

**The Impact of an AIDS Vaccine in
Developing Countries:
A New Model and Preliminary Results**

IAVI Public Policy Department



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This paper was written by John Stover and Lori Bollinger, Futures Institute.

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Publications Unit
International AIDS Vaccine Initiative
110 William Street, 27th Floor
New York, NY 10038 USA
Tel: + 1.212.847.1111
Fax: + 1.212. 847.1112
Email: pubs@iavi.org
Web: www.iavi.org

IAVI's mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world.

The Impact of an AIDS Vaccine in Developing Countries: A New Model and Preliminary Results

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IAVI's Policy Research Working Paper series disseminates important new research findings in order to promote the exchange of information and ideas that facilitate the effective development and global distribution of vaccines to prevent HIV infection.

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Acronyms and Abbreviations

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
HIV	Human immunodeficiency virus
IAVI	International AIDS Vaccine Initiative
IDU	Injecting drug user
MSM	Men who have sex with men
PMTCT	Prevention of mother-to-child transmission
SW	Sex worker
STI	Sexually transmitted infection
WHO	World Health Organization
UNAIDS	Joint United Nations Programme on HIV/AIDS

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Executive Summary

The International AIDS Vaccine Initiative (IAVI), with technical support from the Futures Group, has embarked on a project to estimate the global and country-level impacts of an AIDS vaccine. This analysis is part of a larger effort to document the need for an AIDS vaccine, the benefits that are likely to result from its widespread uptake, and the potential cost-effectiveness of a vaccine to prevent HIV infection, especially in developing countries hard-hit by the AIDS pandemic. Such an effort is particularly important now to ensure that the needed investments are made today, even though a vaccine may only become available a number of years in the future.

Estimates of the potential impact of AIDS vaccines were reported in IAVI Policy Research Working Paper #4, *Estimating the Global Impact of an AIDS Vaccine, 2005*, as part of the first phase of the vaccine impact project. These estimates were based on a review of the vaccine modeling literature and the application of average impacts on lowered susceptibility (i.e., an exposed individual's chances of being protected from infection) from that literature to regional projections of the AIDS epidemic produced by UNAIDS.

In the recently completed second phase of the project, a vaccine model has been developed which explores the potential impact of AIDS vaccines with a range of characteristics consistent with the leading candidates in the R&D pipeline today, including partial protective efficacy, as well as beneficial actions such as reduced infectiousness and slower disease progression. The new impact model also allows for the analysis of a number of different vaccine delivery scenarios, including broad coverage of the adult population and more targeted vaccination of high- and medium-risk groups.

The model relies on data readily available in most countries and is implemented in an easy-to-use interface. It is hoped that teams of national experts will apply the model to their own epidemics to explore the potential benefits of AIDS vaccines in their countries, alone and in conjunction with expansion of existing HIV prevention methods and the possible addition of other new prevention tools in the coming years.

We have used this model to update the previous estimates of the impact of AIDS vaccines in low- and middle-income countries. The model has been applied to seven key countries (Brazil, China, India, Mexico, Nigeria, the Russian Federation and South Africa) using available data in the form of desk studies, and the results have been extrapolated in order to refine the regional projections presented in the previous study.

The model was used to create a baseline scenario that assumes expansion of prevention efforts and anti-retroviral treatment to achieve the United Nations goals of Universal Access by 2015. Several vaccine scenarios were then generated to explore the possible impact of an AIDS vaccine that becomes available in 2015, at the point where prevention and ART coverage have already been scaled up.

These new results indicate:

- An AIDS vaccine with 30% efficacy provided to 20% of the population (the low scenario) would avert 5.5 million new infections between 2015 and 2030 (11% of the

infections that would otherwise be expected), lowering the annual number of new infections in 2030 by 17%.

- In the medium scenario, an AIDS vaccine with 50% efficacy provided to 30% of the population would avert 17 million new infections between 2015 and 2030 (35% of new infections that would otherwise be expected), reducing the annual number of new infections in 2030 by more than half.
- In a high case scenario, a vaccine with 70% efficacy provided to 40% of the population would avert 28 million new infections between 2015 and 2030 (56% of new infections that would otherwise be expected), reducing the annual number of new infections in 2030 by 81%.

A number of additional scenarios were also tested, including ones with higher general population coverage; targeted coverage of high-risk groups only in countries with concentrated AIDS epidemics; and moderate coverage with a vaccine that only lowers infectiousness without reducing susceptibility to infection. In all of these scenarios, the model suggests that a vaccine would avert a significant proportion of HIV infections and AIDS deaths which would otherwise occur. Under these circumstances, an AIDS vaccine would prove to be a highly cost-effective intervention, with its level of cost-effectiveness enhanced by a series of factors, including higher efficacy, greater coverage of high-risk groups, and lower vaccine cost and costs of vaccine delivery.

In conclusion, we would argue that an AIDS vaccine of only modest efficacy, introduced a number of years from now on the heels of other improvements in HIV prevention including new methods such as circumcision, could still be a decisive intervention that effectively helps to curb the global AIDS pandemic, contributing significantly to ending AIDS.

In Phase III of the ongoing project, we intend to conduct an in-depth study of potential vaccine impacts in selected developing countries, in collaboration with national teams and policy-makers, and to implement a costing module that will permit us to carry out cost-effectiveness analysis.

I. Rationale and Objectives

Twenty-five years after the first AIDS case was identified there are 39 million people living with HIV and over four million new HIV infections every year.¹ Although prevention efforts have expanded coverage of key services and led to success in some countries, at the global level coverage of prevention interventions remains inadequate. The epidemic still causes 2.8 million deaths a year. Efforts to scale up prevention coverage, introduce new interventions such as male circumcision, and develop new prevention tools such as microbicides are underway but controlling the AIDS epidemic is likely to require all of these efforts and more. An AIDS vaccine is considered to be the best long-term solution to the AIDS pandemic and should be seen as part of a comprehensive response to HIV/AIDS, combining with other prevention methods to dramatically lower new infections.

In 2005, the International AIDS Vaccine Initiative (IAVI), with technical support from the Futures Group, embarked on a project to estimate the global and country-level impacts of an AIDS vaccine. This analysis is part of a larger effort to document the need, the potential demand for use, and the benefits that are likely to result from widespread use of an AIDS vaccine. Such an effort is particularly important to ensure that the needed investments are made today, even though a vaccine may only become available in the future.

The first phase of this project used the existing modeling literature on AIDS vaccines to assess potential global impact. The work suggested that if an AIDS vaccine were introduced in 2015, such a vaccine could avert 19% - 47% of the new HIV infections that would otherwise occur in the developing world between 2015 and 2030.² There were several limitations to the work done in Phase I; in particular, the analysis was based on traditional notions of how an AIDS vaccine would work as investigated in the modeling literature, and regional and global estimates assumed a uniform pattern of impact for all countries.

In the second phase, reported in this paper, a new model was developed which uses country-specific demographic, epidemiological, and vaccine uptake data to estimate the impact of an AIDS vaccine for individual countries. The model is designed to include three different modes of vaccine action, in line with the latest thinking of leading vaccine scientists, and to incorporate changes over time in the adoption of other prevention interventions and of anti-retroviral therapy. The model was applied to key countries in each of four developing country regions to explore vaccine impacts in low- and middle-income countries³ under several different scenarios. This report describes the model, its application to these countries, and the results generated. The information from these country analyses was then used to update the earlier estimates of global vaccine impact.

Models are mathematical representations of real world phenomena. They can be useful to explore the potential impacts of interventions even when they do not include all the complexity of real epidemics as long as they capture the key dynamics. Models allow us to explore the effects of future developments and understand the range of possible outcomes

¹ UNAIDS. *Report on the Global AIDS Epidemic*. 2006, UNAIDS: Geneva.

² IAVI. *Estimating the Global Impact of an AIDS Vaccine*. Policy Research Working Paper No. 4. 2005, IAVI: New York.

³ Low income countries are those with 2005 Gross National Income (GNI) per capita of \$875 or less, and middle income countries are those with GNP/cap between \$876 and \$10,725, per World Bank definitions.

given our limited knowledge of the future. In this way models can illuminate possible scenarios and the most important influences on their outcomes.

II. Description of the Vaccine Model

The impact model is an easy-to-use tool that can be applied by national teams to explore the impact of potential vaccines on the HIV epidemic in their countries. It is designed to rely on available data and to reproduce key dynamics of the HIV epidemic. It is implemented as a module within the Spectrum Policy Modeling System.⁴ This section provides an overview of the model. Full details including the model equations are provided in a separate manual.⁵

The model simulates the adult population between the ages of 15 and 49 (which accounts for about 85-90% of all adult HIV infections). Demographic information is provided by DemProj, another module within Spectrum, based on assumptions about base year population size, fertility and mortality from the United Nations Population Division.⁶ The population is divided into male and female populations but is not further stratified by age within the 15-49 age group.

