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Cervical cancer screening in Latvia: A brief history and recent improvements (2009–2011)

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Abstract

Screening for cervical cancer (CC) has been an important part of prevention strategies in Latvia since the early 1960s, reducing its incidence from 31.7/100,000 women in 1963 to 8.9/100,000 in 1989. Political and socioeconomic changes after 1991 greatly affected the entire healthcare system, including CC screening, which was temporarily suspended. In 2005, CC screening targeting all women 25 to 69 years old was officially reintroduced in Latvia, with revision in 2007. However, the nature of the screening program remained opportunistic. The inactivity of women, lack of availability of the required services, overloaded general practitioners, and lack of involvement of gynecologists and obstetricians resulted in low coverage of the target population (10% in 2005–2006). Organized screening was finally implemented in Latvia in 2009. Currently, the national Health Payment Center is responsible for inviting women for screening. Cytological smears, principally performed in a 3-year interval, are read by cytopathologists and cytotechnologists at 25 government-based and private laboratories. Cytological testing outside the program is still very frequent and performed on an ongoing basis in parallel with the organized screening. The results of the first round of screening (2009–2011) show encouraging trends, with a stepwise increase in positive responses to the invitation letter, an increase in coverage inside the program, and increasing detection of cervical high-grade lesions and carcinoma in situ. Unfortunately there is still no cytology quality control monitoring in place, and there are no clear recommendations for human papillomavirus (HPV) testing. Because HPV testing is not reimbursed, it is rarely performed.

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Introduction

Over the past two decades, Latvia has undergone major political, social, and economic changes. Latvia was part of the USSR from 1940 to 1991, and its healthcare system was similar to that of other Soviet republics. The Soviet healthcare system was funded from the state budget and claimed to provide health services free of charge to the entire population. After independence in 1991, Latvia became an open market economy country, but healthcare was not completely transformed from a centralized, state-controlled system into a decentralized health insurance–based system, and it is still being reorganized (1).

Cervical Cancer Screening: 1960–1989

In Latvia, there is a longstanding tradition of early diagnosis of cervical cancer (CC) (1–3). As early as the 1930s, there was a well-established morphology school and trained workforce in Latvia, but cytological methods were introduced into routine practice only after the Second World War. The use of cytological testing has been more widespread since the early 1960s, facilitating the propagation of cytology within the laboratories of Latvian healthcare institutions. Standardized cytological forms were created for dispatching material for examination, as well as for reporting the results. Several issues of newsletters and methodology recommendations have been published concerning standardization of all aspects of cytological testing and cytology classification (2, 3). Within the first 10 years, a vigorous cytology tradition was already established in the country, featuring several outstanding specialists in the field. Screening yielded important results already in the first few years after introduction: CC incidence decreased from 31.7 cases per 100,000 women in 1963 to 26.5 cases per 100,000 women in 1968. From 1976 to 1978, the incidence rate was further reduced to 23 cases per 100,000. In 1984, the incidence was 16.8 and in 1992 it was 11.9 cases per 100,000 women, and the lowest number of CC cases was observed in 1989: 8.9 cases per 100,000 women.

From 1970 to 1978, 2.5 million women were cytologically tested as a part of preventive gynecological examinations (3). After 1978, the extent of preventive examinations increased even more. In the early 1980s, this included complex and periodic population-based examinations, both organized and unorganized, and individual testing for people that sought any help at health centers and hospitals. Starting in 1983, preventive gynecological examinations with cytological testing were available for all women age 18 and over. In 1984, cytological screening became compulsory, as part of the broader system for the prevention and treatment of disease for all citizens, known as the "complex computerized population medical examination system". In 1989, compulsory cytological screening was terminated due to political and economic changes.

Opportunistic Cervical Cancer Screening: 1991–2008

After the political and economic changes in Latvia, the number of preventive medical checkups and their effectiveness, including CC screening, declined substantially. As a result, the incidence of CC started to rise again, reaching 18.4 cases per 100,000 women in 2004. According to Appendix 2 of the Preventive Checkups Program (Regulation no. 1036 of the Cabinet of Ministers of Latvia Healthcare Organization and Financing Procedure, issued on 21 December 2004), 1 April 2005 was declared the date of the official reintroduction of CC screening in Latvia. According to the

