POLICY RESEARCH WORKING PAPER 2977

The Strategic Use and Potential Demand for an HIV Vaccine in Southern Africa

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The World Bank
Development Research Group
Public Services
February 2003

Abstract

HIV prevalence in Southern Africa is the highest in the world and the impact of HIV/AIDS in the region are devastating at all levels of society, including the wider economy. Government response has lagged behind the pace of the epidemic, but programs are now beginning to focus on a broad range of interventions to combat its further spread and to mitigate its impact.

Desmond and Greener investigate the issues around the targeting of an eventual HIV vaccine. There is at present no vaccine against HIV. Although several candidates are in the trial stage, it is not likely that a vaccine effective against the sub-type of the virus prevalent in Southern Africa will be available for 10–15 years. When it is, it may be expensive, only partially effective, and confer immunity for a limited period only. Vaccination programs will need to make the best use of the vaccine that is available and effective targeting will be essential.

The authors identify potential target groups for a vaccine, and estimate how many individuals would be in need of vaccination. They develop a method for estimating how many cases of HIV infection are likely to be avoided for each vaccinated individual. The cases avoided are of two kinds: primary—the individual case that might have occurred in people who are vaccinated, and secondary—the number of people that the vaccinated individual would otherwise have caused to become infected. Both of these depend on assumptions about the efficacy and duration of vaccine protection and the extent and nature of sexual risk behavior in the population groups. The authors distinguish between the HIV cases averted per vaccination and the cases averted per 100 recruits into a vaccination program.

The cases averted per 100 recruits is used to develop a priority ranking of the identified population groups for vaccination. The authors discuss the issue of ease of access to those groups and how the differential costs would affect the vaccination strategy. They conclude that an expensive vaccine should be administered to commercial sex workers first, while an inexpensive vaccine would be better administered first to general population groups, in particular, schoolchildren.

Desmond and Greener conclude with a discussion of current levels of public and private expenditure on HIV prevention and treatment, and the implications for an assessment of the willingness to pay for an eventual HIV vaccine.

This paper—a product of Public Services, Development Research Group—is part of the research project "The Economics of an HIV/AIDS Vaccine in Developing Countries: Potential Impact, Cost-Effectiveness, and Willingness to Pay" sponsored by the European Commission and the World Bank. The project was launched in response to recommendations of the World Bank's AIDS Vaccine Task Force. Copies of this paper are available free from the World Bank, 1818 H Street NW, Washington, DC 20433. Please contact Hedy Sladovich, mail stop MC3-311, telephone 202-473-7698, fax 202-522-1154, email address hsladovich@worldbank.org. Policy Research Working Papers are also posted on the Web at http://econ.worldbank.org. The authors may be contacted at desmondel@nu.ac.za or rgreener@bidpa.bw. February 2003. (47 pages)

The Strategic Use and Potential Demand for an HIV Vaccine in Southern Africa

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The authors acknowledge the data collection efforts of other HEARD and BIDPA staff and the useful comments on earlier drafts by Martha Ainsworth and John Stover. This paper is a product of the research project on "The economics of an HIV/AIDS vaccine in developing countries: Potential impact, cost-effectiveness and willingness to pay", sponsored by the European Commission and the Development Research Group of the World Bank (Martha Ainsworth, task manager). The project was launched in response to recommendations of the World Bank's AIDS Vaccine Task Force.

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1. Introduction

Although the HIV virus appeared later in Southern Africa than elsewhere on the continent, Southern Africa now has the highest rates of HIV prevalence in the world. Approximately one adult in five is HIV positive (see Figure 1-1), and Southern African countries face the prospect of the reversal of hard won progress in development, resulting in deepening human poverty and social dislocation. Valuable human resources are being lost, affecting all sectors, public as well as private. HIV/AIDS will hamper governments' ability to manage their economies and to deliver social services.

Figure 1-1. HIV adult prevalence rates and selected development indicators in Southern Africa

Country	Adult HIV Prevalence	Population '000	Adult Population '000	GDP/Capita (PPP$)	Net Secondary Enrolment
South Africa	19.9%	43,421	20,630	$8,908	56%
Zimbabwe	25.1%	11,343	5,771	$2,876	
Zambia	20.0%	9,582	4,137	$756	
Lesotho	23.6%	2,143	998	$1,854	18%
Namibia	19.5%	1,771	790	$5,468	38%
Botswana	35.8%	1,695	775	$6,872	48%
Swaziland	25.3%	1,083	480	$3,987	38%
Overall Total	**21.4%**	**71,038**	**33,581**	**$6,423**	**53%**

Sources: UNAIDS website (HIV prevalence), UNDP (2001).

1.1. Approach of the Paper

The principal goal of this paper is to provide a framework for comparing different AIDS vaccination strategies to guide the process of targeting, should that become necessary. The paper begins with a brief review of the health and developmental impacts of HIV/AIDS in Southern Africa, and the current responses in the seven countries considered with regard to prevention, treatment and vaccine development.

In section 2, the paper presents an analysis based on calculating the total number of cases averted per 100 entrants into a vaccination program, under the assumption that prior screening for existing HIV infection is impractical and is not carried out. This indicator is then calculated for each of 12 identified risk groups and used to rank them in order of effectiveness. This leads to a discussion of access and targeting issues.

In section 3, the paper presents evidence of existing ability and willingness to pay for an HIV vaccine, based upon expenditure on other health items or vaccines, and a brief analysis of economic motivation. The paper concludes with recommendations for vaccination strategies under differing assumptions about the cost, efficacy and duration of protection offered by any potential vaccine.

1.2. The Health and Development Impacts of HIV/AIDS in Southern Africa

HIV prevalence

The estimated adult prevalence of HIV in selected countries of Southern Africa is shown in Figure 1-1. South Africa is by far the largest of the countries listed, with about 61 percent of the adult population of the region, and therefore dominates the overall average rate of 21.4 percent. There are, however, considerable regional variations within South Africa, with rates above 30 percent in KwaZulu Natal, and below 10 percent in the Western Cape. The highest regional rate of 35.8 percent is found in Botswana.

The figure also shows the populations (both total and adult - i.e., aged 15-49), the per-capita GDP and the net secondary school enrollment ratios. All of the totals shown in the table are weighted by population from the countries where data were available.

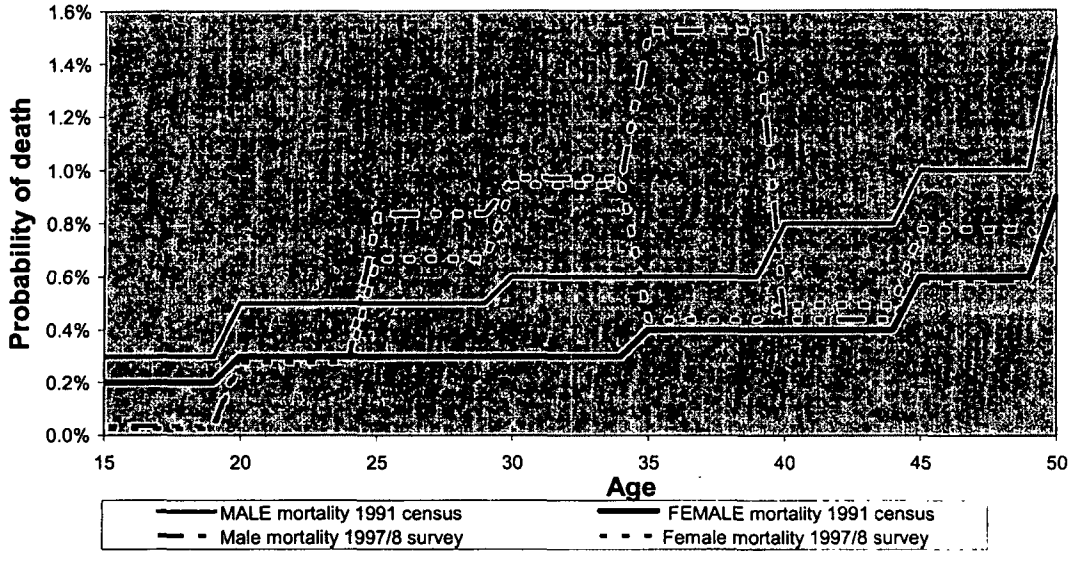
Demographic impact

The demographic impacts of HIV/AIDS arise through its impact on mortality and fertility. Deaths due to AIDS can be expected to cause a dramatic increase in the mortality rates in the 15-49 age group, where they would otherwise be expected to be very low. In the case of infant mortality, there is clear evidence from Botswana and other African countries that HIV/AIDS has caused a stagnation or even a rise in infant and child mortality rates (Timaeus 1998).

