



Cervical cancer screening in Serbia

Skrining karcinoma grlića materice u Srbiji

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Introduction

The article focuses on the beginning of cervical cancer screening in Serbia. The opportunistic screening was introduced in a regular gynecological practice in the early sixties and preventive gynecological examination has been performed since then on a yearly basis. The proportion of population screened was unknown, and the standards for quality assurance and control were not available. The national program for such screening was established in 2011 encouraging women between 25 and 69 years to undergo a preventive gynecological examination together with Pap smear once in a 3-year period ¹.

Based on the experience of countries with effectively organized screening programs, a decision was made in 2006 by the Minister of Health to nominate a group of experts to prepare a proposal for organized cervical cancer screening program after testing the methodology in a pilot study in the District of Braničevo.

The specific objectives were to evaluate the reduction of the incidence and mortality from cervical cancer in the Province by means of an organized low-intensity cervical cytology program, as well as to demonstrate the different aspects of program implementation as a potential model for nationwide implementation.

Screening activities were integrated in the existing health care system. Organized screening for women in the target population (aged 25–69 years) were planned to be free of charge. Sample taking was done by the gynecologists and primary health care personnel in the local health care centers. Sample quality was under continuous control by the cytology laboratories. Confirmation and treatment were integrated into the normal health care routines. The

screening results of the program, including the histologically confirmed diagnosis, were registered at the National Cancer Institute ¹.

The impact of the screening program was assessed indirectly by comparing trends in invasive cervical cancer, changes in coverage, and changes in the interval between Pap smears.

Overview of the cervical cancer screening in Serbia during the years before

According to the data of the Register of Central Serbia for the Malignant Tumors 1,400 new cases of cervical cancer are discovered on the territory of Serbia every year. Considering its frequency, this is the second frequent cancer in women in Serbia, after breast cancer. The standardized incidence rate of cervical cancer in the Central Serbia in 2002 was 27.2 in 100,000 women, which was the highest incidence rate in Europe. Similar, high rates were also recorded in Romania, Albania and Herzegovina. According to the Institute of Statistics of the Republic of Serbia for the year 2002, a total of 452 women died because of cervical cancer. The standardized mortality rate was 7.2 in 100,000 which was lower than in the mentioned countries of the region ².

The incidence rate of cervical cancer was higher in Central Serbia than in the Province of Vojvodina. Apart from this, there were some significant differences in incidences between the districts of Central Serbia. In 2002 the lowest incidences (16.6 per 100,000 were recorded in the District of Mačva) and the highest (more than two times as high) were recorded in the Eastern Serbia, in the border area with Romania and in Belgrade ³.

Age distribution of patients with cervical cancer in Serbia

The risk for occurrence of cervical cancer increases with the age. The highest number of patients is between 45 and 54 years of age. However, the illness may, although very rare, occur even much earlier, e.g. even before 20 years of age. Age distribution of cervical cancer patients in Central Serbia in 2002³ is shown in Table 1.

On the territory of Serbia, screening of cervical cancer is conducted through an organized decentralized program.

The target group for cervical cancer screening

The decision on target group for cervical cancer screening, as well as on interval between check-ups is most usually made on the national level considering the presence of cervical cancer, frequency of human papilloma virus (HPV) infections and available infrastructure means. The World Health Organi-

Table 1
Age distribution of cervical cancer patients in Central Serbia in 2002³

Patient's age (years)	Patients		Age specific rate of cervical cancer per 100,000 patients
	n	%	
0–14	0	0.0	0.0
15–19	1	0.1	0.6
20–24	1	0.1	0.6
25–29	23	2.3	12.4
30–34	40	4.0	22.7
35–39	75	7.5	42.9
40–44	108	10.8	56.7
45–49	162	16.1	75.3
50–54	173	17.2	77.9
55–59	105	10.5	66.3
60–64	89	8.9	55.4
65–69	93	9.3	52.2
70–74	77	7.7	46.5
75+	57	5.7	29.5

According to the available data, less than one third of the cases of cervical cancer are discovered in an early invasive phase in which only operative treatment can be successfully applied. Most of patients are in later stages, when it is only possible to conduct radiotherapy, which results in longer treatment, different complications and significantly increased treatment expenses.

