Preventing HIV in Injection Drug Users: Choosing the Best Mix of Interventions for the Population

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ABSTRACT *Injection drug users (IDUs) transmit the human immunodeficiency virus (HIV) via both needle sharing and sex. This analysis explores the effects of population risk behaviors, intervention effectiveness, intervention costs, and budget and capacity constraints when allocating funds between two prevention programs to maximize effectiveness. The two interventions, methadone maintenance and street outreach, address different types of risk behavior. We developed a model of the spread of HIV and divided IDUs into susceptible (uninfected) persons and infective persons and separately portrayed sex and injection risk. We simulated the epidemic in San Francisco, California, and New York City for periods from the mid-1980s to the mid-1990s and incorporated the behavioral effects of the two interventions. We used the simulation to find the allocation of a fixed budget to the two interventions that averted the greatest number of infections in the IDUs and their noninjecting sex partners. We assumed that interventions have increasing marginal costs. In the epidemic scenarios, our analysis found that the best allocation nearly always involves spending as much as possible on street outreach. This result is largely insensitive to variations in epidemic scenario, intervention efficacy, and cost. However, the absolute and relative benefits of the best allocation varied. In mid-1990s San Francisco, maximizing spending on outreach averted 3.5% of total HIV infections expected and 10 times the 0.3% from maximizing spending on treatment. In late 1980s New York City, the difference is five-fold (2.6% vs. 0.44%, respectively). Our analyses suggest that, even though prevention works better in higher risk scenarios, the choice of intervention mix is more important in the lower risk scenarios. Models and analyses such as those presented here may help decision makers adapt individual prevention programs to their own communities and to reallocate resources among programs to reflect the evolution of their own epidemics.*

KEYWORDS *Economic analysis, Epidemic modeling, HIV prevention, Injection drug users, Resource allocation*

The spread of the human immunodeficiency virus (HIV) among injection drug users (IDUs) remains a significant problem in the United States. IDUs can transmit HIV to needle-sharing partners and to sex partners who may not themselves inject. According to a 1996 study,¹ an estimated 2 million Americans injected illegal drugs at some point in their lives, and 416,000 injected in the previous 3 years. Even as

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late as the mid-1990s, between 40% and 50% of IDUs reported sharing needles,²⁻⁴ and most reported having sex regularly.^{4,5} One study of 96 large metropolitan areas in the United States estimated that 50% of 38,100 new HIV infections occur in IDUs.⁵ More recently, in San Francisco, California, 20% of new HIV infections are estimated to occur in IDUs.⁶

IDUs have sexual contact with non-IDUs, and thus prevention programs aimed to IDUs have the opportunity to avert infections in both populations. Interventions that may directly address sex or drug-related risks include drug treatment, street outreach (SO), counseling and testing, and needle exchange. When successful, drug treatment programs stop drug use and eliminate the HIV infection risk that comes from sharing injection equipment.⁷ Street outreach programs involve counseling for risk reduction and may involve encouraging condom use, the bleaching of injection equipment, or the cessation of needle sharing.⁸⁻¹⁵ Counseling and testing programs provide HIV testing in addition to the kinds of risk reduction counseled in outreach programs.^{11,16} Needle-exchange programs offer sterile syringes to IDUs in exchange for used and potentially infected syringes.^{17,18} These interventions address different aspects of risk for HIV infection and have different costs and varying levels of effectiveness.

Injection and needle-sharing frequencies vary greatly across years and geographic locations.^{3,4,10,19-23} Studies suggest that IDUs have decreased injection risk by reducing or eliminating needle sharing in the last 15 years, since learning about their risk for HIV infection.^{19,24-26} These decreases represent successes of earlier interventions. Some studies also indicate that IDUs have not made commensurate reductions in sexual risk behavior.^{19,26} In fact, one study of IDUs in San Francisco showed that sexual risk factors, rather than injection risk factors, predict seroconversion.²⁷ This change in the ratio of sex to needle-sharing risks suggests that the best prevention strategy of 10 or more years ago may differ from that of today.

Since 1994, state and metropolitan area jurisdictions receiving federal funds for HIV prevention participate in the HIV Prevention Community Planning process.^{28,29} The guidelines issued by the Centers for Disease Control and Prevention (CDC) call for assessments of the current state of the epidemic and the likely effects of interventions in at-risk populations. This process is intended to tailor prevention programs to individual communities and populations. CDC also commissioned a report from the Institute of Medicine (IOM) reviewing HIV prevention efforts in the United States.³⁰ This report recommends that "the nation should have an explicit prevention goal to avert as many new HIV infections as possible with the resources available for HIV prevention" (xii).

