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The Impact of a Partially Effective HIV Vaccine on a Population of Intravenous Drug Users in Bangkok, Thailand: A Dynamic Model

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Summary: Because of the variability of HIV, the first AIDS vaccine is likely to be only partially effective. There is some concern among scientists that a low-efficacy vaccine could worsen the HIV epidemic if vaccinated individuals increase their risk behavior under the false assumption of immunity. To address this concern, we constructed a dynamic compartmental model that simulated the course of the HIV/AIDS epidemic in a population of injection drug users in Bangkok, Thailand. The model calculated long-term HIV prevalence, number of AIDS cases, and total population size for two scenarios: vaccination program versus no vaccination program. We used sensitivity analyses to evaluate the impact of postvaccination risk behavior change on HIV prevalence. A 75% effective vaccine led to a 40-year HIV prevalence of 37% with vaccination and 50% without vaccination. Postvaccination behavior change had only a limited effect on the results with a 75% effective vaccine but a significant effect with a 30% effective vaccine. If 90% of low-risk individuals responded to a 30% effective vaccine with increased high-risk behavior, the benefit of vaccination disappeared. These results agree with analyses of the epidemic among gay men. If injection drug behavior is indeed modifiable, our findings have significant policy and planning implications. **Key Words:** HIV—Vaccines—Risk behavior—Intravenous drug users—Mathematic models.

There are approximately 33 million HIV-infected people, 90% of whom are in developing countries (1). Bangkok, Thailand, where the epidemic exploded in 1988 among injection drug users (IDUs), experienced one of the most rapid outbreaks of HIV. Prevalence among IDUs rose from 1% to 43% in 1 year and then stabilized at 30% to 40% (2). As of 1999, HIV prevalence was 2.2% in Thailand and 33% among Thai IDUs in major urban areas (3).

Bangkok is currently the site of one of only two large-scale AIDS vaccine efficacy trials in the world (4). If clinical trials demonstrate vaccine efficacy, Thailand may be one of the first countries to distribute an AIDS vaccine. Because of the variability of HIV, the first marketed AIDS vaccine is likely to be only partially effective (5). The population effect of a low-efficacy vaccine has been a source of debate in the scientific community (6,7). One source of debate surrounding a low-efficacy vaccine is the possible increase in risky behavior subsequent to vaccination. If the introduction of a vaccine is followed by an increase in risky behavior among individuals who falsely believe they are protected by the vaccine, the incidence of HIV could actually increase rather than decrease. Research has shown that this concern is not unfounded. One study found that participants in early phase I and II vaccine trials in San Francisco increased their high-risk sexual behaviors during the tri-

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als despite being told the vaccine would not provide complete protection (6).

Conversely, it is also possible that risky behavior could decrease after vaccination, because vaccine administration is typically accompanied by risk reduction counseling. Several studies have shown that risk reduction counseling can be an effective way to reduce high-risk behavior. For example, a study on the effect of counseling on injection drug use found that IDUs significantly decreased their high-risk behavior after counseling (8). Individuals who reported practicing safer injection practices were subsequently less likely to have seroconverted during follow-up. Another study found that IDUs in Stockholm demonstrated a significant reduction in needle sharing as awareness about AIDS increased (9).

The true impact of mass vaccination against HIV on a population cannot be known until a vaccine is distributed. Nevertheless, mathematic models can help to predict the impact of a partially effective vaccine before mass vaccination begins. Models of the effect of vaccination in a population of gay men in San Francisco exist, but there are no models based on a population of IDUs in Bangkok. Accordingly, this article describes a mathematic model of the impact of a partially effective AIDS vaccine in a population of IDUs in Bangkok, Thailand. The purpose of our analysis is twofold. First, we use the model to compare HIV prevalence, number of AIDS cases, and total population size with and without vaccination. Second, we evaluate the impact on HIV prevalence of vaccination combined with either favorable or unfavorable risk behavior change.

METHODS

Model Structure

We constructed a dynamic compartmental model to simulate the course of the HIV/AIDS epidemic in a population of IDUs in Bangkok. The structure of the model is adapted from previous simulations of the HIV epidemic in gay male populations (10,11). The model consists of 14 compartments or population subgroups (Fig. 1). Vaccination status, injection-related risk behavior, and disease status distinguish subgroups from each other. There are three levels of vaccination status (unvaccinated; vaccinated, not susceptible; and vaccinated, susceptible), two levels of injection-related risk behavior (low and high), and five levels of disease status (HIV-negative; HIV-positive, asymptomatic, unidentified; HIV-positive, asymptomatic, identified; HIV-positive, symptomatic; and AIDS) defined in the model. We do not distinguish HIV-positive individuals by vaccination status, because we assume vaccination does not produce a therapeutic effect. Transitions among subgroups are governed by difference equations (shown in the Appendix in differential format) (12). Difference equations are available from the authors on request. Parameters that dictate transitions among subgroups include vaccine characteristics, injection characteristics, HIV prevalence, vaccination rate, probability of risk behavior change, and all-cause and disease-specific mortality rates. Transitions occur at yearly intervals for a predetermined number of years. The model tracks the number of people residing in each compartment over time.

AIDS vaccines have been characterized in previous analyses by three parameters: take, efficacy, and duration (7,13). Vaccine take (ψ) is defined as the proportion of people vaccinated in which the vaccine has any effect. Vaccine efficacy (ϵ) is defined as the proportion of people protected from HIV infection among those in whom the vaccine has any take. Vaccine duration ($1 / \omega$) is the number of years that the vaccine provides protection from HIV infection. Conversely, ω is the rate at which vaccine protection wanes. In our model, vaccine failure can occur through any of these three parameters.

