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Cervical cancer screening practices in central and eastern Europe in 2012

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Abstract

The burden of cervical cancer in central and eastern Europe is generally higher compared to western or northern Europe due to a history of mostly opportunistic cervical cancer screening practices and due to the strong influence of political and economic changes in post-communist transition. This article describes the current cervical cancer screening practices, organizational plans for the future, and main obstacles that need to be overcome in 16 countries in central and eastern Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia and The former Yugoslav Republic of Macedonia. Unfortunately, only a few countries have managed to establish an organized and well-functioning cervical cancer screening program in recent years, whereas most countries in the region are still struggling with implementation-related issues of organized cervical cancer screening. Encouragingly, even in the countries where only opportunistic screening is performed, well-prepared plans and strategies have been established for switching to organized screening in the near future.

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Introduction

Cervical cancer represents a major public health problem in many countries, and ranks as the third most common cancer among women worldwide. In 2008, an estimated 530,000 women developed cervical cancer and 275,000 women died of it, corresponding to world age-standardized incidence and mortality rates of 15 and 8 per 100,000 (1). However, developed countries that have implemented cytology screening programs for cervical cancer, traditionally based on cytological evaluation of the Papanicolaou smear (Pap smear) and subsequent treatment of women with high-grade cytological abnormalities, achieved a substantial reduction in cervical cancer incidence and mortality rate, the major burden of the disease thus occurring in developing countries with no established screening programs. These differences are also noticeable in Europe, where the cervical cancer burden in countries with a long history of well-organized screening programs has been reduced up to 80% (2). In 2003, the Council of the European Union recommended implementation of population-based cervical cancer screening programs to European Union member states, with a second updated edition of recommendations published in 2008 (3, 4). According to the recommendations, the Pap smear is the standard cervical cancer screening test and should start at age 20 to 30, and screening should continue at 3- to 5-year intervals until age 60 to 65 (4). High quality should be assured at all steps of the screening process (invitation, screening, diagnostic confirmation, treatment, and follow-up after treatment) and screening should therefore be offered in organized settings, whereas opportunistic screening should be discouraged (4). Monitoring systems and links between appropriate databases should be set up in order to verify performance and impact, and high population coverage should be achieved (4).

Although they shared a similar history under a communist political system in the second half of the 20th century, the countries of central and eastern Europe represent a surprisingly diverse geographic region. Major political and economic changes during the past 20 years of post-communist transition have greatly influenced the healthcare systems in the majority of countries in the region. As a consequence, disease-prevention programs faced serious organizational, professional, and financial problems. Cervical cancer prevention was no exception in this turbulent transition period, leading to a substantially higher burden of the disease in central and eastern Europe compared to western and northern Europe.

This paper provides an update on the current situation of cervical cancer screening programs in 16 countries of central and eastern Europe: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, the Czech Republic, Estonia, Hungary, Latvia, Lithuania, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia and The former Yugoslav Republic of Macedonia. Because data on cervical

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cancer screening practices in these countries are relatively scant in the peer-reviewed literature, this work will hopefully shed light on the current situation, organizational plans, and obstacles that need to be overcome in individual countries of the region.

Albania

Albania's healthcare system faces many challenges in providing appropriate cervical cancer prevention services, starting with very limited awareness among the population about this preventable disease, limited professional and infrastructural capacity, lack of standardization of healthcare services, lack of functioning informational systems, and extremely fragmented data availability.

Because no national cancer registry has been established in Albania yet, the data on the incidence and mortality rates for cervical cancer more likely represent estimates than a reliable reflection of the current situation. According to GLOBOCAN 2008, among the female population of 1.6 million, with an estimated 124 cases of cervical cancer the crude incidence rate was 7.8/100,000 (world age-standardized incidence rate: 7.1/100,000); and with an estimated 49 deaths from cervical cancer the crude mortality rate was 3.1/100,000 (world age-standardized mortality rate: 2.1/100,000) (1).

There is no organized cervical cancer screening program in Albania. The Pap smear is offered in some gynecological-obstetrical centers and private clinics in the capital, Tirana (5). The screening coverage among women of reproductive age is extremely low, probably the lowest in the region: only 3.2% of women 15 to 44 years old reported having ever been screened with a Pap smear, with additional differences observed among women in urban (4.9%) and rural areas (1.8%) (5). Altogether, 2.7% of women 15 to 44 years old reported having had a Pap smear performed regularly every 3 years (4.3% of women in urban areas compared to 1.5% of women in rural areas) (5). One of the main reasons for the extremely low coverage is lack of awareness about cervical cancer prevention among women and also among health professionals: 70% of women in the Albania Reproductive Health Survey answered that the main reason why they have never had a Pap smear was because they had never heard of it, indicating a serious information gap (5). In addition, despite the fact that cervical cancer represents the second most common cancer among women age 15 to 44, and most cancers are diagnosed at stage III to IV, only 8% of women that have ever had a routine gynecological exam also had a Pap smear (5).

In 2011, the Albanian Ministry of Health launched a 10-year action plan called the National Cancer Control Program 2011–2020 with the support of the World Health Organization (WHO) Regional Office for Europe, which includes activities, timelines, and a budget plan based on national priorities (6). One of the important initial steps will be setting up a National Cancer Registry that will form the basis for planning, prioritizing, and monitoring cancer-control activities and will supply important data for developing prevention policies and measures (6). The action plan for the time framework from 2010 to 2015 has set the following goals: (i) to reduce the cervical cancer mortality rate by 5%, (ii) to provide prevention and treatment services for all reproductive tract cancers in the 12 counties, and (iii) to put in place a National Program for Control and Prevention of Cervical Cancer (6).

To the best of our knowledge, the current capacity of the healthcare system in Albania is insufficient to carry out an organized national cervical cancer screening program similar to those in western European countries; instead, a multiple service development approach, involving recruitment of all relevant existing health services in the country—such as the well-functioning maternal health services in planning and implementing the screening program—will gradually yield the much-needed results.

With the international financial, professional, organizational, and training support of European organizations (WHO, European Cervical Cancer Association, United Nations Population Fund (UNFPA), and Union for International Cancer Control, as well as international expert groups (various international scientific and professional societies), Albania has started preparing for the future establishment of a cervical cancer screening program. In the meantime, much work also needs to be done in the accessibility and quality of preventive services, education, and health promotion among the population, developing healthcare infrastructure and systems of reference for screening, diagnosis, and treatment, and improving the knowledge, skills, and practices of healthcare personnel at all levels of care (6).

Bosnia and Herzegovina

Opportunistic screening was introduced into regular gynecological practice in Bosnia and Herzegovina at the same time as in the other republics of the former Yugoslavia, in the 1960s. However, screening practice did not evolve or change substantially during the following years and, as a consequence, there is currently no population-based cancer registry, cervical cancer database, or Pap test database in the country. In addition, there is no adequate plan for establishing a proper cervical cancer prevention program in Bosnia and Herzegovina.

