The effect of the population-based cervical cancer screening program on 5-year survival in cervical cancer patients in Lower Silesia

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Abstract

Background. Poland is considered among the European countries with an average incidence of cervical cancer (CC; about 3,000–3,500/year) and at the same time with high mortality (5-year survival rate – 55.2%). For this reason, in 2006 Poland introduced a Population-Based Cervical Cancer Prevention and Early Detection Program addressed to women aged 25–59 years, in which a cytological test is carried out every 3 years.

Objectives. The aim of the study was to assess the changes in the curability of CC patients brought by the introduction of the Screening Program in the Lower Silesian voivodeship and to identify the subpopulation of women for whom activities aimed at increasing adherence rates must be intensified.

Material and methods. The 5-year relative survival in 3,586 CC patients from 2000–2010 registered in the Lower Silesian Cancer Registry was analyzed.

Results. In the Lower Silesian voivodeship, a 55.1% 5-year survival rate was recorded in 2000–2004 and 70.5% in 2010. The highest increase in 5-year relative survival rates was found in rural communities (from 53.1% in 2000–2004 to 77.7% in 2010) and in Wrocław (56.8% and 74.2%, respectively). In the study group, the number of patients with invasive CC (C53) detected in the local stage of the disease increased systematically from 61.5% in 2000–2004 to 74.3% in 2010.

Conclusions. The introduction of the population-based screening program improved the curability rate in CC patients in the Lower Silesian voivodeship. In order to maintain the recent positive trends, further education should be continued, and activities aimed at increasing adherence to screening tests should be intensified, especially in urban-rural communities.

Key words: cervical cancer, screening tests, cancer epidemiology

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Introduction

Epidemiological statistics list Poland as a country with an increased risk of cervical cancer (CC), where incidence and mortality rates are among the highest in the European Union.[1,2] Cervical cancer accounts for about 6.5% of all cancers in Polish women; it ranks 6th for incidence and 8th for mortality.[3] Increased incidence of CC is observed in women aged over 20 years, and peak incidence falls in the age range of 49–54 years.[1] The risk of death from CC in low-income populations, including these in Poland, is around 2–4%.[4] For the above reasons, this issue is of key importance for social and economic stability of Poland.[5] In 2006, Poland introduced the Population-Based Cervical Cancer Prevention and Early Detection Program addressed to women aged 25–59 years, whose basic aim is to provide women with a possibility to have a cytology test performed every 3 years free of charge.[6,7] The primary function of cytology screening is to diagnose and treat precancerous lesions and preinvasive cancer, as well as invasive cancer at an early stage, which helps avoid the cancer or ensure effective treatment.[5,8,9] In highly developed countries such as Finland, Germany or Sweden, where screening tests were introduced back in the 1960s, the mortality rate of CC decreased by over 80%.[3,10] However, Poland has not managed to reach the optimal percentage of target population adherence, hence CC screening is not fully effective yet.[11] The fact that women rarely use screening tests offered by the healthcare system signifies women's poor health-related awareness and the lack of effects of educational activities undertaken by the government and healthcare system.[12]

Objectives

The aim of the present study was to assess the changes in curability (5-year relative survival) of CC patients (C53 – malignant neoplasm of cervix uteri and D06 – carcinoma in situ of cervix uteri according to ICD-10 classification) after introduction of the population-based screening in the Lower Silesian voivodeship, identify the subpopulation of women for whom activities aimed at increasing adherence to screening tests must be intensified and determine whether there is a positive trend in CC curability despite low adherence to the screening tests.

Material and methods

The 5-year survival rates in 3,586 CC patients (C53 and D06) from 2000–2010 as registered in the Lower Silesian Cancer Registry (LSCR) were analyzed. According to the registry, 271–374 cases were diagnosed annually in the Lower Silesian voivodeship. To exclude the influence of age on 5-year survival, the values of relative survival were calculated based on the life expectancy tables. Statistical calculations were performed using Microsoft Excel 2013 (Microsoft Corp., Armonk, USA) and the χ^2 test with the Yates's correction.

Ethical permission was not applied because the work is based on retrospective data from the LSCR. Our research did not have any influence on patient treatment and survival. No non-routine procedures were performed in the study, so consent from the patients was not taken. The data comes from the LSCR, which is a governmental institution.

