Policy Research Working Paper #4 October 2005

Estimating the Global Impact of an AIDS Vaccine

IAVI Public Policy Department

This paper was written by John Stover, the Futures Group.

The author would like to acknowledge Donald Burke, Jose Esparza, Neff Walker, Daniel Barth-Jones, Sally Blower, Paul Wilson, and Robert Hecht for their comments and contributions to this paper.

International AIDS Vaccine Initiative, 2005
ISBN: 0-9773126-1-5

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Policy Research Working Paper #4
October 2005

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.

Contents

Acronyms and Abbreviations

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
HIV	Human immunodeficiency virus
IAVI	International AIDS Vaccine Initiative
IDU	Intravenous drug use
PMTCT	Prevention of mother-to-child transmission
WHO	World Health Organization
UNAIDS	Joint United Nations Programme on HIV/AIDS

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 and the benefits that are likely to result from widespread implementation. 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 vaccines have been made by a number of scientists using simulation modeling. Researchers have used modeling to investigate the effects of vaccines with different characteristics in different epidemics. Among the characteristics examined are efficacy, duration of protection, and mode of action. Models have also been used to look at various levels of coverage and efforts to target vaccination at particular populations. In general the researchers have found that vaccines can have a significant impact on new HIV infections even if efficacy is as low as 40-50%. However, programs must guard against behavioral reversals by supporting vaccination with other strong prevention programs.

This paper synthesizes the results of these modeling studies and applies them to the worldwide HIV/AIDS epidemic in order to estimate the global benefits of an AIDS vaccine. The modeling results are summarized in a graph that shows the expected reduction in long-term HIV prevalence given different levels of effective vaccine coverage. “Effective coverage” is a combination of vaccine efficacy and the proportion of the population that is vaccinated. These impacts are applied to projections of the future course of the epidemic by region from 2005 to 2030 prepared by UNAIDS. The vaccination programs are assumed to start in 2015 and the benefits are calculated through 2030.

Without any further expansion of prevention efforts except for prevention of mother-to-child transmission (PMTCT) programs and without a vaccine, the annual number of new infections among adults and children would increase from around 6 million today to 10 million by 2030. An AIDS vaccine with 40% efficacy provided to 20% of the population (the Low scenario) would reduce the annual number of new infections in 2030 by 32% from 10.2 million to 7.0 million. It would avert 19% of the 150 million new infections that would otherwise be expected from 2015 to 2030. An AIDS vaccine with 60% efficacy provided to 30% of the population (the Medium scenario) would reduce the annual number of new infections in 2030 by 54% to 4.7 million. It would avert 31% of new infections from 2015 to 2030. A vaccine with 95% efficacy provided to 40% of the population (the High scenario) would reduce the annual number of new infections in 2030 by 82% to 1.8 million. It would avert 47% of new infections from 2015 to 2030, amounting to a total of 70.5 million infections averted.

I. Introduction

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 and the benefits that are likely to result from widespread implementation. 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.

This paper details the first phase of this effort, focused on assessing the global impact of a vaccine. Subsequent phases will entail enhancements to the existing global model, re-estimation of global impacts, and a series of country-level impact studies to be undertaken with national policy researchers and policymakers. The larger undertaking will be embedded in a broader range of analyses of the cost, cost-effectiveness and cost-benefit of vaccines, as well as the development and implementation of country-specific models that can be used by national experts to examine the benefits of vaccines in their specific contexts.

The paper begins by reviewing the existing literature and describing the design of the model used to estimate the impact of a preventive AIDS vaccine. It summarizes the model's results and finally discusses circumstances that could affect the impact of a preventive vaccine.

II. Review of the literature and design of the impact model

The benefits of an AIDS vaccine have been investigated by a number of researchers through the use of simulation models. This body of work illustrates well the likely impact of AIDS vaccines in a variety of specific situations. However, it does not show the global benefits. This work builds on the existing modeling results by applying them at the regional level to investigate the likely benefits in all low- and middle-income countries.

Our approach to estimating the likely future benefits of an AIDS vaccine follows five key steps:

- Review the literature to summarize the results of modeling studies showing the impact of AIDS vaccines on adult HIV prevalence or incidence
- Describe the relationship between effective coverage and adult HIV prevalence found in the modeling studies
- Develop three scenarios encompassing a range of assumptions about vaccine effectiveness and coverage
- Use projections from UNAIDS to describe the future course of the epidemic without a vaccine
- Estimate the benefits of vaccines by applying the impact information from the literature to the UNAIDS projections using the three vaccine impact scenarios.

These five steps are described in detail below.

A. Literature review

A literature search was conducted to synthesize the findings of the research teams that have addressed these issues. The full results of that literature search are reported elsewhere (Stover and Willson 2005). The general conclusion from that review is that even a low-efficacy vaccine can have an important impact on the AIDS epidemic, although it is unlikely that such a vaccine alone would lead to eradication. The characteristics of the vaccine make an important difference, as do the implementation strategies, but the most important factors affecting impact are the efficacy and coverage of the vaccine and whether or not the vaccination program leads to some people adopting riskier behavior.

