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HPV vaccination coverage in the European Region

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Introduction. Human papillomavirus (HPV) is an established cause of cervical cancer and other HPV-related diseases. This study aims to analyze the variation in coverage by HPV vaccination programs, particularly within the European Region countries, and explore possible health outcomes.
Material and methods. A comprehensive literature review and analysis of epidemiological data were conducted, focusing on HPV vaccination coverage rates, the implementation of vaccination programs, and their outcomes across the EU/EEA. The study examined various vaccination models, including school-based and health center-based programs, to understand their effectiveness in achieving high vaccination coverage and the associated reduction in HPV-related disease burden.
Results. The study's analysis identified significant variations in HPV vaccination coverage across the EU/EEA. School-based vaccination programs, in particular, were found to be highly effective in reaching the target population, achieving coverage rates significantly higher than those observed in countries relying on health center-based or mixed-model vaccination strategies.
Conclusions. HPV vaccination programs have played a crucial role in reducing the burden of HPV-related diseases. These programs' success largely depends on achieving high vaccination coverage, which is more effectively realized through school-based vaccination strategies.

Key words: human papillomavirus, HPV vaccination, cancer prevention, cervical cancer, school-based intervention, coverage

Introduction

HPV is a human papillomavirus [1]. There are over 180 types of HPV, including low-risk types that cause benign genital warts (condylomas) and papillomas and high-risk types with a high oncogenic potential, which are responsible for precancerous lesions, cervical cancer, and other types of cancer. An HPV infection occurs sexually, most frequently shortly after the initiation of one's sexual activity. In the course of their lives, 80% of sexually active men and women have been or will be infected with

HPV [2, 3]. HPV infections are the direct cause of nearly 99.7% of cervical cancer cases. The virus is transmitted sexually. Virus transmission is also possible through contact with an infected person's mucous membranes or skin. According to the World Health Organization, cervical cancer is the 4th most common type of cancer worldwide. It is detected in over half a million women every year. It leads to the death of 250,000 women [4].

The introduction of HPV vaccinations has led to a reduction in the number of HPV 6/11/16/18 infections, genital warts, low-grade cervical cytological abnormalities, and histologically confirmed cervical abnormalities [5, 6]. The results of randomized trials demonstrated the high safety profile of HPV vaccines [7]. The most significant benefits are observed in the population of girls vaccinated before exposure to HPV in countries that have achieved high vaccination coverage rates (VCR) [5, 7]. HPV remains a significant source of cervical cancer morbidity and mortality worldwide. Therefore, implementing universal vaccination programs against HPV is vital for improving cancer prevention [5]. In 2018, WHO paid particular attention to cervical cancer and set a target of 90% HPV vaccination coverage of the population by 2030 [8].

According to the World Health Organization's global strategy, every country should achieve the 90–70–90 targets by 2030 to eliminate cervical cancer in the next century:

- 90% of girls fully vaccinated with the HPV vaccine before the age of 15,
- 70% of women after screening tests before the age of 35 (and again before the age of 45), and
- 90% of diagnosed women on treatment (those with the precancerous changes and those with an advanced course of disease).

WHO mathematical models show that implementing the abovementioned activities in the coming years may lead to a global decline of cervical cancer incidence by 42% by 2045 and 97% by 2120 [9].

The first country worldwide to introduce a national, universal HPV vaccination program was Australia. The program was launched in 2007, and the first population group to be vaccinated against HPV was girls. In 2013, boys were also vaccinated. In the European region, Great Britain was the first to launch a universal HPV vaccination program for girls in 2008 [10]. By 2019, almost all EU/EEA countries had introduced the HPV vaccination into their national vaccination programs. 30 out of 31 countries have universal vaccination programs for girls, and 11 also have catch-up vaccination programs dedicated to older age groups [11].

In most countries, universal HPV vaccination programs are fully financed from public funds. In a few countries, the patient covers a part of the costs (this concerns mainly catch-up vaccinations).