The demographic impact of HIV/AIDS is often measured in terms of life expectancy. Life expectancy is, however, an unsatisfactory indicator, since it depends upon assumptions about age and sex specific mortality rates. Accurate measures of age specific mortality are difficult to obtain, and most published estimates of life expectancy make use of mortality rate projections. These projections have not yet been validated against national population census data since such data are usually only collected every 10 years. Both South Africa and Botswana have recently conducted population censuses, and results from these will in due course yield estimates of mortality. Early estimates from the Botswana census (no official publication is yet available) indicate that the projections used to date in life expectancy calculations are not valid.

The evidence from survey data gives some indication of impact. Figure 1-2 below shows measures of adult mortality by age and sex from Botswana (1997 demographic survey) as compared with mortality (in dotted lines) as measured in the 1991 population census. There is clear evidence of substantially raised mortality in the 25 to 40 age groups.

Figure 1-2. Adult mortality in Botswana by age and gender, 1991 and 1997/98



As indicated above, however, these raised mortality rates are substantially below the rates that had been projected for the year 1997/98 – for example, see Botswana MFDP (2000a). In addition, early estimates for the total head count from the Botswana population census in 2001 indicate a total of almost 1.7 million. This is close to projections obtained before HIV/AIDS was accounted for, and is at the very high end of AIDS scenario projections produced prior to the census (most of these were in the range 1.4-1.6 million). In the case of Botswana, it may be that the period from infection to death is higher than was previously expected, but this may not apply across all of the Southern African countries.

A recent study by the Medical Research Council (MRC) in South Africa (MRC 2000) documented the steady rise in adult mortality during the 1990's, with female mortality in the 25-29 age group increasing by a factor of 3.5 between 1985 and 2001. AIDS deaths were broadly compatible with a number of different projection models, in particular the ASSA600 model produced by the Actuarial Society of South Africa (ASSA). The report concluded:

> While there is inevitably some degree of uncertainty because of the assumptions underlying both the model and the interpretation of the empirical data, we estimate that about 40 percent of the adult deaths aged 15-49 that occurred in the year 2000 were due to HIV/AIDS and that about 20 percent of all adult deaths in that year were due to AIDS. When this is combined with the excess deaths in childhood, it is estimated that AIDS accounted for about 25 percent of all deaths in the year 2000 and has become the single biggest cause of death. The projections show that, without treatment to prevent AIDS, the number of AIDS deaths can be expected to grow, within the next 10 years, to more than double the number of deaths due to all other causes, resulting in 5 to 7 million cumulative AIDS deaths in South Africa by 2010.

Economic impact

The expected economic impacts of HIV/AIDS arise through several identified mechanisms. First, the increased mortality among young adults depletes the most economically productive part of the population, reducing the supply of labour across all skill categories. In addition, raised mortality among older, more experienced workers will tend to reduce the average level of work experience among the workforce. The resulting loss of skills will cause a reduction in productivity.

Second, there is an increase in morbidity among workers who are beginning to suffer the symptoms of AIDS. This will have the effect of reducing the average level of productivity, and hence the aggregate level of output.

Third, households will face reduced incomes because of the loss of income earners, at the same time facing higher expenditures because of additional demands for health care. This will have the effect of increasing the levels of poverty and reducing the levels of savings in the economy. The capital available for investment will therefore be reduced, with a negative impact on aggregate economic growth. For example, Greener, Jefferis, and Siphambe (2000a) found that income poverty over a 10-year period might be expected to increase by at least 5 percentage points over what it otherwise might have been.

At a government level, there will tend to be a reduction in revenue from taxation and other sources as a result of reduced economic growth. At the same time, there will be pressure to increase expenditures on health care and welfare to mitigate the impacts of HIV/AIDS. This will have the effect of pushing governments towards the need for deficit spending or reducing expenditure on other development areas. In particular, the costs of AIDS treatment will, in the first instance, be borne by governments. For example, Greener, Jefferis, and Siphambe (2000a) found that the net impact on the government budget over a 10-year period in Botswana would be equivalent to a 20percent reduction in revenue. Pressure on health budgets may also cause a "crowding out" effect, where expenditure on other health priorities may decrease. This effect may cause further economic impacts not directly related to HIV/AIDS.

AIDS will also cause human resource problems for firms and organisations, which may lose employees in vital skill areas and face difficulty in recruitment and training.

Numerous studies over the last 10 years have found estimates of the probable size of aggregate macroeconomic impact, mainly in African countries where the epidemic is the most serious. Results have indicated that HIV/AIDS will probably reduce the growth rate of Gross Domestic Product (GDP) by between 0.5 percent and 2.6 percent. For example, see Over (1992), Kambou, Devarajan, and Over (1992), Cuddington (1993a, b), Bloom and Mahal (1995), Arndt and Lewis (2000), Greener, Jefferis and Siphambe (2000a,b) and Bureau for Economic Research (2001). The overall conclusion of these studies is that the aggregate impact of HIV/AIDS on GDP growth is quite small and well within the

range of variation that would be caused through the normal instruments of economic management.

Development impacts

The HIV/AIDS epidemic is placing a severe burden on all levels of the health care system throughout the region. Hospital admissions are increasing rapidly and more than half of the available hospital beds are occupied by AIDS related cases, including tuberculosis. For example see Botswana MFDP (2000b). The epidemic is threatening to overwhelm the health services, and the expansion of home based care facilities for AIDS patients is inevitable.

The HIV epidemic has fueled a parallel epidemic of tuberculosis (TB), exacerbating the problems of the relatively low coverage of effective TB immunisation in much of the region. For example, see Botswana MFDP (2000a), and the data presented in Figure 3-1.

The education sector has been severely affected by the HIV/AIDS epidemic. The death rates among teachers and lecturers have been increasing sharply in recent years, for example see Botswana MOE and DFID (2000). Although death rates are low among school students, HIV/AIDS has disrupted their home environments as adults fall ill and need to be cared for. There is speculation about how this situation is affecting the quality of teaching and the quality of school work. It is clear that the demographic impacts of HIV/AIDS will create significant planning problems for education in the future.

The rapid spread of HIV/AIDS is exacerbated by a cultural environment in which issues of sexuality and sexually transmitted disease are not openly discussed. There are a number of pervasive culturally based myths about HIV/AIDS which reduce the impact of some of the prevention campaigns and encourage a fatalistic attitude. The issues raised by the epidemic impinge upon long standing taboos and result in a high level of stigma being associated with HIV/AIDS, for example see UNDP (2000).

Despite an apparently high level of knowledge about the nature of HIV/AIDS and how it can be prevented, the steadily rising HIV prevalence (as measured in ante-natal clinics) indicates little evidence of a widespread change in sexual behavior in the region. There is clearly a need to understand the reasons for this and to understand the possible effects that the introduction of an HIV vaccine might have.

1.3. Current responses

The early response to the HIV/AIDS epidemic in Southern Africa, as elsewhere, was essentially biomedical in nature, focusing on increasing national public awareness of HIV, training health workers in AIDS clinical management, and on establishing monitoring systems in ante-natal clinics. This broadened into efforts to prevent the spread of HIV through media campaigns promoting the use of condoms or abstaining from sexual activity. The epidemic progressed unabated however.

Prevention campaigns in most countries have emphasized the message of ABC (Abstain, Be faithful, Condomize). Some assessments (for example UNDP Botswana, 2000) have concluded that the prevention campaigns have not, to date, been able to address the true underlying factors that fuel the campaign. These include intergenerational sex, poverty and the low status of women.

