An Analysis of Optimal Resource Allocation for Prevention of Infection with Human Immunodeficiency Virus (HIV) in Injection Drug Users and Non-Users

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Millions of dollars are spent annually to prevent infection with human immunodeficiency virus (HIV) without a thorough understanding of the most effective way to allocate these resources. The authors' objective was to determine the allocation of new resources among prevention programs targeted to a population of injection drug users (IDUs) and a population of non–injection drug users (non-IDUs) that would minimize the total number of incident cases of HIV infection over a given time horizon. They developed a dynamic model of HIV transmission in IDUs and non-IDUs and estimated the relationship between prevention program expenditures and reductions in HIV transmission. They evaluated three prevention programs: HIV testing with routine counseling, HIV testing with intensive counseling, and HIV testing and counseling linked to methadone maintenance programs. They modeled a low-risk IDU population (5% HIV prevalence) and a moderate-risk IDU population (10% HIV prevalence). For different available budgets, they determined the allocation of resources among the prevention programs and populations that would minimize the number of new cases of HIV infection over a five-year period, as well as the incremental value of additional prevention funds. The study framework provides a quantitative, systematic approach to funding programs to prevent HIV infection that accounts for HIV transmission dynamics, population size, and the costs and effectiveness of the interventions in reducing HIV transmission. The approach is general and can be used to evaluate a broader group of prevention programs and risk populations. This framework thus could enable policy makers and clinicians to identify a portfolio of programs that provide, collectively, the most benefit for a given budget. *Key words*: HIV; AIDS; HIV-1; resource allocation; prevention; cost-benefit analysis. **(Med Decis Making 1999;19:167–179)**

Approximately 30 million people are infected with the human immunodeficiency virus (HIV) worldwide, and approximately 12 million people have died of AIDS.[1] Despite promising advances in treatment of HIV infection,[2,3] prevention remains an urgent public-health priority. HIV infection is spreading rapidly in certain populations: for example, the Chinese Academy of Preventive Medicine estimated that, by the end of 1993, 10,000 people were infected with HIV in China; and that this number had climbed to 100,000 by the end of 1995.[1] Approaches to preventing HIV infection include vaccine development,[4] testing and counseling,[5,6] and educational and behavioral interventions.[7] The efficacy of these interventions is variable and often limited. In addition, the interventions are expensive. Vaccine development has cost hundreds of millions of dollars to date, and many challenges remain.[4] Testing and counseling patients admitted to acute-care hospitals

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in the United States would cost $171 million during the first year alone, and would result in over $2 billion in treatment costs.[8] Educational interventions are costly also, in part because they must be offered to large populations to be effective.

In any specific community or population, a variety of HIV-infection–prevention programs are feasible. How should policymakers decide which programs to implement? How should they allocate resources among programs and populations? Because both the potential benefits and the potential costs of these interventions are high, and because funding for prevention is limited, decisions to implement prevention programs involve high stakes. For example, in 1987, federal health officials in the United States made the decision to implement a nationwide AIDS-awareness campaign with the theme "Anyone Can Get AIDS." The campaign led to significant gains in public support for increased AIDS funding, but has been criticized for channeling substantial funds into a campaign for the general public, and away from interventions targeted to high-risk groups, where funds for prevention are urgently needed.[9] Policymakers must also make choices about resource allocation for HIV-infection prevention at state, regional, and local levels.

How to allocate resources among programs for HIV-infection prevention is a specific case of a more general problem: how to allocate resources to control an epidemic caused by an infectious agent. While resource-allocation problems have been studied in the abstract by economists and operations researchers for many years, resource allocation for epidemic control poses special challenges. Epidemics of infectious diseases are dynamic and are inherently nonlinear: while an epidemic is growing, saving one person today from getting infected could translate into saving scores of people from infection over time. In addition, an epidemic may progress differently in different populations, and different programs for the control of the disease can have very different costs and effectiveness.

Surprisingly little research is available to guide resource allocation for epidemic control. Some authors have considered the appropriate timing of interventions aimed at epidemic control.[10] Others have evaluated the effect of resource allocation on the equilibrium state of an epidemic.[11–13] However, the epidemic equilibrium may not occur for many years after the beginning of the epidemic, and thus these approaches have limited value for decision making in the early stages of an epidemic. Studies of resource allocation before equilibrium is achieved[14–16] have typically considered resource allocation for only a single, closed population. These analyses do not address questions that are of substantial importance in the HIV epidemic, such as the appropriate allocation of resources between a high-risk population (for example, injection drug users) and a lower-risk population (for example, heterosexual adults), nor do they consider the relationship between intervention cost and effectiveness. Some authors have numerically analyzed epidemic models to determine the optimal allocation of resources for control of infectious diseases,[13,17,18] but have not considered the relationship between prevention-program cost and effectiveness. Another approach,[19] suggested for community planners who must allocate HIV-infection–prevention resources, aims to minimize the number of new HIV infections that occur, but ignores nonlinear epidemic effects.

This paper builds on the work of Richter and Brandeau,[20] who developed an analytic framework for determining the optimal allocation of resources for epidemic control among prevention programs targeted to two or more independent populations. They modeled epidemic growth in each population with a compartmental epidemic model, and assumed that policymakers would allocate resources among interventions that reduce the rate of disease transmission. Unlike previous research, their approach explicitly includes cost functions that represent the relationship between expenditures for an intervention and the corresponding reduction in disease transmission. The use of explicit cost functions for preventive interventions provides a more flexible analytic approach; the analytic framework can address directly how differences in cost functions affect the health and economic outcomes of an intervention. The goal is to allocate resources among the prevention programs and populations so as to minimize the total number of new infections that occur over a finite time horizon, subject to a budget constraint and subject to attainable rates of disease transmission.