According to the current data (as of May 2023), 125 countries worldwide have universal vaccinations against HPV (data from the Our World in Data platform) [10, 12].

The study aimed to analyze data on vaccination in the population eligible for the HPV vaccination as part of free national vaccinations in individual European Union/European Economic Area countries.

Material and methods

The material consists of epidemiological data on vaccinations against human papillomavirus in girls and boys under universal preventive programs in individual countries. The data come from collective information on vaccination coverage in eligible populations across countries. A focused literature review was made using the websites of national ministries of health, the WHO database, and the Our World in Data database. The data were collected for the following aspects: vaccination rate in the population per country, date of launching the vaccination per country, and vaccination model, i.e., vaccinations in schools, health centers, pharmacies, or under a mixed model.

Results

Australia was the first country to introduce a universal HPV vaccination program, where girls were vaccinated in 2007 and boys in 2013.

Due to the HPV vaccine's excellent safety profile, efficacy, and population effectiveness, in 2017, the World Health Organization (WHO) published an updated position on HPV vaccinations with a recommendation on HPV vaccinations for persons aged 9–14 years (and, if funds are available, catch-up vaccinations for persons up to 18 years of age) in all countries of the world.

By 2019, almost all EU/EEA countries had introduced HPV vaccinations into the national universal vaccination programs. 30 out of 31 countries (except Poland) have universal vaccination programs for girls, and 11 have also implemented catch-up vaccination programs in older age groups. Universal immunization programs have been extended to the male population in 14 of 30 countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, Germany, Ireland, Italy, Netherlands, Norway, Sweden, United Kingdom), and many other countries plan to extend their programs shortly. In one country (Liechtenstein), catch-up vaccinations are also performed among older boys. In most countries, vaccinations are fully financed from public funds, and in a few countries, it is the patient

who covers a part of the costs (this concerns mainly catch-up vaccinations). Differences between countries are mostly related to the age of the target populations, which is 9–14 years for girls and boys, 10–26 years for girls, and 10–18 years for boys under the catch-up vaccination programs. Poland introduced the HPV vaccination into the national vaccination program in June 2023 as part of the National Public HPV Vaccination Program (tab. I).

The vaccination model in European countries is based on vaccinations in schools, health centers, pharmacies and a mixed model. Population vaccination models include vaccinations in schools. For example, in Belgium, vaccinations in children are scheduled automatically, and only if the guardian declares no consent the child is not vaccinated. Another model includes vaccinations in medical centers or other places, e.g., pharmacies. A mixed model includes vaccination both in health centers and schools (fig. 1).

Since 2014, the HPV vaccination has been introduced in schools in Hungary, where vaccination coverage is almost 80%. In Belgium, the vaccination rate is 90%. In Spain, a reimbursed HPV vaccination program for girls has been operating since 2018. Currently, the vaccination rate is 80%. Subject to reimbursement are vaccinations for girls and vaccinations for high-risk groups: persons with primary immune disorders, HIV carriers, and homosexual men. In Romania, the vaccination program was introduced relatively early, in 2008, but it was suspended and resumed many times, which resulted in poor vaccination rates. A mixed model is used in Romania, i.e., health centers and schools participate in the program.

In Poland, from June 1 to December 29, 2023, 152,000 teenagers aged 12 and 13 (63% girls and 37% boys) were vaccinated under the National Public HPV Vaccination Program, representing approximately 18.3% of the eligible population. The vaccinations are part of recommended protective measures, with vaccine purchases funded by the Ministry of Health starting from June 1, 2023, as per announcements made on February 23, 2023 (Official Gazette of the Ministry of Health, item 16) and September 29, 2023 (Official Gazette of the Ministry of Health, item 88). The Transparency Council of the Agency for Health Technology Assessment and Tariff System (AOTMiT) evaluated the effectiveness of HPV vaccines in preventing cervical cancer, according to which the two vaccines available in Poland —Cervarix, 0.5 ml dose (GlaxoSmithKline Biologicals S.A.) and Gardasil 9, 0.5 ml dose (Merck Sharp & Dohme B.V.)—are effective in preventing cervical cancer. There is no reliable evidence to suggest the clinical superiority of either vaccine in terms of clinically significant endpoints.

