The Impact Of An AIDS Vaccine In Developing Countries: A New Model And Initial Results

A moderately effective AIDS vaccine introduced in 2015 could avert millions of new AIDS infections over the following fifteen years.

by John Stover, Lori Bollinger, Robert Hecht, Clara Williams, and Eva Roca

ABSTRACT: A new model was developed to examine the potential impacts of an AIDS vaccine in developing countries. The findings suggest that even a modestly efficacious first-generation vaccine could have a profound effect on the AIDS pandemic. A vaccine with 50 percent efficacy provided to 30 percent of the population would reduce new annual infections by 34 percent (seventeen million infections avoided) over fifteen years and result in substantial financial savings. A more efficacious vaccine, combined with expanded delivery, would do even more to control the pandemic. It therefore makes sense to continue investing in AIDS vaccine research and development and the eventual manufacture and widespread distribution of a vaccine. [Health Affairs 26, no. 4 (2007): 1147–1158; 10.1377/hlthaff.26.4.1147]

Twenty-five years after the first case of AIDS was identified, there are thirty-nine million people living with HIV and more than four million new HIV infections each year.1 Although expanded prevention programs have led to partial success in some countries, current prevention interventions have proved inadequate in slowing the spread of HIV at the global level. As a result, the epidemic still causes 2.8 million deaths each year.2 Although efforts continue to scale up prevention and develop new tools such as male circumcision, microbicides, and pre-exposure prophylaxis, controlling the AIDS epidemic will require all of these efforts and more. A vaccine is a vital piece in the strategy to defeat AIDS. Combined with other prevention methods, it could dramatically lower the number of new infections and prevent disease associated with AIDS.

By modeling the impact of AIDS vaccines under various scenarios, policymakers can better understand how an AIDS vaccine could be used in their coun-

John Stover is president of the Futures Institute in Glastonbury, Connecticut. Lori Bollinger is its vice president. Robert Hecht (RHecht@iavi.org) is senior vice president, Public Policy, at the International AIDS Vaccine Initiative (IAVI) in New York City. Clara Williams is a senior analyst at IAVI; Eva Roca was formerly a policy analyst there.
tries. This can also help them explore some of the likely challenges in the coming decades, especially as they plan to integrate an AIDS vaccine into a comprehensive response, in an environment of expanded prevention and treatment.

Previous efforts to model the impact of AIDS vaccines have been limited to high-risk populations, focused on a specific geographic setting, or concentrated on a narrow range of strategies. The model presented here improves on prior research by allowing investigators to examine a wide range of strategies and by drawing on readily available, country-specific data that can reproduce the key dynamics of the epidemic in any locale at the regional, national, or global levels.

Much of the previous research on the impact of AIDS vaccines focused on vaccines that were assumed to stimulate protective immune responses in the vast majority of vaccinated people. Such responses would prevent infection from becoming established in the body through the action of “sterilizing immunity,” in which the immune system produces antibodies that block HIV from entering host cells. Vaccinated people would therefore no longer be susceptible to infection.

However, current vaccine research suggests that the first licensable vaccines may be effective only in a modest portion of those vaccinated and may induce a different kind of immune response—a cytotoxic T-cell response, which would not eliminate HIV infection entirely but would keep the amount of virus at a low level so that the vaccinated person would be less likely to transmit HIV to a partner and would also have a slower progression to AIDS-related illness and death.

The model presented here improves on previous efforts by examining combinations of three anticipated mechanisms of vaccine action: reduced susceptibility via a protective immune response, reduced infectiousness, and slower progression to AIDS via control of the viral load at a reduced “set point.”

**Description Of The Model**

- **Risk groups.** The model simulates the adult population ages 15–49. The population is divided into males and females but is not further stratified by age. People reaching age fifteen are considered new entrants to the model and are placed into one of five risk groups when they initiate sexual activity: (1) low-risk heterosexuals (single partner); (2) medium-risk heterosexuals (multiple partners); (3) high-risk heterosexuals (commercial sex workers and their clients); (4) men who have sex with men; and (5) injecting drug users (IDU). A person may leave any higher-risk group by adopting lower-risk behavior, and the model keeps track of this transition.

