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The potential cost-effectiveness of adding a human papillomavirus vaccine to the cervical cancer screening programme in South Africa

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ABSTRACT

This study was designed to answer the question of whether a cervical cancer prevention programme that incorporates a human papillomavirus (HPV) vaccine is potentially more cost-effective than the current strategy of screening alone in South Africa. We developed a static Markov state transition model to describe the screening and management of cervical cancer within the South African context. The incremental cost-effectiveness ratio of adding HPV vaccination to the screening programme ranged from US $1078 to 1460 per quality-adjusted life year (QALY) gained and US$3320–4495 per life year saved, mainly depending on whether the study was viewed from a health service or a societal perspective. Using discounted costs and benefits, the threshold analysis indicated that a vaccine price reduction of 60% or more would make the vaccine plus screening strategy more cost-effective than the screening only approach. To address the issue of affordability and cost-effectiveness, the pharmaceutical companies need to make a commitment to price reductions.

1. Introduction

Human papillomavirus (HPV) causes approximately half a million new infections and around 270 000 deaths from cervical cancer every year worldwide, and 80% of these occur in resource-poor countries such as Africa, Latin America and south-east Asia [1]. Although cervical cancer mortality can be significantly reduced through screening and early treatment programmes, ensuring access to and utilisation of these services is a particular challenge in resource-poor settings [2–5].

Currently there are two prophylactic HPV vaccines: a bivalent vaccine targeted at the oncogenic HPV16 and HPV18 (Cervarix, GSK), and quadrivalent vaccine targeted at these two oncogenic types as well as the HPV types 6 and 11, which are primarily responsible for genital warts (Gardasil, Merck). Both vaccines have been shown to be safe and highly effective against type-specific persistent infection [6,7]. Modelling studies have estimated that a vaccine preventing 75% of persistent HPV (types 16 and 18) infections could be associated with a 70–83% reduction in HPV-related cancer [8].

Economic models are used in estimating cost-effectiveness of a new intervention and in identifying the best strategies for its introduction. In high-resource countries such as Australia, Canada, the United Kingdom and the United States (US), cohort models have been used to estimate cost-effectiveness of HPV vaccines and found that, in a setting of existing cervical cancer screening, the addition of an HPV vaccine has the potential to be a cost-effective use of health care resources [9–13]. In low- and middle-income countries, however, whilst potentially cost-effective, HPV vaccines may be unaffordable at the current market price of US $120 per dose [14–16]. In addition, a number of other very cost-effective public health interventions, such as treatment for tuberculosis, childhood diarrhoea and malaria, hepatitis B vaccine, and HIV/AIDS prevention strategies compete for the same limited resources [17].

In South Africa, cervical cancer is the most common cancer in women with an annual crude incidence rate of 30.2 per 100 000 women [18]. It has been estimated that around 6800 women in South Africa face new cases of cervical cancer, and 3700 deaths occur each year [18]. In 2000, a national cervical cancer screening policy was introduced [19]. The policy goal is to screen at least 70% of women attending public sector services over a 10-year period, using the Papanicolaou cytology technique (Pap smear). Women attending public sector services are entitled to 3 free Pap smears per lifetime at 10-year intervals, starting at age 30. However, the gap between this policy and its implementation is significant [20]. In 2008, both HPV vaccines were licensed and marketed at US $120 per dose in South Africa. At the time of this study, the vaccines were not available in the public sector.

The recent development of the HPV vaccine offers a new approach to cervical cancer prevention in South Africa. This study was designed to answer the question of whether a cervical cancer

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prevention programme that incorporates an HPV vaccine is potentially more cost-effective than the current strategy of screening alone. It was part of a broader study exploring challenges and barriers to potential HPV vaccine introduction in the public sector in South Africa [21].

2. Methods

2.1. Strategies compared in the study

In our model, we compared two different strategies for the base-case scenario: (1) the current strategy within the National Cervical Cancer Screening Programme for diagnosis of cervical disease [19]. According to the public sector national guidelines, screening using conventional cervical cytology is performed 3 times at 10-year intervals starting at age 30; and (2) vaccination of 12-year-old girls followed by screening as described above.

