european cancer ORGANISATION

HPV PROTECT
Izaberi cijepljenje. Spriječi rak.

Croatian Initiative Against Cancers Caused by the Human Papillomavirus (HPV)

Contents

Acknowledgements

We thank all those who provided their time and expertise to make this Initiative possible, and who continue to support the work of all the organisations involved in achieving high-level discussions and actions towards improving cancer care in Europe and beyond.

Authors

Marko Anić
Ella Selak Bagarić
Ivica Belina
Tatjana Nemeth Blažić
Dražan Butorac
Neda Ferenčić Vrban
Adriano Friganović
Marko Gangur
Mirela Šentija Knežević
Jurica Kravaršćan
Marjeta Majer
Danijela Vrdoljak Mozetić
Tatjana Petričević Vidović
Marija Posavec
Mihael Skerlev
Ivana Pavić Šimetin
Miroslav Venus
Ljiljana Vukota

Supported by

Project **'Budi mRAK'**, NGO CroMSIC

Project **'Zdravo Sveučilište'**, The Student Council of the University of Zagreb

NGO **'Impress'**

Abstract

The **Croatian Initiative Against Cancers Caused by the Human Papillomavirus (HPV)** is comprised of a multidisciplinary group of experts dedicated to the goal of preventing diseases associated with HPV infection. The Initiative brings together experts in disease prevention and health promotion among children and youth, epidemiologists, oncology specialists, researchers, patients, representatives of civil society organisations and other stakeholders to jointly contribute to the creation of public health advocacy policies and measures aimed at comprehensive improvement of HPV vaccination rates, prevention of all cancers caused by HPV and early detection of cervical cancer.

The Croatian Initiative Against Cancers Caused by HPV does not intend to focus solely on policy creation, but also aims to provide a platform for exchange of information among experts and interested parties, as well as to amplify the voices of those affected, including the medical community and patients, ensuring that their voices are considered in decision-making processes. Furthermore, the Initiative emphasises the importance of preventing HPV infection and HPV-related diseases through health education for parents, children and youth, and through synergistic actions of stakeholders across health and education sectors, aiming to eliminate the stigma associated with HPV infection as solely a women's issue.

The Initiative is supported by the **European Cancer Organisation (ECO)**, which strives to reduce the impact of cancer and improve the quality of care and outcomes for cancer patients within the European Union through networking, broad cooperation and advocating evidence-based practices and interventions. Currently, ECO supports activities concerning HPV-related cancer prevention not only in Croatia but also in Romania and Bulgaria. In 2023, ECO became active in Croatia with the aim of enhancing prevention of HPV infection and HPV-related diseases, taking into account Croatia's longstanding tradition and progress achieved in prevention and vaccination efforts. This Initiative is organised within the context of Croatia's continuous engagement in combating serious health threats. Furthermore, Croatia's efforts in adopting key strategic documents, such as the National Strategic Framework against Cancer until 2030 and the Action Plan for the Implementation of the National Strategic Framework against Cancer for the period up to 2025, should be highlighted. These documents clearly demonstrate Croatia's commitment to improving the health and well-being of its citizens. Additionally, we commend Croatia for regularly updating and improving its immunisation plan on an annual basis to prevent HPV infection among populations at increased risk. This underscores Croatia's ongoing efforts to ensure a high level of protection against HPV infection. These activities clearly demonstrate Croatia's dedication to improving public health and protecting its citizens.

Summary

The Croatian Initiative Against Cancers Caused by the Human Papillomavirus (HPV) is comprised of a multidisciplinary group of experts dedicated to the goal of preventing diseases associated with HPV infection. The Initiative brings together experts in disease prevention and health promotion among children and youth, epidemiologists, oncology specialists, researchers, patients, representatives of civil society organisations and other stakeholders to jointly contribute to the creation of public health advocacy policies and measures aimed at comprehensive improvement of HPV vaccination rates, prevention of all cancers caused by HPV and early detection of cervical cancer. The Initiative also involves other partners for joint policy creation and advocating for improvements in youth health education aimed at promoting health literacy, HPV vaccination, prevention of all cancers caused by HPV and organised cervical cancer screening programmes.

HPV is the most common sexually transmitted viral infection, and in a portion of infected persons, it may cause several types of cancer. Therefore, it poses a significant public health and clinical challenge. The importance of addressing the issue of HPV infection is underscored by its high prevalence and the fact that it causes about 4.5% of all malignant tumours worldwide. HPV is a DNA virus that infects epithelial cells. Classified based on oncogenic potential, HPV can be divided into low-risk types, which include HPV genotypes which cause genital warts, and high-risk types, which can cause six types of cancer in humans. Infection is often asymptomatic and spreads through intimate skin-to-skin, skin-to-mucosa or mucosa-to-mucosa contact.