Discussion

The most common and dangerous disease caused by the HPV infection is cervical cancer. According to the WHO data, cervical cancer is the fourth most common cancer among women worldwide, and in 2020, it caused the death of over 324,000 women. [2] In Poland, cervical cancer incidence and mortality rates are 12,2/100,000 and 5,4/100,000, respectively, and the incidence of head and neck cancer is 1,27/100,000 (data from 2018). [14] While infection with HPV types 16 and 18 is associated with approximately 70% of cervical cancer cases, HPV infection is etiologically associated with the development of other diseases [15]. It is estimated that worldwide nine out of ten cases of anal cancer, seven out of ten cases of vaginal cancer, one out of two cases of penile cancer, and four out of ten cases of vulvar cancer are caused by the HPV infection [16, 17].

The estimated effectiveness of vaccinations at the population level has been confirmed for HPV infections, genital warts, and advanced precancerous conditions of the cervix. These changes appear relatively quickly after contact with the HPV (the incubation period for genital warts and precancerous conditions of the cervix ranges from a few to several months) [18, 19].

In 2015, a meta-analysis of 20 studies covering 140 million person-years in countries where >50% of girls were vaccinated was published. The results showed that the incidence of HPV infections types 16 and 18 was reduced by 68% (relative risk [RR]: 0.32 [95% CI: 0.19–0.52]). The risk of HPV infections type 31, 33, and 45 was also reduced (RR: 0.72 [95% CI: 0.54–0.96]), which suggests cross-protection. The incidence of genital warts in girls aged 13–19 decreased by 61% (RR: 0.39 [95% CI: 0.22–0.71]). Reduction in the incidence of genital warts was observed in men <20 years of age (RR: 0.66 [95% CI: 0.47–0.91]) and in women aged 20-39 (RR: 0.68 [95% CI: 0.51–0.89]), which indicates the development of population (herd) immunity [19]. These results have been confirmed in recent publications, constituting new evidence of the population effect of the HPV vaccination. The results of a meta-analysis conducted in 2019 by Drolet et al. indicated that after several years of widespread, routine vaccinations among girls aged 13–19 in developed countries, the incidence of HPV 16 and 18 decreased by 83%, and HPV 31, 33 and 45 fell by 54%. The incidence of anogenital warts among boys aged 15–19 decreased by 48% [5]. In Australia, a reduction in the frequency of carrying vaccine HPV types was observed in unvaccinated men [20, 21]. A reduction in the incidence of genital warts was also observed in Italy, Canada, Denmark, Israel, Spain, the United States and Sweden [22–28]. Reduction in the frequency of HPV infections was observed in population-based studies in men and young women in the United States and young women in the United Kingdom [29–31]. Another critical piece of evidence for the effectiveness of HPV vaccination in the prevention of cervical cancer several decades before the expected reduction in the incidence of the invasive form of cancer is the decrease in the incidence of cervical intraepithelial neoplasia that was observed in Australia, Denmark, Sweden, and the United States [32].

Implementing a structured HPV vaccination program is much more common in countries with a high vaccination rate. Importantly, in areas with high HPV vaccination rates, vaccinations took place mainly in schools, the HPV vaccine was always administered on-site, and the reminder communications were sent to children's parents. In areas with meager vaccination rates, the HPV vaccine was administered mainly in health centers or private doctors' offices. Access to HPV vaccinations can be facilitated by increasing the availability of on-site vaccines, sending reminders to parents, and administering vaccines in schools, which results in high vaccination coverage [33–35].

In Poland, the percentage of children vaccinated under the National Public HPV Vaccination Program should be compared with the number of vaccinations carried out as part of health policy programs, including those implemented by local government units. Only then can the total number of girls and boys vaccinated against HPV, both under the National Public HPV Vaccination Program and through health policy programs, be estimated. The estimate should also include children whose parents funded vaccinations privately. However, local government programs are not available in every city, especially in rural areas. Hence, the National Public HPV Vaccination Program increases the coverage of the eligible population for vaccination.

