Optimal Investment in a Portfolio of HIV Prevention Programs

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Objectives. *In this article, the authors determine the optimal allocation of HIV prevention funds and investigate the impact of different allocation methods on health outcomes.* ***Methods.*** *The authors present a resource allocation model that can be used to determine the allocation of HIV prevention funds that maximizes quality-adjusted life years (or life years) gained or HIV infections averted in a population over a specified time horizon. They apply the model to determine the allocation of a limited budget among 3 types of HIV prevention programs in a population of injection drug users and nonusers: needle exchange programs, methadone maintenance treatment, and condom availability programs. For each prevention program, the authors estimate a production function that relates the amount invested to the associated change in risky behavior.* ***Results.*** *The authors determine the optimal allocation of funds for both objective functions for a high-prevalence population and a low-prevalence population. They also consider the allocation of funds under several common rules of thumb that are used to allocate HIV prevention resources. It is shown that simpler allocation methods (e.g., allocation based on HIV incidence or notions of equity among population groups) may lead to allocations that do not yield the maximum health benefit.* ***Conclusions.*** *The optimal allocation of HIV prevention funds in a population depends on HIV prevalence and incidence, the objective function, the production functions for the prevention programs, and other factors. Consideration of cost, equity, and social and political norms may be important when allocating HIV prevention funds. The model presented in this article can help decision makers determine the health consequences of different allocations of funds.*

Key words: *HIV, AIDS, resource allocation, prevention, cost-benefit analysis.* ***(Med Decis Making 2001; 21:391-408)***

Hundreds of millions of dollars are invested annually in HIV prevention in the United States. The allocation of much of these funds is guided by 65 HIV Prevention Community Planning Groups (CPGs). These groups are charged with determining the potential impact of various HIV prevention strategies, prioritizing prevention needs, and developing a resource allocation plan that is consistent with those prevention priorities.[1,2] This process aims to ensure local involvement from communities that receive federal HIV prevention funds and to ensure that knowledge within a community is used to address needs within that community.[3,4]

However, determining the optimal allocation of HIV prevention funds among programs and populations is complex. The effectiveness of a particular intervention may depend on the population to which it is targeted (e.g., a high-risk vs. a low-risk group), the amount already invested in the intervention (e.g., incremental methadone maintenance slots may be less effective than existing slots if individuals enrolled in the new slots are less willing to change their behavior than individuals in existing slots), and the level of investment in other HIV prevention programs (e.g., a television advertising campaign may increase awareness of HIV and thus increase the effectiveness of other HIV prevention programs). Additionally, epidemics of infectious diseases often grow nonlinearly: Incidence of new infections depends on the relative numbers of infected and uninfected individuals in a population. Rules for allocating HIV prevention resources that ignore these fac-

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Received 20 February 2001 from the Ivey School of Business, University of Western Ontario, London, Ontario, Canada (GSZ); and Department of Management Science and Engineering, Stanford University, Stanford, California (MLB). Revision accepted for publication 23 March 2001.

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tors may not yield the maximum health benefit from limited HIV prevention funds.

One resource allocation rule calls for resources to be allocated to interventions in increasing order of cost-effectiveness ratios.[5] However, this approach may not account for nonlinear scaling of interventions, may ignore nonlinear epidemic growth, and may not capture potential interactions between interventions. Resource allocation methods that have been developed to account for some of these problems do not explicitly account for epidemic growth,[6] require very long time horizons,[7] or assume independent, noninteracting populations.[7–11]

Several methods used by CPGs in their planning process have been reported.[2,9,10] One method is to assign priorities by ranking population groups (e.g., according to HIV incidence) and targeting money to groups based on those priority rankings. Another method is to assign priorities to HIV prevention programs and invest in programs based on those priority rankings. Several CPGs have attempted to incorporate equity notions in the ranking process by requiring equal amounts to be spent on various population groups or prevention programs.

In this article, we consider an alternate resource allocation method that is based on an epidemic model combined with optimization techniques.[12] The resource allocation framework that we use explicitly considers nonlinear epidemic dynamics, interactions between populations, and nonlinear "production functions" that relate the amount invested in a prevention program to changes in behavior. We apply the model to determine the allocation of a limited budget among 3 types of HIV prevention programs—a needle exchange program, methadone maintenance treatment, and condom availability programs—in a population of injection drug users (IDUs) and non-IDUs. We determine the set of expenditures (the investment portfolio) that maximizes the number of quality-adjusted life years (QALYs) gained by the population as a result of the resource allocation decision, and we determine the investment portfolio that maximizes the number of HIV infections averted in the population. We compare these solutions to those obtained using alternate resource allocation methods, such as those employed by some CPGs.

METHODS

Resource Allocation Model

We considered the following interventions, indexed by k:

1. A needle exchange program targeted to IDUs ($k = 1$);
2. Incremental methadone maintenance treatment slots for IDUs regardless of HIV infection status ($k = 2$);
3. Incremental methadone maintenance treatment slots for HIV-infected IDUs ($k = 3$);
4. Incremental methadone maintenance treatment slots for IDUs with AIDS ($k = 4$);
5. A condom availability program targeted to IDUs ($k = 5$);
6. A condom availability program targeted to IDUs in methadone maintenance ($k = 6$);
7. A condom availability program targeted to the entire population ($k = 7$).

We denote the amount invested in each intervention k by v_k and the vector of investment amounts by $\mathbf{v}$. The amount of money that can be invested in each intervention k may be limited by an upper bound V_k and by the total budget B. We assume that the decision maker wishes to allocate resources to these interventions to maximize the health benefit that accrues up to time T as a result of the allocation decision. We considered 2 measures of health benefit: the cumulative number of QALYs gained in the population as a result of the allocation decision, which we denote by $QG(\mathbf{v})$, and the cumulative number of HIV infections averted, which we denote by $IA(\mathbf{v})$. QALYs gained is the recommended measure of benefit in cost-effectiveness analyses.[13] However, an implied goal of HIV prevention programs is to maximize the number of HIV infections that are averted; therefore, similar to other methods for allocating HIV prevention resources,[8,10] we also considered cumulative infections averted.

We write the resource allocation problem as

$$\max QG(\mathbf{v}) \text{ or } IA(\mathbf{v}),$$

$$\sum_{k=1}^{7} v_k \le B,$$

$$0 \le v_k \le V_k \qquad k = 1, \ldots, 7.$$

We calculated the functions $QG(\mathbf{v})$ and $IA(\mathbf{v})$ via an epidemic model and production functions that relate the amount of money invested in an intervention to changes in the values of parameters of the epidemic model. Following recommended practice, we discounted health benefits at 3%.[13]

Dynamic Model

We modeled the spread of HIV and the flow of IDUs into and out of methadone maintenance with a dynamic epidemic model that is represented by a system

