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ORIGINAL ARTICLES AND REVIEWS

Key performance indicators of breast cancer screening programmes in Italy, 2011-2019

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Abstract

Introduction. Performance indicators for organised breast cancer screening programmes in Italy, 2011-2019, were evaluated.

Materials and methods. Aggregated data were gathered by the National Centre for Screening Monitoring from over 150 regional or sub-regional screening programmes in Italy. Invitation and examination coverage, participation rate (PR), recall rate (RR), detection rate, positive predictive value (PPV) for the target population as a whole (women aged 50-69), by 5-year age-class, geographical macro-area (North, Centre, South-Islands with the exception of three Regions for missing/uncomplete data) and Region were estimated.

Results. Coverage showed an increasing positive trend, especially in the South-Islands, and PR was stable all over Italy. On the other hand, an increasing RR and decreasing PPV were recorded, especially at the first screening test and in some regions.

Discussion and conclusions. The positive increase in coverage is accompanied by a worsening of some performance indicators for which a better resource allocation and staff training are required. For this reason, further and continuous monitoring is mandatory.

Key words

- breast cancer
- cancer screening
- performance indicators
- early detection of cancer
- Italy

INTRODUCTION

Breast cancer (BC) is a leading cause of disease burden among women in Europe: an estimated 531,086 women were diagnosed with BC and 141,765 died of BC in 2020 [1]. As proved by many studies, mammographic screening (MS) can reduce BC mortality in women aged more than 50 years old. Estimates of mortality reduction range from 20% for women invited to screening to 48% for women who are screened [2, 3].

Many countries, including Italy, offer a population-based mammographic screening programme (breast cancer screening programme, BCSP), to give target women systematic and equal access to screening. In Italy, screening programmes are public health interventions prescribed by a 2001 national law, confirmed in 2017 (Essential Levels of Care) [4]. The quality assurance and data collection are performed in a centralized manner [5].

A cancer-screening programme is a complex process, which effectiveness depends on three main phases: the screening test execution, the referral for further diagnostic assessment, and the surgical/medical therapy [6]. The previous European guidelines for quality assurance in mammography screening underlined three fundamental steps in screening programmes: 1) the identification and information of the eligible population, the delivery of active invitation, the execution of the first level test with high-quality standards; 2) a timely referral of positive cases for further assessment and treatment procedures and the minimization of negative effects; 3) the management of information flows and the provision of constant quality assurance throughout the

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entire process [7]. More recently, the European Commission Initiative on Breast Cancer (ECIBC) recommended implementing organised BCSP for early detection of breast cancer and underlined the importance of comprehensive process monitoring as crucial element to BCSP programmes' success [8, 9]. Since 2004 the National Centre for Screening Monitoring (ONS), on behalf of the Italian Ministry of Health, monitors and supports Italian BCSP programmes. This effort is done together with the Italian group for mammography screening (GISMa), a scientific association whose main goal is to promote the quality of programmes through the development and application of indicators and benchmarks. To this end of primary importance, is the annually data collection of Italian breast screening activities. Data are collected in an aggregated way and gathered through a standardised form to calculate process and impact parameters which have been agreed on a national level [10]. Monitoring results has allowed not only to constantly compare outcomes with national and European standards but also to assess BCSP protocols and organisational features.

This work evaluates the temporal trend (2011-2019) of performance indicators (invitation coverage, examination coverage, participation rate, recall rate, cancer detection rate and positive predictive value) of Italian mammography screening programmes. This assessment is in continuity with a previous survey conducted between 2006-2011 [11]. The parameters assessed in this work were recently proposed as candidate breast cancer screening programmes performance indicators by the European Commission Initiative on Breast Cancer (ECIBC) and they well represent the different quality process domains in MS programmes [12].

METHODS

Setting

In Italy ONS and GISMa provide the common protocol for mammographic screening and each Region is responsible for the organisation and delivery of local BCSP activity. Data are annually gathered by ONS through a structured questionnaire filled by local programme referents and regional coordinators. Logical-formal and epidemiological checks are performed either at the regional or at the national level. In this paper screening programmes' data are analysed aggregated by region and geographical macro-area (North, Centre, South-Islands).

Data

This paper analysed data from the ONS archive, collected from over 150 local breast cancer screening programmes in Italy and collected and managed by the Institute for Cancer Research, Prevention and Clinical Network (Istituto per lo Studio, la Prevenzione e la Rete Oncologica, ISPRO, Florence) where ONS is set up. All data and parameters are referred to 50-69 years target population, and were analysed considering Italy as a whole, by the three Italian macro-areas. *Table 1* showed the Italian female 50-69-year-old target population from 2011 to 2019 (Istituto Nazionale di Statistica, ISTAT, Italian National Institute of Statistics data) the number of tests, recalled women, and screen-detected malignant cancers by the three Italian macro-areas for initial and subsequent screening tests. Target population, invitations and number of performed tests refer to all Italian regions. For South-Islands, the number of tests performed, the number of women with referrals to further assessments, and the number of women with screen-detected cancers by initial or subsequent test, were referred from the following regions from this macro-area: Abruzzo and Basilicata (from 2014), Campania, Sicily and Sardinia. Calabria, Puglia and Molise, were indeed excluded because of some incompleteness of data regarding the above-mentioned variables.

