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Šupe Parun, Andrea; Čukelj, Petra; Tešić, Vanja; Jelavić, Melita; Brkljačić, Boris

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Results of the National Breast Cancer Screening Program in Croatia (2006-2016)

Aim To assess the uptake of the Croatian National Breast Cancer Screening Program from 2006 to 2016.

Methods The Croatian National Breast Cancer Screening Program, a biennial program targeting women aged 50-69, started in October 2006. From 2006 to 2016, four cycles were completed. One cycle lasted two years, with the exception of the first cycle, which lasted three years. To determine the number of detected cancers in each cycle, the screening program data were merged with the data of the Croatian National Cancer Registry. Our results were compared with the reference values from the European guidelines for quality assurance in breast cancer screening and diagnosis.

Results Around 150 000 mammography exams were performed every year. The response rates for cycle 1, cycle 2, cycle 3, and cycle 4 were 63%, 57%, 60%, and 59%, respectively. Further assessment rate was 6.5%. Breast cancer was identified in 5583 women, with 4.8 cancers detected per 1000 mammography exams.

Conclusion The National Breast Cancer Screening Program in Croatia reached a substantial proportion of the target group. Yet, additional efforts are needed to reach at least 70% of the target population.

Andrea Šupe Parun¹, Petra Čukelj¹, Vanja Tešić^{2,3}, Melita Jelavić², Boris Brkljačić⁴

¹Croatian Institute for Public Health, Zagreb, Croatia

²Department of Epidemiology, Dr. Andrija Štampar Institute of Public Health, Zagreb, Croatia

³University of Rijeka School of Medicine, Rijeka, Croatia

⁴Department of Diagnostic and Interventional Radiology, Breast Unit, University Hospital Dubrava, University of Zagreb School of Medicine, Zagreb, Croatia

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Correspondence to:

Andrea Šupe Parun
Department for Epidemiology and
Prevention of Noncommunicable
Chronic Diseases
Croatian Institute of Public Health
Rockefeller str. 7
10 000 Zagreb, Croatia
andrea.supe.parun@hzjz.hr

Breast cancer (BC) is the most common cancer in women, with 2.26 million patients diagnosed yearly (1). Due to a high incidence and relatively good survival rate, its prevalence is also high. Estimated 7.8 million women (diagnosed in the last 5 years) lived with breast cancer in 2020. BC is a good candidate for screening due to the benefits of early treatment and high cancer prevalence (2).

In Croatia, breast cancer is the leading cancer in women, and the average annual number of diagnosed cases in the 2014-2018 period was 2810. According to the latest data from the Croatian National Cancer Registry, there were 2845 new breast cancer cases (crude incidence rate of 134.7/100,000) in 2018, accounting for 24% of all new cancer cases in women (3). In 2020, 722 women died due to breast cancer (crude mortality rate of 34.7/100,000) (4). According to the Euro-



FIGURE 1. Workflow of the Croatian National Breast Screening Program. BI-RADS – Breast Imaging Reporting and Data System; US –ultrasound.

pean Cancer Information System (ECIS) estimates for female breast cancer in 2020, Croatia is the 19th European (EU-27) country when it comes to breast cancer incidence, and the 16th when it comes to mortality (5).

Chemotherapy, surgery, lymph node analysis, and hormone receptor blocking therapy have improved the survival rate of breast cancer patients (6). Despite these improvements, early breast cancer detection remains vital. Programs for early breast cancer detection using mammography, combined with effective treatment, do not only reduce BC mortality but also positively affect the patients' quality of life (2). The Croatian National BC Screening Program, a biennial program targeting women aged 50-69, started in October 2006.

The European guidelines for quality assurance of mammography-based screening, developed within the Europe Against Cancer program (7), provide necessary framework for reducing the adverse effects of screening, such as diagnostic procedures or treatment resulting from false-positive mammography findings. The Croatian version of the Guidelines was published in 2017, with the goal of setting a framework for further implementation and improvement of the National BC Screening Program in Croatia (8).

Results of the Croatian National Breast Cancer Screening Program are not regularly published. Information on the uptake and number of detected cancers is disseminated to interested stakeholders, but this is the first comprehensive overview of available program indicators. The aim is to present the program results for the 2006-2016 period using available data on performance indicators for breast cancer screening programs.