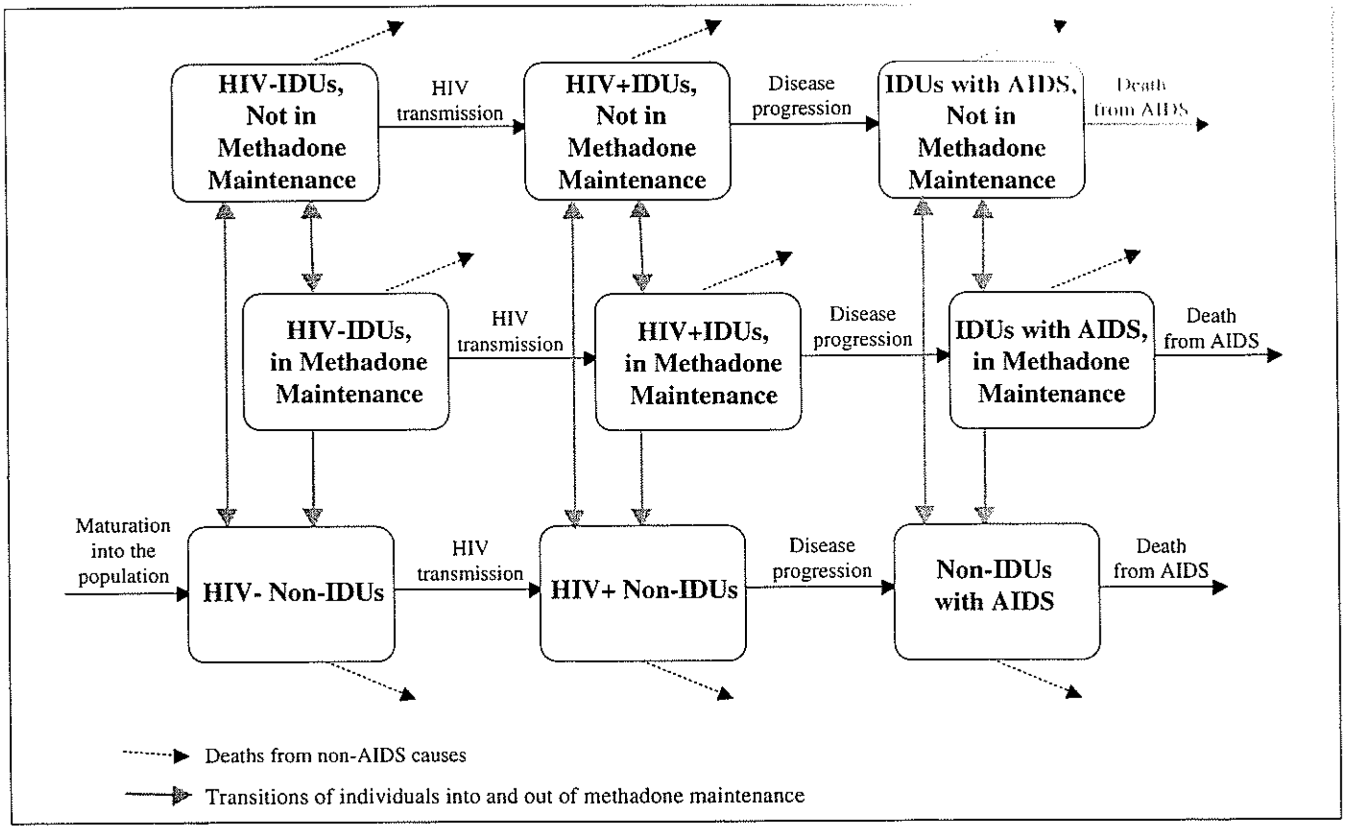

Figure 1. Schematic of dynamic model (IDU = injection drug user).

of simultaneous nonlinear differential equations, a common assumption for models of infectious diseases.[14–16] A version of this model has been described elsewhere.[17,18] The model is illustrated schematically in Figure 1. The model equations are contained in Zaric et al.[18] Selected parameter values and their sources are shown in Table 1; a complete listing of parameter values and sources for the dynamic model can be found elsewhere.[17] We modeled a high-prevalence community of 1 million people with 25,000 IDUs, 3750 methadone maintenance treatment slots, 40% HIV prevalence among IDUs, and 2.7% overall HIV prevalence, and a low-prevalence community of 1 million people with 7000 IDUs, 1050 methadone slots, 5% HIV prevalence among IDUs, and 0.25% overall HIV prevalence. The high-prevalence community is intended to be representative of a city such as New York,[19] and the low-prevalence community is intended to be representative of a city such as Los Angeles.[20]

The population comprises individuals aged 18 to 44 (equal numbers of men and women) and is divided into 9 compartments based on 3 behavior classes (IDUs not in methadone maintenance, IDUs in methadone maintenance, and non-IDUs) and 3 HIV disease stages (not infected, HIV infected without AIDS, and AIDS). Individuals enter the model as HIV-uninfected, 18-year-old non-IDUs. Uninfected individuals become infected as a result of sexual or needle-sharing contacts with infected individuals. Infection transmission is nonlinear, and the sufficient contact rates depend on the number of infected and uninfected individuals. Infection via needle sharing depends on the number of injections, the proportion of injections that are shared, and the probability of transmission per risky injection. Infection via sexual contact depends on the number of sexual partners, the proportion of contacts in which condoms are used, condom efficacy, and the probability of transmission per sexual partner. Individuals move from HIV to AIDS by disease progression. Individuals leave the population because of maturation (attaining age 45), death from AIDS, and death from other causes. Individuals may migrate between risk classes of the same disease stage and may move into methadone maintenance to fill up any empty slots (we assumed

Table 1 Selected Parameter Values and Their Sources

	Base Value[a]	Source
IDUs not in methadone maintenance treatment		
Annual mortality rate from non-HIV causes	3.0%	19, 79-81
Annual number of new sex partners[b]	3.5	24-31
Condom use rate	20%	19, 26, 28-30, 39
Annual number of injections[b]	200, 225[c]	19, 28, 44-48
Fraction of injections that are shared	20%	19, 28, 39, 44, 47, 49-51
Annual rate of injection drug use cessation	1.02%	55
Annual rate of progression from asymptomatic HIV to AIDS[d]	9.2%	18, 82-84
IDUs in methadone maintenance treatment		
Annual mortality rate from non-HIV causes	1.1%	19, 79-81
Annual number of new sex partners[b]	3.5	24-31
Condom use rate	20%	19, 26, 28-30, 39
Annual number of injections[b]	40, 45[c]	44, 48, 52, 53
Fraction of injections that are shared	6%	49, 51, 52, 54
Annual rate of returning to untreated injection drug use	31.5%	20, 55, 57
Annual rate of returning to the general population	3.5%	20, 55-59
Annual rate of progression from asymptomatic HIV to AIDS[d]	8.1%	18, 82-84
Non-IDUs		
Annual mortality rate from non-HIV causes	0.14%	85
Annual number of new sex partners[b]	1.2	32-38
Condom use rate	30%	34, 36, 40, 41
Annual rate of progression from asymptomatic HIV to AIDS[d]	9.2%	18, 82-84
Annual rate of becoming IDUs among uninfected individuals and those with asymptomatic HIV	0.3%, 0.057%[c]	e
Annual rate of becoming IDUs among individuals with AIDS	0%	Assumed
All individuals		
Annual mortality rate from AIDS	37.8%	d

Note: IDU = injection drug user.

a. Value before incremental investment in the HIV prevention programs.

b. Individuals with AIDS were assumed to have only 25% as many new sex partners and injections per year as similar individuals without AIDS.

c. Values for the low-prevalence and high-prevalence communities, respectively.

d. Recent studies show strong survival, CD4 count, and viral load advantages associated with drug regimens that include protease inhibitors, although no exact figure is known.[86-90] We assumed that protease inhibitors lengthen life with asymptomatic HIV by a factor of 1.5. Thus, we assumed that mean time from HIV infection to development of AIDS is 9.8 years with no protease inhibitors[82] and 14.7 years with protease inhibitors, and that mean time from development of AIDS to death is 2.1 years with no protease inhibitors[82,84] and 3.15 years with protease inhibitors. We assumed that 55% of those receiving HIV care receive protease inhibitors.[83] We assumed that 39% of asymptomatic non-IDUs and IDUs not in methadone maintenance treatment receive HIV care (the proportion receiving care varies with stage of infection),[18] 95% of asymptomatic IDUs in methadone maintenance treatment receive HIV care, and 95% of all persons with AIDS receive HIV care.

e. These rates were set so that the proportion of IDUs in the population over time would be relatively stable.

that available methadone slots are always filled). Further details of the dynamic model are included in the appendix.

We used multipliers to reflect the quality of life associated with life years lived in different health states (compartments). For non-IDUs who are not HIV infected, this multiplier is 1.0. The other multipliers were calculated as follows. We assumed a quality multiplier of 0.8 for HIV infection without AIDS and 0.53 for HIV infection with AIDS. These multipliers, based on a self-assessment survey of HIV-infected patients,[21] fall between the values obtained in 2 other studies of HIV-infected individuals.[22,23] We assumed a quality multiplier of 0.80 for untreated injection drug use and 0.90 for time spent in methadone treatment. Little research has been done on the appropriate quality adjustments for substance abuse disorders; however, the quality adjustments we used are similar to those for other conditions that limit activities, including those for moderate angina (0.92), migraine (0.87), ulcer (0.84), and severe angina (0.82).[22] We assumed that the combined effect of HIV infection and injection drug use status on quality of life is multiplicative; for example, an IDU with AIDS was assigned a quality-of-life multiplier of 0.42, which is the product of the multiplier for AIDS (0.53) and the multiplier for untreated injection drug use (0.8).