In recent years, most of the countries considered here have adopted a much more wide ranging multi-sectoral approach to HIV/AIDS which seeks to involve both government and civil society on a broad front. This includes an expansion of community home based care, and an expansion of life skills training, and a phased introduction of a range of treatment options. The number of Voluntary Counselling and Testing (VCT) Centers is increasing rapidly. Botswana has begun to implement a program which ultimately seeks to make AIDS treatment available to a broad sector of the population. This program is at an early stage and is not yet administering ARV treatment to very many people, but it is clear that the logistics associated with widespread ARV treatment will be formidable. The recent policy shift in South Africa is likely to lead to a rapid expansion of ARV and other forms of treatment, particularly for vulnerable groups such as pregnant or breastfeeding women.

1.4. HIV vaccine development

A number of candidate vaccines are currently in or about to begin trials . This is a result of advances in animal models and clinical research (Johnston and Flores 2001). A number of vaccine candidates are ready for, or already undergoing, phase one trials in Europe, the United States and Africa. Not all HIV types are the same, and a number of different subtypes exist. These different subtypes of HIV are prevalent in different parts of the world, but candidate vaccines are often targeted at one subtype. Therefore, a vaccine may become available for some subtypes before others and thus may be used far earlier in some parts of the world. Subtype A is most prevalent in South Africa.

The current candidates are primarily aimed at subtype B, although at least one subtype A candidate has begun trials. The most advanced trials are for the phase three VaxGen candidate aimed at subtypes B and E. These are currently underway in the United States and Thailand, and interim results are expected by the end of this year (Johnston and Flores 2001). The company responsible is already planning for large scale commercial production. This, however, offers little hope to those fighting the epidemic in Africa, since the B and E subtypes are not prevalent in the African epidemic.

In South Africa, where subtype A is dominant, phase one trials are set to begin only this year. Researchers in South Africa believe that a commercially available vaccine for use in the region is 15 to 20 years away, although there appears to be consensus that a viable vaccine can be developed (Morris, Williamson, and Vardas 2001). The South African government strongly supports the vaccine initiative and provides funds from the national budget towards its development and testing, run primarily by the South African Medical Research

Council. The development of an acceptable vaccine for use within in South Africa, and indeed within the continent, is far less advanced than elsewhere in the world.

2. Vaccination strategies

2.1. Introduction

An ideal HIV vaccine would be cheap, freely available, a single dose, simple to administer, one hundred percent effective, and last a lifetime with no side effects. Although one day such a vaccine may become available, the first available vaccines are unlikely to be as ideal. They are more likely to be expensive, multi-dose, less than 100 percent effective and last only a few years. The prohibitively high cost may make the widespread provision of early vaccines unaffordable in many low and middle-income countries, including those in Southern Africa.

In such a situation, interventions will have to make best use of the available finances and apply the most cost effective and politically acceptable strategy. This would involve, amongst other things, the estimation of the effectiveness of targeting different groups within the population and the cost of targeting. The vaccination of members of high-risk groups would likely provide the most effective outcome per vaccine given, but the cost of accessing such groups as opposed to lower risk groups may be sufficient to make easily accessed, but low risk, groups a more cost effective target. The political consequences of targeting high risk groups may also be a major factor influencing target choice.

This section aims to evaluate the conflict between cost and effectiveness and identify the most cost-effective options for a vaccination strategy, with the primary focus on where to begin. While it is not possible to make definitive conclusions while the characteristics and cost of the possible vaccines are unknown, it is possible to raise and discuss a number of issues which will expedite the development of a strategy once the required information has become available.

The section begins with an outline of the method used in the analysis, which is followed by the results and a discussion of their implications. As stated previously, the analysis and discussion concentrates on a vaccine designed to prevent HIV infection rather than one designed to prevent the progression from HIV to AIDS.

2.2. Analysis

The analysis required the estimation of the number of infections averted when vaccinating people with different characteristics, and the relative difficulty of access to the different groups. This section outlines, in brief, the methods used in estimating these parameters, while a more detailed explanation is provided in the appendix.

First, the paper outlines the manner in which the number of infections averted was calculated, broken into two categories:

- The calculation of primary infections averted – i.e., the number of vaccinated individuals who would otherwise have become infected with HIV
- The calculation of secondary infections averted – i.e., the number of people who would have become infected by those vaccinated individuals who became HIV positive

These calculations together yield an estimate of the total number of infections averted for vaccinations of HIV negative individuals for the different groups (i.e., primary plus secondary).

It was felt, however, that ending the analysis at this point could be misleading. Estimating the total number of infections averted masks the problem (and associated cost) of screening for existing HIV infection, particularly among high-risk candidates. For this reason, the number of infections averted per one hundred entrants from a target group was estimated. The method used for this calculation is outlined below.

This section outlines the approach taken to deal with the question of differential access and associated cost. The paper also discusses the method applied in the selection of possible target groups.

The analysis presented in this paper is a simple and easily understandable approach, which is aimed at raising important considerations, rather than at providing accurate numbers. While it is possible to refine the method to improve the estimations, this would dramatically increase the computational complexity, adding little to the discussions outlined.[1] Due to its simplicity, the approach does suffer a number of limitations which are outlined in the appendix. Where they relate to the discussions, they are mentioned in the text.

Method to compare strategies

Primary infections averted. The probability of a "primary" infection refers to whether or not an individual would have been infected with HIV if they had not been vaccinated. It does not include the probability that the individual would have gone on to infect other people. This is referred to as "secondary" infection, and is described in the next section.

The number of primary infections averted for a group of HIV negative vaccinated individuals will depend on four factors:

- The *efficacy* of the vaccine – i.e., the probability that a vaccinated person is protected from infection
- The number of people in the group being vaccinated
- The duration of the period of immunity offered by the vaccine

[1] For a detailed modeling exercise see Stover and others (2002).

- The average probability that a typical group member would otherwise have become infected during the period of protection of the vaccine, called the "period infection probability."

The meaning of the "period infection probability" depends on the length of the period. If the period under consideration is one year, then the period probability is equal to the probability that an individual will be infected during that year. This is also the definition of the incidence of HIV infection for the group. For periods of longer than one year, the period probability will depend on the way in which HIV incidence evolves for the cohort over the period. The evolution of HIV incidence is in turn dependent upon the expected risk behavior within the cohort and will vary considerably among different risk groups.

There is, however, a relationship between the period probability and the HIV prevalence in a cohort. In general, a cohort is likely to experience a high period probability at the early stages of the onset of risk behavior when prevalence is low. As the cohort evolves, the period probability will fall as the prevalence rises, since there are fewer individuals in the cohort left to infect.

The analysis estimated the primary cases averted by simulating the evolution of prevalence and infection probability for different risk groups. This made use of the illustrative risk groups as represented in the simulation model developed by the Actuarial Society of South Africa (ASSA).[2] Although it is no substitute for the use of real data (which are lacking), the benefit of this method is that it gives a realistic estimate of the period probability in a Southern African setting, while arriving at a "best guess" at the differences in likely risk behavior among the different risk groups.

Secondary infections averted. Vaccinating an individual will not only prevent the infection of that individual, but also the secondary infections that would have resulted from that individual infecting others. The number of secondary infections averted will depend upon a variety of factors and will differ substantially for different individuals. For example, preventing the infection of a commercial sex worker will avoid substantially more secondary infections than preventing the primary infection of an older woman in a monogamous relationship. Although there are a host of other factors which must be considered in designing a vaccination program, the number of secondary infections averted is clearly an important component.

A variety of variables is instrumental in determining the number of secondary infections averted. These include:

- the number of sexual partners the individual will have over the period for which the vaccine offers protection
- the number of sexual contacts they have with these partners

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[2] For details of the ASSA 600 model used in this analysis, see www.assa.org.za/aidsmodel.asp.

- their probability of being infected, per sexual contact
- whether they, or their partners, have a sexually transmitted infection (STI)
- whether their partners are already infected with HIV
- the frequency of condom use.

It is necessary to calculate the probable number of people the individual would have infected if he or she had not been successfully vaccinated. The more sexual partners and more sexual contacts they have, the higher the number of people they would infect. Similarly, the greater the individual's probability of having an STI and the higher the STI prevalence of their partners, the higher the probability - per sexual contact - that they would transmit HIV. On the other hand, the higher their condom use, the lower the probability of transmission per contact. Finally, the higher the existing level of HIV among their partners, the lower the chance that their future partners are HIV negative to begin with. Preventing a repeat infection of an already infected individual is not an infection averted. When estimating these variables, it is necessary to consider how behaviors may differ between casual sexual contacts and long-term partners.