2.2. Modelling

We developed a static Markov state transition model to describe the screening and management of HPV infection and cervical cancer within the South African context. The model has two arms: one that follows the study population who were not vaccinated but only

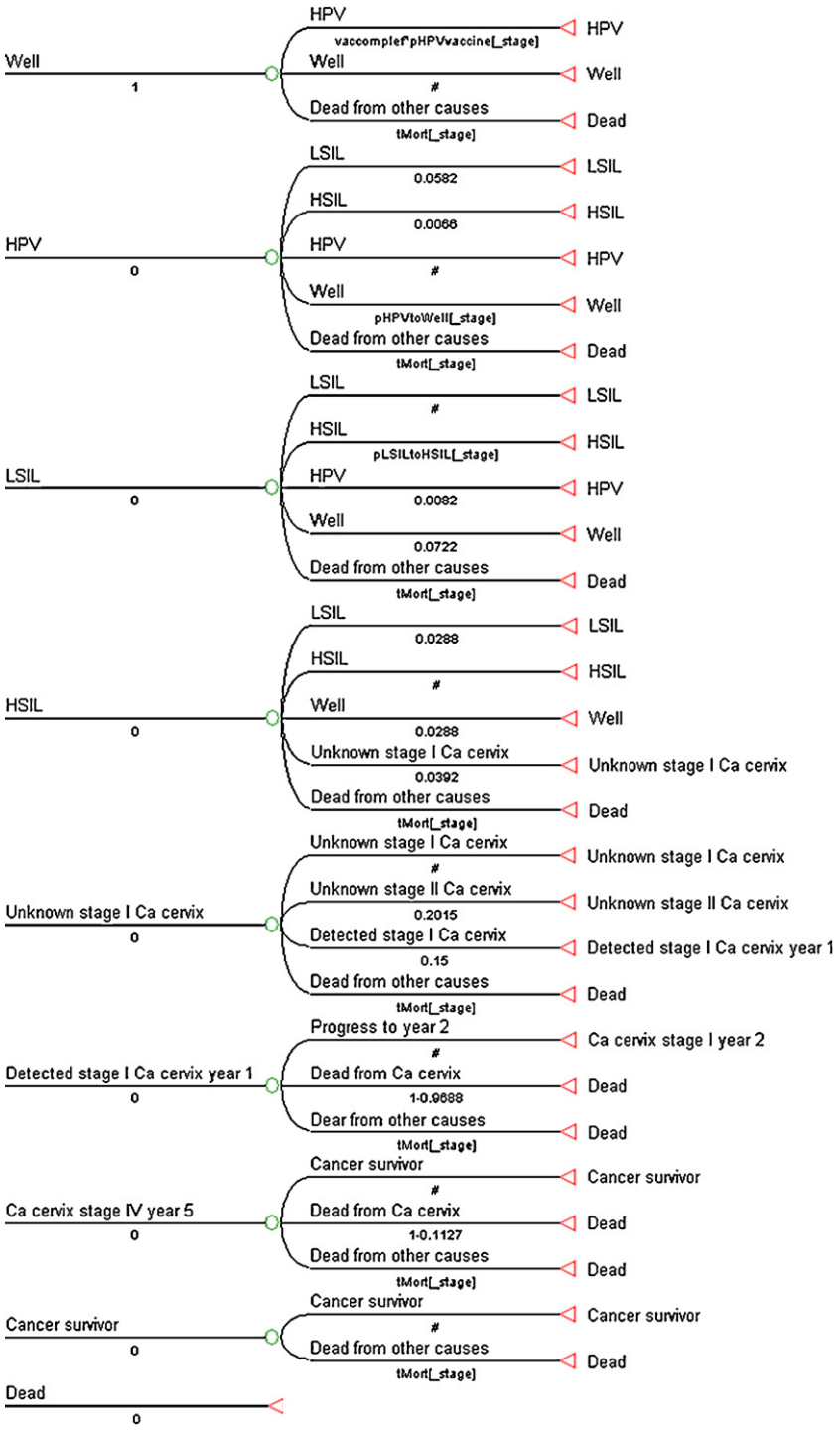

Fig. 1. Health states and possible transitions between states (simplified version of the Markov model, the vaccine arm).

screened and appropriately treated (the non-vaccine arm), and the other which follows the study population who is vaccinated at age 12 and then screened following the national screening protocol and appropriately treated (the vaccine arm).

The model allowed us to compare the two different strategies for prevention of HPV infection and cervical cancer. We adapted a previously published Markov model [12,22] to estimate the lifetime costs and life expectancy of a hypothetical cohort (100 000) of women screened for cervical cancer, and women vaccinated at age 12 and then screened following the national screening protocol. The hypothetical population consisted of women between the ages of 12 and 85.

