



Strengthening cervical cancer prevention in Europe

**Meeting of policy-makers and programme managers
Copenhagen, Denmark, 29-31 May 2007**

Report

Abstract

For many centuries, the diagnosis of cancer was a death sentence. However, in the last 50 years, we have seen progress in the management and control of some cancers, cervical cancer being one of them. It is preventable. Yet, every year, cervical cancer causes the death of more than 30 000 women in the WHO European Region.

The Sixtieth World Health Assembly (2007) reconfirmed the global importance of this problem and the readiness of WHO to assist Member States to resolve it.

The meeting of policy-makers and programme managers on strengthening cervical cancer prevention in Europe provided a forum for sharing the best practices available in the countries of the WHO European Region. Plans were developed on how to overcome existing barriers in those Member States that have expressed their willingness to protect women from this disease. Representatives of 46 Member States and of international partner organizations actively participated in the meeting.

Recent WHO strategies and publications related to the prevention and management of cervical cancer and the introduction of HPV vaccines in countries, and to assisting in the development of national policies and programmes on the use of HPV vaccines within the broader context of cancer control and reproductive health, were presented and discussed. The report of the meeting may assist WHO Member States in strengthening informed decision-making on the prevention of cervical cancer.

Keywords

UTERINE CERVICAL NEOPLASMS –
PREVENTION AND CONTROL
PAPILLOMAVIRUS INFECTIONS –
PREVENTION AND CONTROL
CANCER VACCINES – THERAPEUTIC USE
POLICY MAKING
INTERNATIONAL COOPERATION
EUROPE

Address requests about publications of the WHO Regional Office for Europe to:

Publications
WHO Regional Office for Europe
Scherfigsvej 8
DK-2100 Copenhagen Ø, Denmark

Alternatively, complete an online request form for documentation, health information, or for permission to quote or translate, on the WHO/Europe web site at <http://www.euro.who.int/pubrequest>.

© World Health Organization 2007

All rights reserved. The Regional Office for Europe of the World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either express or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use. The views expressed by authors, editors, or expert groups do not necessarily represent the decisions or the stated policy of the World Health Organization.

Contents

	Page
ACRONYMS.....	1
INTRODUCTION.....	2
OPENING OF THE MEETING.....	2
OBJECTIVES OF THE MEETING.....	3
CERVICAL CANCER PREVENTION IN THE WHO EUROPEAN REGION.....	3
Challenges.....	3
Country examples.....	4
Finland.....	4
Kyrgyzstan.....	5
Discussion.....	5
POLICIES AND APPROACHES IN THE PREVENTION AND MANAGEMENT OF CERVICAL CANCER AT GLOBAL AND REGIONAL LEVELS.....	6
WHO policies in the prevention and management of cervical cancer.....	6
Screening for cervical cancer in the European Union (EU).....	8
Country examples.....	10
Armenia.....	10
Iceland.....	10
Lithuania.....	11
Discussion.....	11
POLICIES AND APPROACHES IN THE PREVENTION AND MANAGEMENT OF CERVICAL CANCER AT GLOBAL AND REGIONAL LEVELS: HPV VACCINES.....	12
Immunization programme in the WHO European Region.....	12
HPV vaccine and immunization policy.....	14
Health economics analyses of HPV vaccination.....	15
Health professionals working with adolescents in the introduction of.....	17
HPV vaccines and the reduction of risk behaviour: areas for consideration.....	17
Discussion.....	18
SETTING PRIORITIES FOR NATIONAL POLICIES ON CERVICAL CANCER PREVENTION.....	18
Cervical cancer prevention in Denmark.....	18
Cervical cancer prevention and HPV vaccine policy in France.....	19
Cervical cancer prevention: considerations for universal HPV vaccination in females aged 12–17 in Germany.....	20
Prevention strategies of cervical cancer in Italy.....	21
Cervical cancer prevention in Turkey.....	22
Discussion.....	22

STRENGTHENING CERVICAL CANCER PREVENTION IN COUNTRIES	23
Issues for consideration when setting priorities	23
Introduction to working group sessions	24
Cervical cancer prevention programmes in countries of the WHO European Region: current situation	25
Country needs for cervical cancer prevention	26
Future directions and planned action in the countries	27
Anticipated assistance from WHO and other partners	27
The role of the mass media: friend or foe?	28
Discussion	29
Ongoing research in the area of cervical cancer prevention.....	29
Discussion	31
RECOMMENDATIONS.....	32
CLOSURE OF THE MEETING	34
REFERENCES	35
ANNEX 1:ASSISTANCE FROM WHO AND OTHER INTERNATIONAL ORGANIZATIONS.....	36
ANNEX 2: LIST OF PRESENTATIONS AND SPEAKERS	41
ANNEX 3: PARTICIPANTS	43

Acronyms

ABC	Abstinence, behavioural change, condom use
ACCP	Alliance for Cervical Cancer Prevention
ASCUS	Atypical squamous cells of undetermined significance
BCG vaccine	Bacillus of Calmette and Guérin (tuberculosis vaccine)
DNA	Deoxyribonucleic acid
DPT	Diphtheria, Pertussis, Tetanus
GAVI	Global Alliance for Vaccines and Immunisation
HIB-conj.	Conjugated Haemophilus Influenzae type b
HIV	Human Immunodeficiency Virus
HPV	Human papillomavirus
LBC	Liquid-based cytology
LEEP	Loop Electrosurgical Excision Procedure
MR	Measles and Rubella
Td	Tetanus and Diphtheria
VIA	Visual inspection with acetic acid
VLP	Virus-like particle

Introduction

Although death from cervical cancer is avoidable, more than 30 000 women in the World Health Organization (WHO) European Region die from this disease each year. The highest mortality rates from cervical cancer are found in parts of central and eastern Europe where they are two to four times as high as in western Europe. These discrepancies are partly due to late diagnoses. There is a great potential to reduce the incidence of and mortality from cervical cancer in this Region through various strategies.

Cervical cancer is almost entirely caused by the human papillomavirus (HPV) and HPV vaccines have recently been licensed in countries of the Region. The vaccines can be used to complement existing cervical cancer prevention strategies, such as those to reduce sexual risk behaviour – and thus exposure to HPV - and cervical cytological screening to detect precancerous lesions. However, planning the introduction of these vaccines so that they complement primary and secondary prevention strategies is complex and challenging. Decision-making on these issues potentially involves a wide variety of programmes including those dealing with reproductive health, cancer control and noncommunicable diseases, immunization programmes, and adolescent health.

The WHO Regional Office for Europe organized this meeting to provide the opportunity for policy-makers and programme managers to discuss existing and possible new strategies for the prevention and control of cervical cancer.

Opening of the meeting

In welcoming the participants (Annex 3) to the meeting, Dr Marc Danzon, WHO Regional Director for Europe, expressed his appreciation of their collaboration and thanked them for coming to the meeting. He noted that cervical cancer poses many challenges to the Member States and that WHO has an important role to play in assisting them to address these problems.

In order to do so, Governments need to know to which extent the disease is a burden in their countries, and understand the factors that influence it and the prevention, early detection and treatment strategies that could provide most benefit. As different options for prevention and control exist, programmes may consider multifaceted strategies, preferably those that balance political, economic and financial issues and value equity and solidarity. At the policy level, countries need to address the accessibility and quality of screening and vaccines. HPV has no boundaries – neither should the response.

Countries need to carefully assess the safety and price of introducing vaccines, especially since the current vaccine is so expensive that many health systems cannot afford it.

Last but not least, cultural aspects have to be taken into account when considering the introduction of vaccines. Information and education are necessary, especially given that negative attitudes towards sexual health issues may impede action.

Objectives of the meeting

In 2006, the WHO Regional Committee for Europe adopted *The European Strategy for the Prevention and Control of Noncommunicable Diseases (1)* that promotes a comprehensive and integrated approach to disease control. During the same year, the first HPV vaccine was licensed in most countries of the WHO European Region. Although this provides a new possibility of preventing cervical cancer, it also provokes a debate on the best combination of strategies to control the disease.

Several programmes were involved in the preparation of this meeting, including those dealing with noncommunicable diseases (including cancer), sexually transmitted infections, reproductive health, adolescent health and vaccine, and immunizations.

The overall objective of the meeting was to assist countries in strengthening informed decision-making on the prevention of cervical cancer.

The specific objectives were:

- to assist Member States in developing national policies and programmes on the introduction of HPV vaccines within the broader context of cancer control and reproductive health;
- to discuss recent WHO strategies and publications relating to the prevention and management of cervical cancer and the introduction of HPV vaccines in the countries; and
- to develop a network of experts and a mechanism for supporting countries in following up the outcome of the meeting.

Cervical cancer prevention in the WHO European Region

Challenges

Why do more than 30 000 women in the region die each year from cervical cancer when the disease is preventable? Are the countries of the Region so diverse that a four-fold difference in cervical-cancer-related mortality between one country and another is justified? Variations in disease burden are obviously influenced by variations in the use and quality of diagnostic procedures, screening tests and the collection of data on outcomes, and the decrease in cervical cancer incidence and mortality that has been observed in most countries. This decline is not sufficient. Preventing cervical cancer in the Region poses multiple challenges that have to be addressed.

One of the challenges is at the level of women and the community. Women need to be better informed and educated about the benefits of prevention programmes. This can be achieved through different channels, including family, schools, health professionals, campaigns and the mass media. It is also important that women have access to prevention services.

Another challenge is how to improve service delivery. It is known that organized screening can prevent up to 80% of cervical cancer cases but it is available in only eleven countries of the Region. In central and eastern European countries and the newly independent states of the former Soviet Union provider-initiated organized screening existed until 1991 but disappeared with the health system reform. This resulted in low-coverage opportunistic screening and increasing cervical cancer incidence and mortality.

A third challenge is how to adapt policies. In many countries, cervical cancer prevention and control are given low priority; in others, updated strategies exist but are not implemented.

Finally, there is the challenge of deciding whether and how to introduce new technologies, such as HPV tests in primary screening, liquid-based cytology and HPV vaccines.

These challenges can only be met through a comprehensive approach that recognizes the roles of the individual, the family and the community and promotes interaction between them. The health systems and policies related to cervical cancer prevention and control also have roles to play in this approach.

Country examples

Finland

Finland is characterized by very low rates of cervical cancer incidence and mortality (age-standardized rates (ASR) of 4.3 and 1.8/100 000 women, respectively) and the disease is no longer a major problem.

An organized, cytology-based cervical cancer screening programme, introduced in 1964, with high coverage and quality control mechanisms, has resulted in a >80% decline in the incidence of and mortality from the disease. An assessment of the use of HPV DNA as a primary screening test, as compared to cytology, is currently being made in a randomized design.

Finland's success in controlling cervical cancer has raised many questions regarding the value of introducing HPV vaccines. Some experts have proposed evaluating the impact of HPV vaccination on cervical cancer as an endpoint within the organized screening programme.

Kyrgyzstan

In Kyrgyzstan, the reported incidence rate of cervical cancer per 100 000 women increased from 9.1 in 1999 to 14.1 in 2006. However, a pilot survey conducted in 2002 suggested serious underreporting. Nearly 90% of invasive cancers are advanced. The inclusion of cancer of the reproductive system, including cervical cancer, as one of the health priorities in the recently approved National Strategy on the Protection of Reproductive Health (2006–2015) offers possibilities for better control. Although the implementation of activities relating to cancer control is planned for the second phase (2010–2015), the action plan will be developed in the near future.

There is no doubt that cervical cancer is an important public health problem given the high incidence of the disease, the large number of advanced cases and the related high mortality. Patients with cervical cancer lack access to quality medical services. Awareness of cervical cancer is low among the general public and among the health care workers. There is a shortage of trained physicians, cytologists, screening infrastructure, supplies and communication services. The main directions for action include: (1) a reform of the nurses' training curriculum to include the early detection of cervical cancer; (2) awareness-raising activities and the development of information and education materials for the general public and patients; (3) training of health workers; (4) the development of guidelines and algorithms for screening and for the treatment of pre-invasive and invasive disease; (5) setting up a screening programme at national level with defined targets; and (6) purchasing sufficient equipment and supplies. Furthermore, an assessment needs to be made of how and when to introduce HPV vaccines. Conceivably, HPV vaccination could be included in the immunization schedule and thus covered by the State Insurance Programme, and vaccine procurement could be implemented through the Ministry of Health. Finally, all international organizations and agencies involved in reproductive health in the country should be encouraged to integrate their efforts to promote cervical cancer prevention and control.