Consistent with the IOM recommendation, a growing body of literature proposes the use of policy modeling to determine the best allocation of resources for HIV prevention.³¹ One study developed a framework to determine the best allocation of resources to HIV prevention interventions and populations.³² They considered three noninteracting subsets of patients in a Veterans Affairs hospital: non-IDUs and low- and moderate-risk IDUs. They examined three interventions: HIV testing with routine counseling, HIV testing with intensive counseling, and these interventions combined with drug treatment. For each population, formulas linked the interventions to a reduction in risky behavior and in turn in HIV infections.

They found that,³² for a low-risk IDU population (with an HIV prevalence of 5%), the best allocation spent \$170 per IDU and \$62 per non-IDU, resulting in all IDUs and some non-IDUs receiving testing and intensive counseling. The remaining non-IDUs would receive testing and routine counseling. In the case of the moderate-

risk IDU population (with an HIV prevalence of 10%), the best allocation spent \$198 per IDU and \$57 per non-IDU, resulting in some IDUs receiving testing and routine counseling and some receiving testing and intensive counseling. All non-IDUs would receive testing and routine counseling under this allocation. The analysis results were most sensitive to HIV prevalence and incidence, available budget, and intervention effectiveness.

An analysis that looked at the best allocation of resources to a needle-exchange program, methadone maintenance (MM), and condom availability programs targeted to different population groups found that best allocations varied by epidemic scenario.³³ They found that, in an IDU community with HIV prevalence of 40%, allocating approximately 75% of the budget to needle exchange and 25% to a condom availability program for IDUs maximized the number of HIV infections averted. In an IDU community of lower prevalence (5%), the best allocation spent nearly all funds on methadone maintenance for HIV-positive IDUs.

The IOM Committee on HIV Prevention Strategies in the United States proposed a resource allocation formulation with inputs that include intervention costs and effectiveness (in terms of reduction in HIV infection rate), estimates of HIV incidence by risk group, a budget constraint, and the distribution of the population by risk group.³⁰ The decision variable is the amount of money allocated to a given intervention for each risk group in each geographic area. The objective of the allocation is to prevent as many HIV infections as possible subject to the budget constraint.

The analyses reviewed above emphasize the increases in cost-effectiveness that can be achieved through a sophisticated quantitative approach to resource allocation for HIV prevention. We believe that the success of past HIV interventions in reducing injection risk behavior in the IDU community and the characteristics of the community (i.e., the transmission to non-IDUs, asymmetries in the number of male and female IDUs, and sexual transmission risk) suggest that resource allocation for HIV prevention in IDUs merits analysis of the prevention implications of these important epidemic characteristics. Community groups will be allocating resources to HIV prevention programs for some time, and we believe that those allocations should change as the epidemic evolves.

Our goal for this analysis was to explore the population and intervention characteristics that have the greatest effect on which interventions work best. While the model we present here addresses a simplified version of the decision faced by community groups, it provides insight as to the influence of population and epidemic characteristics on intervention effects and suggests conditions under which more sophisticated approaches to resource allocation should be taken.

In this article, we consider these factors in addressing the following question: Which combination of two interventions in IDUs minimizes the number of new HIV infections given a fixed HIV prevention budget and limited program capacities? We used a compartmental epidemic model to explore the effects of these factors when allocating a budget between two interventions in a heterosexual IDU population that also includes noninjecting sex partners. Specifically, we looked at MM and SO. We focused on this relatively simple example to emphasize the benefits of using a resource allocation approach that incorporates complex, but real and important, epidemiologic phenomena. We selected this intervention pair to represent distinctly different prevention strategies: an expensive, effective, and narrowly focused intervention versus an inexpensive, moderately effective intervention that addresses both sex and drug risk.

We considered the allocation of resources as a function of intervention cost and effectiveness, as well as population risk behaviors in different times and places. We developed six epidemic settings defined by geographic location (New York City and San Francisco) and time period based on observed risk behaviors and HIV prevalence. Our model portrays IDUs (male and female), both receiving the intervention and not, and their non-IDU sex partners. We differentiated between sex and needle-sharing risk and characterized the interventions with respect to their effects over time on these individual risks. Our analyses expand on the those described above by tying epidemic scenarios to time and place by risk behaviors and HIV prevalence and incidence, by modeling in detail the asymmetries between male-female population sizes and sexual transmission risk, and by including transmission to non-IDU sex partners.