This article illustrates the use of a similar approach, in conjunction with a more sophisticated epidemic model, to evaluate allocation of HIV-infection–prevention resources among programs targeted to injection drug users (IDUs) and non-IDUs in the patient population of a large health-care system. We evaluated three interventions that aim to reduce HIV transmission: HIV testing with routine counseling, HIV testing with intensive counseling, and HIV testing and counseling linked to a drug-rehabilitation program. These interventions are currently being implemented in the health care system; our analysis considered the effects of allocating additional resources to them. To our knowledge, this is the first work on resource allocation for control of an infectious disease that estimates cost functions that represent the relationship between expenditures on an intervention and the corresponding reduction in disease transmission, and incorporates such cost functions into a dynamic disease-transmission model.

Methods

RESOURCE-ALLOCATION MODEL

We considered two patient populations: IDUs ($i = 1$) and non-IDUs ($i = 2$). For simplicity, we assumed that no cross-infection occurs between the two groups. We described the growth of the epidemic in each population by a simple epidemic model, illustrated in figure 1. Each population is divided into susceptible and infected individuals. We assumed that members of the population mix homogeneously (that is, any given susceptible individual is as likely as any other to mix with any given infected individual). The transmission rate (or sufficient contact rate) in each population i ($i = 1, 2$) is denoted by λ_i and represents the average rate of infection-transmitting contacts between susceptible and infected individuals. The quantity λ_i is a function of the number of contacts per unit time between susceptible and infected individuals and the risk of infection transmission per contact. New entrants to each population i are assumed to be uninfected, and to enter at rate δ_i. Individuals in population i exit from susceptible groups at rate μ_{1i} and from infected groups at rate μ_{2i}.

The cumulative number of newly infected people over a given time horizon (from now, time 0, until T time units in the future) in population i is $N_iH_i(\lambda_i)$. The quantity N_i is the size of population i. The quantity $H_i(\lambda_i)$ is calculated from the epidemic model and is a function of the parameters T, λ_i, δ_i, and I_{0i}, where I_{0i} is the fraction of individuals in population i who are infected at time 0. The equations describing the epidemic model are shown in the appendix.

The goal of further expenditures was to reduce the transmission of HIV by reducing the transmission rate. We assumed that an expenditure of c_i dollars leads to transmission rate $\lambda_i(c_i)$ in population i. The total amount of available funds to allocate between the two populations is represented by C.

Using the definitions, we write the resource-allocation problem as:

$$\text{Minimize } N_1H_1(\lambda_1(c_1)) + N_2H_2(\lambda_2(c_2)) \qquad (1)$$

$$\text{such that } c_1 + c_2 \leq C$$

$$a_1 \leq \lambda_1 \leq \lambda_{01}$$

$$a_2 \leq \lambda_2 \leq \lambda_{02}$$

The objective of the resource-allocation decision is to minimize the total number of people who become newly infected up to time T (the number in the first population who become infected, $N_1H_1(\cdot)$, plus the number in the second population who become infected, $N_2H_2(\cdot)$) subject to a constraint on the available resource ($c_1 + c_2 \leq C$) and subject to limits on attainable transmission rates in each population. We assumed a planning horizon of five years, and an HIV-infection–prevention budget of \$1 million. We chose a five-year planning horizon because few programs are planned further in advance than five years. The upper limits on transmission, λ_{01} and λ_{02}, denote the transmission rates in populations 1 and 2, respectively, at time 0 (before any incremental HIV-infection–prevention resources have been allocated); although it is possible that investment in an HIV-infection–prevention program could increase the HIV transmission rate, we enforce the constraint that the level of investment selected must be such that HIV transmission does not increase. The lowest attainable transmission rates in populations 1 and 2, respectively, are denoted by a_1 and a_2. These lower limits could arise because of characteristics of the epidemic, such as inherent infectivity of HIV, or because of limits on the attainable amount of behavior change.

We programmed the model in Mathematica™, and ran it on a SUN-SPARC Station 20/61.

We used this analytic framework to evaluate programs for the prevention of HIV infection at the Department of Veterans Affairs (VA) Palo Alto Health Care System in Palo Alto, California. The VA Palo Alto Health Care System (VAPA) consists of two large medical centers and several associated clinics in the San Francisco Bay Area and in Monterey, California. The VAPA has extensive drug-rehabilitation programs. The VAPA treats approximately 25,000 veterans, and is affiliated closely with Stanford University, Stanford, California.

Our analysis required information about the two patient populations (IDUs and non-IDUs), the characteristics of the HIV epidemic within those populations, and the costs and effectiveness of the preventive interventions. We assumed that HIV testing and routine counseling would include brief pretest and posttest counseling, and that intensive counseling would consist of several follow-up counseling and support sessions.[21] We also considered HIV testing and counseling linked to methadone maintenance programs.

EPIDEMIC AND POPULATION DATA

Using inpatient and outpatient hospital data, we estimated the sizes of the IDU and non-IDU patient populations served by the VA Palo Alto Health Care System; entry and exit rates for each population and each disease group (susceptible and infected); and

Table 1 • Estimated Numbers of Injection-drug-user (IDU) and Non-IDU Patients

Year	Total No. of Inpatients and Outpatients	Total No. of Outpatients	Percentage of Inpatients Who Are IDUs	Total No. of IDUs	Total No. of Non-IDUs
1989	24,478	23,863	9.63	2,299	22,179
1990	23,064	22,475	7.78	1,749	21,315
1991	22,337	21,735	7.71	1,675	20,662
1992	24,531	23,699	6.30	1,333	23,198
1993	24,747	23,556	6.41	1,509	23,238
1994	25,053	23,900	6.86	1,639	23,414
1995	31,748	30,805	8.24	2,538	29,210
AVERAGE				1,820	22,776

the initial HIV prevalence, incidence, and transmission rate in each population. We considered individuals aged 18 to 54 years because this age group captures the majority of IDUs.

