



Towards Prevention of Cervical Cancer in Africa

Report from Meeting at St. Catherine's College, Oxford

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1. EXECUTIVE SUMMARY

Globally there are over 500,000 new cases of cervical cancer annually and in excess of 270,000 deaths, accounting for 9% of female cancer deaths. 85% of cases occur in developing countries and in Africa it is the commonest cancer in women with incidence frequently equating with mortality in the absence of healthcare facilities to deal with the condition.

Mortality rates vary seventeen fold between the different regions of the world. Cervical cancer contributes over 2.7 million years of life lost among women between the ages of 25 and 64 worldwide, some 2.4 million of which occur in developing areas and only 0.3 million in developed countries. Around the world a women dies of cervical cancer every 2 minutes.

Cervical cancer incidence and mortality rates have declined substantially in Western countries following the introduction of screening programmes. Screening programmes in Africa, are however, often rudimentary or non-existent.

The vast majority of women who suffer cervical cancer in Sub-Saharan Africa present with disease advanced far beyond the capacity of surgery or other treatment modalities to offer cure. Palliative care services are very poorly developed and therefore these unfortunate women are sentenced to a miserable end of life, with the cancer penetrating deep into the tissues of the pelvis resulting in pain, bleeding, fistula formation, bowel and ureteric obstruction.

Yet, cervical cancer is one of the most preventable of all cancers through primary and secondary prevention: prophylactic Human Papillomavirus (HPV) vaccination and cervical screening.

A global conference, organised by Oxford University's Africa-Oxford Cancer Consortium (AfrOx) and Cardiff University, was held in Oxford University on March 26th and 27th, to set down a strategy for preventing cervical cancer in Africa and issue an international call for action in combating the disease.

This meeting was organised by Prof David Kerr, University of Oxford and co-founder of AfrOx, and Prof Alison Fiander, Cardiff University.

The landmark conference 'Towards Prevention of Cervical Cancer in Africa' was attended by health ministers from African nations, African doctors, and advisors, the World Health Organization, representatives from the pharmaceutical industry, leading international oncologists, and major global cancer organizations and charities.

The conference delegates issued "**The Oxford Declaration**" (see appendix I) that calls for global support to provide the funds and expertise to eradicate cervical cancer in the developing world.

This report outlines the scale of the cervical cancer problem in Africa, the outcomes of the Oxford meeting on Prevention of Cervical Cancer in Africa and the proposed way forward.

2. BACKGROUND

One in ten female cancers diagnosed worldwide are cancers of the cervix, the most commonly diagnosed cancer among women in Southern or Sub-Saharan Africa and Central America.

Sub-Saharan Africa and South America have the highest incidence of cervical cancer in the world with cervical cancer resulting in 1% of all adult deaths and 2% of all female deaths. Most of these deaths occur in the middle age groups. Population dynamics are currently changing and an increase in middle aged population over the next 50 years will result in a 4 fold increase in deaths due to cervical cancer in middle aged women. Acting now, with screening and vaccination, will reduce deaths in the middle and the end of this century. Approximately 50,000 deaths per year may be avoided in Sub-Saharan Africa. The main challenges in implementing a HPV vaccine programme in Sub-Saharan Africa will be getting an affordable vaccine and ensuring sustainable delivery of the vaccine.

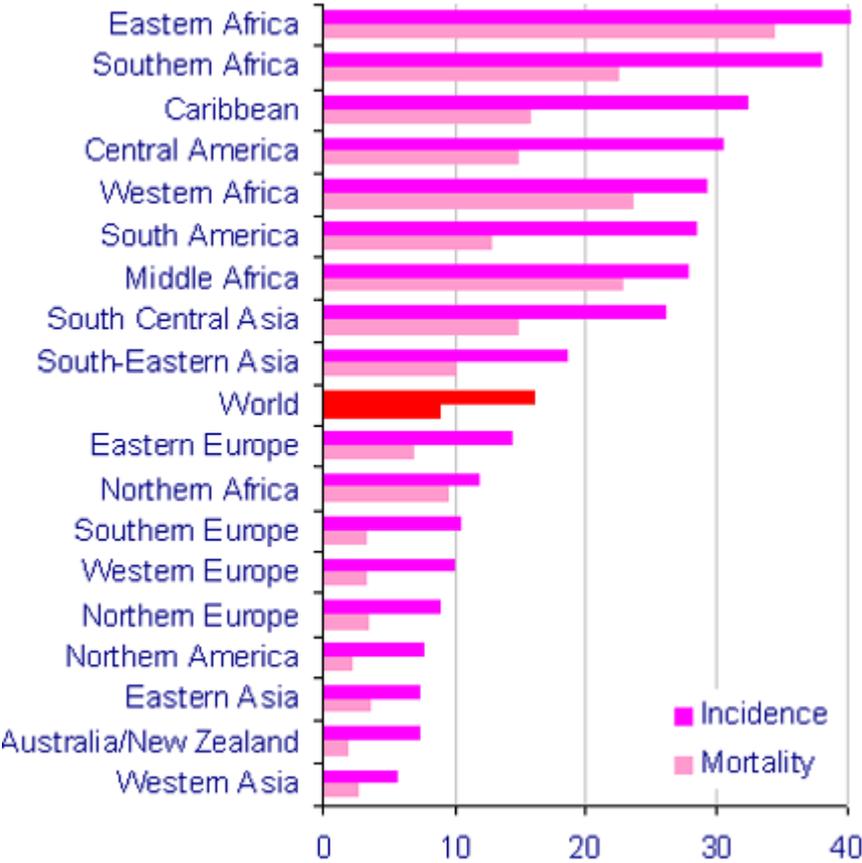


Figure: Age standardised incidence and mortality rates for cervical cancer in the different regions of the world, 2002 estimates (from CRUK Fact Sheet on Cervical Cancer)