MATERIALS AND METHODS

The Croatian National Breast Cancer Screening Program is organized through public health institutes of 21 Croatian

counties and coordinated by the Committee for Organization, Expert Monitoring and Quality Control of the National Breast Cancer Screening Program. The coordinators in each local institute send invitations for a mammography examination, which is conducted by units authorized by the Ministry of Health. Mammography results are categorized from 0-5 according to standardized Breast Imaging Reporting and Data System (BI-RADS) classification (9). Double-reading of the results is conducted by two radiologists. The final result has to be unambiguous, with clear instructions for further steps. It is entered into an application within two weeks, printed out and sent to the participants' home address together with x-ray images and instructions for further steps. The workflow of the program is shown in Figure 1.

All radiology screening units are obliged to perform secondary assessment of their patients (ultrasound) at their institutions, while all hospitals of category I and II need to perform the necessary core biopsy, or minimally, puncture cytology of the detected lesions.

When each screening cycle is completed, county coordinators compile a written report on the program results on the county level, while the National Program Coordinator compiles a written report on the program results on the national level. Reports are sent quarterly to all members of the Committee. The important indicators available from these reports include the number of patients invited to mammography, number of performed mammographies, cancer distribution according to BI-RADS classification, number of patients in whom BC was diagnosed, stage of cancer spread, and reasons for non-response. The uptake includes the women who received the invitation but replied that they had previously undergone mammography outside of the screening program within a period of one year, or had BC symptoms and had been included in regular mammography follow-up outside of the screening program.

TABLE 1. Indicators for the assessment of a breast screening program (9)

| Performance indicator | Acceptable level | Desirable level |
|--|------------------|-----------------|
| Participation rate (%) | >70 | >75 |
| Technical repeat rate (%) | <3 | <1 |
| Recall rate (%) | | |
| initial screening | <7 | <5 |
| subsequent-regular screening | <5 | <3 |
| Additional imaging rate at the time of screening (%) | <5 | <1 |
| Benign to malignant biopsy ratio | ≤1:2 | ≤1:4 |
| Eligible women reinvited within the specified screening interval (%) | >95 | 100 |
| Eligible women reinvited within the specified screening interval +6 months (%) | >98 | 100 |

The European guidelines (7) list a number of epidemiologically relevant performance indicators for breast cancer screening, as well as recommended indicators to assess the performance of a breast cancer screening program (10) (Table 1). The only indicator that we were able to determine was the participation rate, and we also calculated further assessment rate as a possible epidemiologically relevant indicator.

The analysis was performed with descriptive epidemiology methods. The results were compared with the reference values from the European guidelines for quality assurance in breast cancer screening and diagnosis (7). To determine the number of cancers detected in each cycle, the screening program data were merged with the data of the Croatian National Cancer Registry, a registry collecting data on all cancer cases in Croatia.

RESULTS

From 2006 to 2016, four screening cycles were completed. The program targeted women aged 50-69. One reference

cycle lasted two years, with the exception of the first cycle, which lasted three years.

The first cycle lasted from November 2006 until December 2009. Overall, 665 749 women were invited, and 331 609 mammography exams were conducted. The uptake was 63%. The recommended uptake of 70% was reached in six counties (Bjelovar-Bilogora, Istria, Krapina-Zagorje, Međimurje, Požega-Slavonia, Zadar). A total of 2081 cancers were detected (Table 2).

The second cycle lasted from January 2010 until December 2011. Overall, 642 372 women were invited, and 295 605 mammography exams were conducted. The uptake was 57%. The recommended uptake of 70% was reached in four counties (Bjelovar-Bilogora, Međimurje, Požega-Slavonia, Zadar). A total of 1349 cancers were detected (Table 3).