Discussion

It was clear from the presented data that important challenges remain at regional and national levels. Cervical cancer is not given the importance it deserves. In some countries, the reported incidence is not reliable. The example of Finland shows that incidence can be reduced to very low levels, in sharp contrast to countries with higher incidence levels. If a reduction in incidence and mortality is to be achieved, the coordination and integration of intervention measures along the continuum of care are necessary.

To have a realistic idea of the burden of disease in a particular country or region, it is important to have reliable data. Unfortunately, the different databases on cancer incidence and mortality that exist do not always provide exactly the same type of data because they use different sources. WHO mortality data are compiled on the basis of the latest available national data received. Whereas some countries do have up-to-date information, others are several years behind in registering mortality data. Efforts to

generate updated and comparable data should continue. A very interesting database is the WHO/ICO (Institut Català d'Oncologia) Information Centre on HPV and Cervical Cancer (www.who.int/hpvcentre). This includes country-specific data on cervical cancer incidence and mortality, HPV prevalence, sexual behaviour, and screening and immunization programmes. It would also be interesting to have data on severe disability resulting from cervical cancer and the related costs to health systems but these have not yet been collected. It is already a sizeable challenge to have uniform cancer registries and comparable mortality data.

Various countries in the Region are making serious efforts to implement organized screening programmes. Some are more successful than others. An example is Italy where screening is organized in almost the entire country with the exception of the southern provinces. However, organizing a screening programme takes time and requires continuous effort to maintain high coverage and quality. Overtreatment, especially in young women, has to be avoided because of the possibility of adverse effects at a later stage. In Finland, the response rate to organized screening invitations is more than 70%, with higher participation in rural than in urban areas.

Young people and those living in large cities are more difficult to reach. New technologies, such as vaccination, might provide opportunities to reach them but this should be carefully assessed.

The current high cost of vaccines is also an issue and programmes should avoid strategies that provide vaccine and screening (double protection) to one part of the population and neither vaccine nor screening to another part as this would increase the current disparities in the burden of disease.

The importance of clinical vaccine trials with invasive cancer as an endpoint was further discussed. There is indeed a need to know how the vaccine performs at population level and what the impact is on invasive cancer and not only on its precursors. However, it was noted that it would be unethical to conduct a study with cancer as an endpoint without treating detected cases of high-grade dysplasia. Conducting these trials in countries where effective organized screening programmes are in place is a possibility but, as invasive cancer is rare in these countries, large multi-centre studies carried out over several years will be necessary.

Policies and approaches in the prevention and management of cervical cancer at global and regional levels

WHO policies in the prevention and management of cervical cancer

In 2005, there were an estimated 493 000 new cases of cervical cancer and 274 000 related deaths. The age-standardized mortality rates in the WHO European Region vary from 0.8 to 12.5 per 100 000 women. Cervical cancer is especially a problem of

low- and middle-income countries where it is the leading cause of death from cancer in women under 65 years of age. Persistent infection with oncogenic HPV types has been identified as the cause of cervical cancer and HPV 16 and HPV 18 are responsible for ~70% of all cases of invasive cervical cancer.

The risk factors for cervical cancer and the natural history of the disease are well known. Its usual slow progression provides an opportunity for secondary prevention through screening. Several screening tests exist, including cytology, HPV DNA tests and visual inspection tests. New directions in cervical cancer prevention include rapid HPV-based tests and HPV vaccines.

WHO has the mandate of the World Health Assembly to prioritize cervical cancer control. The WHO approach to cancer control is comprehensive and involves the collaborative efforts of several departments and programmes of the Organization. In 2004 and 2005 respectively, World Health Assembly Resolutions WHA57.12 on reproductive health and WHA58.22 on cancer prevention and control were adopted. This year (2007), progress on cervical cancer prevention and control was reported to the Sixtieth World Health Assembly and a global action plan against cancer is being developed.

The vision of the global action plan is to free the world from preventable cancer and to ensure that the best possible treatment and care are accessible to all patients. Cancer control needs a comprehensive approach, encompassing prevention, cure, care and management and including the monitoring of results. For cervical cancer specifically, this means primary prevention, secondary prevention, treatment, palliative care, and monitoring and evaluation. Partnerships are also important to achieving the ambitious goal of reducing the incidence of and mortality from cancer. Therefore, there is a need to: (1) advocate cervical cancer prevention, as well as the treatment and care related to the disease; (2) promote WHO strategies that impact on cervical cancer; (3) promote national cancer control programmes; (4) monitor the implementation and impact of national and global interventions; (5) develop partnerships; and (6) further develop the cervical cancer research agenda.

To facilitate this process in the countries, WHO provides technical support, such as the following modules on cancer control: *Comprehensive cervical cancer control: a guide for essential practice* (2) (a WHO publication available in English and French and soon to appear in Russian) and *Planning and implementing cervical cancer prevention* (3), a manual for managers produced by the Alliance for Cervical Cancer Prevention (ACCP).

In conclusion, cancer is an increasing public health threat, particularly in low- and middle-income countries and is a WHO priority; WHO is developing a global action plan against cancer, which includes cervical cancer control as part of the overall framework; WHO uses a comprehensive and integrated approach to cervical cancer control in the countries in the context of national cancer plans; and partnerships are essential for moving ahead.

Screening for cervical cancer in the European Union (EU)

Articles 95, 152 and 300 of the European Commission (EC) Treaty provide the legal basis for public health action. The objectives of the EC policy in the field of cancer are: (1) to create systems for data collection; (2) to prevent cancer by promoting healthy lifestyles and motivating citizens to participate in screening; and (3) to develop and disseminate evidence-based scientific consensus materials on screening, training in oncology, and other relevant topics.

In December 2003, the Council Recommendation of 2 December 2003 on cancer screening (2003/878/EC) was made on how population-wide screening should be organized for cervical cancer. The Recommendation states that Pap smear screening for cervical cancer precursors should not start before the age of 20 or later than the age of 30.

Future priorities include a scientific report on the implementation of the Council recommendation on cancer screening. The sources of information for this report will be projects of the European Cancer Network (ECN) and the European Network for Information on Cancer in Europe (EUNICE) (with project leaders in the International Agency for Research on Cancer (IARC)) as well as the Member States. The report will be discussed on the occasion of the Cancer Conference, which will be held in February 2008 during the Slovenian presidency of the EU. In addition, a European Commission Communication on cancer will be published.

With regard to HPV vaccination, the EC:

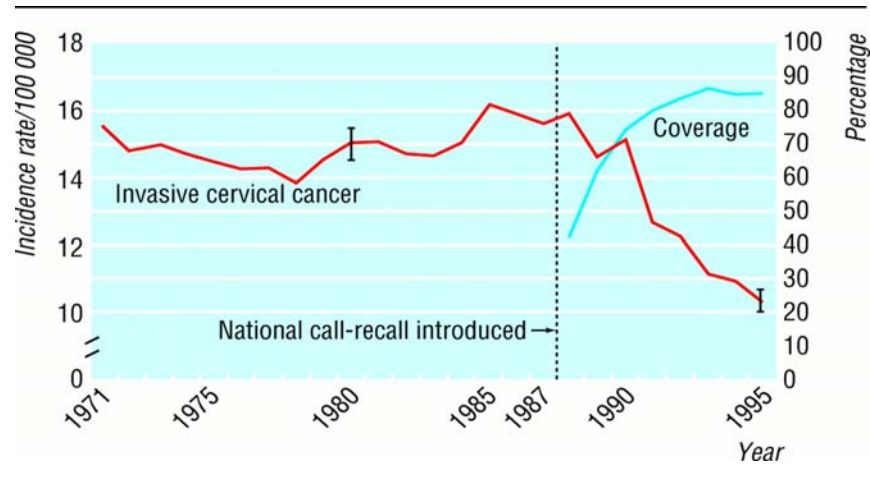
- organized a meeting of EU Member States' officials in May 2007 to discuss the current status of HPV vaccination policies;
- has requested the European Centre for Disease Control (ECDC) to prepare a scientific report on possible policy options, including the advantages and disadvantages of the HPV vaccines;
- is planning to organize a scientific conference, in conjunction with IARC and WHO.

The EU *European guidelines for quality assurance in cervical cancer screening* (4) recommend the organization of screening programmes, the use of cytology as a standard screening method, and the use of the Bethesda system.

There is evidence in Europe that organized screening is more effective and more cost-effective than opportunistic screening, where the initiative for screening has to be taken by the woman herself. In this connection, several case-control studies, cohort studies and trend analyses have been conducted, for example in Finland, Iceland, Norway, Sweden and the United Kingdom, and the results published. Finland and Iceland are examples of how cervical cancer incidence and mortality can be reduced through the introduction of organized, high quality screening programmes with wide coverage. The importance of coverage has also been shown in the United Kingdom, where a dramatic reduction in incidence was observed after the introduction of the

national call-recall system in 1987, which resulted in a two-fold increase in coverage through the screening programme (Fig. 1).

Fig. 1. Cervical cancer incidence rates in the United Kingdom after introduction of national call-recall system



Source: Quinn M, Babb P, Jones J. Effect of Screening on Incidence and Mortality from Cancer of the Cervix in England: Evaluation Based on Routinely Collected Statistics. *British Medical Journal*, 1999, 318: 904-8.

Another example is Norway, where nationwide organized screening was introduced in 1995. Compared to the period 1992–1994 (before organized screening), the overall coverage rate increased only 7% in 1998–2000, whereas in older age groups increases of 20–30% were recorded; in the period 2002–2004, even though 10% fewer Pap smears were taken, cervical cancer incidence was reduced by 22%.

In the Netherlands, the introduction of organized screening resulted in higher coverage, fewer positive tests without an increase in interval cancers, better follow-up of patients with abnormal smears and a reduction in the number of smears without a drop in coverage.

Screening policies vary from country to country. Eleven countries (Denmark, Finland, Iceland, Ireland, Italy, Poland, the Netherlands, Norway, Slovenia, Sweden and the United Kingdom) now have organized screening, at least at regional level. In the other countries, opportunistic screening is still being used. In Finland, Ireland, the Netherlands and the United Kingdom, women are actively invited to take part in screening programmes. Other countries, such as Denmark, Hungary and Slovenia, invite those women who do not spontaneously attend.

Screening intervals vary from one to twelve years depending on the country. The starting age for screening varies from 15 to 30 years. Some countries also recommend that screening be stopped for older women (age group 59–70) who have had two consecutive negative smears.

The conventional Pap screening test is the most commonly used but liquid-based cytology (LBC) is gradually gaining ground in some Member States. Several Member States use HPV DNA testing with cytology in specific cases (ASCUS Pap smears after treatment of precancerous lesions). While most countries now use the Bethesda system, some countries (e.g. Austria, Germany and the Netherlands) use other systems.

HPV testing as a primary screening tool is currently being assessed in the Region through large randomized controlled trials. In several eastern European countries, colposcopy is used as a screening test and not as the diagnostic tool it is intended to be. This is of concern.

Country examples

Armenia

The incidence of cervical cancer in Armenia has slowly risen from 11 to 14 per 100 000 women in the last 15 years but the main problem is the sharp increase in the number of diagnosed women who remain untreated. Whereas the rate was only 15% in 1985, it has been 40–50% for the last 10 years, resulting in an increase in related mortality. Moreover, national statistics are not very reliable. A survey carried out in 2005 showed that 30% more precancerous lesions had been detected than were recorded in the official reports.

In 2006, an opportunistic screening programme was started targeting women aged 30–50 years with a three-year screening interval. Treatment of precancerous and cancerous lesions is according to national standards. With WHO support, cytologists and other health professionals have been trained and cytological laboratories established in the different provinces. A monitoring and evaluation system has been established and a national information system is being developed. Activities have been initiated to raise awareness among the medical staff and women about cervical cancer and prevention mechanisms. In four of the ten regions, screening by mobile teams is also carried out.