The Markov model was developed using TreeAge Pro Healthcare 2007 Suite software (Release 1.4) [23]. Data on cancer related and all-cause mortality rates from the Medical Research Council and the Actuarial Society of South Africa were used to build the model. The prices of screening tests and vaccines were obtained from the local manufacturers. All other data were derived from the literature, including data from South Africa when it was available. The face validity of the model was established by consulting local experts on assumptions regarding the natural history of HPV infection, disease and treatment and resulting model predictions.

Thirty health (Markov) states were determined by consideration of other similar models used for evaluating cervical cancer screening and treatment interventions [8,12,22] (Fig. 1). Due to the slow progression from HPV infection to disease, we used a relatively long time horizon (the model starts at age 0 and finishes at age 85). Each year women face an age-specific risk of acquiring HPV infection that could either persist, progress to a low-grade squamous intraepithelial lesion (LSIL) or a high-grade squamous intraepithelial lesion (HSIL) or resolve. Those who develop LSIL or HSIL could have their disease persist, regress, or progress. Women with cancer could have their disease detected if they have an examination based on their symptoms or remain undetected. When detected, they can survive or die from cancer. We assumed that women who survive five years after cancer diagnosis and treatment become survivors and can die only from other causes. If not detected, they could either progress to the next stage or remain in the same stage. As the natural history of HPV infection is complex, the study does not distinguish between different types of HPV, and incidence, progression and regression estimates are averages for all main viral types.

Each year, women also face age-specific risks of dying from other causes. Mortality from other causes other than cervical cancer was estimated by subtracting age-specific cervical cancer mortality rates from age-specific all cause mortality rates using the Actuarial Society of South Africa (ASSA) 2003 AIDS and Demographic model [24]. Given the potential impact of human immunodeficiency virus (HIV)-related mortality on the effectiveness of the HPV vaccine (according to the ASSA 2003 model, 47% of all deaths were caused by HIV/AIDS), the base-case scenario included HIV-related mortality, whilst in a sensitivity analysis, HIV-mortality was removed.

Model parameters and assumptions for screening, treatment and vaccination are summarised and presented in Table 1. It was assumed that all 100 000 women are disease free at the start of the model (all are in the Well state). The transition probabilities between the different Markov states were derived from a previously published study [22] (Table 1). The cycle length is the time between successive transitions between Markov states. It is chosen depending on the disease and intervention being studied. In this model, a one-year cycle was used.

2.3. Costing methods

An ingredients approach to costing was used for determining provider costs (capital and recurrent) associated with vaccination (through a school-based programme), screening and management

Table 1
Model parameters: base-case estimates and sources.

Parameters	Base-case estimate	Source
Epidemiological parameters[a]		
Age-specific incidence of HPV infection[b]		[22]
15–16	0.1/12 months	
17	0.12/12 months	
18	0.15/12 months	
19	0.17/12 months	
20	0.15/12 months	
21	0.12/12 months	
22–23	0.10/12 months	
24–29	0.05/12 months	
30–49	0.01/12 months	
≥50	0.005/12 months	
Age-specific regression rate (HPV to Normal)[b,c]		[22]
15–24	0.7/18 months	
25–29	0.5/18 months	
≥30	0.15/18 months	
Progression rate HPV to LSIL[c]	0.2/36 months	
Proportion of infections progressing directly to HSIL	0.1	[22]
Regression rate LSIL to HPV or Normal[b,c]		
15–34	0.65/72 months	[22]
≥35	0.4/72 months	
Proportion of LSIL reverting to Normal[c]	0.9	[22]
Progression rate LSIL to HSIL[b,c]		
15–34	0.1/72 months	[22]
≥35	0.35/72 months	
Regression rate HSIL to LSIL or Normal[c]	0.35/72 months	[22]
Proportion of HSIL reverting to Normal[c]	0.5	[22]
Progression rate HSIL to stage I cancer	0.4/120 months	[22]
Progression rates and probability of symptoms in unscreened patients		
Stage I	0.9/4 years	[22]
Progression rate (stage I to stage II)	0.15	
Annual probability of symptoms		
Stage II	0.9/3 years	
Progression rate (stage II to stage III)	0.225	
Annual probability of symptoms		
Stage III	0.9/2 years	
Progression rate (stage III to stage IV)	0.6	
Annual probability of symptoms		
Stage IV	0.9	
Annual probability of symptoms		
Five-year survival after diagnosis		
Stage I	0.83	[22]
Stage II	0.65	
Stage III	0.37	
Stage IV	0.11	
Screening		
Eligibility	Age 30, 40 and 50	[19]
Coverage	0.50	Assumption
Loss to follow-up	0.15	[14]
Treatment[e]		
Proportion of women with HSIL receiving loop electrosurgical excision procedure (LEEP)	0.80	Expert opinion
Proportion of women with HSIL receiving cold-knife conization	0.10	Expert opinion
Proportion of women with HSIL receiving simple hysterectomy	0.10	Expert opinion