The third cycle lasted from January 2012 until May 2014. Overall, 659 975 women were invited, with 262 910 mammography exams conducted. The uptake was 60%. The recommended uptake of 70% was reached in three coun-

TABLE 2. Uptake and screening performance data by county in cycle 1 (2006-2009)

| County | Mammographies (n) | Uptake (%) | BI-RADS* 0, 4, 5 (n) | BI-RADS 0,4,5 relative to number of mammographies (%) | Cancers detected (n) | Cancers relative to BI-RADS 0, 4, 5 (%) | C/1000 M† |
|-----------------------|-------------------|------------|----------------------|---|----------------------|---|-----------|
| Bjelovar-Bilogora | 12 058 | 88 | 1027 | 9.2 | 72 | 7.0 | 6.0 |
| Brod-Posavina | 12 420 | 57 | 2528 | 22.2 | 77 | 3.0 | 6.2 |
| Dubrovnik-Neretva | 8870 | 62 | 934 | 11.4 | 74 | 7.9 | 8.3 |
| Istria | 16 243 | 76 | 732 | 4.9 | 99 | 13.5 | 6.1 |
| Karlovac | 9662 | 58 | 507 | 5.7 | 62 | 12.2 | 6.4 |
| Koprivnica-Križevci | 10 638 | 69 | 2426 | 24.5 | 71 | 2.9 | 6.7 |
| Krapina-Zagorje | 11 589 | 71 | 3694 | 34.2 | 49 | 1.3 | 4.2 |
| Lika-Senj | 3452 | 53 | 227 | 7.2 | 25 | 11.0 | 7.2 |
| Međimurje | 11 431 | 86 | 737 | 6.9 | 80 | 10.9 | 7.0 |
| Osijek-Baranja | 25 769 | 65 | 2118 | 8.9 | 189 | 8.9 | 7.3 |
| Požega-Slavonia | 7296 | 82 | 290 | 4.3 | 40 | 13.8 | 5.5 |
| Primorje-Gorski Kotar | 22 999 | 55 | 1405 | 6.5 | 212 | 15.1 | 9.2 |
| Sisak-Moslavina | 13 711 | 61 | 863 | 6.8 | 56 | 6.5 | 4.1 |
| Split-Dalmatia | 28 477 | 50 | 2117 | 8.0 | 126 | 6.0 | 4.4 |
| Šibenik-Knin | 9736 | 62 | 710 | 8.0 | 45 | 6.3 | 4.6 |
| Varaždin | 13 427 | 57 | 770 | 6.1 | 96 | 12.5 | 7.1 |
| Virovitica-Podravina | 6940 | 66 | 476 | 7.3 | 39 | 8.2 | 5.6 |
| Vukovar-Srijem | 15 123 | 65 | 710 | 5.0 | 123 | 17.3 | 8.1 |
| Zadar | 15 301 | 82 | 1326 | 9.4 | 99 | 7.5 | 6.5 |
| Zagreb County | 18 223 | 51 | 1242 | 7.2 | 96 | 7.7 | 5.3 |
| City of Zagreb | 58 244 | 65 | 5267 | 9.8 | 348 | 6.6 | 6.0 |
| Croatia | 331 609 | 63 | 30 106 | 9.8 | 2081 | 6.9 | 6.3 |

*BI-RADS – Breast Imaging Reporting and Data System.

†Number of detected cancers per 1000 mammographies.

ties (Bjelovar-Bilogora, Međimurje, Požega-Slavonia). A total of 1269 cancers were detected (Table 4).

The fourth cycle lasted from June 2014 until November 2016. Overall, 622353 women were invited, with 249740 mammography exams conducted. The uptake was 59%. The recommended uptake of 70% was reached in three counties (Bjelovar-Bilogora, Međimurje, Požega-Slavonia). A total of 884 BC were detected (Table 5).

In cycles 1-3, the proportion of localized-stage cancers at presentation increased, while the proportion of cancers with regional spread decreased. In the fourth cycle, we detected fewer BCs, possibly because not all cases from the period were reported to the Cancer Registry. An expected retroactive entry of the data will most likely result in more detected BCs. The percentage of unknown stage at diagnosis varied from 19.5% in cycle 1 to 13.9% in cycle 4 (Figure 2).

DISCUSSION

Our results show that, 10 years since its implementation, the National Breast Cancer Screening Program in Croatia

is sustainable and strong. During the first four cycles, 5583 new breast cancers were detected, 4.8 per 1000 mammographies, which is in line with the expectations. The uptake was around 60% depending on the cycle, which warrants additional efforts should to increase the response.