The following indicators were calculated:

- adjusted invitation coverage: percentage of women invited to screening during the analysed period, compared to the target population, excluding undelivered invitations and women with specific exclusion criteria. This parameter may exceed 100% if invitations are not evenly distributed over the years [13];
- examination coverage: percentage of women who performed the test compared to the target population, excluding women with specific exclusion criteria;
- adjusted participation in the screening programme (PR): percentage of invited women who performed the test within 6 months from the invitation, excluding undelivered invitations and women with recent mammography (<12 months);
- recall rate (RR): the number of women recalled for further assessments as a proportion of all women with a screening examination (specificity sentinel parameter);
- detection rate (DR): the number of all malignant cancers detected every 1,000 screened women (sensitivity sentinel parameter);
- positive predictive value (PPV): the ratio of lesions that are truly positive to those that test positive (programme performance sentinel parameter).

While invitation and examination coverages were examined for Italy as a whole, by region and by geographical macro-area (North, Centre, South-Islands), PR, RR, PPV and DR were also examined by 5-year age-classes (50-54; 55-59; 60-64; 65-69).

In calculating RR, DR and PPV by geographical area, Molise, Puglia and Calabria were excluded from South-Islands since data were missing or incomplete. Instead, data of Abruzzo and Basilicata were available from 2014 onwards; RR, PPV and DR were also stratified by initial and subsequent screening test.

Key performance indicators were annually estimated to analyse temporal trends; average annual percent changes (AAPCs) with their 95% confidence intervals (95% CI) were estimated using the Jointpoint Regression Programme (version 4.9.0). Moreover, indicators were combined in two graphs: one plotting invitation coverage versus participation rate or versus examination coverage, and another graph plotting RR *versus* PPV, where DR was shown as isobars, as proposed by Blanks *et al.* [14, 15] This visualization provides an overview of the main performance indicators.

Table 1
Italian National Institute of Statistics (ISTAT). Female 50-69 years old population, number of invited women, number of tests performed, number of women with referrals and with screen-detected malignant cancers in Italy and by geographical macro-areas. Period 2011-2019

			2011	2012	2013	2014	2015	2016	2017	2018	2019
	ISTAT target population		7,613,766	7,612,337	7,751,539	8,005,826	8,178,875	8,349,898	8,440,107	8,529,765	8,533,796
Italy*	Invited women		2,699,403	2,687,657	2,748,500	2,848,716	3,231,733	3,223,356	3,428,234	3,448,500	3,663,316
	Number of tests performed	First screening	260,115	286,029	285,632	302,864	360,624	347,663	338,164	329,148	356,252
		Subsequent	1,070,417	1,083,459	1,137,595	1,200,828	1,296,691	1,348,790	1,389,660	1,415,095	1,496,387
	Number of women with referrals to further assessments	First screening	22,533	27,615	28,223	31,365	34,378	38,157	37,485	39,329	43,173
		Subsequent	49,055	50,662	52,485	54,888	59,466	63,146	67,739	68,249	73,043
	Number of women with screen-detected cancers	First screening	1,237	1,427	1,437	1,644	1,756	1,811	1,750	1,610	1,815
		Subsequent	4,807	5,016	5,428	5,548	6,119	6,159	6,454	6,398	6,425
North	ISTAT target population		3,541,698	3,523,159	3,582,882	3,679,755	3,748,491	3,833,693	3,871,752	3,912,976	3,934,358
	Invited women		1,515,973	1,543,180	1,587,856	1,621,696	1,696,973	1,718,736	1,764,608	1,785,840	1,892,023
	Number of tests performed	First screening	160,055	161,957	162,442	150,358	147,160	149,535	156,975	157,949	158,084
		Subsequent	766,099	778,980	842,134	869,915	917,293	933,045	946,949	951,138	986,668
	Number of women with referrals to further assessments	First screening	14,311	14,964	14,889	15,436	14,411	16,154	16,633	15,829	16,526
		Subsequent	31,526	32,492	35,147	36,543	39,549	40,395	41,262	40,824	40,871
	Number of women with screen-detected cancers	First screening	879	838	923	940	944	906	889	872	895
		Subsequent	3,614	3,756	4,186	4,229	4,571	4,431	4,687	4,634	4,560
Centre	ISTAT target population		1,540,473	1,521,833	1,550,641	1,617,491	1,655,049	1,688,374	1,706,242	1,724,950	1,722,063
	Invited women		619,018	669,551	623,671	627,600	699,792	772,842	791,591	811,444	823,299
	Number of tests performed	First screening	80,266	79,760	77,914	79,694	97,083	94,434	99,595	92,750	96,502
		Subsequent	258,306	272,927	252,771	257,506	284,920	300,524	307,387	323,514	329,781
	Number of women with referrals to further assessments	First screening	6,606	9,178	10,111	9,963	10,054	12,799	13,733	15,039	15,276
		Subsequent	15,395	15,632	15,685	15,310	16,672	17,695	18,846	20,650	20,893
	Number of women with screen-detected cancers	First screening	262	404	353	387	374	542	559	457	447
		Subsequent	1,063	1,202	1,176	1,119	1,257	1,313	1,324	1,332	1,385
South-Islands*	ISTAT target population		2,531,595	2,567,345	2,618,016	2,708,580	2,775,335	2,827,831	2,862,113	2,891,839	2,877,375
	Invited women		564,412	474,926	536,973	599,420	834,968	731,778	872,035	851,216	947,994
	Number of tests performed	First screening	19,794	44,312	45,276	72,812	116,380	103,694	81,594	78,449	101,666
		Subsequent	46,012	31,552	42,690	73,407	94478,90837	115,221	135,324	140,443	179,938
	Number of women with referrals to further assessments	First screening	1,616	3,473	3,223	5,966	9,913	9,204	7,119	8,461	11,371
		Subsequent	2,134	2,538	1,653	3,035	3,245	5,056	7,631	6,775	11,279
	Number of women with screen-detected cancers	First screening	96	185	161	317	438	363	302	281	473
		Subsequent	130	58	66	200	291	415	443	432	480