There are very few available data on cervical cancer incidence and mortality in Bosnia and Herzegovina, and even existing data are mainly estimates based on the incidence and mortality in neighboring countries. The world age-standardized incidence rate based on this methodology was 21.3/100,000 (crude incidence rate: 26.6/100,000) in a study by Arbyn et al. (2007); these estimates were derived from GLOBOCAN 2002 (7). The mortality rate for Bosnia and Herzegovina estimated by averaging rates from neighboring countries was 8.0/100,000 (crude mortality rate 11.1/100,000) (7). A summary report by WHO/ICO (Institut Català d'Oncologia) and GLOBOCAN 2008 reported the crude incidence rate in Bosnia and Herzegovina to be 13.2/100,000 (8), almost half of the crude incidence noticed in the study by Arbyn et al. Both results were derived from estimates of incidence in the countries of the former Yugoslavia and southern Europe, which, according to the same source, noted a decline in the incidence of cervical cancer (particularly in Serbia and Croatia) (8).

The last census in Bosnia and Herzegovina was in 1991, which affects the statistical analysis. The number of new cases of cervical cancer per year in Bosnia and Herzegovina varies depending on the size of the city or region. The most relevant data close to the real incidence in the country were gathered in the cantons of Sarajevo and Tuzla, the two biggest regions in Bosnia and Herzegovina. The crude incidence rate in the Canton of Sarajevo is more homogenous (approximately 30.4/100,000), whereas in the Canton of Tuzla it varied from 18.5/100,000 in 2005 to 43.8/100,000 in 2000 (9). This wide range could be explained with the fact that the Canton of Tuzla is the most populous region in Bosnia and Herzegovina and also the region to which a number of small towns (outside the Canton of Tuzla) in the eastern part of the country gravitate. Considering data from the cantons of Sarajevo and Tu-

zla, the exact crude incidence in the country could be higher than estimated by averaging rates from neighboring countries.

The epidemiological data available for the Canton of Tuzla showed that the most women with cervical cancer were diagnosed in the fifth decade of life; 1.5% of women were younger than 20. In a study by Fatušić et al. (2007), 27.11% of all women with cervical cancer were younger than 30 in the period from 1993 to 2006 (10). This high percentage of younger ages in the incidence rate could be explained by the wartime and postwar period (1993–2000) and the diminished motivation of women to engage in this type of preventive health practice. The high incidence in the Canton of Tuzla, with a significant proportion of young women and a high percentage of women with advanced disease, are a consequence of the lack of a well-functioning screening program. Currently, Bosnia and Herzegovina only has an opportunistic screening program, in theory covering all women age 20 to 64, with one Pap smear every 3 years, after three negative initial smears performed yearly. However, the target population is not well defined due to the lack of appropriate population data, and there are no data on the actual number of tests performed. The type of screening test used in Bosnia and Herzegovina is mostly the conventional Pap test, but HPV DNA detection is also used. There are no clear recommendations by the Ministry of Health on HPV testing indications and reimbursement, and therefore the decision lies in the hands of individual gynecologists.

Through joint cooperation among the Ministry of Health of the Federation of Bosnia and Herzegovina, the UNFPA, and the Non-Governmental Organizations Partnerships in Health, research was conducted in order to obtain real information about the situation in Bosnia and Herzegovina with data about the equipment, professional staff, and laboratory facilities necessary for implementing cervical cancer screening. The research was conducted in 2012 (from August to November) in 10 cantons of the Federation of Bosnia and Herzegovina, Republika Srpska, and Brčko District, and included all public health institutions and most of the private gynecology practices.

In conclusion, the fluctuation of the incidence according to the literature data and this study reflects the situation throughout Bosnia and Herzegovina regarding cervical cancer incidence and mortality. It also indicates the urgent need in the near future to establish a national registry of malignant diseases, and a Pap test database within an organized cervical cancer prevention program as recommended by the Council of the European Union (3).

Bulgaria

The first examinations of women for cervical cancer screening in Bulgaria were implemented in 1956. The National Cervical Screening Program was officially launched in 1970. The target population, screening intervals, and other features of screening were in accordance with the internationally accepted guidelines. Between 1970 and 1985, the cervical cancer incidence and mortality rates in Bulgaria remained relatively stable and were comparable to those of many European countries (11, 12).

Unfortunately, a major collapse in the screening program leading to a serious decline in basic parameters of screening efficacy occurred after 1989 with the democratization of the country and the subsequent health reform. Since the early 1990s, cervical cancer screening in Bulgaria has been opportunistic with little data on the number of Pap smears performed and women screened. As a result of the slow and inconsistent health system reforms and the absence of organized preventive programs, the cervical cancer incidence and mortality rates in the past 20 years have been constantly rising (13). In 2009, the world age-standardized incidence of cervical cancer was 18.7/100,000 women; the crude incidence rate was highest among women age 40 to 49 (over 45.0/100,000). However, during the past few years, overall incidence rates have been relatively constant, with a slight tendency towards a decrease. In the period from 1965 to 2009, mortality rates from cervical cancer also increased from 2.6/100,000 in 1965 to 5.4/100,000 in 2009, with the rate of increase being approximately 0.5% per year.

Currently, there is no national program for cancer prevention in Bulgaria. There are some local initiatives for free preventive checkups that are undertaken rather unsystematically. The reform in the healthcare system has led to a shift from institutionally structured preventive programs to health behaviors dominated by socioeconomic factors, individual knowledge, and personal initiative of both providers and clients. Responsibility for prevention activities has changed from being predominantly collective and resting with the state to individual. This shift is creating significant barriers to regular cervical cancer screening and is increasing disparities in access to screening programs (14).

In 2000, the National Program for Oncological Screening in Bulgaria (2001–2006) was approved by the council of ministers. It provided for cervical, breast, and prostate cancer screening to be covered by the National Health System. Regarding cervical cancer, the program focused on cytology screening for women age 30 to 59 either through primary healthcare providers or through obstetrics/gynecology practitioners, with examinations at specialized laboratories throughout the country. This program was not implemented the way it was planned, and it expired at the end of 2006.

In recent years in Bulgaria, several studies focused on cervical cancer prevention in the context of healthcare reforms. They analyzed women's perspectives towards cervical cancer prevention (14), the determinants of inequalities in cervical cancer screening (15), and the impact of providers' construction of women and their responsibility for prevention (16). Research on health providers' assessment of the opportunity to implement an organized screening program in Bulgaria reveals the lack of instructions and serious organizational problems connected with establishing such a program (17).

Not much is known about the current state of cytopathology in Bulgaria. A few publications have raised concern about a striking decrease in the number of pathologists, insufficient equipment in laboratories, and underpayment of this group of health professionals. Studies on current practices in laboratories have concluded that the level of adherence to the European Guidelines for Quality Assurance for cytopathology is not satisfactory in Bulgaria (18, 19). There are no clear instructions on quality assurance and management of pathology laboratories. Practices for internal and external quality control are insufficient and often do not follow the European guidelines. Due to the lack of national standards for personal and laboratory workloads, the laboratories included in the study significantly differed from one another (19).

There are several national documents related to cancer prevention and screening. However, although health legislation offers a definition of screening, there are no clear regulations and instructions available, except regulations for preventive checkups for high-risk groups and some malignant diseases (e.g., cervix, breast, and colon cancer). There are also some instructions for

good medical practice in outpatient healthcare for prevention and screening. General practitioners (GPs) are responsible for invitations, referrals, and follow-up of people in high-risk groups, as well as for reporting their test results to the National Health Insurance Fund and the regional health centers. GPs therefore function as gatekeepers that decide how to distribute their referrals for prevention, diagnostics, and treatment. Free preventive checkups are available only for people with health insurance. Many Pap smears are performed in the private sector.

