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Extension of organized cervical cancer screening programmes in Italy and their process indicators, 2011-2012 activity

Estensione dei programmi organizzati di screening cervicale in Italia e loro indicatori di processo

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Abstract

Italian national guidelines recommend regional implementation of organized screening programmes for cervical cancer. As we have been doing since 1998, we collected aggregated tables of data from Italian organized cervical screening programmes in order to centrally compute process indicators. Data on women invited during 2011 and 2012 and screened up to April of the subsequent year were considered. In 2012, the target population of Italian organized screening programmes included 14,497,207 women, corresponding to 87.3% of Italian women aged 25-64 years.

Compliance to invitation was 41.2% in 2011 and 40.8% in 2012, with a strong decreasing North-South trend. However, it should be considered that many women are screened outside any organized programmes. In 2012, of the women screened, 3.5% were referred for repeat cytology and 71.1% of them complied; 2.4% of screened women were referred to colposcopy.

Compliance with colposcopy referral was 85.3% among women referred because of ASC-US or more severe cytology and 90.4% among those referred because of HSIL or more severe cytology. The positive predictive value (PPV) of referral because of ASC-US or more severe cytology for CIN2 or more severe histology was 16.9%. The unadjusted detection rate of CIN2 or more severe histology was 3.4 per 1,000 screened women (3.6 standardized on the Italian population, truncated 25-64). CIN2 or more severe histology was detected in 64.6% of colposcopies classified as grade 2 or higher. Of all colposcopies during which a CIN2 or more severe histology was obtained, 33.6% were classified as grade 2 or higher. Follow-up only was recommended to 81.7% of women with CIN1.

Excision by radio-frequency device was the most common treatment for women with CIN2 (52.8%) and CIN3 (57.0%). However 0.4% of all CIN2 and 2.3% of all CIN3 had hysterectomy.

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Keywords: cervical cancer, Pap test, colposcopy, mass screening, Italy

Riassunto

Le linee guida nazionali italiane raccomandano alle Regioni di attivare programmi organizzati di screening per il cervicocarcinoma. Come negli anni precedenti, a partire dal 1998, dai programmi organizzati italiani di screening cervicale si sono raccolte tabelle aggregate di dati per calcolare centralmente indicatori di processo. Si sono considerati i dati delle donne invitate nel corso del 2009 e screenate fino ad aprile 2011.

Nel 2012 i programmi organizzati italiani includevano nella loro popolazione obiettivo 14.497.207 donne, corrispondenti all'87,3% delle donne italiane di età 25-64 anni. La compliance all'invito è stata

41,2% nel 2011 e 40,8% nel 2012, con un deciso trend a diminuire da Nord a Sud. Bisogna comunque ricordare che molte donne vengono screenate al di fuori dei programmi organizzati.

È stato raccomandato di ripetere la citologia al 3,5% delle donne e il 71,1% di esse l'ha fatto. Il 2,4% delle donne screenate è stato inviato in colposcopia. La compliance alla colposcopia è stata 85,3% tra le donne inviate per citologia ASC-US o più grave e 90,4% tra quelle inviate per citologia HSIL o più grave. Il valore predittivo positivo (VPP) dell'invio in colposcopia per citologia ASC-US o più grave per istologia CIN2 o più grave è stato 16,9%. La detection rate (DR) grezza di istologia CIN2 o più grave è stata 3,4 ogni 1.000 donne screenate (3,6 quella standardizzata sulla popolazione italiana, troncata 25-64). Nel 64,6% delle colposcopie classificate come di grado 2 o più elevato l'esame istologico ha dato un responso CIN2 o più grave. Tra tutte le colposcopie con istologia CIN2 o più grave, il 33,6% è stato classificato come di grado 2 o più elevato. All'81,7% delle donne con esito CIN1 si è consigliato il follow-up. L'escissione con radiofrequenza è stato il trattamento più comune per donne con istologia CIN2 (52,8%) e CIN3 (57,0%). Lo 0,4% delle donne con istologia CIN2 e il 2,3% di quelle CIN3 ha avuto un'isterectomia.

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Parole chiave: cancro cervicale, Pap test, colposcopia, screening di massa, Italia

INTRODUCTION

The Italian health system is managed by Italy's 20 regions. Since 1996, Italian national guidelines have recommended to regions to implement organized screening programmes for cervical cancer.¹⁻³ Recommendations, largely based on European guidelines,^{4,5} include personal invitations to women aged 25 to 64 years for a Pap test every three years, a monitoring system, and quality assurance for each phase of the programme.

Surveys designed to assess the level of implementation of organized programmes in Italy and to collect process indicators have been conducted by GISCI (Italian group for cervical screening) since 1997. Their results have been evaluated and published by the ONS (Osservatorio nazionale screening, National centre for screening monitoring), on behalf of the Italian Ministry of Health, since 2002.⁶⁻¹⁵ Diagnostic work-up and particularly treatment have also been monitored in order to reduce under- and over-treatment.

A number of programmes moved to HPV-based screening tests as pilot projects or as routine activity after the recommendation of the national Ministry of Health.¹⁶ Detailed data on HPV-based screening are presented elsewhere.¹⁷

In the present report, data on coverage and compliance and data on second-level activities included all women, independently of the primary screening test. Conversely, process indicators for first-level tests include only women screened with Pap smears.

METHODS

Surveys of organized cervical screening programmes active in Italy in 2011 and 2012 were conducted by the ONS on behalf of the Italian Ministry of Health in 2012 and 2013. A programme was considered active each year if at least 1,000 women were invited during that year. For each year, women invited during that year and screened within the first 4 months of the subsequent year were considered.

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 the relevant year.

We collected tables of aggregated data, in general 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 European⁵ guidelines) and to study their distribution. Data were centrally 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 data were available. In addition, we analyzed 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 organizational 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 underwent re-organization (typically, 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, p. 66) the mean national value, of some indicators and their 10th and 90th percentile. The values of the last three surveys are reported. The year denotes the period of screening activity considered (therefore the year before the conduction of the survey). In addition, we present graphs with the distribution between regions in 2011 and 2012. Figures 2 (p. 67) and 5 (p. 68) report the mean for 2011 and 2012.

Data on second-level activities (about correlation between colposcopic findings and histology and about the management of women with screen-detected CIN or invasive cancer) are presented at an overall national level as tables including data from all programmes that provided them in 2010 and 2011. Colposcopic findings were classified according to the International classification (IFCPC). The Rome 1990 classification¹⁸ was adopted in the first experimental surveys and kept in use

for comparability. In this section each colposcopy was considered as a statistical unit. In case of multiple biopsies during a same colposcopy, the most severe histology was considered. In the section on management of women with screen-detected CIN/cancer each woman was a unit. For this purpose we considered the worst histology before treatment and the first treatment. A “see and treat” approach – i.e., treatment in the absence of a histological diagnosis – is very limited in Italian organized programmes.

RESULTS

Extension of organized programmes and invitation of the target population

Concerning this section of the survey, we obtained questionnaires from 116 and 119 programmes for 2011 and 2012, respectively. The target population of active organized programmes in these and previous surveys is reported in [table 1](#) (p. 64). Target populations are also expressed as the percentage of women aged 25 to 64 years resident in a given area. It must be kept in mind that denominators are based on census for 2012 and estimated for previous years.

Active programmes in Italy had a target population of 14,301,979 women in 2011 and 14,497,209 women in 2012, representing 84.1% and 87.3%, respectively, of the Italian female population aged 25-64, compared to 80.1% in 2010. In 2012, active programmes included in their target population the entire female population aged 25 to 64 years in 15/21 regions, over 95% in 3 regions and close to 80% in 2 regions (Sardinia and Liguria). Incomplete nominal extension is

mainly caused by the choice of not implementing a population-based screening in the region of Lombardia, where only local initiatives are active ([table 2](#), p. 65).

The values above consider the entire target population regardless of the proportion actually invited. It is obviously relevant that active programmes invite women at a rate sufficient to reach the entire target population within the standard screening interval (3 years for cytology-based screening). [Table 1](#) reports 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 2012, actual extension was 70.4% at national level. Because variations between years can result from local criteria of organization, the percentage of women in the target population invited in the last 3 years is reported in [table 2](#). The completeness of invitation is also computed excluding from the denominator women not invited because of recent testing or for other specified reasons (adjusted %). Programmes adopt different criteria for exclusion and some programmes do not exclude any women at all. There is a clear North-South gradient in completeness of invitation. As the interval between HPV-based screens is now 5 years, actual coverage is now underestimated, but this effect is minimal for 2011 and 2012 activity.