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regulation, all women 20 to 35 years old should be screened annually; if the result is normal, the smear is repeated every 3 years. For women 35 to 69 years old, annual screening is recommended. Although this regulation was meant to be the basis of an effective CC screening program in Latvia, regrettably, from the historical perspective, it is clear that the cabinet of ministers' regulation was only a declaration because none of the basic components of the organized screening program were implemented (4, 5). The main responsibility for performing CC screening was placed on the shoulders of the general practitioners (GP), who were responsible for disseminating information, explaining the importance of the screening, interpreting the cytological results, and potential referral. The centralized screening register and register of cytological results have not been created. Fortunately, this solution soon came to be seen as unacceptable, also with assistance from outside experts. Appendix 5 of the Preventive Checkups Program (of 19 December 2006, Regulation no. 1046, Procedure for Organization and Financing of Healthcare) finally clearly stated that the CC screening program should be organized in compliance with European Parliament recommendations: all women 25 to 69 years old should be screened for CC every 3 years. The regulation also finally involved gynecologists and obstetricians in the screening program and defined their role. In addition, in 2007, the cabinet of ministers and the Ministry of Health created two working groups of experts: the first consisted of representatives from ministries and municipalities, as well as medical doctors, specialists, and representatives of non-governmental organizations. The second consisted of representatives of key medical specialists' associations with the common aim of analyzing the situation regarding preventable cancers in Latvia and providing acceptable solutions to improve the situation. Both working groups agreed that acceptable and durable control of preventable cancers in Latvia can be achieved only by implementing organized cancer screening, including organized screening for CC.

Organized Cervical Cancer Screening: 2009-2011

Organized CC screening in Latvia started in January 2009. It finally identified a comprehensive and optimal target group of residents for CC screening and enabled extensive opportunities for each healthcare provider willing to take part in the screening. Currently, the national Health Payment Center *(Veselības norēķinu centrs)*, which has been reorganized as the part of the National Health Service *(Nacionālais veselības dienests)*, is responsible for sending invitations to all women 25 to 69 years old, representing a total target population of 707,460 women. Screening is principally performed in a 3-year interval.

GPs that have contracts with the National Health Service have access to the special screening module in the management information system, which is a central data repository of the National Health Service. The central screening database contains all relevant information on the women eligible for screening and registered with the particular healthcare provider: the date when the invitation was sent out, the reference number of the invitation, the screening date, and the test results. Regular monitoring of the central screening register allows GPs and their assistants or nurses to easily identify all women for whom screening invitations were issued but who have no test results. By identifying and actively contacting non-responding women, the GP can determine the reasons and encourage the women to respond to the screening invitation. If a woman visits the GP due to any medical condition and has no screening result recorded in the register, the GP can take cytological smears (if conditions in the practice allow), but must contact the National Health Service and request an invitation letter and screening examination form electronically. Gynecologists or obstetricians, who are now also involved in screening, act similarly, and they can use any visit (e.g., for birth control counseling) to encourage women to have cytological testing. All participating cytological laboratories must also enter the screening results in the screening module in the management information system. According to Regulation no. 1046 (Procedure for Organization and Financing of Healthcare, issued on 19 December 2006), all screening procedures are fully reimbursed, including taking the smear, cytological testing, and all subsequent examinations and procedures according to the approved algorithm shown in Figure 1. If performed for inpatients, the entire cost of screening is excluded from hospitalization costs.

Cytological smears are read by cytopathologists and cytotechnologists at 25 government-based and private laboratories distributed throughout the entire country. Instead of the conventional methods used in other European countries, the technique used in assessing cytological smears is Giemsa stain in Leishman modification, a unique historical tradition in Latvian cytology (3). A seven-category coding system is used for smear evaluation: C0: uncertain result due to insufficient material or erythrocytes covering the majority of the smear; C1: normal cervical mucosa cells; C2: normal cervical mucosa cells with signs of inflammation; C3: low-grade lesion (LSIL, CIN1); C4: high-grade lesion (HSIL, CIN2/CIN3); C5: cervical cancer cells; and C6: uncertain result due to technical problems or a broken slide. The approved screening algorithm according to different cytological categories is summarized in Figure 1.

Since January 2011, all cytological results within the program (paid from the state budget) and outside the program (paid from the state budget or by the woman herself) have been classified and coded in the same manner. Unfortunately, only results of cytological testing paid from the state budget are available in the screening module in the management information system. In addition, the results of colposcopy and histology findings are not recorded on a routine basis in the management information system; only results of the colposcopy paid from the state budget are currently available in the database.