These variables, as well as those relating to the duration and effectiveness of vaccines, interact with one another to determine the number of secondary infections averted. The implications of these interactions were estimated with a set of equations, which are outlined in the appendix.

It is also possible that a vaccine may lead to changes in sexual behavior resulting from changed perceptions of risk. In the calculations presented in this paper, no attempt has been made to introduce behavior change. The behavior variables used in the calculations are based on the data that are available, which are weak and incomplete. There is, therefore, no quantitative basis for estimating the impact of a vaccine on behavior change in the different risk groups, so it was not included in the calculations. However, possible behavior changes will be very important in vaccination program design, and the implications of changes in behavior prompted by the introduction of a vaccine are discussed below.

Total infections averted. The previous two sections have outlined the basis for the calculation of the number of primary and secondary infections averted. The estimation of the total number of infections averted per vaccinated HIV negative individuals involves the combination of the previous two calculations.

The efficacy of the vaccine will make no difference to the ranking of strategies in terms of their effectiveness, unless vaccination changes risk behavior differently in different target groups. Given the decision to vaccinate, which would in part be motivated by the efficacy, the most effective strategies will be the most effective regardless of the efficacy of the vaccine. A change in the efficacy changes the impact of vaccination of all groups by the same proportion and will not affect their effectiveness in relation to one another. Changes in the duration of protection are, however, more important at this stage.

Changes in the duration change the probability of averting a primary infection. This change will have different implications for the effectiveness of vaccinations in different risk groups. Further the sexual behaviors of different groups will likely vary over time, and a different duration could possibly change the ranking of groups in terms of both effectiveness and cost effectiveness. This issue is discussed in greater detail after the presentation of the results below.

Infections averted per 100 entrants into the program. The method described above estimates the number of infections averted per vaccine administered to an HIV negative individual. The vaccination of an HIV positive individual will result in no infections averted and may well lead to a false sense of security which could increase the risk of others. Considering only the number of infections averted in this way ignores the costs and complications associated with ensuring that only HIV negative individuals receive vaccinations. A more meaningful measure would be the number of infections averted per 100 entrants into a vaccination program. The basis for this calculation is outlined in the appendix.

The vaccination of members of high-risk groups is likely to avert more infections than the vaccination of members of lower risk groups. The impact is, however, likely to be diluted by the need to exclude many vaccination candidates because they are already HIV positive. If the cost of screening is significant, relative to the cost of a vaccine, this may have important implications for policy. Policy decisions may be further complicated by the difficulties associated with locating members of high-risk groups.

Issues of access. The delivery of an HIV vaccine is likely to differ substantially from that associated with currently available vaccines. The majority of currently provided vaccines are administered to young children. The targeting of different population groups will, in some cases, necessitate the active seeking out of participants. The difficulty of access and associated cost are likely to be substantial.

The identified risk groups are classified in terms of their difficulty of access, rated as easy, medium, difficult or very difficult. These classifications are made in terms of once off access and follow up access. The difficulty associated with accessing some groups once off may be very different from the difficulty associated with finding those same people a second or third time for follow up doses. For example, the recruitment of vaccination candidates at a hospital may be very easy for once off doses, but locating those same people for repeat doses would be very difficult.

We do not attempt to quantify the difference in difficulty of access. What is estimated is how large a difference in cost, associated with different levels of difficulty, would change the ranking of different strategies.

If a program aimed at school girls was targeted at fifteen year olds who have very low prevalence,[3] and the vaccination was offered to all entrants, the difference in the costs of access and screening when compared to sex workers would be large. Given the results presented in Figure 2-1, if the additional costs associated with the targeting of sex workers as opposed to school girls was more than 1.2 times the cost of a vaccinating school girls (including the cost of the dose), then the vaccination of school girls would be more cost effective per 100 entrant. Therefore, particularly if a vaccine requires more than one dose, a vaccination intervention may achieve better results by targeting broader population groups than difficult to access high risk groups.

Figure 2-1. Estimated size of risk groups, and cases averted

Group	Size		HIV+	Primary	Secondary	Per HIV-entrant	Per 100 entrants	Access - once	Access - follow up
	Catch up	Maintain							
Sex Workers	700,000	140,000	66%	0.51	7.88	4.53	154	Very Difficult	Very Difficult
High School going girls	2,700,000	94,500	10%	0.34	1.05	0.70	70	Easy	Easy
Military	172,000	10,300	21%	0.25	1.70	0 68	54	Easy	Easy
Prisoners	214,000	10,700	20%	0.25	1.70	0.68	54	Easy	Easy
High School going boys	2,600,000	91,000	1%	0.19	1.68	0.51	51	Easy	Easy
Formal sector male employees	8,181,000	490,860	20%	0.25	1.51	0.63	50	Medium	Medium
High school teachers	189,000	11,000	26%	0.30	1.23	0.67	49	Easy	Easy
High risk transport workers	2,223,000	133,380	56%	0.34	2.17	1.08	47	Difficult	Difficult
Women attending ANC	1,950,000	117,000	26%	0.33	0.86	0.61	45	Medium	Difficult
Formal sector female employees	5,612,000	336,720	26%	0.33	0.80	0.59	45	Medium	Medium
Legal cross border migrants	190,000	11,400	42%	0.20	2 39	0.68	44	Difficult	Difficult
Male STD clinic attendees	700,000	42,000	60%	0.30	1.38	0.71	29	Medium	Very Difficult

Identification of target groups. The above calculations and analysis were performed for twelve different possible target groups. The groups are not mutually exclusive and are not intended as a definitive list, but rather as an array of options to highlight a number of different issues. The groups represent a range across three characteristics: risk behavior, ease of access, and size. Sex workers, high risk transport workers and male STD clinic attendees were selected as the examples of the high risk behavior, while women attending antenatal clinics and high school boys represented low risk behavior. Migrants and sex workers provided examples of difficult to access groups, as opposed to school children whose ease of access depends upon secondary school enrollment (see Figure 1-1).

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[3] The prevalence of all high school girls is assumed to be 10%, the calculations are however carried out based on 1% prevalence assuming that only 15 year olds are recruited into the program.

difficult. A study in Kenya found that there was difficulty in understanding the concept of reduced risk (Forsythe 2000).

Second, by the time a vaccine becomes available (in fifteen or twenty years or even in five), the number of deaths which will have already occurred will be great. The public response to providing a vaccine only to selected individuals may be hostile. People will be afraid and possibly become angry at their exclusion, particularly if it is in favour of sex workers or other high risk groups who they may perceive to be less worthy of protection than themselves.

Third, many of the possible target groups are women, and this may fuel the perception that they are responsible for the epidemic. In the context of high death rates, this may have potentially damaging implications.

Finally, in many instances it will not be politically feasible to separate groups for targeting as they have been in the analysis. The calculation of infections averted separated schoolboys and girls; while this is useful for discussion purposes, such a policy in reality would be inequitable and difficult to defend. The implication would be that school aged children would be the target, rather than girls.

These few problems highlight that effectiveness and cost effectiveness are only inputs into a decision process, and that the final design of a vaccination program will have to consider many other economic, social and political aspects. Indeed, logistics of targeting may be such that the approach will not be considered.

Some similar problems have occurred in vaccination programs for other illnesses and efforts should be made to learn from these experiences (Nichter 1995).

Country-specific issues relating to risk group targeting. The analysis thus far has dealt with the region as a whole and has not discussed specific issues in relation to each country. While there are many similarities across the region, some problems may be country specific.

We have argued above in favour of providing a vaccine to high-school children. Enrollment rates in the region are, however, very different (see Figure 1-1). While they are high in South Africa and Botswana, they are very low in Lesotho. The strength of the cost-effectiveness analysis is, however, that it allows for the ranking of interventions. The most cost effective strategy will always be to begin with the highest ranking group and vaccinate until the budget runs out or all of the groups are vaccinated. Low school enrollment alone would not, therefore, change the recommendations of the analysis.

Country specific issues may make a difference if they change the ranking of groups in terms of their cost effectiveness. If, for example, high-risk groups are easier to access in some countries and the cost of access is low, this would make them a more cost effective option, possibly changing the order of ranking.