For such a program to be successful, it is necessary to have adequate technical and human resources, political and public support, and to regularly evaluate program results and make necessary changes (11).

In European countries that have implemented screening programs for 20 years or more, breast cancer mortality rates are decreasing (12). The European Society of Breast Imaging and the majority of national European breast radiology bodies recommend mammography as the method of choice for a breast cancer screening program. The involvement of radiologists to carry out double reading is also recommended (13).

Age-standardized rates of breast cancer incidence in women in Croatia are increasing, similar to other European countries. Age-standardized mortality rates were stable

TABLE 3. Uptake and screening performance data by county in cycle 2 (2010-2011)

| County | Mammographies (n) | Uptake (%) | BI-RADS* 0, 4, 5 (n) | BI-RADS 0, 4, 5 relative to number of mammographies (%) | Cancers detected (n) | Cancers relative to BI-RADS 0, 4, 5 (%) | C/1000 M† |
|-----------------------|-------------------|------------|----------------------|---|----------------------|---|-----------|
| Bjelovar-Bilogora | 10705 | 81 | 62 | 0.6 | 32 | 51.6 | 3.0 |
| Brod-Posavina | 11228 | 51 | 1686 | 15.6 | 56 | 3.3 | 5.0 |
| Dubrovnik-Neretva | 7147 | 52 | 299 | 4.3 | 34 | 11.4 | 4.8 |
| Istria | 17058 | 65 | 606 | 3.7 | 87 | 14.4 | 5.1 |
| Karlovac | 8962 | 51 | 310 | 3.6 | 31 | 10.0 | 3.5 |
| Koprivnica-Križevci | 9279 | 61 | 612 | 6.8 | 48 | 7.8 | 5.2 |
| Krapina-Zagorje | 10538 | 63 | 2550 | 24.8 | 28 | 1.1 | 2.7 |
| Lika-Senj | 3351 | 55 | 99 | 3.1 | 10 | 10.1 | 3.0 |
| Međimurje | 11285 | 82 | 449 | 4.1 | 54 | 12.0 | 4.8 |
| Osijek-Baranja | 21143 | 52 | 1411 | 6.9 | 116 | 8.2 | 5.5 |
| Požega-Slavonia | 6167 | 71 | 84 | 1.4 | 25 | 29.8 | 4.1 |
| Primorje-Gorski Kotar | 21758 | 51 | 1184 | 5.6 | 127 | 10.7 | 5.8 |
| Sisak-Moslavina | 11504 | 49 | 268 | 2.4 | 33 | 12.3 | 2.9 |
| Split-Dalmatia | 23010 | 35 | 1078 | 4.8 | 108 | 10.0 | 4.7 |
| Šibenik-Knin | 8006 | 54 | 122 | 1.6 | 24 | 19.7 | 3.0 |
| Varaždin | 13082 | 56 | 641 | 5.1 | 53 | 8.3 | 4.1 |
| Virovitica-Podravina | 6191 | 57 | 274 | 4.6 | 23 | 8.4 | 3.7 |
| Vukovar-Srijem | 12705 | 63 | 231 | 1.9 | 76 | 32.9 | 6.0 |
| Zadar | 13159 | 67 | 1513 | 12.0 | 70 | 4.6 | 5.3 |
| Zagreb County | 18720 | 46 | 495 | 2.7 | 70 | 14.1 | 3.7 |
| City of Zagreb | 50607 | 56 | 2321 | 4.8 | 240 | 10.3 | 4.7 |
| Croatia | 295605 | 55 | 16295 | 5.7 | 1349 | 8.3 | 4.6 |

*BI-RADS – Breast Imaging Reporting and Data System.

†Number of detected cancers per 1000 mammographies.

until 2015, with a decrease in the last four years, roughly coinciding with the 10-year anniversary of the implementation of breast cancer screening (4).

The average uptakes of the screening program in cycle 1, cycle 2, cycle 3, and cycle 4 were 63%, 59%, 60%, and 55%, respectively. This is somewhat lower than the 70% uptake recommended by the European guidelines for quality assurance in breast cancer screening and diagnosis (7). The average European participation rate (European total) was 60.2% (14).