METHODS

As described below, we developed a compartmental epidemic model of the spread of HIV through sex and needle sharing. We used this model to estimate the allocation of a \$1 million budget between MM and SO that averts the greatest number of HIV infections in both IDUs and their sex partners. An allocation determined how much money will be spent on each of the two interventions and hence how many IDUs would be reached by each. The epidemic model consists of compartments defined by HIV status (positive or negative), gender, injection behavior, and intervention received. Given a resource allocation, the model estimated the number of HIV infections expected over 5 years, the period evaluated in similar analyses.^{32,34} The full model specification is described elsewhere.³⁵

We modeled a population of 10,000 heterosexual IDUs, 7,500 male and 2,500 female, and 5,000 heterosexual female non-IDU sex partners of male IDUs. The relative sizes of these populations reflect what is commonly observed in IDU populations.^{36–40} We included only female non-IDU sex partners because studies have estimated that half of the sex partners of male IDUs are not IDUs themselves, while most sex partners of female IDUs are IDUs.⁴⁰

Epidemic-Intervention Model

In the epidemic-intervention model, an individual can be in one of two disease states: susceptible or infective (i.e., HIV negative or HIV positive). Disease states are represented by compartments. Compartments are also defined by gender, intervention received, and injection status (e.g., IDU or non-IDU). We assumed that all new entrants were uninfected, and both IDUs and non-IDUs left the population only through death. The rate at which individuals moved from the susceptible to the infective compartments was in part a function of two types of risk parameters: effective infectivity and activity level.

These parameters were defined for both needle-sharing and sex risk behaviors. *Effective infectivity* is the probability of contracting HIV in one exposure to an infected person given typical protective behaviors (e.g., condoms or bleaching). This value combines biological infectivity with the prevalence and efficacy of protective behaviors. Activity level represents the number of potentially infectious exposures per year: the number of sexual partnerships and the number of needle-sharing episodes (using a needle after someone else).⁴¹

We assumed that interventions work by decreasing activity level or by increasing protective behaviors, and these changes can be represented by changes to the

relevant risk parameters. Thus, IDUs receiving an intervention were represented by compartments with lower risk parameter values. If two interventions were implemented, the IDU population was partitioned into four subgroups: individuals receiving no intervention and those receiving only MM, only SO, and both. This partitioning leaves 18 model compartments: (2 IDU genders * 2 HIV statuses * 4 intervention states) + (1 non-IDU gender * 2 HIV statuses).

IDUs can contract HIV through either sexual or needle-sharing activity. In addition to the risk parameters associated with those activities, the rate of infection through either route is a function of the HIV prevalence in the partner population. Partner HIV prevalence varies over time as a function of infection, entry, and death rates. We assumed that risk behavior did not vary within compartments and did not change over time. We assumed no differences between the sexual risk behaviors of female IDUs and those of non-IDUs. We did not consider transmission from mother to child.

In the San Francisco epidemic scenarios, we assumed that proportionate mixing occurs for both sex and needle sharing. *Proportionate mixing* means that partnerships are formed at random, and thus the probability that a given partner is HIV positive is equal to the prevalence of HIV in the partner population. For New York City, we assumed preferential mixing by HIV status occurs. With *preferential mixing*, partnerships are not formed at random. Preferential mixing is likely to occur in populations with substantial HIV spread if partners remain together after one has infected the other. For New York City, we said that a susceptible person was 60% less likely to form a partnership with an infective person than he or she would be if mixing at random, reducing the average prevalence faced by each susceptible person by 60%. This assumption produced baseline HIV incidence predictions that are more consistent with published estimates for New York City during the time periods of interest.