Although the screening programme signifies a big step forward, numerous obstacles exist. These include the limited financial resources of the programme, household poverty, regional diversity and the absence of modern technologies in the rural areas. Efforts are needed to improve the quality of medical services and the collection and analysis of Pap smears, and to attain high coverage of the target population. Only 20% of the target population have participated so far in the screening programme.

Iceland

Iceland, a non-member of the EU, started organized screening in 1964. Intensified call-recall and follow-up measures in the 1980s resulted in an increase in the three-year attendance rate to 82%; this has levelled out to around 75% over the last two decades. In 2004, the age-standardized mortality rate in Iceland was one of the lowest in the world (1.6/100 000). Only about 4–5% of the targeted population had never attended screening. In the period 1980–2004, a significant increase in the incidence of cervical cancer in women under the age of 35 was seen while a continuing decrease was

observed in the older age groups. The increase in age-specific incidence among younger women can be explained by an increase in risk factors: changes in sexual lifestyle resulting in an increase in the number of young women having had multiple sexual partners by the age of 20. As a result, Iceland changed the starting age for screening from 25 to 20 years. An assessment of the impact of HPV vaccines showed that they could further reduce the number of cases of pre-invasive and invasive cancer in Iceland. However, the vaccines could have a negative impact on the performance of the screening programme: if the prevalence of the disease declines, the predicted positive value of the screening test would also decline and a reduction in the number of abnormal screening tests could reduce the alertness of the screeners. If women feel protected by the vaccine, this could also negatively affect screening attendance. The need for molecular markers showing women at real risk for progression of the HPV infection to precancerous and cancerous lesions will increase and the cost-effectiveness of screening will decline. It is, therefore, important to educate the public, the health care personnel and the policy-makers about the benefits and limitations of the new HPV 16 and 18 vaccines. Such education is vital to ensure continued optimal participation in screening and in future vaccination programmes.

Lithuania

Lithuania is a country with a low gross national product (GNP) (US\$ 5200) and high rates of cervical cancer incidence and mortality. A nationwide screening programme was started in July 2004 with a target population of 750 000 women aged 30–60 years. Inviting women to participate is the responsibility of the primary health care centres where facilities exist for taking Pap smears. Ten certified pathology laboratories around the country carry out the analyses of the Pap tests. Funding is provided by the State Patient Fund (state insurance), which reimburses the costs of the services provided (invitations sent, smear taking and Pap smear assessment). Women can attend the primary health care centres free of charge if they are insured. Treatment for women with positive smears is provided according to WHO standards. Referral systems and treatment services have been established at both secondary and tertiary levels.

During the first 2.5 years, 39% of the 750 000 women invited were examined. The overall response rate to the first invitation was 63.4%. The highest response rates were observed in the cities with previous experience of Pap screening. Since the introduction of the screening programme, the number of precancerous lesions detected has increased five-fold and the invasive cancer/in situ cancer rate has declined. It is foreseen that a further reduction of the number of invasive cancers will be seen in the near future.

Discussion

The country examples clearly demonstrate that organization is key to the success of a screening programme. However, in large countries where much of the population lives in rural areas, it might be difficult to reach the target population. How can women be more motivated to participate? And how can funding of the screening programmes be

guaranteed? Some countries have state insurance systems and are thus able to reimburse screening and treatment services while in others this is not the case. For example, in Armenia, where there is no state insurance system, public-funded screening programmes target only the highest risk group, that is, women aged 30–50 years. International organizations try to compensate where governments cannot address the demands. In the case of Armenia, the mobile screening teams are funded by donor agencies. In the long term, it might be attractive for the Government to invest in this approach. In several countries, major efforts to start screening programmes have high-level government support.

Another point of the discussion was the use of cytology as a primary screening test. The introduction of HPV vaccines will probably have an impact on the characteristics of cytology testing. Could HPV DNA tests be an alternative? Large randomized controlled trials are ongoing in five countries of the WHO European Region. These trials compare HPV testing alone or in combination with cytology and have incident CIN3 as the endpoint. The results will be published during 2007–2008.

Policies and approaches in the prevention and management of cervical cancer at global and regional levels: HPV vaccines

Immunization programme in the WHO European Region

The *Global Immunization Vision and Strategy (GIVS)* (5) for the period 2006–2015 was jointly developed by the United Nations Children’s Fund (UNICEF), WHO and other partners and approved by the Member States of WHO at the Fiftieth World Health Assembly (2005). The strategic aims of GIVS are: (1) to protect more people (not only infants) in a changing world; (2) to introduce new vaccines and new technologies; (3) to integrate immunization with linked interventions and surveillance in the context of the health system; and (4) to look at immunization in the context of global interdependence that brings solidarity and equity.

The WHO European regional goal for 2010 and beyond is to achieve and sustain >95% coverage with the vaccines that are being used at present and to accelerate the use of new vaccines and underutilized vaccines, the HPV vaccines among them. To ensure the quality and safety of immunization, the capacity for surveillance and monitoring will be enhanced, including the laboratory network. Partnership, advocacy and communication will be improved.

The WHO European Region is very diverse containing some of the richest countries in the world and also some of the poorest. Thus, it is important to look into the affordability of introducing specific vaccines and to take into account that priorities in the different countries might vary. Despite the differences that exist from country to country, over the last ten years the Region as a whole has progressed a lot towards achieving and sustaining high vaccination coverage. A good example of this is the DPT3 vaccination, which attained 95% coverage 2004. However, it still remains that

more than 500 000 children are not fully protected against diphtheria, tetanus and pertussis by their first birthdays. For this reason, countries of the Region continue to invest in awareness-raising campaigns, for example during the annual European Immunization Week (http://www.euro.who.int/vaccine/20070402_1). To ensure the quality and safety of immunization, global standards are advocated and promoted, and guidance is provided on policy development and the training of clinical staff.

The WHO European Region was declared polio free in 2002. However, some countries remain at increased risk of transmission following the importation of the wild poliovirus and they demand that efforts be made to keep polio under control in the Region. Measures have also been taken to accelerate the control of measles and rubella, with special focus on the prevention of the congenital rubella syndrome, in order to achieve the goal of eliminating measles and rubella by 2010. Because of these vaccination programmes, there is experience in the Region in vaccinating older age cohorts. There is still the unfinished agenda of dealing with the traditional Expanded Programme on Immunization (EPI) vaccines and increasing attention is being paid to underutilized vaccines, for example those against influenza, hepatitis B, conjugated Haemophilus Influenzae type b (HIB-conj), rotavirus and HPV. There are several challenges related to the introduction of new and underutilized vaccines, including a lack of evidence on the disease burden, the relatively high cost of vaccines, and competing priorities – not only vaccines but also other preventable interventions and health needs. The first HPV vaccine, Gardasil® has been licensed in 34 countries of the Region, of which seven have developed guidelines for introducing it.

WHO has developed several tools for decision-making and policy development as well as a regional strategic framework for the introduction of new vaccines. Priorities for country support in relation to the introduction of new and underutilized vaccines include the provision of technical assistance through inter-country activities – such as meetings and workshops – and technical documentation, as well as in-country assistance. In connection with the introduction of HPV vaccines in the Region:

- strong immunization programmes and demonstrated capacity already exist and can be built on;
- informed decision-making is necessary taking account of:
 - evidence on the disease burden, cost-effectiveness and public perception;
 - competing priorities (availability of other new vaccines); and
 - cost and financial sustainability.
- delivery would be through schools, existing adolescent immunization programmes or health visits and should be linked with other vaccine campaigns (Td, rubella, hepatitis B and MR);
- links with other public health interventions are needed; HPV vaccines have to be integrated within a comprehensive cancer prevention and control package;
- the approach should be intersectoral, in partnership with programmes on sexual and reproductive health, immunization, child and adolescent health, and cancer control.

HPV vaccine and immunization policy

Nearly all cases of cervical cancer are associated with HPV. Two HPV vaccines exist: the quadrivalent vaccine (types 6, 11, 16 and 18) Gardasil®, which was approved by the Food and Drug Administration (FDA) and the European Agency for the Evaluation of Medicinal Products (EMA) in 2006, and the bivalent vaccine (types 16, 18) Cervarix®, which has been submitted to FDA and EMA for approval (it has already been licensed in Australia). Both vaccines are indicated for cervical cancer and precancerous lesions caused by HPV 16 and 18. Gardasil® is also indicated for the prevention of genital warts. Relevant to these vaccines is the fact that the distribution of HPV types in cervical cancer cases is quite uniform throughout the world (HPV 16 and 18 are present in ~70% of cervical cancer cases).

Both vaccines are made up of virus-like particles (VLPs) and are non-infectious. The immune response to HPV vaccines is high and persists for at least five years. Antibody levels after vaccination are higher in young people than in adults. Data on the efficacy of both vaccines are broadly similar but published data from large phase III trials are available only for the quadrivalent vaccine. The results show that the efficacy of both vaccines against HPV vaccine-type disease in HPV-naïve women (+/-100% for HPV-related diseases) is extremely high. The vaccines do not have therapeutic efficacy in women already exposed to vaccine-related HPV types. They both have an acceptable safety profile.

To assist countries to prepare for the introduction of HPV vaccines, WHO has published two guidance documents: (1) *Preparing for the introduction of HPV vaccines. Policy and programme guidance for countries* (6), which was the result of the United Nations Populations Fund (UNFPA)/WHO Technical Consultation on HPV Vaccines and Sexual and Reproductive Health Programmes held in March 2006 in Montreux, Switzerland; and (2) *Human papillomavirus and HPV vaccines. Technical information for policy makers and health professionals* (7), which emanated from a meeting of the WHO HPV Expert Advisory Group meeting held in Geneva, Switzerland, on 3–4 August 2006 and is also available in Arabic, Chinese, French, Russian and Spanish. The latter-mentioned document provides updated key information on HPV, HPV-related disease and HPV vaccines, and complements the policy and programme guidance for countries. Both documents were made available to participants during the meeting.

HPV vaccination holds great promise for improving global health. However, the fact that a vaccine is licensed does not mean that it is automatically accepted or that it is accessible and affordable. HPV vaccines are expensive products with a higher cost than other vaccines, and this raises the issue of risk due to increasing health inequalities. Thus, they bring not only opportunities but also challenges. One challenge is how to provide vaccines to young female adolescents, as little experience exists in delivering vaccines or other health services to this age group. It would be interesting to explore whether it might be possible to develop packages for older age groups, including a combination of HPV and other vaccines, as well as educational activities (e.g. on sexual and reproductive health and safe sexual behaviour) and promotional messages.

Other issues to be addressed in connection with the new vaccines in the coming years include duration of immunity, the possibility of their being administered in conjunction with other vaccines and the added value of vaccinating males.

In summary, HPV vaccines have a great potential to reduce the global burden of cervical cancer but they represent only one element of a cervical cancer control strategy. An overarching consideration is to position HPV vaccines within a comprehensive, integrated service delivery structure: partnership is the key. Also, because of the current high cost, critical issues of equity associated with vaccine accessibility must be addressed.

Through the Working Group on HPV vaccines, WHO provides support: (1) to international policy platforms; (2) in decision-making on cancer prevention options; (3) in manufacturing standards and laboratory procedures; and (4) in assessing opinions on and experience in introducing vaccines (Annex 1).

Health economics analyses of HPV vaccination

Analyses related to the health economics of HPV vaccination are difficult to carry out and vary according to the variables considered and the comparisons made. The key factors are the price of the vaccine and the kind of screening programme that is in place or will be developed.

In health economics, various alternatives are considered, and costs and benefits compared. Cost-effectiveness analyses carried out by Professor Sue Goldie, Harvard School of Public Health, on cervical cancer screening demonstrate that very low-cost screening programmes save lives and organized screening, though it costs more, saves more lives. Overscreening is not cost-effective as the cost of a marginal additional benefit is a too high. The question here is how HPV vaccination fits within these analyses.

One of the factors that need to be taken into account is the impact of vaccination at population level. The impact of vaccinating girls of 10-11 years of age will not be felt for 30-40 years, whereas the impact of screening - such as the benefits gained from investing in the detection of precancerous lesions - is felt with much less delay. Thus, in assessing cost effectiveness, assumptions about the future and the value of future health events are very important.

Another factor is that, in contrast to screening, vaccination decreases the risk of infection by immunizing individuals. Part of the population is protected because the vaccinated individuals do not transmit infections. This so-called herd immunity is important with respect to equity in that it might indirectly protect disadvantaged groups that are often hard to reach through screening programmes.

