Population Effects of Preventive and Therapeutic HIV Vaccines in Early- and Late-Stage Epidemics

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Abstract

Background: Development of vaccines against human immunodeficiency virus (HIV) infection is a worldwide public-health priority. We evaluated the population effects of potential preventive and therapeutic vaccines in early- and late-stage epidemics in a population of homosexual men.

Methods: We used an epidemic model that simulated the course of the epidemic for a population designed to reflect that of homosexual men in San Francisco, California. We evaluated vaccine programs by the number of cases of HIV averted, the effect on the prevalence of HIV, and by the gain in quality-adjusted life years (QALYs) for the total population.

Findings: A preventive vaccine prevented 3877 cases of HIV infection during a 20-year period, reduced the projected prevalence of HIV infection from 12% to 7% in a late-stage epidemic, and gained 15,908 QALYs. A therapeutic-vaccine that did not affect the infectivity of vaccine recipients increased the number of cases of HIV infection by 210, resulted in a slight increase in the prevalence of HIV infection from 12% to 15% in a late-stage epidemic, and gained 8854 QALYs. If therapeutic vaccines reduced infectivity, their use could produce net gains of quality-adjusted life years in the population that were identical to gains from the use of preventive vaccines. In an early-stage epidemic, the advantage of a preventive-vaccine program relative to a therapeutic vaccine program was markedly enhanced.

Interpretation: Both preventive- and therapeutic-vaccine programs provided substantial benefit, but their relative merit depended on which outcome measures we assessed. Evaluation of HIV vaccine programs based solely on cases averted, or on prevalence of HIV in the population, underestimates the benefit associated with therapeutic-vaccine programs. The effect of a therapeutic HIV vaccine on the epidemic outcomes depended markedly on whether the therapeutic vaccine reduced the infectivity of the vaccine recipient. Field vaccine trials should evaluate correlates of infectivity, such as HIV viral load. HIV vaccine implementation strategies should be tailored to the dynamics of the epidemic in specific populations.

Approximately 30 million people have been infected with the human immunodeficiency virus (HIV) worldwide, and 5.8 million have died.[1] Up to 20 million additional infections are predicted to occur over the next 4 years alone.[2-4] Although development of an effective HIV vaccine has proved daunting and none are available,[5,6] many candidate vaccines have undergone phase I clinical trials that establish efficacy and antigenicity, several have undergone phase II clinical trials that evaluate dosage regimens, and the World Health Organization recently sanctioned vaccines developed from HIV subunits for phase III trials of effectiveness in countries outside the United States.[7-11] Both preventive and therapeutic vaccines are under development. Preventive (or prophylactic) vaccines prevent infection or disease in uninfected people who are exposed to HIV. Therapeutic vaccines slow the progression of disease in those people already infected with HIV. Because an effective therapeutic vaccine will probably reduce the degree of viral replication and the number of viral particles in blood and other body fluids, such a vaccine may also decrease the likelihood that an infected person will transmit HIV.[12] However, because a therapeutic vaccine may prolong the time during which infected people can transmit HIV (by increasing their length of life), it could have the perverse effect of increasing the number of cases of HIV infection. The mechanism of action of a vaccine (preventive or therapeutic) is important, because it determines who is vaccinated and bears any risk associated with vaccination, who benefits from a vaccine program (the uninfected or the infected population), how many people are vaccinated (usually, the infected population is smaller than the uninfected population), and, perhaps, how the course of the epidemic unfolds.

We report our use of a mathematical model to evaluate the population effects of potential preventive and therapeutic vaccines in early- and late-stage epidemics in a population of homosexual men. We sought to determine the effect of therapeutic or preventive HIV vaccine programs on the number of HIV infections averted, the prevalence of HIV, and the total number of quality-adjusted life years accrued by the population. We performed our analyses by simulating the course of the HIV epidemic under various vaccine programs, in a population matched to resemble a population of homosexual men.

Methods

Model Structure. We used a dynamic, compartmental epidemic model[13-16] that simulated the course of the epidemic for a population designed to reflect that of homosexual men in San Francisco, California (Figure 1). Compartmental models are a standard approach for modeling the course of an epidemic caused by an infectious disease. Mathematical equations govern the rate at which people move over time from one compartment (a population subgroup, represented by a box in Figure 1) to another. For example, when an unvaccinated person becomes infected with HIV, the person moves from box b to box d in Figure 1. The simulation determines how many people are in each box in Figure 1 after a predetermined time (say, 20 years), both with and without a vaccine program. In essence, a vaccine program reduces the rate at which people move from the uninfected population subgroup to the HIV-infected subgroup. We determined the net effect of a vaccine program by calculating the difference with and without a vaccine program, in the number of people with HIV infection, in the prevalence of HIV infection, and in the quality-adjusted life years for the total population. A detailed description of the model, assumptions, and sources of data is available.[17]

The model incorporated the vaccine characteristics of take, efficacy, duration, and effect on infectivity.[15,16] For a preventive vaccine, the take of the vaccine, ψ, is the percentage of people in whom the vaccine has any effect. The efficacy of the vaccine, ε, is the proportion of people protected from infection, among those people in whom the vaccine takes. The duration of the vaccine, $1/\omega$, is the length of time (in years) that the vaccine provides protection. For a therapeutic vaccine, take is defined similarly. For simplicity, we assumed that the effects of therapeutic vaccines on length of life and infectivity were confined to the asymptomatic period of HIV disease. The decrease in the rate of progression to symptomatic disease caused by a preventive vaccine results in additional longevity in the asymptomatic period; this additional longevity is $1/\mu_v$ (in years). We defined infectivity as the probability of transmission of HIV per partnership. The infectivity during the asymptomatic period, β_α, is reduced by a factor,

β_v, the infectivity reduction of a therapeutic vaccine. Thus, the infectivity of a person who received the therapeutic vaccine was equal to $(\beta_\alpha)(\beta_v)$.