The role of Human Papilloma Virus infection in cervical tumours

HPV infection is a major cause of cervical tumours with 99.7% of cancers worldwide containing HPV DNA. HPV infection is the most common viral infection of the lower reproductive tract. Approximately 40 different HPV genotypes infect the genital area of both sexes, including the skin of the penis, scrotum and vulva and the mucosa of the anus, vagina and cervix. These are classified according to oncogenic potential into 'low' and 'high-risk' genotypes. Two high-risk (HR) genotypes, HPV 16 and 18, are responsible for the majority of HPV associated cancers of the ano-genital tract. Two low risk genotypes, HPV 6 and 11, cause a substantial proportion of low-grade cervical dysplasia and more than 90% of genital warts. The peak prevalence of HPV infection occurs in the late teens and early twenties following onset of sexual activity. HPV infection usually resolves spontaneously in 9-12 months, but may persist in a minority of individuals with the subsequent development of pre-cancerous cervical lesions. If untreated these may progress to cervical cancer over a period of 10-30 years. During persistent HPV infection, pre cancerous changes may be detected in the cervix; therefore early detection and treatment of these changes is an effective strategy for the prevention of cervical cancer and forms the basis of cervical screening programmes.

HPV vaccination programmes

HPV is spread through sexual contact and although most women's bodies can fight the infection, sometimes the virus leads to the development of cervical cancer. HPV types 16 and 18 cause 70% of cervical cancer cases, whereas types 6 and 11 cause 90% of genital warts cases. Gardasil is a licensed vaccine that guards against diseases caused by HPV types 6, 11, 16 and 18. It is given as 3 injections over 6 months and is well tolerated, causing only mild irritation, itching and redness at the injection site. Another HPV vaccine, Cervarix, which has been developed by GSK, contains antigens for HPV types 16 and 18, is also given as 3 injections over 6 months and is generally well tolerated.

These vaccines give us the opportunity to eradicate 70% of all known cervical cancer within a generation, saving almost 200,000 lives per annum, the vast majority of whom live in the developing world. There is a large, international trials database that suggests HPV vaccination can offer almost 100% protection against infection by the HPV types included in a given vaccine.

The delivery of HPV vaccination programmes face significant challenges, requiring innovative and multidisciplinary approaches to communication, strengthening of local infrastructure and service delivery. HPV vaccines have several features that require special consideration in that their use requires new approaches to programme delivery; the target population is different to that usually addressed by national immunization programmes; multiple stakeholders need to be involved in advocacy and social communication and the best combination of vaccination and screening for cervical cancers remains unclear at the present time. Sexual and reproductive health communities will be working with a vaccine directed against a sexually transmitted infection that is linked to a common, but under-reported, genital cancer, raising issues that are distinct from experience with other vaccines e.g.

rubella and tetanus. It will therefore be crucial for countries to strengthen existing services and use them as entry points for new interventions, looking for maximum synergy.

Major issues for adolescent immunisation in developing countries include obtaining parental consent, reaching girls in schools, motivation of school teachers and principals and obtaining endorsement by faith leaders, community elders etc.

Prevention of cervical cancer by vaccination against HPV may be a cost effective way of reducing the burden of cervical cancer and other anogenital diseases related to HPV infection in developing countries. Whilst it has been difficult to establish and maintain effective cervical screening programmes in many developing countries these same countries have in many cases developed comprehensive vaccination programmes, which with appropriate adjustment could prove to be instrumental in cervical cancer prevention. As these vaccines are prophylactic, preventing initial infection with HPV, they require to be given prior to contact with the virus and therefore sexual debut. The age of sexual debut may vary between countries but it is generally considered that HPV vaccines should be targeted towards adolescents aged 9 to 13 years (<http://www.who.int/wer/2009/wer8415.pdf>), bearing in mind that even in countries with a relatively late average age of sexual debut, there will be some girls who debut early. The cervix in pubertal girls may be particularly vulnerable to HPV infection due to the physiological changes occurring during puberty. Additionally it has been shown that neutralizing antibody titres are greater in pre-pubertal children compared to older teenagers.

Prophylactic HPV vaccines require refrigeration and maintenance of a cold chain. Vaccine shelf life is estimated at 3 to 4 years from manufacture.

Screening for cervical cancer

The current vaccines only protect against 70% of disease, and are only effective for those not yet exposed to the virus so there is a generation of women who will be helped by screening. In the developed world, potentially dangerous changes in the cervix are usually spotted before cancer emerges due to implementation of national screening programmes. The British system is a good example of a successful screening program, preventing around 4,500 deaths each year in the UK, by detecting cervical disease when it is still at the easily treatable, pre-cancerous stage. In the UK, women are supposed to be called by their General Practitioner to be screened every three years from the age of 25 onwards for pap smear tests reaching up to 80% of the population invited. Smear tests may seem straightforward to health professionals but there is evidence that some women do not know the importance of a smear test, find them embarrassing or even traumatic, and in part this may explain why screening fails to reach everyone who is at risk. However, in many poorer countries screening is less consistent and in most developing countries, screening is virtually non-existent. This is why the death rates from cervical cancer may be ten times higher in East Africa than in some countries in Western Europe. This lack of screening makes the need for a vaccine against cervical cancer even more pressing.

However, since screening using cervical cytology is not feasible in most developing countries, other screening modalities require consideration such as VIA (visual inspection with acetic acid), VILI (visual inspection with Lugol's iodine) and HPV testing.

Several studies have demonstrated that direct visual inspection of the cervix with acetic acid 3-5% (VIA) is a reliable, reasonably sensitive and cost effective screening strategy. It has been shown to have sensitivity in the range of 56-80% and specificity of 64-86% for detecting high grade CIN in several studies. This does mean, however, that visual inspection techniques may miss one quarter to one half of true positives as well as needing access to skilled colposcopy if screen positives are to be assessed further. VIA with magnification (VIAM) and visual inspection after the application of Lugol's iodine (VILI) have also been assessed. VILI was on average 10% more sensitive and equally specific, whilst VIAM showed similar results to VIA alone. These techniques require a lower level of infrastructure compared to cytological screening, providing immediate results and the possibility of treatment in a single visit. However, they have relatively low specificity, possibly related to the high prevalence of other sexually transmitted infections, and there are the attendant problems of over treatment. Another unknown factor is how well VIA performs when genital schistosomiasis is prevalent. Furthermore, standardized initial training and continuing education programmes with supervision and mechanisms for quality control will be required if widespread visual inspection screening is to be successfully implemented. These considerations indicate the need for additional research to define optimal screening strategies in developing countries.

