

# Consensus recommendations for the prevention of cervical cancer in sub-Saharan Africa

## Sub-Saharan African Cervical Cancer Working Group

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## Abstract

Cervical cancer is the second most common cancer and the leading cause of cancer-related death in women in sub-Saharan Africa. It is estimated that more than 200 million females older than 15 years are at risk in this region. This paper highlights the current burden of cervical cancer in sub-Saharan Africa, reviews the latest clinical data on primary prevention, outlines challenges in the region, and offers potential solutions to these barriers. Based on these factors, clinical recommendations for the prevention of cervical cancer from the sub-Saharan African Cervical Cancer Working Group expert panel are presented.

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## Introduction

The sub-Saharan African Cervical Cancer Working Group expert panel was first established in Johannesburg, South Africa, in 2005. The panel comprises specialists in gynaecology, gynaecological oncology, epidemiology, gynaecological pathology and paediatrics who work in cervical cancer research in various institutions within sub-Saharan Africa. The sub-Saharan African Cervical Cancer Working Group meetings provide a forum for these specialists to exchange ideas and strategies on how to reduce the high incidence of cervical cancer in Africa. Their objectives are to raise awareness of the link between human papillomavirus (HPV) and cervical cancer, and to produce clear clinical recommendations for effective and sustainable cervical cancer prevention programmes across the continent.

### Cervical cancer

The sub-Saharan African region faces a number of important public health issues, including HIV/AIDS, infectious diseases and cancer.<sup>1</sup> However, the overwhelming burden of communicable diseases in Africa contributes to a relative lack of emphasis being placed on cancer in the continent.<sup>2</sup> Cervical cancer is a common cancer in women in sub-Saharan Africa, both in terms of incidence and mortality. More than 75 000 new cases are diagnosed, and there are over 50 000 deaths, each year.<sup>3</sup> The overall age-standardised incidence

rate of cervical cancer in sub-Saharan Africa was 31.7/100 000 in 2008. The highest incidence rates in the world were reported in eastern, western and southern Africa.<sup>3</sup> Presently, it is estimated that over 200 million females older than 15 years are in sexual relationships, and are therefore at risk of cervical cancer in sub-Saharan Africa.<sup>4</sup> However, the true burden of cervical cancer in the region may be far greater, as this is only an estimate, due to the failure of women to report cervical cancer in hospital settings and the limited number of cancer registries in sub-Saharan Africa.

### Human papillomavirus

Generally, it is accepted that nearly all cases of invasive cervical cancer are caused by infection with oncogenic strains of HPV.<sup>5</sup> HPV prevalence has been estimated to be 24% in sub-Saharan Africa across all ages, ranging from 17.4% in southern Africa, to 33.6% in eastern Africa.<sup>6</sup> In Africa, HPV distribution data in women demonstrate two peaks at < 25 and ≥ 45 years of age.<sup>6</sup>

To date, of the more than 100 strains of HPV that have been identified, approximately 15 are known to be oncogenic.<sup>7</sup> Most HPV infections are transient, usually “clearing” within two years in more than 90% of women.<sup>8</sup> However, in some cases, oncogenic HPV infections can persist and progress to squamous intraepithelial lesions [cervical intraepithelial neoplasia (CIN) grade 1-3], carcinoma in situ or invasive cervical

cancer over many years, or even decades.<sup>9</sup> Why some women do not clear the HPV infection and go on to develop cervical lesions is still not fully understood.

Irrespective of geographical region, HPV 16 and 18 infections are generally associated with approximately 70% of invasive cervical cancer cases worldwide.<sup>10</sup> HPV 45, 33 and 31 are the next most prevalent, contributing to an additional 14% of cases.<sup>10</sup> This association is apparent in sub-Saharan Africa, according to the results of an epidemiological study of HPV prevalence in Ghana, Nigeria and South Africa, where the combined incidence of HPV 16 and 18 infection in invasive cervical cancer cases was 68.4%.<sup>11</sup> Studies in individual sub-Saharan Africa nations have also shown similar proportions of invasive cervical cancer cases associated with HPV 16 and 18 infections, namely Nigeria (77.9%),<sup>12</sup> Ethiopia (63.9%)<sup>13</sup> and Guinea (62.9%).<sup>14</sup> However, in Senegal, a study of 2 065 consecutive patients aged 35 years or older found that HPV 16 and HPV 58 infections were most frequently associated with high-grade squamous intraepithelial lesions or cervical cancer (23% and 13%, respectively).<sup>15</sup>

### The prevention of cervical cancer

Preventing HPV infection and identifying precancerous cervical lesions are critical elements in reducing the burden of cervical cancer in sub-Saharan Africa.

