Family Medicine & Primary Care Review 2022; 24(2): 177–184, https://doi.org/10.5114/fmpcr.2022.116085

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ISSN 1734-3402, eISSN 2449-8580

Recommendations of the Polish Society of Gynaecologists and Obstetricians, Polish Paediatric Society, Polish Society of Family Medicine, Polish Society of Vaccinology, Polish Society of Oncological Gynaecology and Polish Society for Colposcopy and Cervical Pathophysiology on prophylactic vaccinations against infections with human papillomaviruses in Poland

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

Summary Several hundred million people are infected with genital genotypes of the human papillomavirus (HPV) annually in the world. The infections transmitted mainly through sexual routes are usually asymptomatic, but can lead to the development of cervical, vulvar, vaginal, anal, penile cancers, some head and neck cancers and genital warts (condylomas). The fraction of HPV-related cancers ranges from nearly 100% in the case of cervical cancer to several/over a dozen percent in the case of other cancers and diseases. There are no effective drugs against HPV, but prophylactic HPV vaccines are available free of charge in immunisation programmes in many countries around the world. In Poland, HPV vaccinations have so far been executed out of pocket or in free-of-charge, local-governmental prevention programs, but the vaccination coverage of the target population does not exceed 10%. Starting in November 2021, one of the vaccines has been available with a 50% reimbursement, and work is underway to reimburse the next ones. The National Oncology Strategy assumes the implementation of the HPV immunisation programmes and vaccination of 60% of the teen population by 2028. Three prophylactic HPV vaccines are registered. All of them are safe and their effectiveness in the prevention of diseases caused by vaccine genotypes is almost 100% provided that full post-vaccination immunity is obtained before contact with the virus. Girls aged 11–13 are the priority target cohort for HPV vaccination in Poland. The implementation of routine, free-of-charge HPV immunisation in the Preventive Immunisation Program (PIP) for all adolescents should be pursued. Persons over the age of 13 may also benefit from HPV vaccination and should be vaccinated according to product specifications. In addition to free access under the PIP, the key element for the success of the implementation of HPV vaccinations in Poland will be the education of medical personnel and parents of adolescents to be vaccinated.
Key words: alphapapillomavirus, uterine cervical neoplasms, vaccines.

Nowakowski A, Jach R, Szenborn L, Bidziński M, Jackowska T, Kotarski J, Mastalerz-Migas A, Nitsch-Osuch A, Pinkas J, Sawicki W, Sieroszewski P, Stukan M, WysockI J. Recommendations of the Polish Society of Gynaecologists and Obstetricians, Polish Paediatric Society, Polish Society of Family Medicine, Polish Society of Vaccinology, Polish Society of Oncological Gynaecology and Polish Society for Colposcopy and Cervical Pathophysiology on prophylactic vaccinations against infections with human papillomaviruses in Poland. *Fam Med Prim Care Rev* 2022; 24(2): 177–184, doi: https://doi.org/10.5114/fmpcr.2022.116085.

Human papillomaviruses as an aetiological factor of diseases

Human papillomavirus (HPV) infections are one of the most common genital organ infections in humans, mostly asymptomatic and spontaneously regressing. However, in a few to a dozen or so percent of those infected, lesions develop in various anatomical locations. It is estimated that HPV is responsible for the development of nearly 100% of precancerous lesions and cervical cancers, approximately 64–100% of precancerous conditions and vaginal cancers, 90% of anal cancers, 30% of penile cancers, 15–30% of vulvar cancers [1–3]. HPV also causes some cases of head and neck cancers (oral cavity – approx. 3.7%; nasopharynx – approx. 11%; base of tongue, tonsil – approx. 19.9%; unspecified part of the throat – approx. 25%) [2–3]. HPV is the aetiological factor of genital warts and recurrent laryngeal papillomatosis. So far, around 200 HPV genotypes have been classified, of which currently 14 (designated as: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68) are considered high risk genotypes of neoplastic lesions. The so-called low-risk genotypes 6 and 11 are responsible for the development of most genital warts and recurrent laryngeal papillomatosis. The infection frequency, carrier status, and distribution of HPV genotypes varies depending on the anatomical location of the infection, sex, age, and geographic region and population. About 70% of cervical cancers in the world are caused by HPV 16 and 18 [4] and genotype 16 dominates in all HPV-dependent neoplasms [1]. Based on studies of tissue material form Polish women, it is estimated that genotypes 16 and 18 are responsible for the development of approx. 83% of HPV-DNA positive cervical cancers, and approx. 85% of high-grade intraepithelial lesions (direct precancers) are aetiologically associated with HPV 16, 31, 33, 52, 45 and 58 [5]. It is estimated that 690 thousand cases of cancer globally in 2020 [6] and about three thousand in Poland in 2015 [2] were associated with HPV infections. Cervical cancer is by far the biggest problem for public health in Poland among the diseases aetiologically related to HPV due to the highest incidence, and the threat to health and life of young women. There are no official registers in Poland, but by extrapolating world data [7], the incidence of genital warts and recurrent laryngeal papillomatosis can be estimated at several dozen thousand and several hundred cases per year, respectively.

