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## Description of the national situation of cervical cancer screening in the member states of the European Union <sup>☆</sup>

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### ABSTRACT

This report up-dates information on the national situation of cervical cancer screening in the member states of the European Union. There is yet high diversity in the status of cervical screening, and rapid changes expected to occur in the situation in many countries. It is important to underline differences in the health care and other components in order to allow a proper interpretation of the summary results published elsewhere in this Special Issue. The brief national descriptions along with up-dated information on the recent references are available from all but one member states.

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## 1. Introduction

This report up-dates information on the national situation of cervical cancer screening in the member states of the European Union. Given the high diversity of the status of cervical screening in European countries as well as rapid changes in the situation in many countries, it is difficult to summarise all essential aspects in a few quantitative parameters available for the summary papers among the member states.<sup>1–6</sup>

It is important to underline differences of the healthcare systems, in the action models and historical availability of organised screening, leading to peculiarities of each country in order to allow a correct interpretation of the summary results. Involvement and role of various medical disciplines (pathology, gynaecology, GP, epidemiology, public health) vary meaningfully between the programmes, affecting the organisation of the programmes. The data presented are also relevant for the national decision-making on screening. The brief national

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descriptions along with up-dated information on the recent references are available from all but one member states.

## Austria

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Screening for cervical cancer started in Austria during the 1950s. Screening cytology on a larger scale followed during the 1970s.<sup>7</sup> Up to now the screening is opportunistic in eight of the nine Austrian federal states. In the Vorarlberg (4.3% of the female population), screening for cervical cancer is organised by one central institution. On the national level, screening is not population based as of yet. Smear taking is recommended annually, combined with a gynaecological examination. Expenses are covered by health insurances for women aged 19 years and older.<sup>8</sup> HPV-vaccination is recommended before the age of sexual activity.<sup>9</sup>

Recently, PAP screening data were collected from eight federal states. Based on information available from the social insurance company covering 98% of the population on a compulsory basis, data show differences due to the observation period chosen, region and age. Based on a single year observation (2003–2004), 27% of the target population used the opportunity of a gynaecocytological check. Within 3 years (observation period 2003–2006), 47% of the target female population had a PAP smear. Within the 3-year period the highest participation rate was 75%, seen in women 20–29 years of age. Only 57% of women aged between 50 and 59 years had a PAP smear within the same period.<sup>10</sup> Data on age dependence correspond to those given previously.<sup>11</sup>

Cervical smears are predominantly taken by gynaecologists but sometimes by general practitioners or medical doctors of outpatient clinics. The present screening situation results in about 1.5 million conventional smears, annually. Cytological evaluation of these smears is carried out in hospital and private laboratories. Licensed (cyto)-pathologists are responsible for the reports. The Austrian Societies of Cytology and of Pathology have published quality recommendations for structural conditions, processing features and the validation of results in laboratories for diagnostic cytology. The catalogue includes recommendations for the personal staff and the technical equipment.<sup>12</sup>

In 1998 a voluntary quality assurance programme was introduced by the Austrian Society of Cytology, based on comparison of the reports given by the participating laboratories. Collected data demonstrated that correlation with histology shows a low false positive rate, but adequacy of smears is inappropriate in a high percentage.<sup>13</sup> Now there are ongoing efforts to improve the quality of smears by the undertaking of an intensive search for those instruments which are best for the smear taker. Due to funding policy, liquid based cytology is not common in Austria.

Cervical cancer mortality rate has been reduced by about 50% since 1980 and to a third since 1960.<sup>7</sup> In 2004, 164 deaths from cervical cancer were documented (aged standardised rate 2.2).<sup>14</sup> At the beginning of 2008 an expert committee

was established by the Austrian Federal Bureau of Health to find ways of improving the outcome of screening. There are plans to reach the underserved population by introducing an organised screening programme with a call-recall system and compulsory adherence of the labs to the quality assurance programme; efforts aim at establishing a nationwide basis for a screening programme in accordance with the European guidelines for quality assurance in cervical cancer screening.

## Belgium

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With an age-standardised incidence rate of 12/100,000 and a mortality rate of 5/100,000 (estimates for 2004, European reference population), cervical cancer in Belgium ranks in the middle group of the member states of the European Union.<sup>15</sup> In the 1950s, the standardised mortality rate (corrected for certification inaccuracy) was of the order of 15/100,000. Age-cohort-period analysis has revealed an increased risk of cervical cancer for cohorts born after 1940 that was counteracted partially by screening.<sup>16,17</sup>

In Belgium, the three Communities (Flemish, French and German Community) are responsible for the organisation of preventive health care, whereas financing of most medical acts mainly remains a matter for the Federal State. For instance, consultation of a gynaecologist or GP, taking and reading of a Pap smear are reimbursed by the National Health Insurance Institute. In 1993, the Flemish Community set up a screening programme, in collaboration with the five Flemish provinces, with two major aims: (a) inviting women aged between 25 and 64 years to have a Pap smear taken every 3 years and (b) promoting quality assurance regarding collection of Pap smears, uniform reporting of cytology results and follow-up of screen-positive women.<sup>18</sup> Currently, only two provinces (Antwerp and Flemish-Brabant) still maintain a residual activity of the original Flemish programme. The Flemish programme was successful in working out technical guidelines but failed in setting up a region-wide screening registry and in influencing clinical practice. The two main reasons for failure of the introduction of organised screening were: the lack of agreement between the Federal and Community authorities and the strict and conservative interpretation of the legislation on privacy protection. In spite of laudable efforts of provincial teams and several experts, cervical cancer screening in Belgium remains predominantly opportunistic.

Recently, a comprehensive data file was compiled containing all individual reimbursement claims for Pap smears, colposcopies, cervical biopsies and surgery on the cervix that took place in Belgium from 1996 to 2000.<sup>19</sup> The screening coverage in 2000, derived from this data and defined as the proportion of women aged 25–64 years with at least one Pap smear taken in the last 3 years, was 59% (57% in the Flemish region, 58% in the capital Brussels and 61% in the Walloon region). The increase in coverage ( $P_{2000}-P_{1996}$ ) was 2%, 5% and

3% in the Flemish, Brussels and Walloon regions, respectively. The screening coverage declines by age. The modal screening interval is 1 year, meaning that many women are over-screened. The amount of used smears (1.2 million per year for a target population of 2.5 million) is theoretically sufficient to cover more than 100% of the target population at a 3-year interval. In 2000, 17% of all interpreted cervical cytology examinations were performed in women outside the target age range (10% in women aged less than 25 years old, 7% in women older than 64 years). Gynaecologists take most of the smears. The proportion taken by general practitioners varies substantially by region: 20%, 8% and 3%, in the Flemish, Brussels and Walloon regions respectively. An impressive amount of colposcopies are performed: on average, one colposcopic examination for every three Pap smears.

HPV testing is recommended for triage of women with ASCUS and after treatment of CIN, but not for primary screening.<sup>20</sup> However, hereto, HPV testing is not reimbursed.

The Federal High Council for Health recommends systematic prophylactic HPV vaccination of a 1-year cohort of girls aged 10–13 years.<sup>21</sup> Based on advice from the Flemish Health Council, the Flemish health authority has planned to offer such vaccination in the framework of school health including registration, linkable to a screening and cancer registry, and surveillance of effects.<sup>22</sup> Opportunistic vaccination with the quadrivalent or bivalent HPV vaccine is partially reimbursed for girls aged 12–15 years (co-payment by patient of ~10€/dose). Extension of reimbursement up to the age of 18 is currently considered.

To conclude, structural reduction of the overuse of Pap smears and other related diagnostic and therapeutic procedures and re-investment in coverage increase and quality improvement could potentially result in more life-years saved, without an increase in public funding. In Belgium, translation of European evidence-based guidelines into practice is a long and difficult process, due to the complex political decision making.

## Bulgaria

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In the last 20 years, the incidence and mortality from cervical cancer in Bulgaria have risen constantly, which is in sharp contrast to the steady decline in most European countries. Up to the late 1980s mortality rates from cervical cancer in Bulgaria were comparable to the rates of many EU countries. A dramatic increase in mortality rates has been observed during the political and socio-economic reforms of the last two decades.<sup>25</sup> Thus, in 2004, 1097 new cases of cervical cancer were registered with cervical cancer being responsible for 7.6% of all cancer cases in females, ranked after breast cancer, non-melanoma skin cancer and corpus uteri cancer.<sup>24</sup> Also, more than 30% of the new cervical cancer cases were in advanced (III + IV) stages<sup>24</sup>, and this has not changed during the last 20 years. Moreover, cases of preinvasive cervix uteri cancer are only 20.4%, while invasive ones are 79.6%.

This situation of increasing incidence and mortality rates is due to the fact that the State funded health care system, existing before 1989, has been dismantled. The former health care model in Eastern Europe sought to mount comprehensive and well-organised prevention programmes such as universal childhood immunisations, screening for tuberculosis, sexually transmitted diseases and cervical cancer. Institutionally, the first official National Cervical Screening Programme in Bulgaria started in 1970.<sup>23</sup> For the period between 1970 and 1985, cervical cancer incidence and mortality rates remained relatively stable.

The reform of the health care system started in 1990 and is still ongoing. In 2000, a National Strategy and Programme for Oncological Screening in Bulgaria (2001–2006) was voted for by Parliament, aiming to institute a multifaceted programme of cervical cancer screening for women aged 20 to 60 years. It focused on cytological screening methods and proposed that cervical smears are taken at the primary care units (GPs or OBGYN practitioners) and analysed at specialised laboratories throughout the country. This programme was not implemented in practice in the way it was planned, and it expired at the end of 2006. Currently, Bulgaria has no national programme for cancer prevention; however, there are ongoing efforts to develop one. There are some local initiatives for free of charge preventive check-ups that are undertaken rarely and unsystematically.

As a result, the population based screening programme of the past has been replaced by opportunistic screening that requires a substantial personal initiative of both the providers and the clients.<sup>26,27</sup> The absence of institutionally structured preventive programmes creates significant barriers in access to regular smear tests. A study on psychosocial aspects of cervical cancer screening in Bulgaria has shown that the most important barriers women face are the unwillingness of doctors to offer and to perform Pap smears, the unpleasantness of the gynaecological visits, and the lack of information.<sup>23</sup>

There are no available data on prevalence of HPV infection in Bulgaria. HPV vaccination has now been available in the country for a year on a private basis. Although there were some promotional initiatives, the vaccine is not implemented as an institutional policy.

The challenge in starting an organised cervical screening programme in Bulgaria lies in proper organisation. The country has enough human and physical resources, but clear instructions for the organisation, management, and implementation of a screening programme are needed.

## Cyprus

Azina-Chronides M. On behalf of the Director Medical and Public Health Services. M.A-Ch./d.pa

In Cyprus, the history of cervical cancer screening dates back to 1970 when the Ministry of Health identified the need for screening. Since then, Cypriot gynaecologists in the public and private sectors are recommending and applying Papanicolaou smear tests to all women in their fertile years.

