subjects at first screening, the proportion of positive FOBT was 5.9%, with an elevated homogeneity among the mean values of Regions with a large number of screenees (figure 4). The proportion of FOBT+ reported by each programme ranges from 2.0% to 11% (10th-90th percentiles: 3.2-6.8%).

In subjects at repeat screening, the proportion of FOBT+ is 4.5%, with a lower variability between programmes (range: 2.9-6.5%).

Fifty-nine percent of programmes met the accept-

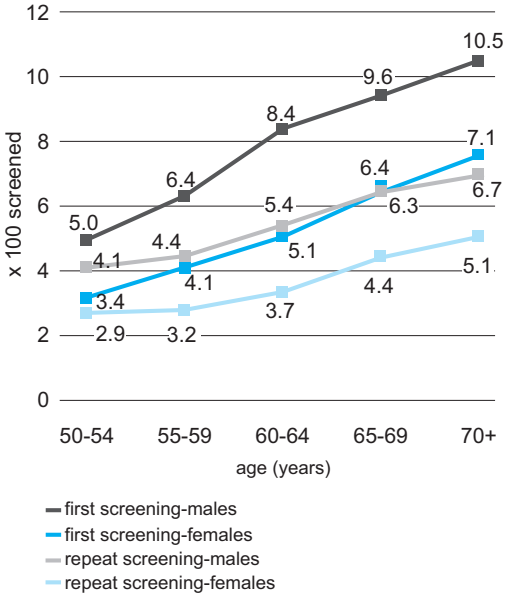


Figure 5. Proportion of FOBT+ by age and gender.

able 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.

Inadequate tests

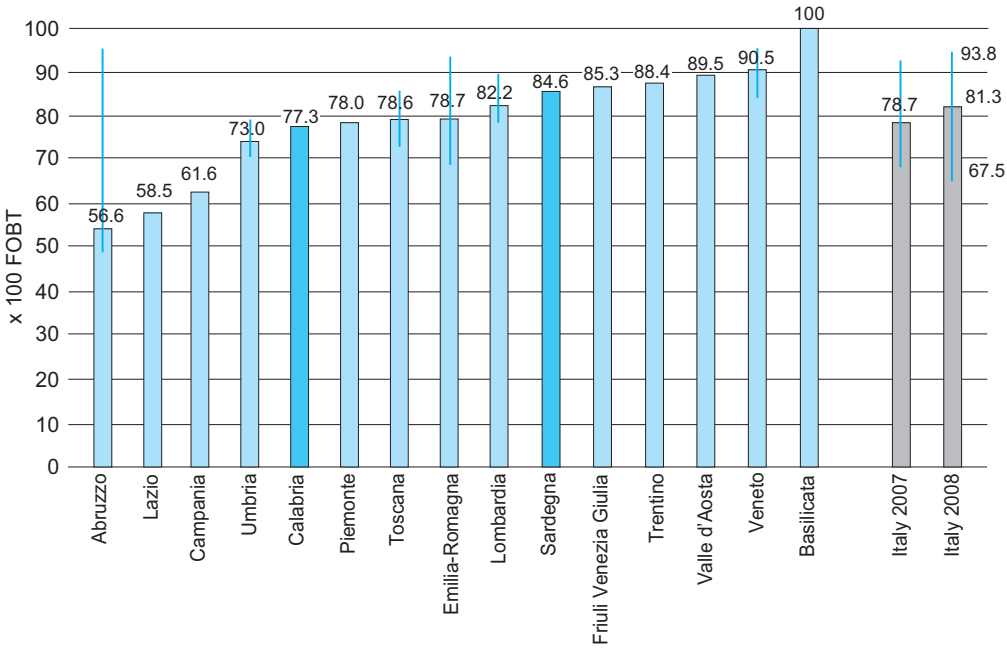
Inadequate tests are essentially due to an incorrect sampling by the subject. During 2008, 88% of programmes reported a proportion of inadequate FOBT lower than 1%, while only five programmes reported a result exceeding 2%. Overall, the national mean value was 0.6%.

Attendance to colonoscopy assessment

Attendance to colonoscopy assessment is essential for screening programmes to achieve colorectal cancer mortality reduction. Overall, 81.3% of FOBT+ subjects attended colonoscopy in 2008. This result is lower than that observed in 2007 (78.7%). Only 22% of programmes met the desired standard (>90%).
Attendance was higher in males (82.3%) than in females (80.0%), as described in the literature.[5] 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.[6,7]
The lowest values were reported in the Regions of the Centre and South of Italy (Abruzzo, Lazio, Campania), the highest in Basilicata, Valle d'Aosta and Veneto (figure 6).

Complete colonoscopies

Besides compliance to colonoscopy, a cornerstone



Note: deep blu columns refer to Regions whose indicators are based on a limited number of cases.

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

element in measuring the effectiveness of a screening programme is the completeness of the endoscopic examination. Overall, 92.2% of the colonoscopies carried out in 2008 were classified as complete, a highly satisfactory result. Eighty-two percent of programmes met the acceptable (>85%) and 61% the desired standard (>90%).
Compared to 2007, we observed an increase in variability among Regions, partly due to the worsening of the quality of data. Mean regional values ranged from 63.8% in Basilicata to 96.8% in Trentino. The values of single programmes ranged from 63.8 to 100%, and the lowest values were due to a small number of outliers (10th percentile: 80.1%).
Programmes generally reported higher proportions of complete exams in males compared to females (overall 94.1 % *vs* 91.5%, respectively), as reported in the literature.[8]
Fifty-four programmes reported data about further assessments in case of an incomplete TC, which took place only in 45% of cases.

Complications at colonoscopy

Fifty-five programmes reported the data about complications at TC, relative to 38,764 examinations overall.
Sixty-nine cases of bleeding were reported, 64 of which were during operative TCs, with a rate of 0.03% for non-operative and 0.34% for operative TCs, both in line with the GISCoR standards (<0.5% and <2.5%, respectively). Twenty-three perforations were recorded (21 during operative TCs), with a rate of 0.01% for non-operative and 0.11% for operative TCs, in line with the GISCoR standards (<0.5% and <2.5%, respectively).
Overall these data are very good; however, a high variability in the collection and recording of 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 ≥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 1,796 carcinomas, 8,633 advanced adenomas, and 5,101 non-advanced adenomas were detected. Therefore the DR was 2.7‰ for carcinoma, 13.1‰ for advanced adenomas, and 7.7‰ for non-advanced adenomas (figure 7). Sixty-eight percent of programmes reached the acceptable standard for carcinoma (>2‰), and 77% for advanced adenoma (>7.5‰).
However, the ratio between the DRs of advanced

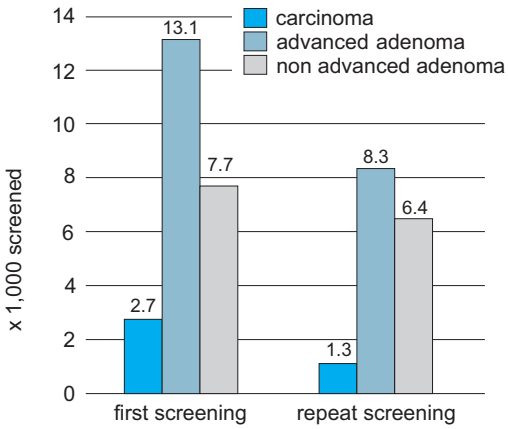


Figure 7. FOBT programmes: detection rates of carcinoma, advanced adenoma and non-advanced adenoma at first and repeat screening.

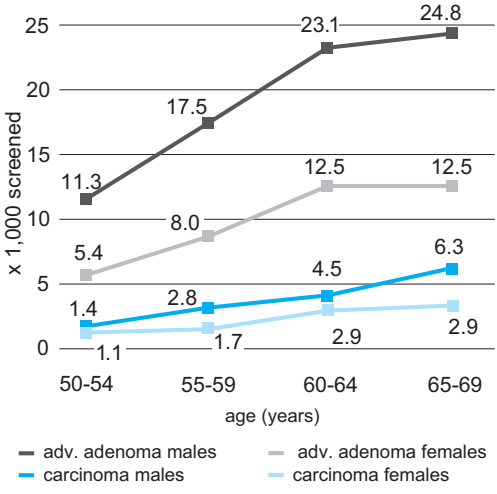


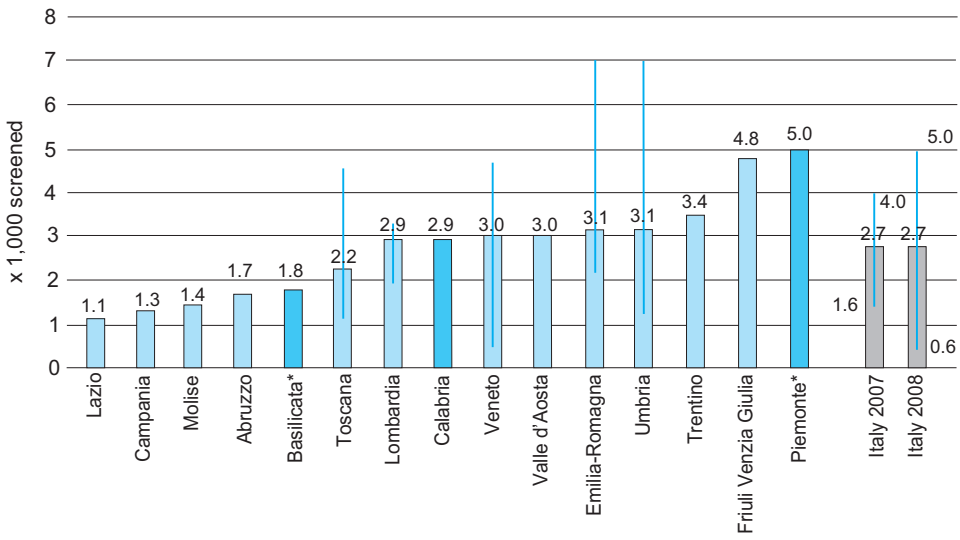
Figure 8. FOBT programmes: detection rates of carcinoma and advanced adenoma by age and sex at first screening.