To illustrate how we developed the equations that govern transition among the population subgroups, we explain the equation for the number of people in the uninfected, unvaccinated subpopulation (Figure 1, box b), $X(t)$, at time t. This number depended on the number of new uninfected susceptible people who entered the population I_u; on the number of people who left the population due to vaccination, infection with HIV, or death from non-HIV causes; and on the number of previously vaccinated people who reentered the uninfected unvaccinated subpopulation because their protection from the vaccine had waned. The terms in Equation 1, noted next, describe each of these groups. The number of people in the population who became successfully vaccinated (Figure 1, transition from box b to a) was the product of the number of uninfected unvaccinated people, $X(t)$, the percentage of the population that participated in the vaccine program, p, and the vaccine take, ψ, or $X(t)p\psi$. The number of people who left the uninfected population due to infection with HIV was the product of the number of susceptible individuals $X(t)$; the average annual number of sexual partnerships, c; and the probability, per partnership, of acquiring HIV, $\lambda(t)$, or $X(t)c\lambda(t)$. The number of people who left the uninfected population due to death from other causes (not shown in Figure 1) was the product of the number of uninfected unvaccinated people, $X(t)$, and the non-AIDS death rate, μ, or $X(t)\mu$. Finally, the number of people who reentered the susceptible population because their vaccine protection had waned was the product of the number of vaccinated people, $X_V(t)$, and the rate of loss of vaccine protection, ω, or $X_V(t)\omega$. Thus, the number of unvaccinated susceptible people varied according to

$$\frac{dX(t)}{dt} = I_u - X(t)p\psi - X(t)c\lambda(t) - X(t)\mu + X_V(t)\omega. \qquad \text{eq. (1)}$$

Transitions between other compartments in Figure 1 were governed by similar equations.[17]

We modeled the effect of a preventive vaccine program as a change in the rate of HIV infection in susceptible individuals exposed to HIV. In the unvaccinated group, the number of

new HIV infections in susceptible individuals was $X(t)c\lambda(t)$. In the vaccinated susceptible group, the number of new infections was $X(t)c\lambda(t)(1 - \varepsilon)$. Thus, the rate of infection of susceptible people was reduced by the term $(1 - \varepsilon)$. For example, if the preventive vaccine efficacy was 70% ($\varepsilon = 0.7$), the rate of new infections was reduced to 30% of the unvaccinated rate.

We modeled the effect of a therapeutic vaccine as a decreased rate of transition from the asymptomatic to the symptomatic state. We assumed that therapeutic-vaccine efficacy was independent of antiretroviral treatment, and, for our base-case analysis, that vaccine programs did not alter sexual risk behaviors. In subsequent analyses, we examined changes in risk behavior. We also assumed that the uninfected population and the infected asymptomatic, unidentified population selected sexual partners preferentially, but not exclusively, from other members of the population who did not have AIDS.[18-20]

Input Data. To estimate input parameters for the model, we used published data as well as an unpublished survey of the behavior of homosexual men in San Francisco, California (Table 1).[21-28] Transmission probabilities were based on epidemiologic studies and model-based estimates.[21,22] We examined the effects of vaccines in both early- and late-stage epidemic. For our analysis, an early-stage epidemic was one in which the prevalence was low but increasing; a late-stage epidemic was one in which the prevalence was high and stable or declining. We modeled our late-stage epidemic to match estimates of the prevalence of HIV in homosexual men in San Francisco (estimated at 49.3% in 1990) and to include a modest number of sexual partners (average 2 partnerships per year), consistent with evidence that homosexual men have reduced high-risk behaviors substantially. For the early-stage epidemic, we modeled a growing epidemic in which the prevalence of HIV was 10% and the susceptible individuals averaged 4 partnerships per year. This higher level of risk behavior may represent an appropriate estimate for young homosexual men.[29,30] The average age of the population was 30 years. Our base-case analysis presents the results from the first 20 years of a simulated vaccination program. Because vaccine programs have effects on the epidemic that persist long

after the vaccination program has ended, we also examined long-term outcomes at up to 150 years, for a vaccination program that lasted for 20 years.

Because the vaccine characteristics for preventive and therapeutic vaccines are unknown, we evaluated the possible future effects of vaccine programs under a wide range of assumptions about vaccine characteristics (Table 1). For our base-case analysis, we evaluated a preventive vaccine that produced a response in all vaccinated individuals (take = 1), protected 75% of these individuals from infection (efficacy = 75%), and provided protection for 10 years (duration = 10 years). Our base-case therapeutic vaccine also produced a response in all vaccinated people (take = 1), extended the life of an HIV infected person by 5 years ($1/\mu_v = 5$ years), and did not affect infectivity ($\beta_v = 1$).