During 2011 and 2012, 41.2% and 40.8%, respectively, of invited women were screened, compared to 39.8% in the previous year ([table 1](#)). A clear decreasing trend in compliance with invitation from northern to central and especially southern Italy (49.1%, 40.2%, and 29.5%, respectively, in 2012) was

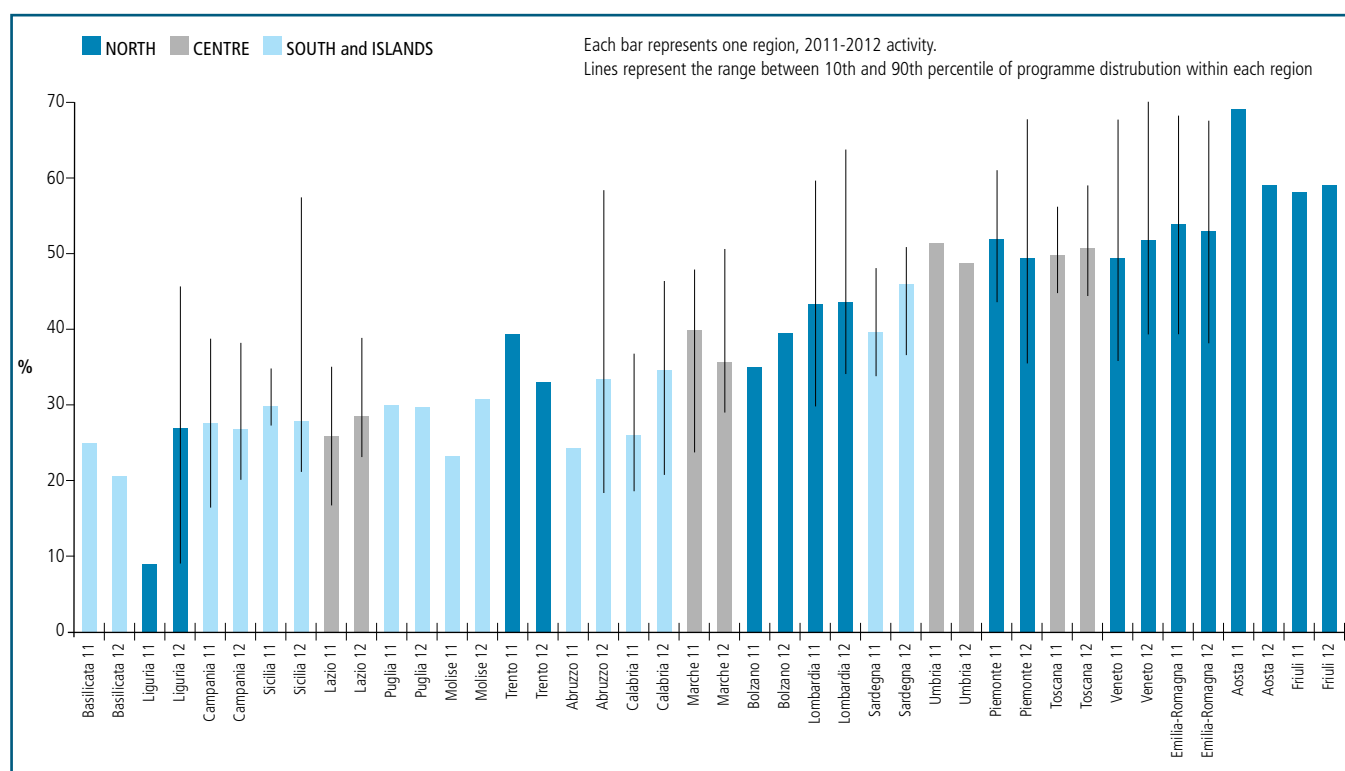


Figure 1. Uptake percentage by region. 2011-2012 activity. / **Figure 1.** Adesione percentuale all'invito, per Regione. Attività 2011-2012.

| | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|--|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|-------------------------------------|
| Number of women 25-64 yrs. included in the target population of organized programmes | 11,362,580 | 11,872,810 | 13,094,025 | 13,133,604 | 13,538,080 | 14,301,979 | 14,497,209 |
| Population 25-64 yrs | 16,463,948* | 16,543,059* | 16,693,052* | 16,812,052* | 16,900,554* | 17,006,946* | 16,600,566** |
| Nominal extension ^a | 69.01 | 71.77 | 78.44 | 78.12 | 80.10 | 84.10 | 87.33 |
| Actual extension ^b | 52.91 (2,873,202/ 5,487,982) | 54.80 (3,021,734/ 5,514,353) | 59.85 (3,330,289/ 5,564,350) | 63.30 (3,547,457/ 5,604,016) | 63.64 (3,584,955/ 5,633,511) | 62.19 (3,525,522/ 5,668,982) | 70.37 (3,893,773/ 5,533,522) |
| Compliance to invitation (%) ^c | 38.49 (1,116,006/ 2,899,817) | 39.83 (1,217,000/ 3,055,353) | 39.69 (1,332,376/ 3,356,931) | 39.27 (1,393,243/ 3,547,457) | 39.84 (1,374,745/ 3,450,755) | 41.17 (1,451,056/ 3,524,863) | 40.76 (1,600,796/ 3,927,403) |
| Percentage of population screened ^d | 20.34% (1,116,006/ 5,487,983) | 22.07% (1,217,000/ 5,514,353) | 23.94% (1,332,376/ 5,564,351) | 24.86% (1,393,243/ 5,604,017) | 24.40% (1,374,745/ 5,633,518) | 25.60% (1,451,056/ 5,668,982) | 28.93% (1,600,796/ 5,533,522) |
| Northern Italy | | | | | | | |
| Number of women 25-64 yrs. included in the target population of organized programmes | 4,911,641 | 4,942,788 | 5,210,405 | 5,133,658 | 5,155,376 | 5,513,736 | 5,590,488 |
| Population 25-64 yrs | 7,545,425 | 7,555,407 | 7,615,828 | 7,674,160 | 7,712,312 | 7,771,110 | 7,564,052 |
| Nominal extension ^a | 65.09 | 65.42 | 68.42 | 66.90 | 66.85 | 70.95 | 73.91 |
| Actual extension ^b | 52.91 (1,330,768/ 2,515,141) | 55.38 (1,394,613/ 2,518,469) | 55.38 (1,525,113/ 2,538,609) | 59.75 (1,528,455/ 2,558,053) | 60.32 (1,550,770/ 2,570,768) | 62.51 (1,619,150/ 2,590,370) | 69.25 (1,745,942/ 2,521,348) |
| Compliance to invitation (%) ^c | 45.62 (612,069/ 1,341,812) | 46.93 (664,344/ 1,415,361) | 47.67 (734,577/ 1,541,010) | 49.15 (751,283/ 1,528,455) | 49.39 (742,219/ 1,502,820) | 49.87 (815,607/ 1,635,630) | 49.12 (867,589/ 1,766,270) |
| Percentage of population screened ^d | 24.34% (612,069/ 2,515,142) | 26.38% (664,344/ 2,518,469) | 28.94% (734,577/ 2,538,609) | 29.37% (751,283/ 2,558,053) | 28.87% (742,219/ 2,570,771) | 31.49% (815,607/ 2,590,370) | 34.41% (867,589/ 2,521,351) |
| Central Italy | | | | | | | |
| Number of women 25-64 yrs. included in the target population of organized programmes | 3,029,340 | 3,008,931 | 3,252,167 | 3,113,448 | 3,277,736 | 3,308,299 | 3,246,268 |
| Population 25-64 yrs | 3,224,341 | 3,275,594 | 3,315,532 | 3,347,197 | 3,367,589 | 3,391,992 | 3,283,420 |
| Nominal extension ^a | 93.95 | 91.86 | 98.09 | 93.02 | 97.33 | 97.53 | 98.87 |
| Actual extension ^b | 75.05 (806,609/ 1,074,780) | 74.54 (813,887/ 1,091,865) | 80.51 (889,801/ 1,105,177) | 80.26 (895,459/ 1,115,732) | 80.62 (904,993/ 1,122,528) | 79.42 (897,918/ 1,130,664) | 81.48 (891,778/ 1,094,473) |
| Compliance to invitation (%) ^c | 35.70 (290,632/ 814,208) | 40.23 (330,925/ 822,548) | 40.17 (357,846/ 890,868) | 38.12 (341,325/ 895,459) | 37.98 (327,029/ 860,981) | 38.52 (346,654/ 899,824) | 40.18 (358,958/ 893,437) |
| Percentage of population screened ^d | 27.04% (290,632/ 1,074,780) | 30.31% (330,925/ 1,091,865) | 32.38% (357,846/ 1,105,177) | 30.59% (341,325/ 1,115,732) | 29.13% (327,029/ 1,122,530) | 30.66% (346,654/ 1,130,664) | 32.80% (358,958/ 1,094,473) |
| Southern Italy and Islands | | | | | | | |
| Number of women 25-64 yrs. included in the target population of organized programmes | 3,421,599 | 3,921,091 | 4,631,453 | 4,886,498 | 5,104,968 | 5,479,944 | 5,660,453 |
| Population 25-64 yrs | 5,694,182 | 5,712,058 | 5,761,692 | 5,790,695 | 5,820,653 | 5,843,844 | 5,753,109 |
| Nominal extension ^a | 65.63 | 68.65 | 80.38 | 84.39 | 87.70 | 95.39 | 98.39 |
| Actual extension ^b | 38.77 (735,825/ 1,898,060) | 42.71 (813,234/ 1,904,019) | 47.66 (915,375/ 1,920,564) | 58.21 (1,123,543/ 1,930,231) | 58.20 (1,129,192/ 1,940,215) | 51.77 (1,008,454/ 1,947,948) | 65.50 (1,256,053/ 1,917,701) |
| Compliance to invitation (%) ^c | 28.68 (213,305/ 743,797) | 27.12 (221,731/ 817,444) | 27.73 (239,953/ 925,053) | 26.76 (300,635/ 1,123,543) | 28.11 (305,497/ 1,086,954) | 29.19 (288,795/ 989,409) | 29.52 (374,249/ 1,267,696) |
| Percentage of population screened ^d | 11.24% (213,305/ 1,898,061) | 11.65% (221,731/ 1,904,019) | 12.49% (239,953/ 1,920,564) | 15.58% (300,635/ 1,930,232) | 15.75% (305,497/ 1,940,218) | 14.83% (288,795/ 1,947,948) | 19.52% (374,249/ 1,917,703) |

^a percentage of the resident 25-64 year-old population that is included in the target population of active organized programmes.

^b numerator: population invited in the relevant year; denominator: 1/3 of the resident population aged 25-64 (invited women include both those invited for cytology and those invited for HPV testing as primary screening test).

^c denominator: number of women invited; numerator: number of women who underwent screening among them (by the first 4 months of the following year).