The literature reviewed spans a period from 1991 to 2005. Many of the earlier studies focused on vaccines that prevent the vaccinated individual from becoming infected. It now appears that it may be easier to develop vaccines that modify the progression of the disease and/or reduce infectiousness rather than ones that prevent infection. As a result, some recent modeling work focuses on the impact of disease-modifying vaccines. However, in order to take advantage of the full body of modeling work carried out over the last decade, this paper focuses on vaccines that prevent infection. A second phase of work to be conducted in the next year will examine the impact of disease-modifying vaccines.

B. Effective coverage and its relationship to vaccine impact

The effects of efficacy and coverage can be combined into a single measure of effective coverage, the proportion of the population that is protected from HIV infection by a vaccine. Figure 1 shows the relationship between effective coverage and reductions in long-term prevalence levels from a number of different studies. There is good agreement among the McLean and Blower (1993) study, which looks at a high-prevalence population group; the two Anderson *et al.* studies, which looked at typical epidemics in southern Africa (1995) and urban, sub-Saharan Africa (1996); the Gray *et al.* (2003) study, which used data from Rakai, Uganda; the Barth-Jones and Longini (2002) study, which examined an Asian epidemic with both sexual and intravenous drug use (IDU) transmission, and the Nagelkerke and De Vlas (2003) study, which examined southern India. The Bogard and Kuntz (2002) study looked at IDU in Bangkok. While the Bogard and Kuntz study found much lower impact for a vaccine of 10 years duration, the impact was similar to the other four studies when a vaccine with lifetime protection was used.

A number of other authors reported the impact of vaccines in terms of the reduction in HIV incidence (Figure 2). Gray *et al.* is the only paper that reported impact on both prevalence and incidence. His results for incidence are similar but somewhat lower than those from Blower *et al.* (2002), which looked at impact in the gay community in San Francisco, and Seitz (2001), which looked at impact in Thailand and Kampala.

This analysis uses the McLean and Blower (1993), Anderson *et al.* (1995 and 1996), Gray *et al.* (2003), Nagelkerke and De Vlas (2003), and Barth-Jones and Longini (2002) results regarding impact on prevalence as its base assumption. There is good agreement among these five studies, and the Bogard and Kuntz study with lifetime protection, and the results are similar, but conservative, when compared with studies reporting impact on incidence. These results show adult HIV prevalence can be reduced significantly within 20 to 25

years of implementing a vaccine. Effective coverage of 20% of the population would reduce prevalence by around 50%, and effective coverage of 50% would eventually reduce prevalence by 80% from the baseline level.

Figure 1. Impact of an AIDS vaccine on adult HIV prevalence after 20-25 years as a function of effective coverage.