Results

The 5-year relative survival rate in CC patients (C53 and D06) in the Lower Silesian voivodeship has been increasing steadily. It increased from 55.1% in 2000–2004 to 60.5% in 2005–2009, and in 2010 it reached 70.8% (Table 1) ($p < 0.00001$). At the same time, the number of cancers diagnosed at the pre-invasive stage (in situ cancers – D06)

Table 1. Five-year survival in cervical cancer patients in the Lower Silesian voivodeship in 2000–2010

Year	Number of C53+D06 cancers	5-year survival	Observed survival [%]	Relative survival [%]	Number of C53 cancers	5-year survival	Observed survival [%]	Relative survival [%]	Number of D06 cancers	%
2000	311	146	46.9	49.5	301	138	45.8	48.3	10	3.2
2001	341	179	52.5	55.4	332	171	51.5	54.4	9	2.6
2002	282	161	57.1	60.3	279	158	56.6	59.7	3	1.1
2003	271	139	51.3	54.2	258	127	49.2	51.9	13	4.8
2004	313	168	53.7	56.7	292	150	51.4	54.3	21	6.7
2005	314	166	52.9	55.3	294	148	50.3	52.6	20	6.4
2006	326	173	53.1	55.5	278	128	46.0	48.1	48	14.7
2007	338	183	54.1	56.5	283	132	46.6	48.7	55	16.3
2008	374	226	60.4	63.1	275	129	46.9	49.0	99	26.5
2009	357	230	64.4	67.3	245	121	49.4	51.6	112	31.4
2010	359	242	67.4	70.8	257	144	56.0	58.8	102	28.4

increased in a statistically significant manner in the analyzed group of patients ($p < 0.00001$), which greatly improved 5-year survival.

In the group of patients diagnosed with pre-invasive (D06) and invasive (C53) cancer, an upward trend in 5-year survival by 1.5% per year in 2000–2010 was observed (linear trend: $y = 1.5 \cdot x + 46.8$). We also found a steady increase in the survival rate in invasive CC (C53) patients by 1% per year, which is described by the trend $y = 0.03 \cdot x + 49.8$ (Fig. 1). In the group of patients diagnosed with invasive CC (C53) a linear reduction in the standardized mortality rate was observed in the years 2000–2015 (Fig. 2).[13] Between 2000 and 2005, in the Lower Silesian voivodeship, an average number of 142 deaths of women due to invasive CC were reported, in 2006–2010 and in 2011–2015 it was 138 and 133, respectively (trend: almost 1 person/year) (Fig. 2).

As the next step, we analyzed the differences in 5-year relative survival rates depending on the patients' residence. The highest increase in relative curability rates was definitely noted in rural communities (from 53.1% in 2000–2004 through 61.5% in 2005–2009 to 77.7% in 2010) and Wrocław (56.8%, 64.4% and 74.2%, respectively) (Table 2). The reasons for this were both a higher number of pre-invasive CC (D06) detected as shown in Table 1 and Table 3, and a better prognosis for invasive CC (Table 4). Both of these were an expected consequence of screening tests.

In the following years, a steady increase in the number of patients treated at the Lower Silesian Oncology Center