This opportunistic screening does not cover women of older ages and no control exists in relation to the frequency of

screening, laboratory quality and follow-up mechanism. Unfortunately, no information on data collection is available for this opportunistic screening. Cervical cancer mortality rates are also not available. The incidence of the disease in Cyprus is 3.9 based on the data of the year 2004 of the Cyprus cancer registry.

Based on the political decision and commitment assigned by the Ministry of Health, the department of Medical and Public Health Services established an ad-hoc cervical screening committee in 2008. The aim of the committee is to prepare a proposal for the development and implementation of a National Screening Programme on Cervical Cancer.

According to the recommendations of the EU Council, Cyprus intends to implement a National Screening Programme on Cervical Cancer in 2009. The aim of the Programme is to reduce the incidence and mortality of cervical cancer by tracing it in the pre-clinical stage.

In cervical screening, one of the most important issues is the collection of a sample from the uterus cervix for cytological analysis. The method used is the Papanicolaou smear test. The smear will be taken by gynaecologists. At least two smears will be collected by using an endo-cervical brush and a spatula.

The ad hoc committee will propose that the target group for cervical cancer screening in Cyprus will be women in the age group from 30 to 60 years. They will be checked every 3 years. The number of Cypriot women in that age group is approximately 167,400. According to the population registry, a written invitation will be sent to every eligible woman. Every year about 57,000 women will be screened.

All Cypriot gynaecologists, in both the private and public sectors, will be involved. The smears will be examined by cytologists/histopathologists. The screening programme will come under the responsibility of the Department of the Medical and Public Health Services (MPHS) of the Ministry of Health of Cyprus. More specifically, MPHS will be responsible for the implementation, monitoring and evaluation of the whole programme. The Medical and Public Health Services in coordination with the Information and Technology Department will also develop a computerised system which will be used for data collection and analysis.

The ad hoc committee intends to propose a follow-up system which will be performed in cooperation with the cancer registry (health monitoring unit). It will be based on a call system and a follow-up form will be developed:

- (1) Women who should have a normal smear will be informed (in writing) of their results and the date of their next smear.
- (2) If the smear should be insufficient or slightly abnormal, women will be contacted by phone and a new appointment, after 3 months, will be arranged.
- (3) If the smear should be abnormal, women should also be informed by phone and should be referred to the gynaecologist for colposcopy/colposcopy directed biopsy or other diagnostic procedures, if necessary.

Over the computerised network system, the Ministry of Health will be able to follow-up further steps.

The Government of Cyprus will fund the whole screening programme. Our target is to achieve coverage of at least 80% of the targeted population. The high response of the eligible women will be achieved mainly by the dissemination of information and by a successful health education campaign involving mass media. In addition, the awareness of health professionals will be raised. After the implementation of the National Screening Programme, the HPV vaccination will be introduced for a certain age group of adolescent girls, possibly at the age of 13–14, through school Health Services.

**Summary and conclusion:** A National Screening Programme for Cervical Cancer will decrease the incidence and mortality of the disease. Cyprus intends to establish a screening programme on cervical cancer in the near future. Women in the age group of 30–60 years will be examined using the Papanicolaou smear test. The Programme will be funded by the Ministry of Health of Cyprus. The Medical and Public Health Services are responsible for the implementation, the coordination, and quality control of the programme. The aim of the programme is to achieve coverage of at least 80% of the targeted population.

#### Czech Republic

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Though lower than in the 1960s, the incidence rates of cervical cancer in the Czech Republic (CR) remain high despite opportunistic screening. In 2005, the incidence was 19.1 and mortality 6.5 per 100,000 women and world standardised rates were 13.5 and 3.9, respectively.<sup>28</sup> The Czech National Health Law from 1966 is still valid and it is the basis for opportunistic screening in the CR today where all women (no age is specified) are entitled to a free preventive gynaecological examination once per year. This prevention visit includes basic colposcopy and a Pap test. All gynaecologists can perform basic colposcopy in their office and it is paid for by the compulsory health insurance. Expert colposcopy is performed only by those specialists who are certified.

Incidence and specific mortality are calculated from data of the National Cancer Registry of the Czech Republic (NCR) (Institute of Health Information and Statistics, Ministry of Health CR) which was established in 1976. Information about cause of death from the Death Certificates is also collected in the NCR database. In the CR, there are 5.2 million women in total and 2.9 million women in the screening age (25–65 years of age).

For the cytological analyses of cervical smears in the CR, there are about 50 laboratories. For the evaluation of cytological slides, the 2001 Bethesda system is used. The data about coverage as well as about the number of annual smears comes from the National Health Insurance Fund. The coverage in women aged younger than 30 years is 33%, 35% in women aged 30–59 years and 17% in women older than 60 years



(period of 3 years). The annual number of cytological smears is approximately 1.5–2 million.

In February 2008, the Ministry of Health of the CR announced the onset of an organised screening programme. The press report announced the following information: (1) The process of the accreditation of the cytological laboratories is to be based on strict criteria. (2) Insurance companies will invite women 25–60 years of age who have not had a cervical smear taken within the last 2 years. Should they not respond, they will be invited again the following year. In 2008, three out of 12 insurance companies sent out the invitation and it is expected that others will follow in the near future. 3. A new screening code for cervicovaginal screening smear has been defined and it is planned that the expected increase in the volume of cervicovaginal smears performed once the organised programme starts will be reimbursed. 4. The cytological laboratories are obligated to keep evidence of the analyses of the screening smears. While these steps are certainly crucial, without the national screening registry, evaluation of the programme performance will not be possible. Nevertheless, the decision of establishment of the registry has been made. Despite EU recommendations, the screening interval in the Czech guidelines is still 1-year but it is planned that if the cytological smear of a woman is normal in two consequent annual examinations, the screening interval will than be extended to 3 years (personal communication).<sup>29,30</sup>

HPV detection is recommended in the Ministry of Health guidelines only for the triage of borderline findings up to 4% of the volume of Pap smears for each laboratory.<sup>30</sup> Even though HPV detection is reimbursed by the insurance companies the test is expensive and therefore not widely used by gynaecologists. On the other hand, there are 30 routine laboratories performing HPV detection which regularly participate in the External Quality Assurance (EQA) programme. The EQA in medical microbiology in the Czech Republic is well organised. It is coordinated by the Accreditation Department of the Centre of Epidemiology and Microbiology of the National Institute of Public Health in Prague. EQA for HPV has been available in the Czech Republic since 2000 and it is prepared by the National Reference Laboratory for Papillomaviruses (NRL PV).<sup>31</sup>

In 2006, deputies of all medical societies, with the exception of the representatives of the Czech Gynaecological and Obstetrical society (CGOS), agreed on the need to implement routine vaccination for girls at the age of 13 years. The CGOS, however, would recommend routine vaccination in girls 15 years old and only on the condition that an organised screening programme in the Czech Republic is established.<sup>32</sup> This recommendation was sent to the Ministry of Health in December 2006 but, so far, there has been no response. Several insurance companies provide partial reimbursement (18–107 EUR; the price of the three doses is approximately 375 EUR) for the vaccination of girls from 12–13 to 15–18 years of age. Several other recommendations for vaccination against HPV were issued by other professional associations.<sup>33,34</sup>

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## Denmark

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Denmark has been a high risk country for cervical cancer. When cancer registration started in 1943, the national age-standardised rate (World Standard Population) was 25 per 100,000. Health care in Denmark is tax-paid and organised by regional authorities. Cervical cancer screening started in the 1960s with population-based, organised screening programmes in some counties and a nationwide agreement in 1969 for payment of general practitioners for the taking of opportunistic smears. Two parallel screening systems thus developed, and this led to a high consumption of smears, being 630,000 in 1983 in a population of five million people.

National screening recommendations were issued in 1986 recommending a screening interval of 3 years for women aged 23 to 59 years. An integrated model was implemented, where all cervical smears in Denmark were centrally registered, and screening invitations were sent only to women not already registered with a cervical cytology within the last 3 years. These recommendations were gradually implemented and only reached national coverage by January 1st 2006, where the last of 14 counties extended a previous programme targeting women aged 25 to 45 to also include the younger and older recommended age groups. The integrated system has considerably reduced the number of cervical smears taken, being 425,000 in 2006.

In 2007, the National Board of Health issued a new programme for cervical cancer screening in Denmark recommending screening every third year for women aged 23 to 50, and every fifth year from age 50 to 65 if the latest two smears within the last 10 years were negative. The programme stills builds on the integrated model where women without a registered cervical cytology within the last 3 years are personally invited to have a smear taken free of charge by their general practitioner. Cervical cytology reading is recommended to be concentrated to pathology departments reading a minimum of 15,000 cervical smears per year. No recommendation is made as to the use of conventional or liquid-based cytology. In 2006, liquid-based cytology was used for 44% of the cervical smears in 2006, and computer-assisted reading was used for 51%. All pathology departments are recommended to use the Bethesda-classification. Human papillomavirus (HPV)-testing is recommended for women with ASCUS and as control after treatment for cervical intraepithelial neoplasia (CIN) 2/3. Use of HPV-DNA or HPV-RNA testing is optional. Where HPV-RNA testing is used, this is also recommended for women with LSIL. Women with other types of abnormal cells are referred to colposcopy. Denmark was, by 1st January 2007, administratively restructured into five regions, and it is up to these regions to implement the new recommendations. A nationwide monitoring with ten quality indicators will be implemented, and the results will be validated both by region and nationwide. HPV-vaccination of girls aged 12 with a catch up programme for girls aged 13–15 has been recommended by the National Board of Health.<sup>35</sup> The proposal is currently being negotiated in the Danish Parliament.