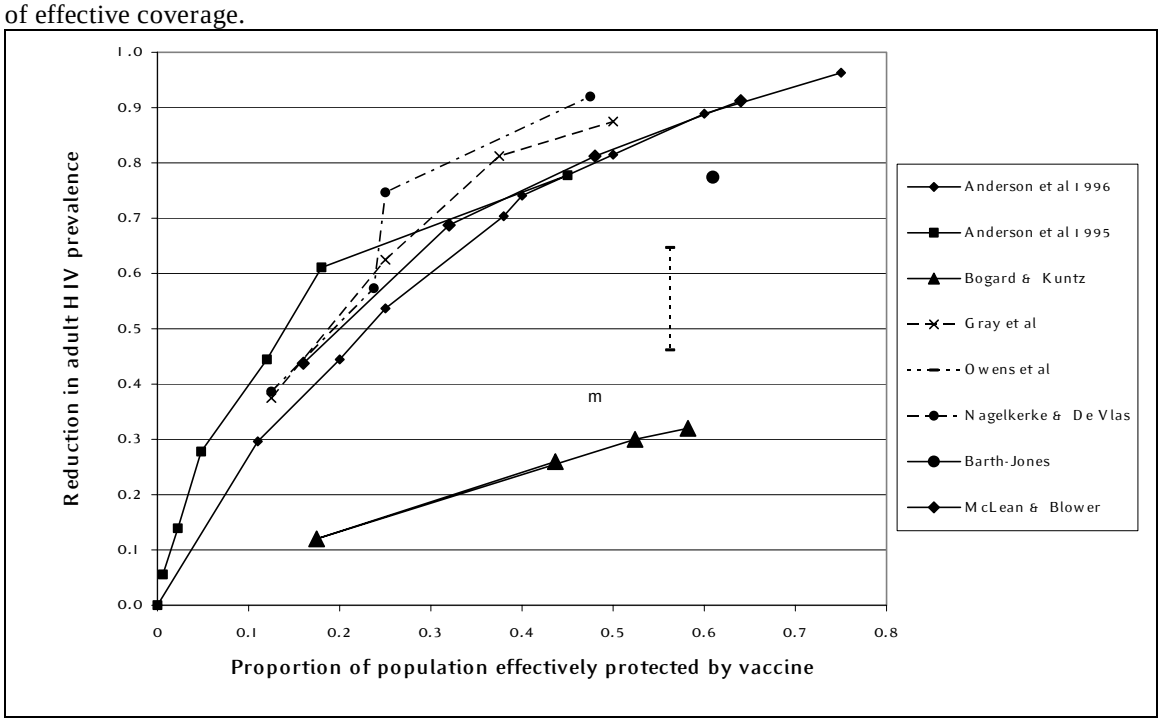
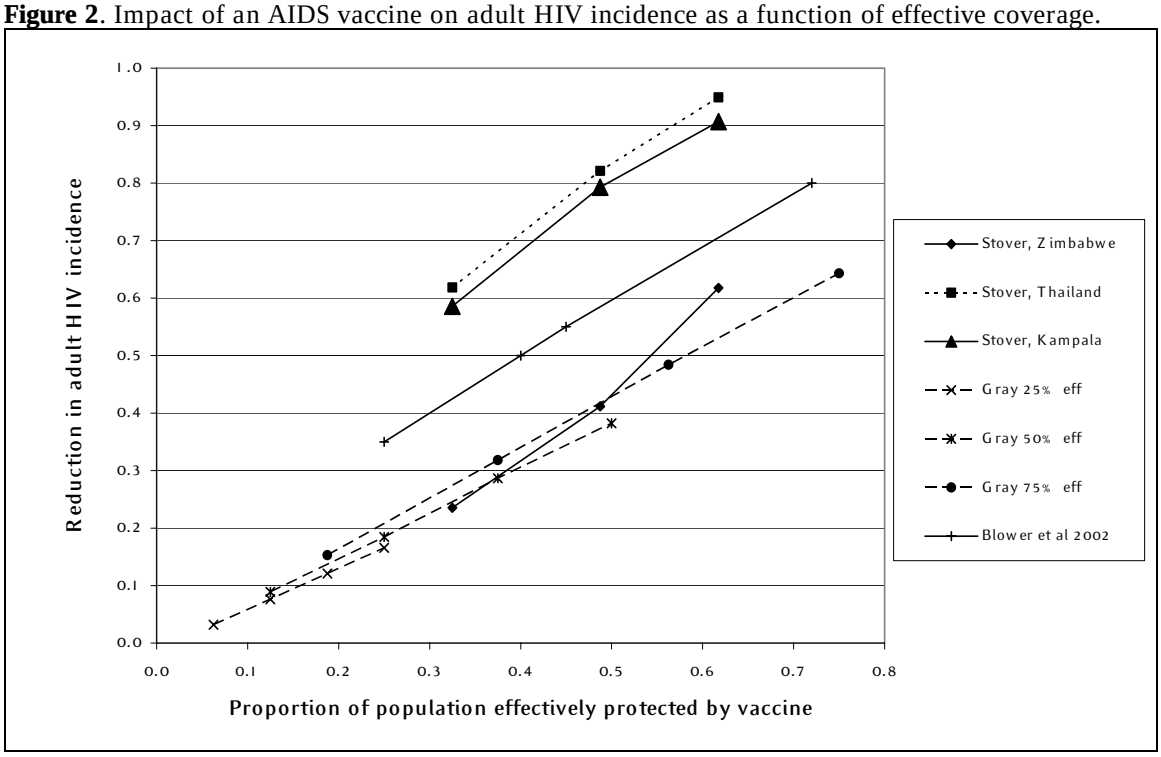


Figure 2. Impact of an AIDS vaccine on adult HIV incidence as a function of effective coverage.



In addition to vaccine efficacy and coverage, several other vaccine characteristics are important to the estimation of impact.

- Duration of protection. Vaccines with longer durations have more impact. However, most of the studies focused on African-type epidemics found little additional impact if the duration of protection was extended beyond 10 years. Duration is more important for very high-risk groups with high rates of turnover. This analysis assumes that for those vaccines providing less than 10 years of protection, the effective duration would be extended by revaccination campaigns. With this approach, duration of protection is not a key characteristic for estimating impact, although it would become important for estimating costs and cost-effectiveness.
- Type of action. Vaccines may have take-type protection (where a person in which the vaccine "takes" is fully protected) or degree-type protection (where every person vaccinated receives some, incomplete protection). The model-based research has found that the type of protection does not have a major effect on the amount of impact, except in populations with very high risk, where take-type protection is more beneficial than degree-type.
- Type of protection. Vaccines may protect against infection (prophylactic) or reduce the severity or progression of the infection (disease-modifying). While there are benefits to disease-modifying vaccines, this analysis assumes that the ultimate goal is to produce a prophylactic vaccine and is therefore confined to the impact of prophylactic vaccines. However, many current vaccine candidates are expected to be disease-modifying, and can reduce transmission of HIV to others, perhaps by reducing viral load during the period of primary infection. Because these could also

have important prevention benefits, their impact will be explored in greater detail in future work.