Prophylactic HPV vaccines

Currently, three vaccines are registered in most countries of the world and in Poland. All of them contain virus-like particles (VLPs) made of purified protein of the main viral capsid L1, produced by recombinant DNA technology, and adjuvants. Vaccines do not contain live viruses or their DNA material. Vaccines cannot cause infection, and the non-infectious VLPs included in vaccines are not replicative. The mechanism of action of HPV vaccines is based on induction a humoral immune response and the presence of neutralising antibodies and their activity at the site of infection. Antibody concentrations obtained after vaccination decrease with the time interval after vaccination and then remain at a stable levels, many times higher than those recorded after natural infection, for many years [8]. Prophylactic HPV vaccines do not have therapeutic properties, do not change the course of the ongoing infection or the clinical course of lesions caused by the virus. Therefore, to obtain the immunity of individual people and the maximum population effect, they should be given to individuals before contact with the virus, i.e., before sexual debut. From a meta-analysis of data covering 60 million vaccinated people over a period of 8 years of follow-up, the highest effectiveness in the prevention of high-grade precancerous conditions of the cervix and genital warts was demonstrated in the group of girls vaccinated up to 19 years of age (lower, but also significant in women up to 29 years of age) [9]. A brief summary of the approved vaccines is presented in Table 1.

Safety

Vaccination safety is a key aspect of ensuring an appropriate balance of benefits against the potential risks of this form of prophylaxis in populations of young, healthy people. All three HPV vaccines have undergone appropriate pre-approval studies, have passed regulatory agencies' positive assessment of their safety, and are subject to ongoing post-approval surveillance (bivalent – HPV2 and quadrivalent – HPV4 vaccines for over 15 years, and nine-valent – HPV9 for 9 years). Post-Vaccine Adverse Reactions (VARs) observed in clinical trials with all three vaccines were similar in profile and incidence. For HPV4, the most common local post-vaccination symptoms were pain (84%), erythema (< 25%), and swelling (25%) at the injection site, with pain more frequent than with placebo (saline – 49%; placebo

Table 1. Characteristics of registered prophylactic HPV vaccines (in order of registration in Europe)