In 2009, a project funded by the European Social Fund started. The project "STOP and Go for a Checkup—National Campaign for Early Cancer Diagnosis" is a nationwide one with the goal of improving infrastructure, increasing capacity, and preparing society for the establishment of population-based screening programs for cervical, breast, and colorectal cancers. It was implemented as part of the Human Resources Development Operational Program 2007–2014. The entire management and administration of the project is performed by the Ministry of Health. Specific aims of the project are to increase the number of early diagnoses of cervical, breast, and colorectal cancer, to raise awareness among the general public about these cancers, to establish a national screening register, and to increase the capacity of health professionals for applying national policies in accordance with good practices in cancer screening. Within a pilot project, it is planned that 250,000 cervical smears will be performed by the end of 2013. Reports on the current situation with screening in the country, good practices across Europe, and indicators for quality control and assurance have been prepared and published, as well as guidelines for good medical practice and screening protocols. The screening registry with a call-recall system is in the development stage, and awareness campaigns for the general public and pilot screening tests are forthcoming. According to this project, management of screening activities should be performed at the local and national levels. There should be a regional coordinator of the project at the 28 regional health inspection centers, and at the national level a managerial team of three experts should be nominated.

Croatia

In Croatia, opportunistic cervical cancer screening has been in place since the 1960s, resulting in markedly decreasing incidence and mortality trends through the 1990s. However, despite the increase in the yearly number of Pap smears in the healthcare system, no further decrease has been observed over the last two decades. Even though the cervical cancer incidence in Croatia (European age-standardized incidence rate: 12.6/100,000 in 2010) is lower than in most countries in the region, the rates are still higher than in countries with organized cervical cancer screening programs, and there are still an estimated 150 cervical cancer deaths yearly (20–22).

In 2003, a working group of the Croatian Ministry of Health was appointed to propose a national cervical cancer screening program. The proposal followed the first edition of the European guidelines for quality assurance in cervical cancer screening. The target population was all Croatian women in the age range from 25 to 64 years. The overall number of Pap smears already performed in Croatia would be enough to cover the target population in the 3-year screening intervals. Pap smears were taken by gynecologists in primary care gynecology offices. There are 35 cytology laboratories reading Pap smears in Croatia. The cytological smear is read using the Zagreb 2002 classification, which is a modification of the Bethesda 2001 classification (23). The test results are recorded and reported to the county institutes of public health.

Organization of the program at the county level was proposed, and the evaluation and monitoring would be performed at both the county level and centrally. Regarding the present costs of treatment and sick leave for cervical cancer patients, it was estimated that introducing the cervical cancer screening program in Croatia would already be cost-effective after the first decade (24).

Due to the higher burden, the Ministry of Health prioritized introduction of the national screening program for breast cancer in the end of 2006 and for colorectal cancer in 2007, whereas the launch of the national cervical cancer screening program was postponed, and was adopted by the government only on 15 July 2010. A pilot screening program was organized in Primorje–Gorski Kotar County in 2006, targeting a sample of 6,000 women in the age group 20 to 64 years. The participation rates were 35.2% in 2007 and 46.5% in 2008. The detection rate of cytological abnormalities was 4.6% (25).

At the end of 2012, the Croatian Ministry of Health launched the national cervical cancer screening program, organized by the Croatian National Institute of Public Health (www.hzjz.hr) according to the European guidelines for quality assurance in cervical cancer screening. According to the program protocol, the target age group is age 20 to 64, and the screening test is conventional Pap smear, with 3-year screening intervals. The program will start by inviting women that have not had a Pap smear taken in the last 3 years according to the health insurance fund data.

The 21 county institutes of public health keep a database of their target population and are responsible for distributing invitations (invitation letters, referrals for Pap smears, and educational leaflets) and coordinating the program at the national level. The screening registry will be kept at the Croatian National Institute of Public Health, which will also be in charge of evaluating and monitoring the program.

Czech Republic

The Czech Republic was one of the first countries in the world to use the Papanicolaou method for cytological diagnosis of atypical cervix cells, as early as 1947, and the first Czech manual on cytodiagnostics was published in 1954 (26). The data from the national cancer registry, which was established in 1976, showed a steady decline in the incidence of cervical cancer from 1960 to 1990 due to yearly preventive gynecological examinations, consisting of basic colposcopy and a Pap smear, guaranteed by the National Health Law of 1966, and due to the establishment of a system of Centers for Gynecology-Oncology Prevention in the 1980s (26).

However, since the 1990s the incidence rate has not changed substantially (European age-standardized incidence rate in 2009: 16.4/100,000) and mortality rates showed only a slight decreasing trend from 2003 to 2008 (European age-standardized mortality rate in 2009: 4.5/100,000), despite the very high frequency of screening visits that could cover the entire target population of 2.7 million women age 25 to 60. This over-screening of a minority of women, with the majority of the target population remaining under-screened due to a lack of coordination and monitoring, resulted in spending considerable resources on cervical cancer prevention, but without an appropriate effect (27). Therefore it was recommended that a nationwide, organized program be

implemented. Due to already existing laboratory infrastructure and sufficient clinical capacity through a nationwide network of gynecologists already in place, it was estimated that implementing an organized program would not require many additional resources to achieve a cost-effective reduction in the incidence of cervical cancer (27).

In January 2008, the Czech Ministry of Health launched a nationwide screening program focusing on the early detection of cervical cancer. Within the program, health insurance companies are responsible for sending invitations to all women age 25 to 60; in 2008, three out of 12 insurance companies sent out invitations, later followed by the others (2). At present, the screening interval is still 1 year (an artifact from the old opportunistic system), but future plans call for it to be extended to 3 years in women whose cytological smears are normal for 2 consecutive years (2). Before implementation of organized cervical cancer screening, there were around 50 laboratories in the country performing cytological analyses without appropriate quality control. Since 2008, stricter criteria have been used for accreditation of cytology laboratories (currently 42 accredited government-based or private laboratories) using a modified Bethesda classification. A national quality control monitoring program has been established within the organized screening program. If the cervical smear test is negative, women are recommended to attend another screening examination within a preventive checkup after 1 year; if there is any other result of the cervical smear test, the registering gynecologist is obliged to send a repeated smear or histology result to the laboratory within the next 7 months in the case of atypical squamous cells of undetermined significance or low-grade intraepithelial lesions, and within the next 4 months for any other cytology result (www.cervix.cz). If there is no second control smear or histology result recorded in the database, the laboratory sends an inquiry to the gynecologist. HPV DNA detection is recommended and reimbursed for the triage of women with borderline cytology, follow-up of women with abnormal screening cytology results and negative colposcopy/biopsy, and prediction of outcome after treatment of cervical intraepithelial neoplasia: CIN2+ (test of cure). HPV testing is performed in 30 routine government-based or private microbiology/virology laboratories and also at cytology laboratories, which regularly participate in the External Quality Assurance program (27). Even though HPV DNA detection is reimbursed for these indications, the test is expensive and not widely used by gynecologists (2).

The overall coverage within the organized cervical cancer screening program in 2008 was 48.4% (28). Compared to the previous opportunistic screening, coverage in the country seems to be increasing: the pooled data from 2004 to 2006 showed an estimated 33% coverage in women younger than 30, 35% coverage in women 30 to 59 years old, and 17% in women over 60 (2). However, to obtain a fully functioning organized screening program and to achieve a substantial impact on cervical cancer incidence and mortality rates in the Czech Republic, an increase in the coverage of the target population will be necessary.