Given the above, it is crucial to work on preventing HPV infection and raising public awareness about the risks and available protection methods. The World Health Organization (WHO), the European Commission and other prominent organisations highlight the need to eliminate cervical cancer, which is primarily caused by HPV infection, in their strategies and documents. In line with this, an approach was proposed which involves three interventions aimed at vaccination, screening and treatment, with global '90-70-90' targets to be met by 2030: 90% of girls fully vaccinated against HPV by the age of 15; 70% of women screened for cervical cancer by the age of 35 and again by the age of 45; and 90% of diagnosed pre-cancerous lesions and invasive cancers treated. Increasing HPV vaccination coverage and cervical cancer screening can significantly reduce the number of cases of HPV-related cancers in the coming decades. Although the incidence of other HPV-related cancers is currently low and no increase in such cancers has been identified in Croatia at the moment, global trends show a rising incidence of these cancers, which may thus be expected in Croatia as well.

The National Strategic Framework against Cancer promotes health awareness and literacy at every age, starting from preschool age. Its objectives include comprehensive health education, preservation of physical, mental and social health, prevention of addictive and other risky behaviours, promotion of vaccination and education on the importance of regular preventive medical examinations. It is therefore essential to initiate broader educational and informational activities as well as campaigns concerning health preservation, including campaigns about HPV vaccination and targeted campaigns aimed at vaccinating boys and young men. These efforts should be preceded by an analysis of the current state and needs in the field of educational and informational activities, to ensure evidence-based planning of educational and promotional activities. In Croatia, HPV vaccination has been available since 2007, and in 2016, it was included in the National Immunisation Programme. However, despite the trend of improvement of vaccination coverage, there is still room for further improvement, particularly among men, in order to achieve WHO's global targets. To meet global and European targets, Croatia needs to enhance the monitoring of the HPV vaccination programme, maintain continuity of promotional and educational activities, especially outside macroregional centres, and improve coordination activities at the county and national levels, in line with intervention needs.

Recommendations pertain to HPV vaccination, the National Preventive Programme (NPP) for early detection of cervical cancer and public health activities in the field of education and information on prevention of HPV infection.

MAIN RECOMMENDATIONS

1. **Information system for monitoring/database**: Improve the information system for monitoring HPV vaccination and cervical cancer screening, focusing on timely reporting – it is necessary to ensure improvements of infrastructure to allow segmented data access. For the purpose of programme evaluation, periodic reports with relevant indicators should be available. It is necessary to ensure data quality for the purpose of reliability of information and in order to facilitate comparison with European and global data. The objective of this measure is to improve the monitoring and evaluation of the programme, contributing to better preventive care for HPV and cervical cancer, in line with the European Council's recommendations on vaccine-preventable cancers.

2. **Education and information/raising awareness**: Establish cooperation with the Ministry of Science and Education and systematically educate young people at appropriate ages for vaccination. Enable direct communication between school medicine specialists and students' parents through e-Citizens or e-Class Register systems to enhance the effectiveness of preventive programmes in school-age children, including health interventions for examination of children, screening and vaccination. Conduct continuous national media campaigns using media and digital platforms to educate about the risks of HPV, emphasising real-life stories and expert recommendations. Design public health messages that clearly communicate that HPV is not only the cause of cervical cancer but also of other malignant diseases, including those affecting the oropharynx, penis, anus and vulva.

3. **Vaccination**: Set a national target for HPV vaccination at 90% of girls vaccinated by the age of 15 by 2030. Continuously increase the number of vaccinated individuals by 2030 – aiming for 60% vaccinated by 2025, 70% vaccinated by 2027 and 90% vaccinated by 2030, with a significant proportion of boys vaccinated in accordance with the European Parliament resolution on strengthening Europe in the fight against cancer.

4. **Connect stakeholders from the health sector, local government and the education sector** – organise annual coordination meetings of local health institutions, local schools and local authorities, creating a synergistic strategy for acting and improving cooperation at the local level, for the purpose of improvement of youth education on preservation of sexual and reproductive health and the promotion of HPV vaccination, thereby increasing the vaccination rate among young people. Additionally, ensure funds for local governments to implement educational campaigns and periodic promotional vaccination actions for young people older than 18, in accordance with local needs, as derived from available databases.

5. **Screening**: Establish the implementation of the National Preventive Programme for early detection of cervical cancer, based on WHO professional guidelines and quality criteria for programme providers, using validated tests approved by regulatory institutions, and conduct activities to inform and educate women about the importance of undergoing preventive gynaecological examinations in accordance with the European Parliament resolution on strengthening Europe in the fight against cancer.