*ISTAT target population and invited women covers all Italian regions; the number of tests performed, the number of women called for further investigation and the number of women with screen-detected cancers detected at screening are for the northern (Piedmont, Val d'Aosta, Liguria, Lombardy, Bolzano, Trentino, Veneto, Friuli-Venezia Giulia, Emilia Romagna) and central regions (Tuscany, Umbria, Marche, Lazio). For the South, data are available for the regions Abruzzo (since 2014), Campania, Basilicata (since 2014), Sicily, Sardinia. For Molise, Apulia and Calabria, data for some years are not available.

RESULTS

Invitation coverage, examination coverage, and participation rate

In Italy, the adjusted invitation coverage followed an increasing trend, from 73.5% in 2011 to 89.1% in 2019, with a significant annual increase of 2.7% (*Table 2*). This trend remained significant in all geographical macro-areas, especially in the South-Islands (AAPC from North: 0.8%; Centre: 2.2%; South-Islands: 6.8%). In the North, Piedmont Region significantly increased its invitation coverage as well as Marche and Lazio in the Centre. However, the most important increases were recorded in the South, especially in Campania and Sicily (*Table 1S* available online as Supplementary Material).

Examination coverage followed an increasing trend, from 40.4% in 2011 to 47.8% in 2019 (+2.0% annually) and this was particularly noticeable in the South-Islands (AAPC from North: 0.7%; Centre: 1.8%; South-Islands: 6.8%). When plotted against adjusted invitation coverage, a slight but evident increasing trend of both indicators was appreciated, with a more relevant increase in the South-Islands (*Figure 1A*). At the regional level, Piedmont, Marche, Lazio, Abruzzo, and Sicily recorded the most important increases (*Table 2S* available online as Supplementary Material).

In Italy, PR showed a slight, though significant, annual decrease of 0.7%: from 59.6% in 2011 to 57.9% in 2019 (*Table 2*). In the North, PR stalled around 68.0%-70.0%, while in the Centre and the South-Islands it was less stable and significantly lower (range in the Centre: 56.2%-60.0%; range in the South-Islands: 37.8%-46.9%), but with no significant trend (*Table 2*). Plotting adjusted PR against adjusted invitation coverage, a substantial stability of PR is observed in the whole period by macro-area, and a growing trend for invitation coverage in the South-Islands and partially in the Centre (*Figure 1B*).

At the regional level, Lombardy region showed a slight significant decrease, while Veneto and Friuli-Venezia Giulia showed significant PR increases. In the Centre Marche, and in the South Abruzzo and Basilicata showed PR increase (*Table 3S* available online as Supplementary Material).

Analyzing PR by age-class, it was higher among women aged over 55 years old across Italy (*Table 4S* available online as Supplementary Material).