#### Screening

Screening is aimed at early detection of premalignant cervical diseases prior to the development of invasive cervical cancer. Methods such as cytology testing, visual inspections, HPV DNA testing and the see-and-treat management of cervical premalignant lesions are available and have been included in World Health Organization (WHO) recommendations<sup>16</sup> and international and national guidelines.<sup>17-19</sup> According to the WHO, successful screening programmes require > 80% coverage, appropriate follow-up and management of patients with positive tests, effective links between screening diagnosis and treatment services, high-quality care and adequate resources.<sup>16</sup> Adequate treatment facilities need to be in place before embarking on screening initiatives.<sup>16</sup>

Establishing the optimal target population and frequency of screening is important, particularly in low-income countries. The development of invasive cervical cancer can take up to 20 years, so screening women who are younger than 30 years of age may not be cost-effective, and there is the risk of overtreatment. Local experience is important in deciding on this. For instance, in Cameroon, screening commences at 25 years of age, based on data obtained over many years. Three-yearly screening intervals are almost as effective

as annual screening, and screening at longer intervals, or just once between the ages of 35 and 45 years, can significantly reduce the mortality that is associated with cervical cancer.<sup>16</sup>

#### Vaccination

The WHO has identified several key approaches to preventing HPV infection and limiting the impact of other risk factors for cervical cancer, including increasing awareness and education with respect to high-risk sexual behaviour, introducing suitable strategies to facilitate behaviour change, discouraging tobacco use and introducing an effective and affordable HPV vaccine.<sup>16</sup> The frequently limited screening and treatment facilities available in the sub-Saharan Africa region make preventing HPV infection of greater importance. According to the WHO, HPV vaccination should be included in national immunisation programmes if cervical cancer prevention is considered a public health priority, if the introduction of HPV vaccination is feasible, if financial sustainability can be secured, and if the cost-effectiveness of HPV vaccination in the particular country or region is taken into account.<sup>20</sup>

Currently, two vaccines are available: a bivalent vaccine (Cervarix<sup>®</sup>, GlaxoSmithKline Biologicals) and a quadrivalent vaccine (Gardasil<sup>®</sup>, Merck & Co). Both of these are prepared from virus-like particles against the most common oncogenic types, HPV 16 and 18. The quadrivalent vaccine also contains virus-like particles against HPV 6 and 11, which confer protection against genital warts. The prevention of genital warts in both girls and boys may help to reduce the risk of transmission of HIV. This is particularly important in regions with a high prevalence of HIV infection, such as sub-Saharan Africa. As at the end of 2012, 51 countries had introduced HPV vaccine into their national immunisation schedule.<sup>21</sup> Currently, both vaccines require three doses administered over a period of six months. However, researches are ongoing to determine whether or not a two-dose strategy would provide adequate levels of protection.<sup>22-24</sup> Selected characteristics of the HPV vaccines are summarised in Table I.

Extensive clinical trial data have shown that both vaccines are well tolerated, safe, highly immunogenic and efficacious against HPV infections and precancerous cervical lesions.<sup>29-30</sup> Long-term follow-up in clinical studies has demonstrated protection for the vaccinated cohort against HPV 16 and 18 infections and associated lesions of 5-9.4 years,<sup>31,32</sup> but the full duration of protection has still not been determined.