HIV transmission dynamics among IDUs are complex and differ from transmission dynamics in a heterosexual or homosexual epidemic. Transmission parameters used in this model are based on previously developed models of injection drug use (14,15). Among IDUs, HIV transmission occurs by the sharing of injection equipment. Injection risk behavior and viral infectivity determine how likely an individual is to become infected with HIV through needle sharing. Injection risk behavior characteristics include contact rate (p), total number of injections per year (k), and the probability that a needle was shared (s). In our model, "shared" means that the needle was used by someone else immediately before injection. Contact rate is defined as the number of different persons with whom needles are shared each year. Viral infectivity is defined at two levels. Per contact infectivity (b) is the probability of viral transmission per infected needle contact. Per partner infectivity (β) is the probability of viral transmission per infected partner contact; it is a function of per contact infectivity, the probability that a needle was shared, contact rate, and the number of injections per year.

IDUs face different annual probabilities of infection depending on their injection practices. Although HIV infection among IDUs occurs by both sexual behavior and sharing of injection equipment, our analysis only examines viral transmission by shared needle use. We consider two categories of injection practices: low risk and high risk. The primary distinction between low-risk and high-risk injection behavior is the number of injections per year. Low-risk IDUs inject fewer times per year than high-risk IDUs. The number of contacts, or individuals with whom needles are shared, and the frequency with which shared needles are used also differ between low-risk and high-risk individuals. We assume "restricted" mixing of IDUs, which implies that IDUs share needles only with those individuals in the same risk group as themselves. The variables $\lambda(t)$ and γ define the risk of infection and the probability of becoming HIV infected, respectively, within each risk group (see Appendix).

Compartment Equations

Compartment equations were developed by adding and subtracting the number of individuals entering and leaving a compartment, respectively, to the number of people already in the compartment. For example, the number of people added to the HIV-negative, low-risk, unvaccinated subgroup (Y_1) at time t is the total of:

1. The number of new uninfected, low-risk, unvaccinated people who enter the population (I_1)
2. The number of people who transition from high-risk to low-risk behavior while remaining unvaccinated and uninfected ($\delta_{2,1}Y_2$)

The number of people subtracted from this subgroup at time t is the total of:

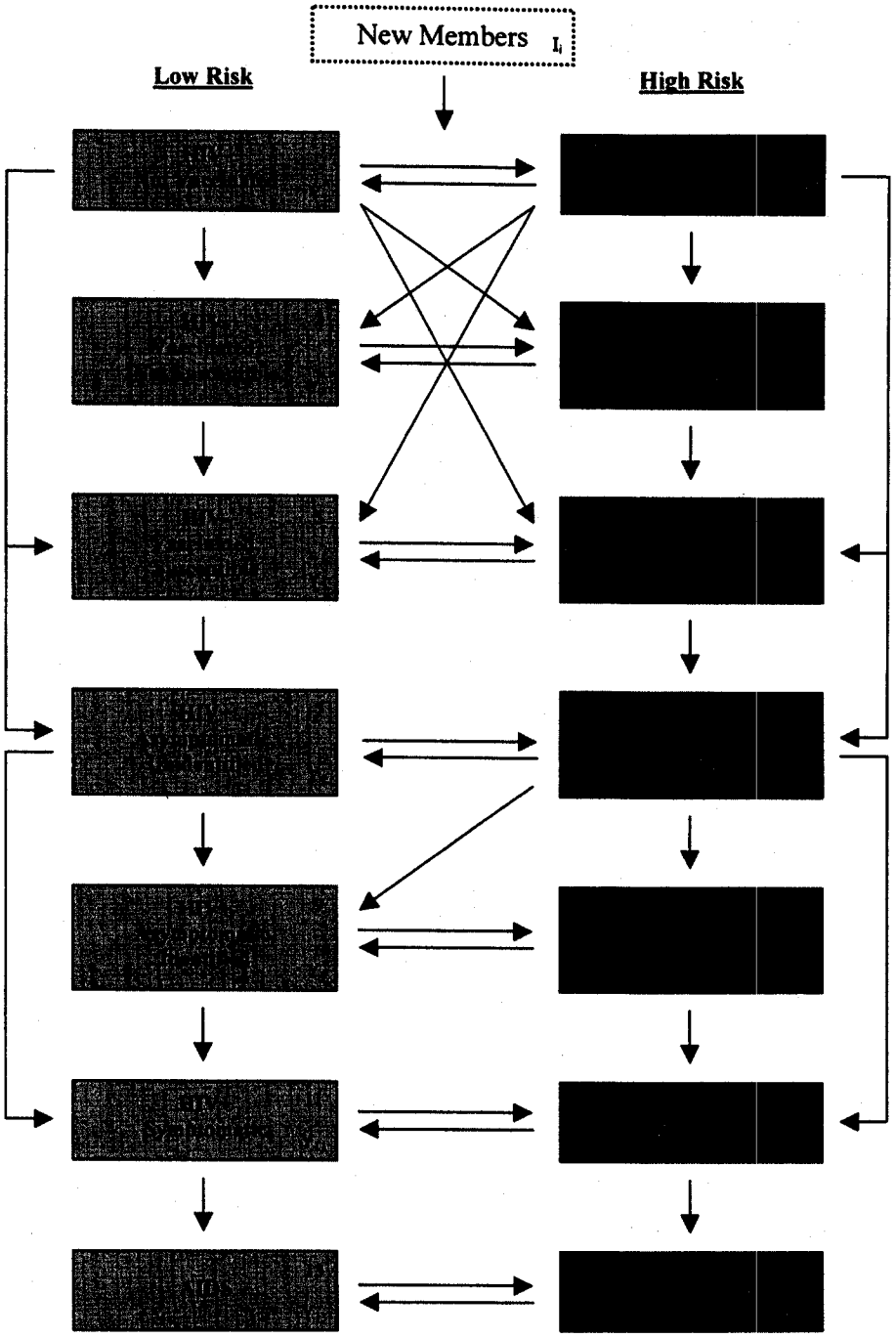

FIG. 1. Graphic representation of the model. Each box represents a population subgroup. Individuals transition from one subgroup to another according to the arrows. Members of any subgroup exit the system by non-HIV–related death; members of both AIDS subgroups (Y_{13} and Y_{14}) also exit by HIV-related death. New members enter the system each year (I_1).

1. The number of people who die of non-HIV–related causes (μY_1)
2. The number of people who become HIV-infected ($\gamma_1 Y_1$)
3. The number of people who are successfully vaccinated (i.e., vaccinated and not susceptible to HIV) and either maintain low-risk behavior or transition to high-risk behavior [$v\psi\epsilon(1 - \delta_{1,4})Y_1$ and $v\psi\epsilon\delta_{1,4}Y_1$, respectively]
4. The number of people who are unsuccessfully vaccinated (i.e., vaccinated and susceptible to HIV) and either maintain low-risk behavior or transition to high-risk behavior [$v\psi(1 - \epsilon)(1 - \delta_{1,6})Y_1$ and $v\psi(1 - \epsilon)\delta_{1,6}Y_1$, respectively]
5. The number of people who transition to low-risk behavior from high-risk behavior while remaining unvaccinated and uninfected ($\delta_{1,2}Y_1$)

The additions and subtractions are combined with the number of people remaining in the compartment after the previous time period ($t - 1$) to arrive at the total number of people in Y_1 in the current time period (t). Equations for compartments 2 through 14 were developed in the same manner. The model was built in Microsoft Excel (Microsoft

Corp., Redmond, WA, U.S.A.) and uses discrete rather than differential equations (i.e., difference equations). The Microsoft Excel code is available from the authors on request.

Input Data

Input data for the model were obtained from the published literature (Tables 1 and 2). Population-specific data were used where possible; in the absence of Bangkok-based research, estimates were taken from epidemic research in the United States. Previous mathematic models of vaccination against HIV among gay men in San Francisco, California, provided estimates of vaccine characteristics, immigration rates, HIV-screening rates, and durations of intermediate disease stages (10,11). The duration of AIDS was estimated using a retrospective study of AIDS patients in an infectious disease hospital in a Bangkok suburb from 1987 to 1993 (22). Our estimate of all-cause mortality among IDUs was based on a longitudinal study of opioid addicts in the United States (18). The value for per contact infectivity was provided by a model-based estimate of HIV infectivity developed using data from a needle exchange program in New Haven, Connecticut (17).

Limited data for risk-sharing characteristics were available. The contact rate and probability that a needle was shared were estimated using a model of the effectiveness of bleach distribution among IDUs (15). Direct data on the probability of an IDU being at low risk and the number of injections per year were available from a cross-sectional survey conducted among HIV-negative IDUs in Bangkok drug treatment clinics (16). Because these data were not categorized according to the subgroups in our model, we applied estimates from the bleach distribution study previously cited (15) to arrive at subgroup-specific data. No data regarding risk behavior change were available; probabilities of risk behavior change were therefore based on assumption and analyzed in sensitivity analyses.

Model Outcomes

For the base-case analysis, the following key assumptions were made. First, 50% of the eligible population of IDUs are to be vaccinated each year. Second, the vaccine provides complete protection against HIV for 75% of those vaccinated and no protection for 25% of those vaccinated. Third, the duration of protection from vaccine is 10 years on average. Individuals are not revaccinated when protection wanes. Fourth, the annual probability of any risk behavior change is 5%. Finally, the initial prevalence of HIV is 30%. The analysis simulated the course of the epidemic in a population of 36,600 male IDUs over both 40 and 150 years.

To evaluate the potential effects of a vaccination program, we used the model to calculate the long-term HIV prevalence, number of AIDS cases, and total population size for two scenarios: vaccination program versus no vaccination program. We performed sensitivity analyses to examine key variables, including vaccine take and efficacy, proportion of IDUs vaccinated, and initial HIV prevalence. We also performed sensitivity analyses to evaluate the impact of postvaccination risk behavior change on HIV prevalence.