Brand name	Gardasil (formerly Silgard)	Cervarix	Gardasil 9
Year of registration in Europe	2006	2007	2015
Composition of one dose (0.5 ml)	20 µg of L1 HPV 6 protein, 40 µg of L1 HPV 11 protein, 40 µg of L1 HPV 16 protein, 20 µg of L1 HPV 18 protein, adsorbed on amorphous aluminium hydroxyphosphate sulphate adjuvant (0.225 mg Al)	20 µg of L1 HPV 16 protein, 20 µg of L1 HPV 18 protein with AS04 adjuvant system	30 µg of L1 HPV 6 protein, 40 µg of L1 HPV 11 protein, 60 µg of L1 HPV 16 protein, 40 µg of L1 HPV 18 protein, 20 µg of L1 HPV 31 protein, 20 µg of L1 HPV 33 protein, 20 µg of L1 HPV 45 protein, 20 µg of L1 HPV 52 protein, 20 µg of L1 HPV 58 protein, adsorbed on amorphous aluminium hydroxyphosphate sulphate adjuvant (0.5 mg Al)
Indications for use	Prevention of precancerous lesions of the genital organs (cervix, vulva and vagina), precancerous lesions of the anus, cervical cancer and cancer of the anus, genital warts (genital warts)	Prophylaxis of precancerous lesions of the genital organs and anus (cervix, vulva, vagina and anus) as well as cervical and anal cancer	Active immunisation against precancerous lesions and cancer of the cervix, vulva, vagina and anus, genital warts (condylomas)
Dosage	Persons 9 through 13 years of age inclusive: Gardasil can be given according to a 2-dose schedule (0.5 ml at 0.6 months). If the second dose is given earlier than 6 months after the first dose, a third dose should always be given. Gardasil can also be given in another schedule – 3 doses (0.5 ml at 0, 2, 6 months). The second dose should be administered at least one month after the first dose and the third dose should be administered at least 3 months after the second dose. All three doses should be administered within 1 year. Individuals 14 years of age and older: Gardasil should be administered according to a 3-dose schedule (0.5 ml at 0, 2, 6 months). The second dose should be administered at least one month after the first dose and the third dose should be administered at least 3 months after the second dose. All three doses should be administered within 1 year	Adults and adolescents from 15 years of age: 3 doses (0.5 ml each) in months 0, 1 and 6; if flexibility in the vaccination schedule is required, the second dose may be administered between 1 and 2.5 months after the first dose and the third dose between 5 and 12 months after the first dose. Children and adolescents 9 to 14 years of age: 2 doses (0.5 ml each) – the second dose administered between 5 and 13 months after the first dose. If the second dose of vaccine is given less than 5 months after the first dose, a third dose of vaccine will be required. The need for a booster dose has not been established	Patients 9 to 14 years of age inclusive at the time of first dose: 2-dose schedule (0, 6–12 months). The second dose should be given between 5 and 13 months after the first dose. If the second dose of vaccine is administered more than 5 months after the first dose, a third dose should always be given. 3-dose regimen (0, 2, 6 months). The second dose should be given at least one month after the first dose and the third dose should be given at least 3 months after the second dose. All 3 doses should be given within 1 year. Patients 15 years of age and over at the time of first dose: 3-dose schedule (0, 2, 6 months). The second dose should be given at least one month after the first dose and the third dose should be given at least 3 months after the second dose. All 3 doses should be given within 1 year. The vaccine should be used according to official recommendations. It is recommended that patients who receive a first dose of Gardasil 9 complete the vaccination course with Gardasil 9. It has not been established whether a booster dose is needed
The route of administration	Intramuscular	Intramuscular	Intramuscular
Contraindications	Hypersensitivity to the active substance or to any of the excipients. Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of Gardasil should not receive further doses of Gardasil	Hypersensitivity to the active substance or to any of the excipients	Hypersensitivity to the active substances or to any of the excipients. Individuals who have developed hypersensitivity after previous administration of Gardasil 9 or Gardasil/Silgard should not receive Gardasil 9

containing aluminium – 75%). These symptoms occurred more frequently after the use of HPV2 and HPV9 [7]. Transient low-grade fever/fever is the only systemic adverse reaction that occurs more frequently (> 10%) in individuals vaccinated with HPV vaccines than in individuals vaccinated with placebo [7]. Common but rapidly reversing VARs after HPV vaccinations include headache and dizziness (> 10%), muscle and joint pain, abdominal pain, nausea and vomiting (frequency 1–10%). The HPV vaccines, as with other vaccines administered to adolescents, have also been associated with syncope, which is classified as a psychogenic needle-stick reaction. Anaphylaxis after HPV vaccinations occurs with a similar frequency similar to that which occurs after administration of other vaccines. Data on the safety of HPV vaccination have been collected in people from 9 years of age and are still collected and analysed, as in case of other preventive vaccines [10].

In post-registration reports, a cause-and-effect relationship was suggested between HPV vaccinations and the occurrence

of Guillain-Barre syndrome, complex regional pain syndrome (CRPS), postural orthostatic tachycardia syndrome (POTS), premature ovarian insufficiency (POI) or autoimmune diseases and others. Due to these reports and the related media controversy, HPV vaccines are among the most thoroughly examined and constantly monitored in terms of safety. So far, none of the suspicions has been confirmed in analyses carried out on large vaccinated populations [11–13]. However, they remain the subject of further observations and debates [14–16]. In the HPV4 safety analysis including data from clinical trials and databases, in the 9-year post-marketing period, only syncope and local skin reactions were associated with vaccinations [17]. Compared to HPV4, local VARs were more frequent after HPV9, but the incidence of serious VARs was the same [19]. Vaccination against HPV is not recommended in pregnant women. However, no differences in the incidence of complications during pregnancy were found in vaccinated and unvaccinated women during pregnancy [18–20].