**Table 1:** Selected characteristics of the bivalent and quadrivalent human papillomavirus vaccines\*

	Bivalent vaccine (Cervarix) <sup>25-26</sup>	Quadrivalent vaccine (Gardasil) <sup>27-28</sup>
<b>Manufacturer</b>	GlaxoSmithKline	Merck & Co
<b>Approval date</b>	EMA, 20 Sep 2007 FDA, 16 Oct 2009	EMA, 20 Sep 2006 FDA, 8 Jun 2006
<b>HPV types covered</b>	16 and 18	6, 11, 16, 18
<b>Adjuvant</b>	AS04	AAHS
<b>Volume per dose</b>	0.5 ml	0.5 ml
<b>Administration</b>	Intramuscular	Intramuscular
<b>Schedule or interval</b>	Three doses: 0, 1 and 6 months	Three doses: 0, 2 and 6 months
<b>Approved age range</b>	≥ 9 years	≥ 9 years

AAHS: amorphous aluminium hydroxyphosphate sulphate, AS04: 3-O-desacyl-4' monophosphoryl lipid A, EMA: European Medicines Agency, FDA: US Food and Drug Administration, HPV: human papillomavirus

\* Sources: USA prescribing information and European Summary of Product Characteristics for bivalent<sup>25-26</sup> and quadrivalent vaccines<sup>27-28</sup>

The overwhelming findings from the published data are that both HPV vaccines are well tolerated, without any proven serious adverse events. The most common reported serious adverse events are pain, redness and swelling at the site of the injection, which tend to be mild.<sup>33</sup> As many more countries plan to initiate vaccination programmes, the panel considers it imperative that a set of recommendations is published to guide the implementation of such programmes in sub-Saharan Africa. This is necessary to complement global efforts to promote global access to cervical cancer prevention.

### Recommendations from the sub-Saharan African Cervical Cancer Working Group expert panel for the prevention of cervical cancer

The sub-Saharan African Cervical Cancer Working Group expert panel has identified a number of actions that, if adopted, could help countries within sub-Saharan Africa to reduce the burden of cervical cancer. The overarching aim of the sub-Saharan African Cervical Cancer Working Group expert panel is to see the establishment of national cervical cancer control programmes that will protect women in Africa from cervical cancer in the long term. The sub-Saharan African Cervical Cancer Working Group expert panel recommends that the prevention of cervical cancer through screening and vaccination should be prioritised in sub-Saharan African nations, initially through demonstration projects. The WHO

has provided recommendations for cervical cancer screening<sup>16</sup> and vaccination.<sup>20</sup> However, the panel recognises that the WHO recommendations need to be adapted to best meet the individual needs of nations in sub-Saharan Africa.

### National cervical cancer control programmes

Establishing national cervical cancer control programmes will provide the framework to implement the policies needed to reduce the burden of cervical cancer in sub-Saharan Africa. Such programmes involve four elements, namely primary prevention, screening and/or early detection, diagnosis and treatment, and palliative care.<sup>16</sup> The sub-Saharan African Cervical Cancer Working Group expert panel, like the WHO Regional Committee for Africa, supports the WHO position that cervical cancer control can be achieved if national policies are adopted.<sup>16,34</sup>

Screening and vaccination have been identified as critical elements on which nations in sub-Saharan Africa need to focus within their respective national cervical cancer control programmes. Cervical cancer screening and HPV vaccination programmes will have to compete for the same limited resources as other cancer-related issues on the political agenda.<sup>30</sup> The healthcare infrastructure, including treatment facilities, will need to be improved in many sub-Saharan African nations. In particular, integrated surveillance programmes and registries must be put in place to monitor the performance, quality and safety of screening and vaccination coverage in many nations. The WHO has identified the paucity of cancer registries in Africa as a concern, and advises all nations to establish cervical cancer registries to monitor the impact of HPV vaccination and screening programmes.<sup>35</sup>

To realise these ambitions, national political will is required to raise the priority level of cervical cancer prevention, as it has for other conditions, like HIV. Only then can cervical cancer screening and HPV vaccination programmes be funded and sustained beyond donation frameworks.

