

# The HPV prevention and control program in Poland: progress and the way forward

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## Abstract

This review assesses Poland's activities in preventing and managing human papillomavirus (HPV)–related diseases, summarizing information from the 2023 HPV Prevention and Control Board meeting. Progress in primary, secondary, and tertiary prevention identifies opportunities to strengthen control of cervical cancer. Poland's national HPV vaccination program, launched in June 2023, initially achieved suboptimal coverage. In contrast, regional initiatives such as the Wrocław immunization program, which has operated for over a decade, demonstrate highly relevant context-specific best practices, including the use of a “train the trainers” model to effectively share information among stakeholders and mitigate crisis. Improved vaccination rates require not only ease of access to vaccines, as the COVID-19 vaccination program has demonstrated, but also addressing parental concerns about vaccine safety and effectiveness. Moreover, innovative strategies—such as integration of adolescent vaccination with cervical screening among women 30 to 45 years old—may have the potential to increase uptake and accelerate elimination in the country. For secondary prevention, Poland is well placed to switch to HPV-based screening, having a centralized registry, validated tests, and standardized colposcopy. The results of a study of the “HPV testing In Polish POPulation” (HIPPO) cervical cancer screening program confirm the superiority of HPV testing over cytology; however, current opportunistic screening poses challenges concerning completeness and equity in data. Expanding organized screening programs and midwife-led services will increase access and help build confidence in public-sector health systems. Tertiary prevention is in line with updated European guidelines. In early-stage cervical cancer, there has been an increase in the use of less invasive surgical approaches, and immunotherapies, such as pembrolizumab, hold promise in locally advanced disease. Initial data suggest that HPV vaccination may help reduce the incidence of cervical intraepithelial neoplasia grade 2 or higher (CIN2+) after excisional treatments, but more data are needed. Poland's coordinated approach shows significant improvements while also highlighting the need for continued innovation, quality control, and public engagement to improve the prevention and treatment of HPV-related conditions.

**Keywords:** cervical cancer prevention programs, human papillomaviruses, Poland, HPV vaccination, HPV-based testing, HPV-related cancer

Received: 22 October 2024 | Returned for modification: 18 November 2024 | Accepted: 23 November 2024

## Introduction

The prevention of human papillomavirus (HPV) disease can be divided into three levels: primary, secondary, and tertiary prevention. Primary prevention primarily focuses on immunization against high-risk HPV types, which are responsible for all HPV-related cancers. HPV vaccines, available since 2006, induce an anti-L1 capsid protein antibody response conferring protection against HPV infections. Secondary and tertiary prevention emphasize early detection and treatment of precancerous lesions to prevent progression to advanced disease and, in some cases, cancer. Despite the efforts, the uptake of HPV vaccination and cervical cancer screening remains uneven. As of 2022, HPV vaccination coverage in the World Health Organisation (WHO) European Region stood at just 31.0%, whereas cervical cancer screening coverage in 2022 varied significantly, ranging from 78.8% in Sweden to as low as 4.5% in Romania (1). Poland, a central European country with a population of approximately 37 million, began efforts to prevent

cervical cancer in an organized cervical cancer screening program from 2006/2007 as recommended by the European Union (2). In 2022, coverage extended to only 10.9% of women 25 to 59 years old screened for cervical cancer within the last 3 years, which was one of the lowest in the WHO European Region (1). The country introduced HPV vaccination nationally starting on June 1st, 2023 (3). However, Poland's investigations of HPV-related disease started well before this, with significant early advancements by the Polish researcher Stefania Jabłońska, who initially postulated the association between HPV and skin cancer in 1966 (4). Her pioneering work preceded Harald zur Hausen's well-known hypothesis linking HPV infections and cervical cancer (5).

The HPV Prevention and Control Board is an independent, international, and multidisciplinary group of experts created in 2015 to provide evidence-based guidance and reflection on strategic, technical, and policy issues regarding the implementation and sustainability of HPV prevention and control programs. The board aims to increase and disseminate relevant information on

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HPV prevention and control to a broad array of stakeholders. It contributes to the control of HPV infection, prevention, and screening strategies of HPV-related cancers by holding two meetings every year: a technical meeting covering topics such as vaccine characteristics, vaccine safety, screening technologies and landscape, treatment strategies, the role of healthcare providers in vaccination programs, and dealing with anti-vaccine messages (6–9); and a national-level meeting covering an analysis of strengths, weaknesses, opportunities, and threats (SWOT) for the country or region (Table 1, 2) (10, 11).

This report covers the fifteenth meeting (held in November 2023), a national meeting discussing the HPV prevention landscape in Poland. The objectives of the meeting were to: 1) review healthcare system and immunization programs within the context of HPV-related disease prevention and control; 2) provide a summary of the epidemiology, burden of disease, and surveillance related to HPV and HPV-related cancers in Poland; 3) analyze the current landscape by identifying key issues and challenges related to HPV prevention and control efforts in Poland; 4) review local and international examples of best practices in HPV prevention and control; and 5) propose strategic directions for advancing HPV prevention and control in Poland.

### Organization of the healthcare system and cancer registries in Poland

Poland’s national health policy is formulated in the National Health Program, which was established in 1990. In its current form (2021–2025), the program is underpinned by five legal acts: the Act on Public Health, the Act on Preventing and Combating Infections and Infectious Diseases in Humans, the Act on Upbring-

ing Sobriety and Counteracting Alcoholism, the Act on Counteracting Drug Addiction, and the Act on Protection of Public Health Against the Effects of Tobacco Use. Therefore, preventive intervention is part of the National Health Program, which is carried out at three levels. At the national level, the program is formulated, implemented by a range of national institutions, and financed by responsible ministries. At the regional level (Poland is divided into sixteen voivodeships, or *województwa*), preventive actions include raising awareness of preventable public health concerns. At the local level (counties, or *powiaty*), prevention programs are carried out and financed by the budget of municipalities (*gminy*). In addition, municipalities can apply for funds from international sources, including European Union grants and/or donations from private individuals or entrepreneurs. Cervical cancer prevention is one of eight programs implemented by the Ministry of Health and financed by the National Health Fund. The program initially focused on secondary prevention through cervical cancer screening. However, in June 2023, an HPV vaccination program using the bivalent or nonavalent vaccine was introduced as a separate component of the National Immunization Plan, expanding the focus to include primary prevention.