New entrants

New entrants into the model are people reaching age 15 each year. They are initially classified as “Not sexually active” and remain in that category until reaching the median age at first sex.

Risk groups

The population becoming sexually active each year is distributed into various risk groups. For women the risk groups are:

- Sex workers (SW) (high risk)
- Injecting drug users (IDU) (high risk)
- Those with casual sex partners (medium risk)
- Married and faithful to one partner (low risk)

For men the risk groups are:

- Clients of sex workers (high risk)
- Injecting drug users (IDU) (high risk)
- Men who have sex with men (MSM) (high risk)
- Those with casual sex partners (medium risk)
- Married and faithful to one partner (low risk)

⁴ Stover J. Projecting the demographic consequences of adult HIV prevalence trends: the Spectrum Projection Package. *Sexually Transmitted Infections*, 2004. 80(Supplement 1):i14-i18.

⁵ Bollinger L and Stover J. A model for examining the effects of an AIDS vaccine. 2006. Futures Group: Glastonbury, CT.

⁶ Department of Economic and Social Affairs. World Population Prospects: The 2004 Revision. 2005. United Nations: New York.

For the purposes of this model, people become potential IDU at the same age as they become sexually active. Although a person may belong to more than one risk group, he/she is allocated to the group with the highest risk of HIV infection.

People are distributed to the risk groups according to a defined percentage distribution that generally remains constant over time, but can be set to vary in response to the higher mortality experienced by the populations with most risk.⁷ The percentages are based on survey data on number of partners and special studies that estimate the sizes of vulnerable populations.⁸

Movement out of risk groups

Once assigned to a specific risk group, a person remains in that risk group until one of the following happens:

- **Reduced risk.** The person ceases high-risk behavior and moves to the low-risk group. This movement is calculated from the average duration of time in a risk group (an input to the model). This could be “lifetime” in which case the person stays in that risk group for life, or a certain number of years that defines the average duration in the risk group. This movement is particularly important for female sex workers, since they may be sex workers for only a relatively short period — 5 to 10 years — of their adult life.
- **Aging.** Once a person reaches the age of 50, he or she “exits” and is removed from the model population. The model uses the simplifying assumption that the same proportion of the population reaches age 50 in each risk group in a particular year. In reality, of course, risk groups will have different age distributions.
- **Non-AIDS death.** At any time, every person has some probability of dying from a cause other than AIDS. The model assumes this probability is constant across all risk groups. In reality, injecting drug users are likely to have a higher non-AIDS mortality rate than other groups.
- **AIDS death.** People who become infected with HIV may die from AIDS and thus exit from the model population.

⁷ A constant distribution to risk groups means that the percentage of the population in the highest risk groups will fall over time as these groups are subject to higher mortality from AIDS than lower risk groups. To compensate for this, the model allows for replacement recruitment. If replacement recruitment is set to 100% for a high-risk group, then the fraction of those newly sexually active that are allocated to that risk group will rise in order to maintain that risk group as a constant percentage of the adult population. If replacement recruitment is set to 50% then recruitment will rise to replace half of the deficit. If replacement is set to 0% then there is no change in the fraction of those newly sexually active allocated to that risk group. One limitation of this approach is that replacement occurs solely from those newly sexually active, whereas in actual epidemics someone from any risk group might adopt high-risk behavior at any time.

⁸ For information on the sizes of vulnerable populations see the special issue of Sexually Transmitted Infections, *Sexually Transmitted Infections* 2006:82 (Supplement III).

HIV infection

Each person entering the model population is assumed to be HIV-negative and to remain uninfected while not sexually active. The sexually active and IDU populations are exposed to a risk of infection each year. The probability of becoming infected depends on a number of characteristics associated with the individual and his or her partner. The factors for sexual transmission are shown in Table 1.

Table 1. Factors influencing the probability of acquiring HIV infection through sexual transmission

Type of characteristic	Factor affecting HIV transmission
Individual	<ul style="list-style-type: none"> ▪ Number of partners ▪ Circumcision status ▪ ART use
Partner population	<ul style="list-style-type: none"> ▪ HIV prevalence ▪ Stage of HIV infection
Partnership	<ul style="list-style-type: none"> ▪ Number of sex acts per partner per year ▪ Condom use ▪ Sexually transmitted infection (STI) prevalence ▪ Type of contact (heterosexual or MSM)
Epidemiological	<ul style="list-style-type: none"> ▪ Probability of transmission per act ▪ Effect of STI on transmission probability ▪ Effect of MSM sex on transmission probability ▪ Relative infectiousness by stage of infection ▪ Effect of circumcision on transmission ▪ Effect of ART on transmission

For medium- and high- risk populations, HIV prevalence among sex partners is assumed to be the prevalence of the opposite sex in the same risk group. For MSM, it is prevalence in the same risk group. Although people in these risk groups may also have contacts with persons in lower-risk groups, those contacts are not considered in the model as they are less likely to add to the overall risk of infection.

For low-risk groups, contacts with other risk groups are a major source of new infection. For example, a married woman who is faithful to her husband would be classified as low risk. If her husband is not infected and they are mutually monogamous, then she has no risk of infection. However, if her husband has other sexual partners or is an injecting drug user she will still have risk because of her partner's engagement in higher-risk behavior.⁹ Therefore, calculations for the low-risk population take these factors into account.

For IDU, HIV transmission depends on a number of factors including: the frequency of injection, the proportion of needles that are shared, the size of the sharing group, and the interactions between different sharing groups. Rather than attempt to incorporate all of these factors, the model estimates new infections based on a single measure of the force of infection (the proportion of the uninfected population that will become infected each year), as an input. The force of infection is set to reproduce the observed trends in IDU prevalence.

⁹ For low-risk groups the partner prevalence is a weighted average of the prevalence of all risk groups. The weights are the proportion of contacts with each risk group. These are estimated from the number of people in each risk group and the percentage that are married.

This approach does not incorporate harm reduction strategies, but it does produce correct trends in IDU transmission for the purposes of estimating vaccine effects.

Progression of HIV infection

A person newly infected with HIV is in the primary infection stage for six months to a year. People in the primary infection category are more infectious than those in other stages. An infected person moves out of the primary infection stage to enter the asymptomatic stage, where he/she remains for six years and has a low level of infectiousness. An infected person then moves to the symptomatic infection stage where he/she remains for two years, before dying from AIDS. Infectiousness is also elevated for people in the symptomatic stage.¹⁰

Adults in the symptomatic stage are considered to be sexually active. This may overstate HIV transmission if many people in this stage have reduced sexual activity due to illness.

Antiretroviral therapy (ART)

People are considered to be eligible for ART when they are in the symptomatic stage. If they receive ART, then their progression to death is reduced by some proportion (specified in the inputs to the model). A person taking ART is assumed to have the same infectiousness rate as someone in the asymptomatic stage.¹¹

Behavior

As shown in Table 1, HIV transmission is influenced by a number of behavioral factors: number of partners, sex acts per partner, condom use, and STI prevalence. Each of these behaviors is specified for each risk group over time. These behaviors can be varied in the model to simulate the effects of spontaneous behavior change or the impact of prevention interventions. The model also contains a behavioral disinhibition component for vaccines. Adults who think they are protected from HIV, because they are vaccinated or because their potential partners are vaccinated, may revert to earlier levels of risk behavior if the vaccination program does not include a strong component supporting safer behaviors. To date, there is little information available to help predict whether behavioral disinhibition would occur significantly with an HIV vaccination program. It is included in the model so that possible effects can be explored and better understood.

¹⁰ These patterns are taken from Stover J. Projecting the demographic consequences of adult HIV prevalence trends: the Spectrum Projection Package. *Sexually Transmitted Infections*, 2004. 80(Supplement 1):i14-i18. and based on data presented in Collaborative Group on AIDS Incubation and Survival including the CASCADE EU Concerted Action. Time from HIV-1 seroconversion to AIDS and death before widespread use of highly-active antiretroviral therapy: a collaborative re-analysis, *Lancet*, 2000. 355:1131-1137.

¹¹ Bertozzi S, Padian N, Wegbreit J, DeMaria LM, Feldman B, *et al.* HIV/AIDS Prevention and Treatment in *Disease Control Priorities*, Jamison D, Breman J, Measham A, Alleyne G, Claeson M *et al*, Editors. 2006. Disease Control Priorities Project. Chapter 18, Table 18.6.

Disinhibition can be applied to those who are vaccinated or to all adults. If applied to all adults, the disinhibition factor is discounted by the vaccination coverage since we expect those who are not vaccinated will be more likely to adopt riskier behavior if they know that most of the population is vaccinated than if they know that very few people are vaccinated. With 100% disinhibition, behavior would return to levels at the beginning of the epidemic. With lower levels of disinhibition, partial reversal would take place.