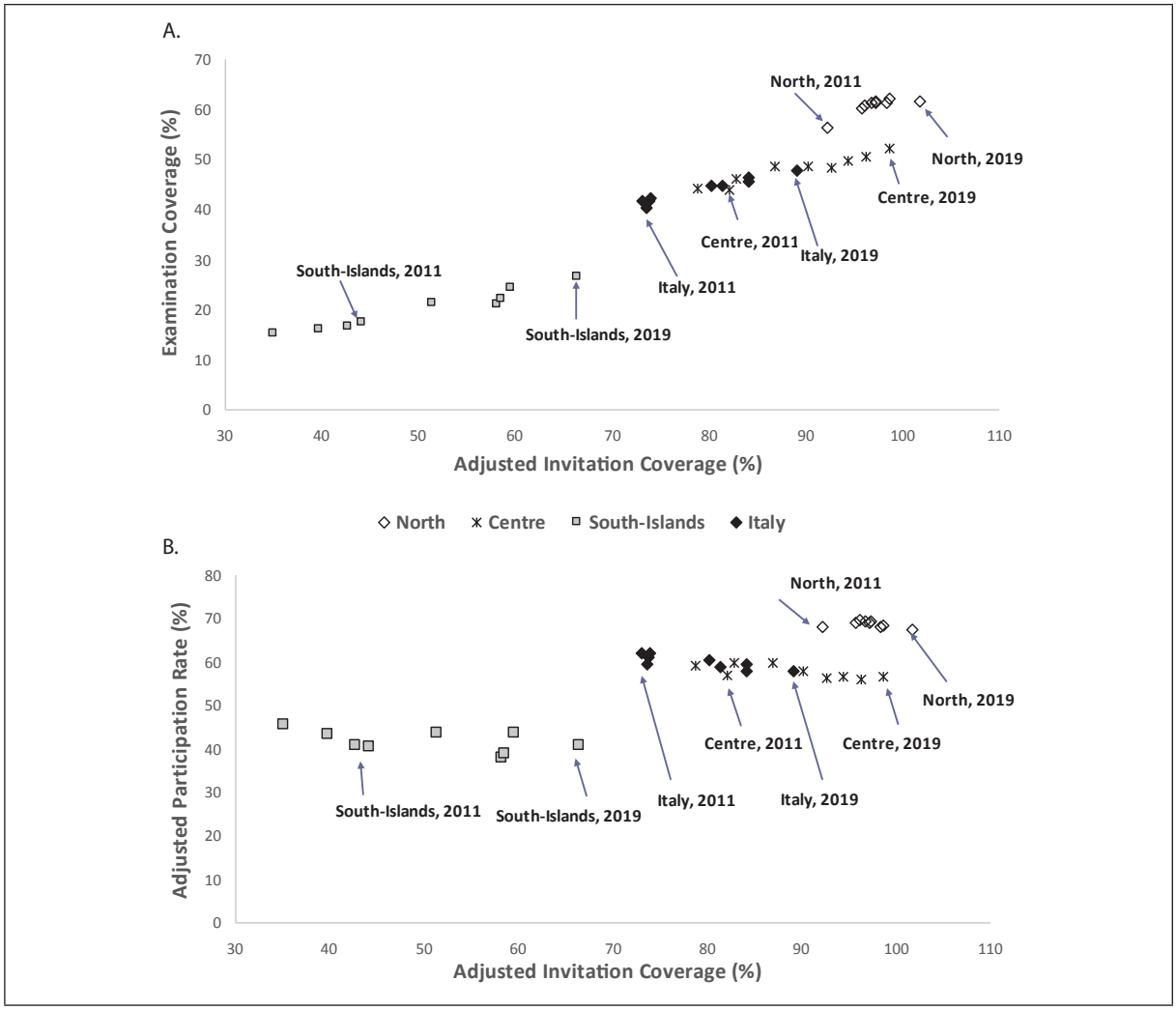

Figure 1
Adjusted invitation coverage *versus* examination coverage (A) and *versus* adjusted participation rate (B) by macro-area.

Main performance indicators: RR, DR, and PPV at the first screening test

Figures of PPV against RR with cancer DR as isobars, showed the relationship between RR, PPV and DR. From 2011 to 2019 for the first screening (*Figure 2A*), RR abscissa values increased, and PPV ordinate values non-proportionally decreased in Italy and in the three macro-areas.

At the same time, DR levels remain stable around the 5‰ DR curve for Italy and the Centre; between the 7‰

Table 2
Adjusted invitation coverage, examination coverage, adjusted participation rate, recall rate, detection rate, positive predictive value with average annual percent change (AAPC) and 95% Confidence Intervals (95% CI) by macro-area (North, Centre and South-Islands, Italy), 2011-2019