^d numerator: number of women who underwent screening among invited women (by the first 4 months of the following year); denominator: 1/3 of the resident 25-64 year-old population.

* estimated by the National institute of statistics (Istat).

** obtained by census.

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

Tabella 1. Popolazione obiettivo dei programmi organizzati di screening cervicale in Italia, quota di donne invitate e donne che hanno effettivamente risposto.

| Region | Programmes active in 2012 | Target population 25-64 yrs (%) (2012) | Nominal extension (%) (2012) | Target population invited (%) (2011) | Target population invited* (%) (2012) | Target population invited* (%) (2010+2011+2012) | Adjusted target population invited** (%) (2010+2011+2012) |
|------------------------------------|---|--|------------------------------------|--|---|---|---|
| Valle d'Aosta | Single regional programme | 35,777 | 100 | 29.6 | 30.4 | 96.59 | 96.59 |
| Piemonte | Regional programme. Fully active ^a Città di Torino, Cuneo, Alessandria, Moncalieri, Rivoli, Ivrea, Biella-Vercelli, Novara, Asti | 1,206,933 | 100 | 27.8 | 30.1 | 87.51 | 87.51 |
| Liguria | Regional programme. Genova 3, Imperia, Savonese | 336,105 | 79.1 | 6.9 | 11.0 | 28.34 [§] | |
| Lombardia | Regional programme. The following are active: Brescia, Cremona, Lodi, Mantova, Pavia, Vallecambonica | 778,096 | 28.7 | 28.1 | 31.6 | 87.31 | 100 |
| Self-governing province of Trento | Single regional programme | 145,719 | 100 | 46.2 | 63.9 | 100 | 100 |
| Self-governing province of Bolzano | Single regional programme | 137,647 | 100 | 24.3 | 23.6 | 71.78 [§] | |
| Veneto | Regional programme. Fully active ^a Adria, Alta Padovana, Alto Vicentino, Asolo, Bassano Del Grappa, Belluno, Bussolengo, Chioggia, Este, Feltre, Legnago, Dolo Mirano, Padova, Vicenza Ovest Vicentino, Verona, Pieve Di Soligo, Rovigo, Treviso, Veneto Orientale, Veneziana | 1,353,553 | 100 | 28.2 | 32.1 | 87.52 | 100 |
| Friuli-Venezia Giulia | Single regional programme | 343,353 | 100 | 28.4 | 30.3 | 83.70 | 100 |
| Emilia-Romagna | Regional programme. Fully active ^a Bologna, Cesena, Ferrara, Forlì, Imola, Modena, Parma, Piacenza, Ravenna, Reggio Emilia, Rimini | 1,255,986 | 100 | 35.6 | 34.2 | 100 | 100 |
| Toscana | Regional programme. Fully active ^a Arezzo, Empoli, Firenze, Grosseto, Livorno, Lucca, Massa, Pisa, Pistoia, Prato, Siena, Viareggio | 1,022,925 | 100 | 31.2 | 33.0 | 95.89 | 100 |
| Umbria | Single regional programme | 265,114 | 100 | 24.2 | 37.7 | 83.82 | 99.48 |
| Marche | Regional programme. Fully active ^a Area vasta 1, Area vasta 2, Area vasta 3, Area vasta 4, Area vasta 5 | 422,224 | 100 | 31.7 | 31.7 | 93.98 | 100 |
| Lazio | Regional programme. The following are active: Latina, Rieti, Roma A, Roma B, Roma C, Roma D, Roma E, Roma G, Roma H, Viterbo | 1,536,005 | 96.4 | 23.6 | 20.8 | 66.48 | 68.41 |
| Molise | Single regional programme | 85,637 | 100 | 13.1 | 14.0 | 53.60 | 53.67 |
| Abruzzo | Single regional programme. Fully active ^a | 368,882 | 100 | 15.9 | 29.5 | 61.05 | 100 |
| Campania | Regional programme. The following are active: Avellino, Benevento, Caserta, Napoli 1, Napoli 2, Napoli 3, Salerno | 1,624,086 | 100 | 14.7 | 15.7 | 46.15 | 54.12 |
| Basilicata | Single regional programme | 167,348 | 100 | - | - | 100 | 100 |
| Calabria | Catanzaro, Cosenza, Lamezia Terme, Locri, Palmi, Reggio Calabria, Vibo Valentia | 530,517 | 97.7 | 19.6 | 14.8 | 57.44 | 60.25 |
| Sicilia | Regional programme. The following are active: Agrigento, Catania, Caltanissetta, Enna, Messina, Palermo, Ragusa, Siracusa, Trapani | 1,375,898 | 99.3 | 19.2 | 30.0 | 78.25 | 78.27 |
| Sardegna | Regional programme. The following are active: Cagliari, Carbonia, Nuoro, Olbia, Oristano, Sanluri | 377,031 | 79.4 | 30.5 | 24.9 | 78.76 | 80.79 |
| Puglia | Single regional programme | 1,131,054 | 100 | 14.0 | 18.3 | 50.43 | 34.5 |

^a fully active means that the entire regional female population aged 25-64 is included in the target population of active cervical screening programmes.
^{*} only women aged 25-64 years are considered both in the 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 due to other reason.
[§] active only for 2 years.

Table 2. Active organized cervical screening programmes and target population (age 25-64), by region. Years 2011-2012.

Tabella 2. Programmi organizzati di screening cervicale attivi e popolazione obiettivo (25-64 anni), per Regione. Anni 2011-2012.

| Year of activity ^a | 2010 | | | | 2011 | | | | 2012 | | | |
|---|------|---------------------------|-------------|------|------|---------------------------|-------------|------|------|---------------------------|-------------|------|
| | N* | Mean (%) (num/den) | centile (%) | | N* | Mean (%) (num/den) | centile (%) | | N* | Mean (%) (num/den) | centile (%) | |
| | | | 10th | 90th | | | 10th | 90th | | | 10th | 90th |
| Population screened ^b | 118 | 1,456,665 | | | 107 | 1,508,595 | | | 104 | 1,467,808 | | |
| Recommendation to repeat cytology ^c | 111 | 4.7 (71,820/1,512,430) | 1.2 | 10.0 | 103 | 4.1 (59,934/1,449,562) | 1.0 | 9.0 | 100 | 3.5 (51,674/1,467,808) | 1.0 | 7.5 |
| Compliance to recommendation to repeat cytology ^d | 100 | 62.7 (33,410/53,288) | 40.8 | 86.9 | 98 | 64.8 (34,591/53,405) | 41.1 | 94.1 | 94 | 71.1 (32,507/45,691) | 41.9 | 95.3 |
| Referral rate ^e | 114 | 2.5 (36,647/1,445,138) | 1.0 | 4.2 | 105 | 2.4 (36,525/1,492,349) | 1.1 | 4.2 | 102 | 2.4 (36,432/1,494,122) | 1.0 | 4.2 |
| Compliance to colposcopy for ASC-US+ ^f | 106 | 85.9 (29,725/34,600) | 64.8 | 98.6 | 101 | 87.7 (30,115/34,346) | 64.8 | 98.3 | 99 | 85.3 (25,510/34,605) | 72.6 | 100 |
| Compliance to colposcopy for HSIL+ ^g | 105 | 88.7 (2,834/3,194) | 64.0 | 100 | 98 | 89.5 (2,749/3,072) | 66.6 | 100 | 99 | 90.4 (2,868/3,172) | 66.7 | 100 |
| PPV of referral to colposcopy because of ASC-US+ cytology for histologically confirmed CIN2+ ^h | 102 | 16.0 (4,597/28,723) | 6.4 | 28.3 | 95 | 15.3 (4,268/27,802) | 5.2 | 29.0 | 92 | 16.9 (4,724/27,988) | 5.8 | 31.1 |
| DR CIN2+ unadjusted ⁱ | 102 | 3.2 (4,597/1,393,654) | 1.1 | 5.2 | 95 | 3.2 (4,268/1,323,390) | 0.8 | 5.0 | 92 | 3.4 (4,741/1,393,544) | 1.5 | 5.2 |
| DR CIN2+ stand. Ita. ^j | 98 | 3.5 | 0.9 | 5.6 | 88 | 3.2 | 1.2 | 5.5 | 89 | 3.5 | 1.2 | 5.8 |

* number of programmes that provided information
^a year before the conduction of the survey; each survey includes women invited during the previous year and screening within the first 4 months of the current year (see text).
^b in some programmes this 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 2013.
^e denominator: number of screened women; numerator: number of screened women referred to colposcopy (any reason).
^f denominator: number of women referred to colposcopy because of ASC-US or more severe citology; numerator: number of the latter who underwent colposcopy.
^g denominator: number of women referred to colposcopy because of H-SIL or more severe citology; numerator: number of the latter who underwent colposcopy.
^h denominator: number of women who underwent colposcopy because of ASC-US or more severe citology; numerator: number of the latter who had CIN2 or more severe detected (histologically confirmed – most severe lesion within six months from cytology considered).
ⁱ denominator: number of screened women; numerator: number of the latter 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 needed data; percentiles were obtained after computing the standardized 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.

Tabella 3. Valore di alcuni indicatori di processo (media nazionale, 10° e 90° percentili) nelle ultime tre survey.

present, as previously observed. In 2012, compliance was over 50% in Umbria, Valle d'Aosta, Friuli-Venezia Giulia, Emilia-Romagna, and the province of Trento (figure 1).

Process indicators in organized programmes

Data in this section include only women screened by cytology. In 2011 and 2012, programmes that provided this type of data were 107 and 104, while screened women were 1,508,959 and 1,467,808, respectively. Some programmes reported data only on women screened after invitation. Decreases in number of programmes and screened women are due to the increase in HPV-based screening. Table 3 reports for each indicator the number of programmes for which that indicator could be computed.