Immunogenicity

The immunogenicity of HPV vaccines has been assessed in many clinical trials. Bridging studies of antibody levels formed the basis of vaccination registration in adolescents (in whom efficacy studies could not be conducted) and a 2-dose vaccination schedule (antibody titres not lower than after the 3-dose schedule) in young people [8]. The percentage of people with seroconversion after receiving the full vaccination course significantly exceeds 90%, and the achieved titres of neutralising antibodies are many times higher than those observed after natural infection [8]. The highest titres are recorded four weeks after the last dose, then antibody concentrations reach a plateau significantly exceeding those after natural infection [21]. Post-vaccination protection is predicted to have a duration of several dozen years [21]. The minimum protective level of antibodies against infection and the need and timing of a booster dose have not yet been established.

Effectiveness

The effectiveness of vaccines assessed in clinical trials depended on many factors, such as: current or past HPV infection, age and sex of the vaccinated person, end point (type, severity, anatomical location of the lesion caused by HPV infection), and the follow-up period after vaccination [22–25]. The highest, up to 100%, efficacy, was observed in the prevention of advanced precancerous lesions caused by vaccine HPV genotypes in people without indicators of current and previous infection [22, 26–27]. For HPV4, the efficacy against high-grade intraepithelial lesions of the cervix (CIN2+), vagina/vulva (VaIN2+/VIN2+) caused by vaccine types 6, 11, 16, 18 was assessed in a combined analysis of three phase II/III clinical trials at 98.2% (95% CI: 93.3–99.8) and 100% (95% CI: 82.6–100), respectively, in HPV-DNA and seronegative women for vaccine types [22]. In the cohort of women with no previous/current infection markers, the effectiveness of HPV2 in preventing HPV-16/18-dependent lesions of CIN3+ and CIN2+ was 100% (95% CI: 85.5–100) [23] and 89.8% (95% CI: 39.5–99.5) [24]. The effectiveness of HPV2 in preventing CIN3+ caused by all HPV genotypes (also not included in the vaccine) was 93.2% (95% CI: 78.9–98.7) [23] in previously uninfected women. The high effectiveness of HPV9 in the prevention of diseases caused by HPV 31, 33, 45, 52, 58 was demonstrated in comparative studies with HPV4 [18]. The effectiveness of HPV4 in the prevention of HPV-6/11/16/18-dependent lesions of the external genitalia in young men with no previous indicators of infection was estimated at 90.4% (95% CI: 69.2–98.1) [25] and the effectiveness in the prevention of advanced precancerous anal lesions reached 74.9% (95% CI: 8.8–95.4). The effectiveness of HPV2 in the prevention of HPV 16/18, HPV 31/45, HPV 31/33/45 infections in the oropharyngeal cavity reached 82.4% (95% CI: 47.3–94.1), 75.3% (95% CI: 12.7–93.0) and 69.9% (95% CI: 29.6–87.1) [28].

Population effects

The high effectiveness of HPV vaccines in clinical trials in reducing the incidence of HPV infections and their clinical manifestations has an impact on the reduction of the incidence of HPV-related infections and diseases, which has been demonstrated not only in models [29] but has been proved also in meta-analyses of population studies [9]. Recently published UK data show a reduction in the risk of invasive cervical cancer and CIN3 by 87% (95% CI: 72–94) and 97% (95% CI: 96–98) respectively in vaccinated girls aged 12–13 years [30]. A nearly 90% reduction in the incidence of cervical cancer has recently also been reported among Swedish girls vaccinated before the age of 17 [31]. In Denmark, after the implementation of the population-based, free-of-charge HPV vaccination programme, a significant decrease in the incidence of cervical cancer was noted, especially in the populations that received vaccines before the age of 16 [32]. The effectiveness of HPV4 in the prevention of genital warts was estimated at 74% (95% CI: 68–79) throughout the whole population of the region of Valencia [33]. Eight years after the introduction of population-based HPV vaccination in Australia, a reduction in the incidence of preterm labour (3.2% 95% CI: 1.1%–5.3%) and low birth weight newborns (9.8% 95% CI 8.2–11.4) was noticed, which may be associated with a reduction in the frequency of cervical excisional procedures in young women [34]. After the implementation of the population-based, free-of-charge HPV vaccination before the age of 16, the risk of developing high-grade intraepithelial neoplasia of the vagina and vulva was reduced by 85% and 78%, respectively, in an analysis of over 500,000 patients [35]. Demonstration of the effectiveness of HPV vaccines in reducing the incidence of less common HPV-dependent cancers such as head and neck, vulva and vagina, and other pathological lesions such as recurrent laryngeal papillomatosis, will require longer observations and large cohorts of subjects. So far, an almost 90% reduction in HPV 16/18/6/11 infections in the oral cavity has been demonstrated in vaccinated versus unvaccinated young Americans [36].