HIV and Population Dynamic Parameters

The model describes how individuals move into and out of compartments through entry (new IDUs entering the population), HIV infection, and death. In this section, we describe parameter values that drive HIV risk and describe population dynamics. Table 1 shows baseline parameter values for effective infectivity, sex activity level, and population dynamics. Table 2 shows needle-sharing activity and baseline

TABLE 1. Baseline parameter values for HIV risk (activity levels and infectivity) and population dynamics

Parameter	Value	Reference
Sex effective infectivity, female to male (probability per partnership)	0.07	42
Sex effective infectivity, male to female	0.10	42
Number of sexual partnerships per year	3	26
Needle-sharing infectivity (probability per needle share)	0.0029	43, 44
Proportion reduction in infectivity due to observed levels of bleaching	0.16	10, 15, 19, 20, 25, 45–47
Needle-sharing effective infectivity* (probability per needle share)	0.0027	—
Entry rate (individuals per person per year)	0.08	—
Susceptible exit rate	0.08	48, 49
Infective exit rate	0.15	50

*Effective infectivity was adjusted for protective behavior.

TABLE 2. Number of needle-sharing episodes per year and baseline HIV prevalence in IDUs for different time periods in San Francisco, California, and New York City

City	Time	Number of shares/year	HIV prevalence	Reference
San Francisco	II	90	0.16	51, 52
San Francisco	III	45	0.15	17, 53
San Francisco	IV	15	0.14	5, 54
New York	I	300	0.50	55, 56
New York	II	90	0.50	55, 57
New York	III	35	0.35	55, 56

Time I = mid-1980s; II = late 1980s; III = early 1990s; IV = mid-1990s.

HIV prevalence for six different epidemic scenarios. These two tables summarize all of the population and risk inputs required by the model; the discussion below provides justification for those values.

We estimated that the infectivity for a single unbleached exposure to an infected needle was 0.0029. This was based on empirical evidence from health care worker exposures,⁴³ our prior examination of needle-sharing data,⁴⁴ and consistency of model-predicted HIV incidence with observed incidence. As with all inputs, we varied this in sensitivity analyses. We decreased infectivity to account for protection afforded by bleach use. Exposure to undiluted bleach for 30 seconds can inactivate the HIV virus⁴⁵; given that they bleached, approximately 20% of injectors achieve this standard.⁴⁶ Of injectors, 10% to 70% bleach^{10,15,19,20,25,47}; we assumed 40% do so.

Thus, we estimated that the proportion of IDUs that bleach and do so effectively enough to eliminate risk through bleaching was $0.2 * 0.4 = 0.08$. The overall baseline effective infectivity for an episode of needle sharing for the whole population was then $0.0029(1 - 0.08) = 0.0027$.

Sexual infectivity was estimated based on per-partnership estimates from the literature, adjusted to annual risk and for condom use. We estimated annual risk by assuming that partnerships last 3 years on average (i.e., we divided by 3). Condom use in partnership studies was very low; we assumed a use rate of 20% in our population. If used, condoms are estimated to be 90% effective in stopping HIV transmission.⁵⁸ Combining these two estimates yields a condom-related risk reduction of $0.2 * 0.9 = 0.18$. Given a 0.38 male-to-female per-partner infectivity,⁴² we arrived at our parameter estimate by adjusting simultaneously for relationship duration and condoms. Hence, the baseline estimate for male-to-female partnership effective infectivity was $0.38 * 1/3 * (1 - 0.18) = 0.103$.

Behavioral studies suggest that IDUs have decreased injection risk (but not sex risk) in the last 10 years, and that these risks vary significantly by location. For example, in eight cities studied between 1987 and 1991, IDUs reported nearly 30% less sharing of needles in the last year than in the first.⁵⁹ We used the reported number of needle-sharing episodes and HIV prevalence to define six epidemic scenarios in San Francisco and New York City in the mid-1980s, late 1980s, early 1990s, and mid-1990s (Table 2). In early 1990s San Francisco, the baseline value for annual needle-associated HIV incidence (the product of sharing frequency, HIV prevalence, and effective infectivity) was $45(0.15)0.0027 = 0.018$.

In the absence of interventions, the model predicted annual HIV incidence rates in the IDU population that correspond approximately to published estimates. For example, in late 1980s San Francisco, our model predicted an HIV incidence rate of 6.1% in IDUs; published estimates of incidence range from 1.9% to 7.9% in that time period.^{60,61} In late 1980s New York City, the model estimated an HIV incidence of 7.5% in IDUs; published estimates range from 3.0% to 9.0%.⁶²

Several difficulties arise when trying to use published estimates of HIV incidence to benchmark the model. For example, time periods for the incidence estimates may not correspond exactly with time periods for the risk behaviors on which the model predictions of incidence are based. Furthermore, the populations on which published incidence estimates are based (e.g., IDUs entering treatment) may not correspond to the population represented by the model.