The model incorporates HIV transmission that occurs due to risky sexual and needle-sharing contacts. The literature reports a range of values for the number of new sex partners per year for IDUs[24–31] and non-IDUs;[32–38] we chose values near the middle of the ranges. We assumed no reduction in sexual activity associated with methadone maintenance. We assumed that all IDUs, whether in methadone maintenance or not, would use condoms 20% of the time in the absence of incremental investment in HIV prevention.[19,26,28–30,39] Among IDUs, condom use rates of 24%,[19] 36%,[39] 10% to 35%,[28] at most 26.5%,[26] 13% to 47%,[29] and 21%[30] have been reported. We assumed that non-IDUs would use condoms 30% of the time, slightly more frequently than IDUs.[34,36,40,41] We assumed that when used, condoms would be 90% effective in preventing HIV transmission.[42,43]

The literature reports a wide range of values for the annual average number of injections per untreated IDU.[19,28,44–48] Rates as low as 287 to 543 injections per year have been reported,[47] as have rates in excess of 1000 injections per year.[19,28,45,46] One model-based analysis estimated that IDUs in New Haven, Connecticut, injected 767 times per year on average.[44] Wide ranges have been reported for the fraction of injections that are shared by untreated IDUs.[19,28,39,44,47,49–51] For example, sharing rates of 51%,[19] 48%,[52] 31.5%,[44] and at least 20%[28,39,50] have been reported. For both rates, we assumed values near the middle of the ranges. We assumed that IDUs in the high-prevalence community would have slightly more injections than those in the low-prevalence community.

We assumed that individuals in methadone maintenance would inject only 20% as often as untreated IDUs.[44,48,52,53] One study reviewed rates of heroin use (identified through positive urinalysis) after 6 months in treatment for individuals in 24 methadone programs.[53] Assuming that the 24 programs are approximately the same size, the reported data[53] indicate that individuals in methadone maintenance injected 16.3% as often as untreated IDUs. We assumed that individuals in methadone maintenance share needles only 30% as often as untreated IDUs (a 70% reduction in sharing);[49,51,52,54] thus, 0.2% × 30% = 6%. One report[52] interpreted a previous study[54] by stating that 9% of IDUs in methadone maintenance shared needles compared to 48% of those not in treatment, indicating that the sharing reduction associated with treatment was (48% − 9%)/48% = 39%/48% = 81%.

We assumed 65% annual continuance in methadone maintenance[20,55] and that 90% of individuals who quit methadone maintenance each year will return to regular injection drug use;[56–59] thus, 0.1% × 35% = 3.5% successfully "graduate" from methadone maintenance each year and 0.9% × 35% = 31.5% leave methadone maintenance each year and return to untreated injection drug use.

Production Functions

Changes in parameter values of the dynamic model as a result of the allocation decision are determined by the intervention production functions. We denote the production function for each intervention k by $w_k(\mathbf{v})$.

For the methadone maintenance treatment programs, the production function describes the number of additional treatment slots that become available as a function of expenditure on methadone maintenance treatment. We assumed a linear relationship between the amount invested in methadone maintenance and the number of additional slots. This may be reasonable because the budgets we consider would lead to small increases in capacity and, thus, would probably not increase fixed costs (methadone slots cost approximately $5250 per person treated per year,[60] so a budget of $1 million could purchase approximately 200 such slots, representing an increase in total methadone maintenance treatment capacity of about 5% in the high-prevalence community and 20% in the low-prevalence community). Moreover, because methadone maintenance treatment programs typically have waiting lists,[61,62] we assumed that per person recruitment costs would be constant for small increases in capacity. The production functions for the methadone maintenance programs are

$$w_i(\mathbf{v}) = v_i/5250 \qquad i = 2, 3, 4.$$

Thus, for example, an investment of $5250 in intervention 3 (methadone maintenance targeted to HIV-infected IDUs) will create 1 new methadone slot to be filled by an HIV-infected IDU. We assumed that new methadone slots are created and filled instantly and that the proportion of IDUs of each disease stage in the newly created methadone slots is equal to the proportion of IDUs of each disease stage in the population.

For the needle exchange program and the condom availability programs, we assumed exponential production functions. Exponential production functions exhibit diminishing returns to scale: The impact of each additional dollar invested decreases as the total amount invested increases. The exponential production function is a special case of the translog production function, which is commonly used by economists in the estimation of production functions.[63,64]

We assumed that the needle exchange program reduces the rate of needle sharing among targeted individuals (but does not reduce the frequency of injection), and we represented the effects of the needle exchange program by a multiplier on the baseline rate of needle sharing among IDUs (before investment in the needle exchange program). Thus, the production function $w_1(\mathbf{v})$ represents a multiplier on the rate of needle sharing among IDUs. For example, $w_1(\mathbf{v}) = 0.9$ means that an investment of **v** leads to a 10% decrease in the rate of needle sharing among IDUs. We estimated the following production function for the needle exchange program:

$$w_1(\mathbf{v}) = 0.67 + (0.33)e^{-(0.011)\frac{v_1}{N_1}}.$$

Details of the parameter estimation are in the appendix. The term N_1 is the number of IDUs. In the high-prevalence community, $N_1 = 25{,}000$; in the low-prevalence community, $N_1 = 7000$. Thus, for example, in the high-prevalence community an investment of \$250,000 in the needle exchange program (which corresponds to an investment of \$10.00 per IDU) would yield a multiplier of 0.96, indicating a 19.2% rate of needle sharing (20% base sharing rate × 0.96) among IDUs not in methadone maintenance, and a 5.8% rate of needle sharing among IDUs in methadone maintenance (6% base sharing rate × 0.96).

We assumed that the condom availability programs increase the rate of condom use among targeted individuals, and we represented the effects of such programs by multipliers on the baseline rate of condom use among targeted individuals (before investment in the condom availability programs). Thus, the production functions $w_5(\mathbf{v})$, $w_6(\mathbf{v})$, and $w_7(\mathbf{v})$ represent multipliers on average condom use by IDUs, IDUs in methadone maintenance, and non-IDUs, respectively. As an example, $w_6(\mathbf{v}) = 1.1$ means that an investment of **v** leads to a 10% increase in condom use among IDUs in methadone maintenance. We assumed that condom availability programs can be targeted to IDUs at no additional cost and that condom availability programs achieve equal levels of behavior change following equal levels of investment per person in each population. We estimated the following production functions for the condom availability programs:

$$w_5(\mathbf{v}) = 2.06 - (1.06)e^{-(0.027)\left(\frac{v_5}{N_5}+\frac{v_7}{N_7}\right)}$$

$$w_6(\mathbf{v}) = 2.06 - (1.06)e^{-(0.027)\left(\frac{v_5}{N_5}+\frac{v_6}{N_6}+\frac{v_7}{N_7}\right)}$$

$$w_7(\mathbf{v}) = 2.06 - (1.06)e^{-(0.027)\frac{v_7}{N_7}}.$$

Details of the parameter estimation are in the appendix. The term N_5 represents the number of IDUs not in methadone maintenance, N_6 is the number of IDUs in methadone maintenance, and N_7 is the number of non-IDUs. In the high-prevalence community, $N_5 = 25{,}000$, $N_6 = 3750$, and $N_7 = 975{,}000$; in the low-prevalence community, $N_5 = 7000$, $N_6 = 1050$, and $N_7 = 993{,}000$.