## Estonia

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Estonia has a population of about 1.3 million (Statistics Estonia, 2007). Reliable cancer incidence data is available for Estonia from 1968 when the cancer registration became centralised. All malignant neoplasms and *in situ* cancers have to be reported to the Estonian Cancer Registry (ECR) by physicians and pathologists.<sup>36</sup> Since 2000, the reported incidence and mortality are affected by the data protection act that prevents linkage of the ECR database with the death certificate database.<sup>40</sup>

In the year 2000, the age standardised (world) incidence rate of cervical cancer was 15.5 per 100,000 women-years in Estonia<sup>38</sup> with 162 new cervical cancer cases being detected. In 2004, the world age standardised incidence rate for cervical cancer was 17.5 per 100,000 women with 181 primarily detected cases (ECR unpublished data, 2007).<sup>41</sup> The age standardised (European) mortality rate of cervical cancer in Estonia was 8.1 per 100,000 women-years in 2000. The incidence and mortality rates are about fourfold higher in Estonia than those in neighbouring Finland.<sup>37</sup>

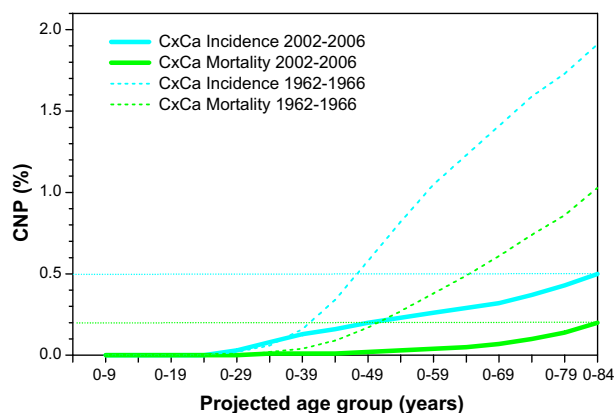
In the year 2006, nationwide organised cervical cancer screening was started in Estonia. According to the National Cancer Strategy, personal invitations to cervical cancer screening have to be mailed to all insured women in the age group of 30 to 59 years with a 5-year interval after a negative test. In 2006, women in the age cohorts of 30, 35, 40, 45, 50 and 55 years were invited to attend cervical cancer screening. Conventional Pap-smear is used for the screening test. Women diagnosed with cervical cancer, without health insurance and having had a Pap-smear in the past 12 months are excluded from the list of invitees.

Pap-smears are taken at 19 clinics by specially educated midwives. Cytological investigations are performed in seven labs. Women have to contact the clinic themselves to be informed about the test result.<sup>39</sup> Gynaecologists treat pathological findings according to the guidelines approved by the Estonian Gynaecologists' Association.<sup>42</sup>

Cervical cancer screening is funded by the Estonian Health Insurance Fund and the National Cancer Strategy. The technical work (mailing of personal invitations and reminders, statistics on attendance rates at different clinics, test results, possible additional investigations) is carried out in cooperation with the Cancer Screening Foundation. To promote participation and increase the awareness of cervical cancer prevention, the Estonian Cancer Society started annual media campaigns in 2007. Human papillomavirus (HPV) vaccination is recommended by the Estonian Gynaecologists' Association, but has not been implemented in Estonia as a national programme.

As the nationwide screening programme started in 2006, only an *ad hoc* audit to check the quality of tests performed in different labs was carried out in 2007.

The unacceptably low population coverage of cervical cancer screening is a major problem to be solved. There is an urgent need for establishing a central electronic screening registry to facilitate the data collection on attendance and test



**Fig. 1 – Cumulative net probability (%) of cervix carcinoma by age in Finland, 1962–1966 versus 2002–2006 (Finnish Cancer Registry, 2008).**

results, and to follow-up women with an abnormal smear. Under-funding and division of work tasks between many parties are main obstacles for improving the efficacy of cervical cancer screening in Estonia.

## Finland

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In Finland (population 5 million), the nationwide organised cervical cancer screening programme has been in action since the early 1960s and has reduced the cervical cancer burden by 80%.<sup>43</sup> The age-adjusted incidence rate of cervical cancer is nowadays 4 and mortality rate 1 per 100,000 woman-years in our country.<sup>44</sup> The cumulative lifetime probability for cervical cancer in Finland is 0.5% and for death from the disease 0.2% (Fig. 1).

Women aged 30 to 60 years are actively invited to screening using information from the National Population Registry. Attending is free of charge, screening is provided by municipalities from the primary health care budget. The screening interval is 5 years if normal screening results. Some municipalities also invite women aged 25 and/or 65 years. Over 35 years, the registered screening invitational coverage has been almost complete within the centrally targeted screening ages. In 2005, invitational coverage was 98% with about 270,000 invitations and 190,000 screening visits in the programme. The attendance rate per one invitational round is 71% but it varies across ages being lowest among the youngest screening ages.<sup>43,44</sup> Detection rates of any histologically confirmed CIN and invasive cancer within the programme is about 0.4% and 0.01%, respectively.

Samples are taken by trained nurses or midwives in local healthcare centres. Sample quality is under continuous internal control by cytology laboratories of the programme. Confirmation and treatment are an integral part of the routine healthcare system. The invitational and screening results, including histologically confirmed diagnosis, are registered at the Finnish Cancer Registry.<sup>45,46</sup>

Conventionally, screening has been based on Pap-smears. However, novel technological alternatives have been introduced as screening tests with an aim to assess screening effectiveness.<sup>46</sup> Approximately 860,000 women have been allocated to automation-assisted cytology (since 1999), human papillomavirus (HPV) DNA testing (since 2003), or to conventional cytology within the organised programme.<sup>47</sup> In the HPV arm, a sole primary HPV test is done and those who test positive initially are tested with cytology (triage). In each arm, women with cytology equal to low-grade squamous intraepithelial lesion (LSIL) or worse are referred for colposcopy.

The detection rates as well as cross-sectional specificity estimates in automation-assisted screening are very similar to conventional screening.<sup>48</sup> There is variation between laboratories in the performance of both conventional and automation-assisted cytology which does not reflect on effectiveness but may affect cost-effectiveness.<sup>49</sup> Initial results from HPV screening suggest slightly increased positivity rates, follow-up screening recommendations and referral rates compared to conventional cytology.<sup>50</sup>

Only small additional impacts on cervical cancer prevention can be expected from any new technologies. However, results on subsequent cervical cancers and screen-detected pre-cancers are needed for planning optimal screening policies for various tests in the future.<sup>47</sup>

Improving screening attendance and compliance into the organised programme, especially among women 25 to 39 years of age, is a key to further prevent cervical cancer in our country. Interventions to achieve better attendance are needed. Reminding (by letter or phone) women initially non-responding is an option. We are also piloting the self-sampling test instead of re-invitation.

In parallel with improving efforts, the stopping of unnecessary actions should also take place. There are wide and wild testing practises outside the screening programme. Unfortunately, we do not have, as of yet, data to study the magnitude and trends in the use of opportunistic screening. Efforts are needed to avoid overuse of services due to spontaneous screening and, hence, to decrease potential adverse effects and improve overall cost-effectiveness.

Currently, HPV vaccines are not included in the Finnish vaccination programme. A cost-effectiveness evaluation on control of HPV-related disease burden is proceeding up to autumn 2010.

## France

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In 2005, the French estimated world age-standardised incidence rate of cervical cancer was 7.1, and the mortality rate reached 1.9 for 100,000 women. Between 1980 and 2000, incidence rates have been regularly declining by 2.9% a year<sup>51,52</sup>; the decrease was smaller between 2000 and 2005 (1.8%). Cervical cancer screening remains mostly opportunistic. Despite over 6 million smears performed each year, only about 57% of the target population is screened within 3 years<sup>53</sup> but among them 45.5% get their second smear between 1 and 2 years.<sup>54</sup>

Nevertheless, since 2003, when the National plan against cancer was launched, several measures have been taken to improve cervical cancer screening. In 2006, the National Committee on Cervical Cancer Screening established Guidelines for organised cervical cancer screening<sup>55</sup> and advised ongoing pilot projects to follow them.

In 2007, the National Institute against Cancer published an update of the cervical screening status, focusing on available data, medical access, local organised initiatives and psychological barriers.<sup>56</sup> In the same year, HPV vaccination guidelines using the quadrivalent vaccine were set,<sup>57,58</sup> recommending vaccination for girls aged 14 and a catch up for girls between 15 and 23 if sexual activity had begun less than 1 year before. It was stated in the document that cervical screening had to be maintained and should be organised. At the moment, a commission on cervical cancer screening is working on how to improve cervical cancer prevention.

Nowadays, only three regional cervical cancer screening programmes are ongoing, financed by National and local grants. One takes place in Martinique, one in Isère and the last one in the Alsace region<sup>59</sup> (the Doubs programme stopped in 2004). These programmes cover about 4% of the French target population (aged 25 to 65 years). At the moment, data are not comparable<sup>60</sup> but starting from 2009 the three programmes will follow the same Guidelines.<sup>55</sup> Two or three new sites should begin organised screening by the end of the year.

Only data from Alsace are presented here. This programme<sup>61</sup> is based on a screening register where all smears taken in the target population are recorded whether the women were invited or not. Almost all smears (95%) are performed by gynaecologists but general practitioners are also involved.

Invitations are sent using the Health insurance lists to women without a smear in the last 3 years. No appointment is given; the choice of the physician is theirs. All smears, opportunistic and organised, are under quality control. Follow-up of abnormal tests is done by contact with the clinicians. Since 2007, a pathology register of all cervical sampling completes the screening register. Interval cancers are known through the two local population-based cancer registers.

Coverage of screening at 3 years reaches 70.6% which is about 10 points above estimated coverage of opportunistic screening in France<sup>53</sup> and quite a good rate in Europe. The overall Positive Predictive Value of colposcopy is low (19.9%) due to the fact that in France, as in Italy, colposcopy is widely available and reimbursed by the health insurance system so that direct referral to colposcopy is a common and recommended attitude for ASC-US and low-grade smears. On the other hand, Positive Predictive Value for col-

poscopy for high grade smears is quite high. Detection rate of CIN2+, projected at 5 years, ranges in the middle values found in the EU.

The Alsatian experience confirms that organising cervical cancer screening in France is possible. The health authorities are still thinking of the best integrated strategy for cervical cancer prevention, including vaccination, screening and treatment of precancerous lesions.

## Germany

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In the 1960s, cervical cancer was the second most frequent cancer site after breast cancer in both parts of Germany.<sup>62</sup> In the past 50 years, incidence and mortality fell by about 75%, whereby the decrease was lower in East than in West Germany<sup>63</sup> (Fig. 2). Today, with an estimated 6200 new cases and 1660 deaths,<sup>64</sup> cervical cancer has become a relatively rare cancer site.

In West Germany, cervical cancer screening started with the statutory cervical screening programme launched in 1971. From the age of 20 and without an upper age limit, statutory health insured women (around 90% of the population) are offered a screening programme without personal invitation including a yearly gynaecological check-up with a conventional PAP smear. Women with private health insurance have equal access to screening. Thus, more than 95% of German women have access to annual screening.<sup>65</sup> The programme is opportunistic and based on self-referral. Currently, 9500 of-

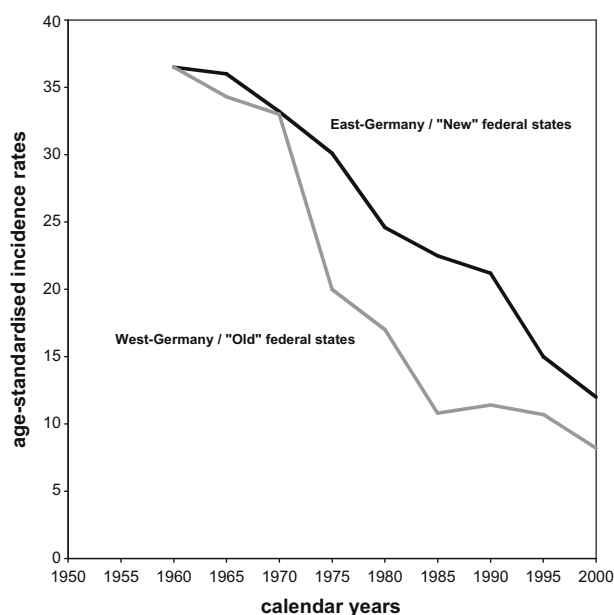


Fig. 2 – Age-standardised incidence rates (world standard) in Germany 1961–2000 (modified from Becker 2003).