A great unknown with respect to HPV is whether persons who become infected have naturally-derived immunity. There seems to be a natural immunity that is not life-long

but this is still uncertain. In the presence of naturally-derived immunity, much higher vaccine coverage is required to eradicate the infection than is otherwise the case.

The impact of vaccination will also depend on the heterogeneity of the population. Targeting high-risk groups for vaccination is very difficult; most benefit is to be expected from vaccinating large proportions of people with moderate-risk sex behaviour. At the moment, little information is available on the advantage of vaccinating boys. Initial analyses suggest that this would only be beneficial if high coverage of girls is not possible. In Finland, large randomized controlled trials are being conducted in order to obtain more data on this question.

There is also uncertainty surrounding the potential interference between vaccine-related and other types of HPV and the existence of cross-immunity. It would be a concern if the removal of vaccine-related types of HPV reduced cross-immunity to other types of HPV, thereby allowing an increase in the incidence of HPV types not included in the vaccine. Epidemiological studies indicate that the level of naturally-acquired cross-immunity is not high but it is questionable whether these studies had the power to detect low-level cross-immunity, which might still be important in the population.

As all these different variables have to be taken into account, models can become very complicated. Moreover it might be difficult to assess the different values for the variables, as some values should be based on population-specific data (e.g. on sexual behaviour).

In low-resource settings, modelling the cost-effectiveness of vaccination and screening strategies has shown that the most effective strategy depends on the cost of the vaccine. If very cheap (US\$ 25 for three doses), vaccines are cost-effective; if they are more expensive (US\$ 100 and up), screening is more cost-effective.

In addition, models developed so far show that:

- vaccination against HPV can substantially reduce precancerous lesions detected in screening and can contribute to lowering cancer mortality;
- vaccinating males is of limited benefit in preventing cervical cancer; the benefits are greater from lower-level vaccine coverage of females;
- the limited duration of protection resulting from discontinuation of screening is of concern;
- vaccinating at a young age, for example 12 years, generates greater long-term benefits; and
- a catch-up programme for vaccinating the 12–18 years age-group speeds up the return of benefits.

Health professionals working with adolescents in the introduction of HPV vaccines and the reduction of risk behaviour: areas for consideration

In connection with the introduction of HPV vaccines and adolescent risk behaviour, the first factors to consider are the social and cultural contexts and the target population. It is important to understand the context in which sexual knowledge is gained and attitudes and behaviours created. These aspects have both country-specific and generic features. Decision-makers need to identify the level of acceptability of the vaccine and any potential barriers to using it. If the HPV vaccine is to be given to children, there is a need for parental consent, which will involve the distribution of appropriate and targeted information. Experience with the Hepatitis B vaccine has shown that adolescents look to their parents for advice about being vaccinated. Furthermore, there are gender-related issues if only girls are to be immunized.

Research shows that there is a lack of knowledge about HPV and its consequences, both among the target populations and among their parents. For example, in one study in the United Kingdom, only 30% of the women surveyed had heard of HPV and they were not clear about how it is transmitted. Providing accurate information involves ensuring that health messages are appropriately constructed and targeted. The knowledge of the lay population in relation to health is based on everyday experiences and is not simply diluted medical knowledge.

The complexity of individual understanding and perceptions of risk also needs to be considered. Research has shown that an individual often perceives his own risk of contracting sexually transmitted infections as low. Research shows that parents tend to underestimate the age at which their children become sexually active and, as a result, may not consider it necessary for them to be vaccinated. The mass media will have an important role to play in shaping perceptions of risk in relation to the HPV vaccine.

In informing the public about HPV vaccines, the irrationalities and complexities connected with sexual decision-making have to be taken into account. The range of audiences and the different social and cultural contexts need to be understood and the risk associated with sexual decision-making needs to be translated into odds that are easily understood. There is a need for transparency: individuals have a right to accurate and comprehensive information about HPV and HPV vaccines. Misinformation provided by anti-vaccination groups on the Internet and groups that promote sexual abstinence, etc., need to be countered. Health professionals are in a trusted position and will have an important role to play in service delivery and in providing accurate and appropriate information

In order to optimize coverage, the HPV vaccination needs to be meaningful to adolescents and it is necessary to find the best way of achieving this, for example, as part of a protection package. The age for vaccination would of course influence the method used. Acceptability could be enhanced through health campaigns during which appropriate information is provided about the protective benefits of the HPV vaccines and about other health-related topics, such as, condom use, smoking and nutrition. It is

important that health messages are positive and that the opportunity is taken to build on the desire of parents to protect their children.

The development of a coherent communication strategy for everyone involved in vaccine introduction and the identification of appropriate health promotion interventions will be challenging.

Discussion

The first point of the discussion was the need to emphasize that immunization does not replace screening programmes. Until now, evidence has only shown that vaccines protect against HPV16 and 18 CIN2/3, not against cancer. It will take decades before the impact of vaccines on invasive cancer can be seen. In addition, there are still many HPV types not covered by the vaccines. Screening vaccinated women is needed primarily to protect them against cervical cancer caused by non-vaccine-related HPV types and to monitor the impact of vaccination. The introduction of vaccines has to be the result of a decision-making process, including an assessment of the burden of HPV and cervical cancer. HPV vaccines should only be introduced if cervical cancer is considered an important health problem in the country, if adequate information has been provided, and if a minimal screening programme exists. Communication and collaboration between programmes are very important.

One of the questions raised related to the impact of natural boosting on population-based protection. Modelling has been used and has been shown to have both possibilities and limitations. It was felt that the outcome depends a lot on the presence or absence of long-lasting immunity, that the age-specific incidence and prevalence of HPV16 suggests at least some naturally-induced immunity, and that re-infection might have a boosting effect on vaccine- or naturally-induced immunity though this is not known.

The safety of HPV vaccines and the related use of aluminium adjuvant was also a concern. There are no data on long-term safety; so far, no major side effects have been attributed to HPV vaccines. The same can be said of other vaccines that have aluminium as an adjuvant.

Setting priorities for national policies on cervical cancer prevention

Cervical cancer prevention in Denmark

Despite the high coverage of the screening programme (80%), the incidence of and mortality from cervical cancer are high compared with other Scandinavian countries. In 2007, the National Board of Health formulated 35 national recommendations on screening. These are in line with the European recommendations (8,9), including three-year screening intervals for women aged 23–50 years and five-year intervals thereafter. A national call-recall system with two recalls has just started. It is recommended that

an HPV test be performed on the cytological results of an atypical, low-grade squamous intraepithelial lesion and as a control measure after conization. All cytological diagnoses, including the HPV test results and the follow-up histological diagnoses, are registered in a national pathology database, which enables quality assurance of the programme.

In May 2007, the National Board of Health published a report on screening for cervical cancer. It is based on information resulting from modelling of HPV transmission and economic assessment and takes the attitude of the public towards HPV vaccination into account.

There are arguments against the introduction of the HPV vaccine, including the fact that it is a new technology and no data exist on the long-term effect and possible long-term side effects. Moreover, the overall impact on public health is not known, the cost involved is heavy and there is a screening programme for the prevention of cervical cancer. However, there are also arguments in favour of introducing the vaccine. It seems to be safe and efficient and, through the induction of herd immunity, a large proportion of the population will be protected. Vaccination can be cost-effective as the disease burden caused by cervical cancer and the expenses incurred by associated interventions are significant. In addition, the quadrivalent vaccine also prevents other HPV-related diseases. Public acceptance of the vaccine does not seem to be a problem in Denmark. Introducing the vaccine through a public programme would enhance social equity.

The report provides the information necessary for decision-making on the introduction of the HPV vaccine in the country and advice on the possibility of doing so is expected in the near future. The major question is whether enough data are available to introduce the vaccine at the present time or whether further results from the phase IV studies are necessary.

If the vaccine is introduced on the basis of the results of the modelling studies, the policy considerations are that: girls should be immunized at 12 years of age; there is uncertainty about the age and gender of the catch-up population; cervical cancer screening should continue; monitoring will be important; and price should be negotiated.

Cervical cancer prevention and HPV vaccine policy in France

In France, there is a steady decrease in the incidence of and mortality from cervical cancer. Screening is opportunistic and carried out by cytology. Population-based pilot experiments are currently in progress. The recommended target population is women aged 25-65 (17 million) and the screening interval is three years after two normal smears. HPV DNA testing is not recommended for primary screening. Approximately 5.5 million tests are performed each year but only 60% of women are screened; 40% of women are under-screened or not screened at all.

After EMEA authorization in September 2006 and licensing in France in November 2006, and in accordance with the recommendations of the Conseil supérieur d'hygiène publique de France (Higher Council of Public Health in France), Gardasil® was included in the national immunization schedule in 2007. The vaccine is recommended for girls of 14 years of age and a catch-up immunization is foreseen for virgin girls and women in the 15–23 years age group. The recommendations also highlight the need for organized screening programmes, which is supported by as yet unpublished cost-effective modelling data. Reimbursement of the vaccine by the national health insurance is in process.

In France, much remains to be done to control cervical cancer. There is a need to monitor the coverage, safety and long-term efficacy of vaccination. A national reference centre for HPV will be created. Screening through pap smears needs to be promoted among health professionals and women, and further studies on the interaction between HPV immunization and cervical cancer screening programmes are required.

Meanwhile, the national health authorities face several issues, one of which is how to improve cervical cancer screening while implementing HPV immunization. Primary and secondary prevention have to be coordinated and clear public health messages provided to the target population. Physicians and health professionals need to be reminded of good prevention practices in relation to both screening and immunization and they should receive training where necessary.

Cervical cancer prevention: considerations for universal HPV vaccination in females aged 12–17 in Germany

Germany has 6500 cases of invasive cancer per year but there is a lack of information on the prevalence of HPV and precancerous lesions.

The recommendation to vaccinate girls in the 12–17 years age group is based on the age of onset of sexual activity and the possibility of reaching young girls through the medical services. At 12 years of age, fewer than 5% are sexually active; at 14 and 17 years of age, the rates are 12% and 73%, respectively. Another important factor is that nearly 30% of girls aged 14 and nearly 90% of girls aged 17 have visited a gynaecologist. Therefore, the vaccine will be delivered through paediatricians, gynaecologists and general practitioners.

The screening coverage is high. Of the female population, 75% have at least one smear taken every three years but only 60% adhere to the national recommendation to be screened yearly.

The following factors contribute to the rationale for recommending HPV vaccination: the high burden of disease among women despite screening (about four deaths per day); the high efficacy shown in the vaccine trials against infection and precancerous lesions in HPV-naïve females; and the good safety profile and excellent opportunities for delivery of the vaccine through health professionals. The vaccine will be included in the national immunization scheme and reimbursed by health insurance companies.

Prevention strategies of cervical cancer in Italy

Data from different regions and studies show that cervical cancer remains an important health problem in Italy. A screening programme targeting women aged 25 and over is in place. Since 2006, the Ministry of Health has been supporting the national prevention programme to improve its coverage.

Public structures are actively involved in both vaccination and screening and HPV vaccines will be delivered by the national health system. Routine vaccination with three doses of quadrivalent HPV vaccine is recommended for 11-year-old girls who will be actively traced and able to receive the vaccine free of charge from January 2008. The goal is to reach 95% coverage within five years.

There are several arguments in favour of introducing HPV vaccines in Italy:

1. The vaccine will be given before the start of sexual activity and exposure to the virus, thus maximizing effectiveness.
2. The target population attends school through which it is possible to achieve wide coverage.
3. There are no problems in communicating with parents on this issue.
4. The National Health System, an expert and reliable network, will deliver the vaccines.
5. It will be possible to reach high coverage in a short time thanks to contact between the target population and the vaccination services for other reasons.
6. The existing computerized register can be used to monitor the implementation and impact of the vaccination programme.
7. Based on estimations of the cost of vaccination made within each region, provisions have been made for the delivery of the vaccine to be free of charge.

Implementation will comprise the following steps: (1) training of health workers; (2) a national information and communication campaign; (3) the synchronized initiation of the vaccination programme in the whole country; and (4) evaluation of the programme. The indicators that will be used for the evaluation are vaccination coverage, frequency of adverse events, and cervical cancer incidence. The impact of vaccination on the screening programme will also be evaluated.