	2011	2012	2013	2014	2015	2016	2017	2018	2019	AAPC	95% CI
Adjusted invitation coverage (%)											
North	92.17	95.74	97.22	96.04	97.20	96.67	98.62	98.24	101.69	0.8	0.4; 1.2
Centre	82.08	90.15	82.78	78.74	86.82	92.63	94.32	96.18	98.55	2.2	1.2; 3.2
South-Islands	44.16	35.06	39.74	42.76	58.16	51.35	59.53	58.52	66.35	6.8	3.5; 10.2
Italy	73.52	73.06	73.94	73.77	81.37	80.23	84.07	84.06	89.05	2.7	1.9; 3.4
Examination coverage (%)											
North	56.58	60.20	61.76	60.87	61.53	61.39	62.26	61.49	61.65	0.7	0.0; 1.4
Centre	43.91	48.64	46.22	44.29	48.74	48.51	49.85	50.63	52.16	1.8	0.7; 2.9
South-Islands	17.32	15.17	15.92	16.54	21.14	21.36	24.38	22.04	26.55	6.8	3.8; 9.9
Italy	40.43	41.87	42.38	41.89	44.74	44.94	46.46	45.60	47.80	2.0	1.5; 2.5
Adjusted participation rate (%)											
North	68.22	69.25	69.51	69.75	69.06	69.45	68.50	68.23	67.44	-0.2	-0.5; 0.1
Centre	56.99	57.99	59.83	59.23	60.04	56.31	56.75	56.17	56.85	-0.5	-1.2; 0.3
South-Islands	40.49	45.57	43.20	40.81	37.80	43.55	43.67	38.83	40.85	-0.6	-2.5; 0.1
Italy	59.58	62.25	62.24	61.34	58.99	60.41	59.56	58.03	57.93	-0.7	-1.3; -0.1
Recall rate (%)											
First screening											
North	8.94	9.24	9.17	10.27	9.79	10.80	10.60	10.02	10.45	2.0	0.6; 3.4
Centre	8.23	11.51	12.98	12.50	10.36	13.55	13.79	16.21	15.83	6.2	2.6; 10.1
South-Islands*	8.16	7.84	7.12	8.19	8.52	8.88	8.72	10.79	11.18	5.7	3.3; 8.2
Italy*	8.66	9.65	9.88	10.36	9.53	10.98	11.08	11.95	12.12	3.9	2.5; 5.2
Subsequent screenings											
North	4.12	4.17	4.17	4.20	4.31	4.33	4.36	4.29	4.14	0.4	-0.3; 1.0
Centre	5.96	5.73	6.21	5.95	5.85	5.89	6.13	6.38	6.34	0.9	0.0; 1.9
South-Islands*	4.64	8.04	3.87	4.13	3.43	4.39	5.64	4.82	6.27	2.8	-4.7; 10.9
Italy*	4.58	4.68	4.61	4.57	4.59	4.68	4.87	4.82	4.88	0.8	0.3; 1.4
Detection rate (‰)											
First screening											
North	5.49	5.17	5.68	6.25	6.41	6.06	5.66	5.52	5.66	0.4	-1.8; 2.7
Centre	3.26	5.07	4.53	4.86	3.85	5.74	5.61	4.93	4.63	2.7	-2.4; 8.1
South-Islands**	4.85	4.17	3.56	4.35	3.76	3.50	3.70	3.58	4.65	0.2	-4.0; 4.6
Italy**	4.76	4.99	5.03	5.43	4.87	5.21	5.18	4.89	5.09	0.3	-1.0; 1.6
Subsequent screenings											
North	4.72	4.82	4.97	4.86	4.98	4.75	4.95	4.87	4.62	-0.2	-1.0; 0.7
Centre	4.12	4.40	4.65	4.35	4.41	4.37	4.31	4.12	4.20	-0.5	-1.7; 0.6
South-Islands**	2.83	1.84	1.55	2.72	3.08	3.60	3.27	3.08	2.67	1.8	-4.7; 8.8
Italy**	4.49	4.63	4.77	4.62	4.72	4.57	4.64	4.52	4.29	-0.6	-1.5; 0.3

Continues

Table 2
Continued

	2011	2012	2013	2014	2015	2016	2017	2018	2019	AAPC	95% CI
Positive predictive value (%)											
First screening											
North	6.14	5.60	6.20	6.09	6.55	5.61	5.34	5.51	5.42	-1.6	-3.4; 0.3
Centre	3.97	4.40	3.49	3.88	3.72	4.23	4.07	3.04	2.93	-3.3	-7.1; 0.7
South-Islands**	5.94	5.33	5.00	5.31	4.42	3.94	4.24	3.32	4.16	-5.0	-8.2; -1.6
Italy**	5.49	5.17	5.09	5.24	5.11	4.75	4.67	4.09	4.20	-3.4	-4.7; -2.1
Subsequent screenings											
North	11.46	11.56	11.91	11.57	11.56	10.97	11.36	11.35	11.16	-0.5	-1.2; 0.1
Centre	6.90	7.69	7.50	7.31	7.54	7.42	7.03	6.45	6.63	-1.4	-3.0; 0.1
South-Islands**	6.09	2.29	3.99	6.59	8.97	8.21	5.81	6.38	4.26	-2.8	-13.5; 9.2
Italy**	9.80	9.90	10.34	10.11	10.29	9.75	9.53	9.37	8.80	-1.4	-2.6; -0.3

*Recall Rates for South-Islands include data from Abruzzo (from 2014), Campania, Basilicata (from 2014), Sicilia, Sardegna. Data for Molise, Puglia, and Calabria regions are not available for every year. Recall rates for Italy include North, and Centre macro-areas plus the above-mentioned Southern regions.
**Detection rates and positive predictive values for South-Islands include data from Abruzzo (from 2014), Campania, Basilicata (from 2014), Sicilia, Sardegna. Data for Molise, Puglia, and Calabria regions are not available for every year. Detection rates, and positive predictive values for Italy include North, and Centre macro-areas plus the above- mentioned Southern regions.