### Screening strategies

In keeping with the WHO recommendations,<sup>16</sup> the sub-Saharan African Cervical Cancer Working Group expert panel emphasises that screening programmes need to be organised, covering the largest possible population linking to suitable treatment and follow-up. Although some countries have established national guidelines,<sup>36</sup> regional guidelines are required for sub-Saharan Africa. Females of reproductive age should receive regular cervical cancer screening, as recommended by the WHO.<sup>16</sup> The WHO further emphasises that cervical

cancer screening is particularly important in areas with a high HIV prevalence. However, HIV status should not affect screening opportunities. Table II summarises the recommendations of the sub-Saharan African Cervical Cancer Working Group expert panel with regard to screening for cervical cancer in individual sub-Saharan African countries.

Cytology, visual inspection and molecular tests can be used to perform screening for premalignant cervical lesions, although each method has advantages and disadvantages in low-resource settings.<sup>38</sup> The specific screening test to be introduced should be determined at national or regional level, based on health system organisation, geography, local infrastructure and available resources.<sup>16</sup>

Cytology testing for cervical lesions is highly specific, with moderate sensitivity.<sup>38</sup> It requires dedicated infrastructure. Women who have been tested must return for results, making it more suitable for urban areas.<sup>16</sup> The effectiveness of cytological screening

is well documented, with associated reductions in cervical cancer incidence having been observed in North America and Europe.<sup>16,39</sup> However, in low-resource settings, cytological screening has not had such an impact.<sup>40</sup> This is related to the lack of widespread services, delays in receiving results, lack of the high-quality laboratories needed for cytology-based screening and absence of adequate centres for the evaluation and treatment of identified patients with abnormal lesions. The Cervical Cancer Working Group expert panel believes that the ultimate goal would be to address these issues. Interim measures include the employment of other less technical, but equally effective and validated, screening methods, for developing countries.

Visual inspection techniques, such as visual inspection with acetic acid (VIA) or visual inspection with Lugo's iodine (VILI), have moderate sensitivity, but relatively low specificity, as screening tests.<sup>38</sup> Such methods do not require the complex organisation

**Table II: Cervical cancer screening recommendations**

Factors	Recommendations
<b>Prior to initiation of screening</b>	Effective treatment strategies and facilities need to be established.
<b>Target populations</b>	<i>Women of reproductive age at risk of cervical cancer:</i> HIV status should not affect screening opportunities.
<b>Structure</b>	Organised nationwide screening programmes should be designed and managed centrally.
<b>Tests</b>	Cytological testing: <ul style="list-style-type: none"> <li>• Consider for primary screening strategy if resources permit.</li> <li>• Consider for use in urban areas primarily.</li> </ul>
	VIA/VILI: <ul style="list-style-type: none"> <li>• Consider for use in low-resource settings as part of a screen-and-treat-strategy.</li> <li>• Consider for use in rural areas primarily.</li> </ul>
	HPV DNA testing: <ul style="list-style-type: none"> <li>• Consider for use in low-resource setting as part of a screen-and-treat-strategy.</li> <li>• Consider for use in rural areas primarily.</li> </ul>
<b>Programme details</b>	<i>New programmes: commence screening in women aged ≥ 30 years:</i> Women aged < 30 years to be included only when the higher-risk group has been covered.
	<i>Existing organised programmes:</i> Women aged < 25 years should not be included in target populations.
	If only one screening opportunity is possible, the optimal age is between 35 and 45 years.
	A three-year interval could be considered if resources are available for women aged 25-49 years.
	An appropriate screening interval is five years for women aged > 50 years.
	Further testing is not necessary <sup>16</sup> in women aged > 65 years who received negative results from the previous two tests.
	Annual screening is not recommended at any age because of a lack of cost-effectiveness. <sup>37</sup>
<b>HPV vaccination considerations</b>	All female vaccine recipients should receive regular cervical cancer screening as recommended.
	Screening for cervical pathology or HPV presence is not required prior to vaccination.
	A female with abnormal screening results is still eligible for vaccination.
<b>Follow-up</b>	Women who are found to have abnormalities on screening need diagnosis, treatment and follow-up in order to prevent the development of cancer, or to treat cancer at an early stage. Countries are required to establish facilities for treatment and palliative care, and to strengthen the facilities if they already exist.