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, which tend to bleed more easily than non-advanced adenomas, as described in the literature.[9]

In subjects undergoing repeat testing, 722 carcinomas, 4,545 advanced adenomas and 3,568 non-advanced adenomas were detected. As expected, the DRs were lower than the corresponding figure at first exams (figure 7). Seventy-four percent of programmes reached the acceptable standard for carcinoma (>1‰), and 91% 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).

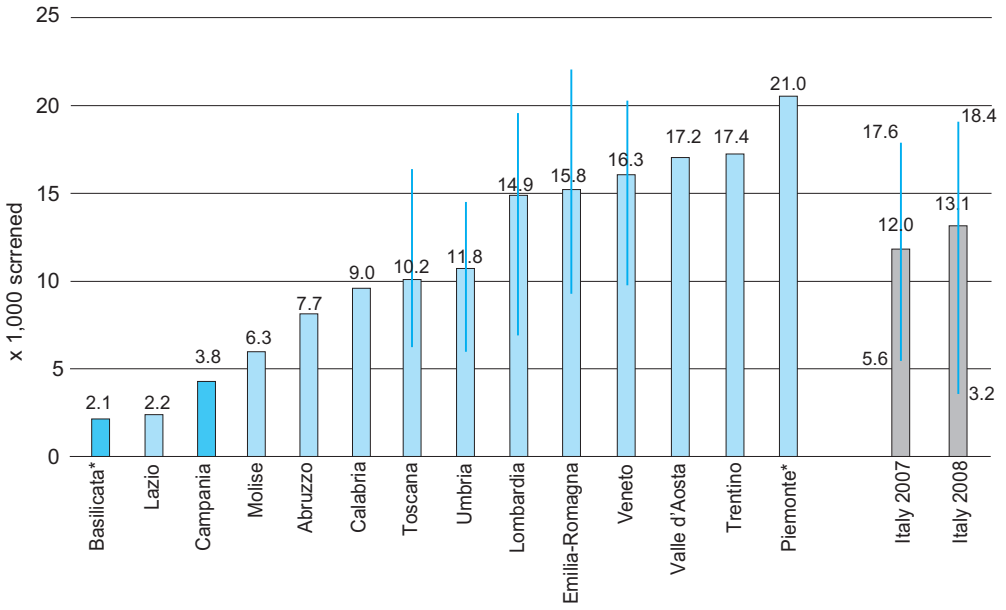
With the exception of Regions with unstable data due to the limited number of screened subjects, we



* not standardised (screenee aged 60+ only).

Note: deep blu columns refer to Regions whose indicators are based on a limited number of cases.

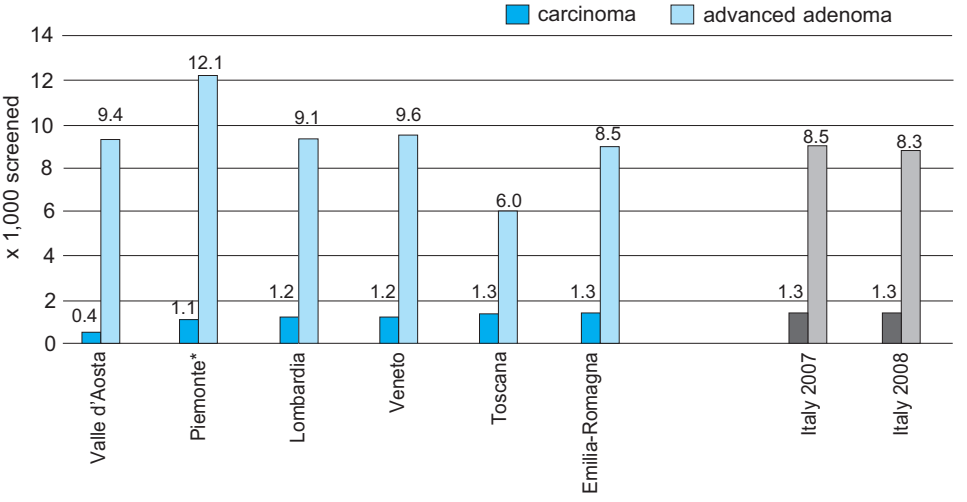
Figure 9. FOBT programmes: standardised (by age and gender, utilising the national media as standard population) detection rates of carcinoma at first screening, by Region, with 10th and 90th percentiles.



* not standardised (screenee aged 60+ only).

Note: deep blu 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, by Region, with 10th and 90th percentiles.



* screenee aged 60+ only.

Figure 11. FOBT programmes: detection rates of carcinoma and advanced adenoma at repeat screening, by Region.

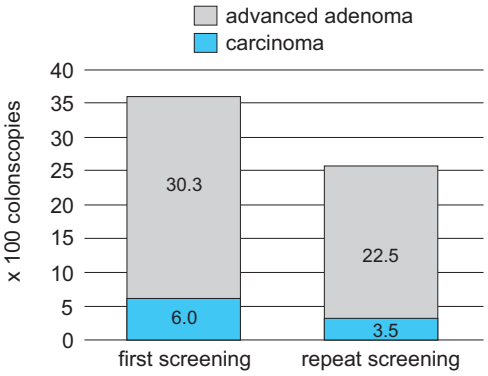


Figure 12. FOBT programmes: positive predictive value (PPV) of colonoscopy for carcinoma and advanced adenoma at first and repeat screening.

observed a high variability among the mean regional values of carcinoma DRs (from 1.1‰ in Lazio to 4.8‰ in Friuli-Venezia Giulia; in Piemonte, programmes screened only subjects aged 60-69 years, figure 9), and advanced adenomas (2.1-2.2‰ in Basilicata and Lazio, 17.4‰ in Trentino, figure 10).

We observed an increasing North-South trend in the detection rates of carcinoma and advanced adenoma, as expected according to the underlying epidemiological figures (carcinoma: North 3.0‰, Centre 2.2‰, South-Islands 1.3‰; advanced adenoma: North 15.0‰, Centre 9.1‰, South-Islands 4.2‰). At repeat examinations, a higher homogeneity was reported among Regions for the DR of carcinoma (Valle d'Aosta: 0.4‰, Emilia-Romagna: 1.3‰) and advanced adenoma (Toscana: 6.0‰, Veneto: 9.6‰) (figure 11).

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 2008, 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 29,495 subjects at first screening round who underwent a colonoscopy after a FOBT+, a diagnosis of carcinoma was formulated in 6% and advanced adenoma in a further 30.3% (figure 11). Among the 20,212 subjects at repeat screening, the corresponding values were respectively 3.5% for carcinoma and 22.5% for advanced adenoma.

Eighty-three percent of programmes reached the acceptable standard for subjects at first screening (>25%) and 93% for those at 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 (data not shown).

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, about 92% 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 44% of cases (41% in 2007) and only three programmes met the acceptable standard (>90% within 30 days). Sixteen percent of subjects had to wait more than two months. The situation was particularly problematic in most Regions, with the exception of Trentino and Basilicata (83% and 80% within 30 days, respectively).

Finally, surgery was performed within 30 days after diagnosis in 64% of cases, and in a further 24% within 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 5.

Overall, during 2008, the 7 programmes invited 20,028 subjects, corresponding to a 58.8% actual extension over their target population (n=49,622): two of these programmes showed values near to 100%, three had very low levels (lower than 33%). Taking all programmes together, 8,135 subjects were screened with FS. Compliance to invitation was 27.2% (range: 12.1-39.6%), slightly lower than that reported in 2007 (27.7%). In all programmes, compliance was higher for males in comparison to females (overall: 29.9% *vs* 24.7%), 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 38% 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, 83% of FSs were classified as complete, with higher levels in males (88%) than in females (79%). This result is worse than the 88% recorded in 2007 and is below the GISCoR acceptable standard (>85%). Quite a high variability between programmes was recorded (range 75-98%) and the average is strongly influenced by the performance of a single programme (Verona: 75%).

Generally, the programmes referred 17.4% of screened males and 9.0% of females, respectively, to colonoscopy assessment. Only in 40% of 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 (85%) was higher than that observed for the FOBT screening, probably due to a greater motivation of the subject to undergo further assess-

	Males	Females	Total
Screened (N)	4,346	3,789	8,135
Screened 2007 (N)	4,489	4,189	8,678
Reason prompting colonoscopy (%)			
advanced adenoma*	7.0	2.9	5.1
other**	10.3	6.1	8.4
Detection rate (‰)			
carcinoma	6.8	2.2	4.7
advanced adenoma	65.0	27.5	47.5
non advanced adenoma	114.1	68.1	92.7
PPV (%)**			
carcinoma	0.5	0.0	0.3
advanced adenoma	7.1	1.5	4.1

* at least one advanced adenoma (with a diameter ≥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.

** proximal colon.

Table 5. Main results of FS programmes.

ment following a diagnosis of advanced adenoma. Colonoscopy completeness rate was 90.3%, and all centres reached high levels (range 84.1-100%). Among the subjects referred to colonoscopy, the prevalence of proximal advanced lesions (advanced adenomas plus cancers) ranged between 0% and 14%.

Overall, FS programmes detected 36 carcinomas, of which 34 in the distal tract of the colon, and 366 advanced adenomas, with a DR of 4.7‰ and 47.5‰, 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 and by the need to consider the cumulative sensitivity of FOBT ensured by repeat screening tests.

Stage at diagnosis

Overall, 1,796 cancers were detected in subjects at first screening and 722 at repeat screening. Seventy-three programmes reported the information about cancerised adenomas, which represented 25.5% of cancers at first screening and 24.2% at repeat screening. FS programmes detected 36 cancers, 11 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 1,957 cases (77.7% of the total). The incompleteness of this information is one of the most critical issues of Italian programmes encountered during 2008.

Table 6 shows the distribution by stage at diagnosis of cases screen-detected by FOBT and FS programmes. Overall, 28.9% of cases were in stage III+ at diagnosis, in agreement with the acceptable standard (<30%). As for the proportion of cases in stage III-IV, small differences were reported between cases at first and repeat screening.