  Every 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 the risk of infection each year. The probability of becoming infected depends on a number of characteristics associated with that person, his or her partners, and the pair (Exhibit 1).

  Most contacts are assumed to be with partners in the same risk group. However, for low-risk groups, contacts with other risk groups are a major source of
new infection. Therefore, calculations for the low-risk population take into account the fact that some people who are faithful to their partners will still be at risk because their partners engage in riskier behavior.

Categories of HIV infection. We used the following categories in the model for people who are HIV-infected. Those who are newly infected with HIV are in the primary infection stage. They remain in this category for six months and are more infectious than people in other stages. An infected person passes out of the primary stage and enters the asymptomatic stage, where he or she remains for six years with a low level of infectiousness. An infected person then moves to the symptomatic infection stage where he or she remains for two more years, before dying from AIDS. Infectiousness is also elevated for people in this last stage.

Eligibility for ART. People are considered eligible for antiretroviral therapy (ART) when they are in the symptomatic stage. If they receive ART, their progression to death is reduced by a proportion specified as an input to the model, and their infectiousness returns to the (low) level of the asymptomatic stage.

Possible vaccine effects. The model captures three possible effects of HIV vaccines: (1) reduced susceptibility to infection (via protective immunity), (2) reduced infectiousness of vaccinated individuals, and (3) slower progression to AIDS morbidity and death. In all cases, it is assumed that the vaccine is effective only when the recipient is HIV-negative. Although a therapeutic effect is theoretically possible, the model does not attempt to capture any kind of therapeutic action—that is, there is no assumed benefit to people who are HIV-positive when vaccinated.

Reduced susceptibility. A vaccine administered to HIV-negative people could provide protection by reducing their susceptibility to a persistent infection, effectively clearing the body of HIV and thus preventing disease; this is the commonly understood action of a vaccine. If the vaccine action is set to “take” in the model, then a certain portion of those vaccinated are fully protected from acquiring HIV—that is, the vaccine is completely effective for some people and has no effect on others. The percentage of people protected is determined by the vaccine’s effi-
cacy, while the portion not protected is fully exposed to the risk of infection. In a “degree” type of vaccine, all of those who are vaccinated are exposed to a risk of infection that is reduced by the efficacy of the vaccine; this causes a reduction in susceptibility for everyone who is vaccinated.

Reduced infectiousness. A preventive vaccine could also keep the amount of virus in a person at a low level so that he or she is less likely to infect others. Studies have shown that viral load is strongly associated with infectiousness; a single log decrease in viral load reduces the probability of transmission by more than half. 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.

Modifying disease. A vaccine given to an HIV-negative person could also provide a benefit by greatly slowing progression to AIDS morbidity. The model implements this by lengthening the asymptomatic period for those vaccinated who obtain this benefit but does not change the length of the primary or symptomatic stages.

Strengths and limitations of the model. Major strengths are that (1) the model includes all three anticipated modes of vaccine action; (2) most of its inputs can be determined from epidemiological surveillance data, national surveys, and behavioral surveillance surveys; and (3) projections can include scenarios with expanded prevention programs, including male circumcision, treatment of sexually transmitted infections, and increased use of ART, so that the impact of vaccines can be assessed in an environment of improved prevention and care. The model could also incorporate other new HIV prevention methods that might emerge in coming years, such as pre-exposure chemoprophylaxis and microbicides. Regarding limitations, the model does not disaggregate the adult population by age. The only risk-group switching is from high or medium to low risk. In addition, the model makes a deterministic projection. It does not represent the uncertainty associated with projections. Uncertainty can be assessed only by making alternative projections with different inputs.

