Vaccine xxx (2008) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Preparing for HPV vaccination in South Africa: Key challenges and opinions

Jane Harries [a,*], Jennifer Moodley [a], Mark A. Barone [b], Sumaya Mall [a], Edina Sinanovic [c]

[a] *Women's Health Research Unit, School of Public Health and Family Medicine, University of Cape Town, South Africa*
[b] *EngenderHealth, New York, United States*
[c] *Health Economics Unit, School of Public Health and Family Medicine, University of Cape Town, South Africa*

ARTICLE INFO

Article history:
Received 19 September 2008
Accepted 13 October 2008
Available online xxx

Keywords:
South Africa
Cervical cancer
Cervical cancer prevention
Human papillomavirus (HPV)
HPV vaccine
Immunization
Health service intervention

ABSTRACT

This article reports on qualitative research investigating key challenges and barriers towards human papillomavirus (HPV) vaccine introduction in the Western Cape Province, South Africa. A total of 50 in-depth interviews and 6 focus groups were conducted at policy, health service and community levels of enquiry. Respondents expressed overall support for the HPV vaccine, underscored by difficulties associated with the current cervical screening programmes and the burgeoning HIV/AIDS epidemic in South Africa. Overall poor community knowledge of cervical cancer and the causal relationship between HPV and cervical cancer suggests the need for continued education around the importance of regular cervical screening. The optimal target populations for HPV vaccination was influenced by the perceived median age of sexual activity in South African girls (9–15 years), with an underlying concern that high levels of sexual abuse had significantly decreased the age of sexual exposure suggesting vaccination should commence as early as 9 years. Vaccination through schools with the involvement of other stakeholders such as sexual and reproductive health and the advanced programme on immunization (EPI) were suggested. Opposition to the HPV vaccine was not anticipated if the vaccine was marketed as preventing cervical cancer rather than a sexually transmitted infection. The findings assist in identifying potential barriers and facilitating factors towards HPV vaccines and will inform the development of policy and programs to support HPV vaccination introduction in South Africa and other African countries.

© 2008 Elsevier Ltd. All rights reserved.

1. Introduction

Cancer of the cervix is the second most common cancer worldwide with approximately 80% of cases occurring in developing countries.

In South Africa, cervical cancer is the second most common cancer amongst women with an overall age standardized incidence rate (ASIR) of 30 per 100,000 per year with the highest rate amongst black women aged 66–69 years [1]. Cervical cancer mortality has been significantly reduced through screening and early treatment programmes in some countries, but this has been difficult to implement in low resource settings [2–4]. Until recently South Africa did not have a national cervical cancer screening policy and cervical screening was performed opportunistically mostly in family planning and antenatal clinics, reaching primarily younger women who are not the optimal target group for screening because they typically experience significantly lower rates of cervical disease than older women [3–5].

The South African National Department of Health in 2000 identified cervical cancer as a national health priority and introduced a national cervical screening policy which states that all women attending public sector services are entitled to three free Papanicolaou (Pap) smears in their lifetime 10 years apart, starting at the age of 30. However, difficulties have been identified in implementing this policy [4].

The human papillomavirus (HPV) is the etiological agent in cervical cancer and has been identified as being a necessary, but not sufficient cause of cervical cancer [6]. HPV is a sexually transmitted infection and almost all individuals become infected with HPV within 2–5 years of initiating sexual activity. Two high-risk genotypes of HPV (16 and 18) are responsible for most cervical cancers whilst low-risk genotypes of HPV (6 and 11) cause a substantial proportion of low-grade cervical dysplasia and more than 90% of genital warts [7].

The recent development of two prophylactic HPV vaccines offers great potential for primary prevention of cervical cancer in South Africa. However, whilst recognizing the potential impact of the vaccines on the incidence of HPV and cervical cancer, screening aimed at secondary prevention of cervical cancer remains vitally important because, for example, all women will not be vaccinated, some cervical cancers are caused by HPV-types the vaccines do not

* Corresponding author. Tel.: +27 21 406 6798; fax: +27 21 406 6788.
E-mail address: Jane.Harries@uct.ac.za (J. Harries).

0264-410X/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.vaccine.2008.10.033

protect against, and the vaccines are not effective in women who already have HPV infection [3,8].

Currently there are two vaccines commercially available: a bivalent vaccine targeting HPV16 and 18 (Cervarix; GlaxoSmithKline) and a quadrivalent vaccine targeting HPV 16, 18, 6 and 11 (Gardasil; Merck, Sharpe & Dohme). Both vaccines show sustained efficacy after five years with good safety profiles and are administered in three divided doses over a six month period, which has implications for attaining effective levels of coverage and uptake [8,10]. Both have recently (March, 2008) been licensed for use in South Africa, but are not yet available in the public health sector.