Table 1 – Cervical cancer screening in Denmark.

Deaths, 2005	137
Invasive cancer cases, 2003	408
Invasive cancer cases, max. count in 1966	964
Treatment of dysplasia, estimate 2003	5000
Non-negative smears, 2006	38,181
Smears, 2006	424,799

fice-based gynaecologists and 1200 cytology laboratories take part in the programme covering 34 million women.

In East Germany, screening for cervical cancer also started in the 1970s; however, full population coverage was not achieved so that the slower decrease of cervical cancer incidence and mortality was largely due to the slower implementation of screening. After the German reunification in 1990, the West German programme was extended to East Germany.

In the past, nationwide regulations for cytology laboratories included standards for qualifications and proficiency testing of the physicians in charge. As from October 2007, additional quality assurance measures have been implemented by the authorities, including maximum workloads for screeners (10 per hour), and standards for re- (or pre-) screening procedures. Furthermore, regular random sample checking of slides for technical quality and correct documentation, as well as mandatory annual statistics on cytological results according to the Munich II classification, and correlation of abnormal PAP smear findings with histopathological results are part of the regulations. Adherence is controlled by the regional Associations of Statutory Health Insurance Physicians (KV), and non-adherence is sanctioned by withdrawal of the licence to settle accounts.<sup>66</sup>

The interpretation of the smears is based on the Munich II classification which deviates in some aspects from the Bethesda system.<sup>67</sup> The main difference is the assignment of moderate dysplasias. In Germany, these abnormalities fall into the category of Group IIID (mild to moderate dysplasia), whereas in the Bethesda system they are assigned to a higher category comprising severe dysplasia and carcinoma in situ. Translatability to the WHO system of histological CIN 1–3 classes is limited since categories are partially overlapping<sup>68</sup>; see also Table 1 in Petry et al.<sup>69</sup>

Recommendations for the management of abnormal PAP smears are published in national guidelines<sup>70</sup> in line with international recommendations comprising early recall after about 6 months in case of mild or moderate dysplasia. For repeated abnormal findings (Group IIID, cytology of mild or moderate dysplasia) or higher abnormalities, colposcopic assessment is recommended. For hospitals (including in and out patients), the Federal Office of Quality Assurance defines a low rate of conisations without histological signs of (pre) malignancy as a quality indicator for gynaecological surgery, and publishes annual results at regular intervals.<sup>71</sup> Similar measures for office-based gynaecological surgery are currently lacking.

According to current evaluations based on billing procedures, participation rates are highly variable in different age groups: 80% of women aged from 20 to 40 receive at least one PAP smear within 3 years. From ages 40 to 65, this rate continuously declines to 60%. Thus, the non-attendance rate is 20–40% in the above named age ranges. Only 25% of women



aged under 50 receive PAP smears in yearly intervals<sup>72</sup> (for data based on specific evaluations see<sup>73–76</sup>).

## Hungary

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The history of *opportunistic* cervical screening in the country goes back to the mid 1950s. It was quite extensive: in the 1980s the annual number of smears taken and analysed exceeded 1 million, the clinical stages of detected cervical abnormalities were favourably shifted, but the mortality levelled off at a rather high level (10 per 100,000 population). It was admitted that the programme had failed, due to the lack of organisation, i.e. personal identification of women screened.

In the early 2000s, a nationwide *organised screening programme* was established in the frame of the National Public Health Programme.<sup>77</sup> Screening strategy is as follows: ‘after one negative smear, once in every three years, full gynaecological examination, comprising both colposcopy and cytology, of women between 25 and 64 years of age’. Since 2004, the cancer screening has been in operation.

The task of the organisation, coordination, monitoring, quality control and evaluation has been delegated by law to the Office of the Chief Medical Officer (CMO). A Screening Coordination Department has been set up which supervises the screening Coordinating Units in the 20 administrative areas (regions, counties), being responsible for management of the implementation. Most importantly, a Central Screening Registry has been established to serve the programme which receives a population list from the database of Health Insurance Fund Administration (HIF), which comprises *personal identification data* (name, date of birth, place of birth, mother's name, address), including a social security number (TAJ), and covers virtually the entire Hungarian population, with the exception of those hysterectomised, those diagnosed and treated with cervical cancer, and those who had received a screening examination for any reasons outside the programme over the last 3-year period (*‘quasi organised screening’*).

The established procedure: the ‘list’ is broken down by counties and sent to the particular primary care physician for validation (migration, deceased etc.). It is then sent back to the Coordination Department and used as a *notification list*. A personal invitation letter (with a perforated ‘slip’) is centrally issued. The ‘gatekeepers’ of the screening are – traditionally – the gynaecologists. The test comprises a complete gynaecological examination including colposcopy; and a smear for cytology, taken by a gynaecologist, analysed by cytologists. Some 40 cytology labs are contracted by the Health Insurance Fund Administration (approximately half of the existing ones where cytological exams are regularly done). The contracted cytology labs are to report back monthly and quarterly, to the Central Screening Registry, data of those who presented themselves for screening. *The rest of the cytology labs not contracted are not obliged to report.* Data collected are the following: the social security number (TAJ) and age of women eligible for screening, the place and date of smear-taking, and cytology examination, and the test results of those smears analysed

and classified as ‘negative’, ‘non-negative’ and ‘unsatisfactory’. The Bethesda categories – though widely used by cytologists – are not reported to the Screening Registry. The test result can be reported in aggregate only, and cannot be linked to an individual, because any data referring to an individual's health status in a way that it might be linked to an individual to communicate to the Screening Registry is strictly forbidden by the data protection law. The same applies to the confirmatory histology.

So far, some 2 million invitation letters have been sent out but less than 5% of those invited have been registered as screened. In the same time, according to the estimate by HIF, approximately 60% of eligible women attended screening in or outside the programme.<sup>78,79</sup>

Consequences: The difficulties of the transition from extensive opportunistic to organised screening are being reflected in the current problems of population screening:<sup>80</sup>

- The gynaecologists working in private clinics do not report the activity even though they are estimated to screen about 30% of eligible women.
- The gynaecologists do perform a colposcopy ‘screening’ before every single smear taking action – hence colposcopy does not play any role in the screening process.<sup>81</sup>
- Due to the partially unregulated privatisations both in the field of the gynaecologist and the cytopathologist (outsourcing activities and real privatisations) most of the data are produced outside the organised programme.

There are attempts to break through by

- Educating alternative health care professionals, e.g. midwives (non MDs) as smear takers.
- Finding, establishing and introducing the proper use of colposcopy in the screening process (e.g. follow-up of those with non-negative test results).
- Establishing a centralised database of all histology proven cervical abnormalities, using the above database to trace back the cytodiagnostic history of the woman by linking histology with previous test results (‘pathobank’).

The insistence of the gynaecological community on their ‘historical role’ seems to be the major impediment to carrying out an effective screening programme.

There is a long way to go until a ‘state-of-the-art’ cervical screening programme can be delivered in Hungary because ‘old habits die hard’.

## Ireland

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The publication of *A Strategy for Cancer Control in Ireland* 2006 advocates a comprehensive cancer control policy programme in Ireland with cancer screening managed by one organisation. Following this *The National Cancer Screening Service* was established.

A national population based Cervical Screening Programme was introduced in Ireland in autumn 2008. The Na-

tional Cancer Screening Service Board provides governance for the Irish Cervical Screening Programme since January 2007. The Board has introduced a contractual model to include the following:

- (1) Contracts with medical practitioners in primary care for smear taking.
- (2) A contract for the provision of cytology services with an accredited laboratory following a procurement process and
- (3) Service level agreements with colposcopy services.

Arrangements will be made for primary treatment of cervical cancers. The Board is committed to delivering a quality assured service for women for smear taking, analysis and diagnosis. The National Cancer Registry of Ireland reports that on average there are 200 cases of cervical cancer per year and 72 recorded deaths. The average age at diagnosis is 46 years and at death 56 years (Women and Cancer in Ireland 1994–2001 NCRI and Women's Health Council February 2006).

Gynae-Cytology laboratory services have been provided in Ireland since the late 1960s on an opportunistic basis. The Irish Cervical Screening Programme Phase One has offered free smear tests through organised cervical screening to women in the Midwest aged 25–60 years since October 2000.

Planning for a National Cervical Screening Programme. Census data from the Irish Central Statistics Office in 2006 indicate that there are over one million women aged between 25 and 60. With an intended 80% uptake rate for the Programme to be successful, and allowing current policy, then the annual number of smears will amount to 300,000 per annum nationally on a call-recall basis.

The Programme Process. Women aged 25–44 in the target screening population are invited for screening every 3 years and women aged 45–60 are invited every 5 years. Eligible women can join the Programme by invitation from the central office based on the screening register or directly at the discretion of their medical practitioner or by self-registration.

A central office administers the Cervical Screening Register information system that maintains call and recall and manages the computerised Clinical Result Register which records women's cytology, colposcopy, cervical histology and hysterectomy status. This organised approach ensures that appropriate follow-up care is provided.

The smear takers are doctors or nurses that are contracted and/or registered with the Programme. An accredited smear taker training programme is available from a number of Irish institutions in partnership with the Programme. The single test in use in all of Ireland is the liquid-based cytology preparation and kits are provided by the Programme.

In preparation for the national Programme a quality assurance framework was established in 2007 and is reviewing the standards and performance indicators to be launched in 2009. The establishment of multi-disciplinary teams in managing women and the monitoring of quality assurance measures are recommendations that will be addressed.

HPV Vaccine. A Health Technology Assessment (June 2008) on the role of vaccination against HPV in reducing the risk of cervical cancer in Ireland shows that universal HPV vaccination of 12-year-old females would be cost-effective in Ireland.

The report also recommends a one-off vaccination programme for 13–15-year-old females. The Minister for Health and Children announced on 5th August, 2008, the preparation and submission of a plan for the introduction of a HPV vaccination programme for 12-year-old girls. This has been delayed due to the current economic climate.

## Italy

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In Italy, where the health service is managed by regions, the implementation of organised screening programmes for cervical cancer, with active invitation every third year of women aged 25 to 64 years, was recommended in 1996.

At the end of 1997 only 13% of Italian women 25–64 years old were included in the target populations of organised programmes. In 2007 the corresponding proportion was increased to 72%. Incompleteness is due to implementation still in progress in southern Italy, where start was mostly delayed, and by absent or minimal activity in a few regions.