All cancer cases are recorded in the Polish National Cancer Registry (<https://onkologia.org.pl>), which was established in 1952. The incidence of HPV-related cancers was determined based on data from the registry from 2000 to 2019. In 2019, Poland (with a population of approximately 29 million adults) recorded 4,418 HPV-attributable cancers in women, with crude incidence rates per 100,000 for cervical cancer at 19.8, oral cavity cancer (gums, floor of the mouth, palate, other parts of the mouth, other non-base parts of the mouth) at 6.68, and vulvar cancer at 3.90. In men, 1,623 cases were reported, with crude incidence rates per 100,000 for oral cav-

**Table 1** | Based on the presentations and discussions, a strengths, weaknesses, opportunities, and threats (SWOT) analysis of the Polish HPV vaccination program was developed.

	POSITIVE	NEGATIVE
INTERNAL	<p>Strengths</p> <ul style="list-style-type: none"> <li>• The Wrocław case study exemplifies the potential success and outcomes achievable through the vaccination program in Poland.</li> <li>• The programs benefit from a multidisciplinary approach, integrating various fields and expertise to enhance their effectiveness.</li> <li>• HPV vaccination is free of charge and targets boys and girls 9 to 14 years old.</li> <li>• The program uses a nationwide information campaign (press, radio, television, internet, social media).</li> <li>• A central system for purchasing vaccines ensures their consistency and reliability.</li> </ul>	<p>Weaknesses</p> <ul style="list-style-type: none"> <li>• The national system for vaccine administration (e.g., mandatory appointments and registration by healthcare providers) is time intensive, potentially deterring participation.</li> <li>• Ambiguity in the recommendations targeting primary and catch-up populations may result in confusion among the public and healthcare providers.</li> <li>• Training for healthcare professionals is costly and demands significant resources.</li> <li>• A limited number of vaccination points and confusion about the availability of two vaccines (bivalent and nonavalent) in the program reduce trust and accessibility.</li> <li>• Propaganda surrounding vaccine options undermines public trust, causing confusion about vaccine selection and its justification.</li> <li>• The lack of a comprehensive and consistent communication strategy among healthcare professionals and policymakers can weaken public trust and confidence in the vaccination program, making it crucial to address this issue.</li> </ul>
EXTERNAL	<p>Opportunities</p> <ul style="list-style-type: none"> <li>• Engage with young individuals to understand their motivations and barriers to vaccination, and reach out to their parents and caretakers as stakeholders.</li> <li>• The global elimination strategy has heightened international awareness and garnered support for implementing the vaccination program.</li> <li>• Best practices and insights from other countries can be leveraged within the Polish program.</li> <li>• Developing tailored interventions based on insights from target groups (healthcare professionals, vaccinees, parents, and social influencers) can effectively promote vaccine uptake.</li> </ul>	<p>Threats</p> <ul style="list-style-type: none"> <li>• Misinformation can lead to increased vaccine hesitancy among the population.</li> <li>• Parental concerns about the safety of the vaccine and the perception that the vaccine is still new, despite 15 years of evidence supporting its safety and effectiveness, pose significant barriers.</li> </ul>

HPV = human papillomaviruses.

ity cancer at 16.30, laryngeal cancer at 14.80, and oropharyngeal cancer (base of the tongue, tonsils, oropharynx) at 6.87. In men, laryngeal cancer incidence (unrelated to HPV) showed a decreasing trend, whereas for cancers of the oropharynx and the oral cavity (related to HPV) the trend increased. Furthermore, a slight upward trend in penile cancer incidence has also been observed. In women, the prevalence of cervical lesions is slightly decreasing, with cervical cancer in situ partly replacing invasive disease, suggesting an impact of screening because women are being diagnosed at earlier stages. A slight increase in cancers of the oropharynx and oral cavity can be observed. Although the cervical cancer incidence in Poland (10.0 per 100,000) has fallen below levels in other European countries (e.g., Norway: 13.0 per 100,000; Czech Republic: 12.0 per 100,000), the same is not true for mortality (Poland: 7.5 per 100,000; Norway: 3.0 per 100,000; Czech Republic: 4.0 per 100,000), potentially because of treatment inequality (barriers in women's access to healthcare and variability in quality and performance of treatment) and underreporting. The cervical cancer survival rate has been slightly improving over time (12), but additional efforts will be necessary to improve survival rates further. In vulvar cancer, the contribution of HPV could have been overestimated. Combined HPV DNA and p16 inhibitor of kinase 4a testing may provide a better estimate of the HPV-attributable fraction, which in Europe may be around 20% (13, 14). In Poland, the mortality-to-incidence ratio (the proportion of women diagnosed with a specific disease that die from it within a given time frame) for vaginal cancer is significantly higher compared to neighboring countries (12, 15). This may, in part, be due to misclassification of the early lesions, which are easier to treat. Ten percent of women with vaginal intraepithelial neoplasia will progress to invasive cancer (16). HIV infection and persistent HPV infection after treat-

ment are both independent risk factors for progression (17).

## Primary prevention: the HPV vaccination program in Poland

### Introduction plan, delivery strategy, communication plan, and reporting system

The Polish National Immunization Program was established in 1960. Although it mostly focuses on infants, the program includes HPV vaccination of adolescents and influenza vaccination of risk groups. Universal vaccination against HPV started on June 1st, 2023. Although a number of vaccines are mandatory (Bacille Calmette-Guérin, hepatitis B, rotavirus, diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* type B, pneumococcus, measles, mumps, rubella) (18), HPV vaccination is recommended and free of charge for gender-neutral vaccination of children 11 to 14 years old, based on a two-dose schedule, with the second dose between 6 and 12 months after the first dose. Vaccinations are administered at all primary healthcare vaccination facilities with an option to carry out vaccinations at schools, provided there is agreement and cooperation between the school and local healthcare staff. An electronic vaccination card is used to confirm eligibility and to record the vaccination. The program launch was accompanied by a nationwide information campaign (press, radio, television, internet, and social media). Currently, the National Research Institute at the National Institute of Public Health–National Institute of Hygiene conducts education and awareness activities on vaccination against HPV (<https://szkolenia.pzh.gov.pl>). The introduction date was carefully chosen to coincide with Mother's Day (May 26th, launch of the nationwide communication campaign) and Chil-

**Table 2** | Based on the presentations and discussions, a strengths, weaknesses, opportunities, and threats (SWOT) analysis of the cervical cancer screening program in Poland was developed.