In 2011 and 2012, 4.1% and 3.5% of screened women were recommended to repeat cytology, compared to 4.7% in 2010

and values between 5% and 7% in 2005-2009. In 2012, in two regions cytology repeat was recommended to more than 15% of screened women and in three others to more than 6% (figure 2). In three of these regions, many repeats were due to «other reasons», likely reactive changes, which represent a relevant source of variability. Repeats for unsatisfactory smears were very high in Molise. In some regions, a proportion of women was recommended to repeat the smear after ASC-US, AGC, and L-SIL cytology. However, these reasons represent a substantial proportion of repeats only in Sardegna and Veneto. Among women who had been recommended to repeat the smear, 65% actually had a new one in 2011 and 71% in 2012, following a monotonously increasing trend (60% in 2007). In 2012 two regions were below 50% and seven were above 80% (figure 3). 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.

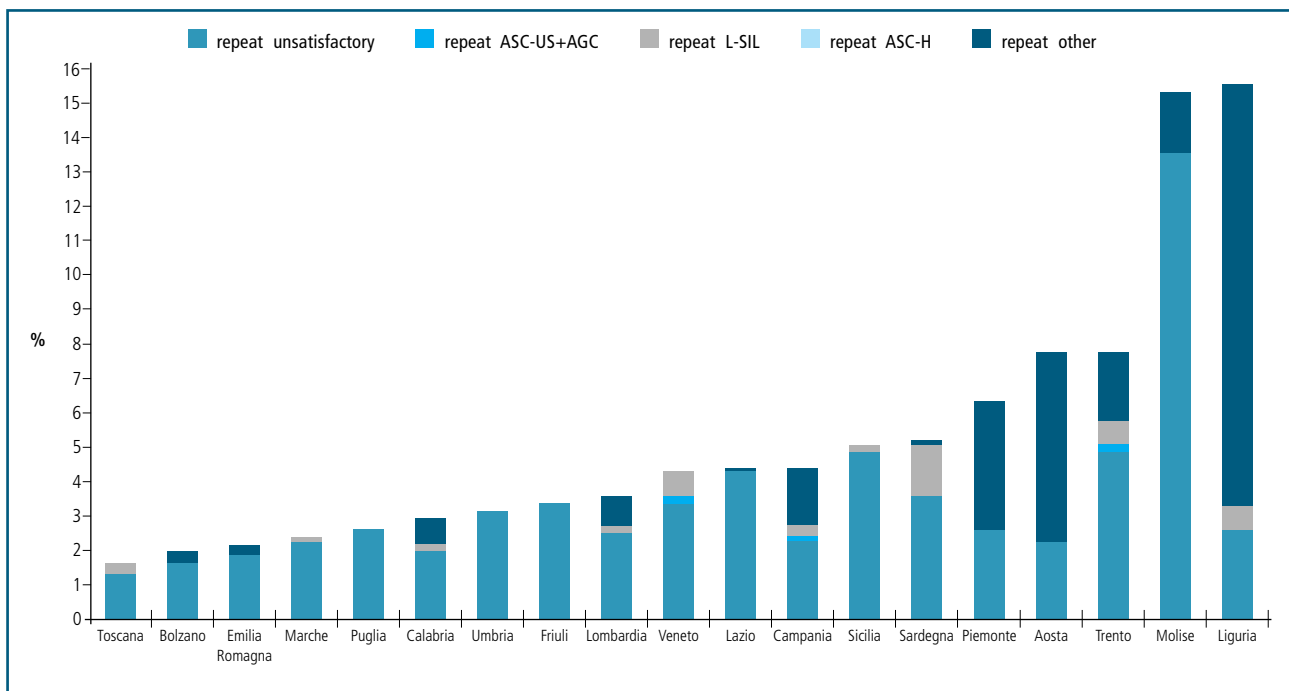


Figure 2. Percentage of screened women referred for repeat cytology, by region. 2011-2012 activity.

Figura 2. Percentuale della popolazione screenata che ha avuto indicazione a ripetere la citologia per qualsiasi causa, per Regione. Attività 2011-2012.

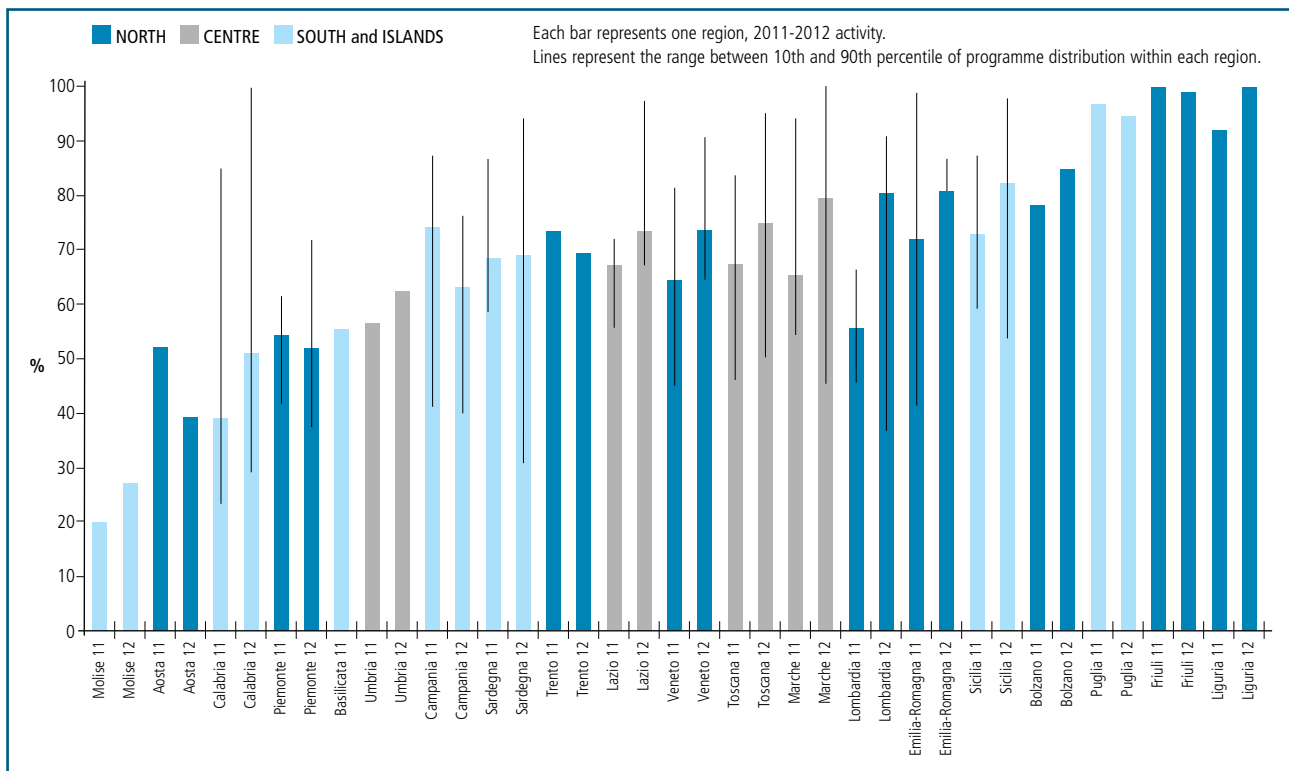


Figure 3. Compliance with repeat cytology. Women who repeated cytology by 15 April 2012 and by 15 April 2013 out of all those referred for repeat cytology. 2011-2012 activity.

Figura 3. Compliance alla ripetizione della citologia. Donne che hanno ripetuto entro il 15 aprile 2012 ed entro il 15 aprile 2013 su tutte le donne che hanno avuto indicazione a ripetere. Attività 2011-2012.

The referral rate to colposcopy was 2.4% both in 2011 and 2012 (table 3). Values between 2.3% and 2.5% had been registered in all years from 2005 to 2010.

The referral rate was above 4% in both 2011 and 2012 in Valle d'Aosta and in 2011 in Molise and Basilicata (figure 4, p. 68). There was a high variability within some regions. In 2012, out