HIV: human immunodeficiency virus, HPV: human papillomavirus, VIA: visual inspection of the cervix using acetic acid, VILI: visual inspection of the cervix using Lugol's iodine

and infrastructure that is required for cytological screening.<sup>40</sup> The potential for immediate results with visual inspection methods may make such tests more suitable for rural areas,<sup>16</sup> and allow for screen-and-treat strategies.<sup>38</sup> Notably, the effectiveness of screen-and-treat strategies has been demonstrated in studies that have been completed in the sub-Saharan African region.<sup>37,41</sup> The evidence supporting visual inspection techniques is increasing. VIA was associated with a 35% reduction in cervical cancer mortality in one study that was conducted in low-resource settings.<sup>40</sup>

HPV DNA testing is highly sensitive, with moderate specificity with respect to screening.<sup>38</sup> The effectiveness of HPV DNA tests has also been demonstrated in low-resource settings.<sup>42-43</sup> Although previously considered to be expensive, the affordability and availability of HPV DNA tests is also increasing.<sup>44</sup>

Regardless of the test used, reaching the largest proportion of women at risk, with quality screening

and treatment, is the key to an effective programme. To achieve this, organised, nationwide, centrally managed screening programmes are preferable to opportunistic screening.<sup>16</sup>

### Vaccination strategies

A dedicated and effective HPV vaccination programme is essential for long-term cervical cancer prevention in the sub-Saharan African region. HPV vaccination programmes should be synergised with other programmes to achieve sustainable delivery. Experts in vaccination, including paediatricians, will be an important resource to ensure the most efficient introduction of HPV vaccination programmes in sub-Saharan Africa. Vaccinated persons should be advised that HPV vaccines do not provide protection against all types of HPV that can cause cervical cancer, and that they will still need to be screened for cervical cancer as they get older, although screening is not a prerequisite for vaccination. It is also important for recipients to

Table III: Human papillomavirus vaccination recommendations\*

	Recommendations
<b>Target populations</b>	<p>Routine vaccination with three doses of the same HPV vaccine is recommended for females aged 9-13 years: The exact age of primary vaccination may vary from country to country to best fit with the available infrastructure. A two-dose HPV vaccination schedule should be considered for implementation if approved.</p> <p><i>Females aged 13-26 years who have not been vaccinated previously should be encouraged to receive the vaccine. Those who have not completed the full three-dose vaccine series should be advised to complete the schedule.</i></p> <p>Females aged &gt; 26 years should be encouraged to discuss HPV vaccination with their healthcare providers, and together must decide if vaccination is appropriate.</p> <p>Population-based male vaccination is not currently recommended until high vaccination coverage in the female population has been achieved.</p>
<b>Strategy</b>	<p>HPV vaccination should be performed as part of a national immunisation programme.<sup>20</sup></p> <p><i>Universal mass vaccination via schools, community centres and health facilities should be considered.<sup>45</sup> Where possible, consider utilising existing age-appropriate national vaccination programmes to save resources.</i></p>
<b>Co-administration</b>	<p><i>HPV vaccines can be administered at the same time as other age-appropriate vaccines. However, each vaccination should be administered individually during the single visit.</i></p>
<b>Special situations</b>	<p><i>The HPV vaccine can be given to females who have an equivocal or abnormal cytology test result, a positive HPV DNA test, or genital warts. Vaccine recipients should be advised that the vaccine does not have any therapeutic effect on existing cytological abnormalities, HPV infection or genital warts.</i></p> <p>Caution should be taken when considering vaccination of the following groups:                      Breastfeeding women.                      Severely immune-compromised females<sup>46</sup> (HIV is not a contraindication to vaccination).</p> <p><i>The HPV vaccine is not recommended for use in pregnancy. If a woman has not finished her three-dose vaccination course and becomes pregnant, she should not receive any other vaccine doses until after delivery, at which point the remaining doses can be administered.</i></p> <p>Interchanging between different HPV vaccines is not recommended, as there are no safety, immunogenicity or efficacy data to support this practice.<sup>25,27</sup></p>
<b>Precautions</b>	<p>The HPV vaccine can be administered to females with mild acute illnesses, e.g. diarrhoea or mild upper respiratory tract infections, with or without fever.</p> <p>Vaccination of females with moderate or severe acute illnesses should be deferred until after the illness improves.</p>
<b>Contraindications</b>	<p>The HPV vaccine is contraindicated in females with a history of immediate hypersensitivity to any vaccine component.</p> <p>The HPV vaccine is contraindicated in females suffering from an acute febrile illness.</p>