Assumptions And Analysis

We applied this model to seven key countries that are among those with the most infections, in four regions that are representative of the epidemic: Nigeria and South Africa (sub-Saharan Africa), Mexico and Brazil (Latin America), India and China (Asia), and Russia (Eastern Europe). Overall, these seven countries contain 46 percent of the people who are living with HIV in the developing world, accounting for around 70 percent of all new adult HIV infections (Exhibit 2). For India, China, and Russia, the future of the epidemic is uncertain, and the baseline projections of the number of infections could be much higher or lower. However, the estimates of the number of new adult infections in 2005 from the model are within the ranges estimated by the Joint United Nations Program on HIV/AIDS (UNAIDS). The results from these countries are scaled up to the region repre-
represented by each country or pair of countries, according to the proportion of all new infections in the region in the modeled countries in 2005.

- **Baseline projections.** A baseline projection was prepared for each country, assuming that no vaccine becomes available but that coverage for other prevention services and treatment increases considerably. Because most countries have adopted plans to work toward universal access to prevention and treatment in the coming years, the baseline projections assume that coverage targets for these programs will be met by 2015 and will continue at that level thereafter; the baseline projections show a corresponding decline in the number of new infections.\(^9\) After 2015, the number of new infections starts increasing again as the coverage of prevention interventions plateaus and population growth contributes to increasing numbers of new infections, even if incidence is stable or declining slightly.

- **Assumptions about impact of prevention.** We assumed that scaled-up prevention programs would result in delays in age at first sexual contact, reduced number of partners for high-risk groups, increased condom use, and reductions in risky behavior among the IDU population. We based these assumptions on earlier model-
ing work on the impact of prevention programs on HIV transmission. The expected impact of male circumcision is included in the projections for South Africa, underpinned by recent encouraging results from trials there and in East Africa. Other new prevention technologies such as microbicides, pre-exposure prophylaxis, and herpes simplex virus-2 (HSV-2) suppressive therapy, being evaluated in clinical trials, are not included because their likely results are less clear.

**Projected ART coverage expansions.** Expanded ART coverage is also included in the model. The baseline projection optimistically assumes that the countries that have not yet achieved universal access will expand the use of ART to 50 percent of those in need by 2010 and to 70 percent by 2015. After 2015, coverage remains at 70 percent. This leads to slightly higher HIV prevalence in the future in countries that now have low levels of ART use.

**Three vaccine scenarios.** We examined three main vaccine scenarios ranging from low efficacy/coverage to high efficacy/coverage (Exhibit 3). Other combinations (for example, a high-efficacy vaccine targeted narrowly to a small population group, or a low-efficacy vaccine reaching a large number of people) are also possible to test using the model. In all three scenarios, the vaccine has “take” type action and covers a plausible range of vaccine characteristics and programs. We explore the sensitivity of the results to changes in the underlying assumptions later.

For all of the scenarios, we assumed that the vaccine will first become available for wide-scale implementation in 2015 and that coverage (percentage of adults vaccinated) will increase linearly from zero in 2014 to the target level in 2020 and then will stay at that level through 2030. The model allows for other start dates for the AIDS vaccine rollout, for different rates of uptake, and for various countries to stagger the introduction of the vaccine over several years.

Any vaccine that reduces infectiousness is also likely to affect disease progression through reduced viral load. This is assumed to lead to a doubling of the time spent in the asymptomatic stage in all three scenarios. The duration of vaccine protection could range from very short (a few years) to lifetime. We chose a long period of vaccine protection in these scenarios but tested a shorter period in the sensitivity analysis. Since each of these scenarios specifies a

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**EXHIBIT 3**

**Specification Of AIDS Vaccine Scenarios**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low</th>
<th>Medium</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>First year of availability</td>
<td>2015</td>
<td>2015</td>
<td>2015</td>
</tr>
<tr>
<td>Coverage in 2020</td>
<td>20%</td>
<td>30%</td>
<td>40%</td>
</tr>
<tr>
<td>Reduction in susceptibility</td>
<td>30%</td>
<td>50%</td>
<td>70%</td>
</tr>
<tr>
<td>Reduction in infectiousness</td>
<td>30%</td>
<td>50%</td>
<td>70%</td>
</tr>
<tr>
<td>Increase in length of progression period</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Duration of effectiveness</td>
<td>20 years</td>
<td>20 years</td>
<td>20 years</td>
</tr>
</tbody>
</table>

**SOURCE:** Authors’ specification of model.
coverage target, a vaccine with short duration will require more frequent revaccinations to maintain the target coverage than one with longer duration.

