

Governing Council



ISSUE BRIEF

# HPV Vaccination in Populations with High HIV Prevalence

## Human Papillomavirus (HPV) and Human Immunodeficiency Virus (HIV)

HPV is a common sexually transmitted disease which can cause cervical cancer and genital warts, as well as less common cancers of the vulva, anus, penis, throat and neck. Cervical cancer is the second most common cancer among women worldwide. It is estimated that about 530,000 new cases and 275,000<sup>1</sup> deaths occur each year. Although preventable if detected at the precancerous stage, cervical cancer is disproportionately prevalent in the developing world where access to pre-cancer screening and treatment is limited. Many countries that have high rates of cervical cancer mortality and morbidity are also burdened with high rates of HIV. Recent findings show that HPV infection doubles the risk of acquiring HIV in women, with similar findings in heterosexual men and men who have sex with men (MSM).<sup>2</sup> Being infected with HIV also significantly increases the risk of persistent HPV infections, which can lead to cervical cancer. Additionally, the development of cervical cancer is much faster in HIV-positive women. Further, women infected with both HIV and HPV are more likely to develop cervical cancer.

## **HPV** Vaccines

Over 100 different HPV genotypes have been identified and 13 are known to cause cervical cancer. Two HPV vaccines have been developed to prevent infection by HPV

HPV infection doubles the risk of acquiring HIV in women and men. HIV also significantly increases the risk of persistent HPV infections, which can lead to cervical cancer. types 16 and 18—the types most often associated with cervical cancer (they cause 70% of cervical cancer cases). One of the vaccines also prevents infections by types 6 and 11, which cause genital warts. Although licensed in more than 100 countries,<sup>3</sup> these vaccines are not yet widely used in the developing world. As of 2013, more than 50 countries have introduced national-scale HPV immunization programs, including several middle-income countries and some low-income countries, and more countries are preparing to offer girls the vaccine, including many African countries with high rates of HIV.

## **HIV and HPV Vaccination**

HPV vaccination is most effective in girls who are not sexually active (and who therefore have not yet been exposed to the virus). The target age group for HPV vaccination is generally pre-adolescent and young adolescent girls prior to sexual debut, with some countries electing to vaccinate older adolescents or young women.<sup>4</sup> While the two available HPV vaccines are approved for use for a wide age range— Gardasil<sup>®</sup> for ages 9 to 26 and Cervarix<sup>®</sup> for ages 9 to 45—the World Health Organization (WHO) recommends a target age of 9 through 13. WHO also recommends selecting the vaccine population based on the age of initiation of sexual activity in the country and the feasibility of reaching girls through schools, health-care facilities or community-based settings.<sup>5</sup> Since the target age for HPV vaccination is so young, HIV prevalence in this population is low and should not greatly impact HPV immunization strategies.

#### HPV Vaccine Safety in HIV-Positive Individuals<sup>6</sup>

Both pre- and post-marketing surveillance show HPV vaccines to be as safe, or safer, than other commonly used vaccines. Further, the Global Advisory Committee on Vaccine Safety (GACVS) at the WHO, and all agencies reviewing and monitoring HPV vaccine safety, have concluded that both HPV vaccines are safe and effective and that the benefits of vaccination far outweigh any risks.<sup>5</sup> HPV vaccines are not live vaccines, are not infectious and can be administered to individuals who are immunocompromised. Recent studies have shown Gardasil<sup>®</sup> to be safe in HIV-infected women19 to 45,<sup>7</sup> in young women,<sup>8</sup> in men,<sup>9</sup> and in children 7 to 12 years old.<sup>10</sup> There are several ongoing clinical trials seeking to further evaluate the safety of HPV vaccines in HIV-infected individuals.<sup>11</sup>

#### Efficacy in Populations with High HIV Prevalence

HPV vaccine efficacy in populations with high prevalence of HIV is still being studied, but results suggest that the vaccine elicits a robust immune response in HIV-infected individuals. A study in Kenya suggested that the efficacy of HPV vaccines may be similar in HIV-infected populations and in non-infected populations.<sup>12</sup> Studies show that HIV-infected women have the ability to mount the necessary immune response to HPV antigens—i.e., they have the biological capacity to benefit from the vaccine.<sup>10,13</sup>