C. Vaccine impact scenarios

Three scenarios are used to explore a range of potential impacts of an AIDS vaccine (see Table 1). These scenarios are intended to capture the full range of likely conditions. The low scenario assumes efficacy is set at 40%, which is probably at the low end of efficacy that would be considered acceptable by health authorities for implementation. Moderate (60%) and high (95%) efficacy are assumed for the medium and high scenarios, respectively.

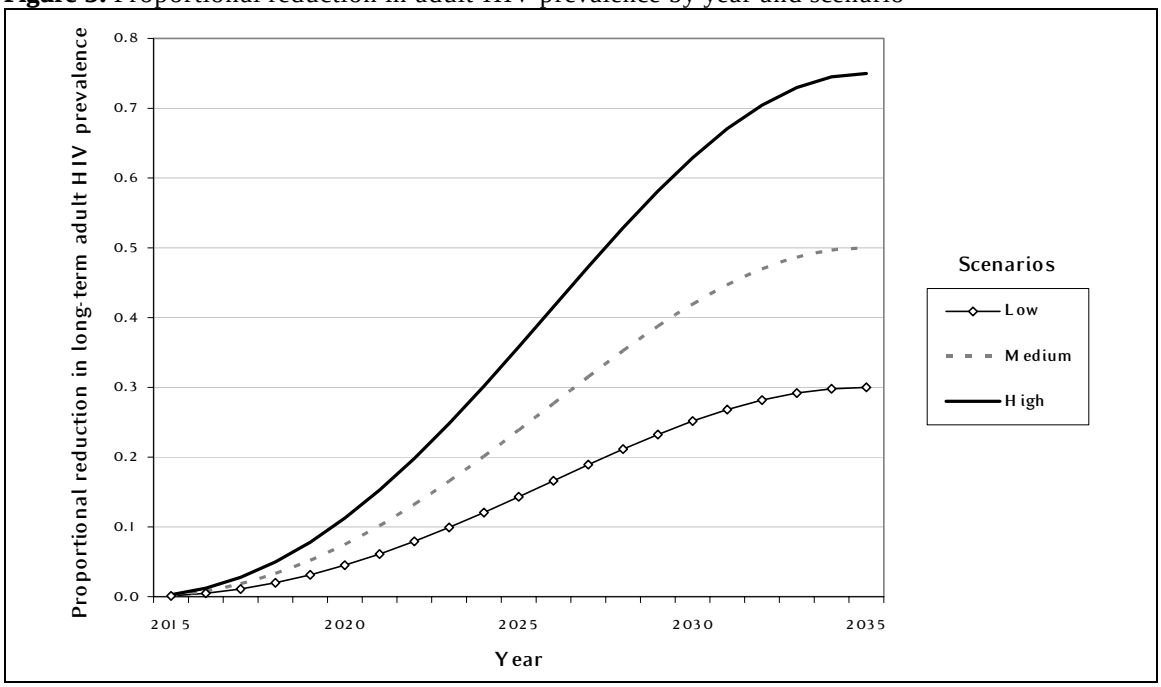
The coverage that could be achieved depends on a number of factors, including the proportion of the population with access to the health system, the proportion of the population targeted for vaccination and the acceptability of the vaccine to the target population. In 2001, WHO, UNAIDS, and IAVI organized a series of regional workshops to assess the demand for vaccination. Participants concluded that low-efficacy vaccines would probably be targeted only to the highest-risk populations and that the acceptability was likely to be low (Esparza *et al.*, 2003). That study estimated that the overall coverage of a vaccine with low/moderate efficacy (30%-50%) would be about 20% and that for a vaccine with high efficacy (80%-90%), it would be nearly 40%. (These levels are considerably less than current coverage of DPT vaccination, which is about 64% in sub-Saharan Africa, 78% in Asia, and 87% in Latin America [World Bank, World Development Indicators 2005].) This analysis uses the lower estimate (20%) for the low scenario, the high estimate (40%) for the high scenario, and the average of the two (30%) for the medium scenario.

Table 1. Coverage, efficacy and effective coverage by scenario

Scenario	Efficacy	Coverage	Effective Coverage
Low	40%	20%	8%
Medium	60%	30%	18%
High	95%	40%	38%

In all scenarios, the vaccine is assumed to become available in 2015. Several of the modeling studies showed that full impact is reached about 20 years after the initiation of a vaccination program. Therefore, as indicated in Figure 3, full impact is assumed to be achieved in 2035. The amount of impact by year is assumed to follow an S-shaped curve in which the impact on prevalence is initially small as program coverage begins, then accelerates rapidly before it gradually approaches the long-term level.