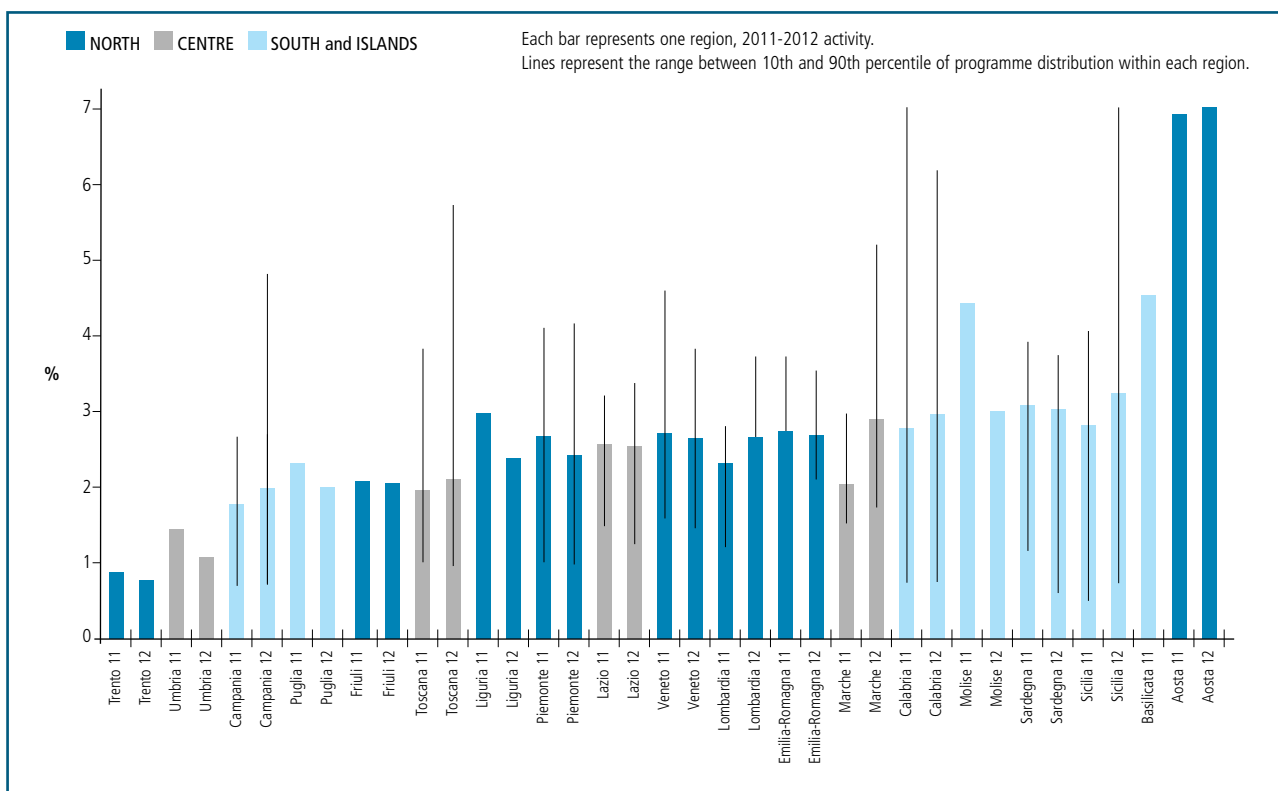


Figure 4. Proportion of women referred to colposcopy for any reason, by region. 2011-2012 activity.
Figura 4. Proporzioe di donne invitate in colposcopia per qualsiasi motivo, per Regione. Attività 2011-2012.

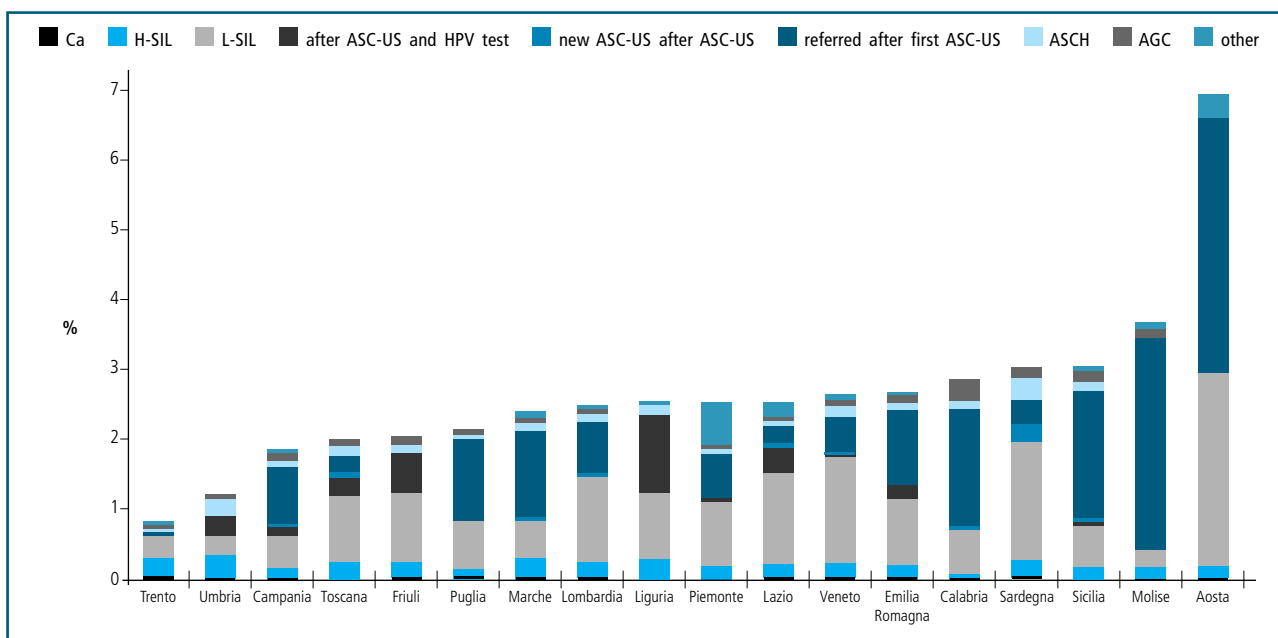


Figure 5. Proportion of women referred to colposcopy, by region and reason. 2011-2012 activity.
Figura 5. Proporzioe di donne invitate in colposcopia, per Regione e motivo. Attività 2011-2012.

of 102 programmes with relevant data, 68 (66.7%) referred to colposcopy fewer than 3% of screened women, and 89 (87.3%) fewer than 4%. However, in 8 programmes the referral rate was >5% and in two of them >6%. With respect to the reason for referral (figure 5), ASC-US cytology was still a major source of variability and reached very high levels in Molise and Valle

d'Aosta. Clearly, the regions with the lowest referral rate invited a very low number of women with ASC-US directly to colposcopy but did a previous repeat of cytology or a triage by HPV testing. However, L-SIL cytology has become now the most frequent reason in many regions and is a second major cause of variability.

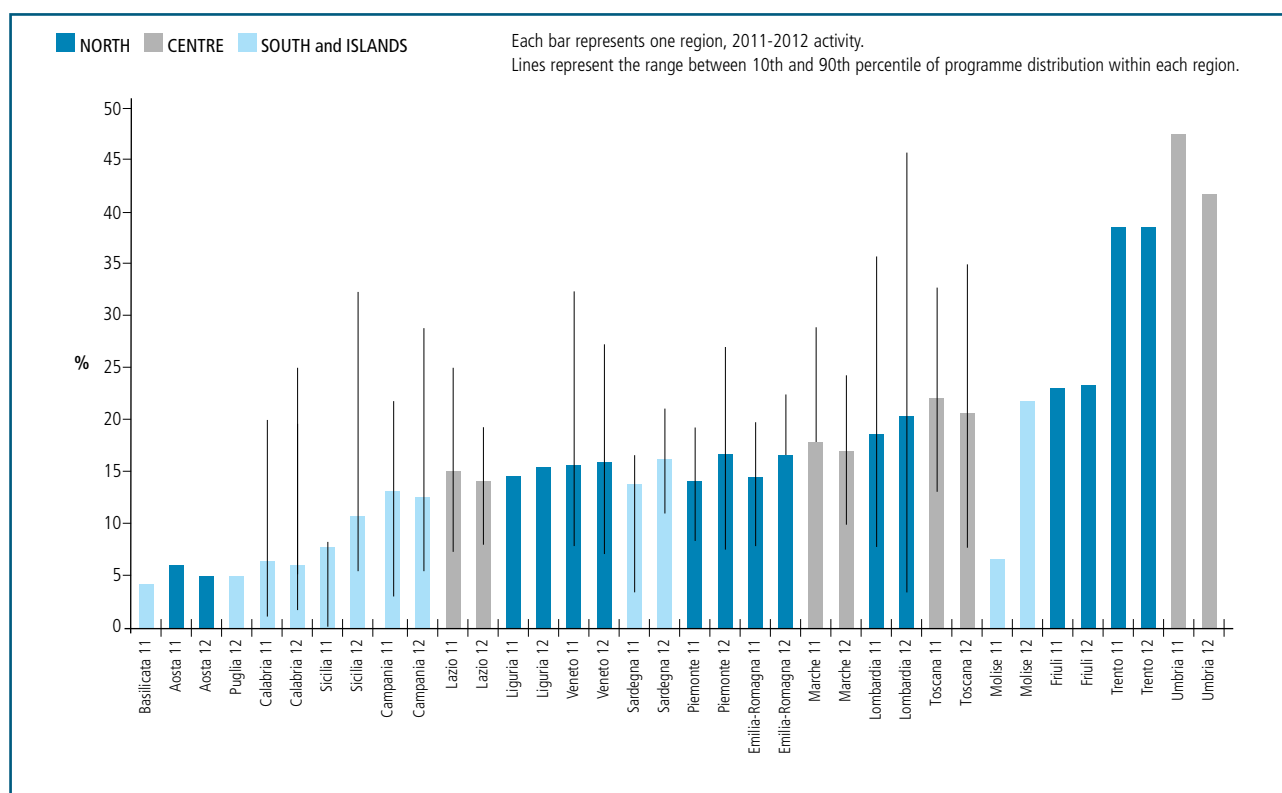


Figure 6. Positive predictive value, by region. 2011-2012 activity. / **Figura 6.** Valore predittivo positivo, per Regione. Attività 2011-2012.

At a national level, the positive predictive value (PPV) of ASC-US or more severe cytology for CIN2 or more severe histology was 15.3% in 2011 and 16.9% in 2012. Its value was just above 16% from 2006, after a rising trend which started in 2000 (when PPV was 11.4%).

Figure 6 shows the distribution of PPV in Italian regions during 2011 and 2012. Its value was inversely correlated to the referral rate (data not shown) and was <10% in Valle d'Aosta and Calabria both years and for one year in Basilicata, Puglia (only one available), Sicilia, and Molise. In 2012 Sicilia was just above 10%, but Molise registered a remarkable increase, reaching 22%. Values stably >20% were observed in four regions (Umbria, province of Trento, Friuli-Venezia Giulia, and Toscana).