Epidemic Outcomes. To assess the outcomes from various vaccine programs, we calculated the number of HIV cases averted, the prevalence of HIV in the population, and the life years saved. Because vaccine programs save years of life both in good health (in the uninfected population) and with HIV disease (therapeutic vaccines prolong the life of people infected with HIV), we converted life years saved to quality-adjusted life years saved (or gained). We calculated the number of quality-adjusted life years gained by multiplying the length of life in a health state by the assessed quality of life (on a 0-to-1 scale) of the health state.[27,31-34] We assessed the model performance by comparing the model output to known or estimated parameters for the population of homosexual men in San Francisco, under the assumption of no vaccine program, for the years 1990 through 1994. Public-health officials estimated the prevalence of HIV in homosexual men in San Francisco at 43% in 1992,[35] the corresponding estimate from the model was 41%. The predicted number of AIDS cases agreed within 15% of the observed rates for the years 1990 through 1994, except for 1992, in which an unusually large number of HIV cases was seen. We performed sensitivity analyses on all model variables.

Results

Our analysis was performed for a population of 55,800 homosexual men.

Effect of Vaccine Type. A preventive vaccine, administered to 75% of the susceptible population, prevented 3877 cases of HIV infection during a 20-year period (Figure 2a), and reduced the projected prevalence of HIV infection from 12% to 7% (Figure 2b) in a late-stage epidemic. With a preventive-vaccine program, an additional 1354 persons were alive after 20 years; also, of those alive, a larger number were living without HIV infection (Figure 3a). A preventive vaccine increased the number of quality-adjusted life years in the population by 15,908 (Figure 3b).

In contrast, a therapeutic-vaccine program administered to the 75% of identified asymptomatic HIV-infected men, increased the number of cases of HIV infection by 210 (Figure 2a), and resulted in a slight increase in the prevalence of HIV infection from 12% to 15% (Figure 2b) in a late-stage epidemic. The number of people alive at the end of 20 years increased by 679, relative to the number of people alive without a vaccine program, but the number of people alive with HIV infection also increased by 871 people (Figure 3a). Despite the increased number of HIV infections, and the modest increase in prevalence, a therapeutic vaccine program resulted in 8854 more quality-adjusted life years for the entire population (Figure 3b).

Our base-case analyses assumed that a therapeutic vaccine did not reduce the infectivity of vaccinated people. However, the population effects of a therapeutic vaccine depend on the balance between the degree to which a vaccine recipient's longevity is increased (and thus transmission of HIV is increased) and the degree to which the recipient's infectivity is reduced. For example, a therapeutic vaccine that increased length of life by 5 years, but reduced infectivity by 50%, could produce net gains in quality-adjusted life years similar to those produced by a preventive vaccine with a duration of 10 years and an efficacy of 62.4% (Figure 4). In contrast to our base-case analysis, a therapeutic vaccine that reduced infectivity by 8.0%, did not increase the number of cases in the population over a 20-year time horizon. For

reductions in infectivity greater than 8.0%, a therapeutic vaccine resulted in a net decrease in the number of cases, thus also providing a benefit of fewer new HIV infections in the uninfected population. Over a wide range of plausible vaccine characteristics, therapeutic- and preventive-vaccine programs produced similar net benefits, as shown in Figure 4. In general, for vaccines of given duration, the more effective the preventive vaccine, the greater the required reduction in infectivity for a therapeutic vaccine to produce similar net gains in quality-adjusted life years for the total population. All results reflected the outcomes of the vaccination program 20 years after its inception.

Epidemic Stage. In an early-stage epidemic, preventive vaccines averted substantially more cases of HIV compared with their use in a late-stage epidemic (Figure 2a). In an early-stage epidemic, the effect of vaccine programs on the prevalence of HIV (Figure 2b) was similar to the effect in late-stage epidemics: preventive vaccine programs reduced the prevalence of HIV, and therapeutic vaccines that do not affect the infectivity of vaccine recipients, resulted in a modest rise in the prevalence of HIV. In an early-stage epidemic, the total number of people alive at the end of 20 years was higher than the number alive for a late-stage epidemic, due to the relatively lower HIV-related mortality (Figure 3a and 3b). Although preventive- and therapeutic-vaccine programs increased the number of people alive after 20 years (2,842 and 498 additional people alive, respectively), a preventive vaccine resulted in a greater number of people alive without HIV, as expected (Figure 3c). In an early-stage epidemic, the advantage of a preventive-vaccine program relative to a therapeutic vaccine program was markedly enhanced: Preventive-vaccine programs saved 5.9 times more quality-adjusted life years than did therapeutic-vaccine programs (31,458 versus 5,355 quality-adjusted life years gained, respectively), compared with a 1.8 times more quality-adjusted life years in a late-stage epidemic (Figures 3b and 3d).