Effects of vaccines

Based on current thinking among scientists, HIV vaccines could affect the dynamics of the model in three ways. First, a vaccine administered to HIV negative populations could *reduce their susceptibility to infection*. This is the commonly understood action of a vaccine — to protect the vaccinated individual from infection. If the vaccine action is set to “take” in the model, then a certain portion of those vaccinated (determined by the vaccine efficacy) are fully protected from acquiring HIV. The portion not protected is fully exposed to the risk of infection. In a “degree”-type vaccine, all those who are vaccinated are exposed to a risk of infection that is reduced by the efficacy of the vaccine.

By way of illustration, consider a group of 100 people who are vaccinated with a vaccine with 50% efficacy. In “take” action, the vaccine would work in 50 of the 100 people and fully protect them, while it would fail to work in the other 50 people and provide no protection to them. In “degree” action, the vaccine would have an effect in all 100 people. It would not fully protect them but would reduce their chances of becoming infected per act by 50%. From a public health perspective, the two types of action may produce similar results in general populations, but the individual results would be quite different. For very high-risk populations, “degree” vaccines that reduce the probability of being infected may not provide enough protection to avert many infections.

Second, a preventive vaccine could *reduce the infectiousness of vaccinated individuals* by lowering the amount of virus in an infected person, so that he/she is less likely to infect others through sexual, IDU, or mother-to-child transmission. The model calculates the reduction in the average probability of transmission resulting from this type of efficacy and coverage of the vaccine, and applies this to all contacts with susceptible populations.

Third, an HIV vaccine given to HIV negative persons could be “disease-modifying” by *slowing significantly their progression* to AIDS death if they become infected with HIV. The model implements this by lengthening the asymptomatic period for those vaccinated. This disease-modifying effect does not change the length of the primary or symptomatic stages.

In practice, scientists believe that the first generation of HIV vaccines may only achieve partial and modest levels of these three actions. Biologically, the second and third kinds of vaccine actions may be closely related — individuals who become infected but have their level of HIV virus held in check by the vaccine may experience both lower infectiousness and slower progression to disease.

The model tests vaccines with any or combinations of all three of these types of action. In all cases, it is assumed that the vaccine is effective only when the recipient is HIV-negative.

People who are HIV-positive when vaccinated obtain no benefit for themselves or for others with whom they may have subsequent contact.

Most of the behavioral data required by this model are available from country-specific surveys such as Demographic and Health Surveys, AIDS Indicator Surveys or other nationally representative surveys. Information on high-risk populations is available for many countries from Behavior Surveillance Surveys. Data on the prevalence of HIV and other sexually transmitted infections is usually derived from sentinel surveillance. (Sources used for country analyses are listed in an annex at the end of this report.)

Vaccine delivery and coverage

The model allows HIV vaccination to be delivered in several ways: coverage may apply to all adults, in which case all risk groups have the same coverage; vaccination may be targeted to specific risk groups by specifying different coverage levels for each group; or vaccinations may be available to all adults or just to those who are HIV-negative (which would require testing before vaccination).

The number of people vaccinated in any year is determined by the coverage, which can vary by time. The model assumes that every vaccinated person receives a full course of shots. The total number of people vaccinated is the cumulative number of people vaccinated who are still alive and in the 15-49 population minus those whose vaccination protection has waned (as determined by the average time of protection). The cost of vaccinations is the number of people newly vaccinated in a year multiplied by the cost to provide a full course of vaccination.

Strengths and weaknesses of the model

The major strengths of the model:

- The model includes all three modes of vaccine action anticipated for an HIV vaccine.
- Policy-makers are able to propose various vaccination strategies and to see quickly and easily how they would help lower the number of new HIV infections and AIDS deaths.
- Risk group discrimination is provided to simulate epidemics in any region.
- Model inputs can mostly be determined from surveillance data, national surveys and behavioral surveillance surveys.
- It is easy to use.
- Model projections can include scenarios with expanded prevention programs, including male circumcision, and expanded ART coverage, so that the impact of vaccines can be assessed in an environment of expanded HIV/AIDS prevention and care.

The model's limitations:

- The adult population is not disaggregated by age.
- Switching between risk groups is only from high risk or medium risk to low risk.
- The model makes deterministic projections and does not represent the uncertainty associated with projections. Uncertainty can only be assessed by making alternate projections with different sets of inputs.
- The cost component is preliminary and uses a constant total cost per person vaccinated, which precludes any analysis of scale effects and does not include details on vaccine delivery costs. The cost component could be developed further in a subsequent phase of the modeling, in order to facilitate calculations of total costs and average cost-effectiveness of a future AIDS vaccine under different scenarios.

III. Analysis

Country case studies

The primary purpose of the model is for country application so that national experts can examine the potential impact of an AIDS vaccine in their country. However, the model can also be used to examine the global impact.

In this study, a series of "desk studies" tested the potential vaccine impact for key countries in each region, exploring the effects of different types of vaccine action, either alone or in combination with other prevention and treatment programs.

For this analysis, seven countries were chosen for model application: Nigeria and South Africa in Sub-Saharan Africa; Mexico and Brazil in Latin America; India and China in Asia; and Russia in Eastern Europe. These countries were selected because they are representative of the epidemic in their regions and because they are among the countries with the most infections.

As Table 2 shows, Nigeria and South Africa contain 35% of all adults living with HIV in Sub-Saharan Africa; Mexico and Brazil represent 42% of all those infected in Latin America and the Caribbean; China and India have 77% of people living with HIV in Asia; and Russia has 63% of those living with HIV in Eastern Europe and Central Asia. Overall, the seven countries contain 46% of people living with HIV in the developing world and account for around 70% of all new adult HIV infections.

Table 2. Case study countries compared to global and regional populations for 2005

Country/Region	Population age 15 and above (Millions)	Number of adults living with HIV (Millions)	Adult HIV prevalence (15-49) (%)
Sub-Saharan Africa	424	22.4	6.1
Nigeria	73	2.6	3.9
South Africa	32	5.3	18.8
<i>Nigeria and South Africa as a percent of Sub-Saharan Africa</i>	<i>25%</i>	<i>35%</i>	<i>--</i>
Latin America and Caribbean	393	1.9	0.7
Brazil	134	0.6	0.5
Mexico	74	0.2	0.3
<i>Mexico and Brazil as a percent of LAC</i>	<i>53%</i>	<i>42%</i>	<i>--</i>
Asia	2819	8.2	0.6
China	1035	0.7	0.1
India	750	5.6	0.9
<i>China and India as a percent of Asia</i>	<i>63%</i>	<i>76%</i>	<i>--</i>
Eastern Europe	252	1.5	0.8
Russian Federation	121	0.9	1.1
<i>Russia as a percent of Eastern Europe</i>	<i>48%</i>	<i>63%</i>	<i>--</i>
All case study countries	2219	15.9	0.9
Low and middle income countries	3888	34.4	1.0
<i>Case study countries as a percent of low and middle income countries</i>	<i>57%</i>	<i>46%</i>	<i>--</i>

Sources: Adult population: *World Population Prospects: The 2004 Revision*, New York: United Nations, 2005. Adults living with HIV and adult prevalence: *2006 Report on the Global AIDS Epidemic*. UNAIDS, 2006.

Methodology

For each of these seven countries, modeling was done using data readily available through published reports. These applications are necessarily incomplete, since national experts were not involved in providing the latest information and interpretation of trends. It is hoped that national experts will have an opportunity to download this model and develop their own applications in the near future. Most of the case study countries are large and have epidemics that are geographically diverse. They do not have a single epidemic that can be modeled easily using national averages for inputs. To address this diversity, future applications of the model in these and other countries may need to be conducted at the sub-national level.

Once each country application was completed, the results were reviewed by comparing the model's estimates of prevalence and numbers infected by risk group with available surveillance data or estimates through 2005. This meant ensuring, for instance, that overall adult HIV prevalence matched results from the 2005 national survey in South Africa, and that the number of people infected by risk group in China matched the latest official

estimate from Chinese experts. When the model estimates did not match these external sources, some of the inputs were adjusted to produce a better match. Adjustments are made to inputs that are most uncertain since they are based on a small number of international studies (such as the probability of transmission in a single sex act) rather than to inputs that are based on national surveys.

Through this tuning process, the model estimates were fitted to what we know about the epidemic for each of the case study countries. For each country, the epidemic was also projected into the future to ensure that results were realistic and consistent with other modeling exercises that do not consider vaccines. This is not a guarantee that the inputs are correct. The same epidemic pattern could probably be matched with many different combinations of input values. Thus the input values used to tune the model for each country represent the authors' best judgment, with some input values having more evidence behind them than others.

