

Methadone Maintenance and HIV Prevention: A Cost-Effectiveness Analysis

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We assess the cost-effectiveness of maintenance treatment for heroin addiction, with emphasis on its role in preventing HIV infection. The analysis is based on a dynamic compartmental model of the HIV epidemic among a population of adults, ages 18 to 44. The population is divided into nine compartments according to infection status and risk group. The model takes into account disease transmission from drug injection and sexual contacts. The health benefits of methadone maintenance and the resulting HIV infections averted are measured in terms of life years gained and quality-adjusted life years gained. Costs considered include all health-care costs (including cost of HIV care and other health care) and the cost of methadone maintenance. The analysis shows that expanding existing methadone maintenance programs is a cost-effective health-care intervention that can play an important role in slowing the spread of HIV and improving the length and quality of life for injection drug users (IDUs), and that such expansion is cost-effective even in populations with low HIV prevalence among IDUs. Incremental expansion of methadone maintenance programs was found to have a cost-effectiveness ratio of between \$9,700 and \$17,200 per life year gained, and between \$6,300 and \$10,900 per quality-adjusted life year gained. Although methadone maintenance treatment is provided to IDUs, the analysis shows that significant benefits accrue to non-IDU members of the population. Sensitivity analysis shows that new methadone maintenance treatment slots will be cost-effective even if they are twice as expensive and half as effective in reducing risky behavior as current methadone maintenance programs.

(Health; Public Policy; Cost-Effectiveness Analysis; Methadone; HIV/AIDS)

1. Introduction

Injection drug use is a principal means of transmission of human immunodeficiency virus (HIV) in many populations. Currently in the United States, some 40% of all new HIV cases and 75% of new HIV cases among women and children are the result of injection drug use, either directly (among injection drug users (IDUs)) or indirectly (among sex partners of IDUs). HIV prevalence among IDUs has been estimated to be 4%–7% in Los Angeles (Bellis 1993), 9%–13% in San

Francisco (Moss et al. 1994), and 40%–60% in New York City (Des Jarlais et al. 1994).

Methadone maintenance treatment is one means of controlling the spread of HIV among IDUs. However, an estimated 1 million–1.5 million people in the United States are injection drug users (Gleghorn et al. 1995, Hahn et al. 1989), but only about 115,000 methadone maintenance slots are available (Rettig and Yarmolinski 1995). In many places, the average wait for an IDU to enter a methadone maintenance program is six months

or more. Restrictive regulations, inadequate funding, and many other factors have limited the number of individuals who receive treatment (Cooper 1989, McAuliffe 1990). In New York City, Mayor Giuliani recently proposed eliminating publicly funded methadone maintenance programs (Swarns 1998).

Some work has been done to assess the costs and benefits of interventions aimed at slowing the spread of HIV among IDUs, such as needle-exchange programs (Kahn 1993, Kaplan 1995), needle-bleaching programs (Siegel et al. 1991), and the introduction of difficult-to-reuse syringes (Caulkins et al. 1998). Less work has been done to assess the costs and benefits of methadone maintenance programs. Empirical studies have shown that methadone maintenance can reduce the risk behaviors that can lead to HIV infection (e.g., Bellis 1993, Hubbard et al. 1989, Meandzija et al. 1994, Metzger et al. 1998) and can reduce HIV incidence among IDUs in treatment (e.g., Metzger et al. 1993). However, these studies have not attempted to measure the economic costs and health consequences of methadone maintenance.

A number of studies have investigated the costs and benefits of methadone maintenance (e.g., Gerstein et al. 1994, Harwood et al. 1995, Maidlow and Berman 1972, Scanlon 1976). These studies analyzed how methadone maintenance treatment reduces the costs that addicted individuals impose on the health, welfare, and criminal justice systems, and losses due to property theft and other crime. These studies found reduced property theft to be the principal benefit of treatment. However, the inclusion of welfare payments and property losses suffered by victims of crime as benefits of treatment deviates from current Public Health Service guidelines for cost-effectiveness studies of health-related interventions (Gold et al. 1996), which specify that analyses should take a societal perspective. Property losses and welfare payments are transfer payments that have no net effect on society. Additionally, none of these studies has measured the effect of methadone maintenance on life years of survival. Failure to consider the effect of treatment on length of life may understate the value of treatment and lead to a "mortality paradox": An analysis that does not value years of survival or quality of life is