1. Introduction

Purpose and relevance of the HPV Initiative

The goal of the Croatian Initiative against Cancers Caused by HPV, established at the initiative of the European Cancer Organisation (ECO), is to eliminate cervical cancer and reduce the incidence of other HPV-related cancers. Specifically, the organisation aims to make it possible for every young person to be vaccinated against HPV, as recommended by Europe's Beating Cancer Plan, and to implement cervical cancer screening programmes in every country, in line with the recommendations of the World Health Organization (WHO).

To accelerate elimination of HPV-related cancers in Europe, ECO launched the 'Action Now' project. This project brings together civil society organisations and professional organisations in countries working to improve HPV vaccination and cervical cancer screening rates, to influence the creation of positive vaccination and cervical cancer screening practices in a timely manner, in accordance with European and global health policies and practices. The project is currently underway in Romania, Bulgaria and Croatia, with plans to extend it to other European countries in 2024.

HPV is the most common sexually transmitted infection. HPV infection is transmitted through intimate 'skin-to-mucosa,' 'skin-to-skin' or 'mucosa-to-mucosa' contact, which includes all forms of unprotected sex (vaginal, oral, anal) and other forms of sexual activity involving mucosal contact, such as petting. Young people, who are often unaware of how easily HPV is transmitted, represent a risk group for spreading the infection, potentially compromising their quality of life. HPV comprises a family of DNA viruses that infect the basal layer of epithelial cells. Regarding oncogenic potential, HPV can be divided into low-risk and high-risk types. Low-risk types, also known as non-oncogenic, can cause genital warts and respiratory papillomas. The most common low-risk HPV types are 6 and 11. High-risk, oncogenic HPV types are closely associated with cervical, oropharyngeal, anal, vaginal, vulvar and penile cancer. The most common high-risk HPV types are 16 and 18, but there are also less common types, such as 31, 33, 45, 52 and 58.

It is estimated that 4.5% of malignant tumours globally are caused by high-risk HPV infection. HPV causes six types of cancer. It is responsible for more than 99% of cervical cancer cases, more than 90% of anal cancer cases, 70% of vaginal and vulvar cancer cases, 60% of penile cancer cases and 60% of oropharyngeal cancer cases. Globally, the majority of cancers caused by HPV are cervical, but in high-income countries, such as the United States, HPV-related head and neck cancers are currently more common than cervical cancer. It is estimated that 630 million people worldwide are infected with HPV, both men and women. While the prevalence of HPV in women is well-known, its epidemiology in men requires further research. A study in The Lancet found that globally, 31% of men have HPV, and 21% carry high-risk HPV (HR-HPV). Prevalence peaks in men aged 25 to 29 and then stabilises. Regions such as Europe, North America and Sub-Saharan

Africa show similar prevalence, but East and Southeast Asia reported half of these rates.

Approximately one-fifth of the global male population carries a high-risk type of HPV. Considering the above, the importance of including men in HPV prevention strategies is emphasised for the purpose of addressing HPV-related health issues and efforts to eradicate HPV-related diseases, such as cervical cancer.

Furthermore, most infected individuals, both men and women, do not exhibit symptoms of the infection. When symptoms do appear, they are most commonly in the form of genital warts, which indicate infection with a low-risk type of HPV. High-risk types of HPV usually do not exhibit symptoms until (and unless) they progress to cancer.

Like other sexually transmitted infections which are transmitted through intimate contact, the prevalence of HPV-related conditions in the population largely depends on collective awareness and preventive measures. In August 2020, the World Health Organization adopted a global strategy to eliminate cervical cancer caused by HPV by 2030. In February 2021, the European Commission adopted Europe's Beating Cancer Plan, which outlines four main health determinants and mentions HPV as a cause of cancer in the chapters on improving prevention (vaccination) and early diagnosis (cervical cancer screening).

There are currently four HPV vaccines available: Cervarix, Gardasil, Gardasil-9 and the recently introduced Cecolin. In Croatia, the nine-valent vaccine is used in the HPV vaccination programme. Numerous studies have confirmed the safety and efficacy of these HPV vaccines in protecting against HPV-related diseases. Since the approval of the HPV vaccine in 2006, more than 100 countries which are members of the World Health Organization have started HPV vaccination programmes. According to data of the European Centre for Disease Prevention and Control (ECDC), 30 countries in Europe currently include HPV vaccination in their programmes.

Compliance with applicable national and European strategic documents

Europe's Beating Cancer Plan emphasises the need to eliminate cervical cancer caused by HPV as well as that all countries must reach and maintain a cervical cancer incidence rate of less than 4 cases per 100,000 women. Achieving these objectives rests on three key pillars and their corresponding targets.

THE THREE PILLARS OF THE EUROPEAN BEATING CANCER PLAN

Vaccination: 90% of girls fully vaccinated with the HPV vaccine by the age of 15

Screening: 70% of women screened with a high-performance test by the age of 35 and again by the age of 45

Treatment: 90% of women with pre-cancer treated and 90% of women with invasive cancer managed.