Figure 3. Proportional reduction in adult HIV prevalence by year and scenario



Vaccination programs might be implemented with blanket coverage (where efforts are made to vaccinate all adults) or cohort coverage (where vaccination is provided to successive cohorts of people reaching a particular age). Programs might also be targeted just at people with the highest risk rather than at all adults. This analysis assumes that programs would start with blanket coverage to vaccinate as many people in the target population as possible, and then might maintain that coverage with cohort vaccination approaches. In concentrated epidemics, where most infections are among those with the highest levels of risk, it might make sense to target public subsidies to those populations, though the vaccine would have to be available to others as well. In this case, the impact of the vaccine on the overall epidemic would derive from its impact among the high-risk populations.

The availability of an AIDS vaccine could lead some people to adopt riskier behaviors if they believe that they or their partners are protected. In the worst cases these behavioral reversals could lead to more infections with the vaccine than without it. The possibility of behavioral reversals could be counteracted by combining strong prevention messages with the vaccination program. The experience with widespread availability of ART in the United States suggests that some behavioral reversals are likely. However, a recent vaccine trial in the United States found no tendency toward riskier behavior among participants in the trial (Bartholow *et al.*, 2005). It should be noted that behavioral reversals could reduce or eliminate the benefits of a vaccine, but there is very little evidence on the magnitude of the behavioral response that might be expected.

D. Epidemiological projections

The impact of a vaccine is assessed using long-term epidemic projections prepared recently by UNAIDS (2005). These projections assume a continuation of current trends in incidence and prevalence. They assume that HIV prevalence has generally stabilized in Latin America and sub-Saharan Africa and continues to increase in Asia, Eastern Europe, and the Middle East and North Africa. Prevalence increases were determined by assuming that prevalence among key risk groups would increase from current levels to saturation by 2010 to 2020 as shown in Table 2.

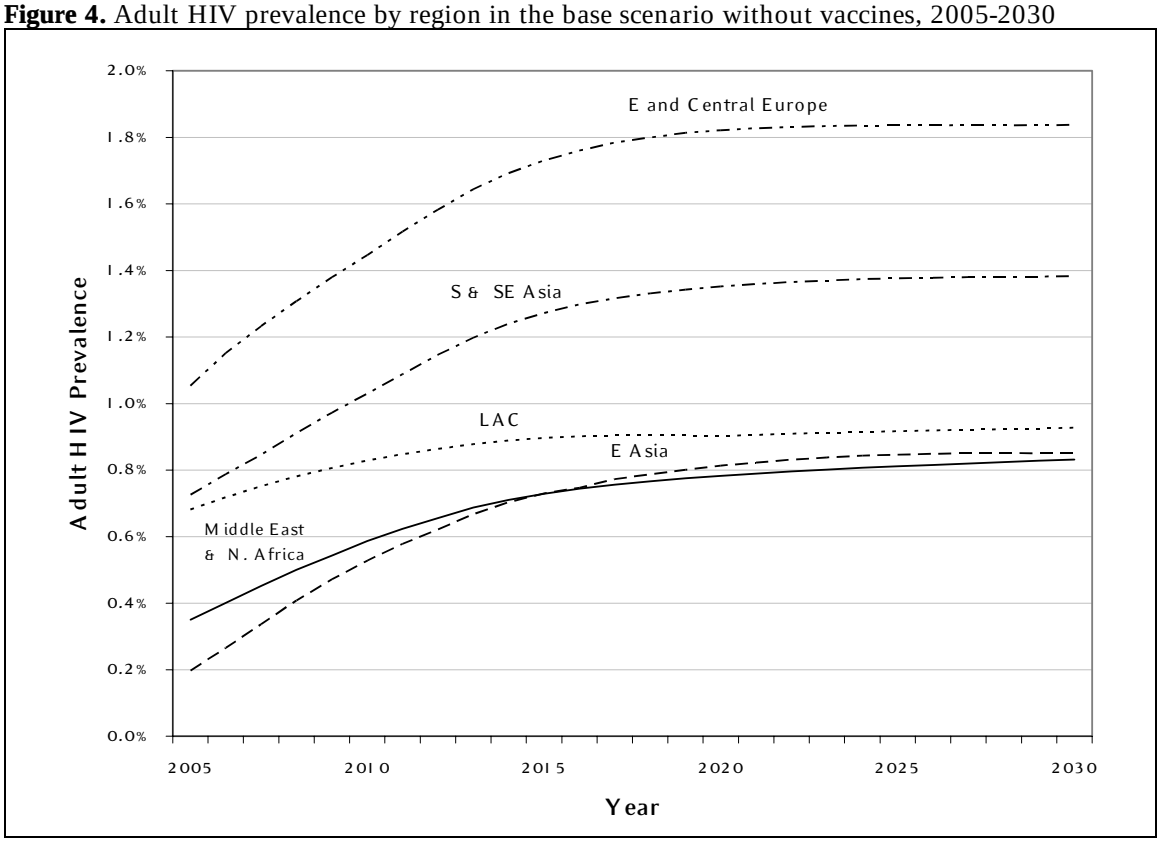
Table 2. Assumed saturation levels and years by risk group