In the case of countries in the region with very high numbers of cross-border migrants, such as Swaziland and Lesotho, they may represent a high risk easy access group. It may be possible to set up vaccination sites on the borders and record in passports the number of doses received. Therefore, while cross border migrants may not be the most cost effective target group in the region as a whole, they may be for specific countries. Similarly, sex workers may be easier or harder to locate in different countries. If sex workers are concentrated in easily identified urban areas or areas associated with particular industries or activities, then the costs of access would be lower than an in agricultural setting where they would be more widely dispersed.

The costs of delivery to all groups may also vary across countries, particularly in relation to urbanisation, population density and the cost of labour. Even if these costs vary by the same proportion for each group, it may still change the differences in cost effectiveness between groups. The importance of delivery costs is a more important component of total costs for the higher risk groups. A decrease in delivery costs of equal proportion across all groups would increase the cost effectiveness of high risk groups compared to other groups. This may even vary the rankings across countries in relation to their costs of labour and transport. Countries with higher labour costs, such as Botswana, would have added incentive to target easy to access groups.

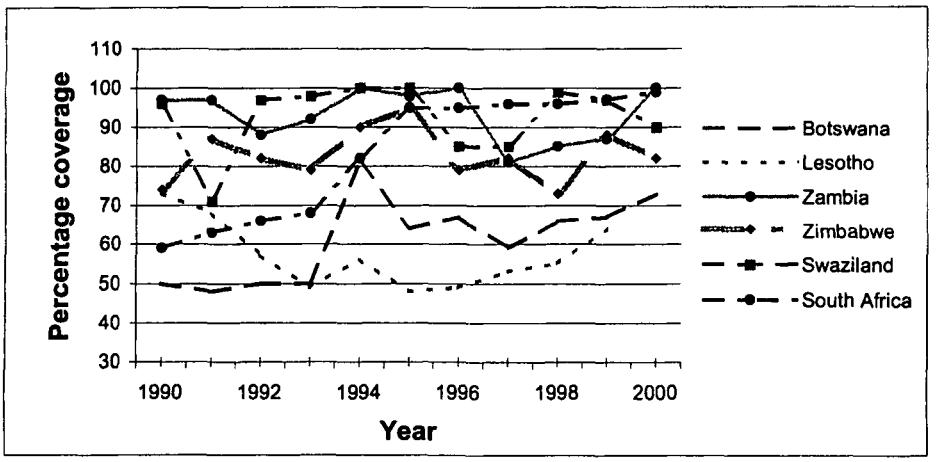
While at this stage when the costs and effectiveness of a vaccine are unknown, it is reasonable to address questions as a region. Once details are available, country-specific assessments and planning will be necessary to identify the most cost effective strategies.

3. Ability and willingness to pay

3.1. Trend in the provision of other vaccines

Governments in the region have displayed a mixed attitude towards the provision of other vaccines. While all of the countries included in the study have vaccination programs, primarily aimed at young children, they have succeeded in reaching very different levels of coverage. In Figure 3-1, the coverage rates of the BCG vaccine against tuberculosis in all the countries is displayed between 1990 and 2000. Lesotho currently has the lowest coverage with 64 percent, while Zambia is close to achieving universal coverage. The coverage rates do not appear to reflect differences in income, as Zambia has achieved some of the highest coverage rates but is the poorest country.

Figure 3-1. BCG vaccination coverage in selected Southern African Countries



Not only does the figure display the very different levels of coverage, but also different trends. Coverage in Lesotho was declining until 1996, while now it is apparently on the increase, although the rise is very slow. South Africa, on the other hand, has been increasing its coverage, with a very dramatic rise since the 1994 elections.

What can be surmised from the above is that governments in the region are willing to use vaccination programs as a major health intervention, but that their commitment towards them is uneven. Zambia and South Africa, and Botswana to some extent have shown very positive attitudes towards childhood vaccines with either high or rapidly increasing levels of coverage.

3.2. Current spending

Estimating the level of government expenditure on HIV/AIDS is difficult, as much of it is too intertwined with other expenditures to be separated. For example, spending on medical care for AIDS patients is difficult to distinguish from other health care spending. It is easier to estimate the level of spending on HIV programs. This spending provides an indication of the level of government commitment to fighting HIV directly. When an HIV vaccine becomes available, government will probably draw on these types of directly allocated funds.

Unfortunately comparable data are not available for all the countries in the region. Figure 3-2 provides estimated levels of government expenditure on HIV related programs. It also shows the level of international donor support and what these funding levels mean in terms of funds per HIV positive person.

Figure 3-2. Reported HIV/AIDS funding at current prices and exchange rates (US$), selected South African countries1996

Country	*National Government*	*International Donors*	*Funds per HIV+ person (total)*	*Funds per HIV+ person (national)*
Botswana	2,711,640	-	14.27	14.27
Namibia	435,700	764,000	8.00	2.90
Zambia	190,878	6,023,688	8.07	0.25
Zimbabwe	43,802	13,933,725	9.23	0.03

Source: UNAIDS (1999).

In South Africa, the national government allocations are somewhat larger. In the most recent budget, one billion Rand is allocated to HIV programs (Hickey 2002). This figure is roughly the same as Botswana in terms of funds per HIV positive individual, although South Africa does receive additional donor support. Included in the funds allocated to HIV in South Africa is the government's support for the AIDS Vaccine Initiative, which displays a commitment to the development and use of a vaccine.

Recently, the above pattern has changed somewhat, Botswana has begun to receive large amounts of international support, and some countries in the region are gaining access to monies from the Global fund. While the figures here may be a little outdated, what is clearly displayed is the variation in the ability and willingness of governments in the region to support HIV programs. This variation is also likely to exist in countries' ability and willingness to pay for vaccine provision. The extent to which these variations will occur is likely to be determined by the constraints on supply. If a vaccine is expensive and there is no international support for purchasing, those countries with more serious budgetary limitations will be more constrained in the development of their programs.

As mentioned previously, the spending outlined above does not include amounts associated with increases in medical care costs or intertwined in other expenditures of government. The middle income countries in the region with better equipped health services, for example, will have greater motivation to vaccinate to avoid costs associated with increased demand.

The low levels of funding and the high level of reliance on international donors are clearly apparent. With the exception of Botswana and South Africa (and possibly Namibia), the large-scale provision of a vaccine with any significant cost would clearly be unattainable with the current expenditure allocation and without the support of the international community. Targeting strategies would have to be used in the context of highly restricted budgets, more so in the low-income countries in the region, unless substantial vaccine purchase support is provided.

3.3. Economic motivation and willingness to pay

Should a vaccine become available, many individuals may be willing to pay for themselves to be vaccinated. HIV in the region is, however, largely perceived

Appendix 1. Data and Assumptions

The assumptions about population sizes, HIV prevalence, HIV incidence and sexual behavior are all contained in the table shown in Figure 1.

Figure 1. Table of Assumptions

		South Africa	Namibia	Botswana	Lesotho	Swaziland	Zimbabwe	Zambia	Total	Assumptions
Total Population	**Population '000**	43,421	1,771	1,695	2,143	1,083	11,343	9,582	**71,038**	SADC website www.sadc.int
Sex Workers	**Population '000**	434	18	17	21	11	113	96	**710**	1% of population
	HIV prevalence	61%					86%	69%	**66%**	SA prevalence the average of available studies
	Partner HIV prevalence	38%							**38%**	SA: average adult population and high risk clients
	5 yr Period probability	50%					14%	28%	**40%**	ASSA simulation, female PRO group
	STI prevalence							19%	**19%**	Country fact sheets
	Partner STI prevalence	12%						14%	**12%**	DHS South Africa
	# regular partners	1						1	**1**	SA split as Zambia
	# regular contacts	600						720	**622**	
	Regular condom use							44%	**44%**	Adetunji and others (2000, 2001)
	# new contacts	3,240						1,560	**2,936**	2 contacts per client
	new condom use							54%	**54%**	Adetunji and others (2000, 2001)
Males attending STD Clinics	**Population '000**	434	18	17	21	11	113	96	**710**	1% of population
	HIV prevalence		42%	54%	54%	50%	65%		**60%**	average of available clinic data
	Partner HIV prevalence	56%		64%			86%	69%	**63%**	sex worker prevalence
	5 yr Period probability		41%	35%	35%	37%	29%	26%	**30%**	ASSA simulation, male PRO group
	STI prevalence	100%	100%	100%	100%	100%	100%	100%	**100%**	by definition
	Partner STI prevalence	12%						14%	**12%**	DHS South Africa
	# regular partners	1							**1**	
	# regular contacts	600							**600**	
	Regular condom use	6%							**6%**	DHS South Africa
	# new contacts							300	**300**	
	new condom use							26%	**26%**	Adetunji and others (2000, 2001)
Military	**Population '000**	85	12	9	2	3	39	22	**172**	The Stockholm International Peace Research Institute (SIRPRI): www.first sipri.org