3. CONFERENCE FORMAT

An international conference was held in Oxford on March 26-27th 2009 to set down a strategy for preventing cervical cancer in Africa and to issue an international call for action in combating the disease. The conference was organised by Prof David Kerr, AfrOx, University of Oxford and Prof Alison Fiander, University of Cardiff.

Over 80 delegates attended the conference, including representatives of the First Ladies of Nigeria and Uganda, health ministers from African nations, African doctors, the World Health Organization, representatives from the pharmaceutical industry, leading international oncologists, and major global cancer organizations and charities (for full list see the Oxford Declaration in Appendix I).

The aims of the meeting were to:

1. Produce a strategy for the prevention of cervical cancer in Africa and agree an action plan for its implementation.
2. Determine how best to implement appropriate screening and vaccination against cervical cancer in Africa.
3. Identify a strategy to raise the necessary funds to enable the implementation of cervical cancer prevention programmes.
4. Set out the training, infrastructure, societal needs for such programmes.

The conference format included a mix of plenary sessions and informal workshops (see Appendix II for the agenda). The combination of plenary sessions and active workshops afforded every delegate the opportunity to share their expertise, views and ideas.

The conference began with two speeches given by representatives on behalf of Her Excellency Dr Turai Umaru Yar'Adua, First Lady of Nigeria and Her Excellency Mrs Janet Museveni, First Lady of Uganda, describing the challenges they face in combating cervical cancer in their countries and their passionate commitment to support cervical cancer prevention programmes in Africa.

The plenary sessions were used to set the scene for the conference and explored the causes of cervical cancer, provided an overview of methods of prevention and screening, and discussed current demonstration projects in developing countries. The plenary sessions also included a talk on the availability of international funding support and talks by representatives of Merck and GSK, the HPV vaccine manufacturers, on the work that they are doing to improve access to the vaccines in developing countries.

Two workshops were held, and both workshops were divided into four sessions. Each session was led by chairman and rapporteur who collated the ideas put forward by the workshop participants and then reported back to the conference at large. The first workshop focused on cervical screening. It looked at the criteria for demonstration projects, discussed the existing and required infrastructure, funding and training needs; focused on how to ensure and evaluate cost-effectiveness and also explored societal issues that would be encountered in trying to make screening culturally acceptable.

The second workshop focused on the practicalities involved in setting up a HPV vaccination programme. The workshop participants discussed the personnel, training & public education needs that would need to be addressed. The delegates also explored the political issues that may arise and how African health ministries might respond to the challenges of preventing cervical cancer. They also examined the key research questions that still need to be explored for prophylactic HPV vaccination and looked at the possibilities for international community support funding for HPV vaccination programmes in Africa.

4. CONFERENCE FINDINGS

Workshop 1 - Introduction of appropriate cervical screening: Planning for delivery

There were four streams for this workshop:

STREAM A - The ideal criteria for a cervical screening demonstration project.

The participants of this workshop stressed that appropriate cancer screening programmes should have high population coverage, use accurate screening tests and have facilities in place to track and treat test positive women. Where possible the numbers treated should be monitored, to help evaluate the service. However, the participants stressed that it would be important to ensure that the screening programmes were feasible, meaning that for example:

- Screening programmes must cover a majority of the population. However, in Africa this may have to be staggered. For instance, by starting at major hospitals where the best practices and training can be carried out, then expanding to major health centres after the complications of expansion have been worked out and in the final stage, screening services could move to small/rural health centres.
- It is difficult in developing countries to do individual call and re-call, and in these circumstances community outreach could be more effective. Using heads of communities would be vital in educating people about the importance of screening. The media, religious and women's groups could also be useful.
- It may be best to start in the capital city so that the central government and health care professionals are on board.
- It would not be feasible to expect every woman in the country to be screened every year. In these circumstances, it is important to screen WELL, if not screening OFTEN.
- The screening should be low tech, ideally run by nurses.
- There should be scope for other interventions to be added.
- Whatever the screening test, the participants agreed that screening and treating in a single visit is ideal. However, at a minimum, treatment must be available – for instance, it may not be possible to treat in very rural areas, so screening could take place in rural health centres and then positive women should be encouraged to travel to district hospitals for treatment. Dr Tsu stated that in her experience women were motivated to travel in order to receive treatment.

The workshop participants also discussed the different methods of screening technologies. They suggested that:

- Although the “see and treat” philosophy acknowledges that there may be overtreatment; overtreatment of the cervix is not harmful. Threatened abortion is less of a problem in Africa as women have generally had their children at a young age so the policy would be to treat all screen positive women.
- Current treatment often uses Cryotherapy which treats the whole of the transformation zone (TZ); but cold coagulation that also treats the entire TZ may have advantages as it is quick, easily sterilizable and the equipment is light to transport, weighing around 2kg.
- The participants agreed that there was an urgent need for the development of new HPV tests to make them more available and less expensive. HPV testing is more sensitive than cytology with a better negative predictive value; 8 years after a negative HPV test CIN 3 rates are lower than 8 years after cytology. VIA has been shown to only have sensitivity of around 40%.
- There are 3 demonstration tests about to begin using CareHPV, which will hopefully lead to greater availability of a reliable low cost test. The CareHPV, will allow for self-sampling so may improve coverage. CareHPV is a cheaper more user friendly test with 89% sensitivity. Lack of specificity may be a problem in Europe and the USA because HPV has a very high incidence among young women. There is a suggestion that HPV prevalence may remain high in some developing countries and further research is required to investigate this in Africa. The CareHPV test will not be available commercially for another 12-18 months. However, they are hoping to make it available on tier pricing with a target price of below \$5 per test.
- The participants agreed that for screening a HPV based test is ultimately the goal. The ideal would be the CareHPV test, with an option for self-testing.