Population	Prevalence at saturation	Year of saturation
Injecting drug users	25%	2010
Female sex workers	15%	2015
Clients of sex workers	7.5%	2020
Men who have sex with men	20%	2015

The projections include 125 countries with the largest number of infected people in sub-Saharan Africa, Eastern and Central Europe, East Asia, South and South East Asia, Latin American and the Caribbean and the Middle East and North Africa. For the purposes of this analysis the individual country projections are aggregated into six regions. For sub-Saharan Africa adult HIV prevalence is roughly stable at about 7.5% from 2015 to 2030. For the other regions, prevalence increases significantly through about 2015 before leveling off as shown in Figure 4.

UNAIDS prepared four separate sets of projections that differ only by the coverage of treatment services. The projection used for this analysis assumes that the coverage of ART for adults and children, cotrimoxazole for children, and PMTCT programs increases from current levels to 80% by 2012 and then remains at 80%. The UNAIDS projections do not include any impact of vaccines, so they serve as the baseline for this analysis.

Figure 4. Adult HIV prevalence by region in the base scenario without vaccines, 2005-2030



E. Vaccine impact calculations

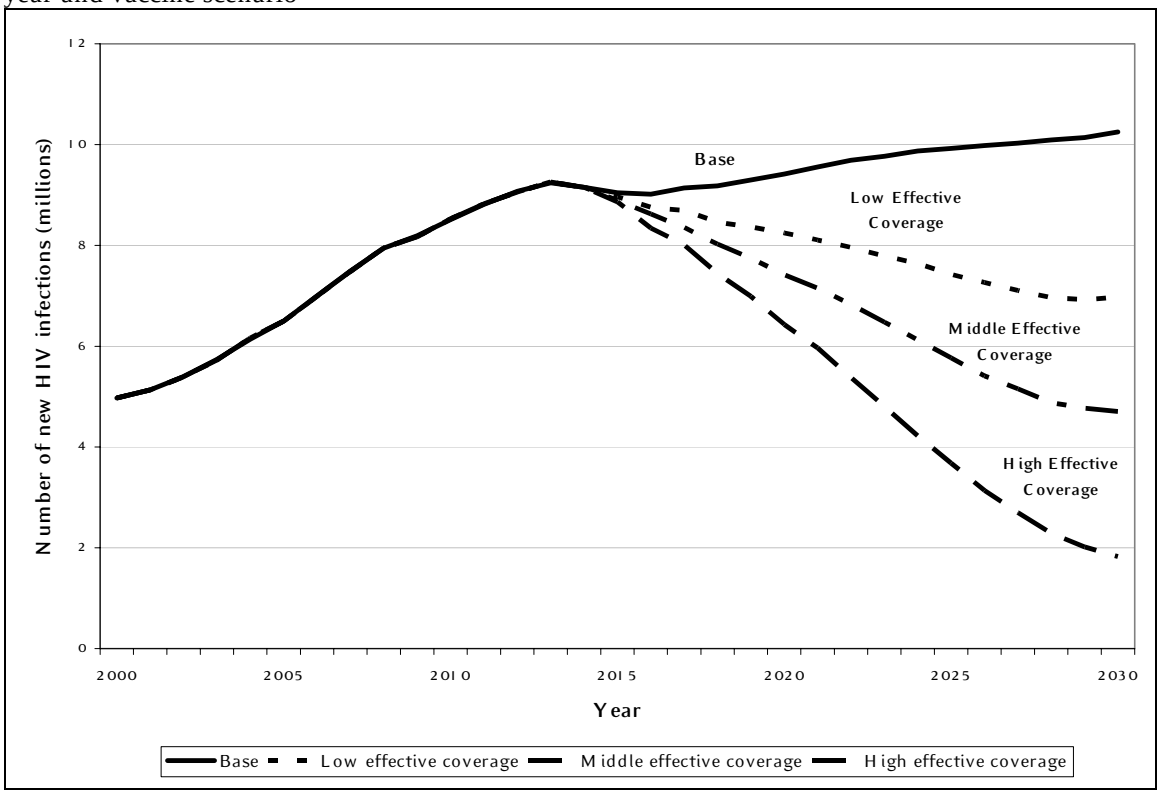
For each vaccine impact scenario, the effective coverage by year is used to estimate the reduction in adult HIV prevalence according to the pattern shown in Figure 1. The results are shown in Figure 3. These reductions are applied to the UNAIDS prevalence projections to estimate a new prevalence pattern for each region.[1] The new prevalence patterns are used in Spectrum to estimate the impact on new infections and AIDS deaths. (Spectrum is a projection model developed by the POLICY Project and used by UNAIDS to project the future consequences of prevalence patterns [Stover 2004].) Projections are made separately for each of the six regions. The same impact patterns (Figure 3) are applied to each region. This results in the same proportional reduction in prevalence by year in each region but, since the baseline prevalence projection patterns are different, the resulting prevalence patterns also differ by region. The projections for each region are aggregated to a global total for low- and middle-income countries.