Intervention Effect Parameters

If an individual responds, interventions work by decreasing the activity level or increasing protective behaviors for sex or drug-related risks. These effects were represented in the model by changes to the sex- and drug-related infectivity and activity level parameters. Thus, we described each intervention by a probability of response and four values describing the magnitude of the effect.

The goal of MM is to stop drug use. It is successful both in reducing the prevalence of injecting and in reducing sharing in those who continue to inject.^{63–66} For example, one study reported a 78% decrease in the prevalence of self-reported drug use 3 months into treatment,⁶⁶ and a second study reported a 59% decrease in the prevalence of sharing given that injection still occurred 3 months into treatment.⁶⁵ We incorporated both types of reduction in the estimates of drug treatment effectiveness and thus assumed that MM reduces injection risk by decreasing activity by 85%. We assumed that MM does not affect infectivity and has no effect on either of the sexual risk parameters.

In this model, SO was defined as a program that includes bleach and condom distribution, as well as risk reduction counseling for both risk behaviors.^{13,67–69} Observed increases in bleach and condom use translate to reduced sex and drug infectivity parameters, and observed decreases in both sex and needle-sharing partners translate to reduced sex and drug activity level parameters. Reductions in effective infectivity are a function of condom and bleach use and effectiveness. We assumed that SO reduces sexual infectivity by 13% and activity by 16% and reduces injection infectivity and activity level by 3% and 30%, respectively.

The preceding estimates for intervention effectiveness reflect the effects of an intervention on an individual's behavior if the individual responds to the intervention. Not all individuals, however, do respond. In this analysis, we estimated that 80% of IDUs respond to MM^{34,70} and 50% to SO.¹² Incorporating these response rates decreased the intervention effectiveness described above by focusing risk reduction in a smaller group of individuals. This is a conservative interpretation that may underestimate intervention benefits.

We assumed that interventions are implemented in the population uniformly with respect to gender and infection status. We assumed that intervention effects on behavior persist throughout the analysis period. We also assumed that these interventions will be in addition to interventions already in place. For example, 10%–20% of the population is in drug treatment at any given time,⁵ and our analysis assessed the benefits of having additional IDUs in treatment.

Intervention Cost Parameters

An allocation determines how many IDUs can be reached by each intervention. We assumed that both interventions exhibited increasing marginal costs reflecting the increasing difficulty of recruiting more clients. Thus, intervention cost parameters consisted of a per-person cost and a rate of increase for each intervention. We assumed that the rate of increase for SO is higher than that for MM to represent the idea that, because SO has a higher client load, each successive person is more difficult, and costly, to contact. For MM, on the other hand, limited treatment capacity usually ensures that new participants are relatively recruitable.²⁵

The baseline intervention delivery cost estimates (per person per year) used in the analysis for MM (P. G. Barnett and J. H. Rodgers, personal communication, 1999) and SO⁷¹ were \$4,750 and \$210, respectively. Details of the cost function are provided elsewhere.³⁵ We also assumed capacity limits for each intervention of 500 clients for MM and 2,500 for SO. An alternative interpretation of the capacity limit is that it represents the maximum number of IDUs reachable by the intervention.³⁰

Implementation

The compartment model consists of a system of dynamic equations that determine the number of individuals in each compartment at any time. To estimate the effects of a given resource allocation, we simulated the system for a 5-year period (updating the compartment sizes every one tenth of a year) and counted the number of new HIV infections that occurred by counting the number of individuals who transitioned from an HIV-negative compartment to an HIV-positive compartment. Simulating the system with no intervention strategies in place yielded a baseline number of infections used to calculate the number of infections averted by any strategy. We modeled the dynamic equations using the Simulink Toolbox (ver. 3), Matlab (ver. 6.0) (both from Mathworks Inc., Natick, MA, 2000) in the Windows 2000 operating system.

RESULTS

We first present detailed results for San Francisco in the early 1990s and then discuss how those conclusions vary by epidemic scenario and under differing assumptions about HIV risk and intervention effectiveness and costs. In this epidemic scenario, the model predicts that 3,556 HIV infections occur in a 5-year period if no intervention takes place; 1,566 of these occur in male IDUs, 750 in female IDUs, and 1,240 in female non-IDUs. This scenario produces an initial annual HIV incidence of 3.9% in IDUs.