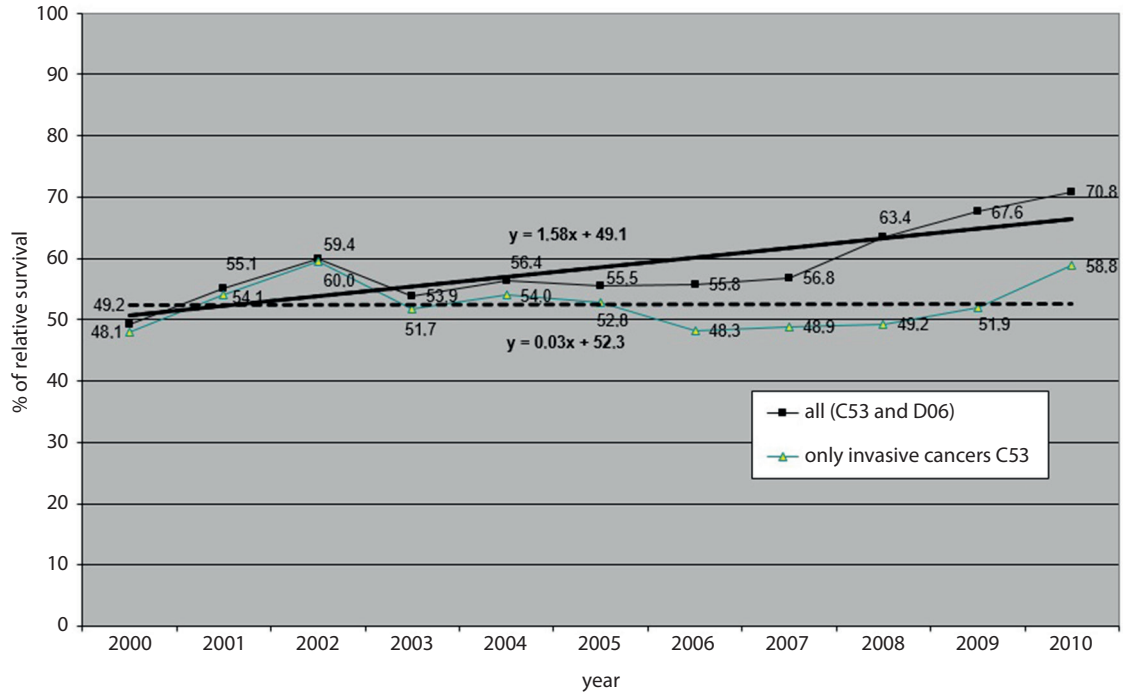

Fig. 1. Five-year relative survival in cervical cancer patients in the Lower Silesian voivodeship in 2000–2010

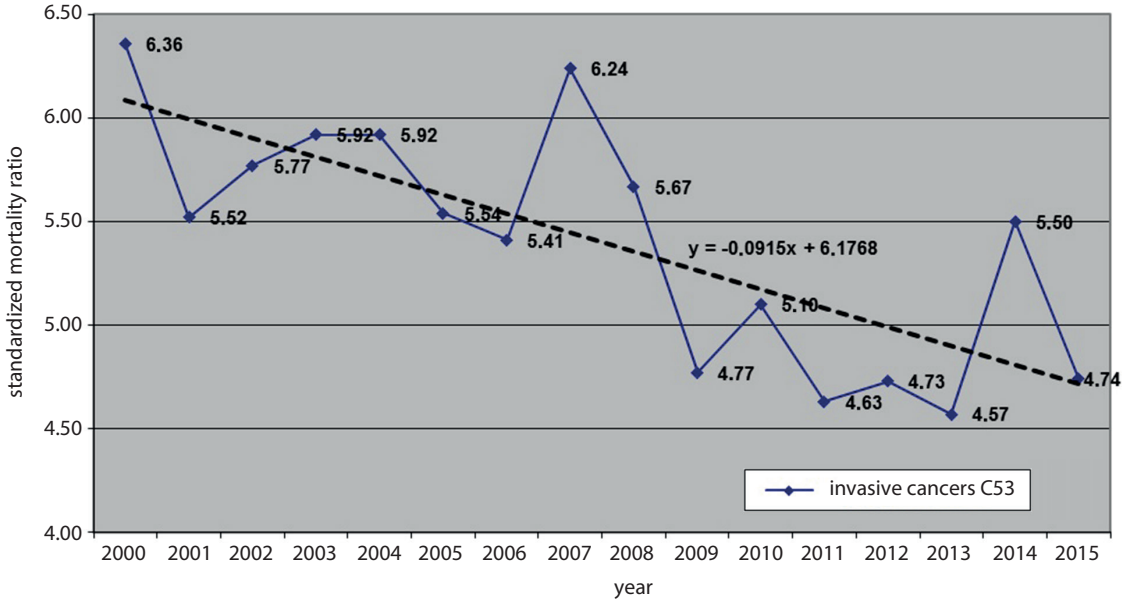

Fig. 2. Standardized mortality rate in invasive cervical cancer patients in the Lower Silesian voivodeship in 2000–2015[13]

Table 2. C53 and D06 (relative) survival by administrative unit

Administrative unit	2000–2004			2005–2009			2010		
	number of cancers	5-year survival	[%]	number of cancers	5-year survival	[%]	number of cancers	5-year survival	[%]
Urban community of Wrocław	321	172	56.8	389	236	64.4	68	48	74.2
Other urban communities	560	306	57.6	611	327	56.7	132	87	68.8
Rural community	296	150	53.1	293	171	61.5	69	52	77.7
Town in an urban-rural community	208	95	49.0	222	128	60.5	43	25	60.9
Rural area in an urban-rural community	133	70	55.4	194	116	63.1	47	30	67.7