The uptake varied substantially between the counties (for example, 37% in Sisak-Moslavina County and 86% in Vukovar-Srijem County during the fourth cycle). Possible reasons include differences in county size and population density, involvement of the local government in the program, and the scope of promotional activities conducted in each county. The availability of mammography units and radiology specialists also differs depending on the county, and can influence the invitation coverage and response rates. Uptake can also be influenced by the degree of involvement

of primary care physicians and patronage nurses. A positive example of this is Međimurje County, with good organization, regular promotional activities, and excellent cooperation of all stakeholders in the program, all of which lead to one of the highest uptakes in Croatia in all four cycles.

The City of Zagreb had an average uptake in all four cycles. We believe that in the City of Zagreb a considerable number of women undergo mammography exams in private clinics, and as a part of regular physical exams organized by their employer. Unfortunately, we do not receive data from these medical institutions.

In the first three cycles, the expected number of detected cancers per 1000 mammography exams was reached, with 5-6 detected cancers per 1000 exams. This number was not reached in the fourth cycle, probably due to data quality, or because not all cancers were recorded in the Croatian National Cancer Registry, especially for later years.

Overall, 5583 breast cancers were detected, translating to 4.8 detected breast cancer cases (both invasive and in

TABLE 4. Uptake and screening performance data by county in cycle 3 (2012-2014)

| County | Mammographies (n) | Uptake (%) | BI-RADS* 0, 4, 5 (n) | BI-RADS 0, 4, 5 relative to number of mammographies (%) | Cancers detected (n) | Cancers relative to BI-RADS 0, 4, 5 (%) | C/1000 M [†] |
|-----------------------|-------------------|------------|----------------------|---|----------------------|---|-----------------------|
| Bjelovar-Bilogora | 8632 | 84 | 19 | 0.2 | 26 | 136.8 | 3.0 |
| Brod-Posavina | 10 155 | 58 | 1046 | 10.3 | 40 | 3.8 | 3.9 |
| Dubrovnik-Neretva | 5598 | 63 | 171 | 3.1 | 38 | 22.2 | 6.8 |
| Istria | 13 494 | 59 | 397 | 2.9 | 63 | 15.9 | 4.7 |
| Karlovac | 8320 | 56 | 146 | 1.8 | 38 | 26.0 | 4.6 |
| Koprivnica-Križevci | 8557 | 61 | 382 | 4.5 | 46 | 12.0 | 5.4 |
| Krapina-Zagorje | 9855 | 64 | 2038 | 20.7 | 37 | 1.8 | 3.8 |
| Lika-Senj | 2705 | 50 | 110 | 4.1 | 8 | 7.3 | 3.0 |
| Međimurje | 10 560 | 78 | 436 | 4.1 | 53 | 12.2 | 5.0 |
| Osijek-Baranja | 17 907 | 56 | 1224 | 6.8 | 89 | 7.3 | 5.0 |
| Požega-Slavonia | 6021 | 76 | 69 | 1.1 | 29 | 42.0 | 4.8 |
| Primorje-Gorski Kotar | 19 548 | 60 | 1168 | 6.0 | 95 | 8.1 | 4.9 |
| Sisak-Moslavina | 11 179 | 55 | 349 | 3.1 | 45 | 12.9 | 4.0 |
| Split-Dalmatia | 20 548 | 52 | 1428 | 6.9 | 135 | 9.5 | 6.6 |
| Šibenik-Knin | 6762 | 50 | 31 | 0.5 | 33 | 106.5 | 4.9 |
| Varaždin | 12 843 | 62 | 421 | 3.3 | 61 | 14.5 | 4.7 |
| Virovitica-Podravina | 4471 | 59 | 208 | 4.7 | 23 | 11.1 | 5.1 |
| Vukovar-Srijem | 10 366 | 60 | 246 | 2.4 | 62 | 25.2 | 6.0 |
| Zadar | 12 040 | 62 | 1228 | 10.2 | 72 | 5.9 | 6.0 |
| Zagreb County | 18 463 | 56 | 615 | 3.3 | 74 | 12.0 | 4.0 |
| City of Zagreb | 44 886 | 59 | 2469 | 5.5 | 200 | 8.1 | 4.5 |
| Croatia | 262 910 | 59 | 14 201 | 5.4 | 1 269 | 8.9 | 4.8 |

*BI-RADS – Breast Imaging Reporting and Data System.