The results obtained in the first round of organized CC screening in Latvia (2009–2011) are summarized in Tables 1–4. Although it is too early to see any influence of organized screening on the incidence and mortality of CC, some encouraging trends are already visible: there has been a substantial increase in positive responses to the invitation letter, an increase in coverage inside the program, and an increase in the number of diagnosed CIN2+ lesions, including carcinoma in situ, in comparison to invasive CC (Tables 1–4). Unfortunately, cytological testing outside the program is still very frequent and continuously performed in parallel with the organized screening, and no cytology quality control monitoring is in place. In addition, there are no clear recommendations for human papillomavirus (HPV) testing. Because HPV testing is not reimbursed, it is rarely performed at present.

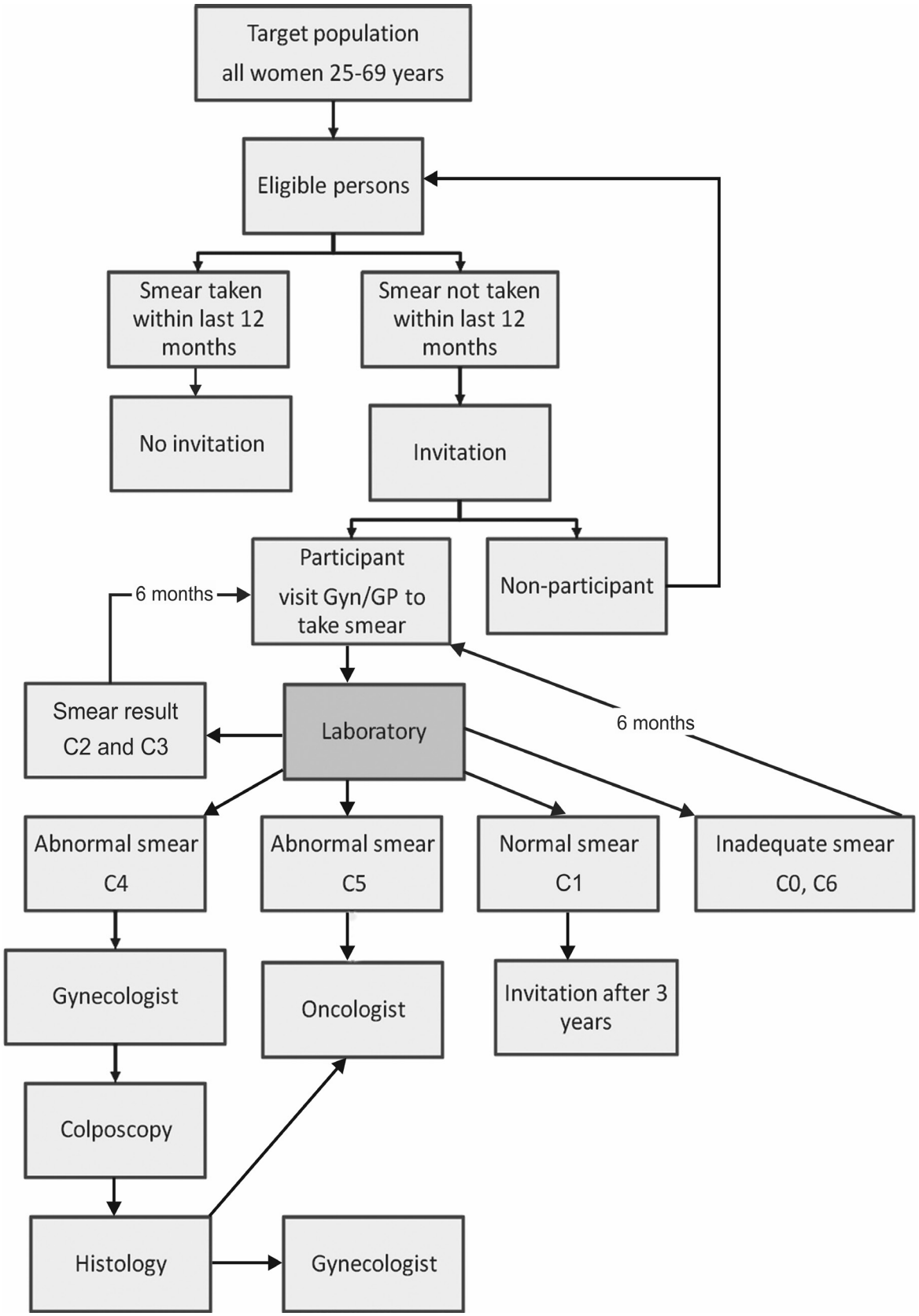

Figure 1 |Current algorithm for management of women involved in organized cervical cancer screening in Latvia. C0: uncertain result due to insufficient material or erythrocytes covering the majority of the smear; C1: normal cervical mucosa cells; C2: normal cervical mucosa cells with signs of inflammation; C3: low-grade lesion (LSIL, CIN1); C4: high-grade lesion (HSIL, CIN2/CIN3); C5: cervical cancer cells; C6: uncertain result due to technical problems or a broken slide.

Table 1 | **Screening uptake of the target group (women age 25–69) during the first round of organized cervical carcinoma screening in Latvia: 2009–2011. (Source: Latvian National Health Service database).**

Indicator	2009	2010	2011
Invitation letters sent out (n)	208,359	224,657	181,808
Women that responded to the invitation (n)	30,942	34,468	62,796
Smears taken (inside and outside program, n)	223,252	225,268	206,846
Screening coverage (%)	14.9	15.3	34.5

Table 2 | **Distribution of cytological findings using a seven-category coding system for smear evaluation among the target group (women age 25–69) during the first round of organized cervical carcinoma screening in Latvia: 2009–2011. C0: uncertain result due to insufficient material or erythrocytes covering the majority of the smear; C1: normal cervical mucosa cells; C2: normal cervical mucosa cells with signs of inflammation; C3: low-grade lesion (LSIL, CIN1); C4: high-grade lesion (HSIL, CIN2/CIN3); C5: cervical cancer cells; C6: uncertain result due to technical problems or a broken slide. (Source: Latvian National Health Service database).**

Cytology category	2009	2010	2011
C0	436	536	573
C1	15,456	17,414	32,326
C2	14,316	15,695	28,667
C3	632	642	960