Table 1 (*Continued*)

Parameters	Base-case estimate	Source
Proportion of women with invasive cancer having surgery (hysterectomy)	0.25	Expert opinion
Proportion of women with invasive cancer receiving chemo-radiation	0.75	Expert opinion
Adherence to treatment for cervical pre-cancerous and cancerous lesions	1.00	Assumption
Vaccine		
Age of vaccination	12	Assumption
Coverage	0.80	Assumption
Efficacy against HPV 16 and 18	0.90	[25]
Proportion of vaccinated women completing 3 doses	1.00	Assumption
Proportion of vaccinated women having a booster	0.50	Assumption
Duration of efficacy	Lifetime	[7]
Health-related quality of life weights for health states		
LSIL	0.91	[27]
HSIL	0.87	[27]
Cancer stage I	0.65	[8]
Cancer stage II	0.56	[8]
Cancer stage III	0.56	[8]
Cancer stage IV	0.48	[8]
Cancer survivor	0.84	[27]

[d]Women with abnormal cytology results classified as LSIL had a repeat Pap smear after 12 months, and if the infection persisted, were referred for further diagnosis. Women with abnormal results classified as HSIL or cancer received colposcopy and biopsy examination.

[a] As the probabilities were expressed as rates (the number of events per unit time), for the Markov model, rates were converted into probabilities.

[b] Acquisition of HPV, LSIL and HSIL was based on age-specific incidence rates.

[c] It was assumed that women can progress and regress (except for the cancer states) between various states.

[e] HPV 16 and 18 infection was asymptomatic and was not therefore treated.

of patients in each arm. Most of these estimates were based on published costing studies from South Africa [2,4]. The reported costs were converted to Rand and were inflated using consumer price index (CPI) figures [26] to 2007 values, and then converted to US $ at the average exchange rate US $ to South African Rand (R) for 2007 of US $1 = R6.5. All costs are reported in 2007 US $.

Cost to the patient included time cost (travelling time and time spent waiting for and receiving care) and transport cost. Patient costs were derived from a previously published study [4].

2.4. Effectiveness measurement

Effectiveness was expressed in life years saved and quality-adjusted life years (QALYs) gained. With QALYs, both the quality and quantity of the years of life a patient is expected to have are assessed. The gain in life years resulting from the intervention, weighted for quality, is the natural way to measure them and they are unaffected by considerations of the average length and quality of life of people that do not need the intervention. On the contrary, disability-adjusted life years (DALYs) were originally developed to measure the current burden of disease for a population where the burden is the gap between the health of a specific, real population and ideal, healthier population. For this reason, we think that the use of QALYs is more appropriate for this study design than the use of DALYs. QALYs are calculated by estimating the total life-years gained from a treatment by weighting each year with a quality of life score (from 0, representing worst health, to 1, representing best health) to reflect the quality of life in that year. Since there were no published health state values or utilities that were applicable to all disease states associated with cervical cancer screening, prevention and treatment in South Africa, quality of life weights from the available literature were used in the model [8,27]. These weights are summarised in Table 1.

2.5. Cost-effectiveness analysis

The cost-effectiveness of adding the HPV vaccine to the secondary cervical cancer prevention programme was estimated in terms of incremental cost per life year saved, and incremental QALY gained (compared with the current strategy—i.e. screening only). The cost-effectiveness analysis was prospectively undertaken from a health service perspective (the costs of providing different screening, treatment and vaccination services borne by the public sector organisations delivering the services and the Provincial Reproductive Health Programme) and a societal perspective (health service perspective and patient's travel and time costs). The analysis focused on the costs (and savings) of an integrated programme. In the base-case, costs and out-

Table 2
Unit cost of vaccination, screening, diagnosis and treatment of SIL and cancer in 2007 US $.

	Health service cost	Patient cost	Total cost
Vaccination[a]	559	11	570
Lifetime screening using cervical cytology[b]	60	33	93
Lifetime screening using HPV DNA[b]	276	33	309
Lifetime screening using VIA[b]	42	33	75
Diagnosis and treatment of low SIL[c]	39	22	61
Diagnosis and treatment of high SIL[d]	689	75	764
Diagnosis and treatment of cervical cancer[e]			
Stage I	3923	692	4615
Stage II	5361	946	6307
Stage III	5361	946	6307
Stage IV	7323	1292	8615

[a] The cost of vaccination included the cost of the HPV vaccine for 3 doses (US $360) and a booster (US $120), four administration visits, and wastage costs of 15%. It was assumed that the vaccine is administered in schools (except for the booster administration which is clinic-based): programme costs of 25% were therefore added to estimate the total cost of the vaccination programme [29].

