



Human Papillomavirus

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DISEASE AND VACCINE CHARACTERISTICS

Human papillomaviruses (HPV) are the most common sexually transmitted infection. Although the majority of infections do not cause illness, persistent infection can result in disease. HPV infection is a necessary cause of cervical cancer, which usually does not occur until decades after infection. The majority of cervical cancers and other HPV-associated cancers are caused by HPV types 16 or 18. In 2012, there were an estimated 266 000 HPV-related cervical cancer deaths in women worldwide (1); > 85% of these deaths occurred in less developed countries. Cervical cancers comprise 84% of all HPV-related cancers worldwide. HPV can also lead to other anogenital cancers (vagina, vulva, penis and anus) and oropharyngeal cancers (head and neck). In addition, HPV can cause anogenital warts, though the HPV types that cause genital warts are different from those that cause cancers.

The World Health Organization (WHO) recommends that HPV vaccines be introduced as part of a coordinated and comprehensive strategy to prevent cervical cancer and other diseases caused by HPV.

Currently, three prophylactic HPV vaccines have been licensed, each containing a different number of types, though all prevent infection from types 16 and 18. Two of these vaccines also target HPV types that can cause genital warts. HPV vaccines do not contain viral DNA, but rather are based on self-assembled, non-infectious virus-like particles (VLPs). HPV vaccines are given according to two- or three-dose schedules, ideally before first sexual activity. All three HPV vaccines have excellent safety, efficacy and effectiveness profiles (2). Cervical cancer prevention remains the priority for HPV vaccination. For cervical cancer prevention, WHO recommends that the primary target group for HPV vaccination is girls aged 9–14 years. Secondary target populations for vaccination are females aged ≥ 15 years and males, if vaccinating those additional target populations is feasible, affordable, and cost-effective and does not divert resources from vaccination of the primary target population or from effective cervical cancer screening programmes.



RATIONALE AND OBJECTIVES OF SURVEILLANCE

In the context of immunization programmes, the primary goal of surveillance for HPV infections is to monitor potential impact of HPV vaccination. However, this surveillance can be quite challenging because of the natural history of HPV infection:

- Most sexually-active individuals will acquire HPV infection at some time in their lives.
- A majority of these infections are asymptomatic and resolve spontaneously within a year or two.
- HPV-related disease may not develop for years to decades following infection.

Therefore, detection and surveillance of every HPV infection is not indicated or recommended.

Routine surveillance for HPV infections is not a prerequisite for vaccine introduction, nor is it required after vaccine introduction, but countries may be interested in monitoring HPV infections to identify vaccine effectiveness and impact. Countries can consider monitoring prevalence of HPV vaccine types among sexually active persons for a period of time before and after vaccine introduction, as an early marker for vaccine impact. This is technically challenging and resource-intensive, and therefore is not suitable or recommended for all countries (1, 3).

Focused surveillance for HPV-related diseases other than cancers may be useful for countries considering implementing or following introduction of HPV vaccination. Countries may consider monitoring for anogenital warts or high-grade cervical lesions within specific target populations.



TYPES OF SURVEILLANCE RECOMMENDED

WHO does not have global-level recommendations for HPV surveillance, and monitoring for HPV infection and HPV-related disease is dependent on country interest and resources. Countries interested in monitoring for HPV-related diseases other than cancer can consider case-based or facility-based surveillance, usually in sentinel sites, for incidence or prevalence of anogenital warts, high-grade cervical precursor lesions or

HPV-related cancers (primarily cervical intraepithelial neoplasia). In some settings, HPV surveillance can be integrated with cervical cancer screening. A key preventive strategy for cervical cancer is screening and treatment for early precancerous cervical lesions, such as through Papanicolaou testing (Pap tests) or clinical HPV tests.



CASE DEFINITIONS AND FINAL CLASSIFICATION

Since WHO does not recommend HPV surveillance in the context of the vaccination programs, standardized

definitions for suspected, possible and probable HPV cases for purposes of surveillance have not been defined.



CASE INVESTIGATION

Individual cases of HPV infection or HPV-related diseases other than cancer do not require investigation

as part of surveillance. They should be referred for appropriate follow-up per clinical guidelines.



SPECIMEN COLLECTION

While routine HPV surveillance is not recommended, certain types of specimens, such as cervical cancer screening tests (Pap tests with or without HPV

co-testing) using a cervical brush, spatula or swab, are gathered as part of cervical cancer screening.



LABORATORY TESTING

Detection of HPV requires molecular testing (4). Clinical tests for oncogenic types of HPV are used for the following:

- cervical cancer screening in conjunction with a Pap test
- triage of abnormal cervical cytology results
- follow-up after treatment of cervical precancers.

For research purposes, type-specific HPV tests may provide useful information on epidemiologic research questions using detection of HPV DNA as the primary endpoint. Serologic assays are currently available only in research settings and were used in the HPV vaccine trials (1). No global laboratory network for surveillance of HPV has been established.



DATA COLLECTION, REPORTING AND USE

DATA COLLECTION

Because routine surveillance for HPV infections is not recommended, there is no standardized set of data to collect or analyse. Burden of vaccine-type HPV infections and HPV-related diseases, including burden of anogenital warts and HPV-related cervical precancerous lesions, can be monitored to assess for vaccine impact (5). In addition, countries should consider implementation and enhancement of cancer registries that include cervical cancers, to measure trends over time following HPV vaccine introduction.

REPORTING REQUIREMENTS AND RECOMMENDATIONS

HPV-related cancers may be notifiable in some countries, depending upon their cancer screening programmes and registries. There are no global reporting requirements for HPV infections, anogenital warts or cervical precancers.



SURVEILLANCE PERFORMANCE INDICATORS

There are no standard surveillance performance indicators for HPV surveillance, as routine surveillance is not recommended.



CLINICAL CASE MANAGEMENT

No specific treatment is recommended or required for asymptomatic HPV infections. Symptoms should be evaluated by a clinician. Various therapies are available

for anogenital warts. Early detection of HPV-related cervical precancerous lesions can enable early treatment and may prevent progression to cervical cancer.



CONTACT TRACING AND MANAGEMENT

Contact tracing is not routinely done for HPV.



SURVEILLANCE, INVESTIGATION AND RESPONSE IN OUTBREAK SETTINGS

Sexual transmission of HPV is extremely common. In general, outbreak investigations are not needed to address epidemiologic questions about HPV

transmission or to make recommendations for potential interventions.



SPECIAL CONSIDERATIONS FOR HPV SURVEILLANCE

The primary aim of HPV vaccine introduction is to prevent cervical cancers. Therefore, every country should establish or strengthen comprehensive population-based cancer registries to track cervical cancer trends. Cancer registries and other sources of administrative data can assess the long-term impact of a comprehensive cervical

cancer prevention strategy including HPV vaccination, cervical precancer screening and treatment, and cancer treatment. However, the full impact on cancer burden would not be observed for decades after vaccine introduction.



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