Each country should meet the 90-70-90 targets by 2030 to get on the path to eliminating cervical cancer within the century.

We can thus conclude that there are two highly effective methods for preventing cervical cancer: HPV vaccination and cervical cancer screening. Screening primarily involves HPV testing, triaging HPV-positive women using effective methods and then treating identified pre-cancerous lesions. The rapid increase of vaccine access and cervical cancer screening programmes worldwide could prevent up to 13.4 million cases of cervical cancer over the next 50 years. By the end of the century, this could lead to a situation where most countries have an annual incidence rate of less than 4 cases per 100,000 women.

A recently published study highlighted as an example of good practice confirmed the high efficacy of the HPV vaccine in preventing cervical cancer, as no cases of the disease have been recorded in fully vaccinated young women. This study was conducted in Scotland, where the HPV vaccination programme, initiated in 2008, ensures that girls aged 12 or 13 are vaccinated. Besides cervical cancer, recent research indicates an increase in the number of HPV-related infections of the anal and oral cavities and oropharyngeal cancer in wealthy countries. A study conducted by Chaturvedi in 2011 showed that the incidence of oropharyngeal cancer in women in the US began to exceed cervical cancer rates in 2010. The US could record nearly a doubling of such cases by 2030. Research conducted in the Netherlands emphasises the effectiveness of HPV vaccination for MSM (men who have sex with men), even when the vaccine is administered after sexual activity. Evaluating the proposed 70% vaccination rate for both sexes, research by Díez-Domingo et al. shows a significant reduction in the incidence of HPV-related

genital warts. These results support the arguments for including boys in HPV vaccination programmes.

According to the National Strategic Framework against Cancer (Official Gazette 141/2020), health education should begin in preschool by introducing it into preschool institutions and integrating it into the curriculum throughout the educational process. Such a curriculum would systematically educate children, young people and their parents about various aspects that contribute to a healthy life and the need to avoid substances that cause addiction and increase the risk of chronic non-communicable and malignant diseases. Furthermore, they would be educated about the need for preventive actions: vaccinations, regular medical examinations and responsible behaviour. Such an educational programme must be accompanied by conditions that enable the preservation of healthy habits in children and young people. This systematic approach, carried out in cooperation with the Ministry of Science and Education and the Agency for Education, is crucial for ensuring a shift in social awareness and a higher level of health literacy among the population. It cannot be replaced by promotional campaigns and public health actions.

The current Curriculum for the Cross-Curricular Topic of Health for Primary and Secondary Schools (Official Gazette 10/2019) defines care for physical health as one component of the cross-curricular topic. Educational expectations are distributed across educational cycles and domains. Although the care for sexuality and sexual health is already represented in educational cycle A.3.1.B , for students in the sixth, seventh and eighth grades of primary school, it defines the recognition of importance of care for reproductive health, and the key content describes the importance and acceptance of conversations about reproductive health, especially with persons with whom students are close, responsible sexual behaviour (available options for preserving sexual and reproductive health) and recognising when and to whom to turn for professional help. Vaccination as a specific protection measure for sexual and reproductive health is offered in the fourth cycle, specifically A.4.1., for students in the first and second years of four-year secondary schools, and for students in the first year of three-year secondary schools.

The National Strategic Framework against Cancer until 2030 (Official Gazette 141/2020) recommends that education of students about the importance of HPV vaccination should start at an earlier age, in primary school, in accordance with the HPV vaccination schedule. Currently, there exist well-developed educational platforms for education of the public in Croatia. Examples of good practice include the websites https://volimzdravlje.hr/ and https://spolnozdravlje.hr/.

A study from neighbouring Italy is highlighted as an example of good practice outside Croatia; it utilised video materials and interactive games for students aged 11 and 12. The video material "Salute e HPV" was used as an educational tool. The video presents the HPV vaccine to children as a standard activity that they should practice at their age in order to stay healthy, similar to physical activity or a healthy diet. Several scenarios are shown where children engage in physical activity, eat healthy food, and brush their teeth with their parents. The importance of getting at least eight hours of sleep at night is also emphasised. At the end of these scenarios, the narrator (a health expert) states that children should also receive the HPV vaccine to stay healthy. The decision to include this activity among several activities with which children in Italy are familiar was made to reduce fear and stigmatisation associated with the HPV vaccine and to emphasise the importance of vaccination at their age, in accordance with the recommendations of the Italian Ministry of Health. Using animated characters and scenarios, the video underscores that HPV vaccination is a standard preventive measure, like physical activity or proper nutrition. The health expert in the video provides accurate information about vaccination, emphasising the importance of discussing any fears. Distribution of this educational material is recommended, through accessible platforms such as YouTube, where it is available – link.