The above production functions reflect the behavior change that may occur among the targeted individuals due to investment in the condom availability programs and the hierarchical interdependence of those programs: We assumed that the untargeted condom availability program would reach IDUs and non-IDUs (in proportion to their relative numbers in the population), that the condom availability program targeted to IDUs would reach IDUs in and out of methadone maintenance (again, in proportion to their relative numbers in the population), and that the condom availability program targeted to IDUs in methadone maintenance would reach only those IDUs. Thus, the level of increased condom use among IDUs ($w_5(\mathbf{v})$) depends not only on investment in the condom availability program targeted to IDUs (intervention 5) but also on investment in the untargeted condom availability program (intervention 7). The level of increased condom use among individuals in methadone maintenance ($w_6(\mathbf{v})$) depends on investment in the condom availability program targeted to individuals in methadone maintenance (intervention 6) as well as investment in the condom availability program targeted to IDUs (intervention 5) and investment in the untargeted condom availability program (intervention 7). The level of increased condom use among non-IDUs ($w_7(\mathbf{v})$) depends only on the level of investment in the untargeted condom availability program (intervention 7). For example, in the high-prevalence community, investment of \$350,000 in intervention 5 (\$14.00 per IDU), \$150,000 in intervention 6 (\$40.00 per IDU in methadone maintenance), and \$500,000 in intervention 7 (\$0.50 per person in the population) corresponds to a total investment of \$14.50 per IDU not in methadone maintenance, \$54.50 per IDU in methadone maintenance, and \$0.50 per non-IDU and will lead to a 34% increase in condom use among IDUs not in methadone maintenance ($w_5(\mathbf{v}) = 1.34$), an 82% increase in condom use among IDUs in methadone maintenance ($w_6(\mathbf{v}) = 1.82$), and a 1% increase in condom use among non-IDUs ($w_7(\mathbf{v}) = 1.01$).

The production functions for the needle exchange and condom availability programs exhibit diminishing returns to scale. For example, spending \$14.00 on condom availability programs per IDU not in methadone maintenance leads to a 33% increase in condom use among such IDUs ($w_5(\mathbf{v}) = 1.33$), whereas investment of \$28.00 per IDU not in methadone maintenance leads to a 56% increase in condom use ($w_5(\mathbf{v}) = 1.56$).

In sensitivity analysis, we considered the following linearized approximations of the above production functions:

$$w_1(\mathbf{v}) = 1.00 - (0.0026)\frac{v_1}{N_1}$$

$$w_5(\mathbf{v}) = 1.00 + (0.025)\left(\frac{v_5}{N_5} + \frac{v_7}{N_7}\right)$$

$$w_6(\mathbf{v}) = 1.00 + (0.025)\left(\frac{v_5}{N_5} + \frac{v_6}{N_6} + \frac{v_7}{N_7}\right)$$

$$w_7(\mathbf{v}) = 1.00 + (.025)\frac{v_7}{N_7}.$$

Details of the parameter calculations are in the appendix.

Solving the Resource Allocation Model

A closed-form solution for the epidemic model that we use is not known. Therefore, we approximated the compartment size functions to derive expressions for $QG(\mathbf{v})$ and $IA(\mathbf{v})$ and applied optimization theory to the approximated model to determine the optimal portfolio of HIV interventions for the approximated model. Details of the procedure are provided in Zaric and Brandeau.[12] For the case of a relatively short time horizon (on the order of several years), the portfolios obtained using these approximation techniques have been shown to be very close to the actual optimal portfolios.[12]

RESULTS

We solved the resource allocation model with the objective of maximizing QALYs gained and also with the objective of maximizing HIV infections averted. We assumed a budget of \$1 million per year, used a 2-year time horizon, and assumed that the same allocation of funds would be made in each year. We set V_k = \$1 million for the needle exchange program and the condom availability programs (interventions 1, 5, 6, and 7) and $V_k = 5250 \times N_k$ for the methadone maintenance treatment programs (interventions 2, 3, and 4), where N_2 is the total number of IDUs, N_3 is the number of HIV-infected IDUs, and N_4 is the number of IDUs with AIDS. Results are shown in Table 2.

In the high-prevalence community, the optimal allocations of resources differ slightly for the 2 objectives but yield similar numbers of QALYs gained (73.5 for the QALYs-gained objective and 72.7 for the infections-averted objective) and infections averted (637.3 for the QALYs-gained objective and 643.5 for the infections-averted objective). In the absence of any interventions, approximately 6100 new HIV infections would occur in the high-prevalence community over the 2-year time horizon (0.31% annual incidence), whereas with the optimal allocations of resources, approximately 5460 new infections would occur (0.27% annual incidence). Both solutions involve allocating approximately two-thirds of the budget to the needle exchange program and one-third of the budget to the condom availability program targeted to IDUs.

In the low-prevalence community, the allocations for the 2 objectives are almost the same but the funds are allocated to different programs: Approximately 95% of the budget is allocated to the methadone maintenance program targeted to HIV-infected IDUs, and the remainder of the budget is allocated to the untargeted condom availability program. The allocation for the QALYs-gained objective leads to 45.0 QALYs gained and 81.8 infections averted, whereas the allocation for the infections-averted objective leads to 44.0 QALYs gained and 86.7 infections averted. In the absence of any interventions, approximately 370 new HIV infections would occur in the low-prevalence community over the 2-year time horizon (0.019% annual incidence), whereas with the optimal allocations of resources, approximately 285 new infections would occur (0.015% annual incidence).

The optimal allocations in the high-prevalence community provide significantly diminished benefits in the low-prevalence community compared to the optimal allocations in the low-prevalence community, and vice versa. For example, the allocation that maximizes QALYs gained in the high-prevalence community yields 7.9 QALYs gained and 69.5 HIV infections averted in the low-prevalence community, whereas the corresponding optimal allocation for the low-prevalence community yields 45.0 QALYs gained and 81.8 infections averted in that community. The optimal allocations for the high-prevalence community involve investment in different programs than the optimal allocations for the low-prevalence community. The allocations differ because the 2 communities have different HIV prevalences (among IDUs and in the overall

Table 2 Budget Allocations and Health Outcomes under Different Allocation Methods

	High-Prevalence Community			Low-Prevalence Community		
Allocation Rule	**Allocation ($1000s)**	**QALYs Gained**	**Infections Averted**	**Allocation ($1000s)**	**QALYs Gained**	**Infections Averted**
Maximize QALYs gained	$v_1 = 617.8$	73.5	637.3	$v_3 = 996.5$	45.0	81.8
	$v_5 = 382.2$			$v_6 = 3.5$		
Maximize HIV infections averted	$v_1 = 737.8$	72.7	643.5	$v_3 = 947.4$	44.0	86.7
	$v_5 = 262.2$			$v_6 = 52.6$		
Proportional to incidence, with program equity	$v_1 = 302.0$	63.9	436.0	$v_1 = 311.0$	19.7	53.1
	$v_2 = 302.0$			$v_2 = 311.0$		
	$v_5 = 302.0$			$v_5 = 311.0$		
	$v_6 = 66.0$			$v_6 = 56.0$		
	$v_7 = 28.0$			$v_7 = 11.0$		
Proportional to incidence, with $/person equity	$v_1 = 278.5$	62.2	411.4	$v_1 = 322.0$	18.8	54.9
	$v_2 = 237.0$			$v_2 = 273.0$		
	$v_3 = 95.0$			$v_3 = 14.0$		
	$v_4 = 17.0$			$v_4 = 2.0$		
	$v_5 = 278.5$			$v_5 = 322.0$		
	$v_6 = 66.0$			$v_6 = 56.0$		
	$v_7 = 28.0$			$v_7 = 11.0$		
Program equity	$v_1 = v_2 = v_7 = 333.3$	44.7	283.6	$v_1 = v_2 = v_7 = 333.3$	20.9	54.9
Group equity, program equity	$v_1 = 166.7$	40.1	278.1	$v_1 = 166.7$	11.5	36.2
	$v_2 = 166.7$			$v_2 = 166.7$		
	$v_5 = 166.7$			$v_5 = 166.7$		
	$v_7 = 500.0$			$v_7 = 500.0$		
Group equity, $/person equity	$v_1 = 147.0$	38.5	260.7	$v_1 = 164.0$	10.6	36.7
	$v_2 = 125.0$			$v_2 = 139.0$		
	$v_3 = 50.0$			$v_3 = 7.0$		
	$v_4 = 9.0$			$v_4 = 1.0$		
	$v_5 = 147.0$			$v_5 = 164.0$		
	$v_6 = 22.0$			$v_6 = 25.0$		
	$v_7 = 500.0$			$v_7 = 500.0$		
$/person equity	$v_1 = 23.0$	14.4	103.9	$v_1 = 6.8$	1.2	7.0
	$v_2 = 19.6$			$v_2 = 5.8$		
	$v_3 = 7.8$			$v_3 = 0.3$		
	$v_4 = 1.4$			$v_4 = 0.1$		
	$v_5 = 23.0$			$v_5 = 6.9$		
	$v_6 = 3.5$			$v_6 = 1.0$		
	$v_7 = 921.7$			$v_7 = 979.1$		

Note: QALY = quality-adjusted life years. v_1 = investment in needle exchange; v_2 = investment in the untargeted methadone maintenance program; v_3 = investment in the methadone maintenance program targeted to HIV-infected injection drug users (IDUs); v_4 = investment in the methadone maintenance program targeted to IDUs with AIDS; v_5 = investment in the condom availability program targeted to IDUs; v_6 = investment in the condom availability program targeted to individuals in methadone maintenance; v_7 = investment in the untargeted condom availability program.

population), different numbers of IDUs, and different levels of risky behavior.