HIV: human immunodeficiency virus, HPV: human papillomavirus

\* Please refer to national prescribing information where available

understand that vaccine clinical trial data do not suggest any therapeutic effect on existing cytological test abnormalities, HPV infection or genital warts.<sup>25-28</sup> Women with abnormal screening results could still be advised to undergo vaccination, if not previously vaccinated, to protect against future HPV infection. Table III summarises the recommendations from the sub-Saharan African Cervical Cancer Working Group expert panel regarding HPV vaccination. These can be modified and easily applied in individual sub-Saharan Africa countries.

#### *Primary vaccination*

The sub-Saharan African Cervical Cancer Working Group expert panel supports the routine vaccination of females aged 9-13 years with three doses of the same HPV vaccine, as recommended by the WHO<sup>20</sup> and recognised professional institutions.<sup>45</sup> Ideally, the HPV vaccine should be administered before potential exposure to HPV through sexual contact.

The sub-Saharan African Cervical Cancer Working Group expert panel recommends that the routine vaccination of pre-adolescent girls should be performed as part of a national immunisation programme, and should be funded by the healthcare system. This would increase potential coverage considerably, and contribute greatly to achieving cervical cancer control at population level. There are several potential approaches to universal mass vaccination, including utilising schools, community centres and health facilities, alone or in combination. Coverage of 88.9% was achieved through school-based HPV vaccination programmes in Uganda.<sup>47</sup> Mixed models that combine both school and health facilities have also been shown to be an effective approach with regard to vaccination in low-income countries, including sub-Saharan Africa nations, with mean coverage approaching 90%.<sup>48</sup> Door-to-door immunisation strategies have been beneficial in Ghana. There is also the potential for the private sector to become involved to maximise vaccination coverage in developing countries.<sup>49</sup>

#### *Catch-up vaccination*

While women are sexually active, they remain at risk of infection with oncogenic HPV and the development of cervical lesions and invasive cervical cancer, as infection does not reliably generate an immune response.

#### *Vaccination of women older than 26 years*

The sub-Saharan African Cervical Cancer Working Group expert panel recommends that females older than 26 years should be encouraged to discuss HPV vaccination with their healthcare providers, and together decide whether or not vaccination is appropriate. Studies have shown the bivalent and

quadrivalent vaccines to be highly immunogenic up to 55<sup>50</sup> and 45 years,<sup>51</sup> respectively. However, mass vaccination of women older than 26 years is not currently thought to be sufficiently cost-effective to merit inclusion.<sup>52</sup>

#### *Vaccination of males*

The sub-Saharan African Cervical Cancer Working Group expert panel does not currently recommend population-based male vaccination until high vaccination coverage in the female population has been achieved. Although male HPV infection often leads to the transmission of HPV to females via sexual intercourse,<sup>53</sup> modelling studies have found that increasing vaccine uptake in pre-adolescent girls is more effective in reducing HPV infection than including boys in existing vaccination programmes.<sup>54</sup> Moreover, economic studies show reduced cost-effectiveness when boys are included in vaccination programmes in low-resource settings.<sup>55</sup>

#### *Individual elective vaccination*

Primary and catch-up vaccination may be funded and delivered by national immunisation programmes. Recommended age ranges vary from country to country. However, any individual who wishes to be immunised should be offered HPV vaccination in the private sector. Overall, the sub-Saharan African Cervical Cancer Working Group expert panel recommends that women and girls and their parents should be encouraged to discuss HPV vaccination with their healthcare providers, and together decide whether or not vaccination is appropriate.

Ideally, all three doses should be given within a 12-month period. If the course is interrupted, it should be resumed using the same vaccine, but not repeated, preferably allowing the appropriate interval between the remaining doses.