	POSITIVE	NEGATIVE
INTERNAL	<b>Strengths</b> <ul style="list-style-type: none"> <li>Robust IT infrastructure, including a country-wide central screening registry.</li> <li>Advancing digital healthcare (e-prescription, referral, and vaccination cards)</li> <li>Multiple well-equipped testing laboratories with molecular testing support.</li> <li>Availability of validated HPV tests.</li> <li>Local pilot data (HIPPO study) supporting HPV-based screening over cytology.</li> <li>Current efforts to standardize colposcopy and screening among gynecologists.</li> <li>Midwives have the capacity to play a greater role in screening, especially for hard-to-reach populations.</li> </ul>	<b>Weaknesses</b> <ul style="list-style-type: none"> <li>Suboptimal program organization and fragmentation of the medical system.</li> <li>Lack of a registry for HPV lesions detected in private opportunistic screening events.</li> <li>Preventive care is deprioritized (low funding).</li> <li>GDPR limits patient data access.</li> <li>Inadequate use of performance and quality control indicators.</li> <li>Non-standardized reimbursement procedures.</li> <li>HCPs' inconsistency in screening and treatment guidelines.</li> <li>Lack of local epidemiological data on HPV-attributable cancers.</li> </ul>
	<b>Opportunities</b> <ul style="list-style-type: none"> <li>High health literacy in the population.</li> <li>High capacity of trained gynecologists (c. 6,000) for screening and treatment services.</li> <li>Good infrastructure (roads) for accessing rural areas.</li> <li>Leveraging IT platforms from the COVID-19 pandemic.</li> <li>Stakeholder interest and potential for organized screening with comprehensive, reorganized, and standardized reimbursement.</li> <li>Tax incentive for users participating in screening.</li> <li>Implementation of structured local screening guidelines.</li> <li>Potential to train midwives for screening services.</li> </ul>	<b>Threats</b> <ul style="list-style-type: none"> <li>Lobbying from medical societies for non-optimal practices (e.g., co-testing and private-based opportunistic screening).</li> <li>Users' preference for private sector opportunistic-based screening.</li> <li>Support for inefficient (non-cost-effective) models.</li> <li>Hesitancy to reveal performance indicators per ESGO guidelines.</li> <li>Social media disinformation.</li> <li>Need for optimal secondary screening for the non-vaccinated cohort (over age 40).</li> <li>Use of pre-/probiotics to treat HPV infection without an evidence base.</li> </ul>
EXTERNAL		

ESGO = European Society for Gynaecological Oncology, GDPR = General Data Protection Regulation, HPV = human papillomaviruses, HIPPO = "HPV testing In Polish POulation" cervical screening program, HCPs = healthcare professionals, IT = information technology.

dren's Day (June 1st, start of the HPV vaccination program).

A government-led central system is used for purchasing and distributing vaccines to vaccination points. It has made 100,000 doses of bivalent and nonavalent vaccines available for vaccination, with a 10-times greater preference for the nonavalent vaccine. Since the introduction of the program on June 1st, 2023, covering individuals born in 2010, 2011, 2012, and 2013, an overall vaccination uptake of 16.70% has been recorded, with girls accounting for 62.97% of the vaccinations and boys for 37.03%. In the initial phase of the program, interest was higher, with 44,000 vaccinations recorded in June 2023, although the number decreased to 9,000 by November 2023. In light of these developments, the Ministry of Health has issued updated recommendations for the HPV vaccination program, effective as of September 1, 2024. The program has been extended to include individuals 9 to 14 years old, encompassing both girls and boys. In addition, all primary healthcare clinics authorized to conduct vaccinations may now also offer HPV vaccinations at primary schools by scheduling field trips as part of the program's expansion.

### Lessons learned from the Wrocław HPV vaccination program

In the 13 years preceding the national HPV vaccination program (2010–2023), a local program operated in Wrocław, with vaccinations being promoted as part of a healthy lifestyle campaign. The program offered annual training for healthcare professionals, teachers, and vaccinators by HPV and vaccination experts. Healthcare professionals and teachers educated parents during school meetings and children during classes using presentations, movies, and games. Free HPV vaccines were offered at all general practitioners' offices, which were equipped with educational materials targeting children and parents. The program achieved a median vaccination coverage of 72% of the target population (13-year-old girls from 2010 onward and boys starting in 2020) with at least one HPV vaccine dose, with a total cost of the program between 2010 and 2023 of €2 million. Simultaneously, the campaign also promoted cervical cancer screening for female caretakers.

Vaccination coverage data were continuously tracked at the Health Department of the Wrocław City Office and analyzed annually. Initial vaccine coverage exceeded 80%, but in 2015 a decline to approximately 60% was observed. To learn from the program, participants, parents, children, and vaccinators were interviewed. Several factors were found to influence vaccine acceptance positively, including education offered within the program, offering vaccinations for free, and experience with earlier vaccinations (19). Barriers to vaccination were fear of side effects and lack of trust in vaccination effectiveness. Many nurses underestimated the importance of their role in building vaccination acceptance, and 7.1% felt uncertain about administering the vaccination. Finally, if unvaccinated children had the chance to decide for themselves, nearly 50% would choose to be vaccinated (19).

A literature review of effective strategies for increasing HPV vaccination uptake, along with local study results, was used by the program supervisors to create a tailored intervention plan aimed at rebuilding vaccination coverage. The information gathered led to the following actions: highlighting vaccine safety, highlighting vaccine effectiveness, providing information on how to handle (perceived) adverse reactions, providing up-to-date online information with a frequently-asked-questions (FAQ) section, targeting vaccinators/nurses and emphasizing the importance of their role in parental vaccine decision making, addressing hesi-

tance and fear, and training the motivational style of conveying messages to parents and children. An increase in vaccine coverage to approximately 70% has been observed since these interventions were implemented, despite the pandemic's negative impact on vaccination efforts (20).

Vaccine hesitancy, identified by the WHO as a top global health threat (21), is driven by distrust in vaccines and authorities (22). Europe has the lowest vaccine confidence, particularly in France (21). Although trust in healthcare providers promotes vaccination (23), skepticism toward scientific experts and reliance on alternative information sources such as the internet can spread anti-vaccination messages (24). Healthcare providers' lack of vaccine confidence further undermines uptake (25, 26). In Poland, barriers to vaccination are parental concerns about the vaccine's safety and the fact that the vaccine is still considered new, although 15 years of experience have shown its safety and effectiveness. Other factors are the limited number of vaccination points and confusion about the availability of two vaccines in the program, which reduces trust in both vaccines. Finally, the limited age group as a target for vaccination is also perceived as a barrier. To tackle the latter, the bivalent vaccine has been made free of charge for all between 9 and 18 years old.