Discussion

We used an epidemic model to estimate the effects of programs with preventive or therapeutic HIV vaccines on a population of homosexual men. Our analysis has three main findings. First, although both preventive- and therapeutic-vaccine programs provided substantial benefit, their relative merit depended on which outcome measures we assessed. Preventive vaccines avert cases of HIV infection, and reduce HIV prevalence. In contrast, therapeutic vaccines that do not affect infectivity increase slightly the number of cases of HIV and HIV prevalence. However, when we evaluated preventive and therapeutic vaccines by the net gain in quality-adjusted life years, the substantial benefit of either type of vaccine became apparent, particularly in late-stage epidemics (Figure 3b). Our use of quality-adjusted life years as an outcome measure[27,31-34] enabled us to account for the benefit of extending the life of people who have HIV infection, yet also maintained the distinction between 1 year of life gained in good health versus 1 year of life gained in poor health. Thus, evaluation of HIV vaccine programs based solely on cases averted, or on prevalence of HIV in the population, provides an incomplete estimate of the benefit of certain vaccine programs, and particularly underestimates the benefit associated with therapeutic-vaccine programs.

Our second finding was that the effect of a therapeutic HIV vaccine on the course of the epidemic depended markedly on whether the therapeutic vaccine reduced the infectivity of the vaccine recipient. Although HIV viral load correlates with HIV transmission,[12] whether a vaccine that reduced viral load would also reduce infectivity is unknown. The greater the degree to which a therapeutic vaccine reduces infectivity, the more the effects of the therapeutic vaccine resemble those of a preventive vaccine. Due to reduced HIV transmission, a therapeutic vaccine that reduces infectivity provides benefit to both the HIV-infected and the uninfected segments of the population. In an extreme case, the logic of this result becomes clearer: A therapeutic vaccine that reduced infectivity to zero would completely protect the uninfected segment of the population, as would a perfect preventive vaccine. For a broad

range of plausible, but imperfect, vaccines, preventive and therapeutic vaccines produce identical gains in the number of quality-adjusted life years lived by the population (Figure 4).

Our third finding is that the relative merits of preventive and therapeutic vaccines also depended on the stage of the epidemic. The relative advantage of preventive vaccines was most pronounced in early-stage epidemics, a finding that held for a variety of vaccine characteristics. In an early-stage epidemic, the number of uninfected persons in whom vaccination can prevent infection is greater than in a late-stage epidemic, or in an epidemic that is growing slowly. Thus, a preventive vaccine holds more promise in an early-stage epidemic compared with a therapeutic vaccine that reduces infectivity modestly, or not at all.

Previous analyses of vaccine programs have not compared preventive and therapeutic vaccines in the same population. Anderson and colleagues evaluated the effects of chemotherapy or immunotherapy (similar to our therapeutic vaccine), and found that the size of the infected population could increase or decrease depending on the growth rate of the epidemic and on the length of the incubation period.[13,14] An analysis of use of a preventive vaccine in homosexual men in San Francisco concluded that a vaccine program without substantial concomitant behavior change was unlikely to eradicate HIV infection.[15,16] Our analysis indicated that a preventive vaccine in a late-stage epidemic would increase the rate of decline in the prevalence of HIV, but that the prevalence of HIV would not reach 0 during the next 50 years. Our model also supports the importance of changes in behavior on the overall effect of vaccine programs (data not shown).[36]

Although no one knows whether preventive vaccines, therapeutic vaccines, or both, will become available, our findings suggest that policy makers could improve vaccine implementation strategies by accounting for both vaccine characteristics and the stage of the epidemic. HIV epidemic growth differs based on geography and population risk behavior. For example, in homosexual men in San Francisco, the rate of incident cases has become relatively stable, suggesting a late-stage epidemic, at least in older homosexual men.[28] In this population, preventive and therapeutic vaccines may have similar effects, depending on the

specific vaccine characteristics. In contrast, the prevalence of HIV among adolescents is increasing, and certain subgroups of adolescents may resemble the population in our early-stage epidemic model, in which most members of the population are uninfected, but have relatively high levels of risk behavior. Preventive vaccines may hold more promise in this group. Although the qualitative results of our analysis may apply to other risk groups, such as injection drug users, analyses of vaccine effects in other groups should account for mode of transmission (for example, sharing of needles) and specific high-risk behavior.

Our analysis also has implications for the design of clinical trials of HIV vaccines. Differences in vaccine take, efficacy, and duration result in predictable patterns of HIV incidence in the study population.[15,16] Our results suggest that field vaccine trials also should evaluate correlates of infectivity, such as HIV viral load. These estimates will help investigators to determine whether therapeutic and preventive vaccines produce similar, or markedly distinct, effects on the course of the HIV epidemic.

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Table 1. Parameter Values and Sources