TABLE 1. *Input data*

Parameter name and description	Symbol	Base case	Range
Vaccination characteristics (10,11)			
Vaccine take	ψ	1.0	0.1–1.0
Vaccine efficacy	ϵ	0.75	0.3–0.9
Vaccine duration (years)	$1/\omega$	10	10–80
Proportion of IDU population vaccinated	ν	0.5	0.1–0.9
Risk behavior characteristics[a]			
Probability an IDU is at low risk (15,16)	π_L	0.29	0.1–1.0
Probability of spontaneous risk behavior change[b]	$\delta_{i,i}$	0.05	0–0.5
Probability of favorable postvaccination risk behavior change	$\delta_{2,3}$, $\delta_{2,5}$	0.05	0–1.0
Probability of unfavorable postvaccination risk behavior change	$\delta_{1,4}$, $\delta_{1,6}$	0.05	0–1.0
Probability of favorable risk behavior change associated with becoming identified as HIV$^+$	$\delta_{6,7}$	0.1	0.05–0.75
Contact rate: low risk(15)	p_L	11	5–12
Contact rate: high risk (15)	p_H	13	12–16
Probability needle was shared: low risk (15)	s_L	0.35	0.1–0.6
Probability needle was shared: high risk (15)	s_H	0.26	0.1–1.0
Per contact infectivity (18)	b	0.0067	
Number of injections per year: low risk (15,16)	k_L	230	
Number of injections per year: high risk (15,16)	k_H	1350	
Population characteristics			
Non-HIV–related annual death rate (19)	μ	0.0138	
Fraction of population screened for HIV annually (10,11)	σ	0.15	
Sensitivity of HIV screening (20)	ξ	0.983	
Initial prevalence of HIV among IDUs (16)	—	0.30	0.02–0.4
Mean age of population (years) (2)	—	30	
Initial population size (16)	N	36,600	
Percentage of men in IDU population (20,21)	—	0.95	

Numbers in parentheses refer to studies cited in reference list.

[a] Risk behavior changes are classified as favorable or unfavorable. Favorable risk behavior change refers to a switch from high-risk behavior to low-risk behavior. Unfavorable change refers to a switch from low-risk behavior to high-risk behavior.

[b] The probability of spontaneous risk behavior change refers to the probability of changing risk behavior status without changing any other health status. This is depicted in the model graphic (see Fig. 1) as any horizontal movement between compartments.

IDU, injection drug user.

TABLE 2. *Subgroup-specific input data*

Population subgroup	Per partner infectivity (β_i) (15,16)	Health state duration (years)	Annual transition rate (μ_i)	Reason for transition	Annual immigration (I_i) (10,11)
Low-risk IDUs					
Group 1: HIV$^-$, not vaccinated	N/A	N/A	N/A	N/A	$\mu * N * 0.9 * \pi_L$
Group 7: HIV$^+$, unidentified	0.0479	7.1	0.1408 (10,11)	Develop symptoms	$\mu * N * 0.04 * \pi_L$
Group 9: HIV$^+$, identified	0.0479	8.1	0.1235 (10,11)	Develop symptoms	$\mu * N * 0.04 * \pi_L$
Group 11: HIV$^+$, symptomatic	0.0479	2.7	0.3704 (10,11)	Develop AIDS	$\mu * N * 0.02 * \pi_L$
Group 13: AIDS	0.0479	1.1	0.9365 (22)	AIDS-related death	N/A
High-risk IDUs					
Group 2: HIV$^-$, not vaccinated	N/A	N/A	N/A	N/A	$\mu * N * 0.9 * (1-\pi_L)$
Group 8: HIV$^+$, unidentified	0.1656	7.1	0.1408 (10,11)	Develop symptoms	$\mu * N * 0.04 * (1-\pi_L)$
Group 10: HIV$^+$, identified	0.1656	8.1	0.1235 (10,11)	Develop symptoms	$\mu * N * 0.04 * (1-\pi_L)$
Group 12: HIV$^+$, symptomatic	0.1656	2.7	0.3704 (10,11)	Develop AIDS	$\mu * N * 0.02 * (1-\pi_L)$
Group 14: AIDS	0.1656	1.1	0.9365 (22)	AIDS-related death	N/A

Numbers in parentheses refer to studies cited in reference list.
IDU, injection drug user; N/A, not applicable.

RESULTS

The results of the base-case analysis showed that after 40 years, HIV prevalence was 37% with vaccination and 50% without vaccination (Table 3 and Fig. 2). HIV prevalence reached equilibrium at 33% with vaccination and 49% without vaccination. The total population size after 40 years was 14,721 with vaccination and 10,569 without vaccination, a difference of 4153 people (Fig. 3). After 150 years, the total population size was 11,966 with vaccination and 9153 without vaccination. Although vaccination ultimately led to lower disease prevalence, there were higher absolute numbers of infections for 18 years starting in year 30 after the initiation of the vaccination program (Fig. 4). Similarly, vaccination led to between 1 and 15 more AIDS cases each year than no vaccination for 18 years beginning in year 32. The excess of infections with vaccination versus infections without vaccination can be explained by the larger total population sized achieved with vaccination because of the reduction in the death rate from HIV.

Sensitivity Analyses

We examined the sensitivity of the model results to changes in key input variables, including vaccine parameters, risk behavior variables, and HIV screening estimates. Sensitivity analyses focused on one outcome variable, HIV prevalence. The results of the model were insensitive to changes in estimates of the fraction of the population screened annually, the sensitivity of the HIV screening test, and most spontaneous behavior changes. The results of the model were highly sensitive to changes in spontaneous behavior among individuals who were either unvaccinated or vaccinated but susceptible to infection. If there was zero rather than a 5% probability of a low-risk unvaccinated person switching to high-risk behavior, HIV prevalence was 37% with vaccination and 24% without vaccination. This was the only single input variable change where no vaccination resulted in a lower HIV prevalence than vaccination. If there was zero probability of a low-risk vaccinated but susceptible person increasing risk behavior, HIV prevalence was 20% with vaccination and 50% without vaccination.