We used the model to examine the impact of targeting on health benefits. As an example, in the low-prevalence community if the money spent on the methadone maintenance program targeted to HIV-infected IDUs were instead spent on the untargeted methadone maintenance program, similar numbers of QALYs would be gained, but only 10% as many HIV infections would be averted (8.2 infections averted vs. 81.8 for the allocation that maximizes QALYs gained, and 9.6 infections averted vs. 86.7 for the allocation that maximizes infections averted). Investment in the methadone maintenance program targeted to HIV-infected IDUs generates significant additional gains in infections averted compared to the untargeted methadone maintenance program. As another example, in the high-prevalence community if the funds invested in the condom availability program targeted to IDUs were instead spent on the condom availability program targeted to individuals in methadone maintenance, both QALYs gained and infections averted would be diminished by about one-third.

We considered the effects of alternate methods for allocating the $1 million budget. One natural allocation method, in the absence of a dynamic model and information about prevention program production functions, is to allocate HIV prevention resources among population groups based on HIV incidence in those groups. For the high-prevalence community, this corresponds to spending $906,000 on HIV prevention for IDUs not in methadone maintenance ($42.60/IDU not in methadone maintenance), $66,000 on IDUs in methadone maintenance ($17.60/IDU in methadone maintenance), and $28,000 on the general population ($0.03/person); for the low-prevalence community, $933,000 would be spent on IDUs not in methadone maintenance ($156.80/IDU not in methadone maintenance), $56,000 on IDUs in methadone maintenance ($53.33/IDU in methadone maintenance), and $11,000 on the general population ($0.01/person).

The money allocated to IDUs not in methadone maintenance could be spent on the needle exchange program (intervention 1), incremental untargeted methadone slots (intervention 2), and the condom availability program targeted to IDUs not in methadone maintenance (intervention 5). If the prevention funds are divided equally among these 3 interventions (3rd row of Table 2), then 63.9 QALYs are gained and 436.0 HIV infections are averted in the high-prevalence community and 19.7 QALYs are gained and 53.1 HIV infections are averted in the low-prevalence community. If the funds for HIV prevention among IDUs not in methadone maintenance are allocated to equalize the amount per person spent on each of the 3 types of programs (needle exchange, methadone maintenance, and condom availability), the results (4th row of Table 2) are similar: 62.2 QALYs are gained and 411.4 HIV infections are averted in the high-prevalence community, and 18.8 QALYs are gained and 54.9 HIV infections are averted in the low-prevalence community. The health benefits realized by these allocations are 50% to 75% as much as those realized by the allocations from our resource allocation model.

Some CPGs have been reported to recommend allocating prevention funds equally among types of prevention programs. This "program equity" allocation (5th row of Table 2)—which we assumed is equivalent to spending $333,333 each on the needle exchange program, on untargeted methadone maintenance (i.e., available to all untreated IDUs), and on the untargeted condom availability program—results in 44.7 QALYs gained and 283.6 HIV infections averted in the high-prevalence community and 20.9 QALYs gained and 54.9 HIV infections averted in the low-prevalence community. In contrast to the allocations determined using the resource allocation model, which allocate no money (or only a very small fraction of the available funds) to HIV prevention for the general population, the program equity rule allocates one-third of the prevention budget to the untargeted condom availability program. The resulting benefits are significantly lower than the benefits realized by the allocations from the resource allocation model.

Another type of equity, which we refer to as "group equity," involves allocating equal amounts of prevention funds to IDUs and to the general population ($500,000 to each group). If the $500,000 for IDUs is then divided equally among the 3 types of prevention programs for IDUs (needle exchange, untargeted methadone maintenance, and condom availability program targeted to IDUs) (6th row of Table 2), then 40.1 QALYs are gained and 278.1 HIV infections are averted in the high-prevalence community and 11.5 QALYs are gained and 36.2 HIV infections are averted in the low-prevalence community. If the same $500,000 is instead allocated to equalize the amount per person spent on each of the 3 types of programs (needle exchange, methadone maintenance, and condom availability), the results (7th row of Table 2) are similar: 38.5 QALYs are gained and 260.7 HIV infections are averted in the high-prevalence community, and 10.6 QALYs are gained and 36.7 HIV infections are averted in the low-prevalence community.

Another allocation method is to equalize across the 7 interventions the amount invested per person. This "$/person equity" allocation (8th row of Table 2) results in 14.4 QALYs gained and 103.9 HIV infections averted in the high-prevalence community and 1.2 QALYs gained and 7.0 HIV infections averted in the low-prevalence community. Using this rule, almost all of the prevention budget is spent on the general population (on the untargeted condom availability program), and the resulting benefits are only a small fraction of the greatest possible level of benefit (those obtained via the allocations from the resource allocation model).

Because of uncertainty with regard to parameters in the model, we performed extensive 1-way sensitivity analyses to determine the effect of changes in parameters on the optimal allocation of resources. We varied all model parameters using wide ranges of values that

Table 3 Summary of Sensitivity Analyses: Optimal Resource Allocations for the High-Prevalence Community with the QALYs-Gained Objective Function

Parameter	Base Case	Low Value	High Value	At Low Value		At High Value	
				Optimal Allocation ($1000s)	QALYs Gained	Optimal Allocation ($1000s)	QALYs Gained
Needle exchange program production functions							
Cost per person[a]	$65.22	$32.61	$100.00	$v_1 = 776.7$ $v_5 = 223.3$	106.3	$v_1 = 413.1$ $v_5 = 586.9$	61.4
Maximum possible reduction in needle sharing[b]	33%	10%	50%	$v_2 = 366.6$ $v_5 = 633.4$	58.9	$v_1 = 831.4$ $v_5 = 168.6$	97.6
Methadone maintenance program characteristics							
Cost per methadone treatment slot	$5250	$3500	$8000	$v_1 = 390.8$ $v_2 = 338.9$ $v_5 = 270.4$	74.8	Base case	Base case
Reduction in annual number of injections	30%	10%	75%	$v_1 = 616.7$ $v_5 = 383.3$	73.3	$v_1 = 620.3$ $v_5 = 397.7$	73.8
Rate at which HIV-infected IDUs enter methadone maintenance relative to their proportion in the population[c]	1.0	0.5	1.5	Base case	Base case	Base case	Base case
Condom availability program production functions							
Cost per person[d]	$11.20	$2.00	$16.00	$v_1 = 648.4$ $v_5 = 351.6$	119.7	$v_1 = 787.7$ $v_5 = 212.3$	67.3
Multiplier for maximum possible increase in condom use[e]	2.06	1.40	2.50	$v_1 = 788.7$ $v_5 = 211.3$	73.5	$v_1 = 552.3$ $v_5 = 447.7$	74.0
Risk parameters							
Annual number of injections among IDUs not in methadone maintenance[f]	225	150	300	$v_1 = 378.3$ $v_5 = 621.7$	59.0	$v_1 = 788.0$ $v_5 = 212.0$	92.7
Baseline condom use among IDUs	20%	10%	30%	$v_1 = 1000$	66.5	$v_1 = 370.8$ $v_5 = 629.2$	90.4
Baseline condom use among non-IDUs	30%	20%	50%	$v_1 = 616.8$ $v_5 = 383.2$	73.6	$v_1 = 619.6$ $v_5 = 380.4$	73.3
Condom efficacy	90%	70%	99%	$v_1 = 773.0$ $v_5 = 227.0$	68.6	$v_1 = 558.0$ $v_5 = 442.0$	76.3
Needle-sharing rate among IDUs not in methadone maintenance[f]	20%	5%	30%	$v_2 = 367.8$ $v_5 = 632.2$	54.3	$v_1 = 857.6$ $v_5 = 142.4$	103.7
Annual number of new sexual partners among IDUs	3.5	2.0	5.0	$v_1 = 929.5$ $v_5 = 70.5$	62.4	$v_1 = 425.5$ $v_5 = 574.5$	90.8
Quality-of-life multipliers							
Quality-of-life reduction associated with injection drug use	20%	0%	30%	$v_1 = 770.3$ $v_5 = 229.7$	84.2	$v_1 = 553.8$ $v_5 = 446.2$	68.3
Quality-of-life increase associated with entering methadone maintenance	12.5%	0%	15%	Base case	Base case	$v_1 = 617.9$ $v_5 = 382.1$	73.5