Among the factors contributing to the low vaccination rate are registration in the central system, which may pose a barrier for parents and providers alike, anti-vaccine propaganda, the presence of fake news related to vaccination, and anti-vaccine movements. Responding to these challenges includes accurate education, promotion, and intersectoral cooperation. The Polish Ministry of National Education website features a message regarding HPV vaccinations, and this information should be disseminated to schools. However, no other actions have been identified to date regarding promoting HPV vaccinations in educational facilities. The experience of countries where vaccinations are administered in schools suggests high effectiveness, as these countries report high HP vaccination takeup rates among children and adolescents. Children and adolescents spend a significant portion of their time in school. In contrast, contact with primary healthcare facilities is less frequent at 12 and 13, as health assessments are not commonly conducted at this age. An interesting initiative appears to be an SMS campaign developed based on experiences from COVID-19 vaccinations.

The literature review on interventions aimed at improving HPV vaccination coverage, which was conducted by Walling et al., stressed community-based interventions as effective in promoting and implementing HPV vaccinations. Community-based interventions, primarily vaccinations in schools, are often associated with high vaccination coverage since they increase access to vaccinations. For example, in Switzerland, where the practical implementation of vaccinations varied

depending on location, implementing a mixed vaccination model showed that the vaccination rate was higher in the areas where vaccinations were performed in schools. School-based vaccination programs have also been particularly effective in achieving high HPV vaccination rates in Australia [33–36].

Conclusions

The effectiveness of population-based HPV vaccination programs has been confirmed in many scientific studies. Monitoring of HPV vaccinations is crucial to ensure vaccination sustainability and, consequently, to ensure population effects related to the prevention of cervical cancer and other cancer sites. Countries that offer reimbursed national vaccinations in the school-based vaccination model achieve the highest vaccination rates. Countries that offer reimbursed national vaccinations in the medical centers-based vaccination model achieve significantly lower vaccination rates. A vaccination model based on primary schools should be considered to increase vaccination takeup within the public HPV vaccination program in Poland.

Article information and declarations

Author contributions

Mariola Borowska – conceptualization, data curation, writing – original draft preparation.
Paweł Koczkodaj – conceptualization, writing – review and editing.
Marta Mańczuk – conceptualization, formal analysis, supervision, writing – review and editing.

Data availability statement

Publicly available data. All sources are indicated in the manuscript.