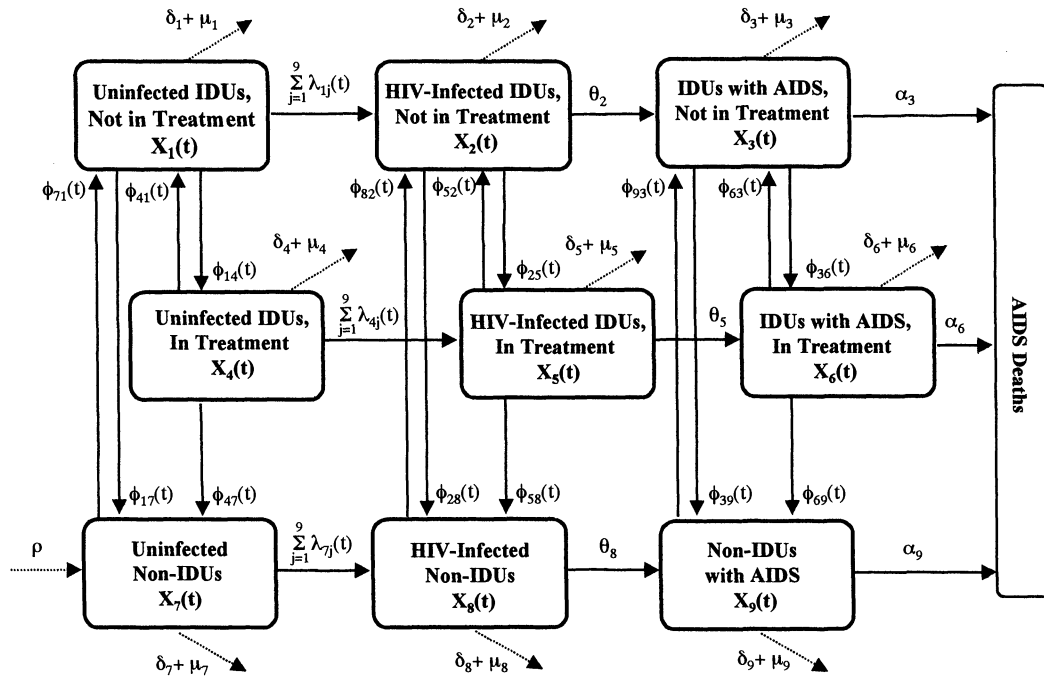
likely to find the intervention with the highest mortality rates to be the most cost-effective.

Barnett (1999) analyzed the cost-effectiveness of methadone maintenance as a general health intervention. Treatment benefit was measured in terms of incremental life years lived among IDUs in treatment. Using data on observed reductions in mortality among IDUs in methadone maintenance programs in Sweden, he estimated that providing IDUs with access to methadone maintenance has a net incremental cost of \$5,915 per life year gained. However, the analysis did not explicitly account for reductions in HIV and related mortality among IDUs and in the rest of the population that would occur due to expansion of treatment programs.

Kahn et al. (1992) used a model-based analysis to estimate the cost of providing methadone maintenance treatment to IDUs in two cities, and to estimate the number of HIV infections that would be averted among IDUs, their sex partners, and offspring over a five-year period as a result of a single year of methadone maintenance. HIV incidence was modeled using a five-year epidemic model comprising 10 six-month cycles. The authors estimated that methadone maintenance treatment would cost approximately \$40,000–\$50,000 per HIV infection averted. The authors considered only the cost of methadone maintenance treatment; they did not consider changes in health-care costs that would occur, nor did they explicitly consider changes in mortality that would occur among IDUs in methadone maintenance.

This paper applies a dynamic model to assess the cost-effectiveness of methadone maintenance treatment (MMT), with particular emphasis on its role in controlling the spread of HIV. Use of a dynamic model allows us to model the flow of IDUs into and out of treatment and into and out of injection drug use, as well as to model changes in HIV transmission among IDUs and in the rest of the population that are brought about by providing IDUs with MMT. We use the model to assess the cost-effectiveness of expanding existing MMT programs in four populations of IDUs, distinguished by the prevalence of HIV among the IDUs (5%, 10%, 20%, and 40%). We also assess the cost-effectiveness of adding incremental treatment slots that are less effective in reducing risky behavior

Figure 1 Schematic of Compartmental Model of HIV Epidemic and Methadone Maintenance Treatment



and/or more expensive than current MMT slots. Following standard cost-effectiveness analyses for health-related interventions (Gold et al. 1996), costs considered include all health-care costs, including HIV care and other health care, as well as the cost of MMT. Health benefits are measured in terms of life years gained and quality-adjusted life years gained.