However, since the vaccine acts by directly affecting susceptibility, infectiousness or progression to disease, rather than through another factor (such as condom use or number of partners), the impact of the vaccine is relatively insensitive to behavioral inputs as long as the model matches the overall characteristics of the epidemic.

The results for the seven countries were then combined to provide totals for each indicator of vaccine impact (such as the total number of infections and the number of new infections). These totals were then extrapolated to represent all low- and middle-income developing countries, by dividing the total for the seven countries by the proportion those countries represent of the developing world total in 2005. This is an approximation because the proportion of new infections represented by these countries will change over time. The same procedure was used to estimate total by region using the specific case study countries in each region.

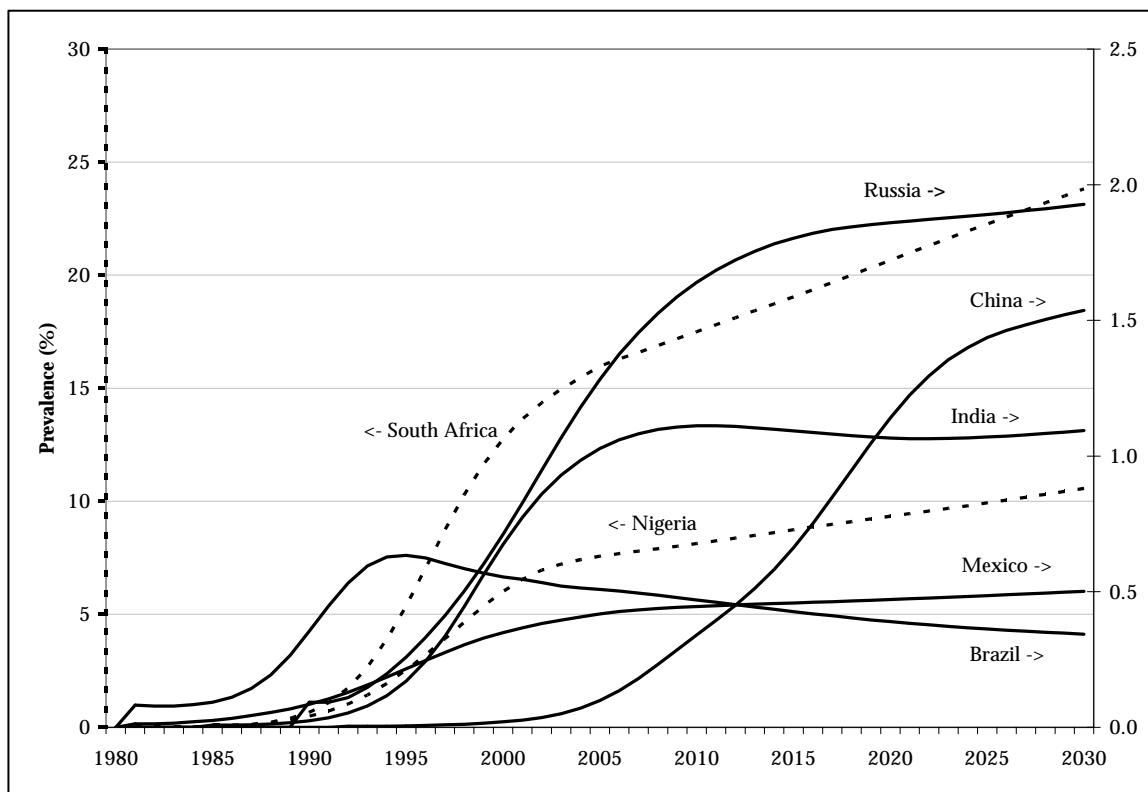
Status quo projections

Once the model has been set up for each of the case study countries and matches the epidemic through 2005, we can project the epidemic beyond 2005. As a first step, projections were done for each country to 2030 assuming no change in any variables after 2005. Those projections are shown in Figure 1. For India, Mexico and Russia these projections are similar to those prepared by extrapolating past trends that have been used to examine the impact of expanded prevention and care.¹² For Brazil, the projection shows a slow decline. For Nigeria and South Africa the projections show slowly rising prevalence as infection stabilizes in the high-risk groups but continues to spread gradually to low-risk populations. For China, the projection used here shows continued rapid growth to about 1.5% before stabilizing. Since the epidemic is still in the early stages in China, it is not clear what the future trajectory will be. A recent attempt to project future prevalence in China estimated that prevalence would stabilize anywhere between 0.5% and 2.5%.¹³

¹² IAVI. *Estimating the Global Impact of an AIDS Vaccine*. Policy Research Working Paper No. 4. 2005, IAVI: New York

¹³ Merli MG, Hertog S, Wang B, Li J. Modeling the spread of HIV/AIDS in China: The role of sexual transmission. *Population Studies*, 2006. 60(1);1-22.

Figure 1. Adult HIV prevalence projected with no change in behaviors or interventions from 2005 - 2030.



Note: Countries shown with dotted lines and preceded by <- (Nigeria and South Africa) refer to the left axis (0-30% prevalence) while those shown with solid lines and followed by -> refer to the right axis (0-2.5% prevalence)

The baseline scenario

The projections above show possible epidemic patterns in the absence of any change after 2005, such as advances in treatment and prevention. However, by the time an AIDS vaccine is ready for implementation, it is expected that other prevention services and treatment will have increased coverage considerably. Most countries have adopted plans to work toward universal access to prevention and treatment in the coming years. Even the partial achievement of these goals will change the epidemic environment for AIDS vaccines. Therefore, expanded prevention and treatment programs have been added to the base projections used for estimating the impact of a vaccine.

Universal access to prevention. The United Nations has called for countries to strive toward universal access to key HIV prevention services. Each country will decide for itself what universal access means and when it can be achieved. Most countries are expected to complete these plans by the end of 2006. In the meantime we have used the targets from the estimation of global financial resource needs. For those estimated, UNAIDS defined a comprehensive prevention package, with services and target coverage levels as shown in Table 3. Target coverage levels vary for each program or intervention, depending on

whether they are being implemented in a country classified as responding to a low stable, concentrated, or generalized epidemic.

Table 3. Universal access: United Nations target coverage levels by type of epidemic

	Low level ¹⁴	Concentrated ¹⁵	Generalized ¹⁶
Programs for vulnerable populations			
AIDS education for primary and secondary students (%)	30	45	100
Programs focused on out-of-school youth (6-15) (%)	10	20	50
Programs focused on sex workers and clients (%)	80	80	80
Programs focused on MSM (%)	80	80	80
Harm reduction programs for IDU (%)	80	80	80
Prevention for people living with HIV (%)	80	80	80
Workplace prevention (%)	0	3	50
Programs for general populations			
Adults reached through community mobilization (%)	0	0	70
Number of mass media campaigns per year (#)	2	4	5
Adult population accessing VCT each year (%)	0.1	1	5
Casual sex acts covered with condoms (%)	80	80	80
Married people with casual partners using condoms in marital sex (%)	30	30	30
Medical services			
Need for post-exposure prophylaxis that is met (%)	100	100	100
Safe blood (proportion of units screened for HIV) (%)	100	100	100
Safe medical injections (%)	77	92	99
Universal precautions (%)	77	92	99
STI treatment (%)	60	75	100
PMTCT (coverage among women attending ANC) (%)	80	80	80

Source: *Resource needs for an expanded response to AIDS in low- and middle-income countries*. UNAIDS, August 2005.

Reaching these target levels of coverage will result in behavior changes. For the purposes of this analysis, increased coverage of prevention services must be translated into an amount of behavior change. This was estimated using the Impact Matrix from the *Goals* model, developed by the Futures Group.¹⁷

¹⁴ Low-level epidemics are those countries where no identifiable population group has HIV prevalence above 5%.

¹⁵ Concentrated epidemics are those countries where prevalence among pregnant women in urban areas is less than 1%, but some groups at high risk have prevalence above 5%.

¹⁶ Generalized epidemics are those countries where prevalence among pregnant women is consistently above 1%.

¹⁷ Bollinger L, Stover J, and Cooper-Arnold K, Where are the Gaps? The Effects of HIV-prevention interventions on behavioral change. *Studies in Family Planning*, 2004. 35(1): 27-38. The Impact Matrix is a summary of all available literature on the impact of interventions on key behaviors: age at first sex, number of partners, condom use, STI treatment seeking behavior and unsafe needle sharing. There are separate matrices for each of the risk groups in the model. The matrix entries show the change in condom use, number of partners and unsafe needle sharing that occurs when a population is exposed to

Interventions in the future to promote adult male circumcision may also have a significant effect on HIV transmission. Male circumcision is already widespread in Nigeria (about 90%), so no additional impact is expected. While circumcision is not common in the other countries examined here, it is unlikely that there would be significant demand for male circumcision in countries with low HIV prevalence. In South Africa, however, studies have shown that there is demand for male circumcision.¹⁸ Therefore, the expanded prevention program for South Africa includes male circumcision services that increase the proportion of adult males that are circumcised from 30% today to 70% by 2015. Other new prevention technologies between now and 2015 could include microbicides, pre-exposure prophylaxis and HSV-2 suppressive therapy, but the impact of these is uncertain, so they are not included in the base scenarios.