Different allocations of the budget between MM and SO yielded different numbers of HIV infections averted, ranging from 17 to just over 141. Spending 80% of the intervention budget on SO, the maximum allowed by capacity constraints, resulted in the greatest number of infections averted (141). Therefore, this is the best strategy and reaches 25% of IDUs with SO and less than 1% of IDUs with MM. The worst strategy would be to allocate the entire budget to MM (resulting in only 17 infections averted). The best strategy resulted in more than seven times as many infections averted. We think of this 710% improvement as a measure of the value of the best allocation.

As suggested, observed changes in the HIV epidemic in IDUs may be explained by changes in the number of needle-sharing episodes and HIV prevalence. In this

section, we explore the best allocation for different time periods in New York City and San Francisco, where each epidemic scenario was defined by baseline values for needle-sharing rate and HIV prevalence. In each of these scenarios, a different number of infections is possible.

To compare results across scenarios, in Fig. 1 the vertical axis indicates the percentage, rather than the total number, of total possible infections averted. The horizontal axis represents the percentage of the total budget allocated to SO (with the remainder allocated to MM).

In all three San Francisco epidemic scenarios, spending as much as allowed on SO averts the greatest number of infections (Fig. 1a). Although the absolute number of infections averted is highest in the riskier late 1980s, the maximum benefit de-

FIGURE. Percentage of possible HIV infections averted by percentage of budget spent on street outreach (SO) (with remainder spent on methadone maintenance, MM) for various periods in (a) San Francisco, California, and (b) New York City.

rived from the best allocation (1,700% improvement over the worst allocation) occurs in the lower risk period, the mid-1990s.

The HIV epidemic among IDUs in New York City has been characterized by higher HIV prevalence than found in San Francisco. As in San Francisco, however, our model predicted that the best prevention strategy was to spend as much as possible on SO (Fig. 1b). In all three scenarios, the best allocation averted approximately 2.5% of total possible infections. In both Fig. 1a and Fig. 1b, a steeper line slope indicates greater difference in effectiveness between MM and SO. The lines are less steep in scenarios with higher (injection) risk, and MM comes closer to being included in the best allocation in these scenarios. The value of the best allocation in New York City was greatest for the least risky, early 1990s scenario, with a 900% improvement. In the highest risk scenario (mid-1980s), the best allocation yielded a 250% improvement. In San Francisco, we also saw that the value of the best allocation increased as the level of riskiness decreased. In both cities, the value of the best allocation was greatest in the low-risk scenarios because the injection risk targeted by the less-effective intervention, MM, contributed less to overall risk.

Sensitivity Analysis

Figure 1 shows that the best allocation does not vary for the different levels of injection risk in these scenarios. In fact, a two-way sensitivity analysis for the scenario corresponding to San Francisco in the early 1990s showed that the best allocation did not vary as a function of two important behavioral risk factors (number of sexual partnerships per year and number of needle-sharing episodes per year).

For example, even if no sexual relationships occurred, the rate of needle sharing had to increase to 600 times per year for MM to be included in the best allocation. We see a similar insensitivity of the best allocation to drug and sex infectivity. Even if both male and female sexual infectivity were reduced to 0, the infectivity of a single needle-sharing episode would have to increase from 0.0029 to 0.036 for MM to be included in the best allocation. And, as sexual infectivity increases, the needle-sharing infectivity would have to increase even further for MM to be included in the best allocation.

Intervention costs, program capacities, and budget define which allocations are possible, as well as affecting which are best. When we varied intervention costs in the early 1990s San Francisco scenario, even for a large amount of uncertainty about costs, SO played the largest role in the best resource allocations. If the cost of SO drops, the capacity limit will be reached more quickly, and MM is more likely to be included in the best allocation. Given increasing marginal costs, there are combinations of high-cost SO and low-cost MM for which the best strategy mixes the two interventions. With constant or decreasing marginal costs, however, the best combination will never be a mix of two interventions unless that mix is forced by capacity constraints.

Our sensitivity analyses also showed that, for these two interventions, the best allocation was relatively insensitive to intervention effectiveness. Recall that SO provided modest relative reductions in sex and drug activity levels and infectivities; MM provided a significant reduction in only one of the four risk factors, drug activity level. Given these intervention foci and baseline costs, it turned out that the best allocation varied little with variation in any one of these individual risk reductions. In the baseline scenario (mid-1990s San Francisco), SO was the most cost-effective strategy no matter the degree that either SO or MM reduced injection activity. Even if MM were shown to reduce sex risk, its significant cost meant it

would have to eliminate nearly all sexual activity to become competitive with SO. If MM encouraged condom use, it would start to become competitive with outreach if it reduced sexual infectivity by 50% (outreach reduced this parameter by 13%).