A key issue raised was the challenge of rebuilding public confidence following crises in HPV vaccination programs, a scenario that many European countries have faced. A central concern is how to address these communication gaps, particularly when health literacy may be a problem, because it varies significantly among the population. How can the public be informed at a level that is understood? The challenge lies in the fact that HPV relates to sexual health, making it a sensitive topic when discussing it with young people and their parents. Focusing the discussion on future sexual health rather than current concerns, and emphasizing cancer prevention, were identified as opportunities to facilitate the conversation. The role of healthcare professionals (HCPs) in the decision-making process was also identified as key. However, this can be an opportunity as well as a barrier. Therefore, a special communication program focused on HCPs is necessary. Moreover, for HPV, the range of HCPs involved is much broader than for other vaccines, which must be kept in mind to tailor the communication. A single individual will never have the same impact as a joint response, and so it is essential to get everyone on the same page, communicating with one voice. Communication will not solve the problem of low coverage if the program is not delivered in the easiest accessible way.

### Secondary prevention: cervical cancer screening in Poland

#### Toward HPV-based cervical screening in Poland

A cervical screening program operated from 2006/2007, targeting women between 25 and 64 years old, once every 3 years. In 2015, invitations were discontinued due to a lack of effectiveness (its implementation has not influenced the burden of cervical cancer in the country), as determined by the Ministry of Health (27). Approximately 3,000,000 cytologies are performed annually; 15% to 30% (depending on the year) are part of the program, with a decreasing trend that reached 11% in 2024, whereas 70% are opportunistic smears. Reimbursement within the program is lower than for opportunistic screening, and the procedures are more time consuming due to necessary data registration. At the same time, there is no central registry for opportunistic tests. Moreover, women have

more confidence in private gynecological care (by peer recommendation) than in reimbursed care in the screening program (28).

Although this number of cytological smears would be sufficient to cover the entire target population at the appropriate interval, 40% to 50% of the target population is not screened at all, and the highest reported screening coverage was only 26%. Nevertheless, in a population-based census survey, more than 70% of women 30 to 59 years old in 2019 reported having participated in cervical cancer screening events within the preceding 3 years (29), with cervical cancer cases being most frequently found among the remaining 30% of under-screened women. A central registry integrating the screening databases is the first necessary step to assess whether the WHO's 70% screening goal can be reached. In the Polish setting, considerations of centralizing this registry between private and public screening events are vital to evaluate actual coverage. A roadmap was published to decrease the burden of cervical cancer in Poland through primary and secondary prevention (30). This included piloting HPV-based screening in an organized setting: the "HPV testing In Polish POPulation" (HIPPO) cervical cancer screening program (31). Poland is well positioned for such a transition due to multiple well-equipped testing laboratories with molecular testing support as well as the availability of validated HPV tests. Preliminary data show that the cervical intraepithelial neoplasia grade 2 or higher (CIN2+) detection rate is higher in the intervention arm, regardless of intention-to-treat or per-protocol analysis (detection rate ratios above 1, with a 95% confidence interval excluding 1). Based on these results, HPV-based screening efforts are in progress to implement HPV-based screening nationwide in the coming months. Complete protocols for screening, triage, treatment, and follow-up have recently been published (32). The aim is to provide broad access to screening, including the possibility of offering vaginal clinician-collected samples or self-sampling. Furthermore, midwives, with their established presence in communities and wide availability in the country, are well positioned to assume a more significant role in screening efforts. Self-sampling is not likely to replace clinician-collected cervical smears, but it may be a good strategy to include the hard-to-reach population. Acceptance and quality assurance need to be further investigated before considering broad implementation of self-sampling because each country's population has different dynamics in the barriers and enablers for women seeking care.

### **Standardization of procedures in cervical cancer screening and colposcopy**

In response to the WHO call for action in 2020, the Cervical Cancer Screening Continuous Quality Improvement Project (also known as the Colposcopy 2020 Project) was set up. This is a comprehensive project for standardizing diagnostic and therapeutic procedures in the secondary and tertiary prevention of cervical cancer screening in Poland, introducing new screening paradigms. The suggested screening algorithm is based on US guidelines, but it is also applicable to the Polish situation because patients with similar test results and screening history combinations have a largely similar CIN3+ risk, regardless of their geographic location, race, ethnicity, or socioeconomic status (33). Loss to follow-up should be minimized by the active capture of women with positive screening results by regional colposcopy clinics. The aim of the project is to standardize the pre-colposcopy stage (pre-colposcopic procedures, including liquid-based cytology, HPV-based screening test selection, and triage test selection), the colposcopy stage

(standardized colposcopy and expedited treatment), and the post-colposcopy stage (excisional or ablative treatment, active observation, and follow-up) (34–38). Starting in 2025, certification will be mandatory for colposcopists. Certification courses will be offered to cytologists and colposcopists free of charge. Recertification will be required every 2 years for physicians working in the screening program. Those that fail the test must complete documented training and retake the test in the next session. Failing recertification twice will result in temporary exclusion from the program until the test is passed. The test has been voluntary since 2020, and improvements in average and top scores have been observed. Proposed key performance indicators for colposcopy clinics include the following benchmarks: documentation of the type of transformation zone in 100% of the cases; colposcopic examination prior to treatment for abnormal cervical cytology in 100% of the cases; definitive histology of CIN2+ in excisional treatments and conizations in at least 85% of the cases; and detection of clear margins in the excisional treatment biopsies in at least 80% of the cases. In addition, each colposcopist should perform a minimum of 50 colposcopies per year for low-grade or minor abnormality and at least 50 colposcopies per year for high-grade or major abnormality.

Another project is the HPV Cytologist Academy, an educational project with certification in gynecological cytopathology for Polish cytotechnologists. The course offers various modules: basics in gynecological cytopathology, liquid-based cytology as a triage test in HPV-related strategy, and dual staining as a triage test in HPV-related strategy.

Implementing a comprehensive cervical cancer prevention plan should be based on several key elements. First, situational awareness and true access for all are essential. Next, there should be centralized databases with continuous updates on key performance indicators. Successful invitations to (potential) participants are crucial, as are population-relevant results. These results include finding cancers in early clinical stages, and reduction in disease risk morbidity and mortality. Short-term solutions proposed to improve prevention include modification of incentives in favor of prophylactic procedures, with rewards for primary and secondary HCP for the provision of preventive services; information technology implementation, from registration to personalized invitations and feedback; increased access, also in remote areas; benchmarking of facilities; and publication of achievement levels of the prevention programs.