[b] The costs of screening included screening test costs (cervical cytology in the base-case analysis), clinic visit costs, and patient costs. In the public sector, the screening service is free of charge at the point of use.

[c] For LSIL, the cost of screening and two clinic visits were included. This is based on the standard practice in South Africa where women diagnosed with LSIL are not offered any treatment but are screened 12 months after the initial diagnosis. If the infection persists, they are referred for further diagnosis.

[d] For HSIL, the medical care costs included the cost of colposcopy and biopsy (100% of cases), LEEP (80% of cases), cold-knife conization (10% of cases) and simple hysterectomy (10% of cases).

[e] For the treatment of cancer, costs were estimated for the four stages of cancer, including the cost of surgery and the cost of chemo-radiation.

Table 3
Cost-effectiveness of adding the HPV vaccine to the existing screening programme in 2007 US$.

Strategy	Lifetime cost in US $	Life years saved	QALY gained	ICER (life years)	ICER (QALY gained)
From the perspective of health service					
Undiscounted					
Screening only	642	51.95	51.74	Dominated	Dominated
Vaccine plus screening	493	52.07	52.04	More cost-effective	More cost-effective
Discounted at 3%					
Screening only	181	24.13	24.08	–	–
Vaccine plus screening	281	24.22	24.15	4495	1460
From the perspective of society					
Undiscounted					
Screening only	755	51.95	51.74	Dominated	Dominated
Vaccine plus screening	517	52.07	52.04	More cost-effective	More cost-effective
Discounted at 3%					
Screening only	216	24.13	24.08	–	–
Vaccine plus screening	289	24.16	24.15	3320	1078

comes were both discounted at the standard discount rate of 3% [28].

2.6. Dealing with uncertainty

To reflect the uncertainty inherent in the analysis, sensitivity analysis was performed using alternative assumptions regarding (1) the screening test (direct visual inspection of the cervix with acetic acid (VIA) and HPV DNA test); (2) screening coverage (20% and 70%); (3) vaccine efficacy (70% and 100%) (4) vaccine coverage (60–100%); (5) delivery options (a clinic-based vaccination programme within the existing national immunisation schedule); (6) mortality rates from other causes (excluding HIV-related mortality); (7) discount rate for both costs and benefits (6%); and (8) health-related quality of life weights (10% reduction for each health state). In addition, a threshold analysis was performed to calculate the price of the vaccine at which the non-vaccine arm would have the same overall cost as the vaccine arm. This represents the point at which vaccination becomes a cost saving strategy for South Africa.

3. Results

The societal cost per vaccinated girl was US $570 (Table 2). The most costly screening strategy is HPV DNA test ($309 per women), followed by cervical cytology ($93) and VIA ($75). The diagnosis and treatment of HSIL is almost 13 times more costly than for LSIL. The cost of diagnosis and treatment of cervical cancer stage IV is almost double the cost of that for stage I. Although screening is free of charge in the public sector, women incur transport costs and time lost from work (11–44% of the total cost).

The undiscounted and discounted lifetime costs, life years, QALYs and incremental cost-effectiveness ratios (ICERs) of adding vaccination to the existing cervical cancer screening are presented in Table 3. When costs and benefits are not discounted, the vaccine followed by screening strategy is more cost-effective, and the screening only strategy is dominated. When cost and benefits are discounted, the ICERs are US $3320 and 4495 per life-year saved (US $1078 and 1460 per QALY gained) from the health service and societal perspective, respectively.

3.1. Sensitivity analyses

The results were robust in sensitivity analyses (Table 4) with the ICER most sensitive to discount rate, vaccine price and vaccine efficacy. As the real benefit of the vaccine is captured in the long-term future (30–40 years after vaccination at the age of 12), the cost-effectiveness of adding the vaccine to the screening programme is significantly affected by discounting. The main cost driver in the vaccine arm is the vaccine price. Using discounted costs and benefits, the threshold analysis indicated that a price reduction of 60% (to US $192 from now US$480 for 4 doses) or more would make the vaccine arm more cost-effective than the screening only arm. The cost-effectiveness of vaccination is sensitive to increases in mortality from HIV/AIDS, and well as changes in the health-related quality of life weights.