- Following a positive HPV test it was recommended that women should have VIA to exclude invasion and then treatment with either cryotherapy or cold coagulation if applicable.

STREAM B - Pre-requisites for cervical screening: infrastructure, funding, training

To set up a cervical screening programme, it is vital to address the associated infrastructure, funding and training needs. The delegates at this workshop recommended that it would be important for:

- Screening to be free at point of service and ideally as close to the people as possible.
- The health systems for African countries differ, and so a unique approach would be required for each country. However, each African Government should be lobbied to set aside a certain amount of money per year to carry out cervical screening. It would be important to have this recognised by a separate sub-section of the national budget. Finding sustainable funding for screening programmes is important – one way to achieve this could be for donors to insist that they would only fund a cervical cancer screening programme if the government agreed to provide funding support for the programme to continue after set-up funding ended.
- Building up political will and support for national funding support towards cervical cancer screening would be required. The First Ladies of Africa could have an important role in leading this. In Nigeria, the Governors' wives have been keen supporters of cervical cancer screening. Community advocates and the media would also need to be mobilised. These groups would also have a key role in raising public awareness about the causes of cervical cancer and why treatment would be important.
- Records and documentation of those being screened should be kept so we can tell how often or if they go for screening. This would also help to monitor whether it was simply the same people getting screened, or if the programme was succeeding in reaching new women.
- If possible, screening should be integrated into existing programmes, such as programmes for breast cancer screening, sexual health programmes, etc
- Training of health professionals to take smear tests and/or HPV tests would be necessary. Training of pathologists to read smear tests would also be critical.

STREAM C - Evaluation & cost effectiveness of cervical screening

The participants of this workshop discussed how to evaluate and measure the cost-effectiveness and success of cervical screening programmes. They identified the following areas as being critical for consideration:

1) Training

- Are programs easy to staff?
- Should pap smears be abandoned for developing countries due to lack of people to read them?
- Work must be done by another health care level other than doctor – but problems arise when empowerment of lower personnel is met by resistance from doctors

- Brain drain an issue – we must address the retention of health care personnel

2) Cost

- Need more interaction with health economists
- Sustainability?
- We must look into different financial flows, the idea of marketing campaigns (i.e. RED, ONE Campaign), and alternate financing schemes to raise substantial sums

3) Coverage

- Feasibility of “mother-daughter” screening and vaccination project?
- Feasibility of self-screening?

4) Political will

- Need to sell a product to the policy makers? It is problematic to make a set of recommendations for African countries. The right screening depends on where you are. This is a highly heterogeneous environment and we can't settle on a one-size-fits-all approach
- As health care leaders, we must push for “dogmatic decisions to be replaced by research-based decisions...lobbying is good if it is on the basis of data, but not on the basis of fear” (Prof Gerhard Lindeque)
- Screening must be made part of a country's health policy
- Demonstration projects are a good way to show political leaders the efficacy of screening programs
- MDG goals 4 and 5 are a useful platform to use – argue that HPV is part of maternal health?

STREAM D - Creating a climate for informed decision-making in screening and vaccination

The delegates at this workshop suggested the following steps should be taken, to create a climate of informed decision-making about screening and vaccination programmes:

- Informed consent has to be tailored appropriately to population. Informed consent means different things in different situations and with different people, so it has to be appropriate to population.
- Screening should become part of routine care.
- Policy makers are not yet aware of the cost/toll of cervical cancer in their countries. Consequently, the development of cancer registries is important.
- Scientific evidence is important but a consensus statement can also be useful, for example from the world health organisation.
- Need to show politicians that the impact of screening would be seen now.
- Survivors' stories and the family stories of the women who have died of cervical cancer need to be told. Doctors and nurses should also tell stories about cervical cancer. We should not be afraid to tell individual stories; these are the ones that touch people.

- Partnerships need to be fostered with developed countries health systems.

Workshop 2 - Introduction of HPV vaccination: planning for delivery

There were four streams for this workshop:

STREAM A - What are the steps required in order to set up a demonstration project?

The participants in this workshop discussed the steps required to set up an HPV vaccination demonstration project, focusing in particular on the personnel, training, politics, and public education needs that would have to be addressed. The workshop participants agreed that if you undertake a good demonstration project in one country, then other countries would be more likely to follow. All demonstration projects should start with training and education which should be a coordinated between health professionals, the government and the public. The media would have an important role to build awareness and dispel concerns about the vaccine programme, and patients should be brought on board to tell their stories and it would be critical to include, and gain the support of, religious leaders in public discussions.

The workshop began by discussing HPV vaccination policies/beliefs/challenges in countries represented. In Nigeria, for example, participants explained that there were problems of awareness, communication, media education and sensitization. “Cancer” is a word in many local languages that implies gravity. However, a key problem would be the lack of knowledge of health professionals about cancer, especially concerning the HPV and cervical cancer link. In Uganda both vaccines (Gardasil, Cervarix) have been registered and are privately available. There are two public demonstration projects with over 90% coverage – here the key issue is what the next steps should be and whether it is now possible to expand to a national programme.

The participants also discussed whether demonstrations are critical and whether it was possible to translate from one country to another? They concluded that:

- Demonstrations are important as they allow for sensitization. They address the ignorance of health care workers and the barriers that may present.
- They also allow for problem solving – after all, long -term delivery mechanisms are not the same as a clinical trial, which is often well funded and tightly controlled.
- It is necessary to determine resources needed and the expectations of the population in each country.
- The group determined that demonstration projects were more important for Africa than for the EU. Africa is starting from scratch, but demonstrations may not be necessary in all countries – neighbouring countries may have acceptable similarities.