		South Africa	Namibia	Botswana	Lesotho	Swaziland	Zimbabwe	Zambia	Total	Assumptions
	HIV prevalence	20%		28%					21%	SA study, Botswana ASSA simulation
	Partner HIV prevalence	25%		35%					26%	SA study, Botswana ASSA simulation
	5 yr Period probability	25%		24%					25%	ASSA simulation, male RSK group
	STI prevalence	12%						14%	12%	DHS South Africa
	Partner STI prevalence	12%						14%	12%	DHS South Africa
	# regular partners	1							1	
	# regular contacts	600							600	
	Regular condom use	6%						19%	9%	Adetunji and others (2000, 2001), DHS South Africa
	# new contacts							300	300	
	new condom use						50%	29%	42%	Adetunji and others (2000, 2001)
Prisoners	Population '000	163	4	6	3	2	19	16	214	website
	HIV prevalence	20%		28%					20%	SA study, Botswana ASSA simulation
	Partner HIV prevalence	20%		23%					20%	SA study, Botswana ASSA simulation
	5 yr Period probability	25%		24%					25%	ASSA simulation, male RSK group
	STI prevalence	12%						14%	12%	DHS South Africa
	Partner STI prevalence	12%						14%	12%	DHS South Africa
	# regular partners	1							1	
	# regular contacts	600							600	
	Regular condom use	6%						19%	7%	Adetunji and others (2000, 2001), DHS South Africa
	# new contacts							300	300	
	new condom use						50%	29%	40%	Adetunji and others (2000, 2001)
Male Formal Employed	Population '000	5,167	204	148	120	17	1,850	676	8,181	gender split in Zimbabwe and Zambia, and employment in Namibia based on averages from other countries
	HIV prevalence	20%		28%					20%	SA study, Botswana ASSA simulation
	Partner HIV prevalence	25%	22%	39%	27%	34%		27%	25%	ANC prevalence
	5 yr Period probability	25%		24%					25%	ASSA simulation, male RSK group
	STI prevalence	12%						14%	12%	DHS South Africa
	Partner STI prevalence	12%						14%	12%	DHS South Africa

		South Africa	Namibia	Botswana	Lesotho	Swaziland	Zimbabwe	Zambia	Total	Assumptions
	# regular partners	1							1	
	# regular contacts	600							600	
	Regular condom use	6%						19%	8%	Adetunji and others (2000, 2001), DHS South Africa
	# new contacts							300	300	
	new condom use						50%	29%	44%	Adetunji and others (2000, 2001)
Female Formal Employed	Population '000	3,533	140	94	102	11	1,269	463	5,612	gender split in Zimbabwe and Zambia, and employment in Namibia based on averages;
	HIV prevalence	25%	22%	39%	27%	34%		27%	25%	ANC prevalence
	Partner HIV prevalence	20%		28%					20%	SA study, Botswana ASSA simulation
	5 yr Period probability	33%	33%	30%	32%	32%		32%	33%	ASSA simulation, female RSK group
	STI prevalence	12%						14%	12%	DHS South Africa
	Partner STI prevalence	12%						14%	12%	DHS South Africa
	# regular partners	1							1	
	# regular contacts	120							120	
	Regular condom use	6%	11%						7%	Adetunji and others (2000, 2001), DHS South Africa
	# new contacts	3							3	
	new condom use	16%	11%				38%	50%	24%	Adetunji and others (2000, 2001)
High Risk Transport Workers	Population '000	1,824	67	49	28	22	147	86	2,223	No. of non passenger vehicles
	HIV prevalence	56%		61%					56%	SA study, Botswana ASSA simulation
	Partner HIV prevalence	56%		64%			86%	69%	59%	Country studies, Botswana ASSA simulation
	5 yr Period probability	34%		31%					34%	ASSA simulation, male STD group
	STI prevalence	30%							30%	DHS South Africa
	Partner STI prevalence							17%	17%	
	# regular partners	1							1	
	# regular contacts	300							300	
	Regular condom use	13%							13%	DHS South Africa
	# new contacts	600							600	
	new condom use	47%							47%	DHS South Africa
Teachers	Population '000	136	2	7	3	3	28	10	189	
	HIV prevalence	26%		36%					26%	SA adult prev 30-44
	Partner HIV prevalence	20%		7%					19%	

		South Africa	Namibia	Botswana	Lesotho	Swaziland	Zimbabwe	Zambia	Total	Assumptions
	5 yr Period probability	30%		29%					30%	ASSA simulation, female RSK group
	STI prevalence	12%						14%	12%	DHS South Africa
	Partner STI prevalence	12%						14%	12%	DHS South Africa
	# regular partners	1							1	
	# regular contacts	120							120	
	Regular condom use	6%						19%	7%	DHS South Africa
	# new contacts	86							86	
	new condom use						50%	29%	44%	Adetunji and others (2000, 2001)
Cross-Border Migrants	Population '000	184							184	
	HIV prevalence	42%	38%	65%	46%	58%		46%	42%	1.7 times the prevalence of adult men
	Partner HIV prevalence	25%	22%	39%	27%	34%		27%	25%	ANC prevalence
	5 yr Period probability	20%	22%	27%	19%	33%		19%	20%	ASSA simulation, male RSK group
	STI prevalence	12%						14%	12%	DHS South Africa
	Partner STI prevalence	12%						14%	12%	DHS South Africa
	# regular partners	1							1	
	# regular contacts	400							400	
	Regular condom use	6%						19%	6%	Adetunji and others (2000, 2001), DHS South Africa
	# new contacts	200							200	
	new condom use	40%					50%	29%	40%	Adetunji and others (2000, 2001)
Pregnant Women (ANC)	Population '000	980	55	46	60	39	360	407	1,947	from fertility data
	HIV prevalence	25%	22%	39%	27%	34%		27%	26%	ANC prevalence
	Partner HIV prevalence	20%		23%					20%	SA average, Botswana ASSA simulation
	5 yr Period probability	33%	34%	29%	33%	31%		33%	33%	ASSA simulation, female RSK group
	STI prevalence	10%							10%	DHS South Africa
	Partner STI prevalence	12%							12%	DHS South Africa
	# regular partners	1							1	
	# regular contacts	120							120	
	Regular condom use	6%							6%	DHS South Africa
	# new contacts	15							15	
	new condom use	16%							16%	DHS South Africa
Newborn	Population '000	1,087	63	48	67	43	463	457	2,228	from fertility data

		South Africa	Namibia	Botswana	Lesotho	Swaziland	Zimbabwe	Zambia	Total	Assumptions
Babies in Clinics	**HIV prevalence**	8%		9%					**8%**	ASSA simulation, average child group
	Partner HIV prevalence	0%							**0%**	N/A
	5 yr Period probability	0%		0%					**0%**	ASSA simulation, average child group
	STI prevalence	0%							**0%**	N/A
	Partner STI prevalence	0%							**0%**	N/A
	# regular partners	0							**0**	N/A
	# regular contacts	0							**0**	N/A
	Regular condom use	0%							**0%**	N/A
	# new contacts	0							**0**	N/A
	new condom use	0%							**0%**	N/A
Adolescent Boys (in school)	**Population '000**	1,892	48	56	28	30	402	161	**2,617**	from enrollment data
	HIV prevalence	0%							**0%**	assumption
	Partner HIV prevalence	10%							**10%**	female assumption
	5 yr Period probability	19%							**19%**	ASSA simulation, male RSK group
	STI prevalence	10%						2%	**9%**	DHS South Africa
	Partner STI prevalence	12%							**12%**	DHS South Africa
	# regular partners	1							**1**	
	# regular contacts	300							**300**	
	Regular condom use	19%							**19%**	DHS South Africa
	# new contacts	300							**300**	
	new condom use	21%							**21%**	DHS South Africa
Adolescent Girls (in school)	**Population '000**	2,052	56	62	40	28	348	99	**2,685**	from enrollment data
	HIV prevalence	1%							**1%**	assumption
	Partner HIV prevalence	20%							**20%**	SA average
	5 yr Period probability	34%							**34%**	ASSA simulation, female RSK group
	STI prevalence	5%						2%	**5%**	DHS South Africa
	Partner STI prevalence	12%							**12%**	DHS South Africa
	# regular partners	1							**1**	
	# regular contacts	300							**300**	
	Regular condom use	19%	11%						**18%**	DHS South Africa
	# new contacts	300							**300**	
	new condom use	21%	11%						**21%**	DHS South Africa