Table 4
The impact of alternative assumptions for vaccine price and efficacy, type of vaccination programme, mortality tables, screening test and discount rate.

Parameter	Increase/decrease in ICER
Screening test	
DNA	−1.4%
VIA	−0.3%
Screening coverage	
20%	−10.4%
70%	+1.9%
Vaccine price	60% reduction in price would make the ICER of the screening + vaccine strategy equal to the ICER of the screening only strategy
Vaccine efficacy	
70%	+53.6%
100%	−19.3%
Clinic-based vaccination programme	+7.3%
Vaccine coverage	
60%	+12.9%
100%	−12.9%
HIV/AIDS-related mortality excluded (for dying from other causes)	−15.3%
Discount rate	
6%	+30.0%
Health-related quality of life weights reduction of 10% for each health state	Between −7.2% and −8.9%

4. Discussion and conclusions

To our knowledge, this is the first study undertaken in South Africa exploring the cost-effectiveness of adding the HPV vaccine to the existing cervical cancer prevention programme. Our study showed that adding the HPV vaccine to the current cervical cancer screening strategy in South Africa is cost-effective. The incremental cost-effectiveness ratio of adding HPV vaccination to the screening programme ranged from US $1078 per QALY gained to US $4495 per life year saved, mainly depending on whether the study was viewed

from a health service or a societal perspective. When patient costs were included in the analysis, the ICER decreased by 26% on average. Therefore, whilst the presence of vaccination has the potential to reduce the cost of cervical cancer to the health system, it also can potentially decrease the cost to the patient—not an insignificant finding taken the current levels of poverty in South Africa.

The study provides evidence on the potential cost-effectiveness of adding a vaccine to the current screening programme to prevent HPV-related diseases. South Africa does not have a willingness to pay threshold per QALY gained. However, if one uses the suggestion of the Commission on Macroeconomics and Health that interventions with an incremental cost-effectiveness per QALY gained below the country's gross domestic product (GDP) per capita would be "very cost effective" [30], then adding the HPV vaccine would be considered very cost-effective since South Africa's GDP per capita is US $5724 [31] and the ICER per QALY gained by adding the vaccine is between US $1078 and US $1460. We have not estimated the budget impact of scaling up of the intervention as this was beyond the scope of the study. It is likely, however, that the budget impact will be considerable because of the larger size of the population eligible for vaccination.

The study findings are similar to earlier analyses of cervical cancer screening in South Africa which reported the cost-effectiveness ratio of cytology screening in the range US $757–1410 per life year saved depending on the number of times the screening is offered and the number of visits associated with the screening (the original findings were expressed in 2000 international dollars but were converted here to US $ using a purchasing power parity of 2.67[15] and exchange rate for 2000 of 6.9 Rand/US $ in order to compare with our results) [3]. The findings also compare favourably with a study on the cost-effectiveness of antiretroviral treatment (ART) interventions in South Africa which estimated the ICER of ART versus no-ART to be US $1102 per QALY gained [32]. It is necessary, however, to consider potential biases caused by differences in methodology and perspectives when making these comparisons.

The cost-effectiveness of vaccination decreases with increasing HIV-related mortality. However, the data on HIV-related mortality used in our model assumes a low access to ART. If ART is scaled-up in the country, it is possible that vaccination will become more cost-effective, particularly given the vulnerability of HIV-positive women to cervical cancer.

It is vital to emphasise that, whilst recognising the potential impact of the vaccine on the incidence of HPV-related disease, and consequently the significantly reduced cost of treating cervical cancer, a well-functioning screening programme aimed at secondary prevention of cervical cancer is crucial as the HPV vaccine does not eliminate, but rather reduces the risk of cervical cancer. On the other hand, in settings where screening coverage is very low, like in South Africa where the coverage is well below 50% and adherence to treatment of pre-cancerous and cancerous lesions is also less than 100% (as very optimistically we assumed in the base-case analysis), having another preventative measure could be desirable.

It is important to emphasise the influence of discounting in the study context. The study used an annual discount rate of 3% in the base-case analysis for both costs and benefits, in line with the majority of similar published studies. As in any economic evaluation of a prevention strategy with long-term effects, the initial intervention costs and the choice of discount rate have a great influence on the resulting cost-effectiveness ratios. In the context of HPV vaccination, the discount rate of 3% made the vaccination followed by screening strategy less attractive, since the costs of the programme are immediate but the benefits (through avoiding disease) are delayed. As the HPV vaccine is assumed to reduce HPV infections, the main impact of adding vaccination is the eventual savings in future costs for treatment of HPV-related diseases.