The introduction of the HPV vaccine presents several unique challenges, for example, to obtain maximum effectiveness the vaccine needs to be administered prior to the onset of sexual activity, which means vaccinating young adolescents [11]. Implementation of an HPV vaccination programme raises several key issues related to target populations including age, sex and uptake; the acceptability of the vaccine to health care providers, adolescents and parents; and the effect of the vaccine on current cervical screening programmes [8,12,13].

As with any new product, there are many questions about how best to promote and deliver the vaccines to ensure optimal population coverage. Uptake will depend on how appropriately social marketing reflects the socio-economic, cultural and programmatic realities, and local knowledge and attitudes towards a vaccine that prevents acquisition of a sexually transmitted disease and targets young girls before they engage in sexual activity.

HPV vaccine introduction offers a unique opportunity to bring together role players across the health spectrum including sexual and reproductive health (SRH), adolescent health, Expanded Programme on Immunization (EPI), and cancer control programmes. The impact of the vaccine on existing cervical screening strategies will also depend on the vaccine's entry point and placement in countries' public health sectors.

A significant body of literature and interest has emerged over the past 6 years around HPV vaccine acceptability issues focusing on knowledge and attitudes towards cervical cancer, HPV and HPV vaccination in relation to uptake and potential opposition to the vaccine [9,13–21]. These studies, primarily undertaken in developed countries and prior to the registration of HPV vaccines, found that most parents and potential recipients had limited knowledge about cervical cancer, HPV and the importance of regular screening measures. However, despite poor levels of knowledge, health care providers were willing to recommend HPV vaccination and parents were interested in having their children vaccinated. Most studies concluded that information and knowledge about HPV, cervical cancer and the importance of regular screening needs to be improved so as to promote informed decision making with regards to HPV vaccination [20,21]. To date little work has been undertaken in developing countries, where the issues may be different [13,22].

Potential opposition to the vaccine ascribed to fears that vaccination will lead to increased sexual behaviour (sexual disinhibition) have been explored [9,13]. Yet, studies to date have suggested that the vaccine's protective effect and ability to prevent cervical cancer override concerns of increased sexual promiscuity [23].

One of the rationales for undertaking this research project was to explore introduction issues before HPV vaccines became available and it was conceptualized within the framework of the WHO strategic approach to contraceptive introduction [24]. Experience with introducing new health technologies has demonstrated the critical importance of understanding the socio-economic, political and cultural contexts before innovations are introduced and to incorporate the perspectives of a broad range of stakeholders, including those of users, providers, managers, policy makers and community groups [25].

This article reports on a qualitative study that explored key challenges and opinions towards HPV vaccination introduction in South Africa. The cost-effectiveness component of this study will be reported on separately. It is intended that this research will inform the development of policy and programmes to support HPV vaccination introduction in South Africa and findings may also facilitate introduction efforts in other African countries as well.

2. Methods

2.1. Study sites

The study was conducted between February 2007 and March 2008 in the Western Cape Province, South Africa. Three study sites were selected to represent the diversity of the Province: two urban areas and one peri urban area. Interviews with health care providers were undertaken in 6 public sector health care facilities (2 in each of the 3 research sites) providing reproductive, maternal and child health and cervical screening services. Interviews with policy influentials were conducted at national and provincial levels.

2.2. Study design

In-depth interviews were held with health care providers, policy makers and key policy influential's at national and provincial levels and focus group discussions were carried out with community members. All data collection was undertaken prior to the licensing of the HPV vaccines in South Africa.

Interview guides were semi-structured, open-ended and probing. Key issues explored included: views and experiences on current cervical screening policy and programmes; knowledge of the HPV vaccine; target populations and optimal age for vaccination; where best to position and manage the HPV vaccine; cost; service delivery issues; and possible opposition to the HPV vaccine. Additional issues explored with the community were knowledge of cervical cancer and of the relationship between HPV and cervical cancer, and the need for regular screening measures.

Interview guides and consent forms were piloted to check for language appropriateness and understanding. Experienced fieldworkers trained in qualitative research methods conducted the in-depth interviews and focus group discussions. Focus group discussions were conducted in the local language of participants. Interviews and focus group discussions were digitally recorded and transcribed verbatim. All participants provided written informed consent. Participants were assured that individual data would be confidential and anonymity maintained. Ethical approval was granted by the University of Cape Town's Research Ethics Committee and the Western Cape Province and City of Cape Town Health Departments granted permission to conduct the study at the selected research sites.

2.3. Study respondents

A total of 50 in-depth interviews and 6 focus groups were conducted. Study participants were selected through purposive and snow ball sampling.