Estonia

Cervical cancer represents a significant public health problem in Estonia because it has a very high incidence and mortality rate, which has not significantly decreased in over 25 years (29). The Estonian cancer registry collects data on all malignant neoplasms and in situ cancers. It should be noted that since 2000 the data on incidence and mortality have been influenced by a data protection act (30).

The highest crude incidence rate in the last decade, 25.8/100,000 women, was recorded in 2007 (the world age-standardized incidence rate for 2007: 18.1/100,000). Crude mortality rates gradually increased between 2000 and 2010, with an observed peak of 10.0/100,000 in 2008 (European age-standardized mortality rate for 2008: 7.5/100,000) and a similar high crude mortality rate in 2010: 9.8/100,000 (European age-standardized mortality rate for 2010: 7.3/100,000).

After pilot studies, which took place from 2003 to 2005, an organized national cervical cancer screening program started in Estonia in 2006 under the authority of the National Institute for Health Development. Screening in Estonia is a routine program, which targets all women from 30 to 59 years old with valid health insurance that have not had a smear taken in the past 12 months. The estimated size of the target population of women is approximately 286,000. A 5-year screening interval is recommended if the previous smear did not show any cytological abnormality and women are screened using conventional cytology. A modified Bethesda classification is used to evaluate cervical smears, which are read by cytotechnologists and cytopathologists.

Trained midwives take Pap smears for the program in 20 clinics around Estonia. There are seven laboratories in the country that perform cytological assessment for the screening program (31). Most of them belong to hospitals, which are owned by the local authorities, but some are private. There is no regular control-monitoring program for cytology laboratories and quality assurance was only carried out once, in 2007.

To obtain the results, women have to contact the clinic themselves. Smears taken within the organized screening program constitute less than 10% of all smears; most smears are taken outside of the organized screening program as regular checkups. These smears are also registered, but their results are not recorded. The proportion of smears taken outside the organized screening program within the target population was 50.4% in 2006 (32). There is no cervical cancer screening registry in Estonia. Therefore, an estimation of the sensitivity of the cytology smear or the estimated detection of high-grade cervical lesions is not possible. A central screening registry was planned to be established in 2012 but is currently still unavailable.

One of the main issues of the national screening program in Estonia is low coverage of the target population. The attendance rate in 2006 was 20.7%, slowly increasing to 24.4% by 2009 (30, 32). To promote participation and increase the awareness of cervical cancer prevention, the Estonian Cancer Society started annual media campaigns in 2007. A recent study concluded that women should have access to more information about cervical cancer risk factors and the screening program itself, and that the information should be personally addressed, with minorities being addressed in their own languages (31).

Implementation of organized cervical cancer screening did not decrease the volume of opportunistic screening (32). Therefore, a substantial number of smears are still taken outside the program. In order to increase the effectiveness of screening, a decrease in smears taken outside the organized screening program is mandatory. Screening availability in urban areas should be monitored.

There is also a need to establish a central electronic screening registry, which would make it easier to collect results and monitor

women with an abnormal smear. Moreover, a screening registry without restrictive data protection legislation is needed. The main obstacles for improving the efficacy of cervical cancer screening in Estonia are underfunding and division of work between many parties (33).

Hungary

Opportunistic cervical screening has a long history in Hungary; it goes back to the late 1950s (34). In 1954, a ministerial decree was issued that stated that "women over 30 need to be screened by colposcopy." Since the mid 1960s, "colposcopy completed by cytology" has become the screening tool. Increasingly more cytology laboratories (based on pathology departments) have been set up, and by early 1970 Hungary was fully covered by screening facilities. Since 1972, a system of pre-screening by trained cytotechnologists has been in place. By the end of the 1970s, sufficient capacity was in place to screen all eligible women every 3 years. In 1978, the Board of Gynecology took the initiative by declaring that "cervical screening should be an integral part of complex gynecological examination, including colposcopy and cytology." During the 1980s, a country-wide cervical screening program was declared (35). The annual number of smears analyzed exceeded one million. The clinical stages of detected cervical abnormalities have shifted favorably, and the survival time of detected and treated cancer cases has been extended, but the mortality rates have not decreased. It was officially admitted that the program had failed (36). The reason for failure was perceived to be the lack of the individual identification of women screened: only the number of smears was registered, and nobody knew who had been screened and who had never been screened. Opportunistic screening, even though very extensive, did not achieve its goal.

In the 1990s, the "close-the-gap" program cosponsored by the World Bank created a favorable policy environment for integrating organized population screening as a core function of the healthcare system in the country, and a golden opportunity presented itself for reorganizing and updating cervical screening in line with international recommendations (37). The proposal to establish evidence-based organized screening as a routine service was well received by the authorities. In 2000, responsibility for implementing, coordinating, monitoring, and evaluating the program was delegated by law to the Office of the Chief Medical Officer. In this office, a National Screening Coordination Department was established that supervises the Screening Coordination Units in the 20 counties of Hungary. Most importantly, a National Screening Registry (linked to the National Cancer Registry) has been set up, which regularly receives the list of the eligible population from the database of the Health Insurance Fund Administration, comprising personal identification data. The list is broken down by county, and is sent to county offices and primary care physicians, who are able to validate it for use as notification list for a call-and-recall screening program. Regarding the screening strategy, the recommendations by international organizations were adapted (women age 25 to 64, every 3 years, conventional Pap technique, Bethesda classification). National guidelines for quality control were issued in 2000 and reissued in 2005 (38).

The personal invitation–based, "quasi-organized" cervical screening program, started in 2003. However, the experiences of the first few years were disappointing. Between 2004 and 2010, about 3.5 million invitation letters were sent out, and 625,000 women (18%) reported back to the screening registry as having participated in screening. In the meantime, the Health Insurance Fund Administration paid for diagnostic cervical cytology almost twenty times more often, meaning that the majority of screened women received screening outside the organized program, preferably attending private clinics, which failed to report the screening tests performed.

It has been realized that this system does not work: the gynecologists have remained the gatekeepers, it was a compromise between traditional screening practice and the current state-of-the-art screening practice in which the invitees were advised to contact the gynecological services for smear-taking, and the smears were transferred to 20 designated cytology laboratories for analysis (39). The extremely low compliance rates need to be increased in the future.

Analysis of the reasons for non-acceptance showed that inconvenient access to gynecological services, particularly for women in rural areas, is the main difficulty to overcome. Therefore the system was reorganized in 2011 with the involvement of primary care personnel in smear-taking, especially district health visitors (nurses). The smears are analyzed in centralized cytology laboratories.

In order to prepare the district health visitors for the new task, education and training sessions have been provided to acquaint them with all aspects of preventing cervical cancer, and in particular smear-taking for cervical screening. After completing training in the screening program, the candidates receive a certificate from the health authorities authorizing them to carry out screening (smear-taking) activities in their localities. In 2011 and 2012, a 4-month pilot program was carried out to demonstrate the feasibility of the concept. The experiences are encouraging: smear-taking by health visitors will gradually be extended.

Latvia

Since the early 1960s, cytology screening for cervical cancer has been an important part of prevention strategies in Latvia, recommended even as a compulsory part of prevention testing from 1984 onwards. The dynamics of the incidence rates showed a steady decline from 31.7/100,000 women in 1963 to 8.9/100,000 women in 1989 (2). However, following the disintegration of the Soviet Union in 1991, major political and socio-economic changes also strongly influenced the healthcare system in Latvia; as a consequence, compulsory cervical cancer screening was terminated, the number of cytological tests performed dropped rapidly, and the incidence rates of cervical cancer started to rise again.