C4	98	145	253
C5	3	5	16
C6	1	4	1

Table 3 | **Newly registered cases of cervical carcinoma among the target group (women age 25–69) during the first round of organized screening in Latvia: 2009–2011. (Source: Latvian National Health Service database, Latvian National Cancer Register).**

Diagnosis	2009	2010	2011
C53: Cervical carcinoma (number/relative incidence per 100,000 women)	221/19.0	252/21.1	250/23.4
D06: Cervical carcinoma in situ (n)	72	195	112

Table 4 | **Newly registered cases of cervical carcinoma among the target group (women age 25–69) during the first round of organized screening in Latvia: 2009–2010 by stage. (Source: Latvian National Health Service database, Latvian National Cancer Register).**

C53 stage	2009	2010
0	2	3
I	68	86
II	31	35
III	54	68
IV	23	43
Unknown	43	14

HPV Vaccination in Latvia

In September 2010, vaccination with bivalent HPV vaccine was integrated into the national immunization schedule. Routine HPV vaccination is provided free of charge to 12-year-old girls. A catch-up program has not been implemented. According to data from a vaccination monitoring system, the coverage for one dose in Latvia increased from 47.4% in 2010 to 61.4% in 2011, and was 58.7% in 2012. Vaccination coverage for three doses was 60.6% in 2011 and 53.4% in 2012.

Conclusions

In conclusion, an organized CC screening program was launched in Latvia in 2009, but not all components of organized screening are operational yet. The results of the first round of screening (2009–2011) show encouraging trends, with a stepwise 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 recommendations (1). HPV testing with clinically validated tests (6) should also be incorporated into patient management as soon as possible for at least two clinical applications: (i) as a triage test to select women whose cytology is equivocal or mildly abnormal and who need referral for diagnosis and treatment, and (ii) as a follow-up test for women treated for high-grade CIN with local ablative or excisional therapy to predict cure or failure of treatment (7). In the near future, there is a plan to modify data collection in the National Health Service database that will allow tracing the follow-up of women with abnormal smears, and linkage with other registers such as the Central Cancer Register.
We strongly believe that recent implementation of CC screening and vaccination against HPV will substantially reduce the incidence and mortality of CC in Latvia in the coming decade and create a solid background for CC to become a rare disease in this part of Europe.

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