This baseline scenario assumes that the prevention coverage targets recommended by UNAIDS will be achieved by 2015. The new values for condom use, number of partners and unsafe needle sharing projected for 2015 and the intervening years are estimated by linear interpolation from 2005 to 2015. Behaviors are kept constant after 2015. Since the UN targets are ambitious and in some cases may prove to be aspirational rather than achievable in the given timeframe, this provides a conservative projection of vaccine impact — the more prevention occurs by other means, the fewer infections will be averted by a vaccine.

Expansion of anti-retroviral therapy. The availability of ART has expanded rapidly in the past few years. In 2005, it was universally available in Brazil and Mexico, and reached about 35,000 persons in Nigeria; 93,000 in South Africa; 16,000 in China; 16,000 in India; and 2,000 in Russia; representing about 5% of need in Russia, Nigeria, and India and about 15% in South Africa and China.¹⁹ In the coming years, treatment will expand further as part of a global effort to achieve universal access to comprehensive prevention programs, treatment, care and support by 2010 as agreed to by United Nations Member States at the June 2006 General Assembly High Level Meeting on AIDS.

Wider ART coverage will lead to a significant reduction in AIDS deaths, but its impact on new infections is not clear. By keeping people alive longer, greater ART coverage could lead to some increase in HIV transmission, although the effect might not be large because ART also reduces viral load. The largest effects may come through behavior change. There might be some disinhibition, where people feel freer to engage in risky behavior because treatment is available. On the other hand, expanded ART could improve the environment for prevention programs by reducing stigma and encouraging more people to get tested. It is important to include expanded ART coverage in this analysis because of the significant impact on AIDS deaths, even though we do not fully understand its likely prevention effects.

each prevention intervention. The impacts are discounted by the increase in the proportion of the population exposed to the intervention, which is the increase in coverage from the base year. Impacts are also discounted if the target population is not the entire risk group. For example, mass media reaches everyone, but AIDS education in the schools reaches students who comprise only a portion of the medium-risk group. The impacts are cumulated across all interventions to determine the final impact.

¹⁸ Scott BF, Weiss HA, Viljoen JL. The acceptability of male circumcision as an HIV intervention among a rural Zulu population, KwaZulu Natal, South Africa. *AIDS Care*, 2005. 17(3):304-13.

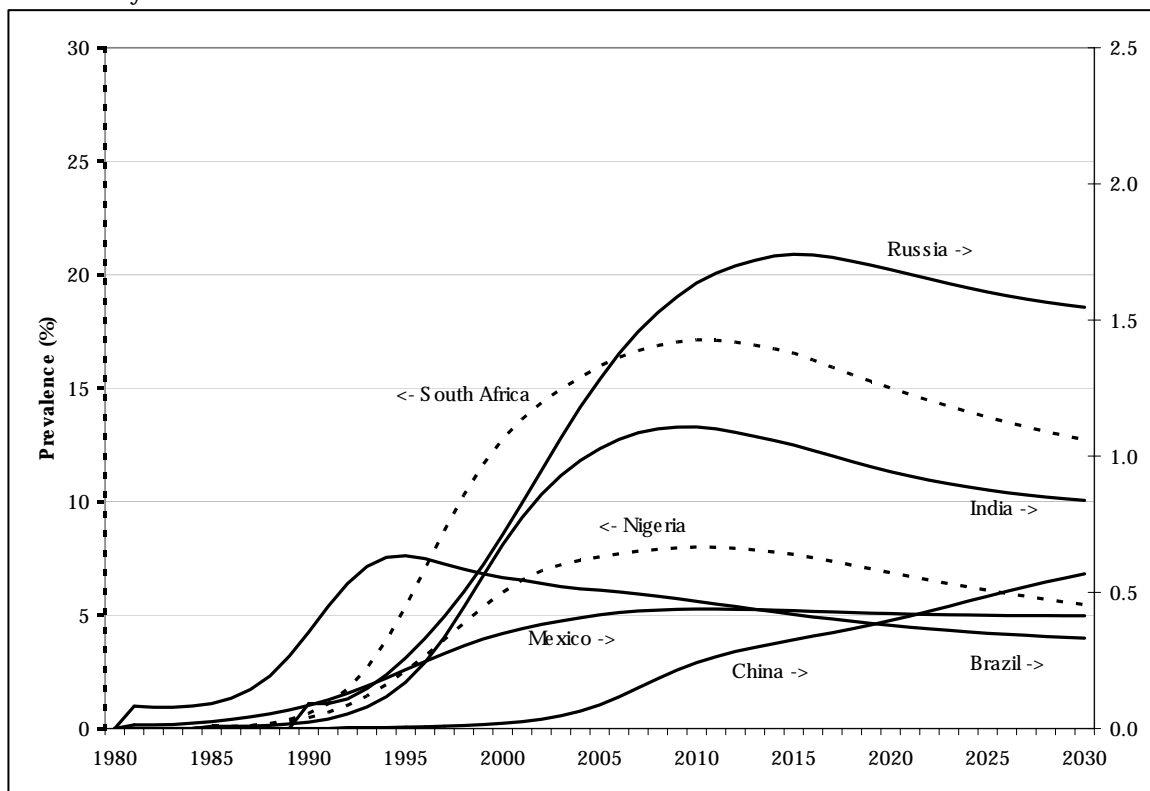
¹⁹ Stover J and Fahnestock M. Coverage of selected services for HIV/AIDS prevention, care and treatment in low and middle income countries in 2005. 2006, Futures Group/POLICY Project: Glastonbury, CT.

In the scenarios described here we have not assumed any behavior change associated with ART use.

Expanded ART coverage is included by assuming the countries that have not yet achieved universal access will expand ART coverage to 50% of those in need by 2010 and to 70% by 2015. After 2015, coverage remains at 70%. This leads to slightly higher future prevalence in countries that currently have low levels of ART coverage, as shown in Figure 2.

The net result of expanded prevention and treatment to the levels proposed for universal access is to reduce prevalence in 2030 by half in Nigeria and China, by one-quarter in Russia and South Africa and by some what smaller amounts in India, Brazil and Mexico. These would be very significant improvements. However, the epidemic would remain serious in all countries, with HIV prevalence still hovering at around 20% of the adult population in South Africa, 4-5% in Nigeria, 1.5% in Russia, and around 0.5% in the other three countries. This translates to about 34 million people living with HIV in 2030, as compared with 26 million today.

Figure 2. Adult HIV prevalence projected with universal access to prevention and treatment services achieved by 2015



Note: Countries shown with dotted lines and preceded by <- (Nigeria and South Africa) refer to the left axis (0-30% prevalence) while those shown with solid lines and followed by -> refer to the right axis (0-2.5% prevalence).

These projections, which include the impact of expanded prevention and treatment (Figure 2), are the baseline projections against which the impact of AIDS vaccines are measured.

Vaccine scenarios

There are many vaccination scenarios and many possible combinations of the different parameters specifying vaccine action, efficacy and coverage. To make the analysis manageable we have selected three vaccine scenarios which span the range from low efficacy and low coverage to high efficacy and high coverage. This provides a range of outcomes that can illustrate the scope for vaccine impact. The specifications of the three scenarios are shown in Table 4. In all scenarios the vaccine has "take"-type action and is assumed to be effective only when administered pre-infection.

For all scenarios the assumptions are that a vaccine first becomes available for wide-scale implementation in 2015 and that coverage increases linearly from 0 in 2014 to the target level in 2020 and then stays at that level through 2030. In the scenarios shown below, coverage refers to the percentage of all adults who are vaccinated. We have used low coverage rates — 20% to 40% — in these scenarios, consistent with the results from earlier work by WHO/UNAIDS on demand and acceptability of AIDS vaccines.²⁰ At the same time, we tested some higher coverage levels to see how they affected the impact results.