Section 2 presents our model and the data we used. Section 3 describes the health and economic outcomes we measured using the model. Section 4 presents our results. We conclude with discussion in §5.

2. Model and Data

Our analysis is based on a dynamic compartmental model of the HIV epidemic in a population of individuals aged 18 to 44. A schematic of the model is shown in Figure 1. All notation is defined in Table 1. The population is divided into nine compartments according to HIV infection status (uninfected, infected without AIDS, and AIDS) and risk group (IDUs not in treatment, IDUs in treatment, and non-IDUs (individuals who do not inject drugs)). The number of individuals in compartment i ($i = 1, \dots, 9$) at time t is denoted by $X_i(t)$.

Entry into the population occurs at rate ρ via maturation of 17-year-olds, all of whom enter the uninfected non-IDU compartment (Compartment 7). Exit out of the population from compartment i occurs via maturation of 44-year-olds at rate μ_i ($i = 1, \dots, 9$), via death from non-AIDS causes at rate δ_i ($i = 1, \dots, 9$), and via death from AIDS at rate α_i ($i = 3, 6, 9$).

Infection transmission, represented by the leftmost horizontal arrows in Figure 1, occurs through drug injection among IDUs and through sexual contact of uninfected individuals with any infected member of the population (anyone in Compartments 2, 3, 5, 6, 8, or 9). The rate of sufficient contact (i.e., the rate of contacts that are sufficient to transmit HIV infection) between uninfected individuals in compartment i ($i = 1, 4, 7$) and individuals in compartment j ($j = 1, \dots, 9$) is denoted by $\lambda_{ij}(t)$. The number of individuals in uninfected compartment i ($i = 1, 4, 7$) who become newly infected at time t is given by

$$X_i(t) \sum_{j=1}^9 \lambda_{ij}(t) \quad i = 1, 4, 7.$$

Table 1 Notation

Indices

- t = time index ($t \geq 0$)
 i, j = index for compartments ($i, j = 1, \dots, 9$)
 R = index for risk level of sexual contacts; H = high risk (no condom), L = low risk (with condom)

Parameters

- ρ = rate of entry into the population
 μ_i = rate of maturation out of the population from compartment i ($i = 1, \dots, 9$)
 δ_i = non-AIDS death rate for individuals in compartment i ($i = 1, \dots, 9$)
 α_i = AIDS death rate for individuals in compartment i ($i = 3, 6, 9$)
 θ_i = rate of AIDS development for individuals in compartment i ($i = 2, 5, 8$)
 I_i = average number of injections per year for individuals in compartment i ($i = 1, \dots, 6$)
 s_i = fraction of injections for which individuals in compartment i share a needle ($i = 1, \dots, 6$)
 τ_{ij}^I = chance of infection transmission to an individual in compartment i ($i = 1, 4$) per risky injection shared with a person in compartment j ($j = 1, \dots, 6$)
 P_i = average number of new sexual partnerships per year for individuals in compartment i ($i = 1, \dots, 9$)
 τ_{ij}^S = chance of infection transmission to an individual in compartment i ($i = 1, 4, 7$) per unprotected sexual partnership with a person in compartment j ($j = 1, \dots, 9$)
 d_i = condom usage rate by individuals in compartment i ($i = 1, \dots, 9$)
 ce = condom effectiveness in preventing the chance of HIV transmission
 G_i = proportion of sexual partnerships of individuals in compartment i ($i = 1, \dots, 6$) that are with other IDUs
 $\phi_{ij}(t)$ = rate of transition between compartments i and j at time t due to movement of IDUs out of treatment and movement of individuals between no injection drug use and injection drug use ($t \geq 0, i, j = 1, \dots, 9$, excluding $(i, j) = (1, 4), (3, 5), (3, 6)$)