TABLE 3. *Results of the base case analysis*

	40 Years		150 Years	
	Vaccination	No vaccination	Vaccination	No vaccination
HIV prevalence, %	37	50	33	49
Population size	14,721	10,569	11,966	9153
AIDS cases	520	505	368	410

We evaluated the sensitivity of the model results to the key components of risk behavior: contact rate, the probability that a needle was shared, and the number of injections per year. The model was more sensitive to changes in some aspects of risk behavior than others. Long-term HIV prevalence was only slightly sensitive to either increases or decreases in contact rate. If all high-risk individuals reduced their contact rate from 13 to 11 contacts per year, HIV prevalence after 40 years was 39% with vaccination and 53% without vaccination. If all low-risk individuals increased their contact rate from 11 to 13 contacts per year, HIV prevalence was 37% with vaccination and 49% without vaccination (Table 4). We also evaluated the sensitivity of our results to the probability of an IDU being at low risk. As this probability ranges from 10% to 100%, the difference in prevalence between vaccinated and unvaccinated IDUs ranges from −18% to −5%.

The results of the model were highly sensitive to changes in the probability that a needle was shared and

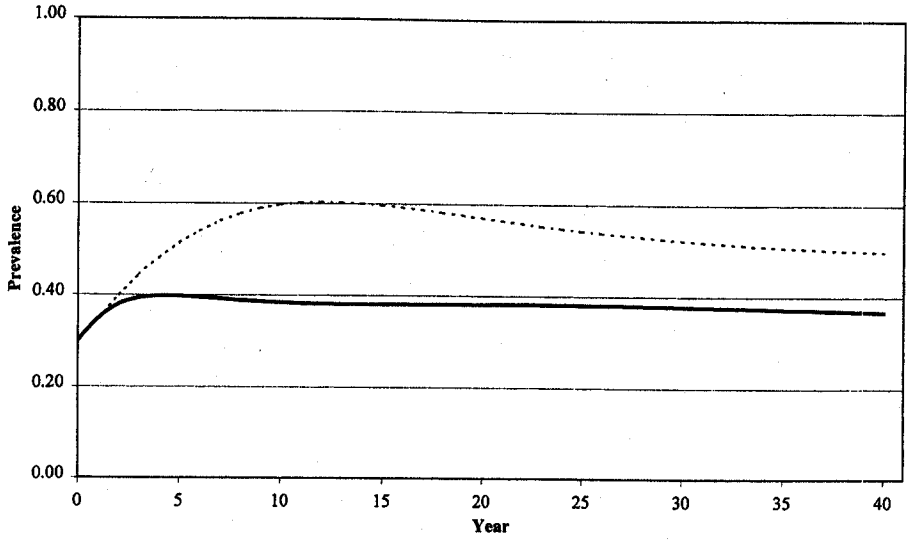

FIG. 2. HIV prevalence over 40 years in the base-case analysis. Plots represent the proportion of the population with HIV each year (*solid line*, vaccination; *dotted line*, no vaccination).

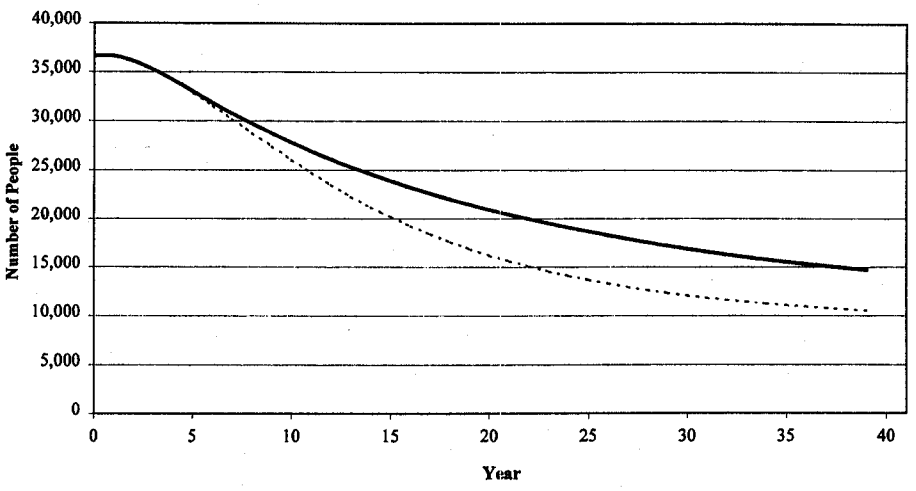

FIG. 3. Total population size over 40 years in the base-case analysis. Plots represent the total number of people in the population each year (*solid line*, vaccination; *dotted line*, no vaccination).

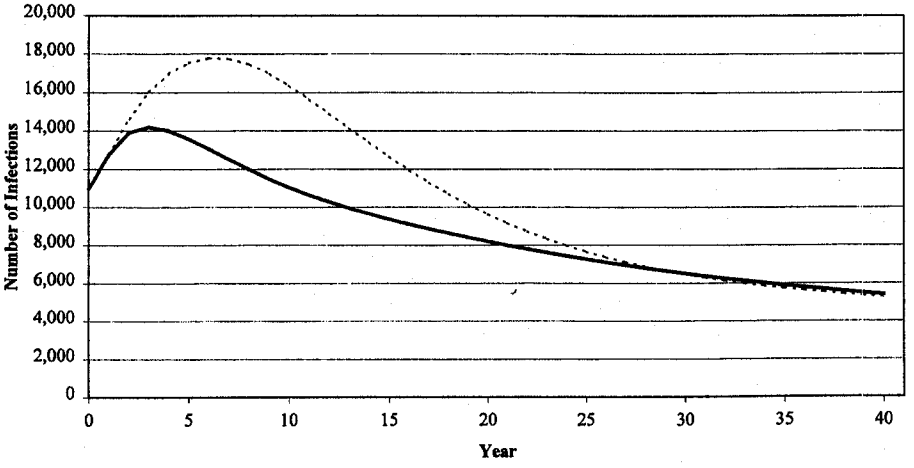

FIG. 4. Total number of HIV infections in the base-case analysis. Plots represent the total number of HIV infections in the population each year (*solid line*, vaccination; *dotted line*, no vaccination).