Appendix 2. Calculations of infections averted

Primary infections averted

The probability of a "primary" infection refers to whether or not an individual would have been infected with HIV without having been vaccinated. It does not include the probability that the individual would have gone on to infect other people. This is referred to as "secondary" infection.

The number of primary infections averted for a group of HIV negative vaccinated individuals will depend on four factors:

- The *efficacy* of the vaccine – i.e., the probability that a vaccinated person is protected from infection
- The number of people in the group being vaccinated
- The duration of the period of immunity offered by the vaccine
- The average probability that a typical group member would otherwise have become infected during the period of protection of the vaccine.

In general, the number of primary cases averted by vaccinating an HIV negative individual may be expressed as a simple product, as follows:

$$PI(t) = VE * N * P_d(t) \qquad (1)$$

where:
- PI(t) = primary infections averted by vaccination at time t
- VE = efficacy of the vaccine (between 0 and 1)
- N = size of the group
- $P_d(t)$ = period infection probability for the group at time t
- d = duration of protection of the vaccine

The meaning of the "period infection probability" depends on the length of the period. If the period under consideration is one year, then the period probability is equal to the probability that an individual will be infected during that year. This is also the definition of the incidence of HIV infection for the group. For periods of longer than one year, the period probability must be calculated from the incidence within the group for each of the years in the period, as follows:

$$P_d(t) = 1 - \prod_{i=0}^{d-1} \left(1 - I(t+i)\right) \qquad (2)$$

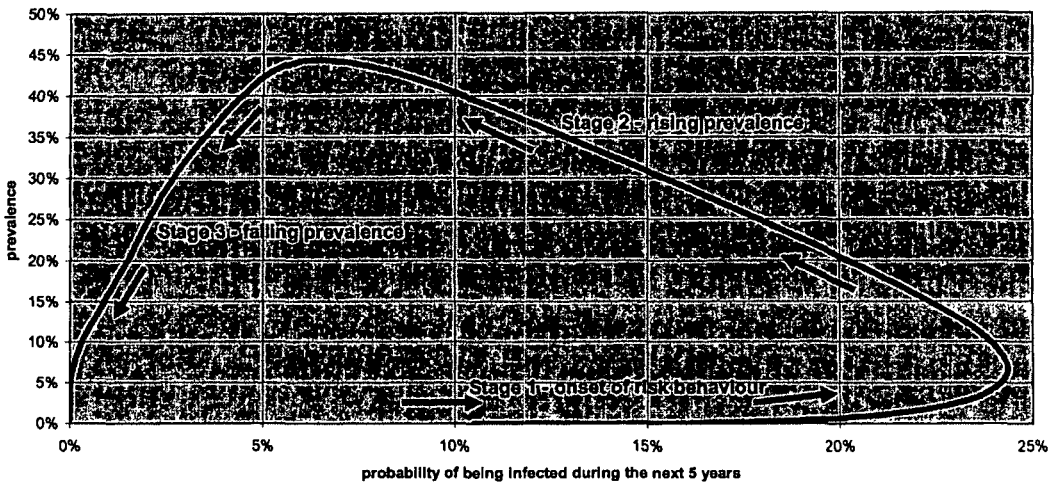
where:
- $P_d(t)$ = period probability of infection at time t
- d = duration of period
- I(t) = HIV incidence at time t (1 year probability of infection)

Equation 6.2 shows that the period probability (and therefore the primary cases averted from equation 6.1) depends on the way in which HIV incidence (labeled I) is expected to evolve for the cohort over the period. The evolution of

HIV incidence is in turn dependent upon the expected risk behavior of the cohort over this period and will vary considerably between different risk groups.

Figure 1 shows the relationship between a 5-year period probability and HIV prevalence for a high-risk group and the way in which it might evolve as the group ages.

Figure 1. Relationship between HIV prevalence and infection probability



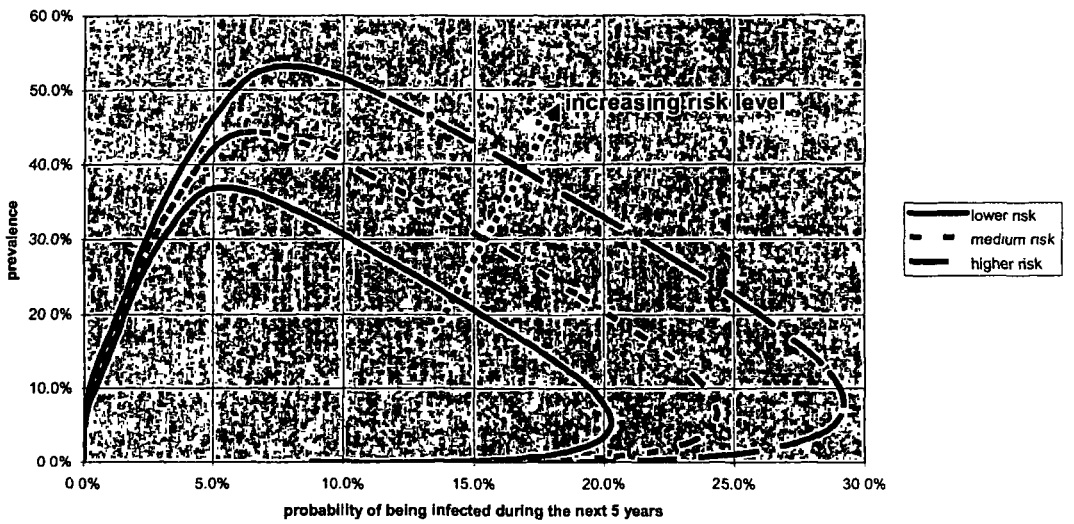
The figure shows an illustrative loop, which the cohort group will traverse in an counter-clockwise direction. For a cohort of HIV negative 12 year olds, both prevalence and period probability are close to zero and will remain so until the cohort begins sexual activity or other risk behavior. When this begins (stage 1), the period probability will rise rapidly, while prevalence rises much more slowly, since few individuals in the group are infected at first. After a few years, prevalence will begin to rise more rapidly and the period probability will begin to fall, as some individuals are already infected and the pool of uninfected members is smaller (stage 2). This trend will continue so that there is a negative relationship between prevalence and period probability (period probability falls while prevalence rises) until significant numbers of the cohort begin to die. At this point, at the top of the loop, prevalence begins to fall, while period probability also falls because there is less risk behavior among older people (stage 3).

Different risk groups are typically in different parts of this cycle. For example, commercial sex workers who have been working for a number of years would exhibit very high prevalence but relatively low incidence - they are near the top of the loop (end of stage 2). Teenage girls who have just begun sexual activity would be expected to exhibit high incidence but low prevalence - they are at the right-hand side (end of stage 1) of the loop.

The size of the illustrated loop would depend upon the degree of risk behavior for the group concerned. Figure 2 shows how these relationships might evolve for a set of illustrative risk groups. As can be seen, the more pronounced

the risk behavior of the group, the larger the scale of the loop, so that the group exhibits higher incidence at the early stages and higher prevalence at the later stages.

Figure 2. HIV prevalence and infection probability for different risk groups



When individuals move from one risk group to another (for example, when an adolescent girl becomes a commercial sex worker, or a commercial sex worker stops sex work), then their risk profile would move from one of these curves to another, representing a change from one type of risk behavior to a different one.