Calculated Quantities

- $X_i(t)$ = number of people in compartment i at time t ($i = 1, \dots, 9, t \geq 0$)
 $\lambda_{ij}(t)$ = sufficient contact rate between members of compartment i ($i = 1, 4, 7$) and compartment j ($j = 1, \dots, 9$) at time t
 $\gamma_{ij}(t)$ = sufficient contact rate between members of compartment i ($i = 1, 4$) and compartment j ($j = 1, \dots, 6$) at time t due to drug injection
 RI_i = average number of risky injections (those with an infected needle) per year for individuals in compartment i ($i = 1, \dots, 6, R = L, H$)
 $\beta_{ij}^R(t)$ = sufficient contact rate between members of compartment i ($i = 1, 4, 7$) and compartment j ($j = 1, \dots, 9$) at time t due to sexual partnerships of risk R ($R = L, H$)
 P_i^R = average number of new sexual partnerships of risk R per year for individuals in compartment i ($i = 1, \dots, 9, R = L, H$)
 $M_{ij}^R(t)$ = chance that an individual in compartment i has a sexual partnership of risk R with an individual in compartment j at time t ($i, j = 1, \dots, 9, R = L, H$)
 $SCI_j^R(t)$ = total number of IDU-with-IDU sexual contacts of risk R that an individual in compartment j has with other IDUs at time t ($j = 1, \dots, 9, R = L, H$)
 $SCO_j^R(t)$ = total number of other sexual contacts (those that are not IDU with IDU) of risk R that an individual in compartment j has at time t ($j = 1, \dots, 9, R = L, H$)
 $\phi_{ij}(t)$ = rate of transition of untreated IDUs in compartment i into treatment compartment j at time t ($(i, j) = (1, 4), (3, 5), (3, 6), t \geq 0$)

The sufficient contact rate $\lambda_{ij}(t)$ is calculated as the sum of the rate of sufficient contact due to drug injection $\gamma_{ij}(t)$ plus the rate of sufficient contact due to high-risk (without condom) and low-risk (with condom) sexual encounters, $\beta_{ij}^H(t)$ and $\beta_{ij}^L(t)$, respectively:

$$\lambda_{ij}(t) = \gamma_{ij}(t) + \beta_{ij}^H(t) + \beta_{ij}^L(t)$$

$$i = 1, 4, 7; \quad j = 1, \dots, 9.$$

random, nonpreferential mixing within (but not across) compartments.

The sufficient contact rate from drug injection is calculated as

$$\gamma_{ij}(t) = RI_i \left[\frac{X_j(t) RI_j}{\sum_{k=1}^6 X_k(t) RI_k} \right] \tau_{ij}^I$$

$$i = 1, 4; \quad j = 1, \dots, 6,$$

To calculate the sufficient contact rates, we assumed

where RI_i denotes the average number of risky injec-

tions per year for persons in compartment i , and τ_{ij}^l denotes the chance of transmission to an individual in compartment i ($i = 1, 4$) per risky injection shared with an individual in compartment j ($j = 1, \dots, 6$). The needle-sharing sufficient contact rate for uninfected IDUs (individuals in Compartments 1 and 4) is the product of: the number of risky injections that these individuals engage in (RI_i , $i = 1, 4$); the probability that the uninfected individual's needle-sharing partner is from compartment j , which is the fraction of all risky injections that are carried out by individuals in compartment j (the bracketed term in the above equation); and τ_{ij}^l , the chance of infection transmission to a person in compartment i per risky injection shared with a person in compartment j . The term RI_i is calculated as the average number of injections per year for persons in compartment i (I_i) multiplied by the proportion of injections that are shared, s_i .

We let R be an index denoting the riskiness of sexual partnerships ($L =$ low-risk, $H =$ high-risk). The sufficient contact rates from sexual partnerships are calculated as

$$\beta_{ij}^R(t) = P_i^R M_{ij}^R(t) \tau_{ij}^S \quad i = 1, 4, 7; \quad j = 1, \dots, 9,$$

where P_i^R is the average number of sex partnerships of risk R per year for persons in compartment i ; $M_{ij}^R(t)$ is the probability that an individual in compartment i has a sexual partnership of risk R with a person in compartment j at time t ; and τ_{ij}^S denotes the chance of transmission to an individual in compartment i ($i = 1, 4, 7$) per unprotected sexual partnership with a partner in compartment j ($j = 1, \dots, 9$).