Table 3. Incidence of D06 in situ cancers

Administrative unit	2000–2004			2005–2009			2010		
	number of all cancers	number of D06 cancers	[%]	number of all cancers	number of D06 cancers	[%]	number of all cancers	number of D06 cancers	[%]
Urban community of Wrocław	321	6	1.9	389	96	24.7	68	17	25.0
Other urban communities	560	25	4.5	611	104	17.0	132	40	30.3
Rural community	296	11	3.7	293	56	19.1	69	24	34.8
Town in an urban-rural community	208	6	2.9	222	35	15.8	43	10	23.3
Rural area in an urban-rural community	133	8	6.0	194	43	22.2	47	11	23.4

Table 4. Only invasive cancers C53 (relative) survival by administrative unit

Administrative unit	2000–2004			2005–2009			2010		
	number of cancers	5-year survival	[%]	number of cancers	5-year survival	[%]	number of cancers	5-year survival	[%]
Urban community of Wrocław	315	167	56.3	293	148	54.4	51	32	66.8
Other urban communities	535	284	56.1	507	225	47.4	92	48	53.3
Rural community	285	141	51.9	237	116	52.1	45	28	64.5
Town in an urban-rural community	202	89	47.4	187	94	53.1	33	17	54.5
Rural area in an urban-rural community	125	63	53.2	151	75	53.1	36	19	56.9

Table 5. Number of patients treated at LSOC by place of residence

Administrative unit	2005–2009			2010		
	number of cancers	number of patients treated at LSOC	[%]	number of cancers	number of patients treated at LSOC	[%]
Urban community of Wrocław	389	212	54.5	68	52	76.5
Other urban communities	611	179	29.3	132	63	47.7
Rural community	293	127	43.3	69	40	58.0
Town in an urban-rural community	222	91	41.0	43	32	74.4
Village in an urban-rural community	194	74	38.1	47	31	66.0
Total	1,709	683	40.0	359	218	60.7

* treated at LSOC by any method, also after surgery performed outside LSOC (but receiving radiotherapy and/or chemotherapy at LSOC); LSOC – Lower Silesian Oncology Center.

in Wrocław (LSOC), which is the referral center for Lower Silesia, was observed. In 2005–2009, 40% of all CC patients from Lower Silesia were treated at the LSOC, whereas in 2010 this number was as high as 60.7%. Such a large change in the number of patients treated at the LSOC probably resulted from the fact that the patients who had undergone screening were referred for multi-specialist consultation to a full-profile reference center and then received treatment at the LSOC.

Table 5 shows the percentage of patients treated at the LSOC by place of residence. Treatment in the LSOC was most often selected by residents of Wrocław (54.5% in 2005–2009 and 76.5% in 2010), while residents of small and medium-sized towns were treated in the LSOC the least frequently (29.3%

Table 6. Five-year (relative) survival, any treatment method, all cancers (C53 and D06)

Period	Treated at LSOC	5-year survival	[%]	Treated only outside LSOC	5-year survival	[%]
2005–2009	683	463	70.8	1,026	515	53.5
2010	218	141	67.5	141	101	75.0

LSOC – Lower Silesian Oncology Center.

Table 7. Five-year (relative) survival rates, any treatment used, only invasive cancers (C53)

Period	Treated at LSOC	5-year survival	[%]	Treated only outside LSOC	5-year survival	[%]
2005–2009	536	322	63.2	839	336	43.2
2010	175	102	61.2	82	42	55.1

LSOC – Lower Silesian Oncology Center.

in 2005–2009 and 47.7% in 2010), which was most probably due to the fact that municipal hospitals have departments dedicated to the care of gynecology patients.