**Study Results**

With expanded prevention and treatment efforts but no vaccine (baseline scenario), the annual number of new adult HIV infections would decrease from around four million today to three million by 2015 and grow slightly after that, largely because of population growth. Seen in this context, a vaccine introduced a decade from now could make a major impact (Exhibit 4).

In the low scenario, an AIDS vaccine with 30 percent efficacy provided to 20 percent of the population would reduce the annual number of new infections in 2030 by 17 percent. It would avert 11 percent of the fifty 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 percent efficacy provided to 30 percent of the population would reduce the number of new infections in 2030 by 53 percent. It would avert 34 percent of new infections from 2015 to 2030—a total of seventeen million infections averted. In the high scenario, an AIDS vaccine with 70 percent efficacy provided to 40 percent of the population would reduce the annual number of new infections in 2030 by 81 percent. It would avert 56 percent of new infections from 2015 to 2030, amounting to a total of twenty-eight million infections averted.

These results are specific to the assumptions made in our projections. To explore how the selected values for some of the key variables in the model might affect the results, we tried several alternative scenarios.

- **Slower progress on prevention and ART.** If the goals of universal access to prevention and treatment are not met, the epidemic will be more severe than shown here. As one alternative, we considered only 50 percent achievement of the universal

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**EXHIBIT 4**

**Number Of New Adult HIV Infections In Low- And Middle-Income Countries, By Year And Vaccine Scenario, 2000–2030**

<table>
<thead>
<tr>
<th>New infections (millions)</th>
<th>Vaccine introduced</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Base</td>
</tr>
<tr>
<td></td>
<td>Low scenario</td>
</tr>
<tr>
<td></td>
<td>Medium scenario</td>
</tr>
<tr>
<td></td>
<td>High scenario</td>
</tr>
</tbody>
</table>

**SOURCE:** Authors’ calculations.

**NOTE:** For details about scenarios, see text.
access goals by 2015. In this case, the proportion of new infections averted by each scenario would be nearly the same as described above, but the absolute number of infections averted would be higher. The number of infections averted from 2015 to 2030 would increase from six million to nine million in the low scenario, from seventeen million to twenty-one million in the medium scenario, and from twenty-eight million to thirty-five million in the high scenario.

Effects of vaccine action. The scenarios presented above assume vaccines that simultaneously do three things, albeit imperfectly: reduce susceptibility, reduce infectiousness, and slow progression to disease. In the medium scenario, a vaccine that only reduced susceptibility would achieve 58 percent of the impact of a vaccine with all three modes of action. A vaccine that only reduced infectiousness and slowed progression without affecting susceptibility would avert about ten million infections over fifteen years in this scenario. This is an important scenario to consider, since the first licensable AIDS vaccine might set the threshold of viral load at a lower set point without offering much protection from persistent infection.

“Degree” versus “take” actions. 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 avert infection. However, the difference is small on a global basis: Changing the type of action from “take” to “degree” in the medium scenario would reduce the number of infections averted by only about 2 percent. The largest impact is in Russia (6 percent reduction).

Higher vaccination levels. Countries could achieve higher coverage levels than the 20–40 percent used in our scenarios if they vigorously pursue policies and programs to deliver the vaccine to their populations. The high scenario (with 70 percent reduction in susceptibility and infectiousness and 40 percent coverage) would reduce the number of new infections in 2030 by 67 percent from the baseline. With higher levels of vaccination, the reductions would be even more dramatic, as shown in Exhibit 5. The epidemic would be virtually extinguished by 2030 with an effective vaccine delivered to more than 70 percent of the population. This reinforces the