Note: QALY = quality-adjusted life years. v_1 = investment in needle exchange; v_2 = investment in the untargeted methadone maintenance program; v_3 = investment in the methadone maintenance program targeted to HIV-infected injection drug users (IDUs); v_4 = investment in the methadone maintenance program targeted to IDUs with AIDS; v_5 = investment in the condom availability program targeted to IDUs; v_6 = investment in the condom availability program targeted to individuals in methadone maintenance; v_7 = investment in the untargeted condom availability program.

a. Cost per person is used to calculate the parameter γ in $w_1(v)$ (see the appendix). At $32.61, $\gamma = 0.0226$; at $100.00, $\gamma = 0.0085$.

b. Maximum possible sharing reduction is used to calculate the parameters α and β in $w_1(v)$ (see the appendix). If the maximum sharing reduction is 10%, $\alpha = 0.9$ and $\beta = 0.1$. If the maximum sharing reduction is 50%, $\alpha = 0.5$ and $\beta = 0.5$.

c. In the base case, we assumed that the ratio of infected to uninfected IDUs entering treatment was equal to the ratio of the number of individuals in each of the 2 groups. In sensitivity analysis, we increased and decreased the entry rate among infected IDUs by 50%.

d. Changing the cost per person for condom availability programs changes the parameter κ in $w_5(v)$, $w_6(v)$, and $w_7(v)$ (see the appendix for details). At $2.00/person, $\kappa = 0.1533$; at $16.00/person, $\kappa = 0.0192$.

e. Changing the maximum possible increase in condom use changes all parameters in $w_5(v)$, $w_6(v)$, and $w_7(v)$ (see the appendix for details). If the multiplier is 1.4, then $\eta = 1.4$, $\mu = -0.4$, and $\kappa = 0.1075$. If the multiplier is 2.5, then $\eta = 2.5$, $\mu = -1.5$, and $\kappa = 0.1845$.

f. By varying the number of injections or rate of needle sharing among IDUs not in methadone maintenance, we implicitly vary the number of injections or rate of needle sharing, respectively, among IDUs in methadone maintenance because our model assumes a constant proportional risk reduction associated with entering methadone maintenance.

Table 4 Optimal Budget Allocations and Health Outcomes When Production Functions Are Linearized

	High-Prevalence Community			Low-Prevalence Community		
Allocation Rule	Allocation ($1000s)	QALYs Gained	Infections Averted	Allocation ($1000s)	QALYs Gained	Infections Averted
Maximize QALYs gained	$v_5 = 1000.0$	55.9	427.1	$v_3 = 1000.0$	45.0	81.1
Maximize HIV infections averted	$v_1 = 444.2$ $v_5 = 555.8$	72.0	607.7	$v_3 = 832.0$ $v_6 = 168.0$	38.9	78.3

Note: QALY = quality-adjusted life years. v_1 = investment in needle exchange; v_2 = investment in the untargeted methadone maintenance program; v_3 = investment in the methadone maintenance program targeted to HIV-infected injection drug users (IDUs); v_4 = investment in the methadone maintenance program targeted to IDUs with AIDS; v_5 = investment in the condom availability program targeted to IDUs; v_6 = investment in the condom availability program targeted to individuals in methadone maintenance; v_7 = investment in the untargeted condom availability program.

have been reported in the literature. Table 3 shows key results of those sensitivity analyses for the high-prevalence community with the QALYs-gained objective function. In almost all of the cases, the optimal portfolio includes just the needle exchange program (intervention 1) and the condom availability program targeted to IDUs (intervention 5), as in the base case, although the relative amount invested in each program varies. For example, if condom availability programs are less expensive than we assumed, then a greater fraction of the budget is invested in the condom availability program targeted to IDUs; and if such programs are more expensive than we assumed, then a smaller fraction of the budget is invested in the condom availability program targeted to IDUs. Similarly, if the needle exchange program is less (more) expensive than we assumed, then more (less) is invested in it.

No money is invested in the condom availability program if condom use among IDUs is significantly lower than we assumed: The condom availability programs are assumed to increase condom use by a fixed percentage for a given investment, so when the baseline condom use rate is low, the magnitude of the increase in condom use is small. Methadone maintenance (in particular, the untargeted methadone maintenance program) becomes part of the optimal portfolio only if the needle exchange program is significantly less effective in reducing needle sharing than we assumed in the base case, if methadone maintenance is significantly less expensive than we assumed in the base case, or if the rate of needle sharing among IDUs not in methadone maintenance is significantly lower than we assumed in the base case.

For the needle exchange program and the condom availability programs, we estimated production functions with decreasing returns to scale: Incremental investments in these programs yield incrementally smaller reductions in risky behavior. In sensitivity analysis, we applied our resource allocation model using linear approximations of the production functions for the needle exchange and condom availability programs (and then used the original production functions to determine the number of QALYs gained and infections averted for each of the resulting allocations). Results are shown in Table 4.

In the high-prevalence community, all of the funds are allocated to the condom availability program targeted to IDUs when the QALYs-gained objective is used, whereas $444,200 is allocated to the needle exchange program and $555,800 is allocated to the condom availability program targeted to IDUs when the infections-averted objective is used. The latter allocation leads to more QALYs gained than does the allocation for the QALYs-gained objective; this occurs because approximated production functions were used to determine the allocations. In the low-prevalence community, all of the funds are allocated to the methadone maintenance program targeted to HIV-infected IDUs when the QALYs-gained objective is used, whereas $832,000 is allocated to the methadone maintenance program targeted to HIV-infected IDUs and $168,000 is allocated to the condom availability program targeted to IDUs in methadone maintenance when the infections-averted objective is used. The former allocation leads to 45.0 QALYs gained and 81.1 infections averted; the latter allocation leads to 38.9 QALYs gained and 78.3 infections averted.

Our base-case analyses assumed a 2-year time horizon. In sensitivity analysis, we also considered a 3-year time horizon. The resulting allocations are similar to those found using a 2-year time horizon. For the infections-averted objective, approximately two-thirds of the funds are allocated to the needle exchange program and one-third of the funds are allocated to the condom availability program targeted to IDUs. For the QALYs-gained objective, approximately three-fourths of the funds are allocated to the needle exchange program and one-fourth of the funds are allocated to the condom availability program targeted to IDUs. Simulation of the epidemic model over a 5-year time horizon showed that for all allocations, the annual number of infections averted increases over time.

DISCUSSION

Other researchers have analyzed the cost and effectiveness of needle exchange programs,[65,66] condom availability programs,[67,68] and methadone maintenance treatment.[17,18] Our work goes a step further by determining the optimal allocation of resources among such programs while considering nonlinear production functions for the interventions (i.e., a nonlinear relationship between the amount of money invested in an intervention and the corresponding level of behavior change), interactions between interventions (in which changes in risky behavior and the chance of HIV transmission are the result of the cumulative impact of different interventions), and nonlinear epidemic growth (via a dynamic epidemic model).

The analysis highlights the usefulness of targeting HIV prevention funds. However, in our analyses, the allocations of funds that maximized QALYs gained or infections averted did not always involve spending all funds on a single program; rather, the optimal investment portfolio comprised a mix of programs and depended on HIV prevalence in the community, risk behaviors, relative numbers of individuals in different risk groups, and the relative cost and effectiveness of each intervention. The pattern of investment in HIV prevention that maximizes health benefits could not be determined by inspection: A model-based analysis was needed.