Several well-equipped laboratories with the capacity to perform molecular (HPV-based) testing are present in Poland. When deciding which HPV test is best suited for clinical, epidemiological, or research purposes, various parameters should be considered. The two most important factors are the set of targeted HPV genotypes and the level of analytical sensitivity. For clinical practice, the HPV test employed should be validated for clinical use, all HPV infections that are associated with or will develop into high-grade CIN should be detected, and they should be differentiated from transient HPV infections. In other words, an HPV test should aim for high analytical specificity, high clinical sensitivity, and high clinical specificity. An optimal balance between clinical sensitivity and clinical specificity for CIN2+ aims to minimize follow-up procedures for high-risk HPV-positive women with transient high risk-HPV infections and/or without cervical lesions. In 2020, 254 distinct commercial HPV assays, with 425 variants, were on the global market. Of those, only about 10% are clinically validated, according to the Meijer guidelines (39, 40). In the context of managing HPV-related diseases, particularly HPV infections,

it is essential to consider the role of the vaginal microbiome and the potential therapeutic approaches being recommended. This is particularly relevant in Poland, where there appears to be an increasing push from private sector interests and private gynecologists to recommend non-validated techniques. Pharmaceutical companies are actively marketing pre- and probiotic agents to Polish healthcare workers as potential treatments for HPV infections, despite limited evidence supporting their use. The female reproductive tract has a specific microbiome, mainly dominated by *Lactobacillus*. Disruption of the microbiome may play a role in vulnerability to HPV infection. Next-generation sequencing (NGS) has made it possible to examine the microbiome in detail. This facilitates investigating the microbiome before and after treatment with pre- and probiotics to determine whether and how they work. Previous studies (without NGS) do not provide sufficient evidence for the use of pre- and probiotics to “treat” HPV infections (41). Generally, the study sizes have been too small, and hardly any placebo-controlled studies have been published. HPV-based screening will lead to an HPV-positive result without lesions in a proportion of women. An HPV-positive result leads to anxiety (42, 43), and these women may be unwilling to wait for the infection to regress on its own. They may be vulnerable to using pre- and probiotic products without any evidence base. Appropriate studies need to be performed to investigate the effectiveness of these products and to define the mode of action if a product is effective.

Experiences from other countries, such as Slovenia’s successful transition from opportunistic to organized screening, offer valuable insights for improving cervical cancer screening in Poland. This was achieved by certifying cytology laboratories and establishing a standardized reimbursement system for both private and public providers. As a result, 3-year screening coverage reached 73%, and 5-year coverage surpassed 80%, leading to a 55% reduction in cervical cancer incidence without increasing costs. In Slovenia, women that have not had a smear in 3 years receive active invitations, and most other women are screened through their gynecologists, fostering trust between patients and providers. The Slovenian experience underscores the importance of a comprehensive and well-structured screening program. Key components such as triage, colposcopy, histology, and treatment must be integrated and routinely certified to ensure high-quality outcomes. Applying similar principles in Poland could enhance program effectiveness and participation rates, especially by building trust and implementing active invitation systems. The meeting also highlighted the importance of addressing disparities in access to screening, particularly in rural areas and among socio-economically disadvantaged groups. These challenges are relevant to Poland and call for innovative solutions such as nurse-led outreach initiatives or mobile screening services. By adapting these approaches, Poland could improve coverage and reduce inequalities in its cervical cancer screening efforts.

The examples shared at the meeting demonstrate how tailored, well-organized screening programs can lead to significant public health improvements, offering valuable direction for enhancing cervical cancer prevention in Poland.

## Tertiary prevention: treatment of HPV-related cancers

### Treatment of gynecological cancers

European guidelines for the treatment of cervical cancer patients have recently been updated (44). In the treatment of cervical pre-

cancer, there is a tradeoff between the risk of treatment failure and the risk of preterm birth after treatment. Therefore, a careful personalized approach is necessary based on age and reproductive plans (45). The impact of HPV vaccination after excisional treatment of CIN2+ has been investigated in clinical trials and observational studies (46). HPV vaccination significantly reduced the risk of CIN2+ recurrence. However, when restricted to observational studies with the least risk of bias, although present, the effect of HPV vaccination was no longer statistically significant. Large, correctly designed randomized placebo-controlled trials are needed to further understand the association of HPV vaccination and CIN recurrence (46).

A large randomized phase III trial showed that simple hysterectomy is non-inferior to radical hysterectomy when used in women with low-risk cervical cancer; that is, stages IA2 and IB1 with stromal invasion below 10 mm (47). In locally advanced cervical cancer (IB2–IIB), the use of pembrolizumab in combination with chemoradiotherapy resulted in limited higher overall survival and 10% higher progression-free survival at 24 months (48), with a higher discontinuation due to immune-mediated adverse events (2.3% versus 0.4%). For recurrent or metastatic disease, tisotumab had improved overall survival and progression-free survival compared to investigator’s choice chemotherapy (49, 50). Overall, surgical treatment of early forms of cervical cancer has been changing to less radical procedures, and adding chemotherapy before chemoradiotherapy improves treatment outcomes in locally advanced disease. Finally, the use of immunotherapy in the treatment of advanced and recurrent cervical cancer is increasing.

### Disease burden and treatment of head and neck cancers in Poland

Globally, the fraction of HPV-positive oropharyngeal cancers (OPCs) varies but is generally between 40% and 60% (51). Variation may be due to the method used for HPV detection, as shown in Polish studies (52–54). In a study of 110 OPC cases, 70.9% of cases were HPV positive, with HPV16 being the most prevalent genotype (96.2%) (55). Among OPCs, the palatine tonsils were the most prevalent tumor site (80%). Currently, standard treatment is associated with high toxicities and compromised quality of life. Therefore, the aim is to de-escalate treatment for these patients. However, recently completed clinical trials to de-intensify chemoradiation in unselected populations failed to demonstrate non-inferiority. On the other hand, immunotherapy (e.g., the use of only anti-programmed cell death protein 1/ programmed death ligand 1 antibodies) has been approved for clinical use. The incidence of HPV-associated OPCs is expected to continue to rise until the benefits of gender-neutral HPV vaccination begin to become manifest.