A total of 26 in-depth interviews were held with national and provincial policy influential's, including policy makers and managers within non-governmental organizations, and academics/clinicians in the field of sexual and reproductive health, virology, infectious diseases and cervical cancer. Policy makers included high-level government managers and directors working in reproductive and sexual health, women's health, maternal and child health and education directorates at both provincial and national level.

Please cite this article in press as: Harries J, et al. Preparing for HPV vaccination in South Africa: Key challenges and opinions. Vaccine (2008), doi:10.1016/j.vaccine.2008.10.033

Twenty four in-depth interviews were conducted with public sector health care providers; 2 doctors, 17 primary care nurses and 5 school health nurses based at the study sites and involved in reproductive health services including cervical screening.

The six focus group discussions consisted of 43 female community members. The median age was 32.7 years (range 21–57), 33 (77%) had completed some secondary school education, 26 (60.5%) were unemployed, and all had children eligible for HPV vaccination. Providers in the six health care facilities assisted in identifying and recruiting focus group participants. On average, there were 7 members per focus group. Focus group discussions were conducted at either the health care facility or at a community venue (the church hall or public library).

A brief introduction to the HPV vaccine was provided to most respondents prior to the interview process as the vaccine was not yet available in South Africa, nor was it part of public discourse. Not surprisingly, apart from academics and clinicians involved in HPV and STI research, knowledge was limited.

2.4. Data analysis

Data analysis was conducted using content analysis. Initial categories for analyzing data were drawn from the interview guides and themes and patterns emerged after reviewing the data within and across the respondent groups. Over several meetings the research team identified key themes across all three respondent categories. Here we present data in terms of the major themes emerging from the interviews and focus groups, and common trends across respondent groups synthesized into key findings that can be used to shape policy and programmatic recommendations.

3. Results

Themes emerging from perceptions and insights expressed by respondents illustrate potential challenges facing HPV vaccine introduction, and are highlighted below. Overall support for the HPV vaccine was largely tempered by negative views around the current cervical screening policy and difficulties associated with secondary prevention, such as Pap smears and reducing cervical cancer incidence.

3.1. Cervical cancer screening policy

Discussion of current cervical screening policy and programmes led many policy makers and providers to speak more generally about the structural constraints endemic to the healthcare system as a whole. This was further underscored by the burgeoning HIV/AIDS epidemic in South Africa and the impact this had on the progression of cervical disease.

A policy influential suggested a re-evaluation of the national cervical screening policy by reducing the 10 year time interval.

> *But now with HIV and AIDS the compromised immune system can speed the progression of HIV and AIDS . . . what would the effect of cervical cancer also have on a patient who's already immune compromised. So in that instance, it might necessitate reducing the period, the 10 year interval between the patients . . . (National Government Representative).*

Respondents involved in service delivery and clinical research similarly suggested adaptations to the cervical screening policy but were mindful of the impact that more frequent screening would have on an already overburdened health care system.

> *At the moment the HIV programme is overwhelming all our budgets for cervical cancer, not cytology itself, but for the further management, because at the moment there's lesions, you have to do histology and follow up and so on and we don't have that capacity at the moment. So actually the screening programme is working too well at the moment to cope with all the clients (Clinician).*

Some nurses expressed concerns about high rates of teen pregnancies and sexual activity amongst a younger age cohort of girls and adolescents and similarly suggested changes to the screening policy by commencing screening as early as age 20.

> *Make our age group a little bit younger because our children become sexually active early and I feel we could make it a little bit younger, probably start in our 20's. Then we can do it at 20, do it at 30 – with the understanding that HIV is now included – because there a person picks up many funny things . . . (School Nurse).*

At the same time, some policy influentials acknowledged that they were not meeting the screening policy's coverage targets. A clinician highlighted the difficulties in reaching adequate coverage coupled with the challenges of implementing cytology-based screening programmes in low resource settings.

> *Half the screening programme is extremely flawed, it's a policy, which if it were properly implemented and had 80% coverage of the target age group, would have an impact on cervical cancer prevention, but we're nowhere near there, we haven't got anywhere near the correct coverage, we're using cytology as a screening test which is okay, but it's got lots of problems and particularly in low resource settings . . . (Clinician).*

Both policy influentials and providers emphasized the continued importance of secondary prevention screening measures particularly amongst older women already exposed to HPV.

3.2. HPV vaccine as a method of cervical cancer prevention

Policy influentials and providers expressed strong support for the HPV vaccine viewing it as an important adjunct to existing cervical cancer prevention strategies. Not withstanding this, many acknowledged the difficulties of introducing a new technology in an environment of limited health care capacity and resources. As an STI specialist/academic explained:

> *When you find an abnormal smear, there's nowhere to send the lady, I mean there is no-one who sees them, there's no colposcopy at all in C so – so that's a big problem you see. So if you can prevent it by vaccination, to me it's much, much better than having a system where you have a health system that's not working properly*.