Vaccination against HPV in special cohorts and clinical situations

Immunodeficiency, e.g., in the course of HIV infections and the use of immunosuppressants, is the strongest known risk factor for the acquisition, maintenance and progression of HPV infections to lesions (precancerous conditions, neoplasms, papillary lesions) [37–38]. It therefore seems that immunocompetent individuals may benefit from HPV vaccination, although there are no results of large, prospective studies in this area. Although prophylactic vaccines have no therapeutic effect, there is a body of evidence showing a lower rate of recurrence of precancerous cervical lesions after treatment in HPV vaccinated women than in unvaccinated women [39–41]. The observations of some of the authors of this position show that Polish women diagnosed and treated due to among the three key goals cervical precancerous conditions are a group willing to undergo HPV vaccinations. These women very often ask their gynaecologists about the possibility of vaccinating their children. Partial reimbursement gives additional opportunities to make use of the vaccination potential in this group of patients.

Recommendations of other organisations and societies

Due to very favourable data from clinical trials regarding the immunogenicity, effectiveness and safety of HPV vaccinations and the registration of the first vaccine in 2006, starting from 2007, HPV vaccinations were recommended by influential societies and organisations, and they began to be implemented in immunisation programmes in a number of countries. So far,

Poland has not joined the group of nearly 90% of the countries classified by the World Bank as high income that have implemented HPV vaccination in PIPs [42]. One of the three key goals of the Global Strategy to Accelerate the Elimination of Cervical Cancer as a Public Health Problem announced by WHO in 2020 is to fully vaccinate 90% of the population of girls up to 15 years of age by year 2030 [42]. The key points of the previous WHO position from 2017 are as follows: 1) HPV vaccinations should be implemented in national immunisation programmes, 2) the prevention of cervical cancer is a priority, 3) HPV vaccinations should be carried out in girls prior to sexual initiation, 4) vaccination should be implemented as part of a coordinated strategy including, inter alia, education on the risk of HPV infections, training of medical personnel and information for women on screening tests, 5) the priority cohort for vaccination is girls between 9–14 years of age, 6) vaccination of secondary target groups (girls > 15 years of age and boys) it is recommended only if it is feasible, cost effective and does not limit the funding of priority cohort vaccinations and cervical cancer screening programmes [7]. From 2020 forward, the position of the European Centre for Disease Prevention and Control is devoted mainly to the vaccination of people with HIV, to boys and to the introduction of HPV9 [43]. Among the key conclusions, it points to: 1) the effectiveness of HPV9 in the prevention of infections and lesions related to HPV 31, 33, 45, 52 and 58 (high quality data) and HPV 6, 11, 16, 18 (indirect data, moderate quality) 2) no direct data in effectiveness of HPV2 in men (evidence of its high immunogenicity), 3) high dependence of cost-effectiveness on priorities and the local situation in a given country (if the priority is cervical cancer prevention, the most cost-effective strategy is to maximise the vaccination of girls; the vaccination of boys may improve effectiveness cost-effective with a low coverage of the cohorts of girls; universal vaccination of girls and boys is recommended if the goal is to prevent various consequences of HPV infections). The United States Advisory Committee on Immunisation Practices: 1) recommends routine immunisation of 11–12 year-olds and catch-up vaccinations for unvaccinated people up to 26 years of age, 2) points to minimal public health benefits of vaccinating people between 26 and 45 years of age and recommends taking combined (doctor-patient) decisions in this regard, as these individuals may benefit from vaccination in individual situations [44]. The National Oncological Strategy for 2020–2030 in Poland assumes the commencement of the vaccination process for girls and boys in 2021 and 2026, respectively, and vaccinating at least 60% of adolescents by 2028, and also points to the need to conduct an information campaign on the benefits of HPV vaccination [45]. HPV vaccines have the recommendation of the President of the Agency for Health Technology Assessment and Tariff System [46–47] and, according to the opinion of experts from 2020, they should constitute an integral part of the comprehensive prevention of cervical cancer in Poland [48].