Addressing HPV-related cancers in Poland is hindered by the lack of detailed local data on HPV subtype prevalence and cancer epidemiology. Without such detailed local data, only limited effectiveness can be achieved in targeted prevention strategies and treatment programs. The greatest priority would be to have a comprehensive cancer registry to track disease staging, metastasis, and treatment outcomes more effectively. One of the major concerns about Poland is the high number of advanced cervical cancer cases diagnosed—more than half are diagnosed at late stages. This is attributed to delays in diagnosis, insufficiently organized screening programs hindering access, and poor coordination among cancer treatment centers. Although the incidence rate of cervical cancer is generally decreasing, the slower de-

crease in mortality points toward gaps in treatment quality and accessibility. There is also growing concern about HPV-driven oropharyngeal cancers, but no organized screening programs in Poland target these cancers. The limited HPV subtype data available, mostly from regional studies, show the most frequent type of HPV infection to be HPV-16. There is also very poor inclusion of targeted high-risk groups—for example, HIV-positive patients and patients treated for diseases related to HPV—into screening programs. Inclusion would improve cancer registries, create more public awareness, and strengthen programs on the prevention and treatment of cancers in Poland. This highlights the need for focused research and organized approaches toward successful reduction of the burdens of HPV-caused cancers.

### Local stakeholders in HPV prevention and control

Kwiat Kobiecości (<https://www.kwiatkobiecosci.pl/>, meaning "the flower of femininity") is an organization founded 17 years ago by Ida Karpińska, a cervical cancer survivor. Following her diagnosis, Karpińska was unable to find sufficient information online, and so she established the organization to address this gap. Leveraging her media expertise, she successfully raised awareness of this often-taboo topic. Kwiat Kobiecości has since evolved into a prominent patient organization, focusing on education and support for women, girls, and healthcare professionals (in training). The organization offers free legal and healthcare support, including emotional and psychological hotlines, and visits women in 50 oncology wards with the help of 120 volunteers. The latest initiative is a mobile medical office providing cytology, HPV testing, ultrasound, and prostate-specific antigen (PSA) testing particularly in underserved areas. Results are disseminated online, and women are referred to local gynecologists or national experts as needed. The organization is fully reliant on sponsorships and receives no government funding.

### The way forward

A clear implementation plan for HPV vaccination and ownership of the prevention plan and the outcome evaluation plan could contribute to a successful program. The Wrocław success story shows that good vaccination rates can be achieved in Poland by using a "train the trainers" program to spread information more quickly. Simplified access to vaccination, based on the COVID-19 vaccination program, would further enhance participation. A comprehensive and consistent communication strategy is necessary to overcome parental concerns (e.g., about the safety and effectiveness of the HPV vaccine). Finally, vaccination (of children

and/or adolescents) may also boost screening (of mothers) and may be used to integrate HPV vaccination and HPV-DNA screening in women 30 to 45 years old, a strategy dubbed HPV Faster. Poland is ready to reach the WHO target of 70% screening of women: a country-wide central screening registry is present, laboratories are ready for HPV-based screening, validated tests are available, and efforts have been undertaken to standardize colposcopy. Moreover, the HIPPO study has shown that HPV-based screening is more efficient than cytology in the Polish setting. Nevertheless, a large part of the female population is reached through opportunistic screening, the results of which may not end up in the centralized registry. Organized screening and treatment will lead to standardized reimbursement. However, this should go hand in hand with building trust in public-sector screening to overcome the user preference for private-sector screening. This can be done by strictly using performance and quality control indicators for screening and treatment, in combination with training and (re) certification. Finally, training midwives for screening services can be particularly valuable for including hard-to-reach populations that rarely visit doctors.

### Conflict of interest

AN declares the following potential conflicts of interest: advisory boards, lectures, grants for research activity, coverage of travel costs, and participation in research events for MSD, and lectures for GSK. LS declares the following potential conflicts of interest: speaker fees or participation in advisory boards for MSD and GSK. DAM has received grants from Seqirus, non-financial support and honoraria from MSD, and non-financial support from Roche Diagnostics, unrelated to this work. AV has received speakers' fees and research advisory board fees through university funds from MSD, Janssen, Hologic, and Novosanis NV. AV has received an unrestricted research grant from MSD and Abbott. All other authors have no known competing financial interests or personal relationships that could appear to have influenced the work reported in this article.

### Funding

The HPV Prevention and Control Board is supported by in-kind contributions and support from the international experts involved and their institutions. To set up the activities and support publication costs, the secretariat obtained unrestricted grants from industry (GlaxoSmithKline Biologicals, Merck). All funds were handled according to the rules of the University of Antwerp. No remuneration was provided for experts or speakers.

### References

1. Eurostat. Cancer screening statistics [Internet]. Luxembourg: European Commission; c2000 - [cited 2024 Dec 7]. Available from: [https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cancer\\_screening\\_statistics&oldid=645013#Cervical\\_cancer\\_screening](https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Cancer_screening_statistics&oldid=645013#Cervical_cancer_screening).
2. von Karsa L, Anttila A, Ronco G, Ponti A, Arbyn M, Segnan N, et al. Cancer screening in the European Union: report on the implementation of the Council recommendation on cancer screening. Lyon: International Agency for Research on Cancer; 2008.
3. Michalek IM, Koczkodaj P, Didkowska J. National launch of human papillomavirus (HPV) immunization program in Poland, 2023. *Vaccine X*. 2024;17:100436.
4. Jablonska S, Fabjanska L, Formas I. On the viral etiology of epidermodyplasia verruciformis. *Dermatologica*. 1966;132:369-85.
5. zur Hausen H. Condylomata acuminata and human genital cancer. *Cancer Res*. 1976;36:794.
6. Vorsters A, Arbyn M, Baay M, Bosch X, de Sanjose S, Hanley S, et al. Overcoming barriers in HPV vaccination and screening programs. *Papillomavirus Res*. 2017;4: 45-53.
7. Vorsters A, Bonanni P, Maltezou HC, Yarwood J, Brewer NT, Bosch FX, et al. The role of healthcare providers in HPV vaccination programs—a meeting report. *Papillomavirus Res*. 2019;8:100183.
8. Waheed De, Schiller J, Stanley M, Franco EL, Poljak M, Kjaer SK, et al. Human papillomavirus vaccination in adults: impact, opportunities and challenges—a meeting report. *BMC Proc*. 2021;15:16.