The final outcome of the programme will depend on a number of critical points, one of which is the degree of coverage achieved. As the HPV vaccine is recommended rather than obligatory, parents are at liberty to refuse vaccination of their daughters. Also, socio-cultural barriers and the organizational challenges of vaccinating young adolescents will have to be overcome. It is still unclear what kind of counselling should be provided in connection with vaccination. As the target population will have limited sexual experience, counselling on sexuality and sexual health could be difficult.

Another issue is the possible impact of vaccination on screening. A comprehensive approach to cervical cancer prevention, integrating primary and secondary prevention,

needs to be developed. Thus, secondary prevention programmes based on screening and the treatment of precancerous lesions should be consolidated.

Finally, there are still many unknown factors that may influence impact, one of them being the possible need for a booster vaccination.

Cervical cancer prevention in Turkey

In Turkey, cancer of the cervix is the eighth leading cause of cancer in women and the age-standardized incidence rate is relatively low (4.5 per 100 000 women). There are several arguments against the introduction of HPV vaccines in Turkey:

1. It is not cost-effective compared to screening. An organized cytology-based screening programme, targeting women aged 35–65 years, with a screening interval of five years, could reduce the incidence by 80%. This would cost only US\$ 150 million per year, which is less than one-third of the cost per year of immunizing one female birth cohort with HPV vaccines at the current vaccine price (estimated at US\$ 500 million per year).
2. The introduction of HPV vaccines into the national immunization programme is not possible at the moment given the high cost. Immunizing 1.5 million children per year with DPT, polio, BCG, MMR, Hepatitis B and Hib costs US\$ 110 million and the addition of HPV vaccines would significantly increase the cost of the programme.
3. The cost of introducing the vaccines at their current price would exceed the budget for treating all cancers in the country.
4. The efficacy of the vaccine in preventing cervical cancer is not known.
5. Screening has to continue in any event.

“Guerrilla marketing” of HPV vaccines gives the impression that their introduction is a high priority. In Turkey, however, introducing organized screening is considered much more important and more feasible at the moment. It is essential that WHO policies are country-based and take the different scenarios into account.

Discussion

As can be seen from the above examples, countries of similar socioeconomic standing can use very different approaches to the introduction of HPV vaccines. Whereas funding is a major issue in some countries (e.g. Turkey), in others (e.g. Germany) health insurance companies play a proactive role in reimbursing vaccination expenses in order to market their services.

A major issue is defining the age of the target population. The proposed age of the primary target population varies from country to country. France and Germany have decided to target the female population at an age when only a small proportion has started to be sexually active (14 and 12 years, respectively). Moreover, they have chosen to vaccinate a catch-up population and a large proportion of this population is

likely already to be HPV-infected. In Italy the age of the target population is 10–11 years of age.

In France, the age of the target population was determined as the result of a recent national survey on the sexual behaviour of adolescents. Catch-up vaccination is only for women who are not yet sexually active and thus HPV-naive. In Germany, the age of the primary target population was decided on the basis of four arguments: (1) few girls are sexually active before they reach the age of 12; (2) it is not yet known if a booster is needed – if immunity wanes, girls vaccinated too early would no longer be protected when they reach the age at which they would be most at risk; (3) as a large proportion of girls visit a gynaecologist between the ages of 14 and 17, there is an opportunity to offer them the vaccine at this time; (4) targeting girls over 12 years of age facilitates counselling on sexual and reproductive health.

A question was raised on how vaccines are offered. Vaccination for cervical cancer is not compulsory in any of the countries of the WHO European Region and needs former parental consent. It is important that, prior to giving their consent, parents be informed about other available methods of cervical cancer prevention.

Several countries stated that the high cost of HPV vaccines is a major barrier to their introduction. For example, in Slovenia, the introduction of the HPV vaccines would double the price of the immunization programme and there are no funds available to provide sexual education at school. Priorities will have to be established.

Strengthening cervical cancer prevention in countries

Issues for consideration when setting priorities

There are several questions to be considered when setting priorities:

1. What is the burden of disease in the country?
2. Is there a control programme? If so, does it include both screening and treatment? Is screening organized? Can the programme be improved? If there is no programme, can one be started? Have alternatives for cytology (HPV testing; visual screening) been considered? Have the target age group and the screening interval been defined?
3. Has the introduction of HPV vaccination been assessed for added value?
4. What steps can be taken to improve screening carried out while implementing vaccination and to coordinate primary prevention and secondary screening (including primary prevention through the promotion of safe sexual behaviour and condom use)?

If HPV vaccination were being considered, it would be useful to have information on the following:

- HPV transmission in the country;
- the estimated cost of introducing HPV vaccines;
- the attitude of the public towards HPV vaccination;
- the cost-effectiveness of introducing HPV vaccines (not only compared to other vaccines but also to other health interventions);
- sources of funding for the vaccines;
- issues of equity/accessibility;
- target population (age group), taking into account the average age of sexual debut in the population and the possibilities of reaching the target population;
- ways to inform and educate the public in order to improve awareness and avoid misperceptions;
- provision of services (providers of the vaccine, administering services, compliance rate);
- training of the providers;
- the impact of vaccination vis-à-vis that of the screening programme;
- monitoring and evaluation of all aspects of HPV vaccination, including safety.

Introduction to working group sessions

The purpose of the seven working groups was to gain more understanding of the issues required to strengthen cervical cancer prevention in the countries and to define future action.

Questions for discussion were:

1. What is the current situation regarding cervical cancer prevention in your country (strengths and weaknesses)? What are the main factors for success or failure?
2. What needs does your country have in respect of cervical cancer prevention? What is the current priority?
3. What are the future directions in your country and what action will be taken with respect to cervical cancer prevention?
4. What kind of assistance does your country expect from WHO and/or other partners?

The following is a summary of the feedback from the working group sessions and the ensuing discussion.

Cervical cancer prevention programmes in countries of the WHO European Region: current situation

The burden from cervical cancer varies a lot from country to country in the WHO European Region, from very high to very low. In Finland, Iceland and the Netherlands, the incidence of the disease is very low, thanks to screening programmes. In countries, such as Italy and Spain, where there is a low prevalence of HPV, the incidence is also low. In some countries, such as Bulgaria, Latvia and Slovenia, cervical cancer incidence and mortality rates are high.

Organized screening is being introduced in an increasing number of countries (e.g. Denmark, Finland, Hungary (quasi-organized), Iceland, Lithuania, the Netherlands, Norway, Poland, Slovenia and the United Kingdom) but most countries rely on opportunistic screening.

Pilot studies on the introduction of organized screening are ongoing in Albania, Croatia and France. Some countries with opportunistic screening are planning to start organized programmes.

Finland is an example of a “model programme”, as the country’s organized screening programme is highly cost-effective. It has proven to be very effective in reducing the incidence of and mortality from cervical cancer by screening a narrow target group (30–60 years) with a wide screening interval (5 years), by using nurses to collect Pap smears and by not referring low-grade smear abnormalities. The country has also integrated research programmes on emerging technologies.

Before taking a decision regarding the introduction of HPV vaccines, many countries are awaiting more information. In some countries, such as France, Germany, Italy and Luxembourg, both the technical and political decisions have been reached. In others, only the technical decision has been taken (e.g. Belgium, Norway, Spain) or further consideration is needed before a decision can be reached (e.g. Bulgaria, Finland, Hungary). In Germany, not only is the prevalence of opportunistic screening high but it has also been possible to introduce HPV vaccines covered by statutory and private health insurance companies.

It was observed that much progress has been made in the Region in controlling cervical cancer. For example, this year (2007) The former Yugoslav Republic of Macedonia introduced a new cytology-based screening programme that targets women aged 19–64, with five-year screening intervals and offers screening to both insured and uninsured women free of charge. Croatia has introduced a good quality control system. Access to quality treatment is available in many countries, e.g. Cyprus. Countries have learned a lot from each other through communication and exchange of experience on, for example: the success of organized screening programmes; the importance of achieving high coverage of a well-defined target population; the fact that yearly screening is not necessary and that the annual Pap smear should be replaced by screening at three- or even five-year intervals; the importance of collaboration with nongovernmental organizations (NGOs), especially with respect to training and gaining access to hard-to-reach populations; and the importance of education.

Community groups, women's groups and teachers have been shown to be important in advocating vaccination and in spreading information about it.

Despite the progress observed in the Region, major problems still exist, such as:

- a lack of political support to start and maintain well-functioning cervical cancer control programmes;
- a lack organized screening programmes and data systems in most countries; where opportunistic screening is in place, it is difficult to switch to organized programmes;
- a lack of trained cytologists and pathologists, although cytology-based screening is the norm in all countries;
- difficulty in many countries in accessing the population most at risk;
- low-quality Pap smears;
- the absence of primary prevention through health education aimed at lifestyle changes;
- limited financial and human resources;
- limited treatment opportunities;
- monitoring and registration difficulties, one reason being the lack of computerized systems;
- the lack of uniform indicators for quality control;
- inadequacy of knowledge about HPV, also among physicians.

Country needs for cervical cancer prevention

1. Political will and commitment, including assured resources, are needed to start and sustain a cervical cancer prevention programme.
2. Health authorities should be instructed to promote organized screening, discourage opportunistic (over-) screening and implement guidelines.
3. Current screening practices have to be improved by optimizing participation and assuring quality. A high coverage rate can only be attained if general practitioners are involved and if the communities are better informed and educated. Training of health staff is an important element in quality assurance.
4. A framework is required for evidence-based decision-making with regard to:
(1) screening policy (start and stop ages, intervals, population groups);
(2) screening method; (3) diagnostic, follow-up and treatment methods; (4) vaccination; and (5) delivery services.
5. There is a need for comprehensive sexual education as well as information and education on the use of innovative methods, such as the ABC approach, HPV vaccination, screening, etc., in cancer prevention.
6. Training tools, such as cervical cancer screening manuals, are needed.

7. A comprehensive information system, including registries of the target population, participation details, screen-test results, follow-up, links to the cancer registry and HPV surveillance systems, would allow monitoring of the quality of the screening and vaccination programmes and evaluation of the impact.
8. In introducing the HPV vaccine, it is important to clarify how to avoid misperceptions and stigmatization in providing sensitive information and how to organize the registration and monitoring of data so that they can be linked with those of the screening registries.
9. It is important to have an international assessment of the effectiveness of new technologies.
10. Involving civil societies, such as anticancer leagues and NGOs, can be helpful in setting up cervical cancer programmes and keeping them high on the agenda.

Future directions and planned action in the countries

1. The focus of a comprehensive cervical cancer prevention and control strategy is on primary and secondary prevention. HPV vaccines can complement screening but the absolute priority is to establish/strengthen organized screening when feasible and affordable. High coverage, a quality assurance system and a call-recall system are important elements of organized screening.
2. For many countries, initiating an organized screening programme and overcoming related barriers are currently the main tasks. For others, the major task is improving and/or expanding the existing programme. As shown in Finland, nurses are excellent for screening, so a lack of physicians should not be a problem.
3. Improving the accessibility of treatment is essential when organizing screening programmes. Treatment should not only be available but also affordable and accessible.
4. Once the results of the studies on HPV as primary screening test are available, countries need to assess the usefulness of other screening tests in their settings. For low-resource countries, a valuable option may be visual inspection.
5. More data and evaluation about screening and vaccination are required.

Anticipated assistance from WHO and other partners

1. Wide distribution of the summary report on the meeting and of a press release to decision-makers and the media, respectively.
2. Advocacy of organized cervical cancer screening so that political commitment can be met.
3. Provision of technical support in connection with designing and implementing organized screening (e.g. to Slovakia), accessing hard-to-reach populations and evaluating the programmes (e.g. Latvia, Uzbekistan). Recruitment of experts to

- support countries requesting WHO assistance, e.g. in cytology (as has already been done in Armenia by experts from Iceland and Norway).
4. Adaptation of evidence-based guidelines and recommendations on screening age and screening interval for the WHO European Region.
 5. Provision of information and educational materials on cervical cancer control and HPV vaccines.
 6. Assistance with communication strategies and the formulation of basic key messages for health education.
 7. Collaboration and negotiation with partners and manufacturers to lower vaccine prices so that they become affordable, particularly for low resource countries.
 8. Monitoring the implementation of best practices in countries.
 9. Assistance with studies on cost-effectiveness, for example of HPV vaccination.
 10. Provision of evidence required for decision-making regarding the introduction of vaccines.
 11. Development of protocols for the study of vaccines that countries could use in addition to the industry-sponsored trials that do not always answer all the questions or reflect practical experience.
 12. WHO vaccine-effectiveness studies using cancer incidence instead of precancerous lesions as endpoint.
 13. NGO support in communicating and organizing meetings between countries of similar standing in developing guidelines and educational material, in networking, and in training.