Polish recommendations for vaccination against HPV

Previously published positions of Polish scientific societies on HPV vaccination are over 10 years old. They emphasised that prophylactic vaccinations should be a practice complementary to regular cytological screening [49]. The important role of paediatricians and family doctors in education and primary prevention of cervical cancer in Poland was also indicated [50].

Local government HPV vaccination programs in Poland and their experiences

Vaccinations against HPV in the years 2010–1017 were the most frequently implemented local government prevention programmes with a positive opinion from the Agency for Health Technology Assessment (currently the Agency for Health Technology Assessment and Tariff System). However, the overall vaccination coverage of the target female population was very low, ranging from just 1% to 1.5% between 2015 and 2017. The highest number of vaccinations in this period was carried out in the Dolnoslaskie, Pomorskie, Slaskie, Wielkopolskie and Mazowieckie voivodships (63% of all vaccinations in Poland). In 2017, HPV vaccines were reimbursed by 223 local governments, including 9 reimbursing also vaccines for boys. During the 10 years of the operation of local government programmes, approximately 180,000 girls were vaccinated. Immunisation coverage depended on the region of Poland – higher in the west than in the east of the country – on average about 55% of the eligible individuals [51]. In 12 editions of the Wroclaw HPV vaccination programme, in 2010–2021, an average of 75.2% of 13-year-old female students (n = 16,301) were vaccinated. The schoolgirls were vaccinated in district clinics. Every year, the implementation of the programme was accompanied by comprehensive educational activities aimed at parents, students of both sexes, teachers, doctors and nurses from vaccination centres. 28,632 parents (60% on average) and 33,949 students (70% on average) participated in educational meetings. In the first 5 years, the average vaccination coverage was 83% [52]. During the peak period of media anti-vaccination propaganda and the broadcast of the film 'Vaxxed' in the 2016/17 and 2017/18 editions of the programme, the percentage of vaccinated people fell to the critical level of 62%. Studies among parents, students and vaccinating nurses were executed. It has been shown that nurses participating in the program were not sufficiently aware of their role in building acceptance of immunisation. Among the determinants of doubts regarding vaccination against HPV among the inhabitants of Wroclaw, the fear of side effects of vaccinations and a lack of trust in the effectiveness of vaccination were identified. Contrary to the results of studies on doubts regarding HPV vaccination from other countries, the respondents from Wroclaw did not report any concerns related to the alleged promotion of promiscuity as a result of vaccination [53]. Changes in educational programs were introduced, which were extended with elements of training in the field of communication skills with the patient, and the monitoring of doubts concerning HPV vaccination was intensified. These changes resulted in a renewed increase in vaccination coverage to a satisfactory level of 70% [54]. Similar conclusions can be drawn from vaccination programmes in Europe and the USA. The highest vaccination rates in the target population were achieved through organised school vaccinations [55], combined with consistent medical recommendations and public education [56, 57].

Recommendations for Poland

1. Prophylactic HPV vaccinations should be an integral part of the comprehensive cervical cancer prevention in Poland. HPV vaccines enable the reduction of the incidence of other diseases aetiologically related to HPV infections.
2. The priority target group for HPV vaccination are girls aged 11–13 years.
3. As a next step, girls over 13 years of age and boys 11–13 years of age should be vaccinated.
4. We should strive for the fastest possible implementation of the free-of-charge HPV vaccinations of adolescents aged 11–13 years Preventive Immunisation Programme.
5. Population-based vaccinations against HPV should be ultimately implemented within the framework of the existing, proven, organisational solutions in the Preventive Immunisation Programme in order to cover the target cohorts as widely as possible.
6. The qualification for HPV vaccination does not differ from other vaccinations. According to the general recommendations, the only permanent, absolute contraindication to