9. Waheed DE, Burdier FR, Eklund C, Baussano I, Mariz FC, Téblick L, et al. An update on one-dose HPV vaccine studies, immunobridging and humoral immune responses—a meeting report. *Prev Med Rep.* 2023;35:102368.
10. Vorsters A, Bosch FX, Bonanni P, Franco EL, Baay M, Simas C, et al. Prevention and control of HPV infection and HPV-related cancers in Colombia—a meeting report. *BMC Proc.* 2020;14:8.
11. Waheed DE, Olivier CW, Riethmuller D, Franco EL, Prétet JL, Baay M, et al. Prevention and control of HPV and HPV-related cancers in France: the evolving landscape and the way forward—a meeting report. *BMC Proc.* 2023;17:18.
12. Caetano Dos Santos FL, Wojciechowska U, Michalek IM, Didkowska J. Survival of patients with cancers of the female genital organs in Poland, 2000–2019. *Sci Rep.* 2023;13:8473.
13. de Sanjosé S, Alemany L, Ordi J, Tous S, Alejo M, Bigby SM, et al. Worldwide human papillomavirus genotype attribution in over 2000 cases of intraepithelial and invasive lesions of the vulva. *Eur J Cancer.* 2013;49:3450–61.
14. Preti M, Joura E, Vieira-Baptista P, Van Beurden M, Bevilacqua F, Bleeker MCG, et al. The European Society of Gynaecological Oncology (ESGO), the International Society for the Study of Vulvovaginal Disease (ISSVD), the European College for the Study of Vulval Disease (ECSVD) and the European Federation for Colposcopy (EFC) consensus statements on pre-invasive vulvar lesions. *Int J Gynecol Cancer.* 2022;32:830–45.
15. Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie – Państwowy Instytut Badawczy, Ministry of Health of Poland, Narodowy Fundusz Zdrowia. Raport Otwarcia Narodowej Strategii Onkologicznej. Warsaw, Poland: Narodowy Instytut Onkologii im. Marii Skłodowskiej-Curie – Państwowy Instytut Badawczy; 2021. Polish.
16. Sopracordevole F, De Piero G, Clemente N, Buttignol M, Manciola F, Di Giuseppe J, et al. Vaginal intraepithelial neoplasia: histopathological upgrading of lesions and evidence of occult vaginal cancer. *J Low Genit Tract Dis.* 2016;20:70–4.
17. Bogani G, Martinelli F, Ditto A, Taverna F, Lombardo C, Signorelli M, et al. Human papillomavirus (HPV) persistence and HPV 31 predict the risk of recurrence in high-grade vaginal intraepithelial neoplasia. *Eur J Obstet Gynecol Reprod Biol.* 2017;210:157–65.
18. Cholewik M, Stepień M, Bieńkowski C, Pokorska-Śpiewak M. Parents' attitudes towards vaccinations regarding the Ukrainian migration to Poland in 2022. *Vaccines (Basel).* 2023;11:1306.
19. Ludwikowska KM, Biela M, Szenborn L. HPV vaccine acceptance and hesitancy—lessons learned during 8 years of regional HPV prophylaxis program in Wrocław, Poland. *Eur J Cancer Prev.* 2020;29:346–9.
20. Ludwikowska K, Szenborn L. Tailored interventions are successful in elevating HPV vaccine coverage: a case study from Wrocław, Poland. In: *ESPID 2024 abstract book.* PDO82:1197. Copenhagen, Denmark.
21. Larson HJ, de Figueiredo A, Xiahong Z, Schulz WS, Verger P, Johnston IG, et al. The state of vaccine confidence 2016: global insights through a 67-country survey. *EBioMedicine.* 2016;12:295–301.
22. Schernhammer E, Weitzer J, Laubichler MD, Birmann BM, Bertau M, Zenk L, et al. Correlates of COVID-19 vaccine hesitancy in Austria: trust and the government. *J Public Health (Oxf).* 2022;44:e106–16.
23. Bish A, Yardley L, Nicoll A, Michie S. Factors associated with uptake of vaccination against pandemic influenza: a systematic review. *Vaccine.* 2011;29:6472–84.
24. Larson HJ, Smith DM, Paterson P, Cumming M, Eckersberger E, Freifeld CC, et al. Measuring vaccine confidence: analysis of data obtained by a media surveillance system used to analyse public concerns about vaccines. *Lancet Infect Dis.* 2013;13:606–13.
25. Wilson R, Zaytseva A, Bocquier A, Nokri A, Fressard L, Chamboredon P, et al. Vaccine hesitancy and self-vaccination behaviors among nurses in southeastern France. *Vaccine.* 2020;38:1144–51.
26. Wilson RJJ, Vergélys C, Ward J, Peretti-Watel P, Verger P. Vaccine hesitancy among general practitioners in southern France and their reluctant trust in the health authorities. *Int J Qual Stud Health Well-being.* 2020;15:1757336.
27. Nowakowski A, Cybulski M, Śliwczyński A, Chil A, Teter Z, Seroczyński P, et al. The implementation of an organised cervical screening programme in Poland: an analysis of the adherence to European guidelines. *BMC Cancer.* 2015;15:279.
28. Kantar Millward B. Study on attitudes towards health behaviors in the area of cancer prevention among residents of Poland, with particular emphasis on the attitudes of Polish women towards cervical cancer and breast cancer. Warsaw: Ministry of Health, Press and Promotion Office; 2017.
29. Michalek IM, Manczuk M, Caetano Dos Santos FL, Macios A, Didkowska J, Nowakowski A. Self-reported participation in cervical cancer screening among Polish women in 2004–2019. *Ginekol Pol.* 2024;95:335–42.
30. Nowakowski A, Arbyn M, Turkot MH, Wieszczy P, Miłosz K, Kamiński MF, et al. A roadmap for a comprehensive control of cervical cancer in Poland: integration of available solutions into current practice in primary and secondary prevention. *Eur J Cancer Prev.* 2020;29:157–64.
31. Głinska P, Komerska K, Janik B, Olkowicz J, Jedrzejewska I, Macios A, et al. HPV testing in Polish population-based cervical cancer screening programme (HIPPO project)—study protocol of a randomised healthcare policy trial. *BMC Cancer.* 2023;23:1118.
32. Łuczyszyn A, Nowakowski A, Bidziński M, Kędzia W, Knapp P, Marszałek A, et al. Algorithms for screening and management of abnormal results within the Cervical Cancer Prevention Program, funded by the National Health Fund—edition after the introduction of high-risk HPV diagnostics. *Gin i Perinat Prakt.* 2024;9:124–32.