The term P_i^H is calculated as the number of new sex partnerships per year for individuals in compartment i , P_i , multiplied by the chance that a condom is not used by individuals in compartment i , $(1 - d_i)$; P_i^L is calculated as the number of new sex partnerships per year for individuals in compartment i , P_i , multiplied by the chance that a condom is used by individuals in compartment i , d_i , multiplied by the effectiveness of condoms in preventing transmission, *ce*. The terms $M_{ij}^R(t)$ are calculated as:

$$M_{ij}^R(t) = \begin{cases} \frac{SCI_j^R(t)}{\sum_{k=1}^6 SCI_k^R(t)} & i = 1, \dots, 6; \quad j = 1, \dots, 6 \\ \frac{SCO_j^R(t)}{\sum_{k=7}^9 SCO_k^R(t)} & i = 1, \dots, 6; \quad j = 7, \dots, 9 \\ \frac{SCO_j^R(t)}{\sum_{k=1}^6 SCO_k^R(t)} \times \frac{\sum_{k=1}^6 SCO_k^R(t)}{\sum_{k=7}^9 SCO_k^R(t)} & i = 7, \dots, 9; \quad j = 1, \dots, 6 \\ \frac{SCO_j^R(t)}{\sum_{k=1}^6 SCO_k^R(t)} \times \frac{\sum_{k=7}^9 SCO_k^R(t) - \sum_{k=1}^6 SCI_k^R(t)}{\sum_{k=7}^9 SCO_k^R(t)} & i = 7, \dots, 9; \quad j = 7, \dots, 9 \end{cases}$$

where $SCI_i^R(t)$ is the total number of IDU-with-IDU sexual contacts of risk R that an IDU in compartment i has with other IDUs at time t and $SCO_i^R(t)$ is the total number of other sexual contacts (all sexual contacts except IDU-with-IDU contacts) of risk R that an individual in compartment i has at time t . These terms are calculated as:

$$SCI_i^R(t) = \begin{cases} X_i(t) P_i^R G_i & i = 1, \dots, 6 \\ 0 & i = 7, \dots, 9 \end{cases},$$

$$SCO_i^R(t) = \begin{cases} X_i(t) P_i^R (1 - G_i) & i = 1, \dots, 6 \\ X_i(t) P_i^R & i = 7, \dots, 9 \end{cases},$$

where G_i is the proportion of sexual contacts of individuals in compartment i ($i = 1, \dots, 6$) that are with other IDUs.

Disease progression occurs from HIV-infected, non-AIDS compartments (Compartments 2, 5, and 8) to the AIDS compartment within the same risk group (Compartments 3, 6, and 9, respectively) at rate θ_i , $i = 2, 5, 8$.

Finally, individuals may change risk groups. Such transitions are indicated by vertical arrows in Figure 1, and occur at rate $\phi_{ij}(t)$ for transitions of individuals from compartment i to compartment j at time t ($t \geq 0$) for various combinations of $i = 1, \dots, 9$; $j = 1, \dots, 9$. Members of the non-IDU population may begin using injection drugs, in which case they move to the corresponding compartment within the same infection state for untreated IDUs. IDUs not in treatment may enter treatment, or they may stop using injection drugs and enter the non-IDU population. IDUs in

treatment may return to untreated injection drug use, or they may stop using injection drugs and enter the non-IDU population.

The population dynamics of the epidemic are represented mathematically by a set of simultaneous nonlinear differential equations that project the number of individuals in compartment i at time t . Following the above discussion, the equations of the model are as follows:

$$X'_1(t) = \phi_{71}(t)X_7(t) + \phi_{41}(t)X_4(t) - X_1(t)(\phi_{17}(t) + \phi_{14}(t) + \delta_1 + \mu_1) - X_1(t) \sum_{j=1}^9 \lambda_{1j}(t) \quad (1)$$

$$X'_2(t) = \phi_{82}(t)X_8(t) + \phi_{52}(t)X_5(t) - X_2(t)(\phi_{28}(t) + \phi_{25}(t) + \theta_2 + \delta_2 + \mu_2) + X_1(t) \sum_{j=1}^9 \lambda_{1j}(t) \quad (2)$$