Consideration of cost, equity, and social and political norms may be important when allocating HIV prevention funds. For example, several CPGs have reported equity as an important factor in their resource allocation decisions.[2] Our model can be used to quantify the cost (in terms of health outcomes) of different allocations of funds. In the resource allocation problem we solved, allocations based on HIV incidence yielded health benefits that were only 50% to 75% as much as the benefits from the allocations based on our model, and allocations based on equity yielded even lower health benefits. Such analysis can be used to help decision makers understand the trade-offs that exist between desirable outcomes.

Our model allows decision makers to perform detailed sensitivity analysis on the parameters of the various prevention programs. Such information could be valuable in determining how close a program is to being included in the optimal portfolio. Although some programs may appear cost-effective when analyzed in isolation, they are less attractive when compared with other possible uses of funds.

Our analysis has several limitations. We estimated production functions with exponential and linear forms. Little is known about the shape of the production functions for most HIV prevention programs. We assumed that no additional costs would be associated with targeting; for example, we assumed that the cost per person of an untargeted methadone maintenance program would be the same as the cost per person of a methadone maintenance program targeted to HIV-infected IDUs. Targeted programs may be more expensive than we assumed if recruitment of targeted individuals incurs additional costs, or may be less expensive than we assumed if targeted individuals have already been identified and referred to such programs. More data on intervention production functions are needed to properly determine optimal expenditures.

Our analysis considered a needle exchange program, condom availability programs, and methadone maintenance treatment. We selected these programs because they target different pathways of infection (needle sharing and sexual transmission) and can be targeted to different population risk groups (e.g., IDUs and non-IDUs) and because we were able to find relevant cost and effectiveness data needed for estimating the programs' production functions. A more comprehensive analysis could include other types of HIV prevention programs. For example, highly active antiretroviral therapy may decrease viral load and thus reduce infectivity. Postexposure prophylaxis may reduce the chance of seroconversion after risky encounters. Vaccines are currently under development that may reduce individuals' susceptibility to HIV. Little is known about the cost and effectiveness of such interventions. However, our model is very general. As more information on the cost and effectiveness of new HIV interventions becomes available, it can easily be incorporated into the model. Similarly, our analysis is easily extended to a model with different population groups and disease stages, as well as to any epidemic that is modeled by a system of differential equations.

The approximation methods used to solve our resource allocation model are accurate only for relatively short time horizons (on the order of several years). We used a 2-year time horizon for determining optimal allocations and considered a 3-year time horizon in sensitivity analysis. We suggest that decision makers consider several time horizons to determine the extent to which the optimal portfolio changes as a function of the time horizon. Note that our resource allocation model is not designed to support cost-effectiveness analyses. To obtain a good estimate of the cost-effectiveness of a particular portfolio of interventions, one could simulate our dynamic model—using the estimated parameter values that result from the set of interventions—over a relatively long time horizon (on the order of 10 years or more[17]). In estimating the cost-effectiveness ratio, a sufficiently long time horizon is needed to fully capture the dynamic epidemic effects that result from the initial investment in prevention.

One of the most difficult steps faced by CPGs in their planning process is estimating the impact of different allocations.[2] The epidemic and optimization model that we described can be used as part of an interactive decision support system to assist members of CPGs in assessing various allocation plans. A similar Web-based decision support system has been described elsewhere.[69]

Our model can be used to determine the allocation of HIV prevention resources that maximizes QALYs (or life years) gained or HIV infections averted. However, maximizing health benefits may not be the only goal of the decision makers: cost, equity, and social and political norms may also be important. Our model can help decision makers determine the health consequences of different allocations of HIV prevention funds.

Financial support for this study was provided entirely by a grant from the National Institute on Drug Abuse. The funding agreement ensured the authors' independence in designing the study, interpreting the data, and writing and publishing the report. This work was also supported by the Societal Institute of the Mathematical Sciences through a grant from the National Institute on Drug Abuse, National Institutes of Health (DA R-01-09531).

APPENDIX

Details of Dynamic Model

Transitions between Compartments

The population is divided into 9 mutually exclusive, collectively exhaustive compartments (see Figure 1). The model incorporates 3 HIV disease stages—uninfected, HIV-infected but asymptomatic, and AIDS—and 3 risk groups—untreated injection drug users (IDUs), IDUs in methadone maintenance, and non-IDUs. Allowable transitions between compartments and into and out of the population are indicated by arrows in Figure 1. All new entrants into the population are assumed to be uninfected non-IDUs; this is represented by the arrow labeled "maturation into the population" in Figure 1. For individuals in all compartments, deaths from non-AIDS causes and maturation out of the population may occur; such transitions are denoted by the diagonal arrows in Figure 1.

When an uninfected individual becomes infected (see below for details of infection transmission), he or she moves to the "HIV-infected but asymptomatic" compartment within the same risk group; these transitions are labeled "infection transmission" in Figure 1. When an HIV-infected, asymptomatic individual develops AIDS, he or she moves to the "AIDS" compartment within the same risk group; these transitions are labeled "disease progression" in Figure 1. Individuals with AIDS may die from AIDS; these transitions are labeled "death from AIDS" in Figure 1.

Individuals may move between risk groups, as follows (in all cases, they remain within the same disease stage, as indicated by the vertical arrows in Figure 1). Non-IDUs may become IDUs; we selected rates for these transitions that would yield a relatively stable proportion of individuals in the population being IDUs. IDUs not in methadone maintenance may enter methadone maintenance; the rates for these transitions were selected so that available methadone maintenance slots are always filled. IDUs not in methadone maintenance may cease injection drug use and become non-IDUs; we assumed this rate was 1.02% annually.[55] IDUs in methadone maintenance may successfully "graduate" from methadone maintenance and become non-IDUs (at a rate of 3.5% per year) or return to untreated injection drug use (at a rate of 31.5% per year); further details with regard to these rates are contained in the Methods section.

HIV Transmission

The model incorporates needle-sharing and sexual transmission of HIV. Mixing is assumed to be random within, but not across, compartments. Needle-sharing transmission to an uninfected IDU can occur from any infected IDU (with or without AIDS, in methadone maintenance treatment or not). When an uninfected IDU shares an injection with an infected IDU, the chance of transmission is assumed to be 0.5%.[44] Sexual transmission to any uninfected individual can occur from any infected individual. We modeled sexual transmission using rates of new partnerships and an average value for the chance of transmission per partnership; we did not model specific sex acts with their associated transmission probabilities. We assumed that in the low-prevalence community, 25% of sexual contacts of IDUs are with other IDUs, and that in the high-prevalence community, 50% of sexual contacts of IDUs are with other IDUs.[24,25,67,70–72] The rate of sexual contacts of non-IDUs with IDUs was determined from the mixing patterns of IDUs (because the number of contacts that IDUs have with non-IDUs must equal the number of contacts that non-IDUs have with IDUs); the rate of non-IDU sexual contacts with non-IDUs was then calculated from the remainder of the total non-IDU sexual contacts.

We assumed that the chance of transmission per unprotected sexual partnership with an infected individual is 5% if the infected individual does not have AIDS and 11% if the infected individual does have AIDS.[73–78] The chance of sexual infection transmission is further modified by the chance that a condom is used multiplied by condom efficacy in preventing transmission (see the discussion in the Methods section). We did not model potential effects of antiretroviral treatments on transmission probabilities.

Effects of Interventions

The needle exchange program is assumed to reduce the rate of needle sharing among IDUs and, thus, the rate of new infection among uninfected IDUs; thus, investment in needle exchange reduces the flow of IDUs along the upper 2 arrows labeled "HIV transmission" in Figure 1. The condom availability programs are assumed to reduce the rate of risky sexual contacts (via condom use) among targeted individuals (IDUs, IDUs in methadone maintenance, or the entire population); thus, investment in any of the condom availability programs reduces the rate of flow along all 3 "HIV transmission" arrows in Figure 1. Investment in incremental methadone maintenance slots increases the number of individuals in the appropriate methadone maintenance compartments (depending on whether the program is targeted to all IDUs, only to those who are HIV infected, or only to those with AIDS) and decreases the number of individuals in the corresponding compartment(s) of untreated IDUs (those within the same disease stage). We assume that new methadone slots are filled immediately at the beginning of the time horizon and that all methadone slots are always filled. A larger proportion of individuals in methadone maintenance leads to reduced rates of new infection among IDUs (the upper 2 "HIV transmission" arrows in Figure 1) because IDUs in methadone maintenance have fewer risky injections than IDUs not in methadone maintenance. Note that the reduced rates of new infection among IDUs that occur immediately due to investment in needle exchange or methadone maintenance lead to future reductions in rates of new infection among non-IDUs: As fewer IDUs become HIV infected, the rate of sexual HIV transmission from IDUs to non-IDUs decreases.