Including children in discussions about their health in general, and specifically about HPV and the HPV vaccine, is important for empowering children and meeting their informational needs. Children responded well to the animated video and online game, which were evaluated in the above study and showed promising results in improving various outcomes. We hope that the results and methods used in this study will inspire other researchers to continue this line of research and further identify and develop strategies and campaigns to encourage children to actively participate in care for their health.

HPV vaccination became available in Croatia in 2007. From 2007 to 2016, HPV vaccination was organised locally for school-aged children in certain cities, towns and counties, depending on the

local government's funding capabilities, through personal payment for the vaccine and at individual request. Nationwide, the vaccine became available and free of charge for certain age groups at the start of 2016. The recommendation for age groups has gradually changed over the past two years, and since 2018, vaccination has been free of charge for boys and girls attending the eighth grade of primary school. As of 2023, HPV vaccination has been made available to students aged 9 to 25, and starting from 2024, the programme has been expanded to include individuals over 25 years of age based on medical status/epidemiological situation. This vaccine is not included in the mandatory vaccination programme.

The HPV vaccination programme is regulated by the immunisation, seroprophylaxis and chemoprophylaxis programme for specific population groups and individuals at increased risk. The vaccination rate among children attending the eighth grade of primary school in 2017 was lower than 10%. Through the implementation of a systematic vaccination programme in the 2022/2023 school year, the level of vaccinated girls and boys up to the age of 15 increased to 51.1% of girls who received at least one dose of the HPV vaccine and 34.3% of boys who received at least one dose of the HPV vaccine. To achieve the targets of the World Health Organization and the European Commission, Croatia will need to increase the number of people vaccinated against HPV, reduce the incidence of malignant tumours caused by HPV infection and systematically educate staff in educational institutions and parents of children in the educational process. The targets set by the World Health Organization can be achieved only through organised cooperation of the Ministry of Health, the Croatian Institute of Public Health, the Ministry of Science and Education, the Agency for Education, local government branches and leading health institutions and associations.

According to the National Strategic Framework against Cancer, the vision for healthcare in Croatia in 2030 involves the improvement, systematic implementation and monitoring of primary prevention programmes, including health promotion. The aim is to raise awareness and educate the population about cancer in order to reduce cancer incidence to an average level compared to other European Union member states. One of the objectives that can contribute to the realisation of this vision is the prevention of cancer caused by HPV infection.

Specifically, as stated in the National Strategic Framework against Cancer, the objectives are:

THE OBJECTIVES OF THE NATIONAL STRATEGIC FRAMEWORK AGAINST CANCER

1. To reduce the risk of pre-malignant and malignant lesions associated with persistent HPV infection in vaccinated individuals
2. To increase the vaccination rate among eighth-grade students by 50% by 2025
3. To reduce the incidence of pre-malignant lesions of the cervix in girls and young women by 30% by 2030.

Some of the measures or activities to achieve these objectives are indicated in the National Strategic Framework against Cancer:

1. Raising awareness among women and the public about cervical cancer prevention
2. Continuous training of healthcare workers involved in the screening programme and educating the public on preventing this type of cancer.

The aim is to improve and monitor the effectiveness of existing screening measures and to introduce new ones, as well as to increase the rate of participation in screening examinations (e.g., educating the public using mass media, promoting patient participation in screenings conducted by family physicians (general practitioners), training personnel to perform screenings, understanding and reducing regional disparities and effectively involving local government).

Croatia can proudly state that it has reached the vaccination targets set out in the National Strategic Framework against Cancer until 2030. To continue the well-established practice of immunisation, the Action Plan for the Implementation of the National Strategic Framework against Cancer for the period up to 2025 states that vaccination continuity must be maintained. This can be improved through up-to-date monitoring of vaccination rates by tracking available data and establishing a centralised and publicly accessible database of vaccinated persons.

The objective of the National Preventive Programme for early detection of cervical cancer is to maintain

women's health, reduce risk, detect cervical cancer early and improve the quality of life for the target group of women. Based on recommendations from the 'Twinning' project, which aims to improve the quality of implementation of the National Preventive Programme for early detection of cancer, organised invitations as part of the National Preventive Programme for early detection of cervical cancer have been suspended until the necessary prerequisites for their implementation are in place.

In Croatia, opportunistic screening for cervical cancer is implemented, which has reduced the incidence and mortality rate of cervical cancer. However, opportunistic screening cannot reduce the incidence of the disease to less than 4 cases per 100,000 women, as most new cases concern women not covered by screening. In December 2012, the Ministry of Health of the Republic of Croatia started implementing an organised national preventive programme for early detection of cervical cancer. The programme's objectives are, firstly, to reduce the incidence of invasive cervical cancer by 60% in the age group 25 to 65, eight years after the start of implementation of the programme; secondly, to reduce mortality from cervical cancer by 80% in the age group 25 to 70, 13 years after the start of implementation of the programme; and thirdly, to gradually reduce opportunistic screening. The programme included all women who had not undergone opportunistic screening (women who had recently had a Pap test did not receive invitations), aged 25 to 64, every three years, with 2013 being the index year. The objectives are as follows:

1. Reduce the incidence and mortality rate of cervical cancer by 50% after three cycles of implementation of the highly organised National Preventive Programme for early detection of cervical cancer
2. Improve the rate of response to invitations for testing to at least 60% by 2030
3. Reduce the mortality rate by 25% by 2030.