Three of them refer to colposcopy no or very few women at the first diagnosis of ASC-US, as a result of the implementation of triage systems for this cytological category. However, PPV was not very high in some regions where no or few women with ASC-US were directly referred to colposcopy but referral because of L-SIL is relevant. Indeed, looking at specific reasons of referral (**table 4**) L-SIL cytology had a PPV for CIN2+ <10%. In addition, women referred to colposcopy because of persistent ASC-US cytology had a lower PPV for CIN2+ than that of women referred at the first ASC-US cytology.

Among women referred to colposcopy because of an ASC-US or more severe cytology during 2011 and 2012, 87.7% and 85.3% respectively actually had one colposcopy, compared to 85.9 in 2010 and 85.1% in the two previous years (**figure 7**, p. 70).

Among women referred to colposcopy because of a H-SIL or

more severe cytology, compliance was 89.5% in 2011 and 90.4% in 2012 (**figure 8**, p. 71).

Figure 9 (p. 71) shows the detection rate (DR) of histologically confirmed CIN2 or more severe lesions. The standardized (on the Italian population truncated 25-64 yrs) DR was 3.2 lesions detected per 1,000 screened women in 2011 and 3.5 in 2012. Previously, DR increased from 3.0 in 2004 to 3.5 in 2010. Overall, there was a decreasing trend from North to South. However, high DRs, despite being lower than in 2009 and 2010, were still observed in Sardegna, where a new programme was recently started, and there was a strong increase in Sicilia in 2012 following invitation extension. An increase from 3.2 in 2011 to 4.9 in 2013 was also observed in Marche (central Italy), again related to an increased proportion of women at their first cervical screen.

Second-level activity

Colposcopic findings and their correlation with histology

Data were reported from 81 programmes both in 2011 and 2012 (**table 5**, p. 72). Most of the 54,776 colposcopies included in the analysis were classified as normal (38.9%), G1 (34.8%) or unsatisfactory (11.9%).

At least one biopsy was performed in 49.5% of all colposcopies: 84.2% of those with abnormal findings, 33.4% of unsatisfactory colposcopies, and 16.8% of normal colposcopies. When considering only colposcopies with biopsy, CIN1 or more severe histology was detected in 69.0% of those classified as grade 1 and CIN2+ in 65.0% of those classified as grade 2 and 89.2% of those suggestive of cancer, but just in

| Criterion of referral | Endpoint | 2011 | | | 2012 | | |
|--|----------|-----------------------|------------|------------|-----------------------|------------|------------|
| | | Mean (%) (num/den) | P10 (%) | P90 (%) | Mean (%) (num/den) | P10 (%) | P90 (%) |
| H-SIL cytology | CIN2+ | 70.2 (1,844/2,626) | 46.0% | 100.0 | 71.7 (1,719/2,397) | 50.0 | 100.0 |
| H-SIL cytology | CIN3+ | 46.4 (1,218/2,626) | 16.0 | 79.3 | 47.2 (1,132/2,397) | 12.5 | 68.4 |
| L-SIL cytology | CIN2+ | 9.7 (1,227/12,622) | 3.3 | 20.0 | 9.1 (1,098/12,022) | 3.0 | 20.0 |
| L-SIL cytology | CIN3+ | 2.9 (362/12,622) | 0.0 | 8.0 | 3.1 (367/12,022) | 0.0 | 8.1 |
| ASC-US cytology followed by TRIAGE HPV | CIN2 | 13.7 (247/1,808) | 2.1 | 33.3 | 12.2 (172/1,416) | 0.0 | 17.2 |
| ASC-US cytology followed by TRIAGE HPV | CIN3 | 4.9 (89/1,808) | 0.0 | 12.3 | 6.0 (85/1,416) | 0.0 | 10.8 |
| Repeat ASC-US cytology | CIN2 | 4.0 (13/324) | 0.0 | 11.5 | 4.5 (17/380) | 0.0 | 10.0 |
| Repeat ASC-US cytology | CIN3 | 0.3 (1/324) | 0.0 | 3.85 | 1.8 (7/380) | 0.0 | 9.1 |
| First ASC-US cytology | CIN2 | 5.6 (440/7,814) | 0.0 | 15.6 | 4.8 (427/8,845) | 0.0 | 13.64 |
| First ASC-US cytology | CIN3 | 2.4 (188/7,814) | 0.0 | 5.8 | 2.1 (187/8,845) | 0.0 | 5.8 |

The table includes data from the 95 programmes that provided data in 2011 and the 92 that provided data in 2012.

Table 4. Positive predictive value for CIN2 or more severe histology and for CIN3 or more severe histology according to different criteria of referral.

Tabella 4. Valore predittivo positivo per istologia CIN2 o più grave e per istologia CIN3 o più grave, secondo diversi criteri di invio.

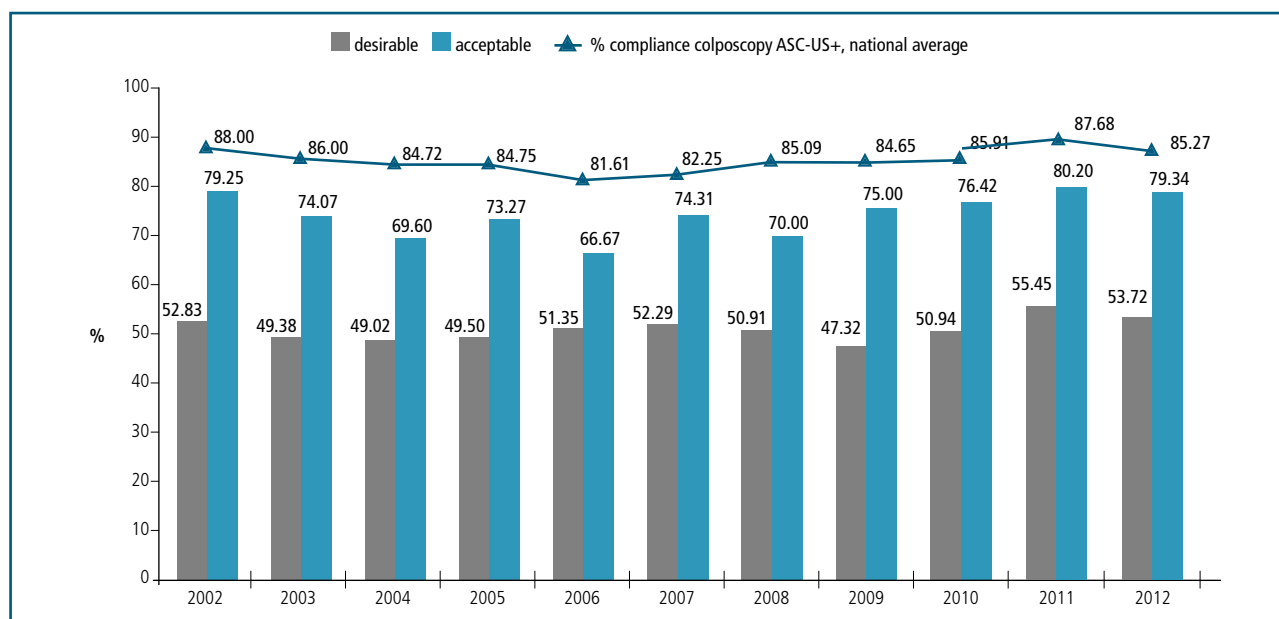


Figure 7. Compliance with colposcopy (referral because of ASC-US or more severe cytology). Percentage of programmes that reach "acceptable" and "desirable" values by year of activity.

Figura 7. Compliance alla colposcopia (invio per citologia ASC-US o più grave). Percentuale di programmi che raggiungono valori "accettabili" e "desiderabili", per anni di attività.

50.8% of those with atypical vessels. When excluding from computations the lesions diagnosed during unsatisfactory or unclassified colposcopies, 95.1% of CIN3+ and 93.7% of CIN2 were identified during colposcopies with abnormal findings (58.9% and 33.6% of CIN3+ and CIN2, respectively, during colposcopies classified as G2, atypical vessels, or suggestive of cancer).

Management and treatment of women with screen-detected biopsy-proven CIN

Data were reported by 86 programmes in 2011 and 93 in 2012 (table 6, p. 73). No information was available for 4.8% of women and the type of treatment was unknown for a further 1.8%.

Of all women with CIN1, 81.7% were recalled for follow-

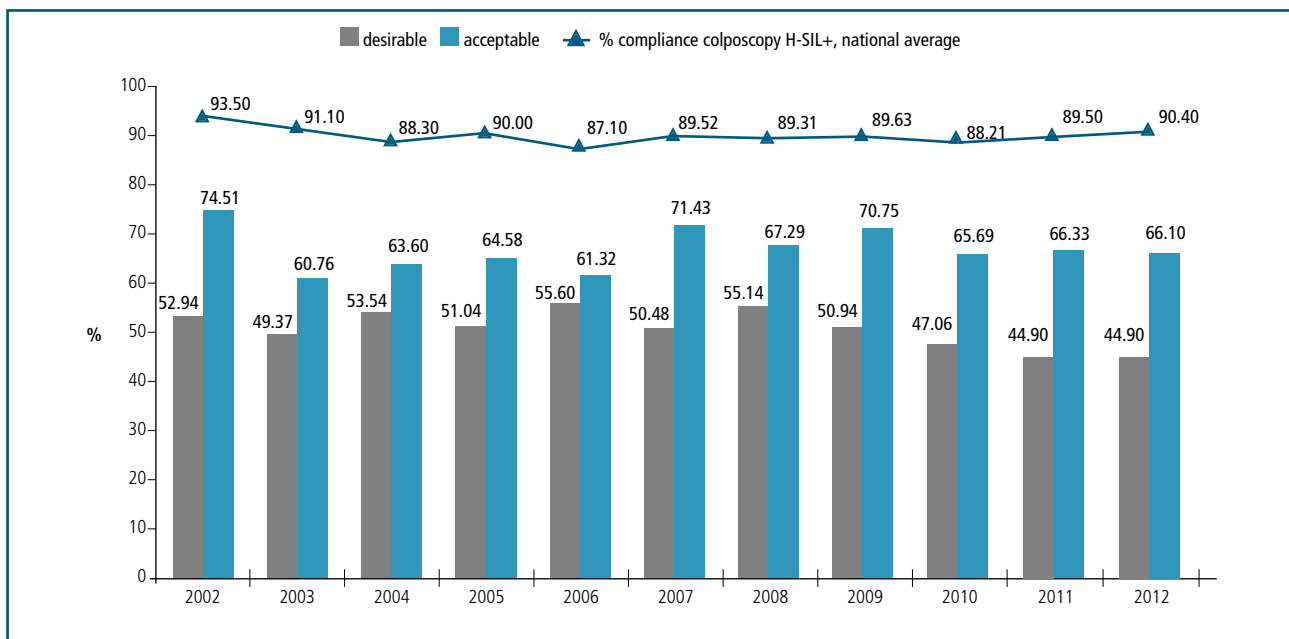


Figure 8. Compliance with colposcopy (referral because of H-SIL or more severe cytology). Percentage of programmes that reach “acceptable” and “desirable” values by year of activity.