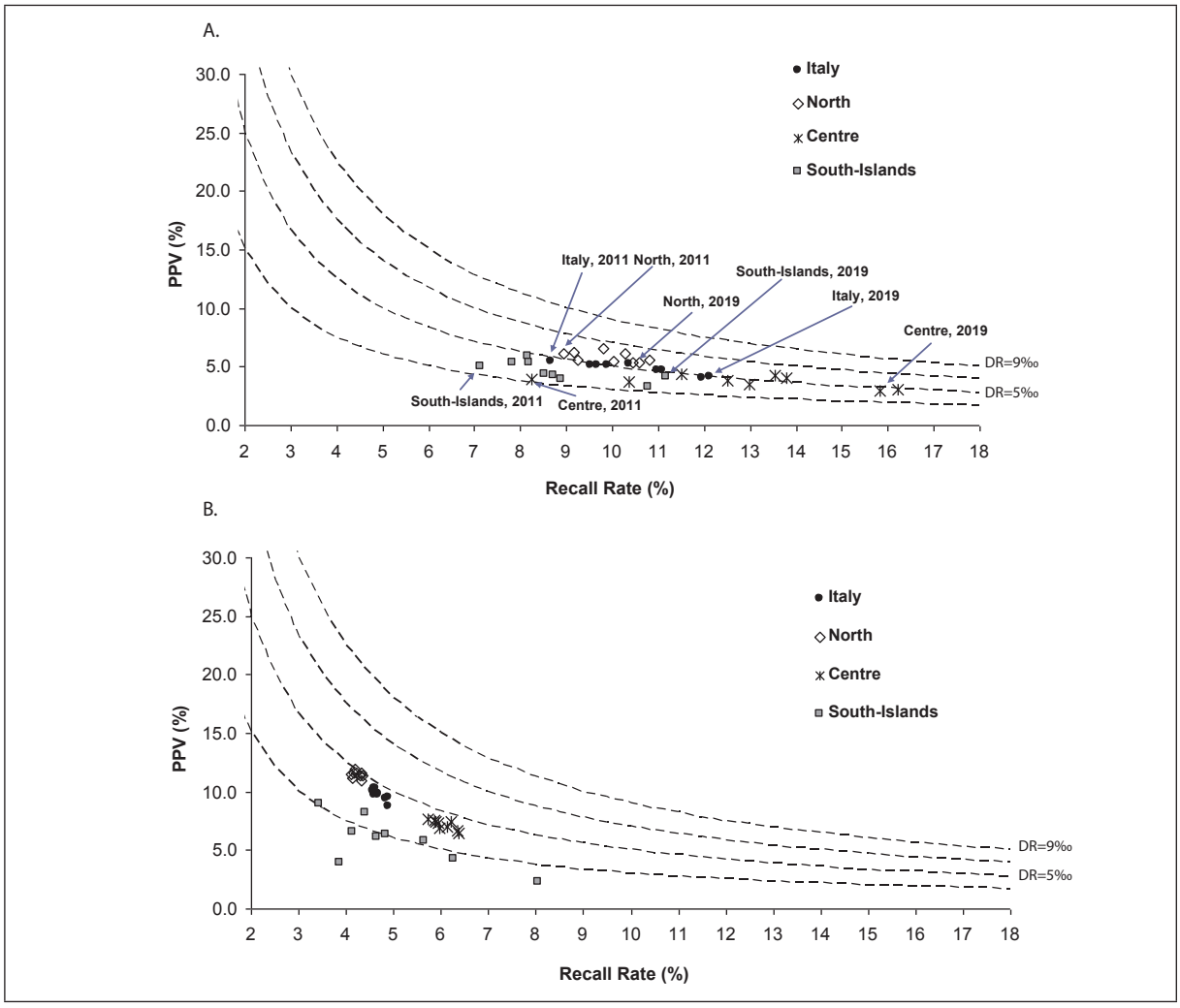

Figure 2
Recall rate (RR) *versus* positive predictive value (PPV) by macro-area; detection rate (DR) shown as isobars. First round (A), subsequent rounds (B).

and 5‰ DR curves for the North, and between the 5‰ and 3‰ DR curves for the South-Islands area. Indeed, RR at first screening showed an increasing trend of 3.9% per year in Italy (from 8.7% in 2011 to 12.1% in 2019); of 2.0% in the North; of 6.2% in the Centre; of 3.9% per year in the South-Islands (with no data from Basilicata, Molise, and Puglia) (*Table 2, Figure 2A*). The RR at the first screening increased substantially in Piedmont and Emilia-Romagna from the North (*Table 5S, Figure 1S* available online as Supplementary Material); for the Centre in Umbria, Marche, and Lazio (*Table 5S; Figure 2S* available online as Supplementary Material); for the South in Campania (*Table 5S; Figure 3S* available online as Supplementary Material). The RR values recorded in Marche since 2015 reached levels over 20%, with a significant increase also in DR (*Table 6S* available online as Supplementary Material). The RR increase was less marked, but still significant in Lombardy and Tuscany. In Autonomous Provinces (PA) of Bolzano and Trento an opposite trend was recorded: the first screening RR decreased significantly by 7.0% and 10.4%, respectively, especially from 2015 onwards.

In all age groups (*Table 4S*), the RR at first screening in Italy increased by 4%-6% per year. The 50-54 age class was the one with a constantly higher RR. In 2016-2018 RR increased considerably in all age groups and in particular for the 65-69 age-class (*Table 4S*).

Positive Predictive Value at the first test decreased by 3.4% per year in Italy as a whole (from 5.5% in 2011 to 4.2% in 2019), and especially in the South-Islands area (reduction of 5.0% per year; *Table 2*). At the regional level (*Table 7S* available online as Supplementary Material), PPV at first screening decreased in most Regions. On the opposite, Veneto showed an improvement in PPV at the first test. In age-stratified data for Italy as a whole (*Table 4S*), PPV increased with age. In women undergoing their first screening at 50-54 years of age, PPV decreased by 3.6% per year. PPV at first screening non-significantly decreased also in the other age groups.