Finally, we chose the best resource allocation by finding the one that averted the most HIV infections. Other analyses have looked at maximizing the number of quality-adjusted life years (QALYs).^{32,33} In general, decreasing HIV infections increases QALYs. Some interventions may further increase QALYs, independent of preventing HIV. For example, successful drug treatment increases quality of life, and hence QALYs, by interrupting an individual's dependence on illicit drugs. If we chose a resource allocation to gain the greatest number of QALYs possible, we would expect MM to be more competitive with SO. On the other hand, a simple calculation suggests that SO would still be the preferred intervention.

For example, if we consider the riskiest scenario, mid-1980s New York City, and assume that each HIV infection averted saves 11 QALYs, we can compare the QALYs gained for SO and MM. If being in MM generates a quality-of-life-based gain of 11% per client-year³³ and MM averts 43 infections in a population of 10,000 IDUs, then the overall gain in QALYs due to MM is approximately 0.05 per client-year. If we conservatively assume no QALYs gained from SO above and beyond HIV prevention, that intervention averts 152 HIV infections and yields an increase in QALYs of 0.17. This rough estimate does not include long-term cessation of drug use after leaving MM. It does suggest that HIV prevention effects are not overwhelmed by QALY effects, and that the results of our analysis would not change significantly if we were to use this outcome measure.

DISCUSSION

Designing the best intervention strategy for the prevention of HIV in an IDU population is challenging because of the multitude of factors that influence prevention effectiveness. IDUs face two types of risk for HIV, and the available interventions may address either or both of those risks to different degrees and at different costs. We used a compartmental epidemic model to explore the effects of these factors when allocating a budget between two interventions to avert the greatest number of infections in a heterosexual IDU population that also includes noninjecting sex partners. Our analysis showed that, given a fixed budget, SO averts more HIV infections than does MM in the epidemic scenarios we considered. The high cost and narrow focus of MM make it less cost-effective for HIV prevention in these scenarios, and the decreasing injection risks among IDUs amplify this finding.

In general, the best resource allocation is a function of budget, drug- and sex-related HIV risks, and intervention efficacy, cost, and program capacity. We explored the effects of most of these factors on the best budget allocation and showed that SO is a more effective HIV prevention intervention than MM for several epidemic scenarios when the budget is limited. Several inputs to the model are independent of these factors, and while they affect the number of infections that occur in a given scenario, they have no effect on the best allocation of resources between the two interventions. These inputs include population dynamics (e.g., entry and death rates) and initial HIV prevalence. We also explored the effects of different entry rates for IDUs and non-IDUs and the effects of increased mortality for susceptible non-IDUs and found that neither affected the best resource allocation.

Another analysis of resource allocation for HIV prevention in IDUs found one case for which MM is most cost-effective in comparison to a condom availability

program targeted to IDUs: for HIV-positive IDUs when HIV prevalence is low.³³ This result is not inconsistent with our analysis, but rather highlights the potential benefits of targeting interventions to infective individuals when the prevalence is very low and the source of infections is concentrated in a small number of persons.

Our analysis should not be used to conclude that MM is a poor use of prevention resources. In fact, other researchers have concluded that methadone maintenance is a cost-effective intervention in general and a cost-effective HIV prevention approach in particular. In fact, one study of both high and low HIV prevalence scenarios concluded that, in both cases, in terms of dollars spent per QALY gained, increasing methadone maintenance capacity was a very reasonable expenditure compared to many other interventions.^{72,73} The authors used an epidemic model to assess the cost-effectiveness of expanded methadone maintenance capacity with respect to costs and QALYs. They concluded that additional MM capacity would result in costs of \$8,200 per QALY gained in a high-prevalence community and \$10,900 per QALY in a low-prevalence community. The cost-effectiveness ratio reflects, in part, reductions in HIV care costs related to averted HIV infections.