Stage	FOBT programmes		FS programmes
	first screening (N=1,156)	repeat screening (N=585)	(N=28)
I	38.3	50.3	39.3
I*	10.1	5.1	14.3
II	21.2	18.6	17.9
III-IV	30.4	26.0	28.6

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

Surgery

This survey collects data about the kind of therapy performed on carcinomas, cancerised adenomas and advanced adenomas, and distinguishes between surgical intervention and endoscopic resection alone. Overall, data were provided for 87% of carcinomas and 85% of advanced adenomas.

Seventy-nine percent of carcinomas underwent surgery, while in 19.8% of cases the treatment was limited to endoscopic resection. This percentage increased to 28.4 considering only pT1 cases. As for advanced adenomas, treatment was exclusively endoscopic in 96.6% of cases.

Discussion

After the pause observed in 2007, the theoretical extension of colorectal cancer screening showed a 6% increase in 2008, with 2,554 carcinomas and 13,544 advanced adenomas being detected by screening, which makes the Italian experience one of the most advanced in the world.

By the end of the year, 14 new programmes were started, 12 of which were in the South of Italy and Islands. A positive sign came from the pres-

ence of new programmes in otherwise uncovered Regions such as Molise (with a regional programme), Calabria and Sardegna. In the North of Italy, we must point out the start of a regional programme in Friuli-Venezia Giulia. Overall, therefore, we observed a partial reduction in the delay in the South of Italy and Islands, where the theoretical extension was 21%. There are still five Regions without any screening programme.

Compared to 2007, extension of invitations was lower, due to the start of many new programmes that were active only for part of the year. If we consider only the programmes that had been activated before 2008, extension of invitations increases to nearly 83%. The situation varies from Region to Region. In many, all programmes reached the desired level of extension, therefore proving that, with adequate planning and fund raising, it is possible to achieve the desired volumes of activity.

On the other hand, the huge variability in extension between programmes underlines a chronic difficulty of many programmes begun in previous years in reaching and maintaining the two-year invitation rate. This determines a lengthening of the inter-screening interval, with possible effects on the programme's efficacy.

Uptake of invitation increased to 47.5%, the best result observed over the last years. 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. This specific analysis shows that attendance to the first invitation was lower than the previous years, probably due to the low performance of the new programmes, while the older ones invited a lower number of subjects for the first time (i.e., those entering the target age class of screening during the year). In 2008, more than half of the programmes had already activated a new round and their population, invited for the first time, was mainly made up of 50 year old subjects, a well-known low-attendance class.

In a biennial FOBT screening programme, a salient issue is whether or not the attendance of invited people can be sustained over time. Overall, 81% of the subjects that had 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, as already described in the literature.[10] Thus, the effect of other factors, which influence response to the first invitation, ceases. It is therefore important for programmes to identify the limitations that may have determined a lack of satisfaction in the screened population.

The low attendance (20%), 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.

These data suggest that the screened population changes across the years: overall the test coverage of the target population may be higher than the number of screened subjects, but for the subjects who do not regularly undergo screening the protective effect of screening will be lower than expected.

This aspect should be taken into consideration when comparing the impact of FOBT *vs* FS programmes. If we assume that the highest protection of FOBT screening is given by regular repetition of the test, while the protection of a single FS lasts for some years, we will expect a reduction in the difference in protection between the two strategies.

The evaluation of diagnostic indicators is difficult because many programmes produced incomplete data and this may be misleading when interpreting the results on a regional basis. In fact, many indicators depend on many factors (e.g., DRs are influenced by the distribution of the screenee by age and sex, by FOBT positivity and by compliance to colonoscopy) and they should be interpreted according to their intra-regional composition. For each indicator we had to select the programmes that sent complete data, with a possible selection bias. Unfortunately, the less complete questionnaires came from the Regions with the lowest number of programmes, leading to an even greater bias.

Overall, we observed for the first time an equilibrium between first and subsequent screening episodes (n=665,264 - 55%; and n=552,391 - 45%, respectively).

The proportion of FOBT+ is quite homogeneous among programmes, particularly at repeat screening. FOBT positivity is affected by many factors that are mainly related to the prevalence of the disease (geography, distribution by age and sex, first *vs* subsequent test) or to the performance of the test (sensitivity, specificity, positivity threshold). Some studies evaluated the effect of the stability of haemoglobin in the faecal sample on the analytic sensitivity of the test. Van Rossum recently showed that the delay between the sample collection by the subject and the delivery of the sample to the laboratory may negatively affect the test's sensitivity with an increase in the proportion of false negative results.[11] The guidelines for lab workers, recently published by GISCoR, recommend a desired maximum delay of 7 days between the sample collection and the performance of the test.[12] However, many programmes are not able to produce the data of the sampling and/or of delivery of the sample by the subject, therefore it is impossible to evaluate the adherence to this recommendation. This is an important aspect, which would be worth studying in the future.

Particular attention should be given to attendance to colonoscopy (81.3% in 2008). The actual proportion of FOBT+ subjects that did not undergo any further assessment is probably lower, since many programmes did not collect data about assessments performed in non-screening settings. However, it must be stressed that the duty of screening programmes is not only that of reaching high levels of attendance to colonoscopy, but also making sure that FOBT+ subjects have undergone assessment, even if outside the programme. The data reported in 2008 suggest that many programmes did not deal with this aspect.

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

Attendance to colonoscopy may also be negatively affected by a long waiting time for the performance of examinations. During 2008 we observed a generalised difficulty for endoscopic services to deal with the excess workload deriving from screening positives.

Compared to the last years, the DRs of carcinoma and advanced adenoma were stable. However, many programmes showed a reduction in DRs at first screening: this is not worrisome, since for programmes 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.

Since DRs are calculated dividing the diagnosed lesions by the screened population, they are inversely associated to the loss of attendance to colonoscopy. In fact, when adjusting the DRs by

attendance to colonoscopy, we observed a levelling off of the differences between regional means. The fluctuations in DRs observed between programmes suggest the presence of factors responsible for this aspect other than the diagnostic sensitivity of the screening programme, such as the quality of endoscopy and the different criteria locally used to classify adenomas as advanced or non-advanced. The detection rate of polyps is one of the indicators for the monitoring of endoscopy quality.[13] GISCoR and ONS carried out a number of «Train the trainer» courses for endoscopists and pathologists which will hopefully be reproduced at regional level.

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 structures.

Moreover, it must be pointed out that most colonoscopies are surgical and should therefore be carried out by expert endoscopists and accurately monitored for quality.

This survey collects little information about the quality of endoscopy. Nevertheless, the data obtained from programmes show a good quality of colonoscopies in terms of completeness and complication rates, both for operative and non-operative TCs.

As for treatment, we collected information about the use of surgical intervention *vs* endoscopic resection alone. Overall, 20% of patients with carcinoma underwent endoscopic resection alone, resulting in improved patient quality of life and cost reduction. However, this percentage increased only to 28% of pT1 cases, which are mostly made up of cancerised adenomas. A possible overtreatment of these subjects should be accounted for.

Overall, 97% of advanced adenomas were treated through endoscopic resection alone. However, we underline the high variability among programmes: surgical intervention was used for 5-10% of adenomas by nine programmes and for more than 10% of cases by two.

	UK Pilot study	Italy 2008
Test	guaiac	immunochemical
Participation (%)	56.8	41.4
Positivity rate (%)	1.9	5.9
Detection rate (‰)		
cancer	1.6	2.7
neoplasia*	6.9	23.5
PPV (%)		
cancer	10	6
neoplasia*	46	54
Attendance to colonoscopy (%)	82.2	81.3

* carcinoma or advanced adenoma or non-advanced adenoma.

Table 7. UK Pilot study (first round) and Italian FOBT screening programmes (first exams): comparison of the main results.

We did not notice any difference between cases at first and repeat screening with respect to the proportion of cases in stage III-IV. This might be due to the sub-optimal sensitivity of FOBT, which fails to identify all tumours present at first screening. Monitoring this indicator over time should clarify this aspect, because as the number of screening rounds increases, the proportion of cancers at an advanced stage detected at subsequent episodes should decrease thanks to the cumulative protection offered by repeat negative episodes. Finally, these data will need to be compared with the frequency and distribution by stage of interval cancers.

Stage distribution, instead, was clearly better for screen-detected cases than the clinical series observed in the absence of organised programmes, since about 40 to 50% were at stage III or IV at diagnosis.