Main performance indicators: RR, DR, and PPV at subsequent screening tests

For subsequent screening tests (*Figure 2B*), less variability in RR and PPV values was observed for all Italy, North and Centre; DR was around the 5‰ DR curve for the North, between the 3‰ and the 5‰ DR curves for Italy as a whole and the Centre, and around the 3‰ DR curve for the South. Even though RR at subsequent tests showed less variability than was observed at the first screening, there was a slight increase of 0.8% per year across Italy, particularly in central regions (0.9% per year; *Table 2*). Within the North area (*Table 8S; Figures 4S, 5S, 6S* available online as Supplementary Material), RR increased in Piedmont and Veneto, while in Autonomous Province of Trento and Liguria RR significantly decreased. In the Centre, RR decreased significantly in Marche, while in Lazio there was an opposite trend. There was also an important but non-significant increase in RR in Umbria, with a relevant and significant reduction in PPV and DR (*Tables 8S, 9S, 10S* available online as Supplementary Material). In the South-Islands, there were fewer variations, but a particularly high RR was observed in Campania in the last year (15.0%; *Table 8S, Figure 6S*).

By age-class, RRs ranged between 5.2%-5.7% across Italy for the 50-54 age group, while it ranged between 4.1%-4.8% in the older age groups (*Table 4S*).

The PPV was about twice as high for subsequent screening as for the first test. For Italy as a whole, there was a slight, but significant annual reduction of 1.4% in PPV for subsequent screenings (*Table 2*). It was higher in the North (above 11.0%); in the South it ranged from 6.1% in 2011 to 4.3% in 2019 and in the Centre from 6.9% in 2011 to 6.6% in 2019. Analyzing data by region (*Table 10S*), Piedmont, Emilia-Romagna and Umbria showed significant annual reductions. In the age group of women over 54, there was a significant annual reduction in PPV of 1%-2% (*Table 4S*).

The DR at first test was higher than that at subsequent screening tests. However, both DR remained substantially stable: DR at first screening ranged between 4.8‰-5.4‰, while DR at subsequent screenings ranged between 4.3‰-4.8‰ (*Table 2*). The lowest DR was observed in the South-Islands (range at first screening 3.5‰-4.7‰; at subsequent screening 1.6‰-3.6‰), while the highest DRs were observed in the North where values always exceeded the Italian average value (range at first screening 5.2‰-6.4‰; at subsequent screening: 4.6‰-5.0‰).

By age-class, the highest DR was observed in the 65-69 age group (first screening, range 7.1‰-11.0‰; subsequent screening, range: 5.8‰-6.5‰), while the lowest DR was recorded in the 50-54 age group (first screening, range: 4.0‰-4.5‰; subsequent screening, 3.0‰-3.1‰; *Table 4S*).

DISCUSSION

Between 2011 and 2019 in Italy, trends in indicators of organized mammography screening showed an increase in the invitation coverage and examination coverage, with a substantial stabilisation of the participation rate, in particular in those areas such as Lazio region and South-Islands macro-area, where screening programmes were not adequately implemented until 2011.

There is still a gap in screening coverage between North-Central Italy and South-Islands; almost all eligible women are reached in the North and the Centre, while slightly more than half of the target population is reached in the South. Nonetheless, the coverage appears to be improving over the years, especially in the South, in Lazio, but also in some areas of the North, as Piedmont and Liguria.

Participation rate is essential in order to record an impact on cancer-specific mortality. European standards for PR consider 70% and 75% an acceptable and desirable level of participation, respectively [7]. In Italy in 2011-2019 PR was constantly below the acceptable level. In the North macro-area PR was close to the acceptable standard in the whole period, while in the South-Islands it was below (40.9% in 2019), confirming a significant North-South gradient.

In particular, in Lazio, Molise, Campania, Sicily, Calabria and Sardinia participation was still below 50% in

2019, while in Val d'Aosta, Autonomous Province of Trento, Veneto, Friuli-Venezia Giulia, Emilia-Romagna, Tuscany, Umbria and Basilicata it was over 70% in 2019. The interpretation of these figures has to be cautious: there may be areas covered by opportunistic screening; participation may vary according to the socio-economic characteristics of the population and to citizens' trust in public health services [16, 17]. The PASSI (Progressi delle Aziende Sanitarie per la Salute in Italia) survey, one of the two National Health Interviews (NHIS) active in Italy, shows that opportunistic screening in the period 2017-2020 accounts on average for one fourth of the screening test coverage in the target population that reaches 75% for breast cancer screening, with differences between macro areas. Indeed, in 2019 it accounted for 14% in North (excluding Lombardy region), 20% for Centre and 23% for South [18, 19].

Comparison between PR recorded in 2011-2019 with those recorded in the previous survey conducted in 2006-2011 confirms the geographical gradient, even if a progressive improvement in invitation and examination coverages emerged in all regions. It is worth noting that a gradual increase in the programmes' coverage may initially lead to a relative decrease in the PR, especially at the first screening test, when invited women have never been invited before and therefore are still not committed to the programme. The higher PR may depict an organizational improvement along with a progressive increase of citizens knowledge and engagement to organized screening [11].

Considering other analyzed parameters, a significant increase of RR and a slight reduction of PPV were recorded, especially at the first screening in some regions of the North (Piedmont, Emilia-Romagna), of the Centre (Marche, Umbria, Lazio), and in Campania for the South.