†Number of detected cancers per 1000 mammographies.

situ) per 1000 mammographies for these four cycles. The rate was higher in the initial cycle, 6.3/1000, while in the

subsequent cycles it was 4.3/1000. In comparison, an average rate for the EU Member States (13) was 6.2 per 1000

TABLE 5. Uptake and screening performance data by county in cycle 4 (2014-2016)

| County | Mammographies (n) | Uptake (%) | BI-RADS* 0, 4, 5 (n) | BI-RADS 0, 4, 5 relative to number of mammographies (%) | Cancers detected (n) | Cancers relative to BI-RADS 0, 4, 5 (%) | C/1000 M† |
|-----------------------|-------------------|------------|----------------------|---|----------------------|---|-----------|
| Bjelovar-Bilogora | 9016 | 75 | 119 | 1.3 | 22 | 18.5 | 2.4 |
| Brod-Posavina | 9018 | 61 | 1061 | 11.8 | 32 | 3.0 | 3.5 |
| Dubrovnik-Neretva | 5297 | 69 | 183 | 3.5 | 21 | 11.5 | 4.0 |
| Istria | 16 122 | 65 | 360 | 2.2 | 42 | 11.7 | 2.6 |
| Karlovac | 7583 | 51 | 174 | 2.3 | 42 | 24.1 | 5.5 |
| Koprivnica-Križevci | 7726 | 58 | 367 | 4.8 | 24 | 6.5 | 3.1 |
| Krapina-Zagorje | 10 050 | 63 | 1643 | 16.3 | 28 | 1.7 | 2.8 |
| Lika-Senj | 2751 | 50 | 87 | 3.2 | 15 | 17.2 | 5.5 |
| Međimurje | 10 873 | 78 | 872 | 8.0 | 35 | 4.0 | 3.2 |
| Osijek-Baranja | 19 562 | 62 | 1086 | 5.6 | 73 | 6.7 | 3.7 |
| Požega-Slavonia | 5549 | 67 | 113 | 2.0 | 20 | 17.7 | 3.6 |
| Primorje-Gorski Kotar | 13 202 | 50 | 608 | 4.6 | 39 | 6.4 | 3.0 |
| Sisak-Moslavina | 7052 | 37 | 314 | 4.5 | 16 | 5.1 | 2.3 |
| Split-Dalmatia | 20 212 | 51 | 1120 | 5.5 | 85 | 7.6 | 4.2 |
| Šibenik-Knin | 4764 | 40 | 29 | 0.6 | 13 | 44.8 | 2.7 |
| Varaždin | 14 298 | 66 | 229 | 1.6 | 48 | 21.0 | 3.4 |
| Virovitica-Podravina | 3611 | 59 | 140 | 3.9 | 14 | 10.0 | 3.9 |
| Vukovar-Srijem | 4273 | 86 | 185 | 4.3 | 13 | 7.0 | 3.0 |
| Zadar | 11 307 | 60 | 897 | 7.9 | 49 | 5.5 | 4.3 |
| Zagreb County | 20 706 | 60 | 569 | 2.7 | 43 | 7.6 | 2.1 |
| City of Zagreb | 46 762 | 60 | 2564 | 5.5 | 210 | 8.2 | 4.5 |
| Croatia | 249 745 | 59 | 12 721 | 5.1 | 884 | 6.9 | 3.5 |

*BI-RADS – Breast Imaging Reporting and Data System.

†Number of detected cancers per 1000 mammographies.