Total population sizes. We used hospital discharge diagnoses to estimate the number of IDUs cared for as inpatients. Because the discharge diagnoses identified only patients with the diagnosis of substance abuse and thus included patients who did not inject drugs, we assumed that all patients with diagnoses of opiate use or amphetamine use, and half of those with diagnoses of cocaine use, were IDUs. We also assumed, based on experience of VAPA providers, that the proportion of outpatients who were IDUs was approximately the same as the proportion of inpatients who were IDUs. To estimate the number of IDUs seen in the outpatient clinics, we multiplied this proportion by the annual number of outpatients (table 1). We estimated the size of the non-IDU population by subtracting the number of IDUs from the total number of patients (table 1).

We used the average numbers of IDUs and non-IDUs as the population sizes for our analysis (table 1). We assumed that all IDUs were at risk for HIV infection (or were already infected), so we estimated the size of the IDU population under age 55 to be $N_1 = 1{,}820$. The percentage of patients less than 55 years of age at the VAPA in 1995 was 49.2%, so for non-IDUs, we estimated the population size to be $N_2 = 0.492 \cdot 22{,}776 = 11{,}206$.

Initial HIV prevalence. Published estimates of HIV prevalences among IDUs in the VA system range from 13%[22] to 18%.[23] Based on a program at the VAPA that screened 3,000 IDUs who had no symptoms of HIV, we estimated HIV prevalence among IDUs to be 5% (unpublished data); thus, $I_{01} = 0.05$. Because prevalence of HIV infection among IDUs in other VA patient populations may be higher than 5%, we considered a second case in which initial HIV prevalence in the IDU population is 10%. We refer to the first case as low-risk IDUs, and to the latter case as moderate-risk IDUs. As described below, we also assumed, following Washington and colleagues,[21] that interventions aimed at low-risk versus moderate-risk IDU populations would have different degrees of effectiveness. For both cases, we evaluated allocation of resources between a non-IDU population and a single population of IDUs, either low-risk or moderate-risk, as illustrated in figure 1; the two cases differ only in the assumptions about initial HIV prevalence in the IDU group and the effectiveness of interventions targeted to IDUs.

Based on unpublished data from the VAPA, we estimated that the prevalence of HIV infection in the under-age-55-years non-IDU patient population was at most 1%; thus, we set $I_{02} = 0.01$. In sensitivity analyses, we varied widely the values for initial HIV prevalences in the IDU and non-IDU populations.

Entry and exit rates. The epidemic model (figure 1) includes entry into and exit from the population. Entry corresponds to maturation into the population (individuals attaining 18 years of age); exit is due to maturation or death. All entrants are assumed to be uninfected. We do not explicitly include migration into and out of the population because we assume that immigrants and emigrants are distributed among the population groups (uninfected and infected, IDU and non-IDU) according to the relative sizes of those groups; thus, such population movement does not affect the epidemic dynamics.

From standard life tables,[24] the maturation rate into and out of a population of 18-to-54-year-old men is approximately 0.027 per person per year, so we assumed that $\delta_1 = \delta_2 = 0.027$. The mean non-HIV death rate among 18-to-54-year-old non-IDU men is approximately 0.002 per person per year.[24] Non-HIV death rates among IDUs are 0.016 to 0.400 per person per year in various IDU populations[25–29]; we used the value 0.017 in our base-case analysis. We assumed that the mean time from infection with HIV to death is 14 years; thus, we set the HIV-related death rate among infected IDUs and non-IDUs at $1/14 \sim 0.074$ per person per year. Summing these rates as appropriate for each population group, we obtained the following exit rates for the four groups: $\mu_{11} = 0.044$, $\mu_{21} = 0.118$, $\mu_{12} = 0.029$, $\mu_{22} = 0.103$. We varied the entry and exit rates widely in sensitivity analyses.

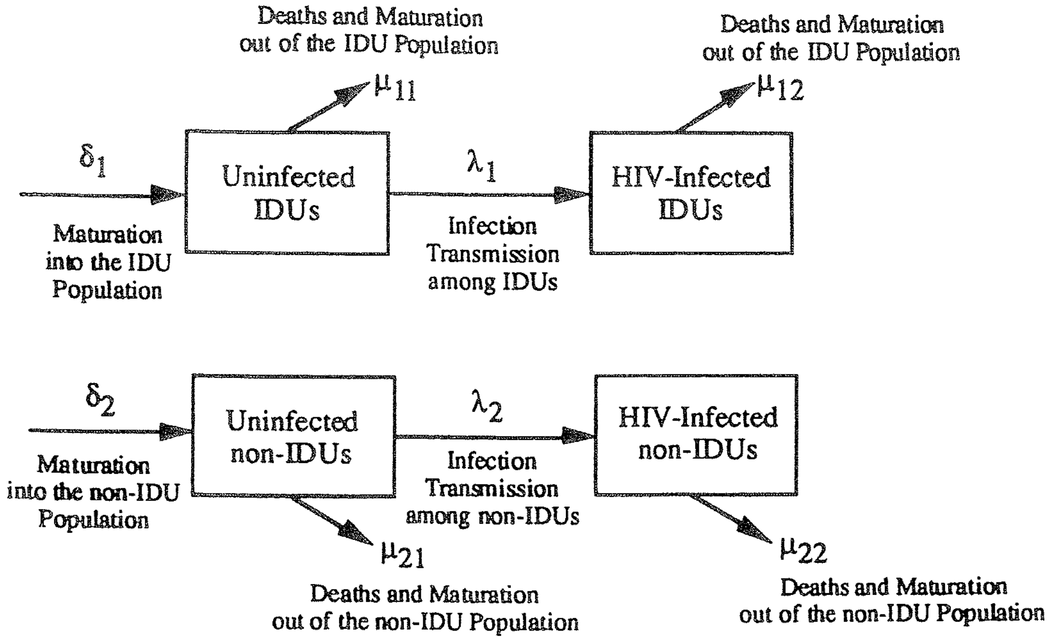

FIGURE 1. Schematic representation of the compartmental HIV epidemic model. The model evaluates the numbers of incident HIV cases in two populations, injection drug users (IDUs) and non–injection drug users (non-IDUs). Resources are allocated between a low-risk IDU population (HIV prevalence 5%) and non-IDUs, or between a moderate-risk IDU population (HIV prevalence 10%) and non-IDUs. Maturation into the target population occurs at the rate δ, deaths and maturation out of the population occur at rates μ, and the HIV transmission rate (or sufficient contact rate) is λ.