The role of the mass media: friend or foe?

There is a need for clear and consistent information about the transmission, detection, and prevention of HPV and its link to cervical cancer and we know that the media can help to increase awareness. However, there are many obstacles: the constant flow of new health care research material; the fact that information provided today is already outdated tomorrow; and the media's constant need for headlines. Moreover, information travels faster and further than ever before, it is not filtered, and people have problems in distinguishing between true and false information. The role of the WHO is to be responsive to public questioning, to establish partnerships with the mass media, to keep WHO staff informed and to react promptly.

The expectations of the media differ from those of WHO. The media needs instant access, great quotes and sound bites; for WHO it is important not to be misquoted, that there are no factual errors or speculation and that, in reporting, journalists reflect sincere interest in the topic.

It is important to realize that the focus should not be on competition but on partnership. To achieve a successful relationship with the media:

1. tell the story so people listen;
2. package information – for example, say what is most important about the HPV vaccine, that it is a great vaccine but unaffordable until the price goes down;
3. plan sound bites;
4. anticipate questions and answers;
5. acknowledge uncertainty – it is better to say that the vaccine will not be available for developing countries in the first couple of years; it is important to be human and modest in our response.

Discussion

Further thought was given to the interaction between health professionals and the media. For example, providing fact sheets to reporters saves time and provides them with accurate information but fact sheets cannot replace personal communication between the health professional and the media.

Health professionals often feel that the media is using them in that reporters contact them for the sole purpose of obtaining data. This can be attributed to the fact that health professionals are not seen as opinion-makers. If health professionals adopted an active approach towards the media, the media would in turn contact them more often.

Ongoing research in the area of cervical cancer prevention

Research in this area focuses on low- and middle-income countries with the knowledge that, in many countries, virtually no services for the early detection and treatment of cervical cancer and its precursors are available. The capability to deal with this problem varies a lot from country to country.

Some countries have been successful in reducing cervical cancer through screening programmes where the link between screening and diagnosis/treatment is considered essential and the quality of screening tests very important. If these two criteria are not met, screening does not work. This is why cytology-based screening does not work in many countries. A comparison of the accuracy of screening tests (sensitivity and specificity) in developing countries is shown in Table 1 (10).

Table 1. Accuracy of screening tests in developing countries

Test	Sensitivity	Specificity
Cytology	31-78%	91-99%
HPV testing	61-90%	62-94%
VIA	50-96%	44-97%
VILI	44-93%	75-85%

The accuracy of visual inspection has been assessed in at least 25 studies. With visual inspection methods, the cervix is looked at with the naked eye after application of vinegar (VIA) or Lugol's iodine. Although the sensitivity and specificity of this method rely on the provider, the results of the studies show that single-approach sensitivity is around 55% and specificity around 80–85%.

The paradigm of cytology-based screening has been repeated screening and high coverage. As the incidence of cervical cancer is highest in women in their fifties and that of precancerous lesions peaks in women in the 30–35 years age group, there is a shift in low- and middle-income countries towards less frequent screening (once or twice in a lifetime) and follow up. Instead, screening and treatment are provided in the same setting (the screen and treat method). Considerable experience in the management of precancerous lesions shows that overtreatment with cryotherapy is safe and can routinely be carried out.

Three specific studies in India assessed the impact of VIA screening. The first study, carried out in 1999–2003, was a cluster randomized controlled trial. Its main objectives were to evaluate: (1) the reduction in cervical cancer incidence and mortality associated with a single round of VIA screening as compared to a control group with no screening; and (2) the cost-effectiveness of VIA screening. In this study, nurses provided screening and cryotherapy and general practitioners carried out the loop electrosurgical excision procedure (LEEP). The results show that, within seven years of follow-up (up to 2006), a 25% reduction in cervical cancer incidence and a 35% reduction in cervical cancer mortality were seen after one single round of VIA screening. The largest effect was observed in the 30–39 years age group.

The objectives of the second study were to evaluate: (1) the reduction in cervical cancer incidence and mortality associated with a single round of VIA screening, cytology or HPV testing, as compared to a control group with no screening; and (2) the cost-effectiveness of the above three approaches. More than 142 000 women participated in this study. The results show that cytology and visual inspection had a similar impact on the cervical cancer three-year moving average, while HPV testing resulted in a higher reduction in incidence and mortality. Important in this study was that, after three years, the incidence of cervical cancer among screen-negative women was much lower in those who were HPV negative at onset than in those with negative cytology or negative VIA results. Long-term follow-up will give very important information on the long-term effect of single lifetime screening and on the optimal screening interval. The study also demonstrated that nurses are competent to carry out screening, colposcopy and cryotherapy.

In the third study, the aim of which was to compare the effectiveness of cryotherapy and LEEP, very high cure rates were shown for CIN1, CN2 and CIN3 treated with cryotherapy.

The results of these studies are very pertinent to low-resource settings in Africa, South-East Asia and Latin America. In India, a national screening policy based on VIA has been introduced in several districts. Thanks to new funding from the Bill and Melinda Gates Foundation, rapid HPV tests are being developed so that HPV testing may be used for a single visit approach when diagnosis and treatment are provided at the same time. A batch test will hopefully be available by the end of 2008; a strip test may be available within four years.

In conclusion, it is very important to keep an open mind. National priorities and expectations are important. In dealing with them, countries should consider how the information obtained from these studies could best be used in policy and practice. Ethics are important and it should be borne in mind that what is ethical in one area may not be so in another. What is most unethical is that, in many places, people are dying from a disease that can be prevented through simple measures.

Discussion

As 50% of the countries of the WHO European Region are low- and middle-income countries, visual inspection could be a valuable option for many of them, especially in connection with screening young women. The use of this test has been shown to be feasible and effective in areas of the United States of America where access to screening is difficult. Countries that face major problems in introducing cytology-based screening programmes should be encouraged to introduce the single visit approach in the near future, based on visual inspection and/or rapid HPV tests.

The possibility of introducing HPV vaccination in countries without screening programmes was also discussed. To do so would have a positive effect on the incidence of cervical cancer even if no screening were in place. However, it would take a generation before the impact of the vaccination could be seen and adult women would not benefit. It is clearly necessary to avoid formulating general recommendations and to design combinations of different interventions. Several technologies exist that can be adapted to specific situations. Vaccination without screening is a possibility but promoting vaccination where no screening is available might be a dangerous shift, as the long-term effects of the vaccine are not known.

Recommendations

Comprehensive cervical cancer control encompasses prevention, early detection, diagnosis, cure and monitoring and requires collaboration among relevant programmes, departments and organizations. To this end, the following recommendations were made.

1. **Strengthen action to consolidate cervical cancer control**

The steps to be taken would vary from country to country depending on the control measures existing in the countries.

2. **Appoint a leading body responsible for cervical cancer prevention**

This body could be an institution or department responsible not only for preventive activities, such as screening, but also for health education, vaccination (if it is to take place), and the collection, monitoring and evaluation of data.

3. **Ensure the availability and accessibility of treatment services before initiating a screening programme**

The treatment of precancerous lesions should be administered on an outpatient basis whenever possible, using LEEP and/or cryotherapy. Centralization of the treatment of cancerous lesions and a referral system are recommended. The needs of women with incurable disease should be addressed by palliative care services. Any cervical cancer programme needs to ensure that morphine is available.

4. **Organize screening programmes**

If an opportunistic screening programme were in place, concrete measures would be needed to organize it according to evidence-based guidance. Evidence is defined at international level but countries also need national data.

In defining the screening methodology, the following WHO guidelines should be taken into account: (1) Cytology is recommended for large-scale cervical cancer screening programmes, if sufficient resources exist. (2) Visual screening methods are recommended for use in pilot projects or other closely monitored settings. (3) HPV tests can be used in conjunction with cytology or other screening tests, where sufficient resources exist. (4) Colposcopy is recommended only as a diagnostic tool (not as a screening tool) and should be performed only by trained and skilled providers.

The manpower required for the different tasks needs to be defined, taking into account the resources (human and financial) available and the international guidelines. Nurses and midwives have the competency to be involved in screening.

Capacity building should be organized according to needs.

In defining the target population and screening interval, it is necessary to take into account that it is more important to achieve high coverage than to repeat

tests on the same women. According to the WHO guidelines: (1) screening should not take place before the age of 25 and should not be done on an annual basis; (2) screening should start at age 25 and continue with three-year intervals until the age of 49; (3) from age 50 to age 64, screening should be with five-year intervals; and (4) screening should stop at age 65 if the last two smears were negative.

5. Allocate the necessary funds for the screening programme

It is important when organizing a screening programme to review the possibilities for funding it. For example, will the programme be financed from public funding, insurance, donors? It is also important to consider accessibility and equity: hard-to-reach groups are often the poorest and thus at highest risk. This means that an optimal rather than a maximal programme has to be set up; it is better to have a minimal programme than no programme at all. Country experiences and demonstration projects have shown that screening every woman once in her lifetime, at age 35, and using visual inspection for rural populations are valid alternatives.

6. Improve screening implementation

Implementation is a continuous process and should be continuously monitored. The evaluation of existing infrastructures and gaps is part of this process.

To achieve a high level of participation, invite the target population through call-recall systems. Start information and awareness-raising campaigns. Seek the active collaboration of service providers and develop communication strategies.

If cytology is used as a screening test, this includes quality control of the whole process of smear taking, fixation, transportation and reading.

7. Make use opportunities for primary prevention

Health education should be an integral part of comprehensive cervical cancer control. Health and sexual health education, including the promotion of condom use, are valuable strategies for the primary prevention of cervical cancer.

8. Make use of existing tools

For example, *Comprehensive cervical cancer: a guide to essential practice*, developed by WHO and available in English, French and Spanish at http://www.who.int/reproductive-health/publications/cervical_cancer_gep/index.htm. The guide will shortly appear in Russian.

9. Assess the introduction of HPV vaccines

Prepare for evidence-based decision-making on the introduction of HPV vaccines as part of a comprehensive cervical cancer prevention package. Make use of WHO guidance and other relevant technical documentation and information.

Preparation may include:

- supporting the national regulatory authorities in determining whether to license HPV vaccines, seeking WHO assistance as needed;
- reviewing global, regional or country-specific data on the burden of disease, epidemiology and risk factors related to HPV and the efficacy, safety and impact of HPV vaccines in the country context (*Human papillomavirus and HPV vaccines: technical information for policy-makers and health professionals* (http://www.who.int/reproductive-health/publications/hpvvaccines_techinfo/hpvtechinfo_nocover.pdf) (www.who.int/hpvcentre));
- exploring how the HPV vaccines might complement and be integrated with existing cancer prevention services, including screening;
- developing strategies and materials for communicating accurate, non-biased information to policy-makers, health care providers, patients, parents and the public about HPV vaccines;
- assessing the cost of licensed HPV vaccines and potential funding mechanisms for the public sector (Global Alliance for Vaccines and Immunization (GAVI) for those countries that are eligible, alternative sources for other countries);
- assessing the potential of monitoring the impact and safety of HPV vaccines, if marketed.

Closure of the meeting

Dr Gunta Lazdane thanked the speakers, participants, interpreters and the organizers of the meeting for their valuable contributions and WHO headquarters for their support.

The report of the meeting will be made available on the WHO web site (www.euro.who.int/reproductivehealth/20070510_1).