Conflict of interest

None declared

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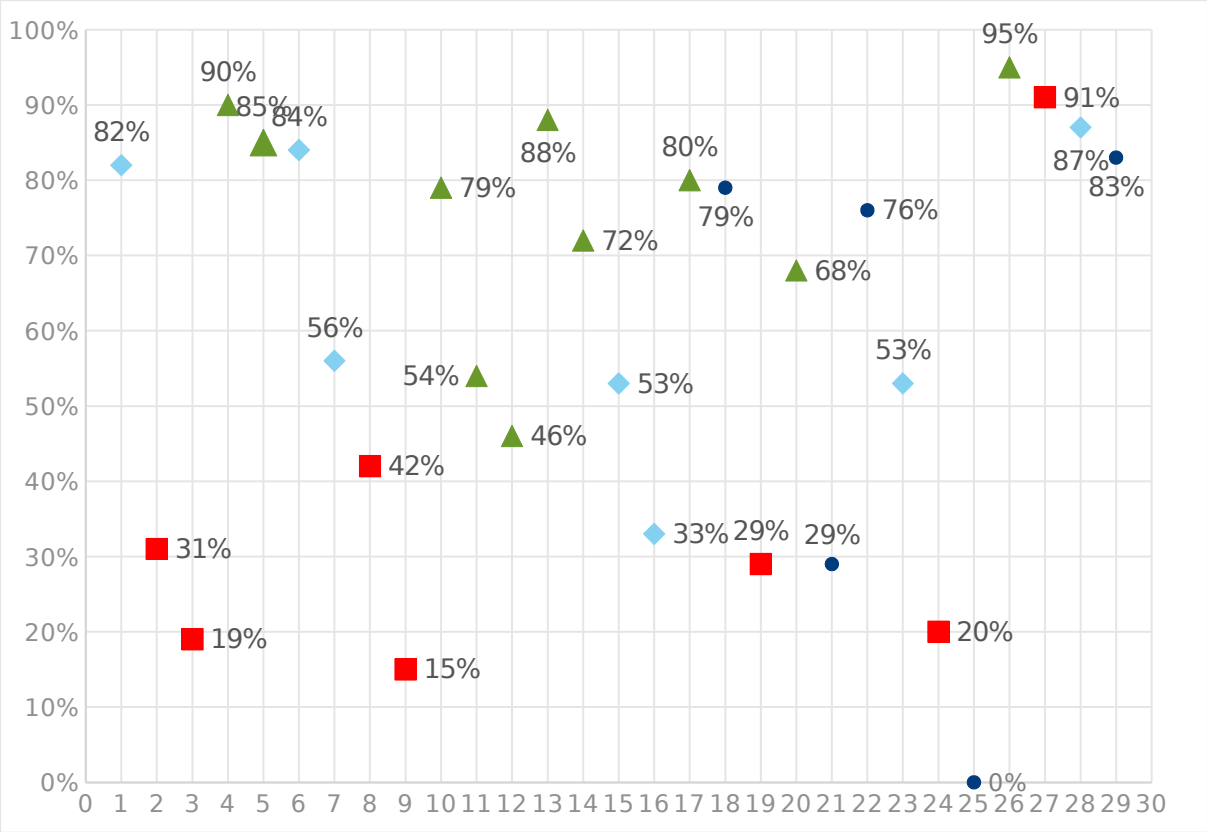
Table I. HPV vaccination coverage in the target populations in Europe

Country	**Implementation**	**Vaccination model**	**Vaccination coverage**
Austria	2014	mixed	53%
Belgium	2008	schools	90%
Bulgaria	2013	health centers	no data
Croatia	2016	schools	no data
Czech Republic	2012	health centers	29%
Denmark	2008	health centers	15%
Finland	2013	schools	68%
France	2007	health centers	19%
Greece	2008	health centers	no data
The Netherlands	2010	mixed	53%
Spain	2007	mixed	82%
Iceland	2010	schools	88%
Ireland	2010	schools	72%
Lichtenstein	no data	mixed	no data
Luxembourg	2008	health centers	no data
Lithuania	2016	no data	no data
Latvia	2010	mixed	33%
Macedonia	2009	schools	54%
Malta	2012	PHCs	79%
Monaco	2006	no data	no data
Germany	2007	health centers	31%
Norway	2009	schools	79%
Poland	2023	health centers	18%
Portugal	2008	mixed	84%
Russia	2014	no data	<30%
Romania	2008	mixed	no data

Slovakia	no data	schools	no data
Slovenia	2009	schools	46%
Switzerland	2008	mixed	56%
Sweden	2011	schools	80%
United Kingdom	2008	schools	85%
Hungary	2014	no data	76%
Italy	2008	health centers	42%

Based on data from the OECD iLibrary: https://www.oecd-ilibrary.org/social-issues-migration-health/eu-country-cancer-profiles_55f07000-en [13] and Our World in Data https://ourworldindata.org/grapher/human-papillomavirus-vaccine-immunization-schedule?tab=table [12]

Figure 1. HPV Vaccination coverage by the year of introduction of the organized vaccination program



Based on data from the OECD iLibrary: https://www.oecd-ilibrary.org/social-issues-migration-health/eu-country-cancer-profiles_55f07000-en [13] and Our World in Data https://ourworldindata.org/grapher/human-papillomavirus-vaccine-immunization-schedule?tab=table [12]