In 2005, cervical cancer screening was officially reintroduced in Latvia; with revision in 2007, all women age 25 to 69 were defined as the target population of the screening program, the screening interval was set at 3 years, and in addition to the overloaded GPs, who bore the entire responsibility for organizing and performing the screening examinations, the role of gynecologists and obstetricians was introduced into the program (40). However, the nature of the screening program remained opportunistic, with no further specifications regarding the organization of the program and any quality assurance. Women's lack of initiative, lack of the required services available, overloaded GPs, and lack of involvement of gynecologists and obstetricians resulted in low coverage of the target population (approximately 10% in 2005 and 2006) and no decline in cervical cancer incidence or mortality rates (2, 40).

Organized cervical cancer screening was implemented in Latvia in 2009. Currently, the Health Payment Center, which has been

reorganized as part of the National Health Service, is responsible for sending invitations to all women age 25 to 69. Cytological smears, principally performed in a 3-year interval, are read by cytopathologists and cytotechnologists at 25 government-based and private laboratories in the country. Interestingly, instead of conventional methods used in other European countries, the technique used in assessing cytological smears is the Giemsa stain in a Leishman modification, a unique historical tradition in Latvian cytology (40). At present, there is no quality control monitoring program for cytology in Latvia. Because there are no clear indications recommended for HPV testing and the test is not reimbursed, HPV testing is rarely performed. Cytological testing outside the program is still very frequent and continuously performed in parallel with the organized screening. It is too early to see any influence of organized screening on the incidence and mortality of cervical cancer; however, the results of the first round of screening (2009–2011) show encouraging trends with a substantial increase in positive response to the personal invitation letter, an increase in coverage inside the program, and increasing detection of cervical high-grade lesions and carcinoma in situ. Nevertheless, there is still room for improvement: the most urgent is implementation of quality assurance at all levels of the program in compliance with European Union recommendations. In the near future, there is a plan to modify data collection in the National Health Service database, which will allow tracing the follow-up of women with abnormal smears and linkage with other registers such as the central cancer register.

Lithuania

Lithuania has one of the highest incidences of cervical cancer. In 2000, the country had the second-highest incidence of cervical cancer in Europe (41). In 2010, the crude incidence was 28.8/100,000 (European age-standardized incidence rate: 25.2/100,000). Before the onset of the national cervical cancer screening program, cervical cancer represented more than 5% of new malignancies among women (2). The crude mortality rate in 2010 was 13.8/100,000 (European age-standardized mortality rate: 10.7/100,000).

The screening for cervical pathology in the previous decade was opportunistic. In 1993, the Ministry of Health helped establish the National Cancer Control Program. From 1993 to 1999, screening for cervical cancer was carried out in six districts throughout the country under the supervision of oncology specialists from the Lithuanian Oncology Center. There are no published data about the organization, methodology, coverage of target population, or results of this screening program. Data from the Lithuanian cancer register database showed that neither this screening system nor opportunistic screening in the remaining part of Lithuania was successful. This was mainly due to a lack of resources, absence of systematic testing, absence of quality assurance, and lack of follow-up (41).

A national screening program started in 2004 under the authority of the National Health Insurance Fund, targeting all women age 30 to 60. In 2008, the age for starting screening was lowered to 25. The recommended interval between two smears is 3 years if a previous smear did not show cytological abnormality. Data on the exact coverage of women is not available; however, the absolute numbers of women tested each year varied from 62,102 women in 2004 to 145,395 women in 2005, and the most recent data show that 101,270 women were tested in 2010.

Lithuania uses conventional Pap smears as the cervical screening test of choice, with a modified Bethesda classification used for cytological classification, which is done by cytologists, cytopathologists, and cytotechnologists. Smears taken outside the screening program are not registered. Eleven pathology laboratories in Lithuania, either privately owned or government based, have been certified to carry out analysis of cervical smears, and all of them are included in a national quality control monitoring program.

Primary healthcare centers are responsible for carrying out the invitations and performing Pap tests. Because there is only general guidance regarding the invitation procedure, there is much variation in invitation methods. For the most part, personal invitations are not sent out and GPs tend to rely on informing women about the screening when they attend their primary healthcare center. Each GP has to cover 1,500 to 2,500 women in the target population. The tests are free for women that are registered with a GP and have health insurance (2).

The effect of the organized screening has yet to be established. From 1998 to 1999, about 50% of cervical cancer cases were diagnosed at an advanced stage (III–IV) (42). After the introduction of organized screening, an increased incidence of stage I cervical cancer and CIN3/carcinoma in situ was observed, so there has been an evident impact on the rates of detection of the early stages of cancer and premalignant lesions, but changes in the incidence of stages III and IV cervical cancer were not evident in the screening group (43). There are still no clear changes in the incidence and mortality of cervical cancer in Lithuania (44). The program still carries opportunistic features because it is strongly dependent on the frequency of women visiting the GP and the activity of the GP in providing information about screening (2, 41). The lack of an organized invitation system is an important weakness of the program.

Montenegro

Montenegro started opportunistic cervical cancer screening as part of the former Yugoslavia in the 1960s. At present, every woman at a preventive gynecological examination can have a Pap smear. However, although a great number of Pap tests are done every year, many women never have a preventive examination due to the lack of an organized screening program, and therefore the cervical cancer incidence and mortality rates are higher than they should be under the current level of medical development and achievements. According to a study by Colaković et al., 550 women in Montenegro developed cervical cancer in the period from 2000 to 2007. This is 45% of all cancers affecting the female genital organs (45). In the first 5 years, the average disease rate was 19.5/100,000, but in the last 3 years it amounted to 25.6/100,000 (around 24% higher); this trend suggested significant growth in incidence rates, whereas the average mortality rate was 4.2/100,000 and very slight growth was observed (45). Almost two-thirds of the cases (64.19%) were age 40 to 59 (45).

Plans for implementing a national screening program grew stronger in 2011, when the Ministry of Health of Montenegro prepared an official proposal for implementing an organized national screening program. One of the first steps is the effort to establish a national cancer registry: so far, forms and instructions for collecting data on malignant tumors have been prepared, which will be followed by the development of an appropriate electronic database and software for data processing, monitoring the imple-

mentation of screening programs, and training medical staff for its use (46).

In May 2011, an organized pilot program was run in four municipalities in Montenegro, covering approximately 2,250 women age 20 to 65 that had not had a preventive gynecological examination at the primary level in the previous 3 years. The examination within the pilot program included a Pap test and basic colposcopy; overall, 45.0% women responded to the invitation (47). Plans for a national organized cervical cancer screening program foresee invitations to women age 25 to 64 (a population of approximately 167,000 women) with a 3-year screening interval using a conventional Pap smear. According to the proposal, the general goals are to achieve at least 50% coverage in the first 3 years after implementing the program, decrease the cervical cancer incidence rates by 50 to 60% in the first 8 years, and decrease cervical mortality rates by 50% in the first 10 years after the start of the program (47). An additional aim is to raise women's awareness about the importance of regular gynecological examinations, prepare national guidelines on management algorithms for women within the program (including appropriate HPV testing), build capacities for implementing a program, and establish a system for collecting and managing data from the national program (47). During implementation, it is necessary to improve the quality of equipment and work, increase the number of gynecology specialists at the primary level, increase the number of specialists in pathological anatomy, educate cytoscreeners, procure microscopes, colposcopes and other standardized equipment, and continue staff education (47).