[1]The vaccine impact is applied to the expected prevalence without ART in order to correctly estimate the impact on incidence. This becomes the input to Spectrum, which then calculates the subsequent effects, including the effects of ART on raising prevalence by postponing AIDS deaths.

III. Results

Figure 5 shows the three different vaccine impact scenarios as well as a "base scenario" that shows the course of the epidemic without a vaccine. The different curves in Figure 5 clearly show that the impact of an AIDS vaccine on the number of new HIV infections can be substantial.

Figure 5. Number of new adult and child HIV infections in low- and middle-income countries by year and vaccine scenario



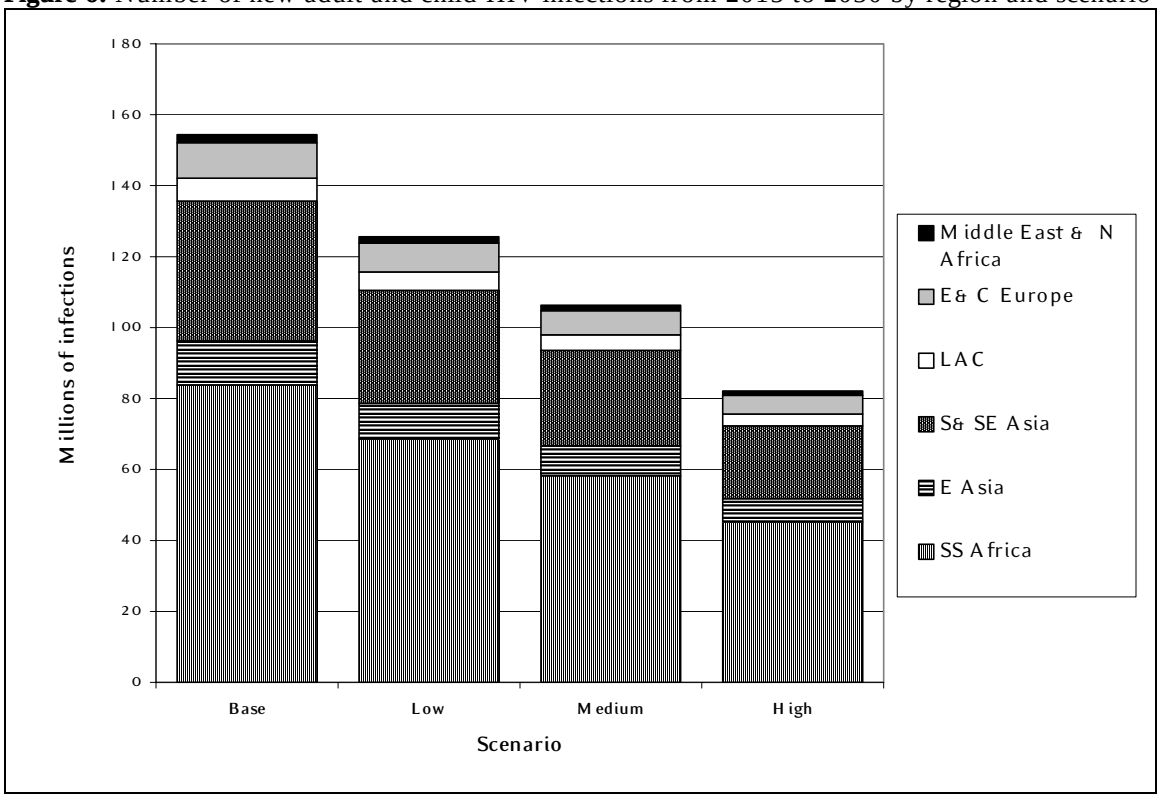
Without any further expansion of prevention efforts, aside from PMTCT programs, and without a vaccine, the annual number of new infections among adults and children would increase from around 6 million today to 10 million by 2030 (the slight dip after 2012 results from the assumption that ART coverage reaches 80% in 2012 and stabilizes at that level and HIV prevalence stabilizes by about 2015 in most regions outside of sub-Saharan Africa).