New cervical cancer screening program in Serbia

On July 3 2006 the Ministry of Health of the Republic of Serbia appointed the Expert Commission for the prevention of cervical cancer primarily aimed at developing a National Program for Prevention of Cervical Cancer.

Regarding the importance of the problem as well as the fact that in Serbia one woman dies per day due to cervical cancer, respecting the recommendations of WHO, and analyzing screening programs of other countries and using the experiences from the Pilot Program from the District of Braničevo, the Commission made the Program to enable the beginning of screening of cervical cancer in our country. This Program was adopted by the Government of the Republic of Serbia issued in Official Gazette No 54 from 23 May 2008¹.

Serbia has enough gynecologists and other medical personnel to conduct screening. A partial change in organization was expected to be achieved by introducing organized screening. This primarily refers to education of cytoscopists and to organization of laboratory service for cytology.

(WHO) recommends that the new screening programs should include women starting from 30 years of age. Women between 25 and 29 should be included only in the case when women of 30 + have been screened. Screening should not include women under 25 years of age. In addition, screening in women older than 65 can be stopped, if they have two consecutive negative findings⁴.

According to data from the Central Serbia the frequency rate of cervical cancer is higher in all age groups in women between 35 and 74 years of age (Table 1). Because of this, establishing the upper age limit, even over 65 years, would enable the revealing of prevalent cases of cervical cancer. Moving the lower limit of target group toward younger age groups, even despite the small risk for cervical cancer occurrence, would enable revealing precancerous lesions.

The screening program included women between 25 and 69 years of age. The target group was identified with the help of election lists or data base of personal identification numbers and list of insured persons of the Republic of Serbia Bureau for Health Insurance. The call for testing was sent to all women from the target group.

Testing included cytological examination of cervical smear (Papanicolaou test) observing the professional-methodological instructions. Screening was performed in every third year. Taking cervical smears was done by the Service for the Protection of Women's Health in the Primary Health Care Center.

Cytological examination of cervical smear (Papanicolaou test) underwent in cytological laboratory in the Primary Health Care Center and only for that Primary Health Care

Center, or in Primary Health Care Center which is responsible for a whole district¹.

Reading the results of tests as well as determining the dynamic and content of further monitoring and referring to the other diagnostics was done by the Service for the Protection of Women's Health in the Primary Health Care Center. The results were read by the gynecologists who initially took smears for cytological diagnostics or the selected gynecologists in the Primary Health Care Center.

In case of negative result, a patient was given a time recommendation for the next control examination and this was evidenced in the suitable Data Base of organized screening of cervical cancer. A patient stayed in a regular screening program and was called for the next check-up³.

A positive result was reported by the doctor so that a patient understood the significance of further diagnostics. In case of inflammatory reversible changes, the patients were treated in the facilities of primary level and cytological test control was scheduled not earlier than 6 weeks after the treatment.

All the other histopathological findings required further procedure in accordance with the protocol for monitoring after receiving results from cytological examination. If a smear was unsatisfactory for cytological analysis, a patient was called again for the control examination in 6–8 weeks.

levels of health care, as well as communication channels taking special care that the procedure be easy, acceptable and understandable for patients with the minimum of stress. It is extremely important to ensure adequate communication with patients at every level. This means explaining all possibilities of the treatment and its results, and getting an acceptance of further treatment, giving a patient an opportunity to freely ask questions in every phase of the treatment.

Women with low-grade lesions are submitted to routine follow-up smears. High-grade preinvasive disease was further evaluated by repeating Pap smear, conization or biopsy and subsequent treatment through surgical removal or ablation. This organized low-intensity cervical cytology programme showed a considerable increase in cervical intra-epithelial neoplasia (CIN) II–III cases and should reduce incidence of and mortality from cervical cancer in the future. Screening with the Papanicolaou smear plus adequate follow-up diagnosis and therapy can achieve major reductions in both incidence and mortality rates.

Uterine cervical cancer was one of the leading cancer among women in Serbia with age-standardized incidence rates of 23–27 per 100,000 in 2002². Cervical cancer incidence rate in Europe is shown in Figure 1.