One of the caveats of the study is that a cost-effectiveness analysis is not an indicator of affordability. A combination of vaccination and screening three times per lifetime is more costly than screening alone but is also more effective. The main cost driver is the vaccine cost. A threshold analysis shows that for the vaccination followed by screening strategy to have the same discounted total cost as the screening only strategy, the vaccine price has to be below US $48 per dose. Whilst potentially cost-effective, vaccination combined with screening in low- and middle-income countries such as South Africa may be unaffordable without financial assistance. Approaches for reducing cost of introducing the vaccine in resource-poor settings could include access to international funding mechanisms, such as the United Nations Children's Fund (UNICEF), and public-private partnerships. The pharmaceutical companies also need to make a commitment to appropriate price reductions. Studies from Brazil and Thailand (middle-income countries with a similar GDP per capita to that of South Africa) also show that a publicly funded HPV vaccination programme would not be a good policy option unless the price of vaccines decreased to an affordable level [14–16].

It is important to indicate that other approaches to cervical cancer screening, such as VIA and HPV DNA testing, have shown to be more cost-effective than cytologic screening in resource-poor settings [2,3]. However, whilst these alternative screening programmes may be desirable policy options in South Africa, this study aimed at estimating the impact of vaccination on the current, cytology based cervical cancer screening programme.

This study has a number of limitations. As there is a lack of epidemiological data on HPV and cervical cancer in South Africa, most of the parameters in the model were derived from the literature which made it difficult to test the validity of the model. The study is context-specific and exploratory in its nature and does not provide any definitive results. A static model that does not consider herd immunity was used. This could have underestimated the indirect benefits of vaccination. The cost of palliative care for invasive cervical cancer was not included in the analysis which could have underestimated the cost of cancer treatment. The study assumed a lifelong duration of vaccine efficacy (after 3 doses plus a booster at 10 years), significantly impacting on cost-effectiveness of the vaccine.

The findings from this model suggest that adding a vaccine to the current screening programme to prevent cervical cancer in South Africa can potentially be a cost-effective strategy. If the vaccine price were to be significantly reduced, vaccination followed by screening might be a very affordable policy option. This new health intervention, therefore, should be publicly funded. However, for the South African government to achieve affordable and appropriate public funding opportunities for HPV vaccination, the pharmaceutical companies need to make a commitment to price reductions.

Conflict of interest

We declare that we have no conflict of interest.