further vaccination, including HPV, is an anaphylactic reaction that occurred after the previous dose of the vaccine or the administration of any of its components. Mild or moderate reactions following the administration of the previous dose of the vaccine, such as pain, redness and swelling at the injection site, slight or moderate fever after the previous dose of the vaccine, are not a contraindication for vaccination. There is no need to do a pregnancy test before administration. The use of hormonal contraceptives has no effect on the immune response. Temporary/relative contraindications include: moderate or severe acute illness, whether with or without fever, e.g. streptococcal angina, influenza, acute bronchitis or acute diarrhoea. Moreover, the exacerbation of the chronic disease process is a relatively temporary contraindication. In these cases, vaccination is postponed until the acute symptoms subside, and in chronic diseases until remission is achieved and the patient's condition is stabilised.

7. HPV vaccines can be administered concurrently or at any intervals with other vaccines, but in a different site – e.g., the opposite arm, or with a minimum distance of 2.5 cm from the site of the first vaccine injection. The safety of concurrent administration of HPV vaccines with pertussis, diphtheria, tetanus, inactivated polio vaccines, hepatitis A and B vaccines, Meningococcal, and COVID-19 has been tested and demonstrated. As part of the vaccination campaign of whole groups of adolescents, VARs may develop in the form of fainting, which in this case is triggered by pain or anxiety. People who pass out can fall and injure themselves if they don't sit or lie down. Giving patients a drink and a snack, ensuring the safety of the procedure, and administering the vaccine to the patient while the patient is sitting or or lying down has been shown to prevent syncope associated with the vaccination procedure. In addition, the patient should be observed for 30 minutes after vaccination. If a patient faints after vaccination, he or she should be monitored by a healthcare professional until consciousness is regained (usually within a few minutes) so that the need for any further medical treatment can be determined.
8. In order to achieve optimal population effects, if it is necessary to select one product for vaccination under the Preventive Immunisation Programme, the selection of the vaccine should be made on the basis of an independent pharmaco-economic analysis taking into account, inter alia, data from clinical trials in terms of efficacy against key endpoints, vaccine price achieved in a tender/auction and distribution of HPV genotypes in lesions in Poland.
9. People older than planned for the free-of-charge immunisation in the Preventive Immunisation Programme may also benefit from HPV immunisation and should be vaccinated in line with the prescribing information for all three approved vaccines.
10. HPV vaccination should be recommended to women diagnosed and treated for precancerous conditions of the cervix, as they may benefit from a lower risk of recurrence of lesions.
11. An extremely important element of the implementation of HPV vaccines are educational activities in target populations for vaccinations and their guardians, for medical personnel and the entire society, which should be conducted both centrally (media campaigns, etc.), regionally/locally (scientific and educational conferences, educational and information activities of producers, etc.) and individually (in clinics and offices) in order to provide maximum information about the benefits of HPV vaccination.

Frequently asked questions and answers on vaccination against HPV will be published on the website of the Polish Society of Family Medicine.

Source of funding: This work was funded from the authors' own resources.
Conflicts of interest: AN – advisory board, lectures, scientific report writing (GSK); RJ – grant (GSK), opinion on Cervarix for the Agency of Health Technology Assessment and Tariff in Poland; LS – lectures and execution of clinical trials (GSK, MSD); MB – no conflict of interest; TJ – no conflict of interest; JK – no conflict of interest; AMM – advisory board (MSD); AN-O – advisory board, lectures (GSK, MSD); JP – no conflict of interest; WS – no conflict of interest; PS – no conflict of interest; MS – lectures (MSD); JW – execution of clinical trials with HPV vaccines, advisory board (GSK, Pfizer, MSD).

Due to the interdisciplinary scope of these recommendations and in order to reach the largest possible audience, this manuscript was simultaneously submitted for publication in the following journals: *Ginekologia Polska, Ginekologia i Perinatologia Praktyczna, Lekarz POZ, Family Medicine & Primary Care Review, Onkologia po Dyplomie, Pediatria Polska, Przegląd Pediatryczny.*

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Tables: 1
Figures: 0
References: 57

Received: 29.04.2022
Reviewed: 03.05.2022
Accepted: 03.05.2022

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