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 (table 7), important

Programmes participating in the survey

Programme	Head of the programme
Abruzzo	
Avezzano Sulmona	A. Sedici
Chieti	S. Martinotti
L'Aquila	A. Agnifili
Lanciano Vasto	G. Ferrini
Pescara	E. Liberatore
Teramo	S. Prosperi
Basilicata	A. Sigillito
Calabria	
Lamezia Terme	M.P. Montesi
Campania	
Avellino 2	V. Landolfi
Salerno 1	V. Gallo, A. Caiazzo, G. Storti
Salerno 2	A. Rossi, MG. Panico
Salerno 3	A. Giuliano, G. Della Greca
Emilia-Romagna	
Regione Emilia-Romagna	A.C. Finarelli, C. Naldoni, P. Landi
Piacenza	F. Fornari, E. Borciani
Parma	A. Franzè, C. Zurlini
Reggio Emilia	L. Paterlini, R. Sassatelli
Modena	R. Corradini
Bologna	N. Collina, M. Manfredi, N. D'Imperio, F. Bazzoli
Imola	R. Nannini
Ferrara	G. Zoli, M.C. Carpanelli, V. Matarese,
Ravenna	O. Triossi
Forlì	F. Falcini
Cesena	P. Pazzi, M. Palazzi
Rimini	M. Giovanardi, D. Canuti
Friuli-Venezia Giulia	L. Zanier
Lazio	
Viterbo	M. Anti, S. Brezzi
Rieti	G. Baldi, F. Barberani
Roma D	P. Grammatico, A. Sorce
Roma H	A. Scozzarro, A. Vella
Lombardia	
Bergamo	R. Paginoni, G. Rocca, L. Tessandri
Brescia	C. Scotti, F. Speziani
Como	M. Gramegna, G. Gola
Cremona	L. Boldori, M. Dal Soldà
Lecco	A. Ilardo
Lodi	A. Belloni, G. Marazza
Mantova	E. Anghinoni
Milano città	L. Bisanti
Provincia Milano 1	M.E. Pirola, P. Ceresa
Provincia Milano 2	L. Fantini
Monza	M. Ignone
Pavia	L. Camana, G. Magenes
Sondrio	L. Cecconami
Vallecamonica	L. Pasquale
Varese	F. Sambo
Molise	P. Mescia, G. Cecere
Piemonte	
Alessandria	G. Faragli
Asti	T. Miroglio
Biella Vercelli	N. Lorenzini
Collegno Pinerolo	M. Sartori
Novara	C. Magnani, A. Cipelletti
Torino	C. Senore
Sardegna	
Cagliari	S. Tilocca
Toscana	
Arezzo	F. Mirri, P. Ceccatelli
Empoli	L. Rossi, M. Biagini
Firenze	G. Grazzini, C. Visioli, N. Ianniciello
Grosseto	R. Rosati, P. Piacentini, S. Quaranta, A. Rechichi
Livorno	P. Lopane, C. Maffei, G. Niccoli
Lucca	G. Finucci, S. Cocciolo, G. Gujana
Massa Carrara	C. Nicolai, P. Vivani, F. Pincione
Pisa	G. Venturini, M. Perco, V. Calvaruso
Pistoia	A. Natali, M. Rapanà
Prato	A. Battaglia, C. Epifani, A. Candidi Tommasi
Siena	A. Ciarrocchi, R. Turillazzi, P. Galgani
Viareggio	C. Ciabattoni, U. Ferro
Trentino	S. Piffer
Umbria	
Città di Castello	D. Felicioni
Foligno	A. Di Marco
Perugia	B. Passamonti, M. Malaspina
Terni	R. Corvetti
Valle d'Aosta	S. Crotta
Veneto	
Alta Padovana	P. Coin
Alto Vicentino	F. Banovich
Asolo	G. Lustro
Belluno	F. Soppelsa
Bussolengo	A. Bortoli
Chioggia	M.L. Polo
Dolo Mirano	A. Montaguti
Este Monselice	M. Penon
Feltre	L. Cazzola
Legnago	F. Vaccari
Ovest Vicentino	M. Lestani
Padova	I. Simoncello
Pieve di Soligo	T. Menegon
Rovigo	L. Gallo
Treviso	G. Gallo
Veneto Orientale	A. Favaretto
Verona	P. Costa, A. Ederle
Vicenza	M. Merzari

differences were evident.[14] 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 neoplasia 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.

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.

Some programmes have already started to monitor interval cancers: it will be important to share these experiences in order to identify the most efficient and feasible method for data collection, analysis, and interpretation.

GISCoR recently proposed a surveillance system for the follow-up of advanced adenomas in order to evaluate locally adopted protocols and to collect data about compliance, detection rates, and workload for the Endoscopy Units.

Data providers for the year 2008:

ABRUZZO: V. Maccallini
BASILICATA: A. Sigillito
CALABRIA: M.P. Montesi
CAMPANIA: R. Pizzuti
EMILIA-ROMAGNA: C. Naldoni, P. Sassoli de' Bianchi (Regione Emilia-Romagna); F. Fornari, G. Gatti (Piacenza); C. Zurlini (Parma); A. Franzè, M. Zatelli, F. Maradini (AOSP Parma); L. Paterlini, C.Campari (Reggio Emilia); R. Sassatelli (AOSP Reggio Emilia); R. Corradini, C. Goldoni (Modena); N. Collina, M. Manfredi, P. Baldazzi (Bologna); R. Nannini, L. Caprara (Imola); M.C. Carpanelli, O. Buriani (Ferrara); O. Triossi, M. Serafini, B. Vitali (Ravenna); F. Falcini, A. Colamartini, O. Giuliani, R. Vattiato (Forlì); M. Palazzi, C. Imolesi (Cesena); D. Canuti, C. Casale, C. Fava (Rimini)
FRIULI-VENEZIA GIULIA: S. Di Bartolomeo, S. Tillati
LAZIO: A. Barca, D. Baiocchi, F. Quadrino
LOMBARDIA: R. Galli (Bergamo); C. Scotti (Brescia); L. Zerbi (Como); M. Dal Soldà (Cremona); A. Ilardo (Lecco); G. Marazza (Lodi); E. Anghinoni (Mantova); E. Tidone, N. Leonardo (Milano città); P. Ceresa (Milano 1); L. Fantini (Milano 2); M. Ignone (Monza); G. Magenes (Pavia); L. Cecconami (Sondrio); F. Sambo (Varese); L. Pasquale (Vallecamonica)
MOLISE: A. Di Credico
PIEMONTE: C. Senore
SARDEGNA: R. Masala
TOSCANA: C. Nicolai, G. Tornabene (Massa e Carrara); S. Coccioli, D. Giorgi (Lucca); M. Rapanà, G. Bini (Pistoia); C. Epifani, L. Abdelghani (Prato); M. Perco (Pisa); P. Lopane, C. Maffei (Livorno); R. Turillazzi (Siena); F. Mirri (Arezzo); R. Rosati (Grosseto); C.B. Visioli, P. Falini, P. Piccini (Firenze); L. Rossi, D. Marovelli (Empoli); C. Ciabattoni (Viareggio)
TRENTINO: E. Barberi
UMBRIA: G. Vinti (Città di Castello); D. Antonini (Foligno); M. Malaspina (Perugia); R. Corvetti (Terni)
VALLE D'AOSTA: S. Crotta
VENETO: S. Callegaro (Alta Padovana); C. Fedato (Alto Vicentino); G. Diacono (Asolo); S. Di Camillo, R. Mel (Belluno); A. Ganassini, C. Fedato (Bussolengo); M.L. Polo (Chioggia); C. Fedato (Dolo); M. Gennaro, F. Talpo (Este Monselice); C. Fedato (Feltre); S. Soffritti (Legnago); N. Scomazzon (Ovest Vicentino); F. Sambo (Padova); T. Moretto (Pieve di Soligo); C. Fedato (Rovigo); M. Pieno, M. Bovo (Treviso); A. Favaretto (Veneto Orientale); M.C. Chioffi, L. Benazzato (Verona); A. Dal Zotto, E. Dal Lago (Vicenza)

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Quality of colposcopy and treatment: data from the national survey of Italian organised cervical screening programmes. 2008 activity

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We collected data from organised Italian cervical screening programmes on (a) the correlation between colposcopic findings (according to the 1990 international classification) and histology, and (b) the treatment/management of screen-detected histologically confirmed cervical intraepithelial neoplasia (CIN).
Data routinely registered by organised programmes were obtained as aggregated tables.
Of the 25,932 reported colposcopies 38.1% were classified as normal and 20.2% as unsatisfactory. CIN2 or more severe histology was detected in 64.0% of colposcopies classified as grade 2 or higher. Of all colposcopies, the outcome of which was CIN2 or more severe histology, 41.7% were classified as grade 2 or higher.
Of the 4,923 women with CIN1, 78.1% had follow-up only. However 0.8% of them had cold-knife conisation, 4.7% were treated by diathermocoagulation and 0.1% had a hysterectomy. Of the 3,788 women with CIN2 or CIN3, 3.9% had not yet been treated when data were collected and no data were available for a further 9.9%. Excision by radio-frequency device was the most common treatment among these women (66.7% of those with known treatment). However 0.7% of all CIN2 and 4.0% of all CIN3 had a hysterectomy. Among the 163 women with invasive carcinoma, 17.2% plausibly with microinvasive disease had only excisional treatment reported.

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Keywords: cervical screening quality treatment assessment survey, Italy

The evaluation of diagnostic assessment and treatment resulting from abnormal cytology is an essential part of quality assurance for cervical cancer screening. It would be impossible to prevent invasive cancer if intraepithelial lesions were not correctly detected during diagnostic procedures – colposcopy and biopsy – and adequately treated. According to the Italian NHS guidelines ≥90% of cases with a recommended treatment should actually be treated.[1,2]
There is also a need to control economic and especially human costs. It is mainly important to avoid over-treatment, particularly of lesions that are not likely to progress to invasive cancer, given also the risk of pregnancy-related morbidity.[3,4] Italian, European and international guidelines suggest applying the most conservative approach among those that provide similar effectiveness.[1-2, 5-7] According to Italian guidelines, no more than 2% of CIN2-3 and no CIN1 should be hysterectomised.[1,2]
Italian data on the correlation between colposcopic findings, histology and treatments have been published since 2004[8-12] after an experimental period started in 1999. Here we report the same data obtained in the survey conducted in 2009 on women invited during 2008.

Methods

Data were obtained through the national survey on cervical screening. Standardised tables of aggregated data were collected, as for the remaining sections of the survey.
Data come from the routine registration system of screening programmes. Providers were asked to check the apparently most abnormal data.