Uterine cancer cervix is the second most common cancer in females in the world with about half a million new pa-

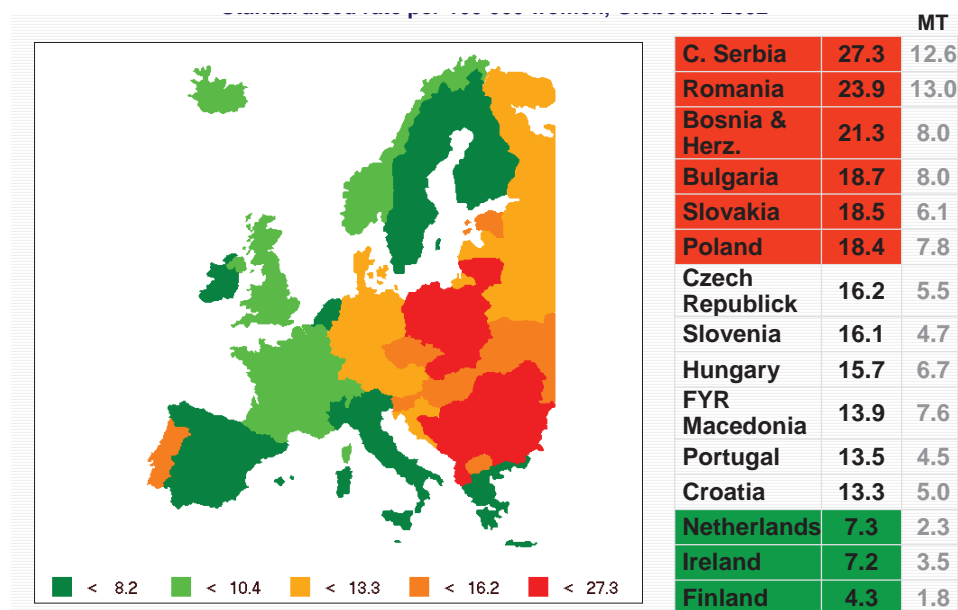


Fig. 1 – Cervical Cancer Incidence Rate in Europe²
(standardised rate per 100,000 women)

Referring the patients to the further diagnostics

A patient was referred to further diagnostics in a regional health facility of secondary level. With histopathological finding the patient returned to the chosen doctor who, depending on the kind of a diagnosed change acted in accordance with the recommendations of the protocol for monitoring women after receiving results from histopathological finding. In order to fulfill the whole value of the procedure it necessary to clearly define all the competences of various

tients per year⁴. Cervical cancer is an important public health problem among adult women in developing countries⁵. Since the introduction by Papanicolaou of cervical smear screening, the incidence of cervical cancer has declined in many developed countries^{2,6}. A decrease in the incidence of and the mortality from cervical cancer is mainly due to the organized mass screening using Pap smear programs. To organize an effective screening program in developing countries it should find adequate financial resources, develop the infrastructure, train the needed manpower, and

elaborate surveillance mechanisms for screening, investigating, treating, and following up the targeted women. The findings from the large body of research on various screening approaches carried out in developing countries and from the available managerial guidelines should be taken into account when reorganizing existing programmes and when considering new screening initiatives⁷.

Cytological screening has reduced the incidence of cervical cancer in countries with organized screening, but in Europe in 1995 there were still an estimated 68,000 incident cases^{5,7,8}. Cytology has limited reproducibility, and both meta-analyses and pooled analyses of cross sectional studies have established that tests for HPV have higher sensitivity than cytology in detecting high grade CIN and that combined HPV and cytology testing have high negative predictive values for CIN⁹⁻¹¹.

Cost-effectiveness modeling of screening strategies, however, depends greatly on reliable and generalisable estimates of the longitudinal, long term predictive values of test-

ing. A long-term negative predictive value is the main determinant of a safe screening interval to use, a key factor for the cost efficiency of a screening program. The long-term positive predictive value is an important measure of the extent of unnecessary procedures induced by screening, another major factor in evaluations of cost-efficiency. Several randomized controlled trials are currently being conducted to compare primary screening based on HPV detection with conventional cytology screening¹²⁻¹⁷. Data from these trials indicate that HPV based screening results in detection of more high grade CIN lesions (a higher sensitivity) but a reduced specificity compared with cytology based screening¹⁸⁻²¹.

Conclusion

The coordinated screening programme provides a low-cost, increases the coverage of the female population, and consequently reduces the rate of invasive cervical cancer.

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