Implementing an organized cervical cancer screening program at the national level was planned for 2012 in Montenegro; however, due to the current economic situation, implementation has been postponed to 2013.

Poland

Poland started opportunistic screening for cervical cancer in the 1970s. However, the programs that were implemented did not have a population-based character and they were carried out using passive prevention (48).

An increase in the incidence of cervical cancer was observed in 1970. Since the beginning of the 1980s, the incidence and mortality rates have been relatively stable with a small decreasing tendency: the crude mortality rate was 10.7/100,000 in 1978 and 10.0/100,000 in 2000. Between 2001 and 2006, the crude mortality rates oscillated between 9.2 and 9.4/100,000. These numbers show that opportunistic programs were inefficient (49, 50).

Therefore, following the example of countries with effective organized screening programs, an initiative was launched to implement a national organized screening program in Poland. Poland started organized screening in 2004; although it was carefully conceptually prepared, for the first 3 years the program was not actively used and was applied only selectively. Some modifications implemented in 2006 created an opportunity for increasing the effectiveness of cancer prevention today (51). An organized screening program is being coordinated by the central and regional coordinating centers and the Polish Gynecological Society. The entire program is monitored by the Polish Ministry of Health.

The main task of an organized screening program was to decrease the cervical cancer incidence and mortality in women by around 50% until 2015. In the National Health Program for 2007 to 2015, the main goal set is to decrease the number of deaths from cervical cancer, from 2,000 to 500 women (by 75%) (52). The main goals of the cervical cancer prevention program are: (i) detecting precancerous stages of cervical cancer (CIN), (ii) singling out high-risk groups of patients that need cytology test more often than every 3 years, (iii) creating the central database for women attending the screening program from 2005 to 2015, (iv) carrying out high-quality screening tests, (v) education and skills development for medical staff (gynecologists, cytopathologists etc.), and (vi) implementing international standards for cervical cancer prevention (www.rakszyjki.org).

Currently, the national program for early detection of cervical cancer provides cytological examination for all women between 25 and 59 that were not screened in the previous 3 years. If an abnormal cytological result is detected, the program provides for patient referral for further evaluation. According to the national guidelines, cytological smears are read by certified cytotechnologists and cytopathologists using a modified Bethesda classification.

To encourage and inform women about cytological examinations, coordinating centers send invitations to women that have not yet been registered in the database or that were not screened in the previous 3 years. The coverage in the target population of approximately 9 million women (about 3.3 million should be screened every year) averaged 21% in 2007, and reached about 27% in 2009 and 2010 (53). Among all cytological smears taken from the beginning of 2007 to September 2010, the proportion of abnormal cytological results was 2.6%. The proportion of inadequate smears oscillated between 0.78 and 1.14%. Unfortunately, among patients with abnormal cytology results, only 12.6% of women were referred for further evaluation (54, 55).

Despite the low attendance of women in screening programs, many cytological examinations are performed outside the screening programs, at private clinics. However, these cytology examinations are not registered by the national program systems. Consequently, in Poland around 3,200 women are still diagnosed with cervical cancer each year and nearly 1,800 die (data from 2010). Compared to the countries of the pre-2004 European Union, where the mortality rate is 1.6/100,000, Poland has one of the highest mortality rates in Europe, about 8.7/100,000 women (49). Data for 5-year survival after disease diagnosis are also alarming; this rate is 48.2% in Poland, compared to the Czech Republic or Sweden, where the survival rates are 63.3% and 69.6%, respectively (53).

HPV DNA testing is available only at private clinics and laboratories because there are no public funds for them. In 2008, guidelines for management of abnormal Pap smears were prepared, in which DNA and mRNA HPV tests were listed as diagnostic tools for verifying abnormal cytology results (54).

Due to the lack of a complex prevention strategy that would effectively apply to all areas of cervical cancer prevention, there are currently no institutions responsible for realization of all the HPV prevention tasks. To improve the screening program, the Polish Gynecological Society and the Polish Gynecological Oncology Society, with the cooperation of the MSD Foundation, created the Polish Coalition against Cervical Cancer in May 2011. The main aim of this coalition is to prepare a complex health program whose implementation will improve cervical cancer prevention in Poland. In 2012, the coalition created a codex and recommendations for changes in cervical cancer prevention that apply to education, primary prophylaxis (HPV vaccination), secondary prevention (cytology), financing, and registration.

In conclusion, implementation of an organized cervical cancer

screening program in Poland has not yet substantially reduced cervical cancer incidence or mortality. The aim of a 50% reduction in mortality by 2015 was shown to be unrealistic; therefore this was extended to 2020. In the meantime, many changes need to be made in the program.

Romania

Romania has one of the highest cervical cancer incidences and mortality rates in Europe. In 2000 the age-standardized incidence rate was 24.6/100,000, and the highest age-standardized mortality rate in the last decade was 11.5/100,000 in 2002. In the last decade, the incidence of cervical cancer in the country ranked second among various female malignancies, after breast cancer, and its mortality ranked third, after breast and colorectal cancer.

Opportunistic screening has been carried out at the national level in Romania since 1965. Before 1990, on average 800,000 smears were performed every year, in an opportunistic manner, discovering 2,400 new cases. After 1990, the number of smears decreased to 170,000 in 2006, for 3,000 new cases of cervical cancer diagnosed. The number of tests performed was low, lacking quality control in diagnosis, treatment, and follow-up (2, 56).

Altogether 187 laboratories, both government-based and private, perform cytological assessment in Romania. There is a national quality-control monitoring program for cytology laboratories, but it is available only for those that have contractual relations with the Health Insurance Agency (the vast majority in the country), for which the internal and external quality control is required. Conventional Pap smear and liquid-based cytology are used as cervical screening tests. Evaluation of smears is done using the Bethesda version 2 classification. The cytological smears are evaluated by cytologists, pathologists, biologists, and clinical laboratory physicians.

Between 1998 and 2001, feasibility studies were conducted for Cluj County and other counties of the northwestern region. One feasibility pilot focused on resources, networking laboratories with gynecological units, test quality, and the response to invitations that were sent to women age 25 to 64 in Cluj-Napoca.

In 2002, the Cancer Commission of the Ministry of Health decided to launch a regional population-based pilot cervical cancer screening program in Cluj County. The pilot program targeted all eligible generations of women 25 to 64 years old. A 3-year interval between two smears was recommended for those that screened negative. The estimated number of target population was approximately 200,000, which represents 3% of the entire female target population in Romania. The global coverage from 2002 to 2006 was 18.4%, due to limited funds allocated by the Ministry of Health. From 2004 onwards, the program was extended regionally to several other districts (57). Since 2006, the Cluj County screening program has been connected to the European Network for Information on Cancer (2).

A Screening Management Unit was founded for this purpose in the Department of Cancer Prevention and Control at the Ion Chiricuţă Institute of Oncology. It is linked to a regional cancer registry and has been a member of the European Network of Cancer Registries since 2003.

The period of the pilot program was too short to register a decrease in the incidence of cervical cancer in Cluj County. The crude incidence rate in 2002 was 30.39/100,000 and 31.68/100,000 in 2006. The crude mortality rate decreased from 15.76/100,000 in 2002 to 14.3/100,000 in 2006 and to 11.16/100,000 in 2008, although it should be noted that the decrease in mortality is skewed due to the inclusion of a number of deaths from other counties.