The effectiveness of mammography screening is closely related to the reading performance of radiologists, the quality of images and the overall organizational quality of the BCSP [20]. If the aim of screening programmes is the early detection of malignant lesions (high sensitivity), this should ideally be accompanied by an acceptable RR and a low frequency of biopsies (high specificity), also to limit anxiety and stress in the involved women [21]. Thus, good RR, DR and PPV values indicate good quality of the programme and a positive impact on breast cancer mortality. Analyzing the RR (a screening specificity indicator), at the first screening, the acceptability threshold (<7%) is always exceeded, both at the national level and by macro-area. Moreover, RR constantly increased, highlighting performance worsening with risks of organizational unsustainability of the programmes [22]. The RR values were particularly high in Marche region (≥20% since 2015) in the Centre, and in Friuli-Venezia Giulia region, in the North, RR exceeded 15% in recent years.

The increase in RR could be explained by several reasons. First, lack of previous mammographic images could explain high RR, especially at first screening test, when women are also younger and with a more dense breast than older women. Second, the transition to digital mammography that occurred in recent years could have enhanced RR, as described in other experiences as well [23]. Third, the involvement in the BCSP of radiologists not mainly dedicated to screening, at least in some regions; fourth, the inadequate training of new health professionals involved in BCSPs. In fact, screening radiologists need dedicated training and should guarantee a minimum annual volume of readings (between 3,500 and 11,000 mammograms/year, as indicated by the European Commission Initiative on Breast Cancer, ECIBC) to reach and maintain high reading performances [8].

Results are better for RR at subsequent screening, as it was consistently below the threshold of acceptability (<5%) and had a constant trend over time. However, stratifying by macro-area, only in the North the RR was actually below this threshold. In particular, all the regions of the Centre and Campania region in the South-Islands area showed values above the acceptability threshold, especially after 2015. The DR of malignant tumours at first screening is higher than in subsequent screening and in older age groups, due to the higher prevalence of disease in this population. Analyzing PPV, as expected, at first screening the values were not only lower than at the subsequent ones, but also less stable. Indeed, a decreasing trend was observed since 2015, especially for women in the 50-54 and 55-59 age groups. While the PPV reached the highest values in the North area, it reached the lowest values in the South-Islands. Comparing the VPP trend in 2011-2019 with that recorded in 2006-2011, a decreasing trend is confirmed overall in both the first and subsequent examinations [11].

In Bolzano and Trento, a general improvement in performance was observed over the period, with good coverage and participation rates and improvements in RR and PPV. In the Province of Trento, this was especially noticeable since 2015; in 2014, Digital Breast Tomosynthesis (DBT) was introduced as the first level screening test, and this may have contributed to the improvement of the PPV [24]. In the Province of Bolzano, tomosynthesis is not used, but the good overall performance can be attributed also to the presence of highly qualified personnel who have been involved in BCSP for years as well as in DBT screening.

Tuscany, Lombardy, Veneto and Liguria showed good performance levels, with high coverage and stability of PPV overtime at first and subsequent screening tests, with slight increases in RR, except Liguria where there was a significant reduction in RR at subsequent screening.

In contrast, in other regions such as Umbria, performance appears to be declining, with an increase in RR and a decrease in PPV and DR.

In the South-Islands macro-area, the snapshot resulting from the present analysis is partial since data from some regions were missing. The fact that some screening programmes do not adequately collect data to estimate performance indicators is an issue that affects programmes monitoring. Regional commitment should be strengthened to address this issue, in accordance with Italian National Prevention Plan 2020-2025 that foresees an improvement of regional screening networks [25]. The complete and timely provision of data

is crucial to monitor the delivery of the LEAs and to ensure a high level of quality in healthcare. In several regions (i.e., Campania, Tuscany, Lombardy, Puglia) regional implementation projects of a unique screening software are being carried on. Those systems may be useful to improve the collection and transmission of data by screening managers in a more efficient and timely manner.

In this analysis, RR and PPV trends suggest an "erosion" of screening programmes performance in many Italian regions. This issue may arise from several causes. In recent years, resources for screening programmes have not been adequately allocated, and, at the same time, quality requirements are increasingly defined and stringent. Moreover, the lack of adequate recruitment, replacement and training policy for screening health professionals may create conditions that weaken the performance of BCSPs. The adequate training of staff dedicated to screening would become a priority to improve programme performances, patient safety and tackling defensive medicine, as well as ensuring equity. This issue has also recently been exacerbated by the deployment of screening staff to manage the pandemic emergency [26, 27].

Indeed, this paper analysed data up to 2019. As highly debated, the pandemic crisis had an impact on screening invitation coverages and tests' execution and also on invited people's propensity to participate to organized screening programmes in Italy (for mammography screening some estimates show 15% lower) [26, 27]. A careful analysis of pandemic and post-pandemic screening performances would become crucial in order to monitor recovery strategies and their effectiveness.

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Author's contribution

GG: conception and design, acquisition of the data, data analyses, critical revision of the article for important intellectual content, final approval of the article; PF: acquisition of the data, final approval of the article; LV: acquisition of the data, data analyses; FB: drafting of the article, critical revision of the article for important intellectual content, final approval of the article; PM, LG, SD, MZ, GS: critical revision of the article for important intellectual content, final approval of the article.

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All Authors declare that they have no conflict of interest.

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