Another study looked at the cost-effectiveness of methadone maintenance solely with respect to preventing HIV infections in a self-contained population of IDUs.⁷⁴ This research estimated average cost per HIV infection averted under different assumptions about active needle sharing, treatment compliance, and relapse. The lowest cost, \$100,000, arose in the scenario with full compliance, the most optimistic assumption about relapse, and the highest level of active needle sharing. The highest cost, nearly \$970,000, arose in the scenario with nearly complete relapse, 50% treatment compliance, and minimal active needle sharing. While this analysis did not explicitly explore cost-effectiveness in different periods of the epidemic, the author did note that treatment is becoming less cost-effective as the rate of needle sharing has decreased over time. The results are less attractive than ours (between \$23,000 and \$211,000 per HIV infection averted) primarily because our model does not account for relapse from treatment and because our model tracks infections averted in non-IDU sex partners. Finally, a study of the overall benefits to society of methadone maintenance found it to be cost-saving.⁷⁵

Some limitations of this research relate to the framing of the question and to available data. Perhaps most important, for purposes of analytic simplicity, we considered only two interventions. Even if they focus only on the IDU population, policymakers who make resource allocation decisions will likely face more than two intervention choices, making the decision even more complex. We chose epidemic scenarios to exhibit a broad range of HIV incidence and thus include the early stages of the epidemic. While our policy conclusions did not vary by scenario, the results showed that the benefit of the best resource allocation was greatest in the most recent scenarios. This suggests that this kind of resource allocation modeling can continue to have relevance for policymakers.

We are now developing other intervention comparisons using the same model. While our analysis used the best available data to estimate the effects of street outreach, we believe that our sensitivity analysis showed that even if we had significantly overestimated the effectiveness of the intervention, it would still outperform MM.

Other limitations involve modeling assumptions. Our analysis estimated the effects of one-time interventions over a 5-year period. This approach is adequate for making a resource allocation in which issues of intervention timing do not arise, as in an annual budget allocation process. To answer questions about the eradica-

tion of the HIV epidemic or the optimal size of an intervention budget or to estimate future HIV incidence or prevalence, it would be appropriate to model repeated applications of interventions and even to model dynamic resource allocation over a multiyear period. If we were to consider repeated interventions, we could analyze the tradeoffs between spending additional budget on reaching more people (perhaps increasing program capacity) and increasing frequency of intervention for a fixed group of people. While we portrayed the effects of the two interventions on HIV risk as independent, the model provides a framework in which these kinds of dependencies could be explored.

We have seen that program capacity constraints may have an effect on the best allocation. This points to the need for further analysis of the fixed and variable costs associated with increasing program capacity. Consistent with IOM recommendations, the goal of our analysis was to find the resource allocation that resulted in the fewest new HIV infections. As discussed, this goal will not favor interventions such as MM that are expensive and have benefits above and beyond HIV prevention.

Finally, our model population did not include men who have sex with men, a population that faces a significant risk for HIV infection. Including this population, which faces a significant risk for sexual transmission, would likely increase even further the advantages of SO over MM.

Allocating resources to HIV prevention programs is a task that will be faced by community planning groups and other decision makers for the foreseeable future. That the ratio between injection- and sex-related risks has changed so dramatically in the last 10 years is a testament to the success of interventions that educate IDUs about the risk of HIV infection inherent in the sharing of injection equipment.

Our analyses suggest that, even though prevention works better in the higher risk scenarios, it is more important to choose the right allocation in the lower risk scenarios. Models and analyses such as those presented here may help decision makers adapt individual prevention programs to their own communities and to reallocate resources among programs to reflect the evolution of their own epidemics. This work adds to the body of knowledge about cost-effective HIV prevention in IDUs and is part of a set of information available to policymakers. In particular, this research points out the apparent cost-effectiveness of street outreach, which has not been addressed elsewhere. In future research, we plan to include other interventions, such as needle exchange and counseling and testing in the resource allocation decision.

ACKNOWLEDGEMENT

Financial support for this study was provided in part by grants from that National Institute on Drug Abuse (R01 DA09531 and R01 DA15612). The funding agreements ensured the authors' independence in designing the study, interpreting the data, and writing and publishing the report.

We thank the following individuals at the University of California, Berkeley, for their comments on the model: Shmuel S. Oren and C. Roger Glassey in the Department of Industrial Engineering and Operations Research; and Robert M. Anderson in the Department of Economics. We also thank Dan Wohlfeiler at the School of Public Health, University of California, Berkeley, and Edward H. Kaplan at the Yale School of Management for their critiques of the manuscript.

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