The effects of vaccines on susceptibility (30% to 70% reduction) and infectiousness (30% to 70% reduction) are meant to span the plausible range of first generation vaccines that might become available. For vaccines with efficacy less than 30% there would be concerns about the behavioral disinhibition effects overwhelming the biological effects. While vaccines with efficacy greater than 70% may be possible, the first vaccines to become available may not reach that goal. Any vaccine that reduces infectiousness is likely to also affect disease progression, so we have included a doubling of the time spent in the asymptomatic stage in all three scenarios. The doubling of the asymptomatic period assumed here is roughly what is being found in animal studies of vaccine candidates. The duration of protection could range from very short (a few years) to lifetime. We have chosen a long period of vaccine protection in these scenarios but test a shorter period in the sensitivity analysis below. Since each of these scenarios specifies a coverage target, a vaccine with short duration will require more vaccinations and booster vaccinations to maintain the target coverage than one with longer duration.

These scenarios were selected to explore a plausible range of vaccine characteristics and programs. The sensitivity of the results to the assumptions is explored later in the section.

Table 4. Specification of vaccine scenarios

Parameter	Low	Medium	High
First year of availability	2015	2015	2015
Coverage in 2020	20%	30%	40%
Reduction in susceptibility	30%	50%	70%
Reduction in infectiousness	30%	50%	70%
Increase in length of progression period	100%	100%	100%
Duration of effectiveness	20 years	20 years	20 years

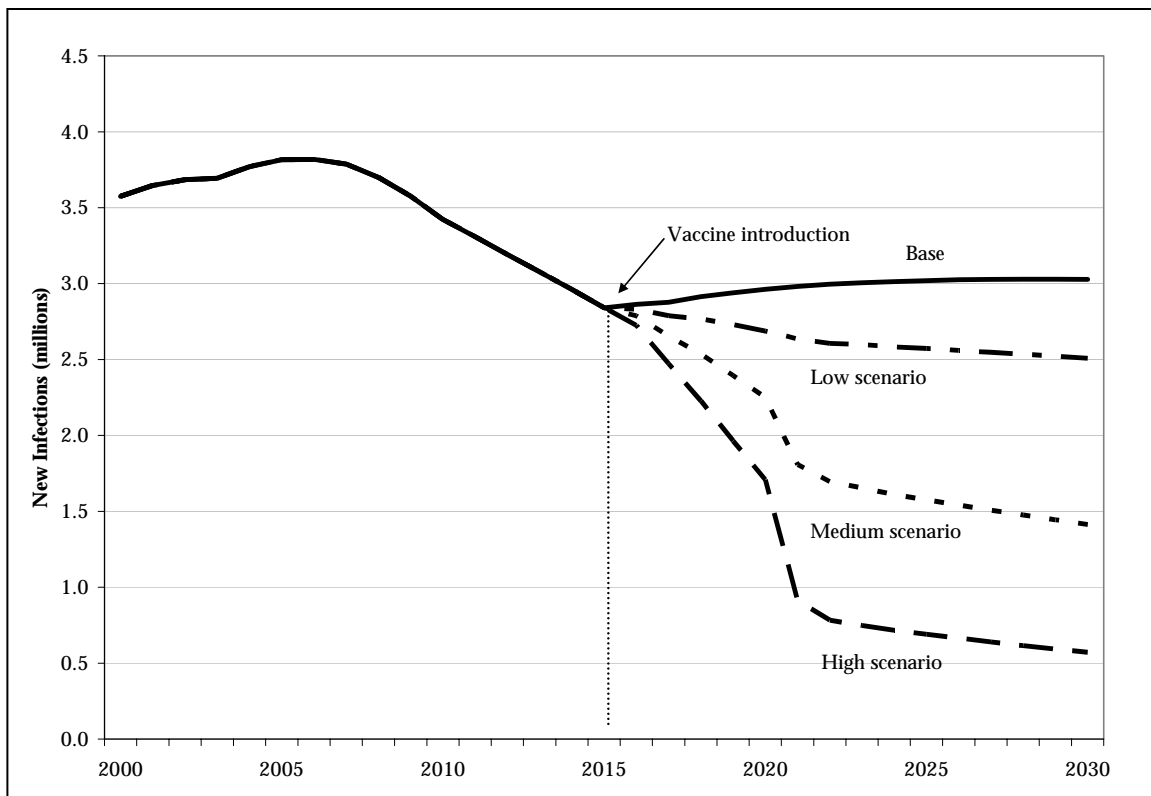
²⁰ Esparza J, Chang M-L, Widdus R, Madrid Y, Walker N, Ghys PD. Estimation of "needs" and "probable uptake" for HIV/AIDS preventive vaccines based on possible policies and likely acceptance (A WHO/UNAIDS/IAVI study). *Vaccine*, 2003. 21: 2032-2041.

IV. Results

Impact of a vaccine on incidence (new HIV infections)

The three main vaccine scenarios. Figure 3 shows the number of new adult HIV infections for all low- and middle-income countries under the three different vaccine impact scenarios compared to the base scenario of expanded prevention and treatment. The different curves in Figure 3 show that the impact of an AIDS vaccine on the number of new HIV infections can be substantial. The base projection shows a decline in the number of new infections up to 2015 as prevention interventions scale up to universal access by that year. After 2015, the number of new infections starts increasing again since the coverage of prevention interventions is no longer increasing and population growth contributes to increasing numbers of new infections even if incidence is stable or declining slightly.

Figure 3. Number of new adult HIV infections in low- and middle-income countries by year and vaccine scenario



With expanded prevention and treatment efforts, but no vaccine, the annual number of new adult HIV infections would decrease from around 4 million today to 3 million by 2015 and grow slightly after that largely due to population growth.

AIDS vaccine scenarios:

- In the low scenario, an AIDS vaccine with 30% efficacy provided to 20% of the population would reduce the annual number of new infections in 2030 by 17% from 3.0 million to 2.5 million. It would avert 11% of the 50 million new infections that would otherwise be expected from 2015 to 2030. This translates into 5.5 million infections averted.
- In the medium scenario, an AIDS vaccine with 50% efficacy provided to 30% of the population would reduce the annual number of new infections in 2030 by 53% to 1.4 million. It would avert 34% of new infections from 2015 to 2030, i.e. a total of 17 million infections averted.
- In the high scenario, an AIDS vaccine with 70% efficacy provided to 40% of the population would reduce the annual number of new infections in 2030 by 81% to 570,000. It would avert 56% of new infections from 2015 to 2030, amounting to a total of 28 million infections averted.

Principal drivers of the results and alternative scenarios. The results shown above are specific to the assumptions made in these projections. To explore how the assumed or selected values for some of the key driving variables in the model might affect the results, and to assess the sensitivity the selected values, we tried several alternative scenarios:

1. *Slower progress on prevention and ART.* The base scenario assumes that international goals for scaling up prevention and treatment are achieved by 2015. If those goals are not met, then the epidemics in these countries will be more severe than shown here. As an alternative base projection, we considered only 50% achievement by 2015 for prevention and treatment scale-up. (That is, the increase in prevention and treatment coverage is only one-half that required to achieve the international goals.) In this case, the *proportion* of new infections averted by the low, medium and high vaccine scenarios would be nearly the same as described above but the *absolute number* of infections averted would be considerably higher. The number of infections averted from 2015 to 2030 increases from 6 to 9 million infections in the low impact scenario, from 17 to 21 million in the medium impact scenario and from 28 to 35 million in the high impact scenario.
2. *Shorter vaccine duration.* All the vaccine scenarios shown above assume vaccines that provide protection for 20 years, but it may be that the duration of protection will actually be less. The way the model is currently structured, shorter duration has virtually no effect on number of infections averted, because the scenarios are driven by coverage levels. The same numbers of people are vaccinated in our calculations no matter how long the protection lasts, since new vaccinations take place once earlier ones wane. With a shortened period of protection more vaccinations are required — four times as many to attain the desired coverage if the duration of protection were only 5 years as opposed to 20 years. This would of course significantly increase costs and lower cost-effectiveness.
3. *Effects of vaccine action.* The scenarios presented above assume that vaccines simultaneously do three things, albeit imperfectly: *reduce susceptibility and infectiousness and slow progression to disease.* The individual effects can be

determined by exploring the results when only one or two modes of action are assumed (summarized in Table 5). In the medium impact scenario a vaccine that:

- Reduces only susceptibility would achieve 58% of the impact of a vaccine with all three modes of action.
- Reduces only infectiousness would achieve 38% of the total impact.
- Lengthens the disease progression period would actually increase new infections by 20% although it would still provide a benefit in terms of additional life years.
- Reduces infectiousness and lengthens the progression period but does not affect susceptibility, would have relatively the same impact as one that only reduced infectiousness, since the additional time spent in the asymptomatic phase would have such low infectiousness.²¹

Table 5. Impact of the different modes of vaccine action in the medium impact scenario

Type of Vaccine Action	Reduction in cumulative number of new HIV infections from 2015 to 2030 compared to medium scenario with all three types of action
Susceptibility, infectiousness, progression	100%
Susceptibility	58%
Infectiousness	38%
Progression	-20%