33. Perkins RB, Fuzzell LN, Lake P, McIntyre M, Nayar R, Saraiya M, et al. Incorporating stakeholder feedback in guidelines development for the management of abnormal cervical cancer screening tests. *J Low Genit Tract Dis.* 2020;24:167–77.
34. Mazurec K, Trzeszcz M, Mazurec M, Streb J, Halon A, Jach R. Triage strategies for non-16/non-18 HPV-positive women in primary HPV-based cervical cancer screening: p16/Ki67 dual stain vs. cytology. *Cancers (Basel).* 2023;15:1595.
35. Trzeszcz M, Mazurec M, Jach R, Mazurec K, Jach Z, Kotkowska-Szeps I, et al. Is primary HPV with secondary p16/Ki67 dual-stain an alternative HSIL-risk detection strategy in cervical cancer screening for women under 30 years? *Diagnos-tics (Basel).* 2021;11:2012.
36. Trzeszcz M, Mazurec M, Jach R, Mazurec K, Jach Z, Kotkowska-Szeps I, et al. Liquid-based screening tests results: HPV, liquid-based cytology, and P16/Ki67 dual-staining in private-based opportunistic cervical cancer screening. *Diagnos-tics (Basel).* 2021;11:1420.
37. Trzeszcz M, Mazurec M, Jach R, Mazurec K, Kotkowska-Szeps I, Kania M, et al. p16/Ki67 dual stain triage versus cytology in primary human papillomavirus-based cervical cancer screening with limited genotyping. *J Med Virol.* 2023;95:e29271.
38. Jach R, Mazurec M, Trzeszcz M, Bartosinska-Dyc A, Galarowicz B, Kedzia W, et al. Colposcopy 2020—colposcopy protocols: a summary of the clinical experts consensus guidelines of the Polish Society of Colposcopy and Cervical Patho-physiology and the Polish Society of Gynaecologists and Obstetricians. *Ginekol Pol.* 2020;91:362371.
39. Poljak M, Oštrbenk Valenčak A, Gimpelj Domjanič G, Xu L, Arbyn M. Commercially available molecular tests for human papillomaviruses: a global overview. *Clin Microbiol Infect.* 2020;26:1144–50.
40. Meijer CJ, Berkhof J, Castle PE, Hesselink AT, Franco EL, Ronco G, et al. Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women 30 years and older. *Int J Cancer.* 2009;124:516–20.
41. Mitra A, Gultekin M, Burney Ellis L, Bizzarri N, Bowden S, Taumberger N, et al. Genital tract microbiota composition profiles and use of prebiotics and probiotics in gynaecological cancer prevention: review of the current evidence, the European Society of Gynaecological Oncology prevention committee statement. *Lancet Microbe.* 2024;5:e291–300.
42. Aker S, Ağar E, Tinelli A, Hatirnaz S, Ortaç F. The impact of HPV diagnosis and abnormal cervical cytology results on sexual dysfunction and anxiety. *Int J Environ Res Public Health.* 2023;20.
43. Alay I, Kaya C, Karaca I, Yildiz S, Baghaki S, Cengiz H, et al. The effect of being diagnosed with human papillomavirus infection on women's sexual lives. *J Med Virol.* 2020;92:1290–7.
44. Cibula D, Raspolini MR, Planchamp F, Centeno C, Chargari C, Felix A, et al. ESGO/ESTRO/ESP guidelines for the management of patients with cervical cancer—update 2023. *Int J Gynecol Cancer.* 2023;33:649–66.
45. Athanasiou A, Veroniki AA, Efthimiou O, Kalliala I, Naci H, Bowden S, et al. Comparative effectiveness and risk of preterm birth of local treatments for cervical intraepithelial neoplasia and stage IA1 cervical cancer: a systematic review and network meta-analysis. *Lancet Oncol.* 2022;23:1097–108.
46. Eriksen DO, Jensen PT, Schroll JB, Hammer A. Human papillomavirus vaccination in women undergoing excisional treatment for cervical intraepithelial neoplasia and subsequent risk of recurrence: a systematic review and meta-analysis. *Acta Obstet Gynecol Scand.* 2022;101:597–607.
47. Plante M, Kwon JS, Ferguson S, Samouëlian V, Ferron G, Maulard A, et al. Simple versus radical hysterectomy in women with low-risk cervical cancer. *N Engl J Med.* 2024;390:819–29.
48. Lorusso D, Xiang Y, Hasegawa K, Scambia G, Leiva Galves MH, Ramos Elias P, et al. LBA38 Pembrolizumab plus chemoradiotherapy for high-risk locally advanced cervical cancer: a randomized, double-blind, phase III ENGOT-cx11/GOG-3047/KEYNOTE-A18 study. *Ann Oncol.* 2023;34:S1279–80.
49. Coleman RL, Lorusso D, Gennigens C, González-Martín A, Randall L, Cibula D, et al. Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study. *Lancet Oncol.* 2021;22:609–19.
50. Vergote IB, Gonzalez Martin A, Fujiwara K, Kalbacher E, Bagameri A, Ghamande S, et al. LBA9 innovaTV 301/ENGOT-cx12/GOG-3057: a global, randomized, open-label, phase III study of tisotumab vedotin vs investigator's choice of chemotherapy in 2L or 3L recurrent or metastatic cervical cancer. *Ann Oncol.* 2023;34:S1276–7.
51. de Martel C, Georges D, Bray F, Ferlay J, Clifford GM. Global burden of cancer attributable to infections in 2018: a worldwide incidence analysis. *Lancet Glob Health.* 2020;8:e180–90.
52. Ribeiro KB, Levi JE, Pawlita M, Koifman S, Matos E, Eluf-Neto J, et al. Low human papillomavirus prevalence in head and neck cancer: results from two large case-control studies in high-incidence regions. *Int J Epidemiol.* 2011;40:489–502.



53. Śnietura M, Jaworska M, Pigłowski W, Goraj-Zajac A, Woźniak G, Lange D. High-risk HPV DNA status and p16 (INK4a) expression as prognostic markers in patients with squamous cell cancer of oral cavity and oropharynx. *Pol J Pathol.* 2010;61:133–9.
54. Szkaradkiewicz A, Kruk-Zagajewska A, Wal M, Jopek A, Wierzbicka M, Kuch A. Epstein–Barr virus and human papillomavirus infections and oropharyngeal squamous cell carcinomas. *Clin Exp Med.* 2002;2:137–41.
55. Durzyska M, Kiprian D, Szumera-Cieckiewicz A, Leszczynski P, Florek A, Śnietura M, et al. Prognostic value of human papillomavirus detection and the eighth edition of the TNM classification staging system in oropharyngeal squamous cell carcinoma: a single-center Polish study. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2022;133:698–705.