Name	Base Case	Range
Vaccine Parameters		
Vaccine Take (as proportion of those vaccinated), ψ	1	0.1 – 1
Preventive Vaccines		
Proportion of susceptibles vaccinated annually, p	0.75	0.25 – 0.9
Vaccine efficacy (proportion who are protected from infection), ε	0.75	0.1 – 0.9
Vaccine duration (years), $1/\omega$	10	5 – 50
Therapeutic Vaccines		
Proportion of asymptomatic, infected people vaccinated each year, $p_t(t)$	0.75	0.25 – 0.9
Increase in asymptomatic period due to vaccine (years), $1/\mu_V$	5	1 – 10
Infectivity multiplier for β_α, change in infectivity due to vaccine, β_V	1	0.10 – 1
Transmission Parameters		
Infectivity, asymptomatic period (per-partner probability of transmission of HIV), β_α,*	0.066	0.044 – 0.081
Infectivity, symptomatic period (per-partner probability of transmission of HIV), β_S†	0.147	0.98 – 0.179
Contact rate, sexual partners, all disease stages except AIDS, late-stage epidemic, c‡	2	1.59 – 5.93
HIV Disease Parameters		
Quality of life, asymptomatic HIV infection§	0.83	0.66 – 1.00
Quality of life, symptomatic HIV infection§	0.42	0.34 – 0.50
Quality of life, AIDS§	0.17	0.14 – 0.20
Duration of Disease		
Asymptomatic HIV infection¶	8.7	7.1 – 9.6
Symptomatic HIV infection¶	2.7	2.2 – 3.2
AIDS¶	2.1	1.7 – 2.5

*Estimated as $0.45\beta_S$ as in Brandeau, et al.[21]

†Calculated from Samuel, et al.[22]

‡Derived from Samuel, et al and Communication Technologies, et al.[22,23]

§Derived from Owens, et al.[33]

¶Estimated as in Owens, et al.[27]

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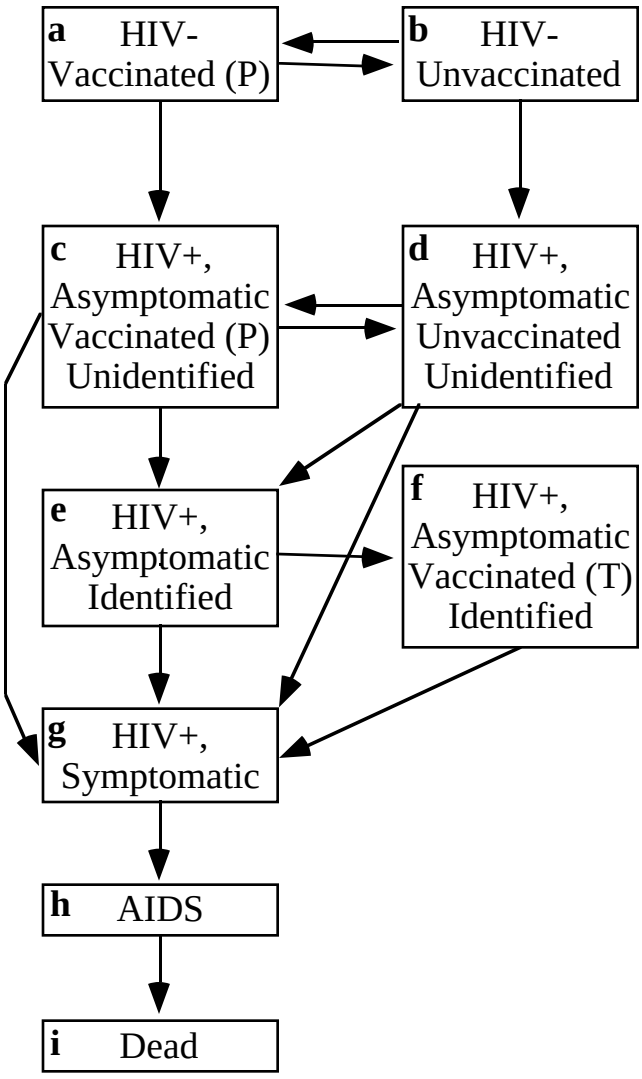
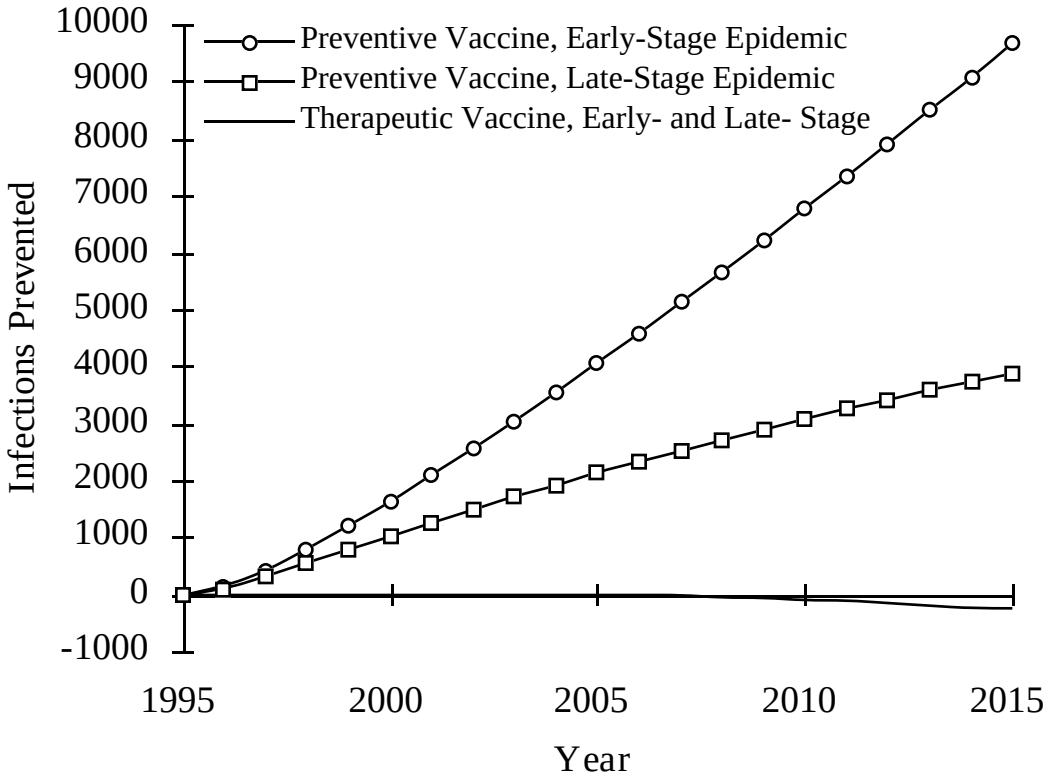