Some of the main effects of the 2002–2008 pilot screening were: (i) screening management unit experience with trained experts, (ii) a screening network with quality assurance and control of tests and treatment, (iii) a cancer registry, screening, and dysplasia registry for monitoring, and (iv) quality control guidelines, training, and protocols.

Difficulties regarding the organized screening program appeared at many levels: in the organization of the management unit and the implementation unit network, in training people in screening management, in setting standards and criteria, and in the protocols for the cytology laboratories, colposcopies, and treatment units (58, 59).

In 2008 Romania started planning the national rollout of a pilot project. On 11 November 2011, the Ministry of Health signed a certificate for the first national organized cervical screening program, which started in 2012. It is based in eight regions managed by eight regional management units, one of them in Cluj County, continuing the 2002–2008 pilot program.

In the first 4 months of the national organized cervical screening, 10 screening networks were conducted in the northwestern region of the country by 10 hospitals with 1,060 family doctors (70.9% of 1,495 in total), 179 gynecologists, 42 gynecology outpatient clinics, and 50 cytopathologists in 28 laboratories. A total of 31,721 tests were carried out from September to December 2012 and the regional response rate to invitations was 62.4%.

Strategies in 2013 are focused on improving management resources in regions and completing implementing resources, with better coverage and proper quality control at all levels. One of the future plans to modify the cervical cancer-screening program is the introduction of HPV co-testing.

Serbia

Cervical cancer is the second most common female malignancy in Serbia, after breast cancer. In 2002, it was the fourth-leading cause of cancer deaths, with 452 deaths and an age-standardized mortality rate of 7.2/100,000 women. With 1,089 new cases registered and an age-standardized incidence rate of 27.2/100,000 women, Central Serbia had the highest incidence of cervical cancer compared with other European countries (60).

A comprehensive, centralized screening program for cervical cancer has never been implemented in Serbia. Cervical cancer prevention has relied on opportunistic screening. This type of screening has been characterized by high coverage in younger women, and by low coverage in middle-aged and older women. Screening of selected groups of women employed at large companies is performed annually by many regional hospitals. This approach, however, has had little effect on morbidity and mortality (61).

In spite of some efforts to initiate screening between 1990 and 1999, the difficult situation in the country did not enable a more organized approach. Since the beginning of 2000, a number of pilot projects have been undertaken and the results were used to develop a national program for organized cervical cancer screening. The program was finalized in 2007 and approved by the Serbian government in May 2008 (62). The preparatory activities have been completed, and cervical screening is now being implemented. Invitations had not yet been issued at the time of writing this article, but the program will be launched in the very near future in order to cover all women age 25 to 65 throughout Serbia. Ap-

proximately 2.300,000 women will be invited for a Pap smear over a period of 3 years.

The program will be run on an organized, decentralized model. The main advantages are the network of primary healthcare units across Serbia, involving more than 500 gynecologists, a coordinated system of public health services, and a well-developed colposcopy service. The major disadvantage of the program is an inherited system of cytology reporting performed by gynecologists trained in cytology and an insufficient number of pathologists with a sub-specialization in cytology. This means that the two important professional groups are lacking: cytotechnologists and pathologists with a sub-specialization in cytology. Overcoming this obstacle and ensuring a quality control system will be the major challenge of organized cervical cancer screening in Serbia. Until new staff are trained in cytoscreening, gynecologists with more than 15 years of experience in cytology and with at least 2,000 cytological examinations per year will function as cytotechnologists. The re-education of this group has already started, and one of the most difficult parts of this process appeared to be the shift to the Bethesda system from the standard Papanicolau cytological reporting. It is also planned for cytological assessment of Pap smears to be performed at 15 accredited laboratories. At the moment, cytological assessment is still performed at more than 120 laboratories without the appropriate quality control (63).

The most recent period, even before the actual implementation of the screening, has been characterized by largely increased awareness of women, medical professionals, and decision-making politicians about the importance of cervical cancer screening. As a result, the incidence of cervical cancer has been steadily decreasing during the last few years: according to the last available data from GLOBOCAN 2008, it now amounts to 20.1/100,000 women (64).

Slovakia

Opportunistic screening as part of regular gynecological practice for women attending gynecological examinations has been in place in Slovakia since 1980. Despite the fact that a great number of smears are taken within the opportunistic screening program, sufficient to cover every woman age 18 to 70, in reality only a minor proportion of women actually have at least one preventive cytological examination every 2 to 3 years. Currently, each woman age 23 to 64 is offered a conventional Pap smear once every 3 years, after two initially negative smears taken in a 1-year period. The coverage in the target population of approximately 2.1 million women is currently approximately 17 to 20%.

The period from 1968 to 2006 showed a stabilized trend in cervical cancer incidence, with an estimated average annual change of −0.008/100,000 (95% CI = −0.048 to 0.032, p = 0.689) and a moderately increasing trend in mortality with average annual increase of 0.049/100,000 (95% CI = 0.033 to 0.065, p < 0.0001); in 2003–2006, the cumulative risk of disease (0–74 years) averaged 1.5%, the cumulative risk of death reached 0.5% (65). According to data from the national cancer registry, the crude incidence rate in 2006 was 19.0/100,000 (world age-standardized incidence rate: 14.1/100,000). The crude mortality rate for 2008 was 7.5/100,000 (world age-standardized mortality rate: 4.8/100,000). The analyses of clinical stages from 1978 to 2003 showed that the number of cases in clinical stage I increased, the stage II rate declined, and the numbers of cases in stages III and IV were still high, with a rising tendency (65). In comparison to other European countries, these trends are unfavorable and the findings have confirmed the necessity of immediate introduction of organized screening in Slovakia (65). Furthermore, an increase in the incidence of invasive cervical cancer has been observed especially in younger age groups.

These data show the inefficiency of opportunistic screening and the need for effectively organized screening programs. However, this activity is linked to the national oncology program, which has still not been adopted by stakeholders and the government. Slovakia lacks a national screening registry of all cytological smears provided by participating cytology laboratories in electronic form. A special regulation has been published with quality standards for cytopathology laboratories and guidelines for managing premalignant lesions, and so equal management can be provided in any region. In general, there are 16 private and state laboratories performing cytological assessment in Slovakia; cytological smears are read by certified cytotechnologists, gynecologists, and cytopathologists, using a modified Bethesda classification.

HPV testing was included in the national screening program in 2009. National guidelines were published in 2010 with algorithms for HPV testing for triage of women with borderline cytology (atypical squamous cells of undetermined significance and atypical glandular cells), triage of women with CIN1, and prediction of outcome after treatment of CIN2+ (test of cure). Gynecologists are fully reimbursed for these indications. Currently, HPV testing is performed in government-based or private laboratories using the same clinically validated HPV DNA test.

In conclusion, the implementation of cytology laboratories offers the possibility of covering the entire target population for Pap screening; however, due to the absence of a national screening program and women's attitudes there is still low coverage of the screened population. This situation is reflected in still high incidence of cervical cancer in Slovakia.