#### *Further vaccination considerations*

Clinical studies have not demonstrated any significant clinical interactions between HPV vaccines and other childhood vaccines, enabling concomitant administration with other age-appropriate vaccines.<sup>25-28</sup> Other vaccination considerations are as stated in Table III.

The sub-Saharan African Cervical Cancer Working Group expert panel recommends that reference should always be made to national prescribing information when making prescribing decisions.

## Challenges and opportunities for achieving cervical cancer control in sub-Saharan Africa

There are a number of unique challenges that face the sub-Saharan Africa region with regard to improving cervical cancer control, including social, cultural, economic and political obstacles.

### *General challenges and opportunities*

The relative importance of cervical cancer as a public health issue remains low across the sub-Saharan Africa region. Public awareness of cervical cancer is still poor,<sup>56,57</sup> and understanding of the importance of the disease is not optimal, even among healthcare professionals.<sup>58,59</sup> Ongoing education of the public, healthcare providers and policy-makers is important. Engaging cervical cancer champions and utilising various media to raise awareness in public and among policy-makers could be a useful strategy for better prioritising cervical cancer, although cervical cancer is not the only major health problem affecting countries in sub-Saharan Africa. The ongoing HIV pandemic also draws on significant healthcare resources. However, as HPV infection has been associated with an increased risk of HIV acquisition, HPV vaccination may also have benefits in reducing the burden of HIV in sub-Saharan Africa.<sup>60</sup> Furthermore, there is evidence that women in sub-Saharan Africa who are HIV positive present with cervical cancer approximately 10 years earlier than those who are HIV negative.<sup>61,62</sup>

Approaches to changing high-risk sexual behaviour through the promotion of abstinence and condom use have been shown to be ineffective in parts of sub-Saharan Africa.<sup>63</sup> This reinforces the need to implement vaccination programmes across the region, and to continue improving screening and treatment facilities.

Local traditional and cultural values in various nations of sub-Saharan Africa need to be considered when considering the implementation of cervical cancer control programmes, and the acceptability of screening and vaccination for cervical cancer prevention. Communicating in an appropriate and sensitive manner is important in ensuring that key messages on cervical cancer prevention are understood.

National health policy-makers in the sub-Saharan Africa region face unique challenges. They are often faced with multiple public health priorities and limited budgets. The burden of cervical cancer in sub-Saharan Africa, the preventable nature of the disease, and available and effective prevention strategies need to be constantly highlighted to political leaders to ensure that cervical cancer prevention is made a priority.

Achieving cervical cancer control across the sub-Saharan Africa region requires a considerable investment of time, resources and expertise. By working together, the sub-Saharan Africa nations can assist each other in reducing the burden of this disease. A collaborative effort, both within and between nations in sub-Saharan Africa, would facilitate the processes needed to reduce the risk of cervical cancer in the region. Regular multidisciplinary meetings, at national and regional level, could assist with the dissemination of expertise and best practices.

### *Screening challenges and opportunities*

Cervical cancer remains largely uncontrolled in high-risk developing countries because of a lack of effective screening.<sup>38</sup> It has been estimated that 95% of women in developing countries have never been screened for cervical cancer.<sup>16</sup>

However, regardless of the specific screening test, low acceptance and compliance can limit coverage of screening programmes in low-resource settings.<sup>64</sup> Women in some cultures may be reluctant to undergo the vaginal examination that is required to conduct screening, which may limit participation.<sup>65</sup> There is evidence that the use of self-collected vaginal samples is an appropriate approach associated with higher participation rates in screening programmes.<sup>66</sup>

The resources required to support the infrastructure, labour force, materials and follow-up needed to deliver effective screening programmes for cervical cancer are considerable, and difficult for developing nations to provide and sustain over a wide age range.<sup>67</sup> However, recent research has shown cervical cancer screening to be highly cost-effective in the sub-Saharan Africa region. Screening with cervical cytology tests or visual inspection with acetic acid, in combination with treatment, costs < US\$ 2 000 per disability-adjusted life year averted.<sup>68</sup> It is imperative that policy-makers are made aware that cervical cancer prevention through screening requires a long-term view, both in terms of clinical and economic considerations.