$$X'_3(t) = \phi_{93}(t)X_9(t) + \phi_{63}(t)X_6(t) + \theta_2 X_2(t) - X_3(t)(\phi_{39}(t) + \phi_{36}(t) + \delta_3 + \mu_3 + \alpha_3) \quad (3)$$

$$X'_4(t) = \phi_{14}(t)X_1(t) - X_4(t)(\phi_{41}(t) + \phi_{47}(t) + \delta_4 + \mu_4) - X_4(t) \sum_{j=1}^9 \lambda_{4j}(t) \quad (4)$$

$$X'_5(t) = \phi_{25}(t)X_2(t) - X_5(t)(\phi_{52}(t) + \phi_{58}(t) + \theta_5 + \delta_5 + \mu_5) + X_4(t) \sum_{j=1}^9 \lambda_{4j}(t) \quad (5)$$

$$X'_6(t) = \phi_{36}(t)X_3(t) + \theta_5 X_5(t) - X_6(t)(\phi_{63}(t) + \phi_{69}(t) + \delta_6 + \mu_6 + \alpha_6) \quad (6)$$

$$X'_7(t) = \rho \left\{ \sum_{j=1}^9 X_j(t) \right\} + \phi_{17}(t)X_1(t) + \phi_{47}(t)X_4(t) - X_7(t)(\phi_{71}(t) + \delta_7 + \mu_7) - X_7(t) \sum_{j=1}^9 \lambda_{7j}(t) \quad (7)$$

$$X'_8(t) = \phi_{28}(t)X_2(t) + \phi_{58}(t)X_5(t) - X_8(t)(\phi_{82}(t) + \theta_8 + \delta_8 + \mu_8) + X_7(t) \sum_{j=1}^9 \lambda_{7j}(t) \quad (8)$$

$$X'_9(t) = \phi_{39}(t)X_3(t) + \phi_{69}(t)X_6(t) + \theta_8 X_8(t) - X_9(t)(\phi_{93}(t) + \delta_9 + \mu_9 + \alpha_9) \quad (9)$$

Additionally, it is assumed that all MMT slots are always filled. Equation (10) ensures that the total flow out of MMT equals the total flow into MMT, and (11) ensures that flow into MMT occurs at the same rate among all untreated IDUs, regardless of HIV infection status.

$$X_4(t)(\phi_{41}(t) + \phi_{47}(t) + \delta_4 + \mu_4) + X_5(t)(\phi_{52}(t) + \phi_{58}(t) + \delta_5 + \mu_5) + X_6(t)(\phi_{63}(t) + \phi_{69}(t) + \delta_6 + \mu_6 + \alpha_6) = \phi_{14}(t)X_1(t) + \phi_{25}(t)X_2(t) + \phi_{36}(t)X_3(t) \quad (10)$$

$$\phi_{14}(t) = \phi_{25}(t) = \phi_{36}(t) \quad (11)$$

The model was programmed in an Excel spreadsheet, using a discretized version of the above equations with a time step of one-tenth of a year. Details of the discretization approach can be found in Zaric et al. (1998). The model was run on a PC platform in Excel 97 with Windows NT 4.0 and a Pentium 166 processor.

Data used in the epidemic model were collected from a variety of sources. Values for all parameters are shown in the Appendix; sources can be found in Zaric et al. (2000). A more detailed data appendix, showing data from each of the sources and relevant calculations, is available from the authors. For some parameters (e.g., number of injections, frequency of sharing, number of sexual contacts, risk reduction due to MMT, death rates among IDUs), data were estimated based on information from a number of sources; in these cases, we chose a value near the middle of the reported range. For other parameters (e.g., quality adjustment for life years lived by IDUs, individuals' knowledge of their HIV status) little data were available, so we either adapted information on closely related quantities or selected parameter values based on the best available information that would lead to reasonable projections by the model.

We created four base cases, corresponding to four different levels of HIV prevalence among IDUs: 5%, 10%, 20%, and 40%. The base cases assume no incremental MMT; thus they assume that approximately

15% of IDUs are in treatment, which reflects the current situation (Rettig and Yarmolinski 1995, U.S. SAMHSA 1992, Watters 1994).