Initial HIV transmission rate. We calculated the initial HIV transmission rate in each population (λ_{0i}), using the epidemic model, as the value that yields the observed number of incident HIV cases in each population. To estimate the initial incidence of HIV infection in each population, we examined the number of incident cases of HIV at the VAPA by year (table 2). From 1991 to 1994, approximately 60% of the incident cases of HIV infection were in IDUs (Holodniy MH, AIDS Research Center, VA Palo Alto Health Care System 1996, personal communication); thus we use data from 1991 to 1994 to estimate the HIV incidence among IDUs. From 1991 to 1994, 39 incident cases of HIV occurred among IDUs and 26 cases occurred among non-IDUs annually, on average (table 2). Using the epidemic model, we found that the values $\lambda_{01} = 0.399$, $\lambda_{02} = 0.221$ yield 39 and 26 annual new HIV cases in the IDU and non-IDU populations, respectively. In sensitivity analyses, we examined a range of values for the initial transmission rate in each population.

ESTIMATION OF COST FUNCTIONS

To the extent possible, we estimated the required cost functions (which express transmission reduction as a function of expenditure) from the published literature. However, substantial uncertainty exists regarding the effects of increased expenditures for HIV-infection–prevention programs and the resulting changes in HIV transmission. Studies of the effectiveness and costs of HIV prevention programs are summarized by Washington and colleagues[21] and Owens and colleagues.[8] As we explain

Table 2 • Incident Cases of Infection with Human Immunodeficiency Virus (HIV)

Year	Cumulative No. of HIV Cases	Incident HIV Cases, Total	Incident HIV Cases, IDUs*	Incident HIV Cases, Non-IDUs
1984	42			
1985	66	24		
1986	84	18		
1987	112	28		
1988	159	47		
1989	220	61		
1990	267	47		
1991	319	52	31	21
1992	393	74	44	30
1993	482	89	53	36
1994	530	48	29	19
1995	557	27		
AVERAGE 1991–1994		66	39	26

*Injection drug users.

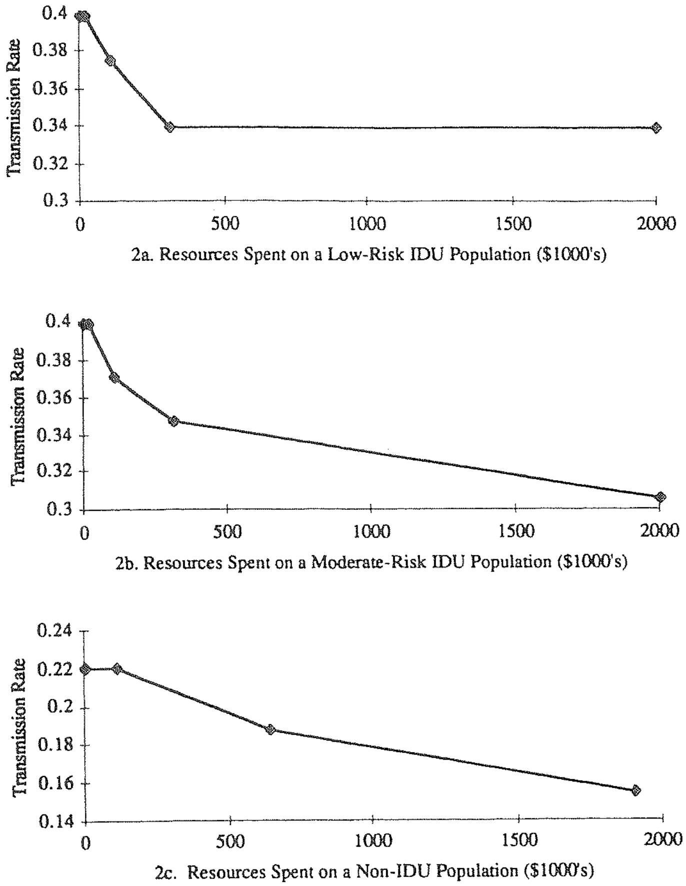

FIGURE 2. Cost functions for prevention programs, representing the reductions in HIV transmission for given levels of expenditure. (a) Cost function for low-risk injection drug user (IDU) population. The first breakpoint on the curve, labeled with a small square, represents expenditures of $18,200 (see text). For smaller expenditures, no transmission reduction occurs. The second breakpoint, at $103,740, represents the expenditure for testing and routine counseling. The third breakpoint, at $309,400, represents the expenditure for testing and intensive counseling. Larger expenditures lead to no further reduction in HIV transmission in this population. (b) Cost function for moderate-risk IDU population. The three breakpoints represent the same expenditures as in (a), but with different associated reductions in HIV transmission. An expenditure of $6,466,460 for methadone maintenance for every IDU (not shown on the graph) will reduce the transmission rate to 0.220. (c) Cost function for the non-IDU population. The first breakpoint represents expenditures of $112,060 (see text). The second breakpoint, at $638,742, represents the expenditure for testing and routine counseling. The third breakpoint represents expenditures of $1,905,020 for testing and intensive counseling.

below, we estimated piecewise linear cost functions (figure 2), and performed extensive sensitivity analysis on the estimated functions.

Cost function: programs targeted to IDUs. We assumed that IDUs could be given HIV counseling and routine testing inexpensively; for a larger expenditure, IDUs could be given intensive counseling and testing; and for an even larger expenditure, IDUs could be enrolled in methadone maintenance.