Figura 8. Compliance alla colposcopia (invio per citologia H-SIL o più grave). Percentuale di programmi che raggiungono valori “accettabili” e “desiderabili”, per anni di attività.

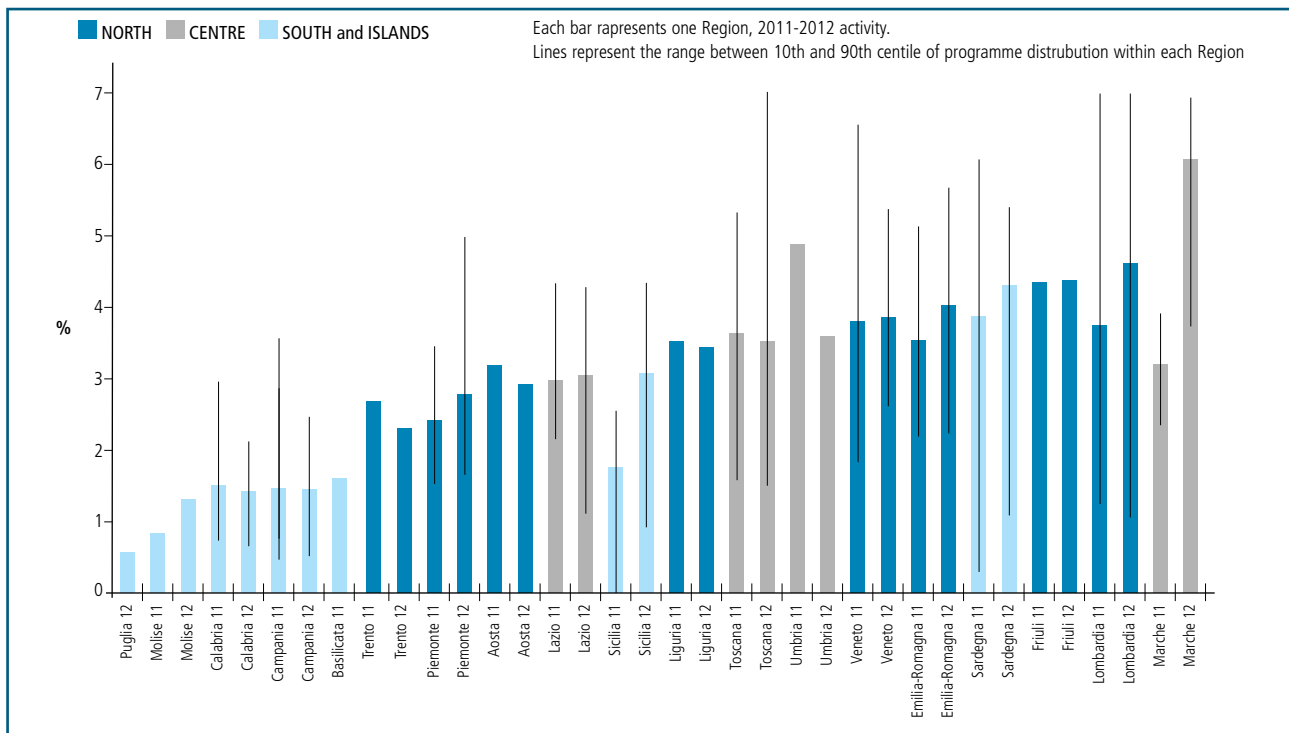


Figure 9. Unadjusted detection rate (per 1,000 women) of histologically confirmed CIN2+, by region. 2011-2012 activity.

Figura 9. Tasso di identificazione grezza di CIN2+ con conferma istologica, per Regione. Attività 2011-2012.

up only, in agreement with the recommendation not to treat these lesions except if persistent.⁵⁻⁷ This proportion increased from previous years (78.8% in 2010 and 73.0% in 2009). Most of women with CIN2 (52.8%) and CIN3 (57.0%) were treated by stand-alone radio-frequency devices. Laser conisation was applied in 7.2% of women with CIN2 and 9.1% of those

with CIN3. Destructive treatments were still used in association with radio-frequency devices (laser in 5.4% and 3.2% of women with CIN2 and CIN3 respectively), but very uncommonly alone, especially for CIN3. Cold knife conisation was limited to 8.8% of women with CIN2 and 14.5% of those with CIN3. Of the women with adenocarcinoma in situ, 35.8% had hys-

| Colposcopic findings | Histology | | | | | | | | | |
|--|---------------------|--------|-------|-------|-------|-------------------------|-----------------------------|--------------------------|-------------------|--------|
| | no biopsy performed | no CIN | CIN1 | CIN2 | CIN3 | adeno carcinoma in situ | invasive squamous carcinoma | invasive adeno carcinoma | total with biopsy | total |
| normal colposcopic findings - transformation zone fully visible (N) | 17,701 | 2,217 | 992 | 215 | 137 | 8 | 4 | 7 | 3,580 | 21,281 |
| % of total | 83.2% | 10.4% | 4.7% | 1.0% | 0.6% | 0.0% | 0.0% | 0.0% | | |
| % of total with biopsy | | 61.9% | 27.7% | 6.0% | 3.8% | 0.2% | 0.1% | 0.2% | | |
| grade 1 (N) | 3,379 | 4,874 | 7,634 | 2,038 | 1,103 | 25 | 25 | 7 | 15,706 | 19,085 |
| % of total | 17.7% | 25.5% | 40.0% | 10.7% | 5.8% | 0.1% | 0.1% | 0.0% | | |
| % of total with biopsy | | 31.0% | 48.6% | 13.0% | 7.0% | 0.2% | 0.2% | 0.0% | | |
| grade 2 (N) | 233 | 460 | 1,092 | 1,125 | 1,626 | 37 | 79 | 15 | 4,434 | 4,667 |
| % of total | 5.0% | 9.9% | 23.4% | 24.1% | 34.8% | 0.8% | 1.7% | 0.3% | | |
| % of total with biopsy | | 11.6% | 23.6% | 24.8% | 36.8% | 1.4% | 1.5% | 0.3% | | |
| atypical vessels (N) | 194 | 51 | 9 | 13 | 27 | 2 | 16 | 4 | 122 | 316 |
| % of total | 61.4% | 16.1% | 2.8% | 4.1% | 8.5% | 0.6% | 5.1% | 1.3% | | |
| % of total with biopsy | | 41.8% | 7.4% | 10.7% | 22.1% | 1.6% | 13.1% | 3.3% | | |
| colposcopic features suggestive of invasive cancer (N) | 11 | 5 | 5 | 4 | 14 | 10 | 39 | 16 | 93 | 104 |
| % of total | 10.6% | 4.8% | 4.8% | 3.8% | 13.5% | 9.6% | 37.5% | 15.4% | | |
| % of total with biopsy | | 5.4% | 5.4% | 4.3% | 15.1% | 10.8% | 41.9% | 17.2% | | |
| other - unsatisfactory colposcopy (N) | 4,343 | 1,262 | 613 | 144 | 141 | 6 | 6 | 6 | 2,178 | 6,521 |
| % of total | 66.6% | 19.4% | 9.4% | 2.2% | 2.2% | 0.1% | 0.1% | 0.1% | | |
| % of total with biopsy | | 57.9% | 28.1% | 6.6% | 6.5% | 0.3% | 0.3% | 0.3% | | |
| Number of colposcopies where colposcopy result is not available (N) | 1,783 | 514 | 284 | 95 | 100 | 3 | 6 | 7 | 1,009 | 2,792 |
| % of total | 63.9% | 18.4% | 10.2% | 3.4% | 3.6% | 0.1% | 0.2% | 0.3% | | 54,766 |
| % of total with biopsy | | 50.9% | 28.1% | 9.4% | 9.9% | 0.3% | 0.6% | 0.7% | | |

Table 5. Colposcopic findings and histology in the colposcopies performed by 81 Italian cervical screening programmes during 2011 and 2012.

Tabella 5. Grading colposcopico ed esito istologico delle colposcopie effettuate da 81 programmi italiani di screening negli anni 2011 e 2012.

terectomy, 15.6% cold knife conisation, and 32.1% other more conservative excisional treatment. As first treatment, some 59% of women with invasive cancer had hysterectomy, 7% cold knife conisation and 10% LLETZ. These plausibly include diagnostic assessment procedures. We do not know about subsequent treatments.