a HIV- Vaccinated (P)
b HIV- Unvaccinated
c HIV+, Asymptomatic Vaccinated (P) Unidentified
d HIV+, Asymptomatic Unvaccinated Unidentified
e HIV+, Asymptomatic Identified
f HIV+, Asymptomatic Vaccinated (T) Identified
g HIV+, Symptomatic
h AIDS
i Dead

Figure 1

a.


Preventive Vaccine, Early-Stage Epidemic
Preventive Vaccine, Late-Stage Epidemic
Therapeutic Vaccine, Early- and Late- Stage
Infections Prevented
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
1995
2000
2005
2010
2015
Year

b.

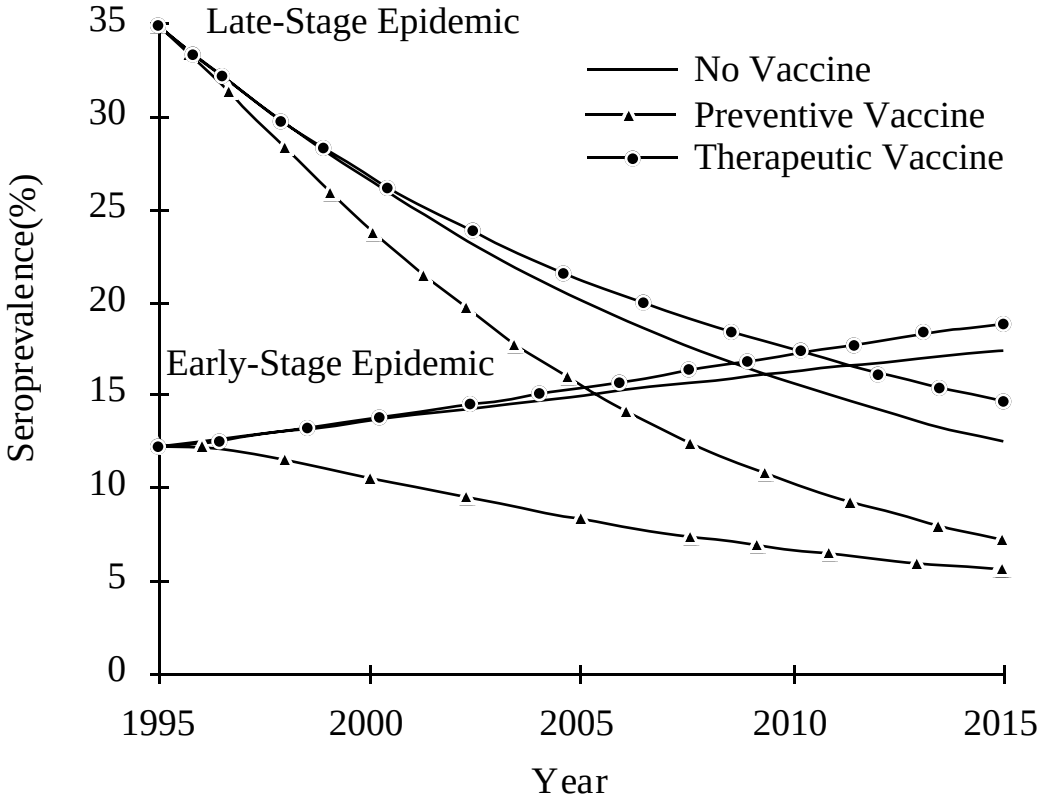

Late-Stage Epidemic
No Vaccine
Preventive Vaccine
Therapeutic Vaccine
Early-Stage Epidemic
Seroprevalence(%)
35
30
25
20
15
10
5
0
1995
2000
2005
2010
2015
Year