The Government of the Republic of Croatia adopted the National Preventive Programme for early detection of cervical cancer in Croatia in July 2010. Implementation of the programme began in 2012, and women aged 25 to 65 were invited to undergo cytological screening (Pap test) under the guidance of the Croatian Institute of Public Health. After the first round of screenings in 2016, the project was suspended due to technical and infrastructural issues. In 2018, the project was reorganised and at the beginning of 2023, it was implemented as a pilot project in the Virovitica-Podravina County.

The purpose and objective of the first phase of the reorganised programme was to test the feasibility of the proposed protocol using a new approach, which would include both Pap tests and HPV testing as the primary screening test. Based on the monitoring data and experiences from the first stage of implementation, the aim was to create a version of the protocol that could be applied at the national level. Pilot project activities were suspended at the beginning of 2020 due to the COVID-19 pandemic. At the end of 2022 and the beginning of 2023, in coordination with the Working Group of the Ministry of Health, the planning and organisation of implementation of the first stage of the reorganised NPP for early detection of cervical cancer resumed, with the programme scheduled to be implemented in Virovitica-Podravina County for 12 months, starting from March 2023.

THE OBJECTIVES OF CROATIA'S NATIONAL PREVENTIVE PROGRAMME FOR EARLY DETECTION OF CERVICAL CANCER

1. Reduce the incidence and mortality rate of cervical cancer by 50% after three cycles of implementation.
2. Improve the rate of response to invitations for testing to at least 60% by 2030.
3. Reduce the mortality rate by 25% by 2030.

Analysis of the current situation and needs

Despite the provision of free vaccines for all eighth-grade students and the availability of vaccines for all young people aged 9 to 25, as well as for those older than 25 according to medical/epidemiological indications, the vaccination rate remains relatively low. According to the latest data of the Croatian Institute of Public Health for 2023, among persons born in 2008 (i.e., 15-year-old children), 51.1% of girls and 34.3% of boys have received at least one dose of the vaccine.

The City of Zagreb, in cooperation with the Committee for the Prevention of HPV Infection and Other Sexually Transmitted Diseases, conducted a survey to determine the level of awareness among parents about the risks of HPV infection. The survey, the results of which were presented on 5 December 2018 at the Zagreb Youth Health Centre, found that every second parent (i.e., 50%) in Croatia does not know that HPV can cause as many as six types of cancer, while a third of the parents have never heard that there is a free HPV vaccine available for all eighth-grade students and, depending on vaccine availability, for all young people up to 25 years old. The SERZAM2020 study shows a low vaccination rate among young people aged 18 to 25. According to the results of this study, only 18.3% of participants (25.0% of women and 11.7% of men) reported being vaccinated against HPV, while 21.9% were unsure of their vaccination status. Of the respondents who were vaccinated, 65.6% were women. These results indicate a need for additional efforts to be made in order to raise awareness and encourage vaccination among young people to improve the HPV vaccination rate.

To achieve global, European and national goals, the priority for Croatia should be, firstly, improving the monitoring of the HPV vaccination programme results and better utilisation of the existing routine HPV vaccination database within the health information system; secondly, developing new software (e.g., an oncology network and oncology database as part of the National Strategic Framework against Cancer or a solution for tracking vaccination status as part of the National Preventive Programme for early detection of cervical cancer), which would lead to improved coordination of activities at the national level, implementation of vaccination and public health education.

VACCINATION IN CROATIA BY THE NUMBERS

Source: Croatian Institute of Public Health (2023)

Number of 15-year old girls that have received at least one dose of the HPV vaccine: **51.1%**

Number of 15-year old boys that have received at least one dose of the HPV vaccine: **34.3%**

Source: Survey conducted by the City of Zagreb in cooperation with the Committee for the PRevention of HPV Infection and Other Sexually Transmitted Diseases (2018)

50% of parents do not know that HPV can cause as many as six types of cancer.

A third of parents have never heard that there is a free HPV vaccine available for eight-grade students.

Source: SERZAM2020 Study

Number of participants that have reported being vaccinated against HPV: **18.3%**

2. Recommendations

Public health

Database and software for NPP: Develop a publicly accessible digital health registry that complies with personal data protection and the General Data Protection Regulation (GDPR), and provides relevant real-time vaccination data and information from the National Preventive Programme for early detection of cervical cancer.