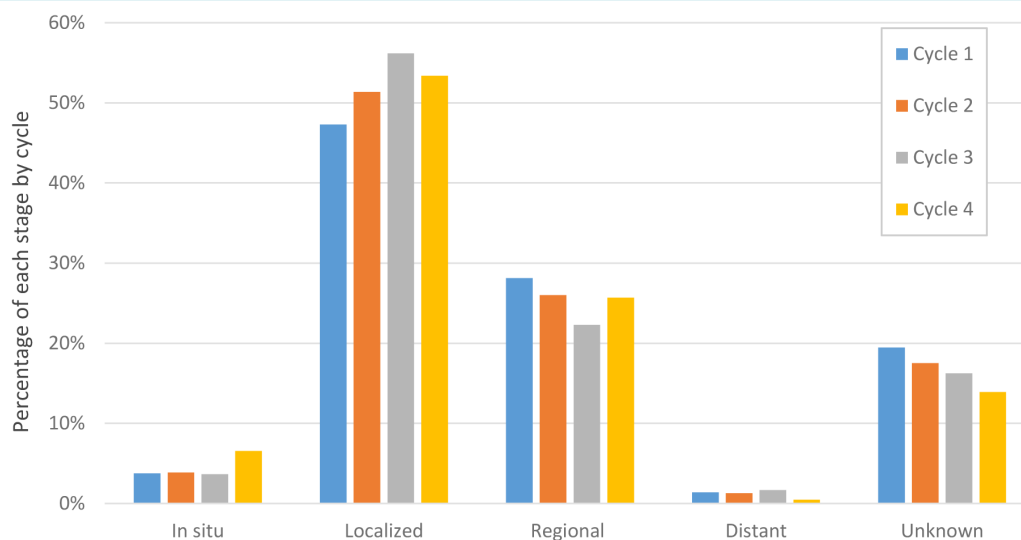


FIGURE 2. Stage at diagnosis for breast cancers detected by screening per cycle, 2006-2016.

women screened (from 2.3 in Portugal, Alentejo to 10.2 in Wales); 7.2/1000 for the initial tests and 5.6/1000 for subsequent cycles. The average further assessment rate in the first four cycles was 6.5%, while the European total was 5.2% (14).

Age-standardized mortality of breast cancer in Croatia decreased by 23% between 2007 (35.9/100,000) and 2020 (27.5/100,000, 2011 Census standard population) (4). Since the only way to determine the effect of a specific breast cancer screening program on breast cancer mortality is to conduct a randomized controlled trial, it is not possible to know if, and to what extent, this finding is the result of the screening, as the improvements in treatment have certainly played a role. However, breast cancer screening can lead to a 30% reduction in breast cancer mortality (15), and although the uptake in Croatia is somewhat lower than prescribed by the screening guidelines, it is presumably still high enough to yield a beneficial effect.

Mammography screening allowed a detection of an increased number of cancers at an early, localized stage, and of a decreased number of cancers with regional and distant metastasis (16,17). These findings indicate that some of the goals of screening program have been achieved. An early diagnosis and early treatment are essential to improve the outcomes of this disease. Therefore, screening programs that allow for early disease detection are a vital public health strategy.

There are some limitations to this study. First, data on almost all of the indicators mentioned in the European guidelines are not routinely collected as part of the program, which limits the possibility of adequate evaluation of the program results. The data on detected cancers and stage at diagnosis were collected by merging the screening database with the Cancer Registry database, and the obtained number of cancer diagnoses was lower than expected when compared with the EU average. We hope that an improved IT infrastructure will enable the follow-up of each woman throughout the whole screening process, from invitation to cancer diagnosis and treatment. Another limitation is the difference in the duration and circumstances surrounding each of the cycles. Due to problems concerning public procurement, the first cycle lasted for 3 years, which limits the comparison with subsequent cycles. Although more breast cancer cases are expected to be diagnosed in the initial cycle, we believe that in this case the difference is in part due to differences in cycle duration.

Despite some difficulties, we are satisfied with the current development of the program. All the studied parameters have significantly improved, which indicates that the program led to true benefits for the patients. These first results show an average screening uptake and an average number of detected cancers. Additional efforts are necessary to obtain other relevant performance indicators and to further improve the uptake.

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Declaration of authorship AŠP conceived and designed the study; AŠP and MJ acquired the data; AŠP, PČ, VT, BB analyzed and interpreted the data; AŠP, PČ drafted the manuscript; VT, MJ, BB critically revised the manuscript for important intellectual content; all authors gave approval of the version to be submitted; all authors agree to be accountable for all aspects of the work.

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