Figure 2

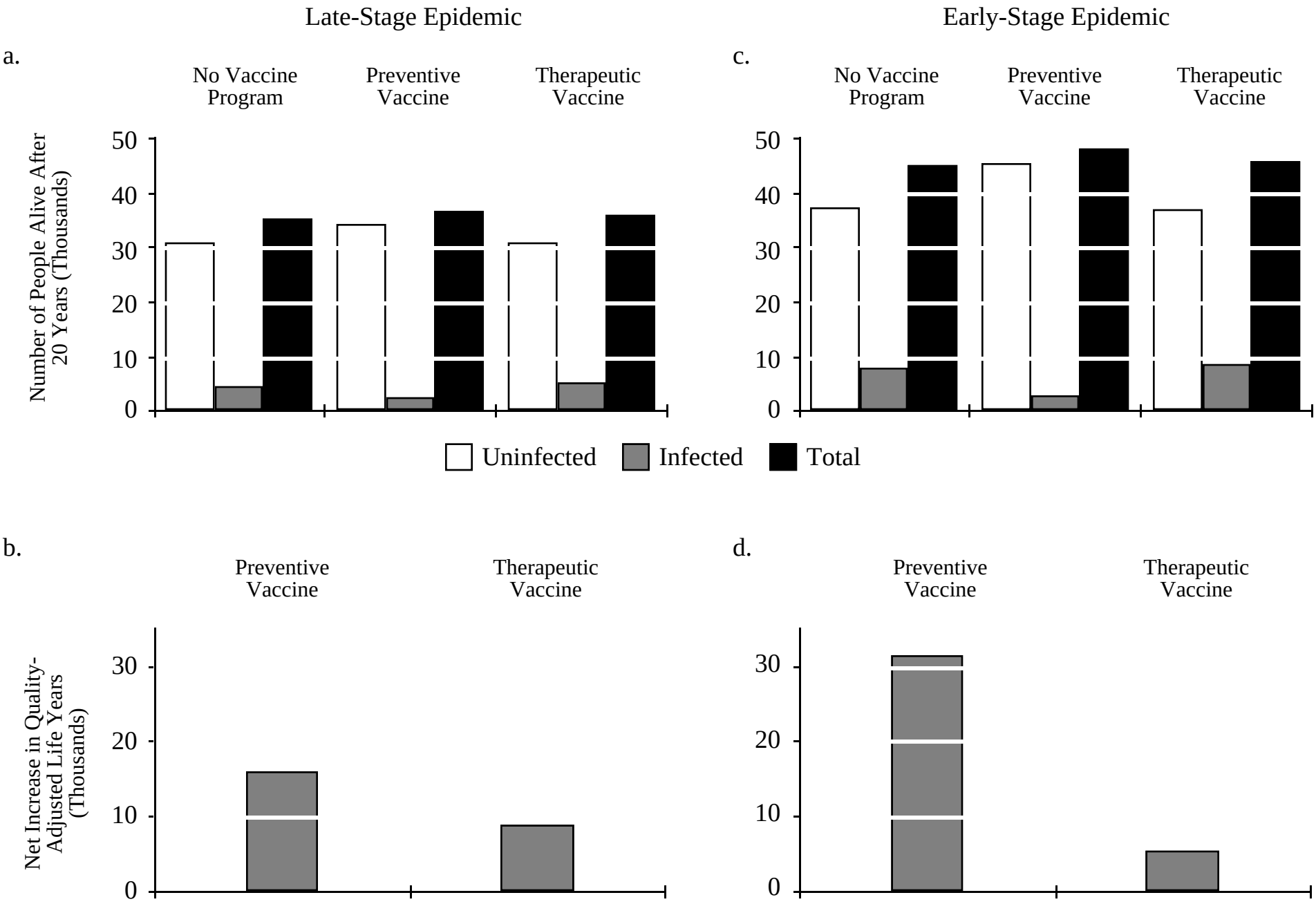

Late-Stage Epidemic
Early-Stage Epidemic
a.
c.
No Vaccine Program
Preventive Vaccine
Therapeutic Vaccine
Number of People Alive After 20 Years (Thousands)
50
40
30
20
10
0
Uninfected
Infected
Total
b.
d.
Net Increase in Quality-Adjusted Life Years (Thousands)
30
20
10
0