Awareness: Establish cooperation with the Ministry of Science and Education and systematically educate young people of appropriate ages for vaccination. Conduct continuous national media campaigns using media and digital platforms to educate about the risks of HPV, emphasising real-life stories and expert recommendations. Design public health messages that clearly communicate that HPV is not only the cause of cervical cancer but also of other malignant diseases, including those affecting the oropharynx, penis, anus and vulva.

Include children in discussions about their health in general, and specifically about HPV and the HPV vaccine, starting in the upper grades of primary school, with use of carefully crafted, scientifically approved interactive educational materials (e.g., animated videos and games), in line with the recommendations of the Croatian Society for School and University Medicine regarding vaccination of students against HPV from the fifth grade of primary school.

Given the importance of Štampar's postulate on the presence of physicians with patients, we strongly recommend **administering HPV vaccinations directly in educational institutions**. This approach facilitates vaccination for school medicine professionals, students and parents, it eliminates administrative barriers and supports educating young people about the importance of preventive healthcare. Additionally, direct communication between school medicine specialists and parents through e-Class Register or e-Citizens systems is recommended to improve the outcomes of preventive programmes in school-age children, including interventions for examination of children, screening and vaccination.

Connect stakeholders from the health sector, local government and the education sector by organising annual coordination meetings of local health institutions, local schools and local authorities, thus creating a synergistic strategy for acting and improving cooperation at the local level. Additionally, ensure funds for local governments to implement educational campaigns and periodic promotional vaccination actions for young people older than 18, in accordance with the HPV vaccination schedule for persons older than 15 (0-2-6 months).

Monitoring: Use advanced data analysis tools to monitor regions with the lowest vaccination and screening rates, enabling targeted interventions and encouraging continuous efforts to increase vaccination coverage at the local level.

Communication: Establish dialogue with representatives of local communities that have achieved high HPV vaccination rates in the target population. The aim is to identify effective methods and strategies that contributed to increased vaccination rates. Special emphasis should be placed on gathering experiences from parents and young people who have already been vaccinated. These testimonies can be crucial in shaping campaigns aimed at promoting awareness, encouraging vaccination and removing the stigma that HPV solely causes cancers which affect women.

Vaccination

Coverage: Set a national target for vaccination at 90% of girls and a significant percentage of boys vaccinated by the age of 15 by 2030.

Stakeholder involvement: Organise annual coordination meetings of local health institutions, local schools and local authorities to create a cohesive strategy and ensure the allocation of resources for vaccination actions.

Screening

Communication: Establish the implementation of the National Preventive Programme for early detection of cervical cancer at the national level, utilising multiple communication channels to ensure that every woman has access to regular healthcare and accurate information about protecting her health.

Innovation: Consider the introduction of self-sampling methods as an additional approach to involving women in the national screening programme. Clear instructions should be provided to ensure the quality and standard of self-collected samples. The decision to implement this approach should be considered particularly for women who have not responded to screening invitations three times in a row or who have difficulties with access to healthcare, for example due to the current lack of gynaecological teams in certain locations. It is important to carefully evaluate this option following a thorough analysis of the current situation and specific needs of the population, to ensure consistent sample quality and patient safety.

Recommendation for quality assurance: Implement quality standards at all screening locations, with special focus on the accuracy of HPV testing and cytological screening. Conduct regular reviews to maintain consistent levels of quality and safety for patients. Cooperate with clinical microbiologists and cytologists to ensure compliance with established standards and adherence to quality guidelines. It is important to emphasise continuous monitoring of implementation of the screening programme and quality assurance as key elements of the process.