TABLE 4. *Effects of changes in single risk behaviors on HIV prevalence*

Target group	Behavior change	40-Year HIV prevalence		
		Vaccination, %	No vaccination, %	Difference, %
Not applicable	None (base case)	37	50	−13
High risk	Decreased contact rate: 13 to 11	39	53	−14
High risk	Decreased probability of shared needle: 26% to 13%	7	11	−4
High risk	Decreased number of injections: 1350 to 730	8	15	−7
Low risk	Increased contact rate: 11 to 13	37	49	−12
Low risk	Increased probability that needle was shared: 35% to 70%	44	61	−17
Low risk	Increased numbers of injections per year: 230 to 730	53	70	−17

the number of injections per year, particularly among high-risk individuals. Decreasing the probability that a high-risk IDU uses a shared needle from 26% to 13% produced HIV prevalences of 7% with vaccination and 11% without vaccination. Decreasing the number of injections from 1350 to 730 injections per year (an average of 2 injections per day) among high-risk IDUs produced HIV prevalences of 8% with vaccination and 14% without vaccination. Comparable increases in these variables among low-risk individuals produced significant but less severe changes in the outcome of the model (see Table 4).

Changes in vaccine parameters had a moderate effect on the results of the model. To evaluate the effect of vaccines with different efficacy, the estimate of vaccine efficacy was varied from 30% to 90%. At a vaccine efficacy of 30%, HIV prevalence with vaccination was 44% after 40 years and reached an equilibrium level of 42%. At a vaccine efficacy of 90%, equilibrium prevalence was 35% with vaccination. Although the benefit of vaccination diminished as efficacy decreased, vaccination remained superior to no vaccination at all levels of expected efficacy. It is important to note that even when vaccine efficacy is set to 1, an unrealistic value representative of a perfectly protective vaccine, the 40-year prevalence with vaccination was 34% and the 150-year prevalence was 29%. The persistence of HIV in the population despite a completely efficacious vaccine can be explained by the constant influx of new members in the population and the waning effect of vaccination.

Increasing the duration of vaccine protection had a significant effect on the model results. If the vaccine's protection was assumed to last 50 years, HIV prevalence was 14% with vaccination, which represents an improvement of 23% compared with the base-case scenario. Reducing the duration of protection from 10 to 5 years increased HIV prevalence with vaccination from 37% to 43%.

Effect of Vaccination-Related Behavior Change

Sensitivity analyses were used to evaluate the impact of vaccination-related behavior change on HIV prevalence. Two types of postvaccination risk behavior change were examined. The first type was desirable risk behavior change, which could result from risk reduction counseling accompanying vaccination. High-risk individuals could respond favorably to vaccination-related risk reduction counseling by changing all aspects of risk behavior, including contact rate, number of injections per year, probability of needle sharing, and per partner infectivity. Sensitivity analysis showed that with a 75% effective vaccine, HIV prevalence is somewhat sensitive to this type of behavior change. If 100% of high-risk individuals switched to low-risk behavior in response to vaccination-related counseling, HIV prevalence decreased to 33% after 40 years, which represents an improvement of 4% compared with the base-case results (Table 5).

TABLE 5. *Sensitivity of HIV prevalence to postvaccination risk behavior decrease*[a]

Vaccine efficacy, %	Probability of postvaccination risk behavior decrease, %	40-Year HIV prevalence		
		Vaccination, %	No vaccination, %	Difference, %
75	5	37	50	−13
75	50	35	50	−15
75	100	33	50	−17
30	5	44	50	−6
30	50	40	50	−10
30	100	36	50	−14

[a] Across all risk behavior variables.

The second type of postvaccination risk behavior change was undesirable. This type of behavior change could occur if individuals increased all aspects of risk behavior after vaccination under the false assumption of immunity. This implied an increase in contact rate from 11 to 13 contacts per year, an increase in the number of injections per year from 230 to 1350, and an increase in per partner infectivity from 0.0254 to 0.5961. Sensitivity analysis showed that simultaneous, unfavorable change in all these variables had a limited effect on the model results when vaccine efficacy was 75% (Table 6). The beneficial effects of vaccination diminished slightly as the probability of unfavorable postvaccination risk behavior change increased, but vaccination with a 75% effective vaccine was superior to no vaccination at any level of unfavorable behavior change.