Programme	Treatment	Colposcopic findings
Abruzzo	yes	yes
Basilicata	yes	yes
Bolzano Self-Governing Province	no	no
Calabria		
Cosenza	no	no
Lamezia Terme	yes	yes
Lercara	yes	yes
Locri	yes	yes
Palmi	yes	yes
Reggio Calabria	no	yes
Vibo Valentia	yes	yes
Campania		
Avellino 1	no	no
Avellino 2	yes	no
Benevento	no	no
Caserta 1	yes	yes
Caserta2	yes	yes
Napoli 1	yes	no
Napoli 2	no	no
Napoli 4	yes	yes
Napoli 5	yes	no
Salerno 1	no	no
Salerno 2	yes	no
Salerno 3	no	no
Emilia-Romagna		
Bologna	yes	yes
Cesena	yes	yes
Ferrara	yes	yes
Forli	yes	yes
Imola	yes	yes
Modena	yes	yes
Parma	yes	yes
Piacenza	yes	yes
Ravenna	yes	yes
Reggio Emilia	yes	yes
Rimini	yes	yes
Friuli-Venezia Giulia	yes	no
Lazio		
Frosinone	yes	yes
Latina	yes	no
Rieti	no	no
Roma A	no	no
Roma B	yes	no
Roma C	yes	yes
Roma D	yes	yes
Viterbo	yes	yes
Lombardia		
Brescia	yes	yes
Cremona	no	yes
Lodi	no	no
Mantova	no	no
Pavia	yes	yes
Valcamonica Sebino	yes	yes
Marche		
Ancona	no	no
Ascoli Piceno	yes	yes
Camerino	no	no
Civitanova	no	no
Fano	yes	yes
Fermo	no	no
Fabriano	no	no
Jesi	no	no
Macerata	yes	no
Pesaro	yes	yes
S. Benedetto Tronto	yes	yes
Senigallia	yes	yes
Urbino	yes	no
Molise	yes	yes
Piemonte		
Alessandria	yes	yes
Asti	yes	yes
Cuneo	yes	yes
Ivrea	yes	yes
Moncalieri	yes	yes
Novara	yes	yes
Rivoli	yes	yes
Torino	yes	yes
Vercelli	yes	yes
Sardegna		
Cagliari	yes	yes
Nuoro	yes	yes
Oristano	yes	yes
Sanluri	yes	no
Sicilia		
Catania	no	no
Messina	yes	yes
Palermo	yes	yes
Siracusa	yes	no
Trapani	yes	yes
Toscana		
Arezzo	no	no
Empoli	yes	no
Firenze	yes	yes
Grosseto	yes	yes
Livorno	yes	no
Lucca	yes	no
Massa Carrara	yes	no
Pisa	yes	yes
Pistoia	yes	yes
Prato	yes	yes
Siena	yes	yes
Viareggio	yes	yes
Trento Self-Governing Province	yes	no
Umbria	yes	no
Valle D'Aosta	yes	yes
Veneto		
ULSS 1 - Belluno	yes	yes
ULSS 2 - Feltre	yes	yes
ULSS 3 - Bassano Del Grappa	yes	yes
ULSS 5 - Ovest Vicentino	yes	yes
ULSS 6 - Vicenza	yes	yes
ULSS 7 - Pieve Di Soligo	yes	yes
ULSS 8 - Asolo	no	no
ULSS 9 - Treviso	yes	yes
ULSS 10 - Veneto Orientale	no	no
ULSS 12 Veneziana	yes	yes
ULSS 13 - Mirano	yes	yes
ULSS 15 - Alta Padovana	yes	yes
ULSS 16 - Padova	yes	yes
ULSS 17 - Este	yes	yes
ULSS 18 - Rovigo	yes	yes
ULSS 19 - Adria	yes	yes
ULSS 20 - Verona	yes	yes
ULSS 21 - Legnago	yes	yes
ULSS 22 - Bussolengo	yes	yes

Table 1. Screening programmes that provided data on treatment and on colpo-histological correlation.

One section considered colposcopic findings and their correlation with histology. Colposcopic findings were classified according to the International classification[13] (IFCPC). The Rome 1990 classification was adopted in the first experimental surveys as it was in use at that time. In order to provide comparability, this classification was not replaced by the Barcelona 2002 classification.[14] Unsatisfactory colposcopies, according to both international classifications,[13,14] include: transformation zone not visible, severe inflammation or severe atrophy or trauma and cervix not visible. Miscellaneous colposcopic findings were not considered if they did not impair examination while if they did impair examination they were included among unsatisfactory colposcopies. In this section, each colposcopy was considered as a statistical unit even in case of repeated colposcopies for the same woman. In case of multiple biopsies during the same colposcopy, we asked to report the most severe histology. For these reasons and because of the different number of programmes that provided data, the total number of histological diagnoses does not correspond to that reported in the section on treatment.

Another section required information on the management of women with screen-detected CIN or invasive cancer. In this section each woman was considered a unit. For this purpose we considered the worst histology before treatment. In case of multiple treatments the first one was considered. A «see and treat» approach – i.e., treatment in absence of a histological diagnosis – is very limited in Italian organised programmes and was applied only in a few centres.

Colposcopic findings	Histology outcome									
	no biopsy performed	no CIN	CIN 1	CIN 2	CIN 3	adeno carcinoma in situ	invasive squamous carcinoma	invasive adeno carcinoma	total with biopsy	total
Normal colposcopic findings. Transformation zone fully visible	8,013	1,216	457	119	74	2	1	6	1,875	9,888
% of total	81.0	12.3	4.6	1.2	0.7	0.0				
% of total with biopsy		64.9	24.4	6.3	3.9	0.1	0.1	0.3		
Grade 1	1,179	2,287	3,575	913	538	8	10	3	7,334	8,513
% of total	13.8	26.9	42.0	10.7	6.3	0.1	0.1	0.0		
% of total with biopsy		31.2	48.7	12.4	7.3	0.1	0.1	0.0		
Grade 2	100	250	414	541	761	30	31	10	2,037	2,137
% of total	4.7	11.7	19.4	25.3	35.6	1.4	1.5	0.5		
% of total with biopsy		12.3	20.3	26.6	37.4	1.5	1.5	0.5		
Atypical vessels	36	13	11	5	19	8	7	3	66	102
% of total	35.3	12.7	10.8	4.9	18.6	7.8	6.9	2.9		
% of total with biopsy		12.7	10.8	4.9	18.6	7.8	6.9	2.9		
Colposcopic features suggestive of invasive cancer	0	0	2	0	14	1	28	10	55	55
% of total	0.0	0.0	3.6	0.0	25.5	1.8	50.9	18.2		
% of total with biopsy		0.0	3.6	0.0	25.5	1.8	50.9	18.2		
Other - Unsatisfactory colposcopy	3,129	1,199	531	163	188	10	14	3	2,108	5,237
% of total	59.7	22.9	10.1	3.1	3.6	0.2	0.3	0.1		
% of total with biopsy		56.9	25.2	7.7	8.9	0.5	0.7	0.1		
TOTAL	**12,457**	**4,965**	**4,990**	**1,741**	**1,594**	**59**	**91**	**35**	**13,475**	**25,932**

Table 2. Colposcopic findings and histology in the colposcopies performed by 71 Italian cervical screening programmes during 2008.

Results

Colposcopic findings and their correlation with histology

We included in this analysis data on 25,932 colposcopies (*vs*. 18,340 in the previous survey).

Table 2 reports colposcopic findings and the corresponding histological diagnoses. Most colposcopies were classified as normal (38.1%) or unsatisfactory (20.2%, overall 58.3%). This reflects the broad use of colposcopy in most Italian screening programmes.[14] A biopsy was performed in 52.0% of all colposcopies.

At least one biopsy was performed in 19.0% of normal colposcopies (*vs* 20.3% in the previous survey). Most of them were normal (64.9%). However a CIN1 was reported in 24.4%, a CIN2 in 6.3% and CIN3 or more in 4.4% of cases. The cases with high-grade CIN or cancer detected in this group need further investigation.

On the other hand, no biopsy was reported during 12.2% of tests with abnormal colposcopic findings, particularly in 4.7% of grade 2 findings and 35.3% of those with atypical vessels. In the previous survey no biopsy was reported in 6.2% of grade 2 colposcopies and 10.0% of those showing atypical vessels.

Grade 1 abnormal findings were reported in 8,513 colposcopies (32.8%). In 13.8% no biopsy was performed. Grade 1 colposcopy should correspond to metaplasia or CIN1 histology. Indeed 79.9% of those cases with biopsy had no CIN or CIN1, but 12.4% reported CIN2 histology and 7.6% CIN3 or more.

Colposcopic abnormal findings of grade 2 should correspond to high-grade intraepithelial lesions. Histology was CIN 2 or more severe in 67.4% of cases with biopsy. Taking into account the overall low prevalence of lesions in women referred to colposcopy, this figure suggests a reasonable specificity for this colposcopic category. On the other hand, even when excluding from computations the lesions diagnosed during unsatisfactory colposcopies, 65.4% of CIN2 and 43.5% of CIN3 were identified during colposcopies reported as «normal findings» or grade 1. In any case, these lesions were detected as a result of colposcopy. Therefore they do not suggest low sensitivity of colposcopy itself, nor, in general, can the results reported in this section be used to estimate colposcopy sensitivity.

In 69.1% of the colposcopies classified as «invasive carcinoma» histology did confirm invasive cancer and in 96.4% it was CIN3 or more severe.

At least one biopsy was reported in 40.3% of colposcopies classified as unsatisfactory. Among these, histology was normal in 56.9% while it was CIN2 or more in 7.2%.

Management and treatment of women with biopsy-proven CIN

Table 3 reports available data about recommendations and actually performed treatment for cases with CIN1 or more severe histology. We included data on the management of 8,958 women (*vs* 6,148 in the previous survey).

Management/treatment of women with CIN1 histology

In 68,7% of CIN1 cases women were recalled for follow-up only, in agreement with the recommendation not to treat these lesions unless persistent.[5-7] There is therefore an increase compared to the 69.3% observed in the previous survey.

For 9,9% of these women (*vs* 4.1%, 6.3%, 8.4%, and 11.6% in the previous years) no data on management/treatment were available.

Out of the overall women treated, 4.2% (0.8% of all women) underwent cold knife conisation, the most radical of conservative treatments.

Hysterectomy, which should not be used for these women,[1,5-7] was performed in three cases (0.1% of those with known managements), possibly because of associated disease.

Diathermocoagulation was performed in 5.3% of cases with known management (*vs* 7.8%, 6.3%, 6.4%, and 9.2% in previous surveys) and 27.3% of treatments.

Treatment of women with CIN2-3 histology

No data on the treatments performed were available for 14.1% (534) of women with CIN2-3. This percentage was 12.7%, 11.2%, and 12.9%, in the previous three years. Overall, 4.8% (166) of women with CIN2-3 were reported not to have been treated. For 94 of them (2.5% of women with CIN2-3) no recommendation for treatment was reported. The latter percent age was higher among women with CIN2 (4.6%) and very small among those with CIN3 (0.3%).

Treatments not performed within three months from recommendation can reasonably be considered as refusal. This occurred for 1.0% of the women for whom a recommendation to be treated was recorded.