Figure 3

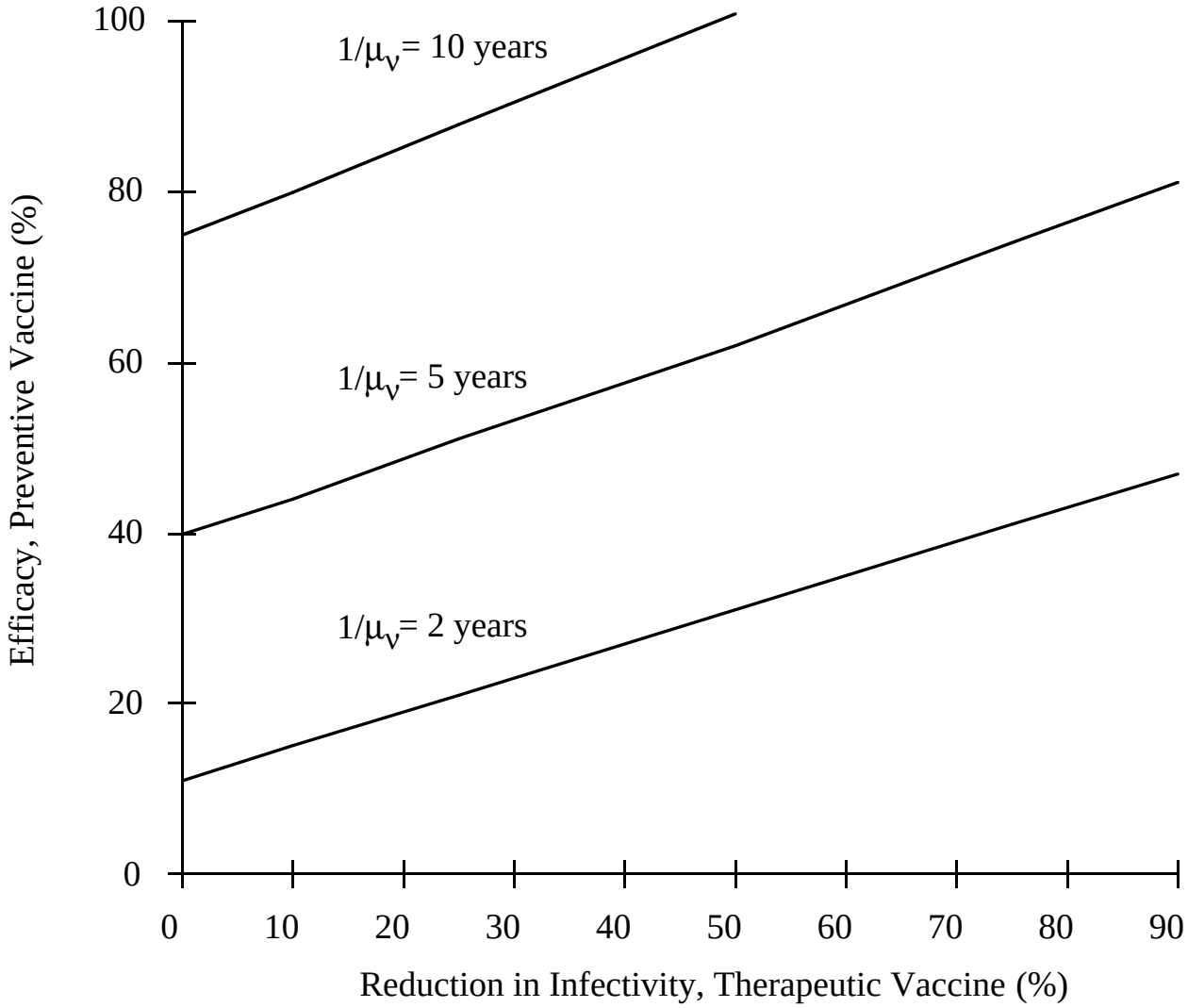

100
80
60
40
20
0
Efficacy, Preventive Vaccine (%)
1/μν= 10 years
1/μν= 5 years
1/μν= 2 years
0
10
20
30
40
50
60
70
80
90
Reduction in Infectivity, Therapeutic Vaccine (%)

Figure 4

Figure Legends

Figure 1 Dynamic compartmental model of HIV vaccine program. Boxes represent population subgroups, and arrows indicate allowed transitions between subgroups. Vaccinated (P) and Vaccinated (T) indicate vaccination with preventive and therapeutic vaccines, respectively; HIV+ indicates infection with HIV; HIV– indicates absence of infection. Transition from population subgroups **a** and **b** to subgroups **c** and **d** occurred because of infection with HIV. Transition from population subgroups **b** and **d** to groups **a** and **c** occurred when members of the population were vaccinated with a preventive vaccine; transition in the opposite direction occurred when vaccine protection waned. Transition from **d** to **e** occurred when a person who was infected but unaware of his infection was identified through screening. We assumed that 15% of the asymptomatic, HIV-infected population was screened and identified annually. Transition from **e** or **f** to **g** occurred from disease progression. Transition from **e** to **f** occurred when an asymptomatic HIV-infected person received a therapeutic vaccine.

Figure 2 Population effects of preventive- and therapeutic-vaccine programs. (a) Preventive vaccines averted more infections in early-stage than in late-stage epidemics. Therapeutic vaccines slightly increased the number of infections in both early- and late-stage epidemics. (b) The prevalence of HIV is shown for early-stage and late-stage epidemics, with no vaccination program, and with preventive- or therapeutic-vaccination programs.

Figure 3 Effect of vaccination programs on population subgroups. In an early-stage epidemic (a and b) and late-stage epidemic (c and d), preventive- and therapeutic-vaccine programs increased the total number of people alive, but therapeutic-vaccine programs resulted in increased number of people alive with HIV. However, a therapeutic-vaccine program increased the net quality-adjusted life years, compared to no vaccination program, despite the slight increase in number of people with HIV (b and d). In a late-stage epidemic, therapeutic

vaccine produced a gain in quality-adjusted life years that was similar to the effects of a preventive vaccine (d).

Figure 4 Equivalence of benefits of preventive and therapeutic vaccines in a late-stage epidemic. The lines indicate combinations for which preventive and therapeutic vaccines provided identical net benefit to the population. As the efficacy of a preventive vaccine increased, a therapeutic vaccine must produce a larger reduction in infectivity to provide equivalent results. The lines are based on a preventive vaccine with take = 1, duration = 10 years, and, for a therapeutic vaccine with take = 1, increase in length of life $1/\mu_V$ years as shown. For preventive vaccines, we assumed that 75% of the eligible population was vaccinated. For therapeutic vaccines, we assumed that 75% of the identified asymptomatic HIV-infected population was vaccinated; because not all asymptomatic HIV-infected persons were identified, after 20 years of the vaccination program, approximately 45% of all people infected with HIV would be vaccinated.