A set of process indicators for monitoring and standardised tables of aggregated data from which indicators are computed was agreed within the association of organised cervical screening programmes (GISCI, Gruppo Italiano Screening Cervicale). This allowed national surveys that were first conducted by GISCI itself and then by the Osservatorio Nazionale Screening on behalf of the Ministry of Health (now of Welfare). Yearly reports have been published from 2002<sup>82</sup>; an English version is available from 2006.<sup>83–88</sup>

Most organised programmes invite all women independently of their spontaneous activity but some only invite women not screened spontaneously. In 2006, invitational coverage was 75%, suggesting problems in performing all the activities needed for full implementation. There is a systematic registration of invitation, smears, colposcopy, histology and, frequently, also of treatment. However, this is true for what is performed within the organised programmes but little is known about spontaneous activity. This is the main limitation of the Italian system. Compliance to invitation was 38.5% in 2005, with a North to South decreasing trend, leading to a projected 29% of the target population screened in 3 years. However, even in areas where organised programmes are active, a large number of women are screened spontaneously, so that the overall coverage is plausibly at least double.

The detection rate of histologically confirmed high-grade lesions shows a decreasing trend from North to South and in northern Italy from East to West. However, the detection rate within organised programmes is a plausible underestimate of the overall one in the screened population, due to the fact that some women have tests both in and outside the organised programmes. The most widely applied protocol, as a result of colposcopy being widely available and relatively inexpensive, is direct referral to colposcopy of all women with ASC-US or more severe cytology, although in the case of ASC-US some programmes repeat cytology and a few have started triage by HPV testing. This results in a low Positive Predictive

Value (PPV) of cytology referral. PPV values, however, have increased over the past years despite the start of many new programmes, while in a previous period the start of new, less experienced, programmes had led to a decreasing trend for many years. This is plausibly also the result of intensive quality assurance programmes conducted by GISCI.

Implementation of organised screening resulted in a 20% reduction of cancer incidence in Turin.<sup>89</sup> Estimation of the impact at a national level is being performed.

The current Italian guidelines, released in 2006, recommend primary screening by cytology, and are awaiting the results of large randomised trials on HPV testing, one of which, the NTCC study, is being conducted in Italy.<sup>90–93</sup> A review is planned. In the meantime, large demonstration projects are starting.

A programme of prophylactic HPV vaccination, with active invitation of women at age 12 recently started in all regions. Some regions also vaccinated other birth cohorts (16 years and in a few 18 and 25 years).

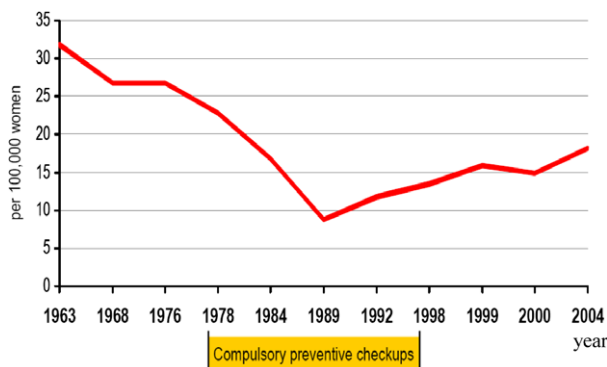
## Latvia

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In the 1960s, cytological testing played an important role in the decrease of cervical cancer incidence in Latvia. From 1970 to 1978, 2.5 million women had been cytologically tested and cervical cancer crude incidence rates decreased from 31.7 per 100,000 women in 1963 to 8.9 in 1989. Until the end of the 1980s, the extent of preventive examinations was increasing. Starting from 1983, preventive gynaecological



**Fig. 3 – The dynamics of the cervical cancer incidence crude rates in Latvia, 1963–2004.**

examinations with cytological testing were available for all women aged 18 and over. In 1984, cytological screening was recommended as a compulsory part of the system for the prevention and treatment of disease for all inhabitants. In 1989, due to political and economical changes in the country, the compulsory preventive examinations were terminated. From the mid-1990s, when the number of women's preventive examinations and, therefore, also the amount of cytological testing was rapidly decreasing, the incidence rates rose again (Fig. 3).

Unfortunately, the last 15–20 years have brought negative changes on the health care system in Latvia. Currently, the cervical cancer incidence and mortality rates in Latvia are very adverse phenomenon (Table 2).

Year 2005 was the date of the reintroduction in Latvia of cervical cancer screening examinations. For women aged between 20 and 35, a cytological smear is done once a year, and, if the findings are normal, the smear is repeated every 3 years. In women between the ages of 35 and 70, a cytological smear is done once a year. The entire responsibility for organising and performing the screening examinations is delegated to the general practitioners. A centralised database for the screening register and collecting the results was not created. The screening model, implemented in Latvia, was opportunistic screening with two target population groups.

From 2007, the cancer screening programme was revised in compliance with the European Parliament recommendations on one target age group: 25 – 70 with repeated cytological smears every 3 years. It also provided a role for gynaecologists/obstetricians in the programme. These most recent regulations from 2007 do not contain any specific reference regarding the organisation of the screening programme. This type of screening is considered an ineffective use of funds. The financial incentives without changes in the organisational principles of the screening did not bring the expected results, because cooperation of the population in the screening activities was and is very low. The small numbers of preventive screening examinations over the first 2 years confirm the idea that the decentralised or opportunistic screening can not guarantee the achievement of goals required. However, it should be noted that the above information refers only to the services paid by the state; it is not possible to obtain accurate information about preventive examinations paid for by individuals. The inactivity and unawareness of people, the insufficient availability of services, the overloaded general practitioners, the lack of involvement of gynaecologists who have private outpatient practices in the programme, and the non-existence of a comprehensive implementation programme of screening are unconquerable obstacles in applying screening as a tool to decrease cervical cancer morbidity and mortality.

**Table 2 – Crude cervical cancer incidence and mortality per 100,000 women in Latvia, 1999–2005.**

	1999	2000	2001	2002	2003	2004	2005
Morbidity	16.4	15.4	14.6	16.6	16.5	18.3	17.7
Mortality	8.3	10.9	9.7	8.7	9.5	10.7	9.9

Currently, in Latvia, there is no management, coordination, and control of cancer, including cervical screening programmes. There is no institution that would collect and store data on the clinical results of examinations (either paid for by the state or by the patient), or which would control the quality of screening examinations – cytological tests, or indeed which would generalise data about the impact of the screening programme on the oncology morbidity rates, the actual improvement of early diagnostics and the decline of mortality. Up to now, no assessment has been made as to the capacity of human resources and technologies in proportion to the required coverage of screening.

As the opportunistic cervical cancer screening initiated in Latvia in 2005 is ineffective, it should be transformed into an organised national cervical cancer screening programme. Now, Latvia is at the stage of needed preliminary activities and preparations prior to implementing the organised cervical cancer screening from 2009.

### Lithuania

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In Lithuania, in 2001–2003, before the onset of the national cervical cancer screening programme, there were high cervical cancer incidence and mortality rates, a low prevalence of early detected cancer and a low detection rate of precancerous lesions. Cervical cancer represented more than 5% of new malignancies among women, and less than 50% of cases were detected at early stages. In 2004, the Ministry of Health adopted the population-based cervical cancer screening programme with a screening interval of 3 years, targeting women at the age of 30–60 years – 750,000 in the country (since 2008 the age interval was increased to 25–60 years). The primary health care centres – more than 350 around the country – were invited to join the screening programme and to implement the screening procedures.

According to the guidelines, the primary health care centre is responsible for the invitation of the women and PAP smear taking. Although general guidance on the invitation procedure has been provided by the programme, much of the practical details were left to be decided by the primary care providers. This led to variation in invitation methods – from verbal communication during a primary care visit to written invitation. A formal individual invitation letter with necessary details to attend is still a rare practice. The visit of the woman to a health care centre in Lithuania is free of charge if she is registered on the list of the centre. It is the responsibility of the GP or a member of the team to provide information to the woman about the screening programme. Each GP is supposed to serve 1500–2500 women of the target population. The funds for cervical cancer screening are allocated at the State Patient Fund (SPF) which is responsible for providing reimbursement for the services. The management of services is enforced by the information system at the SPF and does not allow simultaneous registrations of a woman at different centres. Ten pathology laboratories around the country were cer-

tified to assess the conventional PAP smears. Results are reported by the Bethesda system and are stored at the SPF database.

The implementation of nationwide organised cervical screening along the state insurance based health care system was the new and reasonable approach for cervical cancer screening in a country having relatively low health economy resources. The lack of a population-based invitation system is seen as the weakness of the programme. The first year experience has shown that the programme still carries opportunistic features: it was strongly dependent on the frequency of visits of the woman to the GP, the activity of the GP and experience of the PAP smear takers at each centre. The programme has made an evident impact on the rates of detection of the premalignant lesions (carcinoma *in situ*) and increases the number of cases detected at early stages. Major events (invitation, smear taking, PAP test result, visit to the GP for the test result) of the programme are registered in the IS of the SPF and are monitored and evaluated by the SPF along with the Coordinating Committee at the Ministry of Health. Primary care centres are incentivised for increasing the coverage of the population and detection of precancerous lesions and early stages of cervical cancer.

### Luxembourg

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In 1962, a non-systematic National Cervical Cancer Screening Programme (NCCSP) was established in the Grand-Duchy of Luxembourg. The target population is women aged 15 years and above. Demographic data for the female population are obtained from the annual report of the Central Department for Statistics and Economics Studies (STATEC).

The programme is based on the collaboration of the general practitioners (GPs) and gynaecologists and not on a system of sending out invitations to every woman.<sup>94</sup>

In 1980, the NCCSP was 'institutionalised' by introducing one central division of clinical cytology within the National Health Laboratory responsible for the smear interpretations and the programme administration. In 1990, the second version of the Munich classification, modified by Soost and the recommendations by the Bethesda System, was applied at the national laboratory.<sup>95–97</sup> All materials needed to take the smears are handed out to the doctors involved. The doctors are paid by a system of bonuses given by the Government and a reimbursement by the Health Fund. The number of all doctors taking smears increased from 68 to 105 and the number of gynaecologists increased from 19 (with 28% of smears taken by gynaecologists) to 52 (with 50% of smears taken by gynaecologists).<sup>94</sup> The annual cervical smear is free of charge for every woman. The participation of the women targeted by the programme has increased by approximately 50%



every decade from the early 1970s increasing from 10,950 in 1972 to 70,441 in 1999. Between 1980 and 1999, the number of women at risk taking part in the programme increased from 10.80% to 38.92%.<sup>94,98</sup> The mortality rate has decreased continuously from 6.1/100,000 in 1990 to 0.86/100,000 in 2005.<sup>99</sup>

The success of the Luxembourgish model programme of early diagnosis of cervical cancer is not based on sending out invitations to the target population, but on the principle of one centralised laboratory where all smear interpretation takes place. The strength of this set-up is that the administrative part is reduced to a minimum. The direct collaboration of the three centralised departments (i.e. divisions of cytology and anatomical pathology and the Morphological Tumour Registry) allows an evaluation of each individual case ad hoc. Through a network of closed collaboration between the Department of Preventive Medicine of the National Health Direction and the associations of medical doctors, the programme has improved over time. The target population is informed about the importance of cervical cancer early detection by regular pap smears through the media and through the Family Planning Foundation and the Luxembourgish Foundation against Cancer.