The group then discussed the use of personnel in demonstration projects. They concluded:

- In Uganda, EPI and district personnel can be used for administration of a vaccination project. No new infrastructure would be required other than a few refrigerators.
- The coordination of entities is the most important part of a demonstration project. Helps to have PATH for overarching coordination.

- Personal advocates, and their stories, help to promote HPV vaccination. The media, if used correctly, can have a positive impact. It is important, however, to provide follow-up assistance to any woman who makes her struggle with cervical cancer a public report.

STREAM B - Priorities for research for prophylactic HPV vaccination in Africa

The participants in this workshop discussed the key research questions that need to be examined about prophylactic HPV vaccination in Africa. They identified the following issues as being key areas which should be examined:

- What should the age of vaccination be – childhood is the ideal, but a range of other questions need to be examined. For instance, an interesting research question would be what would happen at a wider range of ages? Also, should HPV be part of the main childhood vaccination programmes for boys as well as girls? In Africa would it be useful to vaccinate boys? Ideally we should vaccinate both sexes at a wide range of ages. At present there is no safety or efficacy data on vaccinating infants or young children. In time the cost will come down so it may be feasible to do this.
- The main issue is HPV vaccine's immunogenicity i.e. how long will the antibodies persist? The most current data is from western world but there are three studies currently in Africa vaccinating 10-25yr olds. Immunogenicity in African populations must be studied. The HPV incidence 'graph' is different in Africa; high incidence is seen in early teens but as opposed to more developed countries, in Africa this incidence does not seem to go down. For childhood delivery i.e. combining HPV with diphtheria and Hep B vaccine already administered in infants, may have to study the effect of HPV vaccine on the others and the effect of the others on HPV. There is currently no data on infant HPV vaccine but infant vaccination is the most successful programme. A key question for research is if we vaccinate infants at six months do they still have antibodies at 12 years?
- Currently combined vaccinations are being looked at. Question would be does HPV modify antibody response for other vaccine or do others affect HPV? Would have to be placebo controlled trials to answer this eg. Diphtheria and Hepatitis B and Placebo or Diphtheria and Hepatitis B and HPV vaccination.
- Where there is a big effect i.e. huge incidence of HPV in Africa, we could just do observational study without randomisation to assess vaccine efficacy.
- Is there a prospect for accelerating development of polyvalent vaccine at a lower cost? If low cost vaccine is available then probably the ideal would be to vaccinate boys also. With polyvalent vaccines the only limit is the number of types that can be put into one vaccine in terms of volume.
- Given that different countries have different type prevalence might we reach a stage where polyvalent vaccines are specifically manufactured to suit different population?
- Although possible this is unlikely as it would be difficult in terms of FDA regulations. However the 8 most common HPV types causing cancer are the same for every continent, only the order of prevalence differs.

- Assessment of anti HPV 16/18 efficacy in Africa can probably be done observationally without randomisation. If 3 types of HPV are present in cervical cancer i.e. 16, 31, 45 we assume that the cancer is driven by 16 and not actually caused by all 3. Current school of thought is that if there are multiple types they are independent of each other.
- In Africa there is a high prevalence of HIV, eg. in some populations HIV prevalence reaches 30%.
 - What happens to girls who have been vaccinated with HPV then seroconvert to become HIV positive? Does the vaccine work equally well?
 - Do antibody levels to HPV maintain or will they need a booster vaccine?
 - Need to get to a stage where the HPV vaccine is being widely used and then undertake studies looking specifically at HIV positive populations.
 - Countries that are struggling with HIV problems however may need to know if there is a benefit to diverting some funds to introduce HPV vaccine.
 - Data on HIV/HPV will be needed ahead of routine vaccination otherwise where will countries put their effort?

STREAM C - How does the international community support funding of HPV vaccine

The delegates of this workshop discussed how the international community could support funding for the introduction of the HPV vaccine to Africa. They made the following recommendations:

- International community must support the HPV vaccine.
- GAVI support and funding for the HPV vaccine would be critical.
- It currently takes about 15 years between a vaccine being available in a developed country and a developing one. The vaccine price has to be affordable for African countries – this will need to be discussed with the pharmaceutical companies.
- When looking at the funding requirements for a vaccine programme, it is important to consider the broad delivery cost in addition to the vaccine cost
- We can look at the PATH projects for examples of good delivery of vaccines- so we don't have to start from scratch when designing implementation plans.
- We must recognise that there are competing health priorities in Africa, which mean there are other key demands for donors and African countries to address. Cost is a big issue and there is variable prioritisation of women's health. Women's health is valued in the western world; this is not always the case in Africa. Advocacy will be crucial in building support for donor and national funding towards HPV vaccination programmes in Africa. For this, there must be a broad advocacy coalition - more champions for HPV should be involved from all levels. Countries need to elect thought leaders. Best practice from demonstration projects will be a useful political tool.

In the plenary sessions of the conference, GSK said that it was committed to tiered pricing. Dr. Kate Taylor from GSK said that nearly 80% of the 1.1 billion doses of vaccines GSK produces annually goes to the developing world. The vaccines are subject to tiered pricing and the price is established by: the value of vaccine; country's ability to pay; volume purchased and duration of commitment. GAVI sponsored countries pay less; typically 10-

20% of the prices paid in the richest countries. GSK have the richest drug development pipeline and a third of this pipeline is aimed at diseases which primarily affect the developing world. Cervarix contains a different adjuvant (AS04) to Gardasil. AS04 appears to give higher antibody levels than than the same antigens formulated with AIOH. Cross protection against HPV types 45, linked with adenocarcinoma and type 52 has also been demonstrated with Cervarix. Both of these types are prevalent in Africa. Cervarix is currently approved in 97 countries and GSK are working with PATH on HPV demonstration projects in Uganda and India.