A two-way sensitivity analysis of vaccine efficacy and the probability of postvaccination risk behavior change was performed to determine whether this result would hold true for various levels of vaccine efficacy. The analysis showed that as vaccine efficacy decreased, the impact of postvaccination behavior change on HIV prevalence increased. In other words, the benefit of vaccination with a low-efficacy vaccine can be mitigated significantly by unfavorable behavior changes. If 50% of low-risk individuals increased their risk behavior in response to vaccination with a 30% effective vaccine, the 40-year HIV prevalence was 47% with vaccination and 50% without vaccination. Without this degree of behavior change (i.e., if only 5% of individuals increased their risk behavior), the HIV prevalence was 44% with vaccination. If 90% of low-risk individuals responded to a low-efficacy vaccine with increased high-risk behavior, the benefit of vaccination disappeared (see Table 6). Similarly, the benefits of a low-efficacy vaccine were enhanced by favorable vaccination-related risk behavior changes. If 50% of high-risk individuals adopted low-risk behavior after risk reduction counseling and vaccination with a 30% effective vaccine, HIV prevalence decreased from 44% to 40% with vaccination. If 100% of high-risk individuals exhibited a favorable behavior change in this manner, HIV prevalence was 36% with vaccination.

DISCUSSION

We used a dynamic compartmental model to evaluate the effect of HIV vaccination on a population of IDUs in Bangkok, Thailand. The analysis addresses two main questions. First, what effect does a partially effective vaccine have on an HIV epidemic among Thai IDUs? Second, does risk behavior change modify this effect? The model provided answers to each of these questions. A 75% effective vaccine can reduce HIV prevalence from 50% to 37% in a population of IDUs after 40 years. The beneficial effect of vaccination persisted in our model even when vaccine efficacy was at the lowest value examined (30%). We observed an initial increase in HIV prevalence followed by a decline to steady-state prevalence; we also found that initial HIV prevalence was lower than steady-state prevalence. Both of these findings are expected in an epidemic model.

We used HIV prevalence after 40 years as our primary outcome measure. It is important to note that different outcome measures such as the number of infections or AIDS cases and different time frames may produce different results. For instance, in our model, a vaccine that successfully lowered HIV prevalence also led to a larger total population by reducing the HIV-related death rate and therefore a greater absolute number of HIV infections for a period of 18 years in the third and fourth decades of the epidemic.

In response to the second question of interest, our results suggested that the effectiveness of vaccination depends on the probability of vaccination-related behavior change only if vaccine efficacy is lower than our

TABLE 6. *Sensitivity of HIV prevalence to postvaccination risk behavior increase*[a]

Vaccine efficacy, %	Probability of postvaccination risk behavior increase, %	40-year HIV prevalence		
		Vaccination, %	No vaccination, %	Difference, %
75	5	37	50	−13
75	50	38	50	−12
75	100	40	50	−10
30	5	44	50	−6
30	50	47	50	−3
30	60	48	50	−2
30	70	48	50	−2
30	80	49	50	−1
30	90	50	50	0
30	100	51	50	+1

[a] Across all risk behavior variables.

base-case assumption of 75%. If 90% of low-risk people increased their risk behavior in response to immunization with a 30% effective vaccine, vaccination would not be beneficial compared with no vaccination. It is unlikely, however, that such a large proportion of low-risk individuals would respond to vaccination in this manner. If half or fewer of the low-risk population exhibited an increase in postvaccination risk behavior, vaccination would reduce HIV prevalence by at least 3% compared with no vaccination. A moderately or highly effective vaccine would be beneficial to a population of IDUs even if risk behavior increased subsequent to vaccination.

There are a number of limitations to our study. First, high-risk sexual behavior contributes significantly to the spread of HIV among IDUs but is not specifically accounted for in this model. We assumed that transmission of HIV among IDUs occurs only by the sharing of injection equipment. Second, we did not consider any potential therapeutic effects of a vaccine. Previous clinical trials have shown no therapeutic effect of vaccination, but these negative findings could be the result of limitations in clinical trial design or implementation rather the result of the true absence of a therapeutic effect. If there were a therapeutic effect of immunization, the vaccination strategy would be even more beneficial than this model predicts. Third, the model assumes "restricted" mixing of IDUs. In reality, there is likely mixing of IDUs between low-risk and high-risk groups. Previous analyses have shown that the assumption of restricted mixing tends to overestimate the effectiveness of an intervention (15). Also, there is likely to be more heterogeneity of risk groups than was modeled by the dichotomous "low-risk" and "high-risk" groups of this simulation. Fourth, we assumed that the behavior of people who were vaccinated but susceptible to infection was not affected by vaccination status. Finally, the results of this model are limited to similar IDU populations and cannot be generalized to other risk groups such as groups at risk for HIV through sexual behavior.

The results of this analysis are in agreement with those from analyses of the HIV epidemic in gay men in San Francisco (13). Such simulations have shown that risk behavior is an important moderator of vaccine effectiveness. Given the overlap between the high-risk sexual behavior population and IDUs, future research should evaluate the effect of vaccination when transmission parameters for both modes of transmission are combined.

Research shows that injection drug use behavior is easier to change than sexual behavior (9,23). The findings from this analysis suggest, first, that a low-efficacy AIDS vaccine is beneficial to a population of IDUs in Bangkok, Thailand, and, second, that this beneficial effect can be enhanced or moderated by risk behavior change. If IDU behavior is indeed modifiable, the findings presented here have significant policy and planning implications.