Since March 2008, the HPV vaccination is free of charge for young women aged between 12 and 18 years. Only 12-year-old girls are invited by personal letter. The vaccine is paid for by the Ministry of Health. The principles of this programme have been defined by a contract between the National Health Fund and the Luxembourgish Government.<sup>100</sup>

## Malta

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At present in Malta, there is no organised National Cervical Screening Programme. Since 1978, the public health care centres, St. Luke's Hospital and Mater Dei Hospital, have offered a free cervical cytology screening service. Furthermore, most of the private laboratories on the islands provide a similar service for payment. Consequently, all cancer screening activity in Malta is opportunistic in nature.

Incidence and mortality rates of invasive cervical cancer in the last 36 years have maintained a steady trend, with minor fluctuations, in spite of the fact that screening has become more available over these last decades.<sup>101</sup> A review of the smear history of women diagnosed with invasive cervical cancer between 1992 and 2002 has shown that 44% of these women did not have any reported smears prior to the diagnosis of the invasive lesion, and that 46% of women diagnosed with cancer had rare smears whilst only 10% had regular smears (once every 3 years).<sup>102</sup>

The Eurochip-2 study,<sup>103</sup> funded by the European Commission, allowed for the first time the quantification of the amount of cervical cytology examinations performed on the Maltese islands. Data were collected from seven laboratories (one public and six private) which perform all the cervical screening activity on the islands. Data collected was limited

to cervical cytology examinations performed by each laboratory from 2003 – 2005 (3 years).<sup>104</sup>

The data revealed that on average 30,000 smears are performed annually. Organised cervical screening programmes usually cover women between 20 and 69 years of age. In population estimates based on mid-2004, the number of women in this age group was 132,473.<sup>105–107</sup> If an organised screening programme is implemented in the near future, and women in the 20–69 year age group are invited for screening every 3 years, the annual volume of activity can be estimated to amount to about 44,000 smears per year. Currently, with the opportunistic screening scenario prevalent in Malta, only 29,000 smears in this age group are being done annually and at face value this amounts to 66% of the target population.<sup>104</sup> However, the opportunistic screening activity is actually resulting in some women being over-screened while others (who may or may not be more at risk for the disease) are excluded from the potential benefits of the screening process.

The data also revealed a number of interesting findings in the distribution of cytological examination by age. Smear taking peaked between the ages of 25 and 49 years. The activity started to slow down from age 50 years, followed by an even sharper drop in the 6th and 7th decades of life. The highest smear taking rates were between the ages of 30 and 49 years, with corresponding lower rates for the 20–29 age group as well as for women older than 50 years.

Most of the smears are still taken using the conventional spatula/brush methods. Only recently has a private laboratory introduced the liquid based technique. At present, no standardised system in the reporting of smears in Malta is in place. The dyskaryosis/cervical intraepithelial neoplasia (CIN) classification is still very much in use whilst the Bethesda system which provides more detailed information about smear results and better criteria for smear suitability is not applied in every laboratory. HPV typing has been introduced by a number of private laboratories, but not as yet by the public laboratory. The Bethesda system together with HPV typing would definitely improve patient management policies, since management would focus on women with high risk HPV lesions.<sup>102</sup>

Following the recent results of the Maltese action for Eurochip-2 project, one can for the first time analyse the situation of cervical screening activity on the islands. This can be used to assess the current situation so as to identify problems of attendance in specific age groups and to estimate the need of healthcare services for establishing the organised cervical cancer screening programme in the future. This should eventually lead to a number of proposed changes which should improve the uptake of cervical screening on the islands.

## Netherlands

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By 2003, the cervical cancer incidence and mortality rates in the Netherlands decreased to 6.2 and 2.0 per 100,000 (European standardised rate), respectively,<sup>108</sup> and were among the lowest in the world. Since 1996, all women aged 30–60 receive an individual invitation every 5 years to have a conventional

Pap smear taken free of charge. The basis for invitations is the population registry. Pap smears are taken by general practitioners (GP) or trained GP assistants.<sup>109</sup> Practice guidelines concerning cervical cancer screening for GPs, pathologists and gynaecologists were published.<sup>110–112</sup> Smears are classified according to the Dutch CISOE-A classification which can be translated into other classifications.<sup>113</sup> While the screening programme is implemented regionally with a complete national coverage, it is financed by central earmarked funds, and is coordinated by a central governmental body. The requirements for the certification of the programme are described in the law on organised screening programmes.

Regular monitoring and evaluation at the regional and the national level are done continuously. Each region appoints a coordinating pathologist who is in charge of the quality control and assurance. This includes providing laboratory-specific feedback. The data used for regional programme monitoring is a combination of information from the organisation in charge of the invitations and that from the regional laboratories, including the linkage to the follow-up data for screened women stored in the computerised national registry of histo- and cytopathology (PALGA). The latter registry is also the basis of the national-level effectiveness evaluation. National evaluation includes programme as well as non-programme screening and its follow-up, and all cancers, screen-detected or not. In PALGA, the woman is identified based on at least her birth date and the first four letters of her maiden name. This registry achieved national coverage in 1990, and the quality of the registration has been improving since.

In 2003, 77% of women aged 30–64 at risk (i.e. with a cervix) had at least one smear in the past 5 years, whereas the response to the screening invitations was 65%.<sup>114</sup> The majority (>50%) of women with cervical cancer are those who were not screened regularly.<sup>115</sup> Whereas the coverage rates among the youngest invited women (30–34 years) improved substantially immediately after 1996, these have not shown any improvement since 1999, and are still lagging behind the rest of the target group by about 10 percentage points. Among the oldest invited women, however, the coverage rate is still increasing. After changes were made to the recommended follow-up (i.e. cessation of follow-up to non-dysplastic smears with inflammatory signs, and those lacking endo-cervical cells), the proportion of primary programme smears requiring any follow-up dropped from 19% to 3% per screening round.<sup>114</sup> This significantly increased the positive predictive value of an abnormal smear. A recent cost-effectiveness analysis estimated that these improvements helped decrease the cost per life-year gained from €15,000 before 1996 to €9000 thereafter.<sup>116</sup>

While at present a conventional Pap smear is the recommended screening tool, much research is also carried out into screening with liquid-based cytology, automated screening, the Human Papillomavirus (HPV) test, and HPV self-sampling. In March 2008, the Health Council advised implementation of the HPV vaccination in 12-year-old girls, and catch-up vaccination for girls aged up to 16 years.<sup>117</sup>

In summary, the 1996 changes helped improve the Dutch cervical cancer screening programme insofar that the uptake of screening within the target age group has increased, whereas the side effects have been considerably limited.

Depending on the outcomes of on-going research on incorporating HPV testing and vaccination, the programme may in the future undergo several important changes.

## Poland

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At the beginning of 2007 the organised nationwide cervical cancer screening programme started in Poland. For administrative and logistic help of the programme, coordinating offices were established by the Ministry of Health. There is one central office and 16 regional offices coordinating the Programme. Each Regional Coordinating Office has a contract with the Ministry of Health for conducting and coordinating the programme in its voivodeship. The Central Coordinating Office has a contract with the Ministry of Health for monitoring the effects of the Programme in Poland. About 8 million women aged 25–59 in 3-year intervals will receive invitations for cytology sent out by the National Health Fund (NHF). In order to collect the data of women participating in organised screening, a computer database of prophylaxis was started. The computer database is hosted in central servers and is available across the whole country. Each participant (e.g. ambulatory, colposcopy clinic, regional coordinating offices) has access to the database online and can enter the clinical data into it. Details of screened women are entered into a computer system which consists of three levels. The first level is filled by the out-patient clinic the moment the Pap smear is taken. The second level is filled by the cytology lab when the smear is evaluated. The last one is filled out in the colposcopy clinic if the cytological smear is abnormal and further diagnostic is necessary. In the database, personal and clinical information of invited patients can be registered. After the first months of screening implementation, the following problems occurred:

- (1) Most women in Poland had a Pap test taken in an opportunistic screening setting, which was better paid by the NHF, rather than cytology done within the programme.
- (2) Gynaecologists were reluctant to enter details of patients into the database system. Moreover, they had to finance computer equipment and access to the internet themselves. Therefore, a very low number of out-patient clinics decided to participate in the Programme.
- (3) Very few women attended the colposcopy clinics participating in the programme (actually less than 10% of women with abnormal results of their cytology).

Therefore, the data gathered were insufficient and diagnostic and treatment indicators were unreliable.

- (1) A large number of invitations sent out in a short time (5.5 million in 3 months) caused, in some regions, a long waiting time for cytological examination.

- (2) Low compliance to invitation (about 10%).
- (3) No central guidelines on management of abnormal Pap smears.

As a consequence, the NHF decided to change assumptions of the programme and at the beginning of 2008 the following modifications took place:

- (A) All gynaecological out-patient clinics which declared an intention to participate in the Programme were accredited by the NHF.
- (B) Details of patients could be entered into the database system in cytologic labs (on the basis of questionnaires filled in by out-patient clinics).
- (C) Doctors for Pap smears taken within the Programme are better paid by the NHF than for Pap smears taken in the opportunistic screening setting.

In summary, the screening programme in Poland is still developing and resolution of the following problems seems to be most important: (a) Access to out-patient clinics where Pap smears are taken should continue to be improved. (b) More efforts are needed to ensure that all screening smears are assessed in well equipped labs with specialised personnel (for example, reimbursement for smears evaluated in labs not complying with standards of equipment, staff qualifications and skills should be stopped). (c) Appropriate financial support should be provided for colposcopy clinics complying with programme standards. Also, only colposcopic clinics participating in the programme should be reimbursed for follow-up of women with abnormal smears. (d) Initiatives should be taken to ensure that Pap smears taken outside the programme are registered in the central database in order to effectively monitor efforts to increase attendance and to reduce the volume of non-programme smears from women eligible to attend screening e) More efforts should be made to inform women about cervical cancer screening and these should be coordinated with improvements in the invitational system.

### Portugal – Central Region

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Mortality from cervical cancer in the central region of Portugal has been experiencing a marked decrease since the introduction of cervical cancer screening in 1990; from 6.3 per 100,000 to 2.7 per 100,000 in 2005. This mortality is somewhat lower than those of the rest of the mainland, 7.1 per 100,000 in 1990 and 3 per 100,000 in 2005, and this difference is statistically significant – SMR = 0.70  $\chi^2 = 4.5$ ,  $p < 0.05$ .<sup>118,119</sup>

The incidence of cervical cancer before the beginning of the screening programme in the Portuguese Central Region was 19.6 per 100,000 in 1989, and rose progressively to 28.4 per 100,000 in 1995. Since then it has decreased progressively.