<table>
<thead>
<tr>
<th>Coverage level reached in 2020</th>
<th>Reduction in number of new infections in 2030 compared to baseline</th>
<th>Reduction in cumulative number of new infections from 2015 to 2030 compared to baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>40% (high scenario)</td>
<td>67%</td>
<td>46%</td>
</tr>
<tr>
<td>50%</td>
<td>76%</td>
<td>53%</td>
</tr>
<tr>
<td>70%</td>
<td>88%</td>
<td>65%</td>
</tr>
<tr>
<td>90%</td>
<td>94%</td>
<td>73%</td>
</tr>
</tbody>
</table>

**SOURCE:** Authors’ calculations.
policy message that higher levels of vaccination are a major driver of vaccine impact and that it is important for countries to plan ahead so that an immediate, large-scale rollout of a vaccine program can take place once a vaccine becomes available.

The impact on AIDS deaths and deaths averted shows a similar pattern to what the model generates for new infections, but the reductions are smaller because some of the deaths would be averted by treatment in the period after 2030. The cumulative proportion of total AIDS deaths averted from 2015 to 2030 is 5 percent in the low scenario, 13 percent in the medium scenario, and 21 percent in the high scenario (Exhibit 6). (The dip in the curve after 2015 is caused by ART coverage reaching its maximum value in that year and remaining constant after that.) Exhibit 7 summarizes key indicators from the three scenarios compared to the baseline projections. The largest benefit is in sub-Saharan Africa, where the epidemic is most severe, but major benefits are also expected for the Asian regions.

Discussion And Policy Implications

With more than four million new infections each year, the HIV/AIDS epidemic continues to spread and cause widespread harm. The results of our simulations show that an AIDS vaccine could greatly reduce the number of new infections and alter the course of the epidemic, even if vaccine efficacy and population coverage levels are relatively modest. In low- and middle-income countries, 11–56 percent of new infections, or 5–27 million new infections, could be averted during 2015–2030 by a moderately effective AIDS vaccine that is introduced in 2015. The baseline projections also show that although expanded prevention and treatment programs will slow the spread of AIDS, they will not halt the disease. Thus, a vaccine should be considered a vital part of a comprehensive response to AIDS.

**Potential of first-generation vaccines.** The potential effects of vaccines modeled here are meant to span the plausible range of first-generation vaccines. Although vaccines with efficacy greater than 70 percent might eventually be developed, the first vaccines might not reach that goal. This analysis indicates, however,
that even a vaccine with only 30 percent efficacy used by 20 percent of the population would have an important impact on new infections. Vaccines with higher levels of efficacy (50 or 70 percent) and modestly higher coverage levels (30 or 40 percent) would have an even greater impact, reducing new infections in 2030 by 53 percent and 81 percent, respectively, and cumulatively averting 34 percent and 56 percent, respectively, of all new infections between 2015 and 2030.

Our modeling results also suggest that a first-generation vaccine that works primarily or exclusively by keeping viral load in check and thus lowering infectiousness and disease progression could still have a considerable positive impact on the epidemic. An AIDS vaccine therefore does not need to be “perfect” to be an extremely valuable weapon in the fight against AIDS.

- **Vaccines and risk behavior.** Because the overall impact could be reduced if receiving the vaccine prompts people to adopt riskier behavior, vaccination should be linked with good counseling and prevention programs. Although a trial of male circumcision in South Africa found that those who were circumcised had more sexual contacts than those who were not, the most recent information from trials in Kenya and Uganda shows no behavioral risk compensation after circumcision.14

  - **Impact of vaccination coverage.** The number of people vaccinated to achieve this impact depends on the delivery strategy and the need for revaccination to maintain effective coverage. In our scenarios, the average number of adults vaccinated per year would be 120–240 million people during 2015–2020 as vaccine coverage expands to 20–40 percent and would then drop to 50–150 million a year to maintain those coverage levels.