Another factor that was analyzed was the impact of experience of the hospital center where the patients received treatment on the curability. Firstly, it is worth noting that before 2008 the LSOC was the only entity that provided oncological radiotherapy services in the Lower Silesian voivodeship. Surgical procedures and systemic treatment in the analyzed period were carried out in various centers in the voivodeship, including the LSOC. Out of the 3,586 patients reported to the LSCR, 1,831 had undergone a surgical procedure, radiotherapy was used in 1,915 patients and 1,022 patients received systemic therapy. No treatment was used in 181 (5%) patients out of the 3,586 patients diagnosed with CC – these were the patients who were not eligible for treatment due to comorbidities or advanced disease. This data was excluded from the analysis. In the study period, we found a significant increase of the 5-year survival rate in the patients treated outside the LSOC (from 53.5% to 75.0%) (Table 6). This increase was undoubtedly attributed to the higher percentage of in situ cancers (D06) that were detected and treated, as well as a decreasing percentage of patients with invasive CC in this group (C53 accounted for 58.2% of diagnoses). By contrast, in patients referred to the reference center (LSOC) for treatment, invasive cancers (C53) still accounted for a high percentage of diagnoses (as high as 80.3%) (Tables 6,7). At the same time, prognosis in patients with invasive CC (C53) who were treated outside the LSOC remained significantly worse, with 5-year survival of 43.2% in 2005–2009 and 55.1% in 2010, whereas in patients treated at the LSOC it was 63.2% in 2005–2009 and 61.2% in 2010 (Table 7). The analysis showed that the treatment results discussed above, namely the 5-year-survival rate in patients with invasive CC (C53) treated outside the LSOC in the study period (2005–2010), were statistically lower ($p < 0.00001$) than for the patients treated at the LSOC. We observed a systematic increase of the percentage, from 61.5% in 2000–2004 through 68.7% in 2005–2009 to 74.3% in 2010, of patients with invasive CC (C53) detected in the local stage of the disease (Table 8).

Table 8. Advancement of invasive cervical cancer (C53)

Period	Number and percentage	Local disease	Regional disease	Metastatic disease
2000–2004	n	643	227	176
	%	61.5	21.7	16.8
2005–2009	n	748	184	157
	%	68.7	16.9	14.4
2010	n	159	31	24
	%	74.3	14.5	11.2

In 2005–2009 in the Lower Silesian voivodeship, we recorded a 63.2% 5-year survival rate among patients diagnosed with invasive CC (C53) treated at the LSOC, and a 43.2% 5-year survival rate in patients treated outside the LSOC. In this group, 69% were patients diagnosed with the local stage of the disease, 17% – with regional stage of the disease and 14% – with generalized disease (Table 9). According to the 25th Annual FIGO (Fédération internationale de gynécologie et d'obstétrique – International Federation of Gynecology and Obstetrics) Report, in Europe the 5-year survival rate in patients with invasive CC (C53) is 82% for the local, 42% for regional and 17% for generalized stages.[14] Taking into account the disease advancement data, the expected relative survival rates in patients from our voivodeship can be calculated using the European standard[14]: $0.69 \cdot 82\% + 0.17 \cdot 42\% + 0.14 \cdot 17\% = 66.1\%$.

The above calculations suggest that 5-year survival rate in the patients receiving treatment at the reference center (LSOC) is at the European level (63.2%). Unfortunately, a much worse prognosis is observed in the patients treated outside the LSOC (43.2%).

Discussion

About 60,000 new cases of CC are diagnosed each year in Europe and as many as half of those patients die.[15] Large-scale studies have shown that screening in women aged

Table 9. Five-year relative survival (RSC) in 1995–1999 and 2000–2007[21,22]

Country	RSC 1995–1999 [%]	RSC 2000–2007 [%]	Change [%]
Northern Europe	71.6	71.5	–0.1
Denmark	69.5	70.7	1.2
Finland	67.9	69.0	1.1
Iceland	76.7	84.6	7.9
Norway	72.8	75.6	2.8
Sweden	71.0	69.9	–1.1
UK and Ireland	65.2	66.6	1.4
Ireland	65.3	66.3	1.0
UK (England)	65.2	66.8	1.6
UK (Northern Ireland)	68.6	71.8	3.2
UK (Scotland)	67.5	66.1	–1.4
UK (Wales)	59.3	63.1	3.8
Central Europe	69.2	68.0	–1.2
Austria	67.5	68.3	0.8
Belgium	69.3	70.2	0.9
France	69.6	63.5	–6.1
Germany	65.0	66.8	1.8
Switzerland	70.6	66.7	–3.9
the Netherlands	73.2	70.3	–2.9
Southern Europe	65.3	66.9	1.6
Croatia	–	68.0	–
Italy	65.6	66.8	1.2
Malta	64.8	54.7	–11.1
Portugal	58.0	63.8	5.8
Slovenia	71.8	75.5	3.7
Spain	66.1	66.1	0
Eastern Europe	63.7	60.3	–3.4
Bulgaria	–	54.8	–
Czech Republic	72.0	67.1	–4.9
Estonia	–	65.6	–
Latvia	–	52.0	–
Lithuania	–	58.9	–
Poland*	53.3	55.2	1.9
Slovakia	65.8	66.5	0.7
European average	64.7	65.4	0.7

* Lower Silesian and Świętokrzyskie voivodeship as well as city of Kraków participated in the study.