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APPENDIX: MODEL EQUATIONS

The following differential equations govern the rate of transition from one compartment to another:

$$\frac{dY_1}{dt} = I_1 + \delta_{2,1}Y_2 - \mu Y_1 - \gamma_L Y_1 - \nu\psi\epsilon(1-\delta_{1,4})Y_1 - \nu\psi(1-\epsilon)(1-\delta_{1,6})Y_1 - \delta_{1,2}Y_1 - \nu\psi\epsilon\delta_{1,4}Y_1 - \nu\psi(1-\epsilon)\delta_{1,6}Y_1$$

$$\frac{dY_2}{dt} = I_2 + \delta_{1,2}Y_1 - \mu Y_2 - \gamma_H Y_2 - \nu\psi\epsilon(1-\delta_{2,3})Y_2 - \nu\psi(1-\epsilon)(1-\delta_{2,5})Y_2 - \delta_{2,1}Y_2 - \nu\psi\epsilon\delta_{2,3}Y_2 - \nu\psi(1-\epsilon)\delta_{2,5}Y_2$$

$$\frac{dY_3}{dt} = \nu\psi\epsilon(1-\delta_{1,4})Y_1 + \delta_{4,3}Y_4 + \nu\psi\epsilon\delta_{2,3}Y_2 - \mu Y_3 - \omega Y_3 - \delta_{3,4}Y_4$$

$$\frac{dY_4}{dt} = \nu\psi\epsilon(1-\delta_{2,3})Y_2 + \delta_{3,4}Y_3 + \nu\psi\epsilon\delta_{1,4}Y_1 - \mu Y_4 - \omega Y_4 - \delta_{4,3}Y_4$$

$$\frac{dY_5}{dt} = \omega Y_3 + \nu\psi(1-\epsilon)\delta_{2,5}Y_2 + \delta_{6,5}Y_6 + \nu\psi(1-\epsilon)(1-\delta_{1,6})Y_1 - \mu Y_5 - \gamma_L Y_5 - \delta_{5,6}Y_5$$

$$\frac{dY_6}{dt} = \omega Y_4 + \nu\psi(1-\epsilon)\delta_{1,6}Y_1 + \delta_{5,6}Y_5 + \nu\psi(1-\epsilon)(1-\delta_{2,5})Y_2 - \mu Y_6 - \gamma_H Y_6 - \delta_{6,5}Y_6$$

$$\frac{dY_7}{dt} = I_7 + \gamma_L Y_1 + \gamma_L Y_5 + \delta_{8,7}Y_8 - \mu Y_7 - \mu_7 Y_7 - \sigma\xi Y_7 - \delta_{7,8}Y_7$$

$$\frac{dY_8}{dt} = I_8 + \gamma_H Y_2 + \gamma_H Y_6 + \delta_{7,8}Y_7 - \mu Y_8 - \mu_8 Y_8 - \sigma\xi(1-\delta_{8,9})Y_8 - \delta_{8,7}Y_8 - \sigma\xi\delta_{8,9}Y_8$$

$$\frac{dY_9}{dt} = I_9 + \sigma\xi Y_7 + \delta_{10,9}Y_{10} + \sigma\xi\delta_{8,9}Y_8 - \mu Y_9 - \mu_9 Y_9 - \delta_{9,10}Y_9$$

$$\frac{dY_{10}}{dt} = I_{10} + \sigma\xi(1-\delta_{8,9})Y_8 + \delta_{9,10}Y_9 - \mu Y_{10} - \mu_{10}Y_{10} - \delta_{10,9}Y_{10}$$

$$\frac{dY_{11}}{dt} = I_{11} + \mu_7 Y_7 + \mu_9 Y_9 + \delta_{12,11}Y_{12} - \mu Y_{11} - \mu_{11}Y_{11} - \delta_{11,12}Y_{11}$$

$$\frac{dY_{12}}{dt} = I_{12} + \mu_8 Y_8 + \mu_{10}Y_{10} + \delta_{11,12}Y_{11} - \mu Y_{12} - \mu_{12}Y_{12} - \delta_{12,11}Y_{12}$$

$$\frac{dY_{13}}{dt} = \mu_{11}Y_{11} + \delta_{14,13}Y_{14} - \mu Y_{13} - \mu_{13}Y_{13} - \delta_{13,14}Y_{13}$$

$$\frac{dY_{14}}{dt} = \mu_{12}Y_{12} + \delta_{13,14}Y_{13} - \mu Y_{14} - \mu_{14}Y_{14} - \delta_{14,13}Y_{14}$$

where

$$\frac{d\lambda_L}{dt} = \frac{p_L\beta_7 Y_7 + p_L\beta_9 Y_9 + p_L\beta_{11}Y_{11} + p_L\beta_{13}Y_{13}}{p_L Y_1 + p_L Y_3 + p_L Y_5 + p_L Y_7 + p_L Y_9 + p_L Y_{11} + p_L Y_{13}}$$

$$\frac{d\lambda_H}{dt} = \frac{p_H\beta_8 Y_8 + p_H\beta_{10}Y_{10} + p_H\beta_{12}Y_{12} + p_H\beta_{14}Y_{14}}{p_H Y_2 + p_H Y_4 + p_H Y_6 + p_H Y_8 + p_H Y_{10} + p_H Y_{12} + p_H Y_{14}}$$

$$\beta_L = 1 - (1 - s_L b)^{k_L/p_L}$$

$$\beta_H = 1 - (1 - s_H b)^{k_H/p_H}$$

$$\gamma_L = 1 - [\lambda_L (1 - s_L b)^{k_L/p_L} + (1 - \lambda_L)]^{p_L}$$

$$\gamma_H = 1 - [\lambda_H (1 - s_H b)^{k_H/p_H} + (1 - \lambda_H)]^{p_H}$$