Washington and colleagues[21] evaluated the costs and effectiveness of these interventions for low-risk and moderate-risk IDUs. HIV prevalences among these groups were approximately 5% and 10%, respectively. Interventions aimed at these different IDU groups had differing levels of effectiveness. The IDU patient group at the VAPA, with 5% HIV prevalence, is most similar to the low-risk IDU group studied by Washington and colleagues.[21] As mentioned, we also considered the case of a moderate-risk IDU patient population, which had a 10% initial HIV prevalence.[21] The cost curves that we estimated for these two groups are illustrated in figure 2.

We estimated that at least $10 per IDU (in either IDU risk group) must be spent before any reduction in the transmission rate would occur, due to the overhead associated with establishing a counseling program. The amount $\$10 \cdot N_1 = \$18,200$ is the first breakpoint in the cost curve for both low-risk and moderate-risk IDU populations; for any expenditure less than $18,200, no change in the mean transmission rate among IDUs occurs. Washington and colleagues[21] found that an expenditure of approximately $50 to $63 per IDU on testing and routine counseling yielded a 6% reduction in overall HIV transmission among low-risk IDUs and a 7% reduction among moderate-risk IDUs. We assumed an expenditure of $57 per IDU on testing and routine counseling, so the second breakpoint in our cost curves for IDUs was $\$57 \cdot N_1 = \$103,740$. Washington and colleagues[21] also found that intensive counseling and testing could be provided at a cost of $170 per IDU, with resulting transmission reductions of about 15% among low-risk IDUs and 13% among moderate-risk IDUs.[21] This third breakpoint occurs at $\$170 \cdot N_1 = \$309,400$.

At the VAPA, IDUs may be treated in a methadone-maintenance program. Methadone maintenance can reduce risky drug injection, and thus can also be considered to be a program for the prevention of HIV infection.[30] Barnett and Rodgers[31] found that methadone maintenance costs were about $296 per month per patient. The usual length of enrollment in a methadone-maintenance program is nine months. Participation in a methadone-maintenance program for 2.5 weeks costs about $170 per patient; this expenditure corresponds to the third breakpoint in the cost curves. A full year's participation in methadone maintenance costs $3,553 per patient. Thus, we assumed the endpoint of the cost curves for interventions targeted to IDUs to be $\$3,553 \cdot N_1 = \$6,466,460$. For clarity, this endpoint is not shown in figure 2, but the curves can be extrapolated up to this endpoint, as we now describe. Washington and colleagues[21] found that, for low-risk IDUs, a 15% reduction in HIV transmission was attainable with such intensive treatment; thus, for these IDUs, methadone maintenance did not provide any additional HIV risk reduction beyond that gained from testing and intensive counseling. For moderate-risk IDUs, Washington and colleagues[21] found that a year of methadone maintenance reduced HIV transmission by about 45%.

Cost function: programs targeted to non-IDUs. We assumed that $10 per person in the non-IDU population would have to be spent before any behavioral change would occur. Thus, $\$10 \cdot N_2 = \$112{,}060$ is the first breakpoint in the non-IDU cost curve. Using data from Washington and colleagues,[21] we estimated that testing and routine counseling would cost $57 per person in the non-IDU population; following Owens and colleagues,[8] we assumed that the associated risk reduction would be 15%. Thus, we calculated the second breakpoint of the cost curve as $\$57 \cdot N_2 = \$638{,}742$, corresponding to a 15% reduction in the transmission rate.

Washington and colleagues[21] found that intensive counseling and testing for IDUs cost $170 per person. We assumed that such an intervention for a non-IDU population would also cost $170 per person, and would result in a 30% reduction in HIV transmission in the non-IDU population. Thus, we estimated the endpoint of the cost function for prevention programs targeted to the non-IDU population to be $\$170 \cdot N_2 = \$1{,}905{,}020$, with an associated 30% reduction in the HIV transmission rate. Because of uncertainty about the degree to which intensive counseling would reduce risky behaviors among non-IDUs, we used sensitivity analyses to examine lower levels of risk reduction.

The values of input data for the analysis are summarized in table 3.

Results

Chart 1 shows the numbers of HIV-infection cases averted for different allocations of the $1-million budget. For the case of a low-risk IDU population, the total number of incident cases of HIV infection is minimized by allocating $309,400 to the IDU population and allocating the remaining $690,600 to the non-IDU population. This allocation provides HIV testing and intensive counseling for every IDU ($170 per person). For the non-IDU population, an average of approximately $62 per person is spent on HIV prevention: this cost corresponds to HIV testing and routine counseling ($57 per person) for about 95% of the 11,206 people in the non-IDU population and HIV testing and intensive counseling ($170 per person) for the remaining 5% of the non-IDU population $\{(0.95)(\$57) + (0.05)(\$170) = \$62\}$. We estimated that this allocation of resources would avert a total of 106

Table 3 • Summary of Input Data

	Low-risk IDUs*	Moderate-risk IDUs	Non-IDUs	Source
Epidemic data				
Population size (N_i)	1,820	1,820	11,206	Calculated, VA data
Initial HIV† prevalence (I_{0i})	5%	10%	1%	Calculated, VA data
Entry rate (δ_i)	0.027	0.027	0.027	Census[24]
Exit rate, uninfected individuals (μ_{1i})	0.044	0.044	0.029	Des Jarlais et al.[25] Selwyn et al.[26] van Haastrecht et al.[27] Pehrson et al.[28] Galli and Musicco[29]
Exit rate, infected individuals (μ_{2i})	0.118	0.118	0.103	Assumed
Initial HIV transmission rate (λ_{0i})	0.399	0.399	0.221	Calculated, VA data
Intervention data				
Minimum expenditure per person	$10	$10	$10	Estimated
Testing and routine counseling				
(Maximum) expenditure per person	$57	$57	$57	Owens et al.[8] Washington et al.[21]
Associated transmission rate reduction	6%	7%	15%	Owens et al.[8] Washington et al.[21]
Testing and intensive counseling				
(Maximum) expenditure per person	$170	$170	$170	Washington et al.[21]
Associated transmission rate reduction	15%	13%	30%	Washington et al.[21]
Methadone Maintenance				
(Maximum) expenditure per person	$3,553	$3,553	—	Barnett and Rodgers[31]
Associated transmission rate reduction	15%	45%	—	Washington et al.[21]
Available budget		$1 million		Assumed
Time horizon		5 years		Assumed

*Injection drug users.
†Human immunodeficiency virus.

cases in the two populations over the five-year time horizon; thus, these prevention programs cost approximately $9,400 per HIV-infection case averted. Chart 1 shows that an alternative allocation, in which $198 per person is spent on IDUs and $57 per person is spent on non-IDUs, achieves almost the same results: 105 cases are averted.