4. *Enhanced reduction in infectiousness.* The first successful AIDS vaccines, if they are based on the leading vaccine candidates in Phase IIb trials today, may reduce infectiousness and lengthen the time to disease progression, but not lower susceptibility. This is because these candidate vaccines do not appear to stimulate protective antibodies but could induce a strong cellular response that lowers infectiousness and keeps disease in check for a long time. We explored the impact of such a vaccine by assuming a 30% reduction in susceptibility (versus 50% in our medium scenarios above), 70% reduction in infectiousness (versus 50%) and 5 years duration (instead of 20 years). In this case the total number of infections averted between 2015 and 2030 would be relatively the same as the medium scenario.
5. *Degree action.* If the vaccine has "degree"-type action (causing a reduction in susceptibility for everyone vaccinated) as opposed to "take"-type action (completely effective for some people and no effect in others) the impacts would be somewhat different, especially for groups with the highest risk, where "degree"-type action might not provide enough protection to avoid infection. However, changing the type of action from "take" to "degree" in the medium scenario only reduces the number of infections averted by about 2%. The largest impact is in Russia where it reduces the impact by 6%.
6. *Higher coverage.* It is possible that an effective vaccine could achieve higher coverage levels than the 20% to 40% used in the scenarios above. The high scenario (with 70% reduction in susceptibility and infectiousness and 40% coverage) reduces

²¹ This is one possible profile for some of the leading AIDS vaccine candidates today, which may not stimulate protective antibodies but might induce a strong cellular response that lowers infectiousness and keeps disease in check for a long time.

the number of new infections in 2030 by 67% from the baseline. With higher levels of coverage, the reductions would be even more dramatic, as shown in the table below (Table 6). The epidemic would be virtually extinguished by 2030 with an effective vaccine delivered to more than 70% of the population. This reinforces the policy message that higher levels of population coverage are a significant driver of vaccine impact.

Table 6. Impact of higher coverage on incidence of HIV infections²²

Coverage Level Reached in 2020	Reduction in the Number of New Infections in 2030 Compared to the Baseline	Reduction in the Cumulative Number of New Infections from 2015-2030 Compared to the Baseline
40% (High scenario)	67%	46%
50%	76%	53%
70%	88%	65%
90%	94%	73%

²² Assume vaccine is capable of achieving a 70% reduction in susceptibility and in infectiousness.

Impact on AIDS mortality

The impact on AIDS deaths averted has a similar pattern to what the model generates for new infections, but the reductions are smaller because some of the deaths will be averted by treatment in the period after 2030. Figure 4 shows the annual number of deaths under the different vaccine scenarios:

The cumulative number of deaths averted from 2015 to 2030 is 5% in the low scenario, 13% in the medium scenario and 21% in the high scenario.

Figure 4. Annual number of adult AIDS deaths in low- and middle-income countries from 2015 to 2030 by vaccine scenario

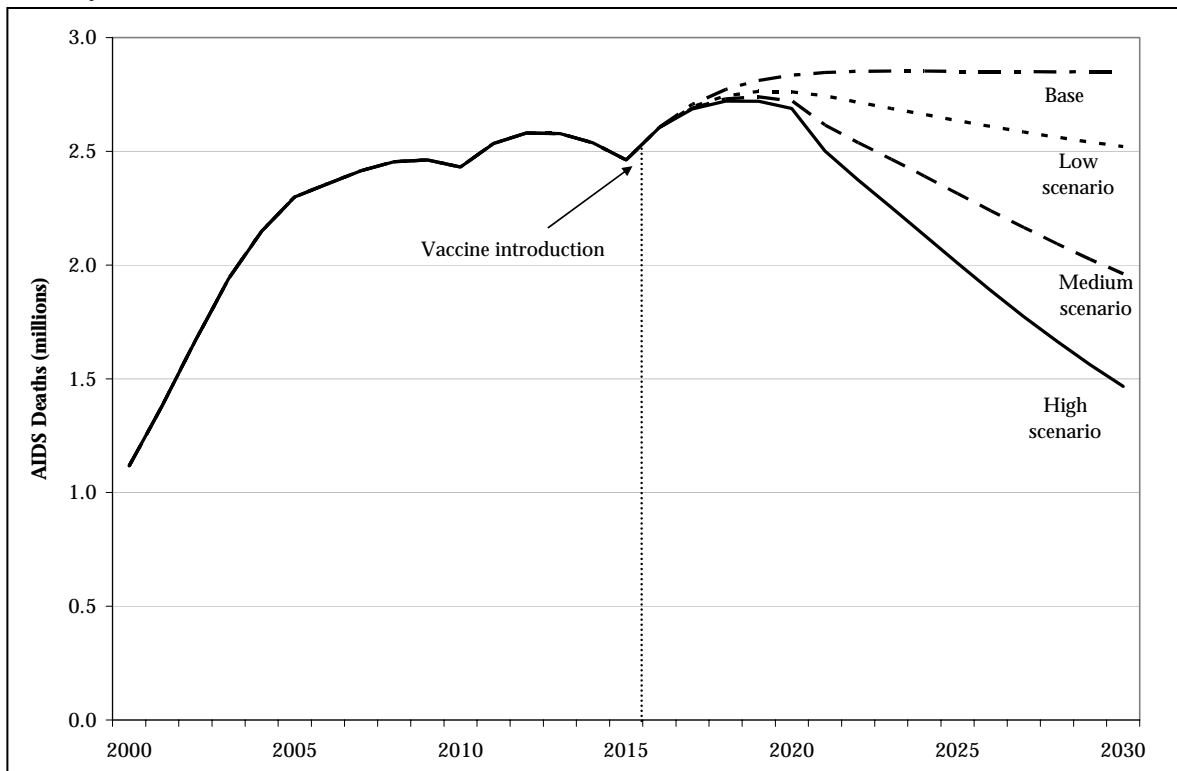


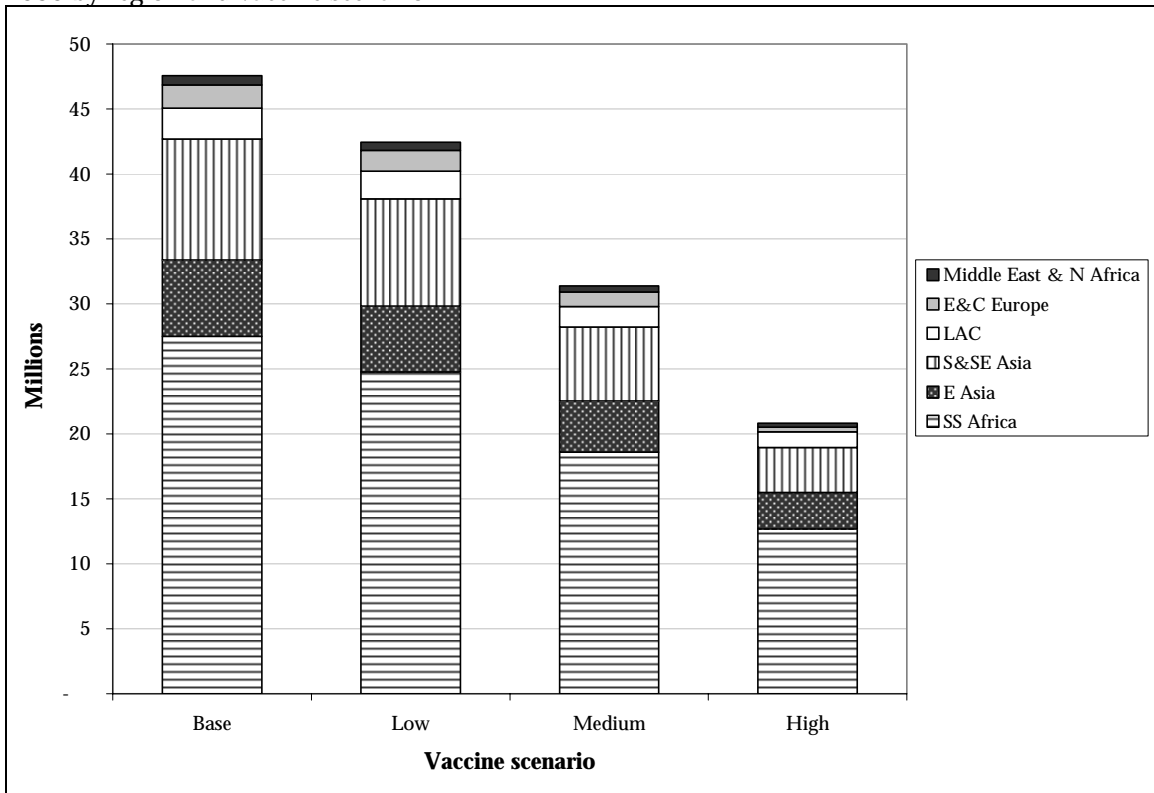
Table 7 summarizes the key indicators from the three scenarios compared to the baseline projections, while Figure 5 shows news adult HIV-infections by region.