## HPV Immunization Strategy for Individuals Infected with HIV

In general, immunization strategies do not differ for people living with HIV, except in the case of live attenuated vaccines, which the HPV vaccine is not. Such strategies are based on evidence that a particular vaccine is effective and does not negatively impact Studies show that HIVinfected women have the ability to mount the necessary immune response to HPV antigens—i.e., they have the biological capacity to benefit from the vaccine.<sup>10,13</sup> HIV disease. The HPV immunization strategy for HIV-positive individuals would likely be similar for those who are not infected; however, results from ongoing safety and efficacy trials are needed to confirm this. There currently are no published international guidelines for administering the HPV vaccine to HIV-positive individuals.

### Conclusions

Given that in general, the recommended target population (age 9 through 13) for the HPV vaccination is too young to have significant levels of HIV infection and that the vaccine has been shown safe for HIV-infected individuals, general HPV immunization strategies should not be altered in settings with high HIV prevalence.<sup>5</sup> The potential benefit of the vaccine may be great due to this group's increased risk for HPV-related disease. The WHO states that any concerns regarding safety and efficacy among HIV-positive individuals should not deter large-scale HPV immunization programs.<sup>5</sup> In addition, they recommend that HIV testing should not be a prerequisite for routine HPV immunization. Results from ongoing studies evaluating the safety, efficacy and immunogenicity of HPV vaccination in HIV-positive individuals will shed further light on this issue.

#### **Cervical Cancer Action**

Cervical Cancer Action: A Global Coalition to Stop Cervical Cancer (CCA) was founded in 2007 to expedite the global availability, affordability, and accessibility of new and improved cervical cancer prevention technologies to women in developing countries.

#### For more information: Cervical Cancer Action www.cervicalcanceraction.org info@cervicalcanceraction.org

I WHO, GLOBOCAN, http://globocan.iarc.fr

- 2 Houlihan CF et al. HPV infection and increased risk of HIV acquisition. A systematic review and meta-analysis. AIDS 26: online edition. DOI: 10.1097/QAD.0b013e328358d908, 2012.
- 3 As of April 2011, Gardasil<sup>®</sup> was approved in 123 countries and Cervarix<sup>®</sup> in 114.
- 4 Kane MA et al. Chapter 16: HPV Vaccine in the developing world. Vaccine 2006:24 (Suppl 3)S:132-139.
- 5 Human papillomavirus vaccines WHO position paper. Weekly Epidemiological Record 2009; 84(15):118-32.
- 6 For more information on the safety of the HPV vaccines, see the Cervical Cancer Action Network's Issue Brief: HPV Vaccine Safety. www.cervicalcanceraction.org/pubs/CCA\_HPV\_vaccine\_safety.pdf.
- 7 E.M. Kojic, et al. Safety and immunogenicity of the quadrivalent human papillomavirus vaccine in HIV-positive women. Presented at AIDS 2012.
- 8 J. Kahn, et al. Immunogenicity of the HPV-6, -11, -16, -18 vaccine in HIV-positive young women. Presented at AIDS 2012.
- 9 Wilkin T, Lee JY, Lensing SY, et al. Safety and Immunogenicity of the Quadrivalent Human Papillomavirus Vaccine in HIV-1 Infected Men. J Infect Dis. 2010; 202: 1246-53.
- 10 Levin MJ, et al. Safety and Immunogenicity of a Quadrivalent Human Papillomavirus (Types 6,11,16, and 18) Vaccine in HIV-Infected Children 7 to 12 Years Old. J Acquir Immune Defic Syndr. 2010; 55 (2):197-204.
- 11 See trials information at www.clinicaltrials.gov (NCT00604175, NCT00798265, NCT00667563).
- 12 DuVuyst et al (2008). Human papillomavirus types in women with invasive cervical carcinoma by HIV status in Kenya.
- 13 Vaccine volume 24, supplement 3, August 31, 2006 pg. 143.