For the case of a moderate-risk IDU population, we minimize the number of incident cases of HIV infection by allocating $360,360 to the IDU population ($198 per person) and allocating the remaining $639,640 to the non-IDU population ($57 per person). This allocation corresponds to testing and routine counseling for all non-IDUs, testing and intensive counseling ($170 per person) for 99% of IDUs, and methadone maintenance ($3,553 per person) for 1% of IDUs {(0.99)($170) + (0.01)($3,553) = $198}. We estimated that this allocation would avert 136 cases over the five-year period, yielding a cost of about $7,400 per HIV case averted. Chart 1 shows that an allocation of $170 per IDU and $62 per non-IDU achieves almost the same results: 135 cases are averted.

Our results were most sensitive to the available budget, to the effectiveness of methadone maintenance in reducing HIV transmission among IDUs, to the effectiveness of testing and intensive counseling in reducing HIV transmission among non-IDUs, and to the HIV-infection incidences and prevalences among the IDUs and the non-IDUs.

Figure 3 shows the optimal allocation of resources as a function of the available budget. If the budget for prevention programs ranges from $18,200 (the minimum expenditure) to $948,142, then the optimal solution—for the case of a low- or a moderate-risk IDU population—is to spend available funds on IDUs, up to $170 per IDU (a total of $309,400), and then to spend any remaining funds on testing and routine counseling for non-IDUs. At a budget of $948,142, the optimal solution in each case is to spend $170 per IDU for testing and intensive counseling (an expenditure of $309,400), and to spend $57 per non-IDU for testing and routine counseling (an expenditure of $638,742).

For budgets of more than $948,142, the optimal allocations for the low- and moderate-risk IDU populations differ. For the low-risk case, it is not optimal to spend more than $170 per IDU ($309,400 in total) because methadone maintenance in a low-risk IDU population may not achieve greater risk reduction than testing and intensive counseling[21]; thus, any available funds beyond $948,142 are spent on testing

Chart 1 • Cases of HIV Infection Averted as a Function of Resources Allocated*

Allocation to IDUs	Allocation to Non-IDUs	Case 1: Low-risk IDUs (5% HIV prevalence)	Case 2: Moderate-risk IDUs (10% HIV prevalence)
$0 per IDU: No intervention targeted to IDUs	$89 per non-IDU: Some non-IDUs receive testing and routine counseling, and some receive testing and intensive counseling	45	45
$57 per IDU: All IDUs receive testing and routine counseling	$80 per non-IDU: Some non-IDUs receive testing and routine counseling, and some receive testing and intensive counseling	80	96
$170 per IDU: All IDUs receive testing and intensive counseling	$62 per non-IDU: Some non-IDUs receive testing and routine counseling, and some receive testing and intensive counseling	106	135
$198 per IDU: Some IDUs receive testing and routine counseling, and some receive testing and intensive counseling	$57 per non-IDU: All non-IDUs receive testing and routine counseling	105	136
$550 per IDU: Some IDUs receive testing and intensive counseling, and some receive methadone maintenance	$0 per non-IDU: No intervention targeted to non-IDUs	85	123

*This chart shows the total numbers of cases of infection with human immunodeficiency virus (HIV) averted among injection drug users (IDUs) and non-IDUs over a five-year time horizon, given different investments of $1 million in HIV prevention (as described in the first two columns), for the case of a low-risk IDU population (third column) and the case of a moderate-risk IDU population (fourth column). Each row corresponds to a different allocation of the $1 million budget.

and counseling of non-IDUs. For the case of a moderate-risk IDU population, however, for budgets of more than $948,142, the optimal allocation is to spend $639,640 on testing and routine counseling in the non-IDU population ($57 per person), and to allocate the remaining resources to the IDU population; in this case, at least $170 per IDU is spent, so all IDUs receive at least testing and intensive counseling ($170 per person), and some IDUs receive methadone maintenance ($3,553 per person).

We assumed a base-case budget of $1 million. One can use the information in figure 3, along with information about HIV-infection cases averted, to determine the incremental value of additional funds. Such information could be used by a policymaker to determine the value of increasing the budget. For the case of the low-risk IDU population, each incremental $100,000 in available funds leads to 2.5 incremental cases averted, so the cost per incremental HIV-infection case averted is approximately $40,000. For the case of the moderate-risk IDU population, each incremental $100,000 above the $1 million leads to 3.7 cases averted, which translates to approximately $27,000 per case averted. Thus, for both populations, increasing the budget above $1 million is cost beneficial.

We also examined the effects of changes in the effectiveness of interventions on the optimal allocation of resources. Sensitivity analysis indicated that investing a proportion of funds in methadone maintenance for low-risk IDUs becomes optimal when the resulting reduction in the transmission rate (the endpoint of the cost curve) is 50% or more. For moderate-risk IDUs, investment in some methadone maintenance remains optimal if the transmission rate reduction is 35% or more (the base-case analysis assumed a 45% reduction).

Our base-case analysis assumed that testing and intensive counseling would reduce the rate of HIV transmission among non-IDUs by 30% for an expenditure of $170 per non-IDU. For the low-risk IDU population, so long as testing and intensive counseling of non-IDUs is more effective than testing and routine counseling of non-IDUs (i.e., transmission reduction greater than the 15% achieved by testing and routine counseling), it remains optimal to spend $62 per non-IDU (and thus to invest in testing and intensive counseling for about 5% of non-IDUs). For the case of a moderate-risk IDU population, the reduction in the transmission rate among non-IDUs from testing and intensive counseling would have to be 37% or more before it would be worthwhile to invest in such programs. However, this degree of behavioral change may not be attainable in many clinical settings.