Note that the sharp dip in the curve after 2010 is due to the fact that the coverage of prevention services reaches its peak in 2010 and remains constant after that. The dip in the curve after 2015 is caused by ART coverage reaching its maximum value in that year and remaining constant after that.

Table 7. Comparison of new infections and AIDS deaths across all scenarios

	Baseline Scenario	Low Impact Scenario	Medium Impact Scenario	High Impact Scenario
New Infections in 2030	3.0 M	2.5 M	1.4 M	0.6 M
Cumulative New Infections 2015-2030	47 M	42 M	31 M	21 M
AIDS deaths in 2030	2.8 M	2.5 M	2.0 M	1.5 M
Cumulative AIDS deaths 2015-2030	45 M	42 M	39 M	36 M

Figure 5. Number of new adult HIV infections in low- and middle-income countries from 2015 to 2030 by region and vaccine scenario



V. Discussion

The results of these simulations of the potential impact of an AIDS vaccine indicate that under three scenarios based on modest population coverage levels and partial vaccine efficacy, between 11% and 56% of new infections could be averted between 2015 and 2030. That represents 5 to 27 million people who would be protected from HIV infection during that period.²³

These estimates of impact are somewhat higher than those produced in the previous analysis using similar levels of coverage and vaccine efficacy. The previous analysis focused on vaccine impacts on susceptibility, while this analysis adds impacts on infectiousness as well, which enhances the overall impact. This analysis also considers vaccine impact on extending the progression period, which tends to reduce the impact on new infections, but because the extension occurs during the asymptomatic phase, transmission rates are not high and the additional benefit of reduction in infectiousness outweighs the effects of extending the progression period. Modeling results suggest that a vaccine with a weak ability to protect vaccinated individuals from HIV infection but with substantial ability to lower infectiousness could still have a major positive impact on the course of the epidemic in developing countries.

These estimates are based on modeling the HIV epidemic in seven key countries. For India, China, and Russia, the future of the epidemic is highly uncertain. Thus, the projections of the number of infections in the base projection could easily be much higher or lower. The estimates of the number of new adult infections in 2005 are somewhat higher than those released recently by UNAIDS²⁴ but are well within the UNAIDS range for that year. However, the estimates reported here of the proportion of all new infections that could be averted by a vaccine are relatively insensitive to the absolute number of new infections.

With over four million new infections each year, the AIDS epidemic continues to cause widespread harm. A recently published analysis of the impact of scaled-up prevention programs estimated that half of new infections could be averted between 2005 and 2015 and that new infections in 2015 could be reduced by two-thirds over what would be expected without expanded prevention.²⁵ But even with this reduction there would still be a large number of new infections occurring each year. Thus, even if an AIDS vaccine is not available until 2015 or later, there is still an important role for an effective AIDS vaccine if new infections are to be reduced to negligible levels.

This analysis indicates that even a vaccine with only 30% efficacy used by 20% of the population would have a measurable impact on new infections: it would reduce the number of new infections by 17% in 2030 and by 11% from 2015-2030. However, vaccines with higher levels of efficacy (50% or 70%) and modestly higher coverage levels (30% and 40%) would have much greater impact, reducing new infections in 2030 by 53% and 81%

²³ These results are indicative when applied to long-term epidemiological projections in all low- and middle-income countries.

²⁴ 2006_GR-Epicore_en.ppt available at www.unaids.org

²⁵ Stover J, Bertozzi S, Gutierrez JP, Walker N, Stanecki KA, Greener R, Houws E, Hankins C, Garnett GP, Solomon JA, Boerma JT, DeLay P, Ghys P. The Global Impact of Scaling-Up HIV/AIDS Prevention Programs in Low- and Middle-Income Countries *Science*, 2006. 311(5766): 1474-1476.

respectively and cumulatively averting 34% and 56% of all new infections between 2015 and 2030.

The overall impact could be less if the use of the vaccine prompts people to adopt riskier behaviors. In the worst cases with a low efficacy vaccine, behavioral reversals could lead to worse outcomes than without the vaccine. It will be important to link vaccination with good counseling and strong prevention programs to promote safer behaviors. A recent trial of male circumcision in South Africa found that while the men who were circumcised had more sexual contacts than those who were not, male circumcision still significantly reduced the number of new infections.²⁶

The number of people vaccinated in order to achieve the impacts presented in this paper depends on the vaccine delivery strategy and the need for re-vaccination to maintain effective coverage. In the scenarios presented here, which assume vaccination coverage applied to all adults, the average number of people vaccinated per year would range from 120-240 million people during 2015-2020 as vaccine coverage expands to 20-40%, and would then drop to 50-150 million a year to maintain those coverage levels. However, in concentrated epidemics vaccination may be targeted to high-risk populations. If the vaccination coverage level of 40% used in the high scenario were applied to just the high-risk heterosexual populations, men who have sex with men and injecting drug users in concentrated epidemics and to all adults in generalized epidemics, then the total number of people vaccinated would be just 20% (24-48 million) of the total when coverage is applied to all adults in all countries. This targeted vaccination approach would still achieve 85% of the impact.

This paper does not address the issue of cost or cost-effectiveness of a vaccine. The cost of a future vaccine is highly uncertain. However, the total medical, social and economic costs of the AIDS epidemic are clearly enormous, so any program that can reduce the number of new infections by 10% to 50% may be expected to produce significant savings.

In spite of the uncertainties regarding cost, the availability of a vaccine would be a clear and significant benefit in the effort to control the AIDS epidemic. Although prevention programs are expanding rapidly in many countries, they have not yet been enough to reverse the trend of prevalence in any but a handful of countries. An effective vaccine and a successful vaccination program would likely make a significant impact on the course of the epidemic. In the best scenario, an effective vaccine coupled with broad coverage and accompanied by other scaled-up prevention interventions could come close to eradicating the epidemic.

²⁶ Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, Controlled Intervention Trial of Male Circumcision for Reduction of HIV Infection Risk: The ANRS 1265 Trial. *PLOS Medicine*, 2005, 2(11):1-11.

VI. Next steps

The HIV vaccine model developed in this activity has been designed to be appropriate for use by national experts. The model is included as a module within the Spectrum System of Policy Models. The Spectrum Model and manual for the HIV Vaccine module are available for downloading at the Futures Group website (www.FuturesGroup.com). We hope that teams of national experts will apply the model to their epidemics using the best available data to explore the effects of different types of vaccines and implementation strategies. IAVI plans to support several national teams to carry out this work.

This modeling project should be seen within in the larger context of AIDS vaccine policy analysis and advocacy. IAVI is supporting other activities to build country demand and uptake scenarios for AIDS vaccines, with demand levels dependent on several key factors including efficacy, price, and HIV prevalence. These demand scenarios can then be combined with the impact model and with cost estimates in order to calculate the cost-effectiveness of an AIDS vaccine.

In addition, WHO-UNAIDS and IAVI are supporting a complementary HIV vaccine modeling program called *HIV VaccSim*, a more complex vaccine model which can be used to explore the range of uncertainty and the resulting distributions of potential impact estimates.^{27,28} That model also allows greater flexibility in exploring highly targeted vaccine delivery strategies (e.g., to sex workers, primary school age children, etc) and their relative cost-effectiveness, in the face of potentially limited vaccine supplies.

²⁷ Barth-Jones DC, Cheng H, Kang LY, Kenya PR, Odera D, et al. Cost effectiveness and delivery study for future HIV vaccines. *AIDS*, 2005. 19(13):w1-6.

²⁸ Barth-Jones, DC & Longini Jr., IM. Determining Optimal Vaccination Policy for HIV Vaccines: A Dynamic Simulation Model for the Evaluation of Vaccination Policy. *Proceedings of the International Conference on Health Sciences Simulation 2002* in Eds. Anderson JG, Katzper, 2002 *Western Multiconference*, January 27-31, 2002. San Antonio, Texas.

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IAVI—East Africa
 Floor 16, Rahmutulla Tower
 Upperhill Road
 PO Box 340 KNH 00202,
 Nairobi, Kenya

IAVI—India
 193 Floor 1, Jorbagh
 New Delhi, 110003
 India

IAVI—Headquarters
 110 William Street
 New York, NY 10038
 United States

IAVI—Europe
 Herengracht 206-216
 1016 BS Amsterdam
 The Netherlands

IAVI—Southern Africa
 6 Aubury Park, Unit 0006
 Magalieszicht Ave,
 Dunkeld West 2196
 South Africa