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References

[1] World Health Organisation. Projections of mortality and burden of disease; 2007 [Available from http://www.who.int/healthinfo/statistics/bodprojections2030/en/index.html].
[2] Goldie SJ, Khun L, Denny L, Pollack A, Wright TC. Policy analysis of cervical cancer screening strategies in low-resource settings. JAMA 2001;285(24):3107–15.
[3] Mandelblatt JS, Lawrence WF, Gaffikin L, Limpahayom KK, Lumbiganon P, Wrakamin S, et al. Costs and benefits of different strategies to screen for cervical cancer in less-developed countries. Journal of the National Cancer Institute 2002;94(19):1469–83.
[4] Goldie SJ, Gaffikin L, Goldhaber-Fiebert JD, Gordillo-Tobar AB, Levin C, Mahe C, et al. Cost-effectiveness of cervical cancer screening in five developing countries. New England Journal of Medicine 2005;353(2):2158–68.
[5] Denny L. Prevention of cervical cancer. In: Ljumba P, Padarath, editors. South African health review 2006. Durban: Health Systems Trust; 2006.
[6] Harper DM, Franco DL, Wheeler C, Ferris DG, Jenkins D, Schuind A, et al. Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised control trial. Lancet 2004;364:1757–65.
[7] Villa L, Costa R, Petta A, Andrade R, Ault K. Prophylactic quadrivalent human papillomavirus (types 6, 11, 16 and 18) L-1 virus-like particle vaccine in young women: a randomised double-blind placebo-controlled multicentre phase II efficacy trial. Lancet Oncology 2005;6:271–8.
[8] Goldie SJ, Kohli M, Grima D, Wienstein MC, Wright TC, Bosch FX, et al. Projected clinical benefits and cost-effectiveness of a human papillomavirus 16/18 vaccine. Journal of the National Cancer Institute 2004;96(8):604–15.
[9] Kulasingam S, Connelly L, Conway E, Hocking JS, Myers E, Regan DG, et al. A cost-effectiveness analysis of adding a human papillomavirus vaccine to the Australian National Cervical Cancer Screening Program. Sexual Health 2007;4(3):165–75.
[10] Brisson M, Van de Velde N, De Wals P, Boily M. The potential cost-effectiveness of prophylactic human papillomavirus vaccines in Canada. Vaccine 2007;25(29):5399–408.
[11] Jit M, Choi YH, Edmunds WJ. Economic evaluation of human papillomavirus vaccination in the United Kingdom. British Medical Journal 2008;337:a769.
[12] Kulasingam SL, Myers ER. Potential health ad economic impact of adding a human papillomavirus vaccine to screening programs. JAMA 2003;290(6):781–9.
[13] Sanders GD, Taira AV. Cost effectiveness of a potential vaccine for human papillomavirus. Emerging Infectious Diseases 2003;9:37–48.
[14] Goldie SJ, Kim JJ, Kobus K, Goldhaber-Fiebert JD, Salomon J, O'Shea MKH, et al. Cost-effectiveness of HPV 16, 18 vaccination in Brazil. Vaccine 2007;25(33):6257–70.
[15] Tangcharoensathien V, Limwattananon S, Chaugwon R. Research for development of an optimal strategy for prevention and control of cervical cancer in Thailand. Research report submitted the World Bank. Thailand, Nonthaburi: Ministry of Public Health; 2008.
[16] Goldie SJ, O'Shea M, Campos NG, Diaz M, Sweet S, Kim SY. Health and economic outcomes of HPV 16.18 vaccination in 72 GAVI-eligible countries. Vaccine 2008;26(32):4080–93.
[17] World Health Organisation. Choosing Interventions that are Cost-Effective (WHO CHOICE); 2008 [Available from http://www.who.int/choice/results].
[18] Mqoqi N, Kellet P, Sitas F, Jula M. Incidence of histologically diagnosed cancer in South Africa 1998–1999. National Cancer Registry of South Africa. Johannesburg: National Health Laboratory Service; 2004.
[19] South African Department of Health. Guideline for cervical cancer screening programme. Pretoria: National Department of Health; 2000.
[20] Moodley J, Kawonga M, Bradley J, Hoffman M. Challenges in implementing a cervical screening programme in South Africa. Cancer Detection and Prevention 2006;30(4):361–8.
[21] Harries J, Moodley J, Barone MA, Mall S, Sinanovic E. Preparing for HPV vaccination in South Africa: key challenges and opinions. Vaccine 2009;27(1):38–44.
[22] Myers ER, McCrory DC, Nanda K, Bastian L, Matchar DB. Mathematical model for the natural history of human papillomavirus infection and cervical carcinogenesis. American Journal of Epidemiology 2000;151(12):1158–71.
[23] TreeAge Software Inc. TreeAge Pro 2006 users manual. Williamstown, MA; 2006.
[24] ASSA. AIDS and Demographic Model of the Actuarial Society of South Africa; 2003 (release 15 March 2006) [Available from www.assa.org.za].
[25] Koutsky LA, Ault KA, Wheeler CM, Brown DR, Barr E, Alvarez FB, et al. A controlled trial of a human papillomavirus type 16 vaccine. New England Journal of Medicine 2002;347:1645–51.
[26] Statistics South Africa. Consumer Price Index; 2007 [Available at http://www.statssa.gov.za/keyindicators/CPI/CPIhistory.html].
[27] Elbasha EH, Dasbach EJ, Insinga RP. Model for assessing human papillomavirus vaccination strategies. Emerging Infectious Diseases 2007;13(1):28–41.
[28] Russell LB, Gold MR, Siegel JE, Daniels N, Weinstein MC. The role of cost effectiveness analysis in health and medicine. JAMA 1996;276(14):1172–9.
[29] Kumaranayake L, Kurowski C, Conteh L. Costs of scaling up priority health interventions in low-income and selected middle-income countries: methodology and estimate. In: WHO Commission on Macroeconomics and Health, Working Group 5 Paper 18. Geneva: World Health Organisation; 2001.
[30] World Health Organisation. Macroeconomics and Health: investing in health for economic development: report of the commission on macroeconomics and health. Geneva: World Health Organisation; 2001.
[31] World Bank. World development indicators database. 14 September 2007. Washington: World Bank; 2006.
[32] Cleary SM, McIntyre D, Boulle AM. The cost-effectiveness of antiretroviral treatment in Khayelitsha, South Africa—a primary data analysis. Cost-Effectiveness and Resource Allocation 2006;4(20).