We also examined the effects on the optimal resource allocation of different levels of initial HIV

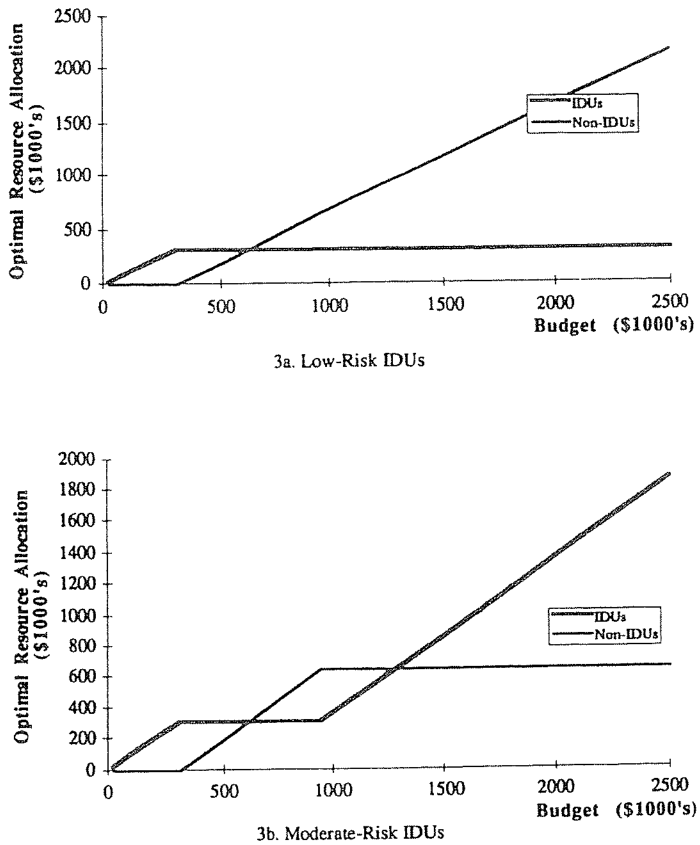

FIGURE 3. Optimal allocation of resources as a function of the available budget. (a) Optimal allocation for the case of a low-risk IDU population. (b) Optimal allocation for the case of a moderate-risk IDU population.

prevalence in the IDU and non-IDU populations. Our base-case analyses assumed that initial HIV prevalence in the non-IDU population was 1%, and that initial HIV prevalence in the IDU population was either 5% (for the low-risk IDU case) or 10% (for the moderate-risk IDU case). For the low-risk IDU case, even if initial HIV prevalence in the non-IDU population is only one-fifth as high as we assumed, it is still optimal to spend $170 per IDU for testing and intensive counseling, and then to devote the remaining funds to non-IDUs ($62 per non-IDU). For the moderate-risk IDU case, even if initial HIV prevalence among IDUs is as high as 40%, the same solution remains optimal: All non-IDUs receive testing and routine counseling. Conversely, assuming that initial HIV prevalence among IDUs is 10%, as in the moderate-risk base case, if initial HIV prevalence among non-IDUs is 1.5% or higher, then it becomes optimal to spend only $170 per IDU (for testing and intensive counseling), and to spend $62 per non-IDU (with some non-IDUs receiving testing and intensive counseling, and all other non-IDUs receiving testing and routine counseling); the increased HIV prevalence among non-IDUs makes it optimal to devote more resources to non-IDUs than in the base case.

Finally, we performed sensitivity analysis on the length of the time horizon. For one-year and three-year horizons, the optimal allocation of resources was the same as for the base-case allocation.

Discussion

We analyzed the optimal allocation of resources for prevention of HIV infection among two different populations (IDUs and non-IDUs) and three different prevention programs: HIV testing with routine counseling, HIV testing with intensive counseling, and HIV testing and counseling linked to methadone maintenance programs. We used a resource-allocation model that is based on a model of the HIV-infection epidemic and on cost functions that describe the relationship between expenditures for prevention programs and subsequent reductions in HIV transmission. Our goal was to determine the allocation of resources among populations and interventions that minimized the number of incident HIV cases over a five-year time horizon, subject to a given budget constraint.

The optimal allocation of resources between a low-risk IDU population (5% HIV prevalence) and a non-IDU population was to provide testing and intensive counseling to all IDUs, and to spend the remaining funds on testing and counseling of non-IDUs. The funds available for the non-IDU population were sufficient for testing and routine counseling for the majority of non-IDUs, and for the more expensive testing and intensive counseling for the remaining non-IDUs. The optimal allocation of resources between a moderate-risk IDU population (10% HIV prevalence) and a non-IDU population was to fund testing and routine counseling for all non-IDUs, and to spend the remaining funds on IDUs. The funds available to the IDU population were sufficient for most IDUs to receive testing and intensive counseling, and for a proportion of IDUs to receive the more expensive testing and counseling linked to drug rehabilitation.

Why are such patterns of resource allocation optimal? The primary determinants of the optimal resource allocation are the sizes of the populations, the HIV-transmission dynamics in the populations, the relative effectiveness of the preventive interventions in the populations, the cost of the interventions, and the available budget. In our analytic framework, the relative effectiveness of the preventive interventions in each population, and the interventions' costs, were reflected in the cost functions for each population (figure 2). Our estimated cost functions indicated that HIV testing and counseling associated with drug rehabilitation did not provide additional reduction in HIV transmission in a low-risk IDU population, but did provide additional benefit in the moderate-risk IDU population. Our cost function for the non-IDU population indicated that HIV testing and routine counseling provided modest but important reductions (15%) in HIV transmission, and that testing and intensive counseling provided substantial reductions (30%) in HIV transmission.