In Portugal, cervical cancer screening had been kept as an opportunistic action for many years, in almost the entire country. However, at the Central Region in the mainland, a population based cervical cancer screening programme

started in 1990.<sup>120</sup> As of June 2006, the coverage attained all of the 109 municipalities of the Central Region.

In 2007, the Southern Region (Alentejo) began the implementation of a cervical cancer screening pilot in 44 municipalities, aiming at launching a national programme in 2009.

The Portuguese Ministry of Health set the goal of covering all of the mainland health regions by the end of 2009 - according to the National Oncologic Plan 2007/2010.<sup>121,122</sup>

In October 2008 the National Directorate of Health began HPV quadrivalent vaccination (covering 6, 11, 16 and 18 types) in young girls aged 13 years, according to the new national vaccination schedule.<sup>123</sup>

The Central Region has a target population of 476,000 women (aged between 25 and 64 years), and approximately 448,000 as eligible population (after removing the women who meet the exclusion criteria). The screening has had a formal centralised organisation since 2005.

The women registered on a health database (each one with a national health number), receives a personal invitation (considering the exclusion criteria) every 3 years. This invitation is issued by the local health centres, providing a specific date to perform the test.

The programme uses conventional Papanicolaou Smear as a primary screening test, performed at local health centres by family doctors. The introduction of liquid-based cytology (routinely used in the Southern Region's pilot) is under evaluation, and it may be adopted in 2010, thereby enlarging the screening interval from 3 to 5 years. The screening is free of cost for women.

Two cytopathology laboratories, with quality assurance methodology, provide support to the screening at the Central Region. Bethesda 2001 classification is used for reporting the smear results. The procedures to maximise quality assurance in these two laboratories include: double registration of results; re-evaluation by a 3rd experienced cytopathologist in case of disagreement; review of previous screening smears for positive cases; review of false positive smears after anatomic-pathological diagnosis; review of negative smears on randomised samples in a fixed periodicity, and cito-histological correlation.

These laboratories have a permanent linkage with the local health centres (feedback of smear results) and with the nine Cervical Pathologic Units (referral centres for gynaecological diagnosis and treatment).

Between 1990 and 2005, this regional programme only had a database system monitoring cytopathologic laboratories. During 2005–2006, a new database system was developed which monitors all interactive modules (family physician/GP, cytopathology laboratory, cervical pathologic units and epidemiologic monitoring, with linkage to the Regional Cancer Registry). This database system still has some difficulties concerning the above mentioned linkages.<sup>124</sup>

Data from 2005 showed a standardised incidence ratio of 14.4 per 100,000 (5.5 per 100,000 of *in situ* cancer, and 8.9 per 100,000 of invasive cancer).<sup>125</sup> These regional data are lower than those of the rest of the mainland; however, we are slightly above the average in the EC.

Before the onset of cervical cancer screening in the Central Region, the staging analysis of cervical cancers in a Central Oncologic Hospital revision (1985) showed that less than



30% of lesions were diagnosed as stage 0–I, and over 50% of lesions were stage III and IV. With the screening implementation, the same authors, in 1997 and 2001 and in the same hospital, found that 89.5% of lesions correspond to stage 0–I, and only 5.9% were advanced cancers (stage III–IV).<sup>126</sup>

## Romania

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With an age standardised mortality rate of 10.64% in 2005, Romania reports the highest mortality from cervical cancer in Europe.<sup>127,128</sup> From 1927, when Aurel Babeș used cervical cytology for diagnosis of cervical cancer,<sup>129</sup> until now, opportunistic screening has been in practice in our country. However, a low number of tests performed with an extremely low coverage of the target population and lack of quality control in diagnosis, treatment and follow-up<sup>130</sup> has taken us to the situation that Romania has the highest incidence and mortality rate of cervical cancer in Europe.<sup>131</sup>

In 2002, the Ministry of Public Health (MPH) took the decision to finance a regional pilot screening programme, using conventional smear, organised by the “Prof. Dr. Ion Chiricuță” Cancer Institute from Cluj-Napoca.<sup>132</sup> For the rest of the country, opportunistic screening activities were financed too. The pilot programme is population based, targeting 195,000 women aged 25–64 years (3% from the whole of the female target population in Romania).<sup>133</sup> From 2004, the programme was extended regionally to five counties, representing administrative North-West European development regions of the country.

Starting in 2006, the set of indicators for monitoring and standardised tables of aggregated data, proposed by the EU-NICE-ECN network, was used to evaluate the regional screening programme. In the first round of the organised screening programme, 16.23% from the target population were tested, due to limited financial resources provided by the MPH. Difficulties appeared first in organising the management unit and then in the implementation unit network, in training people in screening management, in setting standards and criteria, as well as in the protocols for the cytological laboratories, colposcopies and treatment units. There were also problems in financing.<sup>132,134</sup>

The invitational system consists of a limited number of letters of invitation - personal invitations performed by the general practitioners, mediators from nongovernmental organisations, city-halls and churches. At the beginning, opportunistic screening was also enrolled in the programme.<sup>134,135</sup>

The screening database is connected to the regional cancer registry, which has been a member of ECNR from 2003. Although the cytological results of the screening programme are registered 100%, the histology and treatment data include less than 10%. The referral rate to colposcopy is high, but few are reported,<sup>134</sup> which explains the extremely low positive predictive value of the referral to colposcopy CIN2+. This is the reason why, since 2008, we are implementing new data reporting rules (colposcopy registries).

Quality control guidelines used are regional, according to the European recommendations.<sup>134,136,137</sup> National guidelines

are a part of the planning for a potential rollout of the regional programme to the national level, started in 2007, and the national strategy is based on eight regional management units for screening programmes, corresponding to the administrative European development of new regions of Romania.

Organising a national screening programme needs important EU assistance. At the level of screening management, no regional resources are in place. The infrastructure of the screening network is insufficient; the estimated resources available are less than 10% of the necessary amount of resources. It is an urgent necessity to organise a complex project of training, certification and accreditation, as well as some criteria for training centres, management units and implementation units. We also consider less labour-intensive HPV primary screening as a useful new method.

Decision makers in public health at the national and European level do not seem to understand the importance of the screening management units. Their existence, as well as a European School of Screening Management, is mandatory for the quality of all national screening programmes.

## Slovak Republic

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The Section of Gynaecological Oncology and Section of Colposcopy and Cervical Pathology, as part of the Slovak Gynaecological and Obstetrics Society, recently prepared proposals oriented to the realisation of systematic cervical cancer screening across the whole territory of Slovakia. This proposal was accepted by members of the Slovak parliament and is now a law, No. 661/2007 (since January 1st 2008).

According to this law, cervical cancer screening in Slovakia will be organised from one central point which has the working name ‘Reference centre’. The Reference centre will be a governmental institution. The Slovak Ministry of Health Care is responsible for constituting the centre. This centre has been designed to facilitate the written invitation of women to cytological examination and for the monitoring and feedback of the entire cervical cancer screening process.

The screening test is via conventional cytology. Screening starts for women at the age of 23 years and finishes at the age of 64 years if the three previously performed tests have been negative. During the first 2 years of screening we apply 1 year examination intervals. If the first two smears are negative the next examinations should be performed at 3-year intervals. If the woman starts screening later than age 23 years the schedule is the same.

The smears should be evaluated in accredited cytological laboratories which are able to apply and respect the principles accepted by European Union. The results should be evaluated and formulated according to the Bethesda classification.

The detection of HPV is not at the present time a part of screening due to the high price of this test. Health insurance companies are obliged to pay for the detection of HPV for women with cytological confirmation of ASCUS and for women 6 months after conisation for dysplasia using the method HC2.

Of great importance in the introduction of systematic screening is the health education of the female population,



oriented to information on the importance and advantages of screening and its performance and positive consequences.

In our country, the vaccines Cervarix and Silgard (Gardasil) are accepted and have been available since 2007. Both vaccines could be used for girls from the age of 9–10 years and for women under 25–26 years of age. Vaccination is not covered by health insurance companies. Health insurance companies reimburse 10% of the price of the vaccine to girls aged 12 years.

## Slovenia

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In Slovenia, opportunistic screening was introduced in regular gynaecological practice in 1960. According to the data of the Cancer Registry of Slovenia, the crude incidence rate of invasive cervical cancer increased from 22.5/100,000 in 1950 to 34/100,000 in 1962 and then decreased to 14/100,000 in 1979, when the incidence was the lowest.<sup>138</sup> Since then, till 1993, there were no major changes, but in 1994 the incidence rate started to increase again and reached 20/100,000 in 2000.<sup>139</sup> Cervical cancer mortality, however, has never been as high in Slovenia as in some Eastern European Countries, though the official cervical cancer mortality is underestimated for about 20%; on the basis of death certificates it is not always possible to distinguish between cervix, corpus and unspecified uterine cancer deaths.<sup>140</sup> The increase in cervical cancer incidence rates in the 1990s was ascribed to the inefficiency of opportunistic screening in Slovenia and in 2003 (after the initial pilot study) the organised screening programme was established.<sup>141</sup> It has its legal basis in several regulations: the Screening Registry with its database on all smear reports and histology reports was included in the Act on Databases in Health Care.<sup>142</sup> The special regulation with standards for cytopathology laboratories was published by the Ministry of Health and laboratories have been reviewed to evaluate whether they comply with these standards.<sup>143</sup> The screening policy was defined with the ministry's recommendation on preventive examinations in primary reproductive health care.<sup>144</sup> National guidelines for quality assurance and control of all procedures involved in cervical cancer screening and treatment of intraepithelial lesions and of cervical cancer were published at the beginning of the programme<sup>145–147</sup> and reviewed in the following years.<sup>148–150</sup> All of these guidelines are available at the web-site of the programme also (<http://www.onko-i.si/zora/>), but currently in Slovenian language only.

According to the new recommendations, each woman between ages 20 and 64 is to be invited to perform a preventive gynaecological examination together with a PAP smear once every 3 years (after two negative smears) – either by her 'personal' gynaecologist with whom she has already been registered or from the Screening Registry in case she has not been registered yet.<sup>142</sup> All smear reports (in electronic form) from all cytological laboratories are gathered in the central database of the Screening Registry which is linked to the central Population Registry.<sup>142</sup> The Screening Registry also enables the sending of invitations to women whose smear has not been registered in the past 4 years.