For each base case, we chose model parameters consistent with observed data that would generate the required HIV prevalence among IDUs in that population (i.e., 5%, 10%, 20%, or 40%). We assumed that differences in HIV prevalence among IDUs in the four populations were due solely to factors related to risky injection drug use (e.g., the number of IDUs in the population, the rate at which non-IDUs enter the IDU population, the number of injections per IDU per year) and the overall HIV prevalence in the population. We held as constant across the base cases all other parameters (e.g., other demographic factors and factors relating to risky sexual contacts). Thus, in addition to assuming differences in HIV prevalence among IDUs (5%, 10%, 20%, and 40%, respectively), we assumed differences in overall HIV prevalence in the populations (0.17%, 0.26%, 0.61%, and 3.01%, respectively), the fraction of individuals in the population who are IDUs (0.7%, 0.7%, 0.9%, and 2.5%, respectively), the average number of injections per IDU per year (200, 200, 200, and 225, respectively), and the fraction of IDU sexual partnerships that are with other IDUs (0.10, 0.10, 0.25, and 0.50, respectively). These values were selected based on the best available estimates of HIV prevalence in different U.S. cities (California Department of Health Services Office on AIDS 1997, CDC 1998, Karon et al. 1996), the fraction of individuals who are IDUs (Gleghorn et al. 1995, Hahn et al. 1989, Spencer 1989), and rates of injection in different IDU populations (e.g., Booth et al. 1996, Des Jarlais et al. 1994, Kaplan and Heimer 1992, Koblin et al. 1990, Meandzija et al. 1994, U.S. General Accounting Office 1990a, U.S. General Accounting Office 1990b). We also assumed differences in the annual per person transition rate of non-IDUs into injection drug use (0.00057, 0.00057, 0.0009, and 0.0030, respectively); these rates were chosen because they generated a relatively constant fraction of the population being an IDU over the 10-year time horizon.

The base cases were validated by projecting the epidemic forward for 10 years and comparing our model's projections with recent growth of the epi-

demic. The base cases were designed to generate relatively stable HIV prevalence among IDUs and non-IDUs, at levels consistent with current data, and with a relatively stable proportion of the population being IDUs. In addition, the base cases were designed to generate approximately 25%–30% of HIV cases caused directly by injection drug use, in order to reflect current U.S. estimates. The base cases were created to enable us to compare the effects of expanding MMT programs in different IDU populations, but were not intended to provide detailed epidemic projections.

3. Health and Economic Outcomes

We modeled the effects of expanding MMT programs by changing parameters in the model that relate to methadone maintenance capacity (e.g., the fraction of IDUs in MMT and the flow of IDUs into MMT). Then we projected the epidemic model forward. The incremental effects of such changes were determined relative to the corresponding base case. The projections were compared over a 10-year time horizon.

We measured health and economic outcomes. Health outcomes were measured in terms of discounted life years gained and discounted quality-adjusted life years (QALYs) gained. Costs considered were the discounted incremental costs of health care and MMT compared to the corresponding base case. Following standard practice (Gold et al. 1996), we discounted costs, life years, and QALYs using a 3% discount rate.

We measured the number of incremental life years lived compared to the corresponding base case in each population compartment. We also measured the number of quality-adjusted life years lived: This is the number of life years lived multiplied by a quality-adjustment factor that is specific to each compartment. Quality adjustment, a standard tool in health economics, is a means of valuing the quality of life in different health states (Gold et al. 1996). As shown in Table 2, one year of life for a healthy non-IDU was valued with a multiplier of 1.0, and multipliers of less than 1.0 were used to reflect the diminished quality of life associated with injection drug use, HIV infection, and AIDS. For example, with quality adjustment, a year of

life in the non-AIDS, HIV-infected, untreated IDU compartment was valued at 72% as much as a healthy year of life for a non-IDU (a multiplier of 0.72).

Little research has been done on the appropriate quality adjustment for substance abuse disorders. We assumed quality-adjustment multipliers of 0.8 for untreated injection drug use and 0.9 for methadone maintenance. These values may be compared to quality adjustments for other conditions that limit activities, such as the quality adjustments for moderate angina (0.92), migraine (0.87), ulcer (0.84), and severe angina (0.82) (Owens et al. 1997). We used information from a self-assessment survey of patients by Bayoumi and Redelmeier (1999) to estimate the quality-adjustment multipliers for life years lived with