Techniques compatible with local anaesthesia (which should be ≥85% according to NHSCSP

First treatment	Most severe histology before treatment										
	CIN 1*	%	CIN 2*	%	CIN 3*	%	adeno Ca in situ	%	invasive Ca	%	total
laser vaporisation	233	4.7	74	3.9	21	1.1	0	0.0	0	0.0	328
cryotherapy	4	0.1					0	0.0	0	0.0	4
radical diathermy	1						0	0.0	0	0.0	1
diathermocoagulation	260	5.3	14	0.7	1	0.1	0	0.0	0	0.0	275
excision by radio-frequency device	282	5.7	1,067	55.6	984	52.6	13	15.5	12	7.4	2,358
cold knife conisation	40	0.8	194	10.1	320	17.1	18	21.4	11	6.7	583
laser conisation	32	0.7	98	5.1	149	8.0	2	2.4	4	2.5	285
excision by radio-frequency device + laser vaporisation	27	0.5	28	1.5	8	0.4	17	20.2	1	0.6	81
hysterectomy	3	0.1	13	0.7	74	4.0	24	28.6	99	60.7	213
other treatments											
conisation NOS	1		14	0.7	10	0.5					25
photothermocoagulation	10	0.2									10
chemotherapy									1	0.6	1
chemotherapy + radiotherapy									1	0.6	1
polypectomy			1	0.1	1	0.1					2
vaginal laser vaporisation (VAIN)	3	0.1	2	0.1							5
cervicectomy									1	0.7	1
type of treatment unknown	56	1.1	81	4.2	79	4.2	6	7.7	12	7.4	234
not treated - no treatment recommended	3,431	69.7	89	4.6	5	0.3	0	0.0	2	1.2	3,527
not treated - treatment recommended since <3 months	23	0.5	19	1.0	15	0.8	0	0.0	0	0.0	57
not treated - treatment recommended since ≥3 months	86	1.7	40	2.1	13	0.7	0	0.0	2	1.2	141
unknown if treated	431	8.8	185	9.6	189	10.1	4	4.8	17	10.4	826
TOTAL	**4,923**	**100.0**	**1,919**	**100.0**	**1,869**	**100.0**	**84**	**100.0**	**163**	**100.0**	**8,958**

* including VAIN of same grade

Table 3. Treatment or management of the intraepithelial lesions detected by 84 Italian organised cervical screening programmes during 2008.

standards[7]) were applied in 79.6% of known treatments. Excision by radio-frequency devices was the most frequently applied technique (2,051 cases, 66.7% of the 3,073 with known treatment). Laser conisation (247 cases) represented 8.0% of known treatments. Laser vaporisation was employed in 3.2% of cases with known treatment, while combined excision by radio-frequency devices and laser vaporisation (usually applied in the presence of both large exocervical-vaginal and endocervical lesions) was employed in 1.2%. Overall, stand-alone destructive treatments were employed in 3.6% of known treatments for CIN2/3. Hysterectomy, which should not be used in more than 2% of these lesions[1], was actually performed in 2.3% of women with a diagnosis of CIN2/3 (2.8% of known treatments). There was an increase with increasing histological grade: 0.7% of the CIN2 and 14.0% of the CIN3 with known treatment.

Cold knife conisation (which, given the higher risk of pregnancy-related complications[3,4], should be limited to selected cases, justified by morphological or clinical reasons or by diagnostic uncertainty) was applied in 514 women, 16.7% of those with known treatment. Its use increased with increasing histological grade: 10.1% for CIN2 and 17.1% for CIN3.

Diathermocoagulation was infrequent (0.5% of cases with known treatment) but still used, although less than in previous surveys and basically only for CIN2.

Adenocarcinoma in situ and invasive carcinoma

Invasive adeno- and squamous carcinoma were mostly treated by hysterectomy (76.2% of cases with known treatment). To date, the staging of invasive carcinoma and its relation with radicality of treatment has not been studied. In 15 cases (11.5% of known treatments) treatment was conservative, with cold knife or laser conisation, and in 13 cases minimally invasive techniques were applied. These treatments should be limited to cases in PT1a1 stage with free margins.[5,6] However it is possible that diagnostic excisions were misclassified as the first treatment.

For in situ adenocarcinoma cold knife conisation was reported in 21.4% of known treatments. Indeed this approach is considered as the preferred conservative interventions. In 30 cases, 40.5% of known treatments, an excisional minimally invasive technique was employed. Overall, 67.6% of known treatments were conservative, while hysterectomy was used in 32.4% of cases with known treatment. For adenocarcinoma in situ, a conservative approach, although with a sufficient volume of tissue excised, taking into account multifocality and the need for free margins, is now recommended.[6,15]

Histology in punch biopsy *vs* excised specimen

We experimentally collected data comparing histology on punch biopsy and on the tissue obtained by excisional treatment. Out of 2,062 available cases with CIN2-3 histology on the punch biopsy, histology on the excisional specimen was CIN1 in 8.5%, CIN2-3 in 79.3%, adenocarcinoma in situ in 0.4%, microinvasive Ca in 1.9% and fully invasive Ca in 1.4%. Of the 245 cases with CIN1 histology on punch biopsy 59.6% still had CIN1 histology on the excisional specimen while 27.3% had CIN2-3 or adenocarcinoma in situ and in 9.4% no CIN was detected.

Quality of margins of excised specimens

No data on interpretability of margins was available in 743/2,104 (34.9%), 172/339 (50.7%) and 62/314 (19.7%) while the margin was reported as interpretable in 93.7%, 94.6% and 96.4% of cases with available data of radio-frequency excisions (loop or needle), cold knife conisations, and laser conisations respectively.

The endocervical margin was reported as free of disease in 78.1%, 84.5% and 87.6% of cases with available data respectively but no data was

available in 36.9%, 52.5% and 20.4% of radiofrequency excisions (loop or needle), cold knife conisations and laser conisations respectively.

Discussion

This survey now provides a good picture of diagnostic activity and an almost complete picture of therapeutic practice within organised cervical screening in Italy. However, given the routine nature of data, we cannot exclude that apparent cases of inappropriate management actually correspond to errors in registration. For this reason, and in order to fully apprecate complex situations, peer review procedures should be conducted at a local (regional) level on apparently abnormal cases.

Concerning colposcopic findings, it must be considered that Italian screening programmes apply broad criteria of referral compared to other countries. This results in low prevalence of disease in examined women and therefore in a low positive predictive value of abnormal colposcopic findings. In addition, the present data are based on routine data and apparent discrepancies between colposcopic findings and histology could result from errors of registration of the former. A remarkable proportion of CIN2 and 3 was detected among women with normal or unsatisfactory findings. However it must be considered that these lesions were detected as a result of colposcopy. Therefore they do not show low sensitivity of the entire colposocpic process nor, in general, can the results reported in this paper be used to estimate the accuracy of the entire colposcopic procedure. Nevertheless they are in agreement with data on low sensitivity of colposcopic findings[16] and suggest that biopsies should be broadly applied.

A higher centralisation (also suggested by the English NHSCSP[7] and by Italian national standards[1,2]) would improve the capacity to identify the most severe but less frequent lesions.

Despite more cases of CIN included in the survey, the proportion of cases with unknown management increased compared to previous years. Assuring that recommended treatments are actually performed is an essential task of organised screening programmes.

The proportion of women with CIN1 who had just follow-up, in agreement with Italian guidelines, further increased and is now close to 80%. The use of hysterectomy in women with CIN it is now almost limited to CIN3 and approximates the value recommended by Italian guidelines.

Diathermocoagulation (not to be confused with radical diathermy that showed results similar to those obtained by surgical conisation)[17] is not included among methods acceptable for the treatment of CIN[5-7] as it does not reach a sufficient average tissue destruction. In addition, possible diagnostic problems during follow-up can result from persistent lesions in deep glandular crypts obliterated by thermal damage. The use of diathermocoagulation was very limited among women with high-grade CIN, but was still frequent for CIN1.

In conclusion, these results show increasing application of guidelines, but data on actual management are unknown for a too large a proportion of women with CIN.

No systematic information is available on important aspects, like complications and side effects of treatments and the rate of persistence/recurrence. An *ad hoc* project of collection of these data has begun in some Italian Regions.

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Audit system on Quality of breast cancer diagnosis and Treatment (QT): results of quality indicators on screen-detected lesions in Italy, 2007

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Abstract

This survey, conducted by the Italian Breast Screening Network (GISMa), collects individual data yearly on about 50% of all screen-detected, operated lesions in Italy. The 2007 results show good overall quality of diagnosis and treatment and an improving trend over time. Critical issues were identified concerning waiting times, compliance with the recommendations on not performing frozen section examination on small lesions and on performing specimen X-rays. Preoperative diagnosis reached the acceptable target, but there is a large variation between Regions and programmes. For more than 80% of screen-detected invasive cancers the sentinel lymph node technique (SLN) was performed on the axilla, avoiding a large number of potentially harmful dissections. On the other hand, potential overuse of SLN deserves further investigation.

The detailed results have been distributed, also by means of a web data-warehouse, to regional and local screening programmes in order to allow multidisciplinary discussion and identification of the appropriate solutions to any problem documented by the data. Specialist Breast Units with adequate case volume and enough resources would provide the best setting for making audits effective in producing quality improvements with a shorter waiting times.

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Keywords: breast cancer screening quality treatment survey, Italy

Mammography screening acts through a delicate balance of human benefits and costs which is highly sensitive to the quality, not only of the screening itself but of the entire process of care of screen-detected lesions. Therefore, screening programmes should perform audits of further assessment, histopathology, diagnosis, and treatment, as well as the screening test itself.[1,2]

The mammography screening movement in Europe has been on the front line in introducing quality assurance and monitoring in all stages of breast cancer management and care. In the framework of the European Breast Cancer Screening Network an individual records database and audit system, called QT (audit system on Quality of breast cancer Treatment) has been produced, which can be downloaded at www.cpo.it/qt or the EUSOMA (European Society of Breast Cancer Special-

ists) website (www.eusoma.org). It is available in six languages (English, French, German, Italian, Spanish, and Hungarian) and has users in several European countries.

Within the Italian Breast Screening Network (GISMa) a quality assurance programme on the care of screen-detected breast cancers has been ongoing since 1997,[3] and results of this activity are published yearly in the Reports of the National Centre for Screening Monitoring. The aim of this report is to show the results of the monitoring of diagnosis and treatment indicators in screen-detected lesions operated with open surgery in Italy in 2007. Some preliminary results are also shown for 2008.