Data from the Screening Registry at the Institute of Oncology in Ljubljana also serve to monitor coverage and compliance with screening together with other screening performance indicators. The condition for establishing such an information system was uniform smear reports and standardisation of work in cytopathology laboratories and was introduced during the pilot stage.<sup>143</sup> The National Board nominated by the Ministry of Health supervises the results of the programme.<sup>151</sup>

Four years after the start of the national programme, 70% of women in the target age group (20–64 years) had at least one smear registered in the Screening Registry. The percentage is about 80% till the age of 45 and smaller among older women.<sup>151</sup> In 2006, 228,593 smears have been registered from 205,036 women aged 20–64; 6.1% of screening smears were less adequate or inadequate and in 10.3% some cell abnormality has been found. In 71.8% of women with high grade intraepithelial lesions, the pathology report revealed CIN2 or worse lesions (positive predictive value). In 2006, 160 new cervical cancer patients were registered in the Cancer Registry of Slovenia. The linkage of their data with the Screening Registry enables us to review their screening history; nearly three quarters of these patients did not attend for regular screening. According to the data from the Cancer Registry of Slovenia, the incidence rate of cervical cancer started to decrease, especially in the age group from 35 to 49 years.<sup>151</sup>

## Spain

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Incidence and mortality from cervical cancer (CC) in Spain are in the lower end of the world rankings, similar to those observed in the USA and Canada but double that of Finland. The age-standardised incidence and mortality rates for 100,000 women are 7.6 and 2.2, respectively.<sup>152</sup> These relatively low rates prevented Spanish health authorities from prioritising a population-based screening programme against cervical cancer.

Spain is divided into 17 autonomous communities and each is responsible for its own health policy and management. There is not a unified health data collection system but there are 13 population-based cancer registries that provide good quality data and some also collect information on pre-neoplastic cervical lesions. Spain has a universal Health System and women can access gynaecological clinics free of charge.

All regions have progressively adapted cervical cancer screening recommendations from scientific organisations, especially those issued by the European Union leading to an overall 14 regions with established protocols. Most programmes target women sexually active between 25 and 65 years of age. Over the last decades, opportunistic screening has been the prevalent preventive intervention throughout the different communities. More recently, La Rioja and Castilla & Leon have initiated an organised screening programme while in all other communities there exist organised strategies with limited call-recall systems and monitoring.<sup>153,154</sup>

Currently, cytology is the reference method for cervical screening. Sample collection is performed by gynaecologists and/or midwives in both reproductive and primary health care centres. Colposcopy is widely available and is often performed as a complementary evaluation. Cytologies are to be performed on a 3 yearly basis after two consecutive negative ones. In some regions there is an active educational effort to inform women on cervical cancer prevention activities.<sup>154</sup>

HPV DNA testing is starting to be included as a novel detection and triage tool in Spain. Catalonia is the first region that has included HPV DNA testing in the publicly financed screening protocol and introduced it as a tool in clinical management algorithms of screened women. Women with inadequate screening (aged over 40 years and with no Pap in the previous 5 years), those with atypical squamous abnormalities with unknown significance and those who underwent surgical conisation are eligible for this testing. This new programme was fully implemented during 2007 and first results are expected for 2009. Castilla & Leon is using HPV testing among women over age 34 as an adjuvant to cytology. Extremadura and Andalusia are likely to follow suit and include HPV DNA as a triage tool for abnormal results.

Each community actively evaluates screening coverage and access as well as sexual behaviour through surveys. All communities participate in the 'Encuesta Nacional de Salud' carried out every 2–3 years by the National Office of Statistics. Other sources of information are specific surveys aimed at evaluating screening coverage at a national level.<sup>155,156</sup> Global overall coverage data (% of those female respondents aged 18–69 who self-reported receiving a past smear during the last 3 years) ranges from 50% to 69%.<sup>155–158</sup> In the most recent survey, younger women (30–39 years) reached a coverage of 67%, while women aged 60–69 only 35%.<sup>157</sup> Women in the richest income quintile reached a screening coverage of 65% while among those most disadvantaged only 32% women are screened.<sup>157</sup> Despite general recommendations, many women are often overscreened with annual cytologies. Of the total women screened, approximately 30% undergo cytologies with their private health insurance companies.

Both commercially available HPV vaccines have been authorised in 2006 and 2007 and will be implemented in the immunisation schedules free of charge for one cohort of girls aged between 10 and 14 years in all communities before 2010.<sup>159</sup>

## Sweden

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The Swedish screening programme has been in action since the end of the 1960s. There are National recommendations, the latest revision in 1998, but the 21 counties are autonomous in providing health care and the implementation is therefore regional.<sup>160</sup>

Age limits and intervals for invitation to cervical cancer screening are every 3 years for ages 23–50 years and every 5 years for ages 51 to 60 (with one or two exceptions). Invitations are issued by the laboratories except in Stockholm

where there is a special screening office covering several laboratories in the metropolitan area.<sup>161</sup>

Invitations are sent to women who have not had a smear registered in the morphology database for 3 (or 5) years. Fees for a cytological smear differ between 0 and 200SEK (approx. 20€). In some counties a specific time and place for the test is issued in the invitation, while in others, women need to make their own reservations at the antenatal centres.

In Sweden, routine smear taking is performed by midwives at antenatal centres supervised by gynaecologists. The screening invitation usually gives an appointment to such a clinic, but if the woman prefers to go to a doctor on her own initiative, that test is registered and the next invitation is postponed. This is what we call integration of opportunistic and organised screening. Smears outside the programme are usually taken by private gynaecologists, whereas GPs are seldom involved. Coverage is higher in the rural areas where organised screening dominates and personal invitations to screening are the rule.

Computer systems linking cytology registers and invitation have been in action since the 1960s. Today, there are two different database systems used. Terminology for diagnosing cervical cytology varies slightly between laboratories. Since about 2000, a common terminology with only 14 SNOMED codes is recommended but there are still variations regarding the interpretation of ASCUS (atypical squamous cells of undetermined significance).<sup>162</sup>

Sweden has a national population register and every individual has a Personal Identification Number used in all contexts of health care from birth throughout life. This makes it possible to collect and compare health data from registers. A National Cancer Registry has been in practice since 1958 and it is mandatory for all laboratories and clinicians to report all cases of invasive cancers as well as Cancer *in situ*/CIN3 by location (T83) and by the SNOMED classification code. Since 2004 all gynaecological tumours have also been classified by FIGO stage.<sup>163</sup>

There is a list of quality indicators, the most important being coverage of testing within the recommended screening interval in the screening ages.<sup>164</sup> A nationwide audit of cervical screening was performed in connection to the establishment of a national register for the quality control of cervical cancer screening. The screening history of all cervical cancer cases in 1999–2001 could be related to that of population based controls. This audit was published in 2008.<sup>165</sup>

Recent development – a professional network for the coordination of the regional screening programmes is formed in order to optimise the computer systems. The national board of health and welfare and its national registries cooperates with this network in developing standards for mandatory reports of morphology and HPV data concerning all HPV related cases of disease to the central registers.

The responsibility of long term follow-up after diagnosis and treatment of atypical smears is being moved from individual clinics to the screening invitation systems, taking advantage of the computerised call and recall and the use of trained midwives to take the tests. HPV-testing data are to be registered in a detailed standardised format that can be integrated in the screening registers to facilitate the flow of the screening algorithms.

Strengths – Good registers with possibilities of complete linkage allow for good monitoring. Coverage is 79% in the screening ages, Total cervical cancer incidence is 6.6 per 100,000 women (world standard rate).<sup>166</sup>

Drawbacks – Decentralisation has slowed down the coordination necessary for the integration of novel technologies into cervical cancer prevention.

### United Kingdom – England

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Currently, the NHS Cervical Screening Programme screens 3.4 million women of all ages in England each year.<sup>167</sup> Coverage has dropped to 79.2% of women having been screened in the last 5 years and this is a matter of some concern, particularly as younger women now are less likely to attend for screening than their counterparts in previous generations.<sup>168</sup> Cervical screening coverage rates were maintained at over 80% for a number of years and cervical cancer rates fell from 15 per 100,000 population in 1986 (just before the national screening programme was introduced) to 8.7 per 100,000 in 2005.

In 1988 the organisation of call and recall signalled the official beginning of the NHS Cervical Screening Programme. Screening was targeted at women aged 20 to 64 and performed at least 5 yearly. Smears were largely taken by doctors in general practice and in 1990 a system of payments for General Practitioners (GPs) depending on coverage rates was introduced. Over the next few years coverage rose to over 80% of eligible women having been screened in the previous 5 years.

Quality Assurance (QA) was introduced to the programme in 1994 with the introduction of regional teams which monitor the service locally. They also validate statistical reports produced by the service and ensure services work to national minimum standards. Regular QA visits are carried out for all parts of the service with recommendations for improvement made where needed and followed up as appropriate.

The biggest changes to the screening programme have come in the last 5 years. The requirement for women to be screened 'at least every 5 years' had resulted in a mix of screening frequencies around the country. As a result of an independent audit in 2003 screening intervals were standardised at 3 yearly for women aged 25–49 and 5 yearly for women aged 50–64.<sup>169</sup> The same audit led to the policy decision to raise the age of first invitation to 25. The decision was also made in the same year to convert to Liquid Based Cytology (LBC).<sup>170</sup>

Conversion to LBC is now complete. The latest year's figures from the screening indicate that the proportion of inadequate smears had dropped to 2.9% whereas it had been consistently over 9% since reporting began 10 years earlier.<sup>167</sup> Other benefits of LBC conversion include test results being available sooner for women, with 49% reported within 2 weeks compared with 34% in 2 years previously. Two-week turnaround in laboratories was not even reported before conversion to LBC began.

Over 100,000 women per year are referred to hospital colposcopy clinics for investigation of abnormal cytology following a non-negative screening result.<sup>167</sup> Information systems in cervical screening are not all-encompassing and obtaining timely and accurate information on colposcopy outcome, including histology where appropriate, is difficult and time-consuming. The regional quality assurance teams are a key feature in effective monitoring of colposcopy and histology.

The next few years see a number of challenges ahead for the cervical screening programme in England. Automation of cytology reporting is the subject of a major trial,<sup>171</sup> as is primary HPV testing.<sup>172</sup> Six sentinel sites have implemented HPV triage of borderline and mild abnormalities (equivalent to ASCUS and LSIL) with a view to eventual national roll out.<sup>173</sup>

The Department of Health announced the introduction in September 2008 of an HPV immunisation programme to routinely vaccinate girls 12–13 years of age, with a catch-up for girls up to age 18 years over the next 2 years.<sup>172</sup> This is not expected to have any impact on the screening programme for some years, but may assist in addressing the danger of increasing incidence caused by falling coverage in younger women.

The NHS Cervical Screening Programme is estimated to be saving currently around 3000 lives each year in England.<sup>174</sup> It has been hugely successful in controlling cervical cancer. Over the next few years new technologies will be the topic of much debate and could possibly lead to a redesign of the Programme. However, the basic issue of recruiting women to be screened remains of the highest importance.

### Conflict of interest statement

None declared.

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