Estimation of Production Functions

Needle Exchange Programs

We estimated the cost and effectiveness of a sample program based on the New Haven needle exchange program. Kaplan and O'Keefe[65] estimated that the New Haven needle exchange program could reduce incidence by 33%. We assumed that needle exchange programs do not reduce the frequency of injection but do reduce the probability that an injection will be with a shared needle. This implies a 33% reduction in the rate of risky needle sharing among those who participate in the needle exchange program. We assumed a participation rate of 1200/2300 = 52%,[65] yielding an average needle-sharing reduction of 17.2% (= 0.52 × 0.33). The total annual cost of the New Haven needle exchange program was estimated to be \$150,000,[66] which corresponds to \$65.22 per IDU (\$150,000/2300).

We fit an exponential production function with the following form:

$$w_1(\mathbf{v}) = \alpha + \beta e^{-\gamma \frac{v_1}{N_1}},$$

where N_1 is the total number of IDUs and α, β, and γ are parameters of the production function. For the high-prevalence community, $N_1 = 25{,}000$; for the low-prevalence community, $N_1 = 7000$. We assumed that a very high intensity needle exchange program could draw the participation of all IDUs in New Haven, corresponding to an average multiplier of $w_1(\mathbf{v}) = 0.67$ (i.e., all IDUs experience the 33% reduction). Thus,

$$\lim_{v_1 \to \infty} w_1(\mathbf{v}) = \lim_{v_1 \to \infty} \alpha + \beta e^{-\gamma \frac{v_1}{N_1}} = \alpha + 0 = 0.67,$$

so $\alpha = 0.67$. When no money is invested, $w_1(0, v_2, \ldots, v_7) = 1 = \alpha + \beta$; thus, $\beta = 0.33$. Based on our cost and effectiveness estimates for the New Haven program (which served a population of 2300 IDUs),

$$w_1(150000, v_2, \mathrm{K}, v_7) = 0.828 = 0.67 + 0.33 e^{-\gamma \frac{150000}{2300}},$$

so $\gamma = -(2300/150{,}000) \times \ln((0.828 - 0.67)/0.33) = 0.011$.

We considered the following linear approximation of $w_1(\mathbf{v})$ in sensitivity analysis:

$$w_1(\mathbf{v}) = \alpha' + \beta' \frac{v_1}{N_1}.$$

When no money is invested, $w_1(0, v_2, \ldots, v_7) = 1 = \alpha' + 0$; thus, $\alpha' = 1.00$. Based on our cost and effectiveness estimates for the New Haven program,

$$w_1(150000, v_2, \mathrm{K}, v_7) = 0.828 = 1.00 + \beta' \frac{150000}{2300},$$

so $\beta' = -0.0026$. We assumed that the maximum possible reduction in sharing is 33% and set the upper limits on investment accordingly; thus, V_1 = \$3.2 million in the high-prevalence community and V_1 = \$880,000 in the low-prevalence community.

Condom Availability Programs

The terms $w_5(\mathbf{v})$, $w_6(\mathbf{v})$, and $w_7(\mathbf{v})$ are multipliers for average condom use by IDUs, IDUs in methadone maintenance, and non-IDUs, respectively. Data on the effectiveness of condom availability programs are limited. Many studies are based on high school students and patients at sexually transmitted disease clinics and, thus, may not be generalizable to the general population or to groups of IDUs. However, we based our estimates of program effectiveness on these studies in the absence of better data.

We estimated the condom-use multipliers based on a study of a condom availability program in a Los Angeles high school.[68] Among men who engaged in vaginal sexual intercourse in the past year (50.6% at baseline, 51.8% at follow-up), condom use increased from 37% to 50%. Among women who engaged in vaginal sex in the past year (42.0% at baseline, 44.0% at follow-up), condom use increased from 27% to 32%. Assuming equal numbers of men and women, the average baseline rate was 32% and the average follow-up rate was 41%, indicating a 28% increase in condom use.

To implement the condom availability program, baskets with packets containing 2 condoms and an information card were made available around the school. A donation container to accept $0.25 per packet taken was located near each basket. The program's implementation was publicized around the school. During the 1st year, approximately 1800 to 2000 packets were distributed per month and almost no money was collected. We assumed that 20,000 condom packets were distributed per year at a cost of $1.20 each ($0.50 per condom and $0.20 for the information cards), for a total materials cost of $24,000. We assumed that restocking the baskets and publicizing the program takes 5 hours per week, performed by a school nurse earning $20/hour, for a labor cost of 5 × 40 weeks/school year × $20/hour = $4000. Thus, we estimated the total annual cost of the condom availability program to be $28,000. The school has 2500 students, yielding a cost per person of $28,000/2500 = $11.20.

For the rate of condom use among non-IDUs, we assumed a production function of the form

$$w_7(\mathbf{v}) = \eta + \mu e^{-\kappa \frac{v_7}{N_7}},$$

where N_7 is the total number of non-IDUs and η, μ, and κ are parameters of the production function. We assumed a maximum average condom use rate at follow-up of 66%, which corresponds to a multiplier of 2.06 = 66%/32%. Thus,

$$\lim_{v_7 \to \infty} w_7(\mathbf{v}) = \lim_{v_7 \to \infty} \eta + \mu e^{-\kappa \frac{v_7}{N_7}} = \eta + 0 = 2.06,$$

so $\eta = 2.06$. When no money is invested in intervention 7 (the untargeted condom availability program), $w_7(v_1, \ldots, v_6, 0) = 1 = \eta + \mu$; thus, $\mu = -1.06$. Finally, based on our above cost and effectiveness estimates for the high school program (which served a population of 2500 students), we have

$$w_7(v_1, \ldots, v_6, 28000) = 1.28 = 2.06 - 1.06 e^{-\kappa \frac{28000}{2500}},$$

which yields $\kappa = -(2500/28{,}000) \times \ln((2.06 - 1.28)/1.06) = 0.027$.

To fit production functions for the other 2 condom-use multipliers, we assumed that the same level of expenditure per person would be required to achieve comparable results in a smaller segment of the population. Thus, an expenditure of $11.20 per IDU would achieve a 28% increase in condom use among all IDUs, and an equal expenditure targeted specifically to IDUs in methadone maintenance would increase the condom use rate among such IDUs by the same amount (28%). Thus,

$$w_5(\mathbf{v}) = 2.06 - (1.06) e^{-(0.027)\left(\frac{v_5}{N_5} + \frac{v_7}{N_7}\right)}$$

$$w_6(\mathbf{v}) = 2.06 - (1.06) e^{-(0.027)\left(\frac{v_5}{N_5} + \frac{v_6}{N_6} + \frac{v_7}{N_7}\right)}.$$

We considered the following linear approximations in sensitivity analysis:

$$w_5(\mathbf{v}) = \eta' + \mu'\left(\frac{v_5}{N_5} + \frac{v_7}{N_7}\right)$$

$$w_6(\mathbf{v}) = \eta' + \mu'\left(\frac{v_5}{N_5} + \frac{v_6}{N_6} + \frac{v_7}{N_7}\right)$$

$$w_7(\mathbf{v}) = \eta' + \mu' \frac{v_7}{N_7}.$$

When no money is invested in intervention 7 (the untargeted condom availability program), $w_7(v_1, \ldots, v_6, 0) = 1 = \eta'$; thus, $\eta' = 1.00$. Based on our above cost and effectiveness estimates,

$$w_7(v_1, \ldots, v_6, 28000) = 1.28 = 1.00 + \mu' \frac{28000}{2500},$$

so $\mu' = 0.025$. We assumed that the maximum achievable rate of condom use would be 66% and set the upper limits on investment accordingly: thus, in the high-prevalence community, we set V_5 = $660,000, V_6 = $99,000, and V_7 = $26 million; and in the low-prevalence community, we set V_5 = $184,800, V_6 = 27,700, and V_7 = $26 million.

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