Slovenia

Slovenia started opportunistic screening in 1960 as a part of regular gynecological practice in women attending preventive gynecological exams. Although enough smears were taken to examine every woman age 20 to 64, in reality less than half of the women actually had at least one gynecological exam every 3 years (66). From the end of the 1970s until 1993, the incidence of cervical cancer has been relatively stable, followed by a substantial increase with a peak in 1997 (European age-standardized incidence rate for 1997: 21.7/100,000), which placed Slovenia in the upper third of European countries regarding the incidence of cervical cancer. Furthermore, an increase in the incidence of invasive cervical cancer has been observed especially in younger age groups.

Due to the inefficiency of opportunistic screening and based on experience from countries with established and effectively organized screening programs, an initiative was launched to implement a national organized screening program in Slovenia. After an initial pilot study from 1998 to 2001, a national screening registry linked to the Central Population Registry of Slovenia was established (2, 66). This computerized information system has enabled the centralized registration of all cytological smears provided by participating cytology laboratories in electronic form, identification of non-attendees, and sending invitations to women that had not yet been registered with a gynecologist or had not been screened in the previous 5 years (2, 66). In addition, complete screening activity and screening quality is monitored through the

screening registry. A special regulation with quality standards for cytopathology laboratories was published, and compliance with the standards was reviewed at all laboratories (66). In general, all 10 laboratories performing cytological assessment in Slovenia are government-based and cytological smears are read by certified cytotechnologists and cytopathologists, using a modified Bethesda classification. National guidelines for quality assurance and control of all procedures were published at the beginning of the program, and the national screening policy and management of women with abnormal smears was precisely defined.

In 2003, a national organized cervical cancer screening program named ZORA was fully implemented. Currently, each woman 20 to 64 years old is invited to perform a conventional Pap smear once every 3 years (details below), after two initially negative smears taken in a 1-year period. The coverage in the target population of approximately 630,000 women exceeded 70% from 2006 onwards, and reached 81.2% in the first 5 years after implementation of the screening program (from 2004 to 2008) (67). As a consequence of successfully implementing an organized screening program, the incidence of cervical cancer in Slovenia decreased from 210 cases in 2003 (European age-standardized incidence rate: 18.8/100,000) to 130 cases in 2009 (European age-standardized incidence rate: 10.9/100,000) (a nearly 40% decrease); cervical cancer mortality ranged between 40 and 50 cases per year (www.slora.si).

In general, a substantial proportion of women have a regular gynecological exam at least once every 3 years and have a regular Pap smear on this occasion. Those that do not have a regular exam at their own initiative are invited by their gynecologists and, if there is no response, they receive an official written invitation from ZORA in the 4th year. If there is still no response from a non-attending woman and no Pap smear is recorded in the central system, a second invitation is sent 9 months later (67). In addition, ZORA sends inquiries to gynecologists regarding women with pathological screening smears, if there is no second control smear recorded in the database in the next 6 months, in order to remind gynecologists to adhere to the guidelines (67). Among approximately 260,000 cytological smears performed annually, the proportion of smears with borderline or abnormal cytology detected as part of the screening program in 2010 was 5.7%. The proportion of inadequate smears was 0.3% (67). In 2010, the national screening program was upgraded with the inclusion of HPV testing. In 2011, new national guidelines were published with algorithms for HPV testing for the following indications: (i) triage of women with borderline cytology (atypical squamous cells of undetermined significance and atypical glandular cells), (ii) triage of women over 35 with low-grade intraepithelial lesions, (iii) triage of women with CIN1, and (iv) prediction of outcome after treatment of CIN2+ (test of cure) (68). HPV testing is only performed at two certified government-based laboratories using the same clinically validated HPV DNA test, and gynecologists are fully reimbursed for HPV testing for these indications.

In conclusion, with the implementation of an organized cervical cancer screening program, Slovenia has achieved a substantial reduction in the cervical cancer incidence in a relatively short period of time. In addition, a further decline in HPV-related tumors is expected in the future due to the implementation of HPV vaccination within the national immunization program.

The Former Yugoslav Republic of Macedonia

The former Yugoslav Republic (FYR) of Macedonia has run an opportunistic cervical cancer screening since 1967. Although the coverage of the target population of approximately 580,000 women has been relatively low (estimated on 15–25%), a positive impact of screening was observed at the end of the 1990s when the ratio between invasive and precancerous lesions diagnosed in women has changed in favour of the latter. However, a great amount of money is spent on opportunistic screening with unsatisfactory results regarding overall coverage and cervical cancer incidence rates.

At present, there is no national or regional cancer registry. The crude incidence rates from 2000 to 2007 ranged between 20.9/100,000 (year 2002) to 38.0/100,000 (year 2001). Every year around 40 to 50 women die from cervical cancer (crude mortality rates range 4–5/100,000); in most cases death occurs in older age, but it is necessary to emphasize that the very high death rate from this disease is observed also in women age between 45 and 54 (about 13 per 100,000 women) (69). Cervical cancer ranks as the 3rd most frequent cancer among women in the FYR Macedonia and the 2nd most frequent cancer among women between 15 and 44 (70). The current screening policy which predicts a 3-year screening interval among women age 19 to 65, does not provide any decline in the incidence rates. The type of screening test used in the FYR Macedonia is not uniform: 80% of the testing is done with a conventional Pap smear, and 20% with liquid-based cytology. Cytotechnologists and cytopathologists at 12 government-based or private cytology laboratories use modified Bethesda classification to evaluate cervical smears; however, there is no quality control monitoring program for cytology laboratories in the country. Women with borderline or abnormal cytology results undergo HPV testing and colposcopy if they are HPV positive. The proportion of smears with abnormal cytology result in 2007 was fairly high, approximately 18–20%. Recommended and reimbursed indication for HPV testing in addition to borderline and low-grade cytology is also prediction of the outcome after treatment of CIN2+ (test of cure). HPV testing is performed in government-based or private microbiology/virology laboratories, mostly by in-house PCR tests.

There is an obvious need to establish a national organized cervical cancer screening program in the FYR Macedonia. A large amount of money is currently spent on opportunistic screening; however, the outcome of this approach is disappointing in a view of a low coverage rates and high cervical cancer incidence rates. The main reasons for these problems are lack of awareness of effective cancer prevention measures, lack of priorities within public health institutions, local government involvement in activities that promote women's health, non-compliance of the order of using the services of various healthcare levels in the FYR Macedonia, insufficient training of staff to implement screening, lack of necessary equipment and information system support, and lack of sufficient funding for national organized screening program (69). The encouraging news is that an initiative has been launched to reorganize the national screening program and to switch from opportunistic to organized screening based on a conventional Pap smear. This reorganization is predicted for 2015. So far, The Ministry of Health set up a coordinating body with the principle task of preparing a draft action plan for implementing organized screening and offering suggestions for the national program. In 2011, a pilot program was run in four municipalities of the FYR Macedonia (69). However, much work needs to be done in the near future, starting with establishment of a national cancer registry, a population-based cervical cancer screening registry, a

computerized information system, education of the cytoscreeners, preparation of national guidelines for managing women included in the screening program, and quality control programs.

Conclusions

This article describes the current situation of cervical cancer screening programs, organizational plans for the future, and the main obstacles that need to be overcome in 16 countries in central and eastern Europe. Unfortunately, only a few countries have managed to establish an organized and well-functioning cervical cancer screening program in the past years, whereas most of the countries in the region are still struggling with the problems of early and preparatory stages of implementing organized cervical cancer screening. Encouragingly, even in the countries where only opportunistic screening is performed, well-prepared plans and strategies have been established for switching to organized screening in the near future.

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