No recommendation of treatment was registered for 7.0% of CIN2 and 2.2% of CIN3. On the other hand, hysterectomy was reported in 0.1%, 0.4%, and 2.3% of women with CIN1, CIN2, and CIN3, respectively. Italian guidelines recommend no more than 2% hysterectomies on CIN2/3 and virtually none on CIN1.^{1,2} Diathermocoagulation, which is not recommended by guidelines,^{5,19} was still applied for 4.3% of CIN1 and 1.6% of CIN2.

No treatment was registered, despite referral, in 3-4% of women with CIN2/3 or adenoCa. In most of these cases, referrals were made >3 months in advance, suggesting refusal.

Correlation between colposcopy-guided biopsy and excised specimen histology

Excisional histology was CIN1 or lower in 13% of women with a CIN2-3 colposcopy-guided biopsy, similar to what was ob-

served in 2010 (14%). Among women with CIN1 who had a colposcopy-guided biopsy, 23% had CIN2 or more severe histology on the excised specimen. Higher values had been observed in previous years: 30% in 2009 and 32% in 2010 (table 7).

DISCUSSION

Organized cervical screening programmes have now reached almost complete nominal extension. Italian women not included in organized programmes are substantially only those from most of Lombardia, which chose not to implement invitational programmes. However, the programmes active in northern and central Italy now frequently reach complete or almost complete invitational coverage, while in some regions of southern Italy the invitation rate is much lower than needed. Some decrease in invitational coverage, compared to previous years, was observed in regions of southern but also northern and central Italy.

It is important to avoid that funding restrictions due to the economic crisis result in an inversion of the growing trend observed up to now: this would mean losing the results of a great amount of efforts and resources allocated for many years. Recent national results^{20,21} confirm the early local observation²²

| | Most severe histology before treatment | | | | | | | | | | total |
|--|--|--------------|--------------|--------------|--------------|--------------|-------------------------|--------------|--------------------|--------------|---------------|
| | CIN1* | % | CIN2* | % | CIN3* | % | adeno carcinoma in situ | % | invasive carcinoma | % | |
| First treatment | | | | | | | | | | | |
| laser vaporisation | 231 | 2.3 | 103 | 2.5 | 24 | 0.7 | 0 | 0.0 | 0 | 0.0 | 358 |
| cryotherapy | 1 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 |
| radical diathermy | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 |
| diathermocoagulation | 436 | 4.3 | 65 | 1.6 | 6 | 0.2 | 0 | 0.0 | 0 | 0.0 | 507 |
| excision by radio-frequency device | 469 | 4.7 | 2,147 | 52.8 | 1,929 | 57.0 | 24 | 22.0 | 25 | 10.0 | 4,594 |
| cold knife conisation | 84 | 0.8 | 359 | 8.8 | 490 | 14.5 | 17 | 15.6 | 18 | 7.2 | 968 |
| laser conisation | 47 | 0.5 | 293 | 7.2 | 308 | 9.1 | 10 | 9.2 | 4 | 1.6 | 662 |
| LLETZ + Laser | 20 | 0.2 | 220 | 5.4 | 108 | 3.2 | 1 | 0.9 | 0 | 0.0 | 349 |
| hysterectomy | 13 | 0.1 | 15 | 0.4 | 79 | 2.3 | 39 | 35.8 | 147 | 59.0 | 293 |
| Other treatments | | | | | | | | | | | |
| conisation NOS | 0 | 0.0 | 2 | 0.0 | 2 | 0.1 | 0 | 0.0 | 0 | 0.0 | 4 |
| radio/chemotherapy | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 3 | 1.2 | 3 |
| photo-thermocoagulation | 3 | 0.0 | 1 | 0.0 | 1 | 0.0 | 1 | 0.9 | 0 | 0.0 | 6 |
| trachelectomy | 0 | 0.0 | 1 | 0.0 | 1 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 |
| polipectomy | 2 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 |
| type of treatment unknown | 66 | 0.7 | 122 | 3.0 | 112 | 3.3 | 4 | 3.7 | 19 | 7.6 | 323 |
| not treated - no treatment recommended | 8,233 | 81.7 | 285 | 7.0 | 73 | 2.2 | 3 | 2.8 | 0 | 0.0 | 8,594 |
| not treated - treatment recommended <3 months before | 36 | 0.4 | 29 | 0.7 | 24 | 0.7 | 0 | 0.0 | 2 | 0.8 | 91 |
| not treated - treatment recommended ≥3 months before | 74 | 0.7 | 92 | 2.3 | 85 | 2.5 | 4 | 3.7 | 5 | 2.0 | 260 |
| unknown if treated | 365 | 3.6 | 331 | 8.1 | 140 | 4.1 | 6 | 5.5 | 26 | 10.4 | 868 |
| Total | 10,080 | 100.0 | 4,065 | 100.0 | 3,382 | 100.0 | 109 | 100.0 | 249 | 100.0 | 17,885 |

Table 6. Treatment or management of the intraepithelial lesions, performed by 86 Italian screening programmes in 2011 and 93 in 2012.

Tabella 6. Trattamento o gestione delle lesioni intraepiteliali effettuati da 86 programmi italiani di screening nel 2012.

| worse histology before treatment | Histology on excised specimen | | | | | | | total |
|----------------------------------|-------------------------------|-------------------|---------------------|----------------------|------------------------------|-----------------|-------------------|-------|
| | negative (<CIN) (%) | CIN1 (%) | CIN2/3 (%) | adeno Ca in situ (%) | invasive cervical cancer (%) | total available | not available (%) | |
| CIN1 | 188 (20.4) | 521 (56.6) | 205 (22.3) | 5 (0.5) | 2 (0.2) | 921 | 51 (5.2) | 972 |
| CIN2/3 | 154 (2.9) | 537 (10.2) | 4,428 (83.7) | 43 (0.8) | 126 (2.4) | 5,288 | 184 (3.4) | 5,472 |
| Adeno Ca in situ | 4 (5.7) | 2 (2.9) | 8 (11.4) | 42 (60.0) | 14 (20.0) | 70 | 1 (1.4) | 71 |
| Invasive cervical cancer | 7 (3.7) | 0 (0.0) | 40 (21.2) | 7 (3.7) | 135 (71.4) | 189 | 9 (4.5) | 198 |

The number of women is given, followed by percentages in brackets. "Not available" percentages are computed on row totals. The other percentages are computed based on the "total available" data.

Table 7. Correlation between colposcopy-guided biopsy and excised specimen histology.

Tabella 7. Correlazione tra biopsia guidata dalla colposcopia e istologia del campione prelevato.

that organized programmes can increase the overall proportion of women screened within the needed interval, thus showing their utility. A recent nationwide analysis of the screening histories of women who developed invasive cancer²³ also showed (in agreement with previous local analyses^{24,25}) that the large majority of those women did not comply with invitation. Therefore, an effort to increase compliance and reduce its negative North-South trend is needed.

When 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 organized 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. In some areas, this phenomenon was however compensated by an increase in immigrants from high migration pressure countries, who have a higher prevalence of high-grade CIN than Italian women.²⁶⁻²⁹

Performance indicators show little variation in the last years at a national level. There is surely a long-term trend to reduce recall for cytology repeat (which is plausibly attributable to the training activity in cytology interpretation, mainly performed by GISCi) and increasing compliance to recall for repeat. Referral to colposcopy was stable or slightly on the rise. However, PPV was also substantially stable, after a previous increase from 2000. Many indicators show increased homogeneity between regions for the past few years. A number of outliers, however, are still present: two regions recall over 10% of screened

women to repeat cytology and a group of regions has an extremely low PPV. A crucial factor in determining PPV is clearly the management of ASC-US, and its heterogeneity explains part of the heterogeneity in PPV. However, variability in criteria of interpretation of cytology still plays a relevant role. Although implementation of triage systems for ASC-US is needed in order to obtain high PPVs, it is not always sufficient. In fact, triaging ASC-US by repeat cytology did not reach high PPVs, possibly because criteria of interpretation were too loose in any case. In addition, high frequency of ASC-US was replaced by high frequency of LSIL reports, without reaching high PPVs.

Programmes with low PPV are mainly (but not only) from southern Italy, where organized programmes started their activity more recently. The very low CIN2+ detection rate observed in a few regions in southern Italy also requires attention. In southern Italy recent data showed a prevalence of HPV infection similar to that in central and northern Italy. This suggests a similar baseline risk at least in younger cohorts.³⁰ Therefore, the low detection rate could be the result of a selective uptake of invitation of women who had already been intensively screened, low sensitivity of cytology and/or histology, or low compliance to colposcopy. Part of the low compliance to colposcopy may depend upon incomplete registration (especially of colposcopies performed outside reference centres). Moreover, part of the low detection rate may depend upon in-

complete registration or missing links with histology results. In any case, it is essential to strive for the implementation of good fail-safe systems. Lack of diagnostic work-up can make the efforts made for primary screening useless.

In conclusion, data suggest that most of the programmes that have been active for many years reached a good quality, likely thanks to the long-lasting monitoring and intensive activity of quality assurance. On the other hand, the newly started programmes in southern Italy need strong support to improve quality, particularly as for the specificity of first-level cytology and the completeness of follow-up and registration. There is a need for intervention, as, in some areas, the current situation does not guarantee effectiveness of screening and acceptable levels of undesired effects. A shift to HPV testing could solve problems concerning quality of cytology interpretation, but it would not be an effective solution to problems of loss to follow-up.

The application of appropriate treatments has largely improved during the last few years and has now reached levels that are acceptable – although still not optimal – in almost all geographical areas. In addition, these data are still missing from many programmes. High quality of diagnostic work-up and treatment and strict adherence to positive women management algorithms are needed in view of a shift to HPV-based screening.

Conflicts of interests: none declared

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