  - **Importance of infrastructure.** Developing countries would find it challenging to create and maintain the immunization infrastructure required to deliver an AIDS vaccine to so many people, especially since they would include marginalized adult groups, not the children who receive the bulk of Expanded Program of Immunization (EPI) vaccines. On the other hand, these are not impossible orders of mag-
nitude, particularly for countries facing the terrible consequences of the AIDS epidemic. By comparison, the United Nations Children's Fund (UNICEF) delivers 185 million doses of measles vaccine and more than two billion doses of oral polio vaccine to low-income countries each year.15

**Targeting the vaccine.** In countries with concentrated epidemics (low overall prevalence, with pockets of high prevalence in high-risk groups only), vaccination might be targeted to high-risk populations. If the vaccination coverage level of 40 percent (high scenario) is applied to high-risk heterosexual populations, to men who have sex with men and IDUs in countries with concentrated epidemics, and to all adults in countries with generalized epidemics, the model suggests that the total number of people vaccinated would be limited to 24–48 million per year. Because of the importance of the high-risk groups in fueling the epidemic, this targeted approach would still achieve 85 percent of the impact of a generalized vaccination program. This finding suggests that in some countries with concentrated epidemics and limited financial and human resources, governments might want to promote vaccination for everyone but direct limited public funds to support vaccination for the highest-risk groups, where the public health benefit would be the largest.

**Cost and cost-effectiveness analysis.** This paper does not address cost or cost-effectiveness. The cost of a future vaccine is still highly uncertain, since manufacturing technology and associated costs are still unknown, and there are few precedents for estimating the costs of delivering a vaccine to adult populations. However, the combined medical, social, and economic consequences of the AIDS epidemic are enormous, so a vaccine that can reduce the number of new infections by 10–50 percent may be expected to produce sizable savings.

One possible approach to cost-effectiveness analysis would be to establish benchmarks for cost per infection averted, cost per person treated with ART, and cost per disability-adjusted life-year (DALY) gained, based on the literature covering available HIV prevention services and other health interventions considered to be “good buys.” These benchmarks could then be converted, using the model described in this paper, into a series of corresponding figures representing the total cost of the vaccine delivered. Any combination of manufacturing and delivery costs below these thresholds would point to an AIDS vaccine that is more cost-effective than the alternative AIDS or public health intervention.

**Other possible uses of the model.** Other possible future analyses using this model include examining vaccine effects under other conditions, such as incomplete vaccination (that is, a portion of those vaccinated do not receive all doses recommended) or the adoption of other new HIV prevention methods such as microbicides, should these methods be shown to be efficacious. The model also can be used by policymakers to determine how a vaccine may affect their response to the AIDS epidemic, mobilize political support for intensified vaccine research, increase national participation in vaccine trials, and develop plans to ensure access to a vaccine when one becomes available. The AIDS epidemic is heterogeneous, and strategies to
stop the epidemic must be tailored to the unique needs of each country and region. The model presented here lends itself to these tasks.\footnote{Preliminary results from the modeling work were presented during a satellite session at the Toronto AIDS conference, 13–18 August 2006, as well as the HIV Vaccine Conference in Amsterdam, 29 August–1 September 2006. Preliminary results were also discussed during the World Health Organization (WHO)/Joint United Nations Program on HIV/AIDS (UNAIDS) Cost-Effectiveness and Delivery Study for HIV Vaccines in Beijing, September 2006. John Stover and Lori Bollinger conducted the research under contract with the International AIDS Vaccine Initiative (IAVI); the research was also funded in part by the U.S. Agency for International Development (USAID) and IAVI’s many other generous donors. The authors thank Neff Walker, Daniel Barth-Jones, Philip Musgrove, and Raymond Hutubessy for their insightful comments during the research and analysis.}

\textbf{NOTES}
2. Ibid.
6. This population accounts for about 85–90 percent of all adult HIV infections. The model is implemented as a module within the Spectrum Policy Modeling System. Full details, including the model equations, are given in ibid., as well as in J. Stover, “Projecting the Demographic Consequences of Adult HIV Prevalence Trends: The Spectrum Projection Package,” \textit{Sexually Transmitted Infections} 80, no. 1 Supp. (2004): i14–i18.
10. Ibid.