Methods

Individual data on diagnosis and treatment of screen-detected operated lesions (benign or malignant) are recorded on QT either by clinical staff in charge of the patients or by local screening organisation and evaluation units. Regional programmes report data yearly to the national co-ordination office, which performs data quality control and analysis of outcome measures. The definitions of performance indicators which are being monitored are from Italian[4,5] and European[2,6,7] guidelines. The definition of indicators can be found at www.qtweb.it/index.php?id=14&l=E . Regional cases were excluded from the analysis of an indicator if missing values exceeded 30%. Ranges by screening programmes or Region are also shown. Even if most programmes in Italy have designated surgical units where the majority of the cases are referred, to avoid selection bias the study protocol required that participating programmes record all screen-detected cases, no matter where treatment has taken place. The index year for this report is 2007. Piemonte, Valle d'Aosta and Toscana use as an index date the date of the screening test that originated surgical referral, while the remaining Regions use date of surgery. To avoid selection bias, the study protocol requires that participating programmes record all screen-detected operated lesions. Known interval cases, operated in the index year, are also included.

This document reports results that, in their preliminary version, were presented at the National Centre for Screening Monitoring annual meetings in December 2008 (Milan) and December 2009 (Turin). Data for the index year 2007 have been checked locally, updated, and discussed at specific multidisciplinary meetings in each of the Regions involved. Data for 2008 are at present available to regional and screening coordinators on a web data-warehouse which allows for analysis and benchmarking, in order to be checked, updated, and discussed prior to publication.

Results

In 2007, fifty of 130 screening programmes belonging to GISMa participated in the QT project and individual data on 3,432 cases (age 50-69) in seven Regions were recorded (table 1). After exclusion of self-referred cases, interval cases (2.3% of cancers recorded in the 2007 QT database) and double lesions, the remaining 3,151 cases (2,679 malignant, 334 benign, 138 post-operative diagnosis unknown) represent 47% of cancers and 36% of benign lesions reported by the National Centre for Screening Monitoring aggregated data survey, the results of which appear in another chapter of this Supplement (Giorgi et al., p. 9).

All Regions reporting data for 2007 co-ordinated the QT survey at the regional level including all or nearly all (Veneto, Lazio) of their screening programmes. In the time period 2000-2007, more than 20,000 screen-detected lesions in ten Italian Regions were documented in QT (table 1).

Distribution of cases by histopathological diagnosis and age at diagnosis is reported in table 2. Operated benign lesions represent 10.4% of cases with known diagnosis and ductal carcinoma in situ (DCIS) 15.2% of all malignant screen-detected lesions.

Number of programmes	2000	2001	2002	2003	2004	2005	2006	2007
Piemonte e Valle d'Aosta	8	9	10	10	10	10	10	10
Lombardia	1	-	-	-	1	1	1	-
Veneto	2	1	12	12	12	12	10	9
Emilia-Romagna	6	8	9	9	8	10	11	11
Toscana	1	1	1	1	1	9	9	11
Umbria	-	-	1	-	-	-	-	-
Lazio	2	5	3	7	7	6	6	8
Campania	1	-	-	-	-	-	-	-
Sardegna	-	-	-	-	-	-	-	1
Sicilia	2	1	2	-	1	-	-	-
TOTAL	**23**	**25**	**38**	**39**	**40**	**48**	**47**	**50**

Number of cases	2000	2001	2002	2003	2004	2005	2006	2007
Piemonte e Valle d'Aosta	589	709	812	852	1,170	1,175	1,212	1,098
Lombardia	69	-	-	-	51	138	139	-
Veneto	158	76	270	426	369	432	392	191
Emilia-Romagna	394	796	663	742	856	920	992	984
Toscana	144	138	151	195	213	522	526	710
Umbria	-	-	33	-	-	-	-	-
Lazio	137	142	128	245	339	239	286	375
Campania	9	-	-	-	-	-	-	-
Sardegna	-	-	-	-	-	-	-	74
Sicilia	135	23	36	-	10	-	-	-
TOTAL	**1,635**	**1,890**	**2,093**	**2,460**	**3,008**	**3,426**	**3,547**	**3,432**

Table 1. Italian survey on diagnosis and treatment of screen-detected breast lesions: number of screening programmes and cases, by Region, 2000-2007.

Histopathological diagnosis	All cases		Age 50-59		Age 60-69	
	N	%	N	%	N	%
benign	339	9.9	197	14.7	142	6.8
lobular carcinoma in situ (LIN)	36	1.0	20	1.5	16	0.8
ductal carcinoma in situ	446	13.0	183	13.7	263	12.6
micro-invasive	67	2.0	29	2.2	38	1.8
invasive	2,405	70.1	851	63.6	1,552	74.6
unknown	139	4.1	57	4.3	69	3.3
TOTAL	**3,432**	**100.0**	**1,337**	**100.0**	**2,080**	**100.0**

Table 2. Italian survey on diagnosis and treatment of screen-detected breast lesions: distribution by final histopathological diagnosis and age, 2007.

Outcome measure	Eligible cases	Missing %	Result (CI 95%) %	Target %
pre-operative diagnosis in cancers (C4-5, B4-5)	2,873	4.0	88.1 (86.9-89.3)	-
pre-operative diagnosis in cancers (C5, B5)	2,873	4.0	75.2 (73.5-76.8)	≥70
non-inadequate cytology if final diagnosis is cancer	2,054	2.3	92.0 (90.7-93.1)	≥90
absolute sensitivity C5	2,088	2.3	65.2 (63.1-67.3)	≥60
grade available	2,303	3.2	98.9 (98.3-99.3)	≥95
estrogen receptors available	2,303	5.1	97.4 (96.7-98.0)	≥95

Results are calculated on eligible cases minus cases with missing information.

Table 3. Summary on diagnostic indicators, 2007.

More descriptive data follow (not in the table): 62.2% of patients with cancer diagnoses were 60-69-years old, 37.6% 50-59-years old (2% age not known), 27.7% of invasive cases is N+ (missing 6.9%). Grade of invasive carcinoma is distributed as follows: 21.5% grade I, 53.9% grade II, and 24.6% grade III (missing 3.2%). Nuclear grade of DCIS is 28.6% grade I, 41.4% grade II, and 30.0% grade III (missing 14.7%).

Results of outcome measures are shown in tables 3 and 4. The number of eligible cases for each outcome measure and the number of missing values are also shown. Seventy-five per cent of cancers had pre-operative cytological or micro-histological diagnosis (table 3), unvaried compared to 2006 and over the acceptable target of 70%. However, considerable variation exists between Regions (range 70.5%-80.9%) and programmes (range 51.2%-100%).

Cases for which pre-operative diagnosis was not available are distributed by reason in table 5. Failure in performing any non-operative diagnosis is responsible for 12% of these cases (15% in 2006). Non-operative diagnosis being «suspect of malignancy» (C4 or B4), rather than holding a higher degree of certainty, is responsible for 52% of the cases.

Waiting times are well below the targets and worsened compared to 2006. Fifty-five per cent (59% in 2006) of cancers receive surgery within one month of referral (range between Regions 47.4%-82.7%, range between programmes 17.5%-100%), and 44% within two months of the screening date (table 4). Almost 25% of cases with surgical referral had

Outcome measure	Eligible cases	Missing %	Result (CI 95%) %	Target %
waiting time for surgery from referral ≤30 days	3,213	8.9	**55.3 (53.5-57.1)**	≥80
waiting time for surgery from screening test ≤60 days	3,149	15.2	44.1 (42.4-46.1)	-
waiting time for surgery from screening test ≤90 days	3,149	15.2	75.7 (74.0-77.3)	-
frozen section examination not performed in cancers ≤10 mm	827	13.8	**75.3 (72.0-78.4)**	≥95
specimen X-ray (invasive cancers ≤10 mm treated by conservation surgery)	512	23.2	**54.7 (49.6-59.7)**	≥95
only one operation after pre-operative diagnosis	2,051	3.5	91.6 (90.2-92.7)	≥90
conservative surgery in invasive cancers ≤20 mm	1,639	2.6	93.1 (91.7-94.3)	≥85
conservative surgery in DCIS (ductal carcinoma in situ) ≤20 mm	346	0.9	91.3 (87.6-93.9)	≥85
margins >1 mm after last surgery	2,399	8.7	**94.7 (93.6-95.5)**	(95)
number of lymph nodes >9 in axillary dissection (level I or II or III)	810	5.7	**90.8 (88.5-92.7)**	95
axillary staging by SLN only in pN0	1,523	0.7	**83.9 (81.9-85.7)**	≥95
no axillary dissection in DCIS	433	7.2	**94.5 (91.7-96.5)**	≥95
no axillary dissection or SLN in benign lesions, LIN, and DCIS low or intermediate grade	690	5.2	**66.4 (62.6-70.0)**	≥95
immediate reconstruction after mastectomy	402	14.4	61.6 (56.2-66.8)	-
immediate reconstruction after mastectomy (DCIS and invasive ca ≤30 mm, pN0)	174	14.4	**67.1(58.9-74.5)**	≥80

Results are calculated on eligible cases minus cases with missing information.
Results short of numerical target are shown in bold.
The following Regions have been excluded from calculation for certain quality objectives due to missing values >30%: Veneto and Emilia-Romagna (specimen X-ray).

Table 4. Summary of surgical indicators, 2007.

	N	%
pre-operative diagnosis not performed	83	12.1
unsatisfactory	87	12.7
false negative (C2 or B2)	32	4.7
dubious (C3 o B3)	125	18.2
suspicious (C4 o B4)	358	52.3
TOTAL	**685**	**100.0**

Table 5. Distribution of malignant cases without pre-operative diagnosis, (C5 or B5) by reason, 2007.