Some policy influentials and clinicians raised concerns that the current HPV vaccines may not target HPV strains prevalent in South Africa as little is known about the natural history of HPV and HPV-types associated with cervical disease.

Community respondents' understandings around cervical cancer, HPV and the need for regular cervical screening were explored. Overall knowledge of cervical cancer was either poor or anecdotal and the causal relationship between HPV and cervical cancer was unknown amongst all participants. In some instances, Pap smears were conflated with an intervention to treat and "cleanse the womb". However, women who attended health care facilities with established cervical screening services were more knowledgeable about cervical cancer and the importance of regular cervical screening.

Community respondents were eager to learn about the vaccine and its role in cervical cancer prevention and made innovative suggestions how best to disseminate vaccine information by identifying a broad range of role players (church leaders, school teachers and health care providers) best suited to provide information and

Please cite this article in press as: Harries J, et al. Preparing for HPV vaccination in South Africa: Key challenges and opinions. Vaccine (2008), doi:10.1016/j.vaccine.2008.10.033

support. A focus group participant reflected on the vaccine's potential for a future generation of women and girls:

If it can improve the future for all our daughters then it is a good thing. In the past we never knew about things like this and a lot of women's reproductive organs were removed because they contracted cancer. So I think it is a good thing.

3.3. Target populations: age and gender

The optimal target populations for HPV vaccination was explored with all respondent categories and appeared to be influenced by the perceived median age of sexual activity in South African girls, considered between 9 and 15 years. A more "robust immunological response" amongst a younger aged cohort was cited as reason to vaccinate as young as 12 years, whereas, some providers and community respondents suggested commencing at the age of 9 due to high levels of sexual abuse and early onset of sexual activity in many communities. A nurse provider explained:

We need to include the 9 year old as well because they're very sexually active now at a very early age. At first it used to be the 19, 18 year old, but now they start in primary schools already, becoming active and of the molestation and all those things.

A mother in one of the focus groups concurred with these sentiments:

I will actually insist on it – the vaccine that you are speaking about especially for the children of the age 9 because I, as a mother, if I look at our community . . . the children in our community are very sexually active because they are already starting at the age of 10 and 11, they start with boyfriends and things like that. Prevention is better than cure.

3.4. Immunizing boys

Recognizing the high burden of cervical disease amongst women and competing health resources, most policy makers and providers had reservations about immunizing young males, despite the benefit of protection against ano-gential warts. The main reasons cited were the cost-effectiveness of including males at this early stage and the practicality of reaching a difficult to reach population. A clinic manager alluded to the difficulties that are generally associated with attracting men to health services that have historically tended to focus more on women's health issues.

I don't know how receptive they're[boys] going to be to you know – reproductive health has always been focused on females more, then we have to have a whole mind set about, and reasons why, education as to why it is necessary, because it[HPV vaccine] can protect, you know, them. So I think it would be very difficult . . .

Community respondents' views about immunizing boys were largely attributed to women's greater vulnerability to STIs. Thus a vaccine that could protect both women and men was of mutual benefit.

Because men today have lots of women and maybe the girl is not as active as the man and now he comes from a lot of women and maybe he comes and gives that to his steady girlfriend. I think it is something good to be given to them both for their protection.

3.5. Distribution and service delivery strategies

Potential distribution strategies were explored as the vaccine has the possibility of bringing together a wide range of constituents; including sexual and reproductive health, adolescent health, EPI and cancer prevention programmes.

Whilst differing views in terms of service delivery and possible location of the vaccine programme emerged, a "multifaceted" collaboration between different stakeholders was envisaged. The EPI programme was considered suitable due to extensive experience with procuring, managing and monitoring vaccine delivery. However, some policy influentials cautioned that optimal coverage would need to reach an older cohort of children than EPI traditionally targets. Similarly, delivery through schools was considered appropriate in terms of accessing the target population. However, the feasibility of a school-based health system managing the HPV vaccination programme was called into question by many policy makers and providers. A lack of human resource capacity and experience were considered potential barriers to effective vaccine roll out in this setting. A school nurse alluded to the difficulties of a service managed by a "Department that did not regard HPV vaccination as their focus" and suggested that many school nurses "would not be very happy accepting an extra project".

For the most part policy influentials felt that adolescent health had been neglected in South Africa, and that distributing the HPV vaccine at youth and adolescent clinics, which were few in number and located only in urban areas, would result in limited coverage.

A provider highlighted the possibilities of an intersectoral collaboration by relating to her experience with a recent polio campaign.