21–65 years with a cytology test significantly reduces the CC incidence and mortality rate.[16,17] Although widely available, free-of-charge prophylactic cytology tests has been available in Poland for a few years and access to diagnostic tests has become easier, the number of new cases remains high despite the downward trend.[18] The reason behind the low adherence of the target population to screening cytology tests is low awareness of the benefits of such tests, as well as insufficient knowledge among the target group about the screening tests offered.[19,20] It should also be underlined that some cases of CC develop despite women's participation in screening (adenocarcinomas), and some of the cases occur in groups not covered by regular screening.[15] In order to compare the effectiveness of conducted activities aimed at reducing mortality from malignant neoplasms, EUROCARE studies were conducted in Europe. In the EUROCARE-5 study (2000–2007), an average of 65.4% for 5-year relative survival was obtained, with the highest values found in Northern Europe (71.5% on average) and Central Europe (68%), and the lowest values noted in Eastern Europe (60.3%).[21] In comparison with survival rates in 1995–1999, no unequivocal increase in survival rates was noted in Europe or in individual countries (Table 9).[22]

The 5-year survival rate in Poland in 2000–2007 (55.2%) was among the lowest in Europe, being almost 10% lower than the average for Europe, and almost 30% lower than the average for Iceland.[21] In 1995–1999, this rate in Poland was lower by a further 1.9%.

In the Lower Silesian voivodeship in 2000–2004, relative survival was 55.1%, in 2005–2009 it was 60.5% and in 2010 it was 70.5%. It is worth noting that if a survival rate of over 70% is maintained in the following years, the Lower Silesian voivodeship may rank high in the planned EUROCARE-6 study because only 8 European countries had a rate value of over 70% (Table 9) in EUROCARE-5.[21] Considering the upward trend in detecting in situ cancers, an extremely beneficial effect of population-based screening on 5-year survival rate in CC patients is observed (Table 4). The highest increase in the relative curability rates was noted among patients residing in rural communities (from 53.1% in 2000–2004 through 61.5% in 2005–2009 to 77.7% in 2010) and in Wrocław. While in the case of Wrocław better results may be attributed to easily available cytology test and screening information, the deciding factor in rural communes might have been the provision of free of charge medical service and significantly and gradually rising public awareness regarding cancer prevention. At the same time, it is unclear why such a major effect of screening was not observed in communal towns, i.e., small and medium-sized towns. The higher 5-year survival rate in CC patients was accompanied by a higher percentage of patients undergoing treatment at the LSOC. In 2010, compared to 2005–2009, the number of patients treated at the LSOC increased by over 20% from 40% to 60.7% of all cancer patients in the Lower Silesian voivodeship. The authors believe that centralized therapy in the center with the most extensive experience in the treatment of CC contributed to better treatment outcomes for the patients.

Conclusions

The 5-year survival rate in 2000–2007 in Poland (55.2%) was among the lowest ones in Europe, being almost 10% lower than the European average. In the Lower Silesian

voivodeship, a 55.1% 5-year survival rate was recorded in 2000–2004, 60.5% in 2005–2009 and 70.5% in 2010. The highest increase in relative survival rates was found in rural communities (from 53.1% in 2000–2004 through 61.5% in 2005–2009 to 77.7% in 2010) and in Wrocław (56.8%, 64.4% and 74.2%, respectively). In the group under study, the number of patients with invasive CC (C53) detected in the local stage of the disease increased systematically from 61.5% in 2000–2004 through 68.7% in 2005–2009 to 74.3% in 2010. Five-year relative survival rates in Lower Silesian patients receiving treatment at the LSOC (63.2% and 61.2%) were significantly better than those in patients treated in other centers (43.2% and 55.1%) and close to the expected relative survival rates for Lower Silesian patients with invasive cancers (66.1%). In conclusion, the introduction of the population-based screening program improved the curability rate for CC patients in the Lower Silesian voivodeship. However, to ensure that the recent positive trends are continued, women must be educated further, and activities aimed at increasing adherence to screening tests must be intensified, particularly in urban-rural communities. At the same time, patients diagnosed with CC must be systemically referred to highly specialized centers where comprehensive treatment is provided.

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