	N	%
normal tissue	9	2.7
fibroadenoma	39	11.7
cysts	4	1.2
atypical ductal hyperplasia	70	21.0
atypical lobular hyperplasia	5	1.5
atypical apocrine metaplasia	4	1.2
fibrocystic mastopatia	53	15.9
benign phylloid tumour	3	0.9
sclerosing adenosis	36	10.8
radial scar	14	4.2
papilloma/papillomatosis	47	14.1
other	39	11.7
unknown	11	3.3
TOTAL	**334**	**100.0**

Table 6. Distribution by histological type of benign lesions operated using open surgery (excluding syncronous lesions), 2007.

not yet received surgery three months after screening (range between Regions 71,1%-79,9%, range between programmes 27.9%-100%). Guidelines recommend avoiding intra-operative examination or frozen section examination (even on margins) in lesions under or equal to 10 mm because of limited accuracy and the risk of deteriorating the specimen and impairing subsequent examination.[1,4-7] The result of this indicator (table 4) is still below the target and about stable compared to the previous year, as in 2007 frozen section examination was performed in about one fourth of cases (range between Regions 67.6%-97.8%). If the indicator is calculated not counting as failures intra-operative examinations of margins only, the result is still short of the target: 87.5%. Italian guidelines recommend the performance of two-view specimen X-rays on all non-palpable lesions and set the numerical target at 95%.[4] Given the high proportion of missing values for number of views and palpability, a simplified indicator has been calculated (table 4) on invasive cancers within 10 mm of size that gives a result of 54.7%, short of the target and below the result reached in 2006 (60.3%). The number of missing values is high (23.2%), It should also be taken into account that no information on any specimen ultrasound has been collected.

Breast conservation, both for invasive cancer and

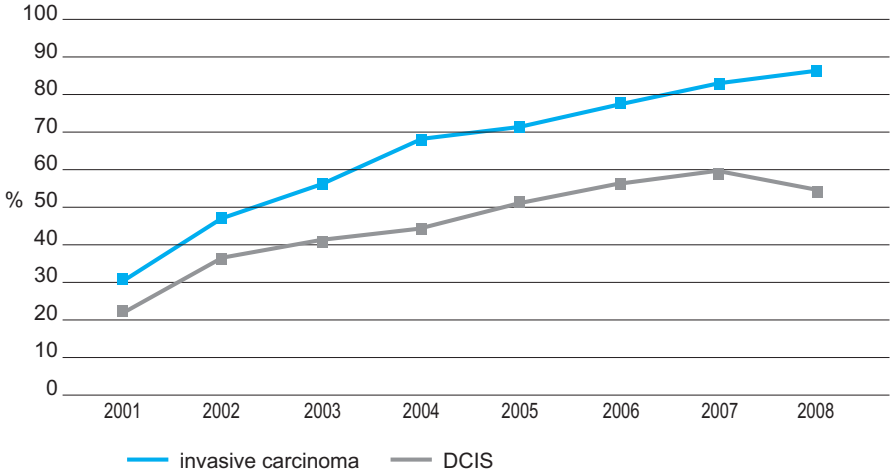

Figure 1. Italian survey on diagnosis and treatment of screen-detected breast cancers: trend in the use of SLN technique, 2001-2008.

DCIS, is at very high levels (table 4), which have been maintained over the years (table 7). When a mastectomy is performed, only 62% of the cases receive immediate breast reconstruction (table 4). However, this figure has greatly improved compared to 2006 (38.2%).

This survey also allows investigating the gradual introduction of the sentinel lymph node (SLN) technique, a less harmful operation compared to axillary clearance. An increasing proportion of invasive cancers (82.6% in 2007) and, similarly but less appropriately, of DCIS (58.9%) were treated with SLN overtime. It is worth noticing that in 2008 (preliminary data) the use of SLN in DCIS, often inappropriate, decreased for the first time (figure 1). The proportion of node negative invasive cases staged by SLN only (table 4) was 83.9% in 2007 (with a high variability by Region: 51.6% - 90.0%), compared to 81% in 2006 and 72% in 2005. The result for 2008 (preliminary data) is 88%.

Notwithstanding the introduction of SLN, 5.5% of DCIS (range between Regions 2.6%-15.1%) in 2007 received clearance of the axilla (table 4), a procedure known for its complications and one that is unnecessary in these cases. This result has improved compared to 2006 (axillary clearance in 8.2% of DCIS). Merging together benign lesions, LIN and DCIS of low and intermediate grade, SLN has been performed on 33.6% of these cases (range 0%-61.9% by Region) (table 4).

Overtreatment may also result from unnecessary surgical breast surgery on benign lesions. This issue is illustrated in table 6, where benign lesions operated using open surgery are distributed by histopathology type. An indicator measures the benign lesions at no increased risk for malignancy (all except papilloma, sclerosing adenosis, radial scar, atypical hyperplasia, phylloid tumours) as the proportion of all operated benign lesions (excluding double lesions and lesions with missing histological type). Benign lesions at no increased risk were 139 in 2007 (43.0% of all operated benign lesions versus 47.1% in 2006).

Table 7 shows time trends from 1997 to 2007 for selected performance parameters, with analysis limited to the three screening programmes having contributed cases during the whole period. The frequency of pre-operative diagnosis and avoidance of frozen section examination in small lesions showed improvement overtime, while waiting times grew longer.

%	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	Target
pre-operative diagnosis in cancers (C4-5, B4-5)	67.6	72.6	74.9	78.7	81.3	82.0	86.8	84.2	88.4	88.3	90.6	-
frozen section not performed in cancers ≤10 mm	**53.3**	**65.2**	**60.0**	**48.8**	**58.7**	**68.5**	**77.5**	**87.7**	**85.3**	**85.2**	87.0	≥95
conservative surgery ininvasive cancers ≤20 mm	88.9	93.2	92.9	90.2	93.4	91.7	94.7	92.1	95.2	92.8	95.4	≥85
conservative surgery in situ cancers ≤20 mm	87.0	97.1	92.9	91.0	88.7	91.8	88.5	93.3	92.4	87.9	93.8	≥85
number of lymph nodes >9 in axillary dissection	**94.1**	**93.9**	**92.0**	**90.7**	**92.4**	**92.6**	**94.5**	96.2	**94.8**	96.2	95.3	≥95
no axillary dissection in DCIS	**92.1**	**85.7**	**90.0**	**79.7**	96.0	96.9	**87.4**	95.3	95.5	**94.4**	93.3	≥95
waiting time for surgery since referral ≤21days	56.1	51.1	33.3	37.0	22.7	32.3	32.8	31.1	30.0	30.5	21.4	-

Only programmes having contributed data for the whole period (Firenze, Modena, Torino) are included.

Table 7: Time trends for selected indicators, 1997-2007.

Discussion

In 2007, most outcome measures were near or met the target set by GISMa.[5] Major exceptions, similar to 2006, were waiting times for surgery, compliance with the recommendation on avoiding frozen section examination on small lesions, performing specimen X-rays, and the performance of immediate reconstruction after mastectomy. Although reaching the acceptable target, the indicator on non-operative diagnosis deserves a comment. The proportion of cancers with pre-operative diagnosis has clearly increased over the years, due to increasing use of micro-histology techniques, and reached the acceptable target for the first time in 2005. However, the result was stable in 2007 compared to 2006, and only marginally increased (77%) in 2008, according to preliminary data, although a wide margin for improvement in order to reach the European desirable target of 90%[7] still exists. This is also supported by the finding of a considerable variation between programmes: about 40% do not reach the acceptable target, while 10% meet the desirable target.

Pathologists and radiologists should be involved with surgeons in analysing reasons for underperformance in programmes scoring in the lower part of the range.

Waiting time from screening to surgery embraces much of the entire screening process (time from screening to first assessment, time from first assessment to result, time from result of assessment to first surgery). Results were already poor and worsened further between 2006 and 2007. Preliminary results from 2008 show the decreasing trend is continuing: 53% of lesions were operated within 30 days of surgical referral and 71% within 60 days of the screening examination. Regional authorities should inspect the reasons for this considerable delay especially in regard to programmes in the lower part of the range.

Avoiding the use of frozen section entails a difficult change in attitude by the surgeon, when it is not due to lack of pre-operative diagnosis. This procedure, even when aimed at the evaluation of margins in impalpable lesions, should be substituted by two-view specimen Rx.[4]

The proportion of mastectomies followed by immediate reconstruction has dramatically improved compared to 2006 but is still too low, especially in light of a marginal decrease measured in the preliminary 2008 data (58%). This is probably due to low availability of plastic surgeons and should improve with specialised training in this area of surgery.

Axillary dissection in DCIS almost reaches the target (5%) but should further decrease, since this treatment is useless in DCIS and a potential cause of complications. Pre-operative multidisciplinary discussion is the way to minimise this problem, as only from the confrontation with the pathologist and radiologist can the surgeon learn about the non-invasiveness of the lesion.[8] This should also help in decreasing the use of SLN in benign lesions, LIN and low and intermediate grade DCIS.

Missing values, although improved since 2006, are still relatively large for waiting time, performance of the specimen Rx and reconstruction.

Although this survey includes a large share of screen-detected cases in the country (about 50%), a selection towards inclusion of cases from better-organized Regions cannot be excluded. Benign operations, furthermore, seem to be under-recorded. A larger participation in the survey by Italian Regions and programmes would be appropriate, perhaps coupled with simplified data collection methods. On the other hand, it will be important to maintain the connection between screening and clinicians that this project has put forward during the years.

Quality of data, including proportion of missing values, and results of outcome measures emerging from this survey should be verified and discussed in detail at the level of local screening programme or clinical Breast Unit, with regional co-ordina-

tion; this way the most useful information and indications for action should emerge.

Conclusions

The establishment of specialist multidisciplinary Breast Units is essential in order to be able to improve waiting times as well as the quality of care.[8] Running a monitoring system for quality of screening and care requires dedicated resources, particularly data managers with some clinical expertise, and an appropriate organisation for collecting data and making the best use of them.[8] One individual, be it a physician, a breast nurse or a data manager should be made responsible for co-ordinating data collection and reporting to the screening programme evaluation unit as well as to each Breast Unit collaborating with the programme. For auditing to produce change, feed back and careful analysis of emerging problems is necessary, and the best setting for these activities is multidisciplinary meetings.

Although many of the indicators relate to individual skill or knowledge of recommendations, most involve the team as well. Discussion of data analysis reports during multidisciplinary meetings often prompts improvement of the quality of data itself, such as the reduction of missing values and accurate item definition, classification, and coding. Detailed results of this survey have been distributed to regional screening programme co-ordinators in order to allow identification of the appropriate solutions to any problems documented by the data. Quality improvement and experience gained during audits are likely to promote update and corrections in guidelines and the monitoring system itself, thus closing the quality cycle.

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