The optimal resource allocation depends on the balance of these factors. As the funds available for prevention increased, allocation of resources to the low-risk IDU population did not continue to increase, because the cost function indicates that no further benefit accrues. In contrast, allocation of funding for the moderate-risk IDU population continued to increase as the available budget increased because the cost function indicated increased benefit with allocation of resources for the most expensive intervention: testing and counseling associated with drug rehabilitation

Our analytic framework provides a quantitative, systematic approach to funding HIV-infection–prevention programs. The approach accounts for transmission dynamics, population size, and the effectiveness of the interventions. The approach is general and could be used to evaluate a broader group of programs (e.g., needle exchange, bleach distribution, condom distribution) and a broader array of risk populations, given sufficient data. Alternatively, the framework could be used to evaluate both prevention and treatment programs, which may compete with each other for resources. Whether treatment and prevention programs compete for resources depends on whether these programs are funded from the same or different sources. Our framework could accommodate either situation. The framework thus could enable policymakers and clinicians to identify a portfolio of programs that provide, collectively, the most benefit for a given budget. Currently, no such framework is available, despite the enormously difficult decisions that policymakers must make about funding HIV-infection–prevention programs.

Such a framework could be useful for modeling problems in a variety of policy domains. Although investigators have used dynamic models for analysis of screening for cancer,[32–34] coronary heart disease,[35] and stroke prevention,[36] our framework is particularly useful for disease processes in which the interaction of two or more groups is an essential component of the analysis, as is the case for infectious diseases. Thus, the framework would be useful for allocation of resources among prevention programs such as vaccines for HIV infection[5,37]; vaccines for control of *Helicobacter pylori* infection, which causes ulcer disease and gastric cancer[38,39]; and prevention or amelioration of a variety of other infectious diseases.

Although the use of our analytic framework for such decisions has advantages, the approach depends on the availability of evaluative studies that characterize the relationship between expenditures for a prevention program and the rate of HIV transmission. Although such evaluations are inherently difficult, the use of observable behaviors and surrogate markers is a feasible alternative. For example, Kaplan and colleagues used mathematical modeling in conjunction with detection of HIV on returned needles to evaluate the effect on HIV transmission of a needle-exchange program.[40] Holtgrave and colleagues[41,41] have studied the effectiveness of HIV counseling and other programs for prevention of HIV infection. Although evaluations of the effectiveness of HIV counseling must rely on self reporting —a method with known limitations—such studies provide useful information that can be related to transmission dynamics via modeling. Nonetheless, rigorous economic evaluations of prevention programs are uncommon, and this deficit poses a substantial obstacle to the use of any method for quantitative evaluation of resource allocation for prevention of HIV infection. The limited information available for the development of cost curves indicates that further evaluative studies of interventions are needed. The value of the information obtained from such evaluations should be assessed with respect to the cost of obtaining the information with evaluative studies; methods to make such an assessment exist.[43,44]

Our study has several limitations. First, we assumed that no HIV transmission occurs between IDUs and non-IDUs. Although this assumption does not hold in the general population, there is little interaction between IDUs and non-IDUs within the specific population that we examined; therefore, the assumption is not likely to have significantly influenced our conclusions. If there were significant transmission between the populations, prevention programs for the IDU population would provide greater benefit than we estimated in our analysis. Second, because the focus of our analysis was on prevention of HIV transmission, we considered the effect of drug-rehabilitation programs on reduced HIV transmission among IDUs only. An analysis of resource allocation with a broader scope might indicate that increased funding of drug rehabilitation is optimal because of the other health benefits associated with such programs.[30] Third, the health and economic outcomes of the HIV-infection–prevention programs we considered have not been evaluated rigorously. We used the best available data to construct our cost functions, and our sensitivity analyses suggest that our findings are robust to modest changes in these cost functions. However, further evaluation of the costs and benefits of these programs would refine our estimates substantially. Finally, planners attempting to control the spread of HIV infection must balance many considerations, including fairness, desires of advocacy groups, community standards, and competing agendas among the planners themselves. Our framework does not explicitly account for these elements of the allocation process.

Resources for programs for the prevention of HIV infection currently are allocated through a complex political process. These processes often involve community planning, and differ from state to state. Our framework provides a systematic method for evaluating the medical costs and benefits of portfolios of prevention programs. Policymakers must balance the medical costs and benefits of candidate programs along with questions of equity, fairness, and ethics. In addition, decision makers may differ about which objectives they aim to satisfy. Our framework does not explicitly include these important additional considerations. Rather, we believe our analytic framework provides an additional tool[45] to help policymakers as they aim to strike this difficult balance so as to allocate scarce prevention resources effectively.

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APPENDIX

Epidemic Equations Underlying the Resource-Allocation Model

The epidemic in each population is described by the following differential equations:

$$dS_i(t, \lambda_i)/dt = \delta_i - \lambda_i I_i(t, \lambda_i) S_i(t, \lambda_i) - \mu_{i1} S_i(t, \lambda_i)$$
$$dI_i(t, \lambda_i)/dt = \lambda_i I_i(t, \lambda_i) S_i(t, \lambda_i) - \mu_{i2} I_i(t, \lambda_i)$$

where

$S_i(t, \lambda_i)$ = the fraction of population i that is susceptible at time t
$I_i(t, \lambda_i)$ = the fraction of population i that is infected at time t
λ_i = transmission rate (sufficient contact rate) for population i ($\lambda_i > 0$)
δ_i = entry rate into population i ($\delta_i > 0$)
μ_{i1} = exit rate of susceptibles from population i ($\mu_{i1} > 0$)
μ_{12} = exit rate of infectives from population i ($\mu_{i2} > 0$)

for $i = 1, 2$, $t \geq 0$.

The total number of newly infected people over a given time horizon (from now, time 0, until T time units in the future) in population i (calculated as a percentage) is

$$H_i(\lambda_i) \equiv \int_{t=0}^{T} \lambda_i I_i(t, \lambda_i) S_i(t, \lambda_i)\, dt$$