Dr. Joan Benson, from Merck, said that the company seeks to accelerate access to vaccines in the developing world through its research, relevant policy activities, no-profit pricing policy for Gardasil and RotaTeq, programs and partnerships. Merck is committed to offering GARDASIL (quadrivalent HPV vaccine), at a no-profit price - a price at which the company will not profit to the public sector of GAVI eligible countries. Merck understands that it will take multiple global partners to accelerate access to vaccines and seeks to identify potential partners to accomplish this goal. Merck is working with PATH on projects with Gardasil in India, Vietnam and Peru. Under the Gardasil access programme MSD will donate at least 3 million doses of Gardasil over 5 years to GAVI eligible countries. Gardasil is being registered in the poorest countries and currently approved in 14 countries in Africa. Merck is seeking WHO prequalification of Gardasil, which would help facilitate GAVI funding by GAVI and procurement by UNICEF and UN agencies.

These are fantastically generous offers from the pharmaceutical companies which give us a great opportunity to raise the necessary funds to get the vaccine into countries in Africa.

STREAM D - How should African health ministries respond to the challenge of preventing cervical cancer?

Whilst health ranks high in Africa, cervical cancer is ranked low. Consequently, the participants in this workshop suggested that efforts would need to be made to increase the priority that African health ministries give to cervical cancer prevention.

They recommended that:

- Cervical cancer should be included in cancer control plans which should be approved by parliament.
- It will be important to also form bridges and coordinate efforts between ministries of education for school-based programmes, and ministries of finance who should be made aware of women's affairs and encouraged to assign this a specific budget.
- Lobbying should also focus on getting cancer prevention designated a priority for aid from groups such as the Gates foundation and European Union.
- African ministers of health should advocate for cancer control to be seen as a priority within African union.

5. CONCLUSIONS FROM THE MEETING AND WAY FORWARD

This international meeting in Oxford took place to map out a strategy for cervical cancer prevention in Africa.

There was great excitement from the delegates about the impact that the introduction of the HPV vaccine could have in Africa. The costs of doing this have so far been prohibitive, as a course of vaccine jabs costs \$360 per girl, and is therefore way beyond the budget of most African governments. The delegates agreed that efforts need to be made to lower the cost of the vaccine for developing countries.

Early detection is also crucial in combating cervical cancer. In the last few years there have been some phenomenal improvements in screening technology, due to the development of low cost DNA tests aimed at detecting the HPV virus. Research suggests that even if women in developing countries had access to just one screening in their life-time, it could reduce their risk of cervical cancer by a third. The development of a rapid, point of care HPV test is welcomed and now requires implementation.

There was complete agreement among delegates that the only way to effectively prevent, detect and treat the rising numbers of cervical cancers in Africa is to develop broad partnerships of research institutions, international organizations, national governments in developed and developing countries, the pharmaceutical industry and international organizations. Strong local and international leadership is essential. The relevant organisations and individuals, with funds from government and private donors, must be brought together to develop achievable and sustainable cervical cancer prevention programmes for African countries.

At the end of the meeting, the delegates signed the Oxford Declaration committing, for the first time, to global cooperation to eradicate cervical cancer in Africa.

Participants (African First Ladies, African health ministers, clinicians, activists and representatives of NGOs and the pharmaceutical industry) attending this conference have unanimously agreed to the following three resolutions:

- We call upon all African governments to recognise and acknowledge the magnitude of the problem of cervical cancer in Africa and the need for immediate, coordinated international action.
- We will work with African Governments, NGOs and other international partners through consensus to implement effective cervical cancer screening including treatment programmes, taking into account the latest technology and ensuring equity of access for all women and girls.
- We will galvanise African Governments, the GAVI Alliance, the pharmaceutical industry, and other international partners to utilise newly emerging tools to deliver an effective and affordable programme of HPV vaccination to the nations of Sub-Saharan Africa and support research which will advance knowledge in this field.

The implementation of this declaration requires immediate, vigorous and collective action.

6. APPENDICES

APPENDIX I



PREVENTION OF CERVICAL CANCER IN AFRICA: A CALL TO ACTION THE OXFORD DECLARATION, 27 March 2009

Every 10 minutes, a woman in Africa dies from cervical cancer, despite the fact that almost every case is preventable through a programme of screening, treatment and vaccination against the Human Papilloma Virus (HPV).

Participants (African First Ladies, African health ministers, clinicians, activists and representatives of NGOs and pharmaceutical industry) attending this convention, organised by Afrox, have unanimously agreed to the following **three resolutions**:

1. We call upon all African governments to recognise and acknowledge the magnitude of the problem of cervical cancer in Africa and the need for immediate, coordinated international action.
2. We will work with African Governments, NGOs and other international partners through consensus to implement effective cervical cancer screening including treatment programmes, taking into account the latest technology and ensuring equity of access for all women and girls.
3. We will galvanise African Governments, the GAVI Alliance, the pharmaceutical industry, and other international partners to utilise newly emerging tools to deliver an effective and affordable programme of HPV vaccination to the nations of Sub-Saharan Africa and support research which will advance knowledge in this field.

We unanimously agree that implementation of this declaration requires immediate, vigorous and collective action.

All attendees at the AfrOx HPV Convention hereby commit their support to this Declaration:

Her Excellency Dr	Turai Umaru	Yar'Adua	First Lady of Federal Republic of Nigeria
Her Excellency, Mrs	Janet	Museveni	First Lady of Republic of Uganda and member of Parliament
Professor	Isaac	Adewole	College of Medicine, University of Ibadan, Nigeria
Ms	Rebecca	Affolder	GAVI Alliance, Switzerland
Dr	Raghib	Ali	University of Oxford, UK
Sir	John	Arbuthnott	University of Oxford, UK
Miss	Suzanne	Ashman	University Hospital of Wales, UK
Mr	Lekan	Asuni	GSK Pharmaceuticals, Anglophone West Africa, Nigeria
Mr	Hassan	Azadeh	Foundation for Research on Women's Health, Productivity and the Environment, The Gambia
Dr	Joan	Benson	Merck & Company Inc, USA
Dr	William	Bosu	Disease Control and Prevention Dept, Ghana
Mrs	Carolyn	Burgess	Language is Everything, UK
Dr	Mark	Clanton	American Cancer Society, USA
Mrs	Ramou	Cole-Ceesay	Dept of State for Health, The Gambia
Mr	Mark	Connolly	Global Market Access Solutions, Switzerland
Professor	Heather	Cubie	Royal Infirmary of Edinburgh, UK
Dr	Myfanwy	Davies	University of Cardiff, UK
Dr	Philip	Davies	ECCA, France