References

1. *Gaining Health. The European Strategy for the Prevention and Control of Noncommunicable Diseases*, Copenhagen, WHO Regional Office for Europe, 2006 (http://www.boneandjointdecade.org/HTML/musconline/images/highlights/WHO_European_Strategy_for_Prevention_and_Control_of_NCD_2006.pdf, accessed 11 November 2007).
2. *Comprehensive cervical cancer control: a guide for essential practice*. Geneva, World Health Organization, 2006 (http://www.who.int/reproductive-health/publications/cervical_cancer_gep/index.htm, accessed 11 November 2007).
3. Alliance for Cervical Cancer Prevention (ACCP) *Planning and implementing cervical cancer prevention and control programs: A manual for managers*. Seattle, ACCP, 2004 (http://www.who.int/reproductive-health/cancers/cervical_cancer_prevention_control_programs.pdf, accessed 11 November 2007).
4. European Commission. *European Guidelines for Quality Assurance in Cervical Cancer Screening - 2nd Edition*. Luxembourg: Office for Official Publications of the European Communities, 2007.
5. World Health Organization, United Nations Children's Fund. *Global Immunization Vision and Strategy (GIVS)*, Geneva, World Health Organization, 2005 (http://www.who.int/vaccines-documents/DocsPDF05/GIVS_Final_EN.pdf, accessed 11 November 2007).
6. *Preparing for the introduction of HPV vaccines. Policy and programme guidance for countries*. Geneva, World Health Organization, 2006 (http://www.aidsvaccineclearinghouse.org/pdf/HPV/reports_bg/WHO_HP_V_Guidance_Document_2006.pdf, accessed 18 November 2007).
7. *Human papillomavirus and HPV vaccines. Technical information for policy-makers and health professionals*. Geneva, World Health Organization, 2007 (http://www.who.int/reproductive-health/publications/hpvvaccines_techinfo/hpvtechinfo_nocover.pdf, accessed 18 November 2007).
8. Wiener HG et al. European guidelines for quality assurance in cervical cancer screening: recommendations for cytology laboratories. *Cytopathology*, 2007, 18:67-78.
9. *IARC Handbooks of Cancer Prevention*, Vol.10: Cervix Cancer Screening. Lyon, IARC Press, 2005.
10. Sankaranarayanan R et al. A Critical Assessment of Screening Methods for Cervical Neoplasia. *International Journal of Gynecology and Obstetrics*, 2005, 89(Suppl.2):4-12 (http://www.rho.org/files/IJGO_89_S2_2005_02.pdf, accessed 18 November 2007).

Annex 1

Assistance from WHO and other international organizations

World Health Organization

WHO provides technical advice and assistance; it is not a funding agency.

WHO support to the international policy platform

- Information-sharing with professional organizations: EC meeting October 2007, Conference on cancer – Slovenian Presidency – 2008, 10th Congress of the ESC – Prague – 30 April–3 May 2008.
- Provision of policy guidance and technical information to policy makers and health professionals in preparation of the introduction of HPV vaccines (2006-2007):
 - *Policy and programme guidance for countries* (available in English, French, Russian);
 - *Human papillomavirus and HPV vaccines: Technical information for policy makers and health professionals* (available in English, being translated to other languages).
- Fostering discussion by WHO vaccine policy bodies:
 - Strategic Advisory Group of Experts (April 2007);
 - Global Advisory Group on Vaccine Safety (June 2007).
- Organization of meetings in all WHO Regions to explore the possibility of introducing HPV vaccines in 2007-2008.
- Gathering information for the annual meetings of international/regional advisors and the meetings of the HPV Expert Advisory Group.
- Coordinating with different organizations, e.g. ECDC, on the harmonization recommendations.

WHO support to decision-making on cancer prevention options

- Assistance to Member States in developing of national policies. The WHO Regional Office for Europe works in 29 of the 53 countries in the region on the basis of bi-annual agreements between the Ministries of Health and the Regional Office. The Ministry of Health decides whether work on cancer prevention will be part of the agreement.
- Assistance to Member States in identifying sources of funding.

- Providing access to data compiled by the WHO Information Centre on HPV and Cervical Cancer, led by the Institut Catala d'Oncologia, Barcelona. Country-specific data on HPV and cervical cancer data are available on the WHO web site www.who.int/hpvcentre.
- The web site also includes information on current and novel options for cervical cancer prevention.
- Publication of:
 - *Comprehensive cervical cancer: a guide to essential practice*, available in English, French and Spanish at http://www.who.int/reproductive-health/publications/cervical_cancer_gcp/index.htm; being translated into Russian).
 - *Cancer control: knowledge into action. WHO guide for effective programmes. Planning* (<http://www.who.int/cancer/modules/Planning%20Module.pdf>).
 - *Cancer control: knowledge into action. WHO guide for effective programmes. Prevention* (<http://www.who.int/bookorders/anglais/detart1.jsp?sesslan=1&codlan=1&codcol=15&codcch=2674>).
 - *Planning and implementing cervical cancer prevention and control programmes*, a manual for managers (http://www.who.int/reproductive-health/cancers/prevention_control_cervical_cancer.html).
- Elaboration of a strategic note on the introduction of HPV vaccines in the European Region.
- Development of a WHO European regional strategic framework for the introduction of HPV vaccines, adjusting global HPV recommendations to reality in the Region.
- Support to countries in the introduction of vaccines through policy guidance and technical assistance.
- Support provided by the programme for noncommunicable diseases.
- Provision of advice on licensing procedures (WHO headquarters).
- Fact sheets are underway and will be available in English and Russian (WHO headquarters).
- Assistance to Member States in organizing training (exchange of experience).

WHO support related to manufacturing standards and laboratory procedures

- Dissemination of *WHO Guidelines to Assure the Quality, Safety, and Efficacy of HPV vaccines* (2007).
- Provision to countries of the WHO pre-qualification status of HPV vaccines and dissemination of information on standards through Expert Committee on Biologicals Standardization (ECBS) Technical Series Reports.
- Establishment of global HPV laboratory network and access to international standard reagents.

- Support to training on standard laboratory operating procedures to facilitate vaccine licensing and monitoring.
- Support to national regulatory authorities in evaluating HPV vaccines for possible licensing.

WHO support in assessing experience with vaccine introduction

- Launching communities of practice, a web-based forum (HPV-vaccines.net) through which the experiences and opinions of health professionals in relation to cervical cancer prevention and HPV vaccines will be collected.
- Planning an evaluation of how the introduction of HPV vaccines influences children, adolescents, and reproductive health programmes.
- WHO tools for decision-making on and the policy development relating to the introduction of vaccines (*Preparing for the introduction of HPV vaccines. Policy and programme guidance for countries* and *Human papillomavirus and HPV vaccines. Technical information for policy-makers and health professionals.* respectively.)
- *Vaccine Introduction Guidelines. Adding a Vaccine to the National Immunization Programme: Decision and Implementation, 2005*
- A plan of action for the introduction of new and underutilized vaccines in the WHO European Region is being finalized.

WHO support in research

- Publication of trial protocols to be used in normal settings: ethical and legal aspects have been discussed – special interest to operational research. WHO can be contacted regarding involvement.
- Organization of vaccine effectiveness studies using cancer impact as an endpoint. The role of WHO in these large trials needs to be assessed.

Potential support from partner organizations

European Commission (EC)

The EC can, as part of a public health portfolio, facilitate an exchange of information between Member States.

European cervical cancer association (ECCA)

The objectives of the European Cervical Cancer Association (ECCA) are to raise awareness about cervical cancer and how it can be prevented in Europe and to promote the implementation of comprehensive organized cervical cancer prevention

programmes. Its target audiences are the general public, health professionals and policy makers.

ECCA is a network with 60 member organizations in 26 countries. The central office is based in Lyon, France.

Information for the general public includes introductory brochures on cervical cancer screening, HPV, abnormal Pap smear and HPV vaccination, as well as information booklets on cervical cancer prevention and follow-up of an abnormal pap smear. These are adapted for countries and translated.

For health professionals, a patient communication tool kit is available. Information for all audiences is available through www.ecca.info.

The European Parliament Cervical Cancer Interest Group, which includes 36 Members of European Parliament, works within the European Parliament and the EC to keep cervical cancer prevention high on the political agenda. The Group is now being expanded to include national politicians. In January 2007, the first cervical cancer prevention week was also organized; it will be repeated on 21-28 January 2008.

International Planned Parenthood Federation (IPPF)

IPPF has a worldwide network of 150 autonomous member associations, working in 181 countries. It has five main areas of work: access, abortion, adolescents, HIV/AIDS and advocacy. The Internationally Medical Advisory Panel (IMAP) produced a statement on cervical cancer prevention and HPV vaccines in April 2007. IMAP recommends: (1) the promotion of safe sex; (2) the strengthening of cervical cancer screening programmes (visual inspection for resource-limited settings); (3) that member associations be strong advocates for the availability of low-cost vaccines and for partnership; (4) that girl-only focus be avoided – everyone, including men, should be informed of the benefits and limitations of the vaccines; and (5) that HPV vaccines be provided. With regard to the last point, the cost and accessibility of the vaccines pose a challenge.

IMAP statements are published in the IPPF bulletins (www.ipf.org)

International Union for Cancer Control (UICC)

The International Union for Cancer Control has 260 members from 80 countries, and 4 strategic directions, prevention and early detection being one of them.

Support is provided through:

- training: support in developing workshops with the partners, targeted fellowships, e.g. for cytologists, training in situation analysis.
- the organization of meetings (e.g. UICC World Cancer Congress 2008, Geneva, Switzerland, 27-31 August 2008).
- the provision of tools: books, guides, web-info, networks. E.g.: handbook on evidence-based cancer prevention.

- the provision of experts for site visits and technical assistance.
- pilot interventions, e.g. Latin America cervical cancer screening programmes: completion and audit in 4 countries; cervical cancer screening in Cambodia.
- advocacy and lobbying.

United Nations Population Fund (UNFPA)

UNFPA is assisting countries in Southern and Eastern Europe, on population issues and support for comprehensive RH programmes. Cancer prevention has not been a particular area so far, but UNFPA has been involved in preparatory work on HPV vaccines and is committed to continue this work. UNFPA will be an advocate for affordable vaccines and more broad-scale availability. UNFPA can also provide support to implementation of screening programme, in countries where UNFPA is present (e.g. training of health workers).

Annex 2

List of presentations and speakers

Cervical cancer prevention in Europe and countries

Challenges in the prevention of cervical cancer in the WHO European Region

Dr Gunta Lazdane, Regional Adviser, Reproductive Health and Research, WHO Regional Office for Europe

Country examples:

Finland

Dr Nea Malila, Director, Finnish Cancer Registry

Dr Merja Saarinen, Ministerial Counsellor, Health and Medical Affairs, Ministry of Social Affairs and Health;

Kyrgyzstan

Dr Gulnara Atantaeva, Head, Consultant Polyclinic, Kyrgyz Scientific Centre of Human Reproduction

Policies and approaches in the prevention and management of cervical cancer at global and regional levels

WHO policies in the prevention and management of cervical cancer

Dr Andreas Ullrich, Medical Officer Cancer Alliances, Chronic Diseases and Health Promotion, WHO headquarters

Screening for cervical cancer in the European Union

Dr Marc Arbyn, Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium

Mr Jaroslav Waligora, European Commission, Luxembourg

Country examples:

Armenia

Dr Gayane Avagyan, Chief Specialist, Maternal and Child Health Protection Unit, Ministry of Health

Iceland

Dr Kristian Sigurdsson, Medical Director, Cancer Detection Clinic, The Icelandic Cancer Society

Lithuania

Dr Ausrute Armonaviciene, Head, Subdivision of Mother and Child Health, Ministry of Health

Policies and approaches in the prevention and management of cervical cancer at global and regional levels: HPV vaccines

Immunization programme in Europe

Dr Nedret Emiroglu, Regional Adviser, Vaccine Preventable Diseases and Immunization, WHO Regional Office for Europe

HPV vaccine and immunization policy

Dr Teresa M. Aguado, Coordinator, Initiative for Vaccine Research, Product Research and Development, WHO Headquarters

Health economic analyses of HPV vaccines

Professor Geoffrey P. Garnett, Division of Epidemiology, Public Health and Primary Care, Imperial College, London, United Kingdom

Health professionals working with adolescents in the introduction of HPV vaccines and the reduction of risk behaviour

Dr Tina Miller, School of Social Sciences and Law, Oxford Brookes University, United Kingdom

Setting priorities for national policies on cervical cancer

Cervical cancer prevention – Denmark

Dr Beth Bjerregaard, Chairman, Department of Pathology, University of Copenhagen, Herlev Hospital

Dr Sigrid Poulsen, Senior Medical Officer, Communicable Diseases, National Board of Health

Cervical cancer prevention and HPV vaccine policy in France

Dr Hervé Creusvaux, Direction Générale de la Santé, Ministère de la Santé, de la jeunesse et des sports

Dr Sylvia Guyot, Direction générale de la santé, Bureau de la politique vaccinale et des maladies transmissibles, Ministère de la santé, de la jeunesse et des sports

Cervical cancer prevention: considerations for universal HPV vaccination in females aged 12–17 in Germany

Dr Yvonne Deleré, Sekretariat der Ständigen Impfkommission, Robert-Koch-Institut, Berlin

Prevention strategies of cervical cancer in Italy

Dr Maria Grazia Pompa, Communicable Diseases Unit, Directorate General of Prevention, Ministry of Health

Cervical cancer prevention in Turkey

Professor A. Murat Tuncer, Head, Department of Cancer Control, Ministry of Health

Strengthening cervical cancer prevention in countries

Role of mass media and key opinion makers: friend or foe?

