Human papillomavirus (HPV) vaccines

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Human papillomavirus (HPV) infection has been estimated to cause 270 000 deaths worldwide annually from cervical cancer and approximately 80% of these occur in resource-poor countries.[1] In South Africa, cervical cancer is the second most common malignancy among women, with the highest rate among black women aged 66 - 69 years.[2] With the development of prophylactic HPV vaccines there are prospects of significant reduction in morbidity and mortality due to HPV infection and its complications.[3]

Currently, two prophylactic HPV vaccines are available commercially (Table I). Cervarix (GlaxoSmithKline Biologicals) is a bivalent vaccine and Gardasil (Merck & Co) is a quadrivalent vaccine. HPV genotypes 16 and 18 currently contribute to approximately 70% of cervical cancer cases.[4]

From a public health perspective, the primary target population for vaccination with the HPV vaccine is females naïve to vaccine-related HPV types. Therefore the focus has been on adolescent girls prior to initiation of sexual activity, often cited as age 9 - 13 years.[6] The main aim is to attain high vaccine coverage, exceeding 70% in this population group. This approach has been shown to have the most cost-effective reduction in disease burden. Vaccination of older females (already sexually active) has been suggested as a possible secondary target group worth investigating. Vaccination in males has been debated. The WHO does not advocate vaccination in this population group based on cost-benefit analyses.[4]

Vaccine safety has been evaluated as part of licensing requirements as well as in post-licensure monitoring studies.[3,7] All available data currently point to adequate safety for use in routine vaccination programmes.[10] Inadvertent vaccination of pregnant women has been described and it has not been associated with any adverse effects.[4] Similarly, reports of vaccination during breastfeeding, specifically with the quadrivalent vaccine, have not been associated with any vaccine-associated adverse effects.[8]

Efficacy studies at this point are limited to evaluation of reduction in infection with HPV genotypes present in the vaccines.[3] However, as the final end-point of vaccination efficacy, the reduction in malignancies remains important and this has to be evaluated in long-term studies.[9] Follow-up studies for Cervarix and Gardasil have shown efficacy for up to 5 years.[3] The need for subsequent booster vaccines has not been established, and these data will become evident upon continuation of long-term follow-up studies.[4] Inter-changeability of these vaccines in the three-injection course has not been studied, and this practice is not encouraged. However, should the particular vaccine used not be available for subsequent doses, vaccination should not be deferred and an alternative may be used.[4]

Both HPV vaccines contain non-live, non-infectious particles and co-administration with other non-live or live vaccines is considered safe, provided separate syringes and injection sites are used.[4] The potential benefit of HPV prevention among immunocompromised persons may be far-reaching as these patients are at increased risk of HPV-associated disease morbidity and mortality.[10] Safety and immunogenicity have not been definitively established in this population,[4] and further research is required.

The WHO[4] advocates introduction of routine HPV vaccination as part of a national EPI programme provided HPV prevention is considered a health priority, and the programme is logistically feasible and financially sustainable. High vaccine costs are often cited as barriers to national public health usage. However, a recent study in Cape Town showed a cost benefit for routine HPV vaccination use.[1] Cervical cancer screening programmes should continue,[11] as genotypes not included in the vaccines may still cause malignant transformation.[12]

A further theoretical obstacle remains public acceptance. However, in a survey evaluating patient and clinician perceptions, cost remained the greatest barrier to vaccination, with the commonly cited misconception of promotion of promiscuity being an issue in less than 2% of subjects.[13] Adequate education of both clinicians and patients is an essential component to ensure effective implementation of a national vaccination programme.[4]

References available at www.cmej.org.za

Table I. Characteristics of Cervarix and Gardasil prophylactic vaccines

	Cervarix	Gardasil
Genotypes included[5]	16, 18	16, 18, 6, 11
Vaccination schedule[5]	0, 1 and 6 months	0, 2 and 6 months
Administration[5]	0.5 ml dose IM	0.5 ml dose IM
Adjuvant[6]	ASO4 which includes 3-O desacyl-4'monophosphoryl lipid A and aluminium salt	Aluminium hydroxy-phosphate sulphate
Duration of proven efficacy[3]	Proven efficacy studied up to 4.5 years	Proven efficacy studied up to 5 years
Registration in South Africa[2]	Since March 2008	Since March 2008
Availability in South Africa		
Private sector	Available	Available
Government sector	Not available	Not available
Cost per vaccine (wholesale)	R550.96	R770.00[7] - R877.80