The analysis estimated the primary cases averted by simulating the evolution of prevalence and infection probability for different risk groups. This made use of the illustrative risk groups as represented in the simulation model developed by the Actuarial Society of South Africa (ASSA). The results are shown in Figure 2. Although it is no substitute for the use of real data (which are lacking), the benefit of this method is that it gives a realistic estimate of the period probability in a Southern African setting, while arriving at a "best guess" at the differences in likely risk behavior between the different risk groups.

Secondary infections averted

A variety of variables is instrumental in determining the number of secondary infections averted. These include:

- the number of sexual partners the individual will have over the period for which the vaccine offers protection
- the number of sexual contacts with these partners
- their probability of being infected, per sexual contact
- whether they, or their partners, have a sexually transmitted infection (STI)

- whether their partners are already infected with HIV
- the frequency of condom use.

It is necessary to calculate the probable number of people the individual would have infected if he or she had not been successfully vaccinated. The more sexual partners and more sexual contacts they have, the higher the number of people they would infect. Similarly, the greater the individuals' probability of having an STI and the higher the STI prevalence of their partners, the higher the probability - per sexual contact - that they would transmit HIV. On the other hand, the higher their condom use the lower the probability of transmission per contact. Finally, the higher the existing level of HIV among their partners, the lower the chance that their future partners are HIV negative to begin with. Preventing a repeat infection of an already infected individual is not an infection averted.

The number of secondary infections averted was calculated for each risk group based on the above variables and the following formula:

$$\begin{aligned}&\text{Secondary infections averted (SI) =}\\&\text{Casual Partners Infections Averted (CPIA) +}\\&\text{Regular Partners Infections Averted (RPIA)}\end{aligned} \qquad (3)$$

Individuals are likely to have different sexual behavior with regular partners than with casual partners. These different behaviors necessitate the use of different formulae to calculate secondary infections averted, as follows:

$$CPIA = [CCT_d * (1-PP)] * [(NC*RNC) + (C*RC)] \qquad (4)$$

Where:

CCT_d = The number of sexual contacts with casual partners
PP = The probability that the partner is already HIV positive
NC = The proportion of contacts where a condom is not used
RNC = The risk of HIV transmission per sexual contact without a condom
C = The proportion of contacts where a condom is used =(1-NC)
RC = The risk of HIV transmission per sexual contact with a condom
d = duration of efficacy of the vaccine

The equation is broken into two sections. The first estimates the probability that the contact was with an HIV negative partner. The second half estimates the probability that the contact would have resulted in transmission of HIV if the individual had not been vaccinated. The second half consists of a weighted average of the risk of transmission with and without the use of a condom (the weight is determined by the level of condom use). The risk with and without a condom is calculated as follows:

$$RNC = STD*STII*(IPS+PPS) \qquad (5)$$

$$RC = RNC*CE \quad (6)$$

Where:

STD = The risk of transmission between otherwise healthy adults (differs depending on the sex of the individual)

STII = The STI inflator, the factor by which the presence of an STI in one partner increases the risk of transmission

IPS = The individuals probability of being infected with an STI

PPS = The partners probability of being infected with an STI

CE = Condom efficacy

The equation implies that the STI inflator is doubled when an STI is present in both partners. The expression assumes that the prevalence of STIs is independently distributed from that of HIV infection. Without this assumption, calculations become cumbersome and time consuming and change little in the final result.

The calculation of secondary infections among regular partners is somewhat different. If the method outlined above for casual partners were used, it would be possible for a situation to arise where the prevention of one infection would be counted more than once. It is necessary, therefore, to adjust the formula as follows:

$$RPIA = NP * (1-PP) * [NC(1-(1-RNC)^{RCT_d}) + C(1-(1-RC)^{RCT_d})] \quad (7)$$

Where:

NP = The number of regular partners

RCT_d = The number of sexual contacts per regular partner

The calculation of risk with and without a condom remains the same.

The values of the variables included in these equations will be determined by the duration of efficacy of the vaccine. The number of contacts and the number of sexual partners will apply to the period for which the vaccine is effective. The efficacy of the vaccine makes no difference to the calculations at this stage. These calculations are based on the assumption that the primary infection has been averted.

The above calculations effectively assume that had the individual not been vaccinated, he or she would have become infected the very next time having sex. The combination, in the following section, of primary and secondary infection calculations will address this problem. Secondary infections averted will only be included for primary infections averted, averaged over the period. Although there are more sophisticated methods to achieve this correction, they would complicate the analysis and would have little effect on the magnitude of secondary infections or the ranking of target groups in terms of effectiveness.

It is also possible that a vaccine may lead to changes in sexual behavior resulting from changed perceptions of risk. In the calculations presented in this paper, no attempt has been made to introduce behavior change. The behavior variables used in the calculations are based on the data that are available, which are weak and incomplete. There is therefore no quantitative basis for estimating the impact of a vaccine on behavior change in the different risk groups, so it would not affect the relative ranking of the groups in terms of effectiveness. The implications of changes in behavior prompted by the introduction of a vaccine are, however, discussed below.

The above approach to calculating secondary infections has a number of limitations. First, the method assumes that sexual partners can be divided into two groups—casual one-time partners and long-term partners. In reality, these are the two extremes and there exists a host of different combinations. These could be included by estimating an equation 2.8 for all the different number of sexual contacts. This would however greatly increase the computational burden, and given that such desegregated data does not exist, such an approach was not used. This omission results in an over estimation of secondary infections averted, as a result of double counting for groups with a high number of infrequent but not once off sexual partners. Effectively this means that the calculations over estimate the effectiveness of vaccinating high-risk groups

Second, the calculations do not consider the possibility that future partners may also have been vaccinated. The method, therefore, over estimates the effectiveness for all groups. However, the focus of the paper is on where to begin a vaccination strategy, and this issue is not of critical importance at this stage. Evaluating a broad based vaccination programs requires the use of complex simulation models, which have been deemed beyond the scope of this work (see Stover and others 2002 for an example of this work).

Third, the calculations make the simplifying assumption that STIs and HIV among future partners are distributed independently of each other. Again, this simplification was made to avoid over complicating the analysis.

Total infections averted

The previous two sections have outlined the calculation of the number of primary and secondary infections averted. The estimation of the total number of infections averted per vaccinated HIV negative individuals involves the combination of the previous two calculations as follows:

$$\text{Infections averted} = VE * [\text{primary} + (\text{primary}*\text{secondary})] \quad (8)$$

Where:

VE = the efficacy of the vaccine

primary = the probability that the individual would have been infected had they not received the vaccine

secondary = the number of infections averted by avoiding a primary infection

Unless the possibility of behavior change as a result of vaccination is introduced into the calculation, the efficacy of the vaccine will still make no difference to the ranking of strategies in terms of their effectiveness. Given a decision to vaccinate, which would in part be motivated by the efficacy, the most effective strategies will be the most effective regardless of the efficacy of the vaccine. A change in the efficacy changes the impact of vaccination of all groups by the same proportion and will not affect their effectiveness in relation to one another. Changes in the duration of protection are, however, more important at this stage. While behavior change is not included in the calculations, it is discussed in the text

Changes in the duration change the probability of averting a primary infection. This change will have different implications for the effectiveness of vaccinations in different risk groups.

Infections averted per 100 entrants into the program

The method described above estimates the number of infections averted per vaccine administered to an HIV negative individual. The vaccination of an HIV positive individual will result in no infections averted and may well lead to a false sense of security which could increase the risk of others. Considering only the number of infections averted in this way ignores the costs and complications associated with ensuring that only HIV negative individuals receive vaccinations. A more meaningful measure would be the number of infections averted per 100 entrants into a vaccination program. This calculation was as follows:

Per100 = Total infections averted * (1-target group prevalence)*100 (9)

The vaccination of members of high-risk groups is likely to avert more infections than the vaccination of members of lower risk groups. The impact is, however, likely to be diluted by the need to exclude many vaccination candidates because they are already HIV positive. If the cost of screening is significant relative to the cost of a vaccine, this may have important implications for policy. Policy decisions may be further complicated by the difficulties associated with locating members of high-risk groups.

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