Mr Christopher Powell, Communication Officer, Family and Community Health, WHO headquarters

On-going research in the area of cervical cancer prevention

Dr Rengaswamy Sankaranarayanan, Head, Screening Group, International Agency for Research on Cancer

Annex 3

Participants

Albania

Dr Ilirjana Kadare
EPI Manager, Institute of Public Health
Tirana

Prof Shahin Kadare
Chairman, Interregional Programme for the Prevention and
Management of Cervical Cancer in Albania
Hospital University Center 'Mother Teresa'
Tirana

Armenia

Dr Gayane Avagyan
Chief Specialist, Maternal and Child Health Protection Unit, Ministry of Health
Yerevan

Azerbaijan

Dr Zaur Safarov
Associate of the Oncology Department
Azerbaijan State Medical University

Belarus

Dr Svetlana Shilova
Chief Obstetrician-Gynaecologist, Ministry of Health
Minsk

Belgium

Dr Marc Arbyn
Epidemiologist, Unit of Cancer Epidemiology, Scientific Institute of Public Health
Brussels

Dr Jessy Hoste
Flemish Agency for Health and Care, Ministry of Welfare, Health and Family of the Flemish
Community
Brussels

Bosnia and Herzegovina

Dr Vesna Juric
Specialist in Obstetrics and Gynaecology, Clinical Hospital
Mostar

Dr Sladjana Petkovic
Public Health Institute of Republika Srpska
Banja Luka

Bulgaria

Dr Radosveta Filipova
EPI Manager, Directorate of Public Health, Ministry of Health
Sofia

Dr Petya Kostova-Zlatkova
Gynaecological Clinic, National Specialized Hospital for Oncology
Sofia

Professor Victor Borissov Zlatkov
Gynaecological Clinic, Specialized hospital for Midwifery and Gynaecology
Sofia

Croatia

Dr Ante Corusic
Clinic for Gynaecology and Obstetrics, University Medical School
Zagreb

Dr Damir Eljuga
Klinka 2A Zenske Bolesti, KB 'Sestre Milosrdnice'
Zagreb

Cyprus

Dr Marios Televantos
Medical Officer, Archbishop Makarios III Hospital
Nicosia

Czech Republic

Dr Lenka Krejcova
Senior Official, Health Care Department, Ministry of Health of the Czech Republic
Prague

Denmark

Dr Beth Bjerregaard
Chairman, Department of Pathology, University of Copenhagen, Herlev Hospital

Dr Sigrid Poulsen
Senior Medical Officer, Communicable Diseases, National Board of Health
Copenhagen

Estonia

Dr Ülla-Karin Nurm
Head, Public Health Department, Ministry of Social Affairs
Tallinn

Finland

Dr Nea Malila
Director, Finnish Cancer Registry
Helsinki

Dr Merja Saarinen
Ministerial Counsellor, Health/Medical Affairs, Ministry of Social Affairs and Health

France

Dr Hervé Creusvaux
Direction Générale de la Santé, Ministère de la Santé, de la jeunesse et des sports
Paris

Dr Sylvia Guyot
Direction générale de la santé, Bureau de la politique vaccinale et des maladies transmissibles
Ministère de la santé, de la jeunesse et des sports
Paris

Georgia

Dr Rema Ghvamichava
Associate Professor, Oncology Prevention Center
Tbilisi

Dr Levan Metreveli
Member of Parliament, Committee of Health and Social Affairs, Parliament of Georgia
Tbilisi

Germany

Dr Yvonne Deléré
Sekretariat der Ständigen Impfkommission, Robert-Koch-Institut
Berlin

Hungary

Dr Attila Kovacs
Deputy National Chief Medical Officer
Budapest

Iceland

Dr Kristjan Sigurdsson
Medical Director, Cancer Detection Clinic, The Icelandic Cancer Society
Reykjavik

Ireland

Mr Christopher Fitzgerald
Principal Officer, Public Health Services, Department of Health and Children
Dublin

Dr Tony Holohan
Deputy Chief Medical Officer, Department of Health and Children
Dublin

Italy

Dr Maria Grazia Pompa
Director, Communicable Diseases Unit, Directorate General for Prevention
Ministry of Health
Rome

Dr Marco Zappa
Director, CSPO Center for the Study and Prevention of Cancer
Scientific Institute of the Tuscany Region
Florence

Kyrgyzstan

Dr Gulnara Atantaeva
Head, Consultant Polyclinic, Kyrgyz Scientific Centre of Human Reproduction
Bishkek

Latvia

Dr Ludmila Engele
Head, Department of Methodology and Strategy, Riga's Eastern Hospital
Dr Skaidrite Vasaraudze
Head, Division of Family Health, Department of Public Health, Ministry of Health
Riga

Lithuania

Dr Ausrute Armonaviciene
Head, Subdivision of Mother and Child Health, Ministry of Health
Vilnius

Malta

Dr Miriam Dalmas
Medical Officer, Department of Health Information
Guardamangia

Netherlands

Dr Hans Houweling
Health Council of the Netherlands
The Hague
Ms Annemarieke Rendering
Policy Adviser, Public Health and Disease Prevention, Cervix Screening Programme, Ministry
of Health, Welfare and Sport
The Hague

Norway

Dr Bodolf Hareide
Senior Adviser, Directorate for Health and Social Affairs
Oslo
Dr Rita Steen
Head, Department of Screening-based Research, Cancer Registry of Norway
Oslo

Poland

Dr Barbara Dabrowska
Chief Specialist, Department of Health Policy, Unit of Oncology, Ministry of Health
Warsaw

Portugal

Dr Maria da Graça Freitas
Deputy Director General for Health, Ministry of Health, Directorate-General of Health
Lisbon

Dr Joaquim Gouveia
National Coordinator, Oncological Diseases
Lisbon

Republic of Moldova

Dr Olga Cernetchi
Deputy Rector for Quality Assurance and Integration, State University of Medicine and
Pharmacy 'Nicolae Testemitanu'
Chisinau

Dr Laura Turcan
Epidemiologist, National Scientific Centre of Preventive Medicine
Chisinau

Russian Federation

Dr Vera Prilepskaya
Deputy Director, Scientific Centre of Obstetrics, Genecology and Perinatology
Moscow

Dr Cofia Rogovskaya
Vice President, Russian Association on Cervix Pathology and Colposcopy
Federal Research Institute for Obstetrics Gynecology and Perinatology
Moscow

Serbia

Professor Vesna Kesic
Head, Department for Gynaecological Diagnosis, Institute for Gynaecology and Obstetrics
Clinical Center of Serbia
Belgrade

Dr Nevenka Pavlovic
Section Head, Unit for Chronic Diseases and Conditions, Center for Disease Control and
Prevention
Institute of Public Health of Belgrade

Slovakia

Dr Oliver Sadovsky
President, Slovak Society for Cervical Pathology and Colposcopy
National Oncology Institute
Bratislava

Slovenia

Dr Bojana Pinter
Department of Obstetrics and Gynecology
University Medical Centre Ljubljana

Spain

Dr Isabel Pachon del Amo
Coordination Centre of Health Emergencies, Directorate General of Public Health
Madrid

Sweden

Dr Anders Tegnell
Head, Communicable Disease Prevention and Control Unit
National Board of Health and Welfare
Stockholm

Tajikistan

Dr Muborak Kurbonova
Head, Department of Gynecology, Scientific Institute of Obstetrics, Gynecology and Pediatrics
Ministry of Health
Dushanbe

The former Yugoslav Republic of Macedonia

Dr Jovanka Kostovska
Head, Department for Primary and Preventive Health Care
Ministry of Health
Skopje

Dr Adela Stefanija
Director, Clinic of Gyneacology and Obstetrics, University Clinical Center
Skopje

Turkey

Professor A. Murat Tuncer
Head, Department of Cancer Control, Ministry of Health
Ankara

Turkmenistan

Dr Nurberdy Saryev
Head, Department of Cancer – Gyneacology, Scientific-clinical Centre of Oncology
Ashgabat

Ukraine

Dr Liudmila Vorobyova
Head, Oncological Department, Oncological Research Institute
Kyiv

United Kingdom of Great Britain and Northern Ireland

Dr Sowsan Atabani
Senior Registrar, Immunization Policy, Monitoring, Surveillance
Department of Health
London

Uzbekistan

Dr Said Sultanov
Chief Obstetrician-Gynaecologist, Ministry of Health
Tashkent

Temporary Advisers

Dr Geoffrey P. Garnett
Professor of Microparasite Epidemiology, Division of Epidemiology, Public Health and
Primary Care
Imperial College
London
England

Dr Tina Miller
School of Social Sciences and Law
Oxford Brookes University
England

Dr Rengaswamy Sankaranarayanan
International Agency for Research on Cancer (IARC)
Lyon
France

Representatives

Catalan Institute of Oncology (ICO)

Dr Silvia de Sanjose Llongueras

European Cervical Cancer Association (ECCA)

Dr Philip Davies
Dr Magdalena Grce

European Commission (EC)

Mr Vincent Houdry
Mr Jaroslaw Waligora

International Planned Parenthood Federation (IPPF) European Network, Brussels

Dr Peter Safar

International Planned Parenthood Federation (IPPF), London

Dr Kiran Asif

Medical Women's International Association (MWIA)

Dr Vibeke Jorgensen
Dr Aggi Kjaer

PATH-Europe

Dr Robin Biellik

International Union against Cancer (UICC)

Professor Hélène Sancho-Garnier

United Nations Development Fund for Women (UNIFEM)

Dr Astrid Perez-Pinan

United Nations Population Fund (UNFPA)

Dr Assia Brandrup-Lukanow

Observer

Dr Jan Stjernswärd
Consultant
Sweden

World Health Organization

Regional Office for Europe

Dr Nedret Emiroglu
Regional Adviser, Vaccine Preventable Diseases and Immunization

Dr Jill Farrington
Coordinator, Noncommunicable Diseases

Ms Helen Gill
Administrative Assistant, Family and Community Health

Ms Elizabeth Kyed
Administrative Assistant, Communicable Diseases

Dr Gunta Lazdane
Regional Adviser, Reproductive Health and Research

Dr Andrei Lobanov
Medical Officer, Vaccine Preventable Diseases and Immunization

Dr Aiga Rurane
Head of WHO Country Office, Latvia

Ms Tetyana Friederich-Vlasyuk
Secretary, Making Pregnancy Safer

Regional Office for the Americas/Pan American Health Organization

Dr Merle Lewis
Immunization Unit

Headquarters

Dr Teresa M. Aguado
Coordinator, Initiative for Vaccine Research Product, Research and Development

Dr Kathleen Irwin
Scientist, Implementation Research
Initiative for Vaccine Research Programme

Mr Christopher Powell
Communication Officer

Dr Andreas Ullrich
Medical Officer, Cancer Alliances

Rapporteur

Dr Patricia Claeys
University of Gent, International Center for Reproductive Health
Belgium

Interpreters

Mr Vladimir Ilyukhin
Simultaneous Interpreter
Russian Federation

Mr Georgy G. Pignasty
Conference Interpreter/Translator
Russian Federation