### *Vaccination challenges and opportunities*

A number of barriers have been identified in attempts to establish paediatric vaccination programmes in developing nations. The introduction of HPV vaccination programmes has similar challenges.

Cultural and religious resistance to a vaccine that primarily targets young females, and which is associated with a sexually transmitted infection, is thought to have a significant impact on vaccine uptake from country to country. As a result, communication and advocacy strategies should be carefully tailored

to the needs of each individual country, and to the different communities being targeted.

There is also documented evidence of the challenges facing developing nations with respect to ensuring vaccine safety,<sup>69</sup> and maintaining the logistical requirements for a sustained vaccination programme, including cold chain and transport infrastructure, as well as vaccine supply and quality.<sup>70</sup>

Another important barrier to HPV vaccine introduction is cost. In November 2011, the Global Alliance for Vaccines and Immunization (GAVI) took the first decisive steps in supporting the implementation of HPV vaccination in countries with limited resources.<sup>71</sup> Therefore, it is vitally important to disseminate the GAVI criteria for co-funding widely at national level. Eligible countries need to take action now. They must determine their vaccination needs, apply for co-funding and oversee the implementation of HPV vaccination programmes.

Policy-makers should be aware that economic modelling has demonstrated HPV vaccination to be cost-effective in developing nations, such as Brazil<sup>72</sup> and South Africa,<sup>73</sup> although this was dependent on the price at which the vaccine was offered. In 2013, GAVI announced a record low price for HPV vaccines of US\$4.50 per dose.<sup>74</sup> A two-dose HPV vaccination strategy, which would have considerable financial benefits, has also been investigated with encouraging results.<sup>22</sup>

The available HPV vaccines are still waiting to be licensed in many African countries and, even in those that have approved the use of these products, important political decisions are pending before the introduction into national immunisation programmes. In Africa, national immunisation programmes are improving vaccination coverage. It is estimated that 71% of infants received routine vaccinations in 2011, as measured by diphtheria, tetanus and pertussis immunisation coverage.<sup>75</sup> However, most national immunisation programmes do not have a sufficient number of vaccine doses to cover the adolescent and adult populations, and HPV vaccination is not yet on the WHO's Expanded Program on Immunization.

The sub-Saharan African Cervical Cancer Working Group expert panel recognises the difficulty in establishing nationwide vaccination networks, and advocates the WHO recommendations for demonstration projects to be initiated as the first step.<sup>76</sup> The nationwide introduction of HPV vaccine could be challenging for nations that do not have prior experience in delivering multi-dose vaccines to young adolescents, as the target population is not normally served by routine vaccination programmes, the

burden of cervical cancer is not well appreciated and the benefits of HPV vaccination are not immediately observable.<sup>71</sup> Demonstration projects allow national groups to develop effective communication strategies and delivery mechanisms on a smaller scale. Such projects also provide evidence to inform national policy-makers, who can then be leveraged for nationwide roll-out of HPV vaccination programmes.<sup>71</sup>

GAVI offers support with regard to setting up demonstration projects and further funding for national HPV vaccination programmes once a demonstration project has been successfully completed. GAVI requires evidence of the delivery of multi-dose vaccines to  $\geq 50\%$  of a target population of 9- to 13-year-old girls in an average-sized district.<sup>71</sup> The sub-Saharan African Cervical Cancer Working Group expert panel encourages each respective Ministry of Health, through their governments, to approach GAVI for financial assistance regarding demonstration projects.

## Conclusion

Cervical cancer is a disease of inequity. It is a preventable disease that leads to considerable morbidity and mortality across the African continent. The sub-Saharan African Cervical Cancer Working Group expert panel advocates a plan of action for cervical cancer prevention through the establishment of national cervical cancer control programmes that involve the implementation of screening and vaccination programmes within the sub-Saharan Africa region. The recommendations provided by the sub-Saharan African Cervical Cancer Working Group expert panel have been developed through recognition of the challenges that face nations in sub-Saharan Africa. They were advanced with the aim of providing a platform from which clinicians could work, and to be used to engage key healthcare and political stakeholders in the region. The ultimate aim is that in the long term, greater protection from cervical cancer will be provided to African women.

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