I think . . . with everyone, if they have inputs in it, it could work . . . if you have the different sectors working together it could work, because if you allocate it only to child health, okay, then there's going to be like now our services are so defragmented. Like now with our polio campaigns – it's working excellently because everybody's involved, you have local authority and the provincial and everyone is involved, you know – then it can work . . .

Similarly, a maternal and child health manager referred to the planned introduction by the Department of Health under the EPI of the combined diphtheria and tetanus vaccine at age 12 and suggested that the HPV vaccine could be administered in tandem with this vaccine.

Focus group participants were similar to other respondent groups about where they thought the vaccine should be delivered. Health care clinics were often named as the most suitable location for the distribution of the vaccine as "most people come to the clinic with their children to receive other immunizations". Some participants expressed support for delivery through schools to ensure coverage for all and to dovetail with the life skills school curriculum. However, some called into question the capacity of such a system to administer the vaccine and maintain hygienic standards and appeared unsure as to who would be responsible for vaccination.

Will the person know where to put the injection and that is why I say the health measures and standards have to be maintained with any type of injection and I don't know I don't trust the High Schools to do that, I honestly don't know?

3.6. Vaccine cost

Regarding user cost, many community participants due to their socio-economic circumstances wanted the vaccine to be free (like other childhood immunizations) or available at low cost. However, there was a perception that something paid for would be superior in quality. Yet, experience of introducing costly vaccines, more recently, the rotavirus vaccine into the public health sector induced skepticism amongst policy influentials about the affordability of the HPV vaccine to the South African public health care sector.

Please cite this article in press as: Harries J, et al. Preparing for HPV vaccination in South Africa: Key challenges and opinions. Vaccine (2008), doi:10.1016/j.vaccine.2008.10.033

The private sector's contribution to HPV vaccine awareness and promotion was explored with policy influentials. Some speculated that the private sector would play a minimal role in promoting the vaccine as most medical insurances due to a curative bias do not cover vaccines, traditionally the domain of the public sector.

The vaccine programme in general, across the private sector, is generally not funded, because most medical schemes agree generally that that's a public sector service which you can access and many people then access that on an out-of-pocket basis... Unfortunately the private sector is not geared towards preventative health, they're largely curative, and so the challenge would be how that vaccine then would be placed within the private health system, for someone to access it (National Department of Health Representative).

General Practitioners (GPs) in the private sector were seen as playing a role in vaccine awareness as many saw a broad range of patients throughout the life. A physician commented that GPs with a particular interest in women's health could play a role in catch-up programmes and vaccine delivery:

The GP has a role to check, ... checking has it happened. There will be people that move into the country from other places, that may not have had it when they were at school, there'll be people who missed it when they went to the schools, so I think GP's obviously do have a role, it's a question of how they remember to do it. Because you know, they're busy, you come in with a swollen knee or a sore throat, it takes a lot to suddenly think ooh this person's 13, or this person's 15 or 16, have they had their vaccination, I can't honestly see it happening unless that GP has a really, really strong interest in say for example cervical cancer, women's issues.

A policy influential reflected on the role of pharmaceutical companies in driving the process and cautioned against being "seduced" by drug companies at the expense of continued secondary prevention measures.

3.7. Possible opposition

Most policy influentials and health care providers interviewed did not foresee opposition to the introduction of the HPV vaccine from parents, the wider community or religious organizations. Many felt opposition could be avoided by providing comprehensive counseling and information and by communicating with stakeholders about the long term health benefits of the vaccine in preventing cervical cancer.

Some policy influentials felt that opposition to the vaccine from various religious groups including groups who generally oppose vaccines was to be expected. However, parental and public opposition could be overcome by providing clear health messages to both parents and recipients prior to introduction.

A number of policy influentials suggested marketing the vaccine as a "cancer vaccine" rather than a "STI vaccine" as a means of minimizing opposition and referred to past experiences with the Hepatitis B and the more recent GlaxoSmithKline (GSK) HPV vaccine in the United Kingdom.

Hepatitis B is also sexually transmitted, nobody ever talks about that side of it at all, they never talk about well let's vaccinate our kids because they might get Hepatitis B when they become sexually active, but it's a reality, especially in South Africa with the high carrier rates, so I think that's a good thing to look at ... (Academic Virologist).

To my understanding there's been a lot of outreach by the various pharmaceutical companies to those groups to kind of alleviate any concerns and I think they've been relatively successful in saying this is a cancer vaccine, it's not about STI's, but protecting young girls from cervical malignancy that's highly prevalent, it's preventable now with this vaccine and I think that's a tactic that can be successful (Infectious Diseases Physician).

Community respondents concurred with these sentiments by suggesting that marketing the vaccine as prevention against cancer rather than against an STI could help educate parents about its health benefits. Furthermore, negative perceptions of cancer within communities had changed over time particularly in the face of treatment options.

Those years cancer was a sin. One couldn't just speak about their cancer then the other people gossiped. It was almost like they had a big virus but today you can speak about it if there is a chance for you to be helped.

3.8. Safety and efficacy

Some focus group participants raised concerns about vaccine safety and efficacy; however, this did not dissuade them from supporting the vaccine in principal. A few community respondents anticipated that a South African HPV vaccine service might be inherently inferior as frequently vaccines used in South Africa are "not of the same standard as first world countries or in the private sector". Vaccines available in the government/public sector were considered "cheaper" and hence inferior. Concerns were raised that an inferior vaccine could have a negative impact on fertility as this interchange suggests:

Many a time we use vaccines that are not on the same standard as first world countries even private vaccines and government vaccines in South Africa are totally different. Are they going to give us a cheaper vaccine with more side effects which we only see in 30 years and anything to do with the womb? Is it going to affect fertility later on in the child's life? That is something I would be a bit conscious about, a bit scared.

Yes, maybe the women can become sterilised because of that injection and they can perhaps never have children again. These are things that will be discovered.

4. Discussion and conclusions

This is the first study undertaken in South Africa exploring key challenges and opinions towards HPV vaccination and provides important insights into introduction and acceptability issues should the public health sector move forward to make one or both of the HPV vaccines available. With the recent licensing of both commercially available HPV vaccines in South Africa, considerable information sharing and advocacy with all pertinent stakeholders including civil society and non-governmental organizations working in the field of sexual, reproductive, adolescent and women's health is necessary.

Despite some concerns around cost and application to local context, the need for a product to prevent cervical cancer resonated strongly with all respondent categories. Whilst there seemed to be general support for the HPV vaccine, it is not clear whether such support for a hypothetical product would necessarily translate into practice. For many providers and policy influentials an overriding concern was the overextended health care system with limited capacity to provide adequate cervical screening services to the general population of women using public sector services. This was further compounded by the impact of the HIV/AIDS epidemic on women's overall health and screening for pre-cancerous cervical

lesions, and suggested a need to create cervical screening policies for HIV-positive women.

The HPV vaccine's public health potential in preventing cervical cancer will only be realised if the vaccine is introduced on a large scale in the public health sector, where cervical screening and treatment options are limited. HPV vaccines have already been endorsed by physicians in the private sector and there has been widespread support in the media and government, however, cost will continue to be an important issue to address as currently the vaccine is priced at ZAR 700 (USD 100) per injection [26]. Not withstanding, if the vaccine could be made available at significantly reduced cost it would improve the chances of rapid and widespread introduction. To reduce cost in resource constrained settings, public–private partnerships and access to international funding mechanisms needs to be pursued.

Studies have shown that the HPV vaccine is a highly cost-effective health intervention [27]. An important component to this study was a cost-effectiveness analysis of integrating cervical cancer prevention programmes by adding the HPV vaccine to the existing screening programme in the public sector, and will be reported elsewhere. The findings of this analysis suggest that adding a vaccine to the current screening programme to prevent HPV related diseases in South Africa is a cost-effective strategy.

Besides cost, the logistical challenges of vaccine delivery will need to be addressed including decisions about the target population and partnerships between different stakeholders and government health and other (e.g. education) programmes to ensure optimal coverage. Given that cervical screening will need to continue after the introduction of HPV vaccination it will be important to re-evaluate current screening programmes and the impact that early HPV vaccination of a younger aged cohort of women will have on the overall burden of cervical cancer.

The optimal target population for HPV vaccination is likely to vary from country to country because of differences in age of sexual debut (i.e. first potential sexual exposure to HPV), epidemiology and available vaccination infrastructure. It is likely that vaccination will target school going girls aged 9–15 years and raises a number of issues. Most respondents felt that age of immunization should be prior to sexual activity (9–15 years), with an underlying concern by many that the high levels of sexual abuse and violence in South Africa had significantly decreased the age of sexual exposure and so vaccination should commence at the lower end of the age range. This is not surprising given the high levels of gender-based violence in South Africa and has been reported in other studies in similar settings [28,29].

Vaccinating pre adolescents and adolescents is a relatively new phenomenon and one that poses challenges in both developed and developing countries [9,10]. In South Africa, a regular health care visit for immunization at age 11 or 12 is currently not well established. This may well change with the planned introduction of the combined diphtheria and tetanus vaccine at age 12 and would be an ideal time for the HPV vaccine to be administered and would form part of the EPI programme.

Although some countries for example in the European Union and United Kingdom have successful school-based health programmes, many, including South Africa, do not have well established school health programmes [30]. The delivery and uptake of a three dose vaccine has raised some concerns as continued success of an HPV vaccination programme will depend on high levels of coverage of all three doses and points to the need for a pilot study in advance of a national immunization programme [10,31]. In South Africa 95.5% of school aged children are enrolled in primary schools and thus school-based programmes would be a good way to reach a large number of girls in the target age group relatively easily and could facilitate ensuring uptake of all three doses. However, other strategies would be needed to try to reach out-of-school youth.

The ways in which a vaccine against genital HPV is promoted will be critical to its acceptance and compliance amongst young girls and parents. The notion that vaccinating against an STI might encourage risky sexual behaviour has received media attention and academic interest in other settings [9,13,31]. At present it is unclear whether vaccination would actually encourage risky behaviour, or if fear of sexual disinhibition or implied consent for sexual initiation is a significant barrier to HPV vaccine acceptance [31]. However, the general feeling amongst respondents in our study was that opposition could be overcome with adequate counselling and information and focusing on the vaccines cervical cancer preventive properties, as opposed to focusing on the fact that HPV is sexually transmitted. Most respondents anticipated minimal opposition to the HPV vaccine and alluded to their experiences of introducing other programmes associated with sexual and reproductive health such as the 1996 Choice on Termination of Pregnancy legislation which despite controversy and some opposition had been successfully implemented in South Africa.

In common with studies from other settings, our findings suggest that considerable continued health promotion efforts are needed to improve knowledge about cervical cancer, HPV and the need for regular cervical screening, and highlight the importance of continued prevention and treatment strategies [13,17,21]. Moreover, health care providers not directly involved in cervical screening programmes need further training and education regarding the rationale behind the current national cervical screening policy. Significantly, there was a noticeable difference in levels of cervical cancer knowledge noted at one research site, largely attributed to a previous cervical health intervention aimed at developing and improving public sector cervical screening services in selected sites in South Africa [4]. Research published to date on knowledge about HPV and attitudes towards HPV vaccination relies on data collected prior to the availability of HPV vaccines and this may well change as more information about HPV and HPV vaccination is disseminated into the public domain.

National and provincial programmes will need to undertake the following: define the primary target populations taking into account earliest age of sexual activity and/or exposure; and develop partnerships between the different implementing stakeholders including Department of Education and school-based health care, EPI, Sexual and Reproductive Health, Women's Health and Cancer directorates. In addition, national cervical cancer control strategies will need to be updated to incorporate the new HPV vaccines. In planning a service delivery strategy for the introduction of the HPV vaccine, information, education and counseling (IEC) materials need to be developed to include a broad range of recipients, taking community members' poor levels of knowledge about cervical cancer, HPV and the need for prevention measures into account. Furthermore a comprehensive approach to cervical cancer prevention needs to be developed by ensuring access to secondary prevention programmes and treatment options.

Acknowledgments

The study was supported by EngenderHealth's Alliance for Cervical Cancer Prevention grant from the Bill & Melinda Gates Foundation. The authors thank: field researchers, the Western Cape Province and City of Cape Town Health Departments and the National Department of Health and all participants who gave of their time, as well as Janet Bradley and Marcia Mayfield, formerly with EngenderHealth in New York for assistance early on with development and design of the study.

References

[1] Mqoqi N, Kellett P, Sitas F, Musa J. Incidence of histologically diagnosed cancer in South Africa 1998–1999. Johannesburg: National Cancer Registry of South Africa; 2004.
[2] Lazcano-Ponce EC, Moss S, de Ruiz PA, Castro JS, Avila MH. Cervical cancer screening in developing countries: Why is it ineffective? The case of Mexico. Arch Med Res 1999;30(3):240–50.
[3] Denny L. Cervical cancer: the South African perspective. Int J Gynaecol Obstet 2006;95(1):S211–4.
[4] Moodley J, Kawonga M, Bradley J, Hoffman M. Challenges in implementing a cervical screening programme in South Africa. Cancer Detect Prev 2006;30(4):361–8.
[5] Fonn S, Bloch B, Mabina M, Carpenter S, Cronje H, Maise C. Prevalence of pre cancerous lesions and cervical cancer in South Africa—a multi centre study. S Afr Med J 2002;92(2):148–56.
[6] Muñoz N, Castellsagué X, Berrington A, de González AB, Gissmann L. Chapter 1: HPV in the etiology of human cancer. Vaccine 2006;21(24 Suppl. 3):S1–10.
[7] World Health Organization. Preparing for the introduction of HPV vaccines: policy and programme guidance for countries. Geneva: World Health Organization; 2006.
[8] Jacob M, Bradley J, Barone MA. HPV vaccines: what does the future hold for preventing cervical cancer in resource-poor settings through immunization programs? Sex Transm Dis 2005;(32):635–40.
[9] Zimet GD, Shew ML, Kahn JA. Appropriate use of cervical cancer vaccine. Annu Rev Med 2008;59:223–36.
[10] Brabin L, Roberts S, Stretch R, Baxter D, Chambers G, Kitchener H, et al. Uptake of first two doses of human papillomavirus vaccine by adolescent schoolgirls in Manchester: prospective cohort study. BMJ 2008;336(7652):1056–8.
[11] Wright T, Bosch F, Franco E, Cuzick J, Schiller J, Garnett G, et al. Chapter 30: HPV vaccines and screening in the prevention of cervical cancer; conclusions from a 2006 workshop of international experts. Vaccine 2006;24(3):251–61.
[12] Ault K, Reisinger K. Programmatic issues in the implementation of an HPV vaccination programme to prevent cervical cancer. Int J Infect Dis 2007;11(2):S26–8.
[13] Zimet GD, Liddon N, Rosenthal SL, Lazcano-Ponce E, Allen B. Chapter 24: psychosocial aspects of vaccine acceptability. Vaccine 2006;24(3):201–9.
[14] Giles M, Garland S. A study of women's knowledge regarding HPV infection, cervical cancer and HPV vaccines in Australia. Aust NZ J Obstet Gynaecol 2006;46(4):311–5.
[15] Rosenthal D, Dyson S, Pitts M, Garland S. Challenges to accepting a HPV vaccine: a qualitative study of Australian women. Women Health 2007;45(2):59–73.
[16] Noakes K, Yarwood J, Salisbury D. Parental response to the introduction of a vaccine against HPV. Hum Vaccin 2006;2(6):243–8.
[17] Moreira ED, Oliveira BG, Ferraz FM, Costa S, Costa Filho JO, Karic G. Knowledge and attitudes about human papillomavirus, pap smears and cervical cancer among young women in Brazil: implications for health education and prevention. Int J Gynecol Cancer 2006;16(2):599–603.
[18] Ogilvie GS, Remple VP, Marra F, Mcneil SA, Naus M, Pielakk L, et al. Parental intention to have daughters receive the HPV vaccine. CMAJ 2007;177(12): 1506–12.
[19] Pitts M, Clarke T. Human Papillomavirus infections and risks of cervical cancer: what do women know? Health Educ Res 2002;17(6):706–14.
[20] Vanslyke JG, Baum J, Plaza V, Otero M, Wheeler C, Helitzer DL. HPV and cervical cancer testing and prevention: knowledge, beliefs, and attitudes among Hispanic women. Qual Health Res 2008;18(5):584–96.
[21] Mosavel M, El-Shaarawi N. I have never heard that one": young girls' knowledge and perception of cervical cancer. J Health Commun 2007;12(8):707–19.
[22] Kane MA, Sherris J, Coursaget P, Aguado T, Cutts F. HPV vaccine use in the developing world. Vaccine 2006;21(24):132–9.
[23] National Board of Health, Danish Centre for Health Technology Assessment (2007). Reduction in the risk of cervical cancer by vaccination against HPV—a health technology assessment Danish Center for Health Technology Assessment 9 (1). www.dacehta.dk. Retrieved 17 August 2007.
[24] World Health Organization. Making decisions about contraceptive introduction: a guide for conducting assessments to broaden contraceptive choice and improve quality of care. Geneva: World Health Organization; 2002.
[25] Simmons R, Hall P, Diaz J, Diaz M, Fajans P, Satia J. The strategic approach to contraceptive introduction. Stud Fam Plann 1997;28(2):79–94.
[26] Thomas C. HPV vaccines: bring me your daughters! S Afr Med J 2008;98(4):259–61.
[27] Goldie S, Kohli M, Grima D, Wienstein M, Wright T, Bosch F, et al. Projected clinical benefits and cost-effectiveness of a human papillomavirus 16/18 vaccine. J Natl Cancer Inst 2004;96(8):604–15.
[28] Orner P, Harries J, Cooper D, Moodley J, Hoffman M, Becker J, et al. Challenges to microbicide introduction in South Africa. Soc Sci Med 2006;63(4): 968–78.
[29] Dunkle K, Jewkes R, Brown H, Gray G, McIntryre J, Harlow S. Gender-based violence, relationship power, and risk of HIV infection in women attending antenatal clinics in South Africa. Lancet 2004;363(9419):1415–21.
[30] Wright T, Van Damme P, Schmitt H-J, Meheus A. Chapter 14: HPV vaccine introduction in industrialized countries. Vaccine 2006;24(3):122–31.
[31] Waller J, Wardle J. HPV vaccination in the UK. BMJ 2008;336(7652):1028–9.

Please cite this article in press as: Harries J, et al. Preparing for HPV vaccination in South Africa: Key challenges and opinions. Vaccine (2008), doi:10.1016/j.vaccine.2008.10.033