Sources

1. Bruni L, Albero G, Rowley J, Alemany L, Arbyn M, Giuliano AR, et al. Global and regional estimates of genital human papillomavirus prevalence among men: a systematic review and meta-analysis. Lancet Glob Health. 2023 Sep;11(9):e1345–62.
2. Akhatova A, Azizan A, Atageldiyeva K, Ashimkhanova A, Marat A, Iztleuov Y, et al. Prophylactic Human Papillomavirus Vaccination: From the Origin to the Current State. Vaccines. 2022 Nov 11;10(11):1912.
3. Occa, Aurora et al. "Helping Children to Participate in Human Papillomavirus-Related Discussions: Mixed Methods Study of Multimedia Messages." JMIR formative research vol. 6,4 e28676. 11 Apr. 2022, doi:10.2196/28676
4. Canfell K. Towards the global elimination of cervical cancer. Papillomavirus Res. 2019 Dec;8:100170.
5. Díez-Domingo J, Sánchez-Alonso V, Villanueva RJ, Acedo L, Tuells J. Impact of a Gender-Neutral HPV Vaccination Program in Men Who Have Sex with Men (MSM). Int J Environ Res Public Health. 2021 Jan 22;18(3):963.
6. Ntanasis-Stathopoulos I, Kyriazoglou A, Liontos M, Gavriatopoulou M. Current trends in the management and prevention of human papillomavirus (HPV) infection.
7. Roman BR, Aragones A. Epidemiology and incidence of HPV-related cancers of the head and neck. J Surg Oncol. 2021 Nov;124(6):920–2.
8. Tim J Palmer, Kimberley Kavanagh, Kate Cuschieri, Ross Cameron, Catriona Graham, Allan Wilson, Kirsty Roy, Invasive cervical cancer incidence following bivalent human papillomavirus vaccination: a population-based observational study of age at immunization, dose, and deprivation, JNCI: Journal of the National Cancer Institute, 2024;, djad263, https://doi.org/10.1093/jnci/djad263
9. McIlwain WR, Sood AJ, Nguyen SA, Day TA. Initial Symptoms in Patients With HPV-Positive and HPV-Negative Oropharyngeal Cancer. JAMA Otolaryngol Neck Surg. 2014 May 1;140(5):441.
10. Rezolucija Europskog parlamenta o jačanju Europe u borbi protiv raka – European Parliament resolution of 16 February 2022 on strengthening Europe in the fight against cancer – towards a comprehensive and coordinated strategy, 2022, available at: https://www.europarl.europa.eu/doceo/document/TA-9-2022-0038_EN.html, accessed: 17.12.2023.
11. Europski plan za borbu protiv raka – Europe's Beating Cancer Plan, 2021, available at: https://health.ec.europa.eu/system/files/2022-02/eu_cancer-plan_en_0.pdf, accessed: 17.12.2023.
12. Nacionalni plan protiv raka 2020.-2030. – National Plan Against Cancer 2020–2030, available at: https://www.iccp-portal.org/system/files/plans/NPPR_program_HR_2020_17-01.pdf, accessed: 17.12.2023.
13. Global strategy to accelerate the elimination of cervical cancer as a public health problem, WHO, 2020., available at: https://www.who.int/publications/i/item/9789240014107, accessed: 17.12.2023.
14. Arbyn, M et al. "European Guidelines for Quality Assurance in Cervical Cancer Screening. Second edition--summary document." Annals of oncology : official journal of the European Society for Medical Oncology vol. 21,3 (2010): 448-458. doi:10.1093/annonc/mdp471
15. Arbyn, M et al. "European Guidelines for Quality Assurance in Cervical Cancer Screening. Second edition--summary document." Annals of oncology : official journal of the European Society for Medical Oncology vol. 21,3 (2010): 448-458. doi:10.1093/annonc/mdp471
16. Kurikulum međupredmetne teme Zdravlje za osnovne i srednje škole – Curriculum for the Cross-Curricular Topic of Health for Primary and Secondary Schools, available at: https://mzo.gov.hr/UserDocsImages/dokumenti/Publikacije/Medupredmetne/Kurikulum%20medupredmetne%20teme%20Zdravlje%20za%20osnovne%20i%20srednje%20skole.pdf, accessed: 17.12.2023.
17. Akcijski plan za provedbu Nacionalnog strateškog okvira protiv raka za razdoblje do 2025. godine – Action Plan for the Implementation of the National Strategic Framework against Cancer for the period up to 2025, available at: https://vlada.gov.hr/UserDocsImages//2016/Sjednice/2024/Sije%C4%8Danj/282%20sjednica%20VRH//282%20-%205%20Akcijski%20plan.docx, accessed: 01.03.2024.
18. Europska komisija, Prijedlog preporuke Vijeća o vrstama raka koje se mogu spriječiti cijepljenjem – European Commission, Proposal for a Council Recommendation on vaccine-preventable cancers, available at: https://health.ec.europa.eu/publications/proposal-council-recommendation-vaccine-preventable-cancers_en, accessed: 01.03.2024.
19. Chaturvedi AK, Engels EA, Pfeiffer RM, Hernandez BY, Xiao W, Kim E, Jiang B, Goodman MT, Sibug-Saber M, Cozen W, Liu L, Lynch CF, Wentzensen N, Jordan RC, Altekruse S, Anderson WF, Rosenberg PS, Gillison ML. Human papillomavirus and rising oropharyngeal cancer incidence in the United States. J Clin Oncol. 2011 Nov 10;29(32):4294-301. doi: 10.1200/JCO.2011.36.4596. Epub 2011 Oct 3. PMID: 21969503; PMCID: PMC3221528.

As the not-for-profit federation of member organisations working in cancer at a European level, the European Cancer Organisation convenes oncology professionals and patients to agree policy, advocate for positive change and speak up for the European cancer community.

Publication: September 2024

european cancer ORGANISATION

Rue de la Science 41
1040 Brussels, Belgium

+32 2 775 02 00

europeancancer.org

FOLLOW US:
@EuropeanCancer