Ms	Maria Stella	De Sabata	Fondo Anglesio Moroni, Italy
Professor	Francis Abayomi	Durosinmi-Etti	National Consultative Committee on Cancer Control, Nigeria
Prof Dr	Ahmed	Elzawawy	ICEDOC, Egypt
Ms	Julia	Emanuel	
Professor	Alison	Fiander	Cardiff University, UK
Dr	Kenneth	Fleming	University of Oxford, UK
Dr	Silvia	Franceschi	IARC, France
Dr	Felix	Frempong	Ghanaian Cancer Society, Ghana
Dr	Hadiza	Galadanci	Aminu Kano Teaching Hospital, Nigeria
Prof	Winald	Gerritsen	VUmc Cancer Centre, The Netherlands
Dr	Joe	Harford	National Cancer Institute, USA
Dr	Danielle	Heideman	VU University Medical Centre, The Netherlands
Dr	Luc	Hessel	Sanofi Pasteur MSD, France
Dr	Mariatou	Jallow	Ministry of Health, The Gambia
Dr	Mark	Jit	University of Birmingham, UK
Miss	Shoned	Jones	University of Cardiff, UK
Miss	Victoria Isabelle	Kay	UICC, Switzerland
Miss	Susan	Keese	Qiagen UK Ltd, UK
Prof	Sean	Kehoe	The Womens Centre, Oxford Radcliffe NHS Trust, UK
Prof	David	Kerr	SIDRA, Qatar and University of Oxford, UK
Prof	Henry	Kitchener	University of Manchester, UK

Dr	Nicholas	Kitchin	Sanofi Pasteur MSD, UK
Dr	Mark	Krul	Aglaia Oncology Fund, The Netherlands
Dr	Jeremy	Lauer	WHO, Switzerland
Prof	Gerhard	Lindeque	University of Pretoria, South Africa
Miss	Isabel	Litwin-Davies	University of London, UK
Dr	Julian	Lob-Levyt	GAVI Alliance, Switzerland
Mr	Attahirli	Maccido	Federal Ministry of Women Affairs & Social Development, Nigeria
Dr	Helen	McShane	University of Oxford, UK
Dr	Rachel	Midgley	University of Oxford, UK
Professor	Florence	Mirembe	Makerere University, Uganda
Dr	Jo	Morrison	University of Oxford, UK
Dr	Emmanuel	Mugisha	PATH, Uganda
Dr	Twalib	Ngoma	AORTIC, Tanzania
Hon	Sarah	Nyombi	Parliament of Uganda, Uganda
Lady	Theresa Nkeoma	Nwosu	Princess Nikky Breast Cancer Foundation, Nigeria
Professor	Ifeoma	Okoye	Dept of Radiation Medicine, College of Medicine, University of Nigeria, Nigeria
Princess	Nikky	Onyeri	Princess Nikky Breast Cancer Foundation, Nigeria
Dr	Patience	Osinubi	Federal Ministry of Health, Nigeria
Professor	Julian	Peto	London School of Hygiene & Tropical Medicine and the Institute of Cancer Research, UK
Prof Sir	Richard	Peto	University of Oxford, UK

Mr	Tom	Peto	London School of Hygiene & Tropical Medicine and the Institute of Cancer Research, UK
Mr	Doug	Pyle	American Society of Clinical Oncology, USA
Dr	Anne	Reeler	Axios International, France
Mr	Dave	Roberts	Morgan Roberts Ltd, UK
Ms	Anne	Ruglys	Sanofi Pasteur MSD, UK
Dr	Joseph	Saba	Axios International, France
Rev Fr	Victor	Sackey	Cancer Society of Ghana, Ghana
Miss	Panayota	Sakulias	GSK, UK
Dr	Rengaswamy	Sankaranarayanan	IARC, France
Professor	Peter	Snijders	VU University Medical Centre, The Netherlands
Professor	Margaret	Stanley	University of Cambridge, UK
Hon Minister	Salamatu	Suleiman	Federal Ministry of Women Affairs & Social Development, Nigeria
Dr	Kate	Taylor	GSK Biologicals, Belgium
Dr	Julie	Torode	International Union Against Cancer, Switzerland
Dr	Amanda	Tristram	Cardiff University, UK
Dr	Vivien	Tsu	PATH, USA
Dr	Deborah	Watson-Jones	London School of Hygiene and Tropical Medicine, UK
Professor	Edwin	Wiredu	University of Ghana, Ghana
Mr	Scott	Wittet	PATH, USA

APPENDIX II

Agenda for the Oxford Meeting



Towards Prevention of Cervical Cancer in Africa

Thursday 26 to Friday 27 March 2009

Bernard Sunley Building, St Catherine's College, Oxford, UK

Day 1: Thursday 26 March

08.30 – 09.00

Arrival/Registration (tea and coffee)

09.00

Welcome/Introduction

Prof Sir Richard Peto

09.10

Introduction of First Ladies

Princess Nikky Onyeri

09.20

Views from Africa: the Ugandan experience from the First Lady of Uganda (Chairperson of the African Forum against Breast and Cervical Cancer)

Her Excellency Hon. Mrs Jane Museveni

09.30

Views from Africa: Nigerian experience from the First Lady of Nigeria

Her Excellency Hon. Dr Hajiya Turai Umaru Yarl Adua

09.40 – 13.10

Plenary Talks

Session Chair:

Princess Nikky Onyeri

09.40

The cause of cervical cancer - HPV infection

Dr Amanda Tristram

10.10

Opportunities for cervical cancer prevention

Prof Isaac Adewole

10.40

Acceptability of cervical cancer prevention programmes repercussions for uptake

Dr Myfanwy Davies

11.10

Tea/Coffee

Session Chair:

Professor Gerhard Lindeque

11.40

Appropriate cervical screening (Future developments in cervical screening)

Dr Rengaswamy Sankaranarayanan

12.10	Prophylactic HPV vaccination	Prof Margaret Stanley
12.40	International funding effort: the view from GAVI	Dr Julian Lob-Levyt

12.50 Lunch

14.00 Addressing the problem of cervical cancer in Africa – answering the unknowns, evaluating interventions, demonstration project(s) (Introduction to workshops) **Professor Alison Fiander**

14.30– 16.00 Workshop 1: Introduction of appropriate cervical screening: Planning for delivery

Each stream to have facilitator and short introduction to set scene and task of group

- (A) The ideal criteria for a cervical screening demonstration project
 - What are the essential questions to answer?

Chair: Dr Silvia Franceschi
Rapporteur: Dr William Bosu

- (B) Pre-requisites for cervical screening: infrastructure, funding, training
 - What's in place already and what's needed?

Chair: Dr Mariatou Jallow
Rapporteur: Dr Mark Clanton

- (C) Evaluation & cost effectiveness of cervical screening
 - How to evaluate and measure cost effectiveness i.e programme evaluation

Chair: Dr Julie Torode
Rapporteur: Professor Sean Kehoe

- (D) Creating a climate for informed decision making in screening and vaccination: more than just facts?
 - Societal issues: key issues for a successful programme in creating a climate for prevention

Chair: Dr Twalib Ngoma
Rapporteur: Mr Scott Wittet

16.00 Tea

16.20 – 17.00 Plenary session (Chair: Francis Abayomia Durosinmi-Etti)
Feedback from each workshop stream & discussion

19.30 Reception - JCR Lounge
8.00 Dinner - Hall

Day 2: Friday 27 March

Session Chair: Dr Joseph Saba

- 08.45 Health investment modelling and vaccination programs: applications to HPV **Dr Mark Connolly**
- 09.15 Enabling sustainable access for cervical cancer vaccine – one company’s approach **Dr Kate Taylor**
- 9.30 Accelerating HPV Vaccine Access in Developing Countries **Dr Joan Benson**
- 09.45 Practical examples from prevention of cervical cancer demonstration projects **Dr Vivien Tsu**
-

10.15 – 11.30 Workshop 2: Introduction of HPV vaccination: planning for delivery

- (A) What are the steps required to set up a demonstration project (personnel, training, politics, public education)?
Chair: Dr Emmanuel Mugisha
Rapporteur: Professor Winald Gerritsen
 - (B) Priorities for research for prophylactic HPV vaccination in Africa
Chair: Sir Richard Peto
Rapporteur: Professor Ahmed Elzawawy
 - (C) How does the international community support funding of HPV vaccine?
Chair: Dr Joe Harford
Rapporteur: Ms Rebecca Affolder
 - (D) How will the African Health Ministries respond to the challenge of preventing cervical cancer?
Chair: Dr Philip Davies
Rapporteur: Mrs Ramou Cole-Cessay
-

11.50 Coffee/tea

11 50 – 12.50 **Plenary session (Chair: Professor Edwin Wiredu)**
Feedback from each workshop stream & discussion

13.00 Lunch

14.00 Action/taking forward the prevention of cervical cancer in Africa **Dr Twalib Ngoma/
Prof Alison Fiander**

14.30 Formulating the Oxford Declaration - Calling for International Action on Cervical Cancer **Sir John Arbuthnott/
Princess Nikky Onyeri**

15.00 Close of meeting

APPENDIX III

Media Coverage of Oxford Meeting

1. Africa faces 'cancer steam train', Thursday 26th March 2009

BBC News Website

<http://news.bbc.co.uk/1/hi/health/7964413.stm>

2. Good morning Wales, interview with Alison Fiander, 6.25am, Thursday 26th March 2009

BBC Wales

3. World Briefing, 3.16pm, Thursday 26th March 2009

BBC World Service

4. Newshour, 8.50pm, Thursday 26th March 2009

BBC World Service

5. Radio 4 news, 5.30pm, Friday 27th 2009

BBC Radio 4

6. Interview with David Kerr, How to make drugs more accessible, genetics and access to counterfeit drugs, Health Check, Monday 30th March 2009

BBC World Service Radio

7. Kill or Cure: The Real Lady Killer, aired Tuesday 21 July 2009 (Rockhopper Productions)

This documentary on cervical cancer in Uganda featured interviews with Sarah Nyombi (MP, Uganda) and Julian Lob-Levyt (Executive Secretary, GAVI Alliance) at AfrOx's "Towards the Prevention of Cervical Cancer" conference.

BBC World News

<http://www.rockhopper.tv/programmes/260>

8. David Kerr on Preventing Cervical Cancer in Africa

British Medical Journal Blog

<http://blogs.bmj.com/bmj/2009/03/30/david-kerr-on-preventing-cervical-cancer-in-africa/>

9. Providing Hope in Africa's Battle Against Cervical Cancer

www.Physorg.com

<http://www.physorg.com/news157305596.html>

10. Oxford Declaration prompts urgent action in fight against cervical cancer in developing countries

www.uicc.org

http://www.uicc.org/index.php?option=com_content&task=view&id=16610&Itemid=664

11. Oxford Declaration

www.gavialliance.org

http://www.gavialliance.org/resources/declaration_final_draft_2.pdf

12. "Towards Prevention of Cervical Cancer in Africa", forthcoming September 2009

Interviews with Julian Lob-Levyt (GAVI Alliance), Princess Nikky Onyeri (Princess Nikky Breast Cancer Foundation) and Dr. Sankaranarayanan (IARC).

"Cancer in the Developing World" podcast series, Oxford University

<http://podcasts.ox.ac.uk/>

8. ACKNOWLEDGEMENTS

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