- In the Low Scenario, an AIDS vaccine with 40% efficacy provided to 20% of the population would reduce the annual number of new infections in 2030 by 32% from 10.2 million to 7.0 million. It would avert 19% of the 150 million new infections that would otherwise be expected from 2015 to 2030. This translates into 28.5 million infections averted.
- In the Medium Scenario, an AIDS vaccine with 60% efficacy provided to 30% of the population would reduce the annual number of new infections in 2030 by 54% to 4.7 million. It would avert 31% of new infections from 2015 to 2030, i.e. a total of 46.5 million infections averted.

- In the High Scenario, an AIDS vaccine with 95% efficacy provided to 40% of the population would reduce the annual number of new infections in 2030 by 82% to 1.8 million. It would avert 47% of new infections from 2015 to 2030, amounting to a total of 70.5 million infections averted.

The number of new infections by region in each scenario is shown in Figure 6. As half of new infections occur in sub-Saharan Africa and one-quarter in South and South-East Asia, those regions would also receive the greatest benefit from a vaccine. In sub-Saharan Africa, a vaccine would avert between 15 and 28 million infections from 2015 to 2030, just over half of the global total. South and South-East Asia would have about a quarter of the global benefit, with 7 to 19 million infections averted from 2015 to 2030, depending on the scenario.

Figure 6. Number of new adult and child HIV infections from 2015 to 2030 by region and scenario



IV. Discussion

The results of a number of simulations of the impact of an AIDS vaccine, when applied to long-term epidemiological projections in all low and middle income countries, indicate that between 19% and 47% of new infections could be averted between 2015 and 2030. That represents 30 to 70 million people who would be protected from HIV infection during that period.

The estimates of the impact of a preventive vaccine used here are derived from studies that primarily examined stable epidemics. Owens *et al.* (1998) showed that the impact could be 40% greater when implemented early in an epidemic before prevalence has stabilized. Therefore the overall impact could be even larger. However, according to UNAIDS projections, the epidemics in all regions are expected to nearly stabilize by 2015, so if a vaccine is not available until then the impact would be as shown.

The overall impact could be less if the use of the vaccine prompts people to adopt riskier behaviors. A number of researchers have shown that, in the worst cases, behavioral reversals could lead to worse outcomes than without the vaccine. Of course, that is relevant only for countries where significant positive behavior change has already occurred. It is not likely that a vaccination program would lead to more risky behavior than existed before the AIDS epidemic started. Behavioral reversals among those vaccinated could cut the benefits of a vaccine by half (Stover 2002), but behavioral reversals by those not vaccinated as well could lead to perverse results. The effects would be most severe with a low efficacy vaccine that provides degree-type protection. In vaccines with high efficacies that provide take-type protection, behavior reversals would have little effect if high rates of coverage could be achieved.

It is expected that prevention programs will continue to scale up in the coming years so that projections of continued trends in prevalence may be overly pessimistic and may overstate the impact of an AIDS vaccine. Optimistic estimates of the effects of comprehensive prevention programs indicate that as many as 2/3 of new infections could be averted in the next 8 years (Stover, Walker *et al.*, 2002). In this case, the number of infections averted by a vaccine would be less, but the proportional impact would likely be similar. Anderson and Garnett (1996) find that, at all but the very highest levels of vaccination coverage, the effects are likely to be additive to other prevention efforts. In other words, the same relative impact could be expected. The combination of an effective vaccine and other comprehensive prevention services could drive HIV prevalence to very low levels everywhere.

This paper does not address the issue of cost or cost-effectiveness of a vaccine. The total costs of the AIDS epidemic are clearly enormous, so any program that can reduce the number of new infections by 20 to 50% may be expected to produce significant savings. The cost of a future vaccine is highly uncertain. Efforts are underway to estimate the future costs of vaccine purchase in order to establish a guaranteed purchase fund. But the cost of the vaccine itself will be only part of the total costs, and it is unclear now how much public subsidy would be required. The costs of implementing the program could also be substantial, especially if several doses are required, or if re-vaccination campaigns are

needed because the duration of protection is short. There could also be extra counseling costs in the case of a low efficacy vaccine.

The number of people vaccinated in order to achieve this impact depends on the strategy for implementation and the need for re-vaccination to maintain effective coverage. The WHO/UNAIDS/IAVI study (Esparza *et al.*, 2003 estimated that the number of people vaccinated in the first five years of a global program would range from about 49 million for a low-efficacy vaccine to 260 million for a high-efficacy vaccine.

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.

V. Next steps

This paper focuses on estimating the global impact of a preventive AIDS vaccine based on results published to date in the modeling literature. It is intended as a first step. In the next 6 to 18 months IAVI will conduct additional work to refine these estimates. The new work will use country-specific models to examine vaccine impact in several key countries with different epidemic types. New models will also be used to look at vaccines that reduce the transmission of HIV and those that modify disease progression in addition to the preventive vaccines examined in this report. We will aim to continue a dialogue with the specialists who are modeling vaccine effects and involve developing country experts through the use of an easy-to-use model that can be quickly applied to specific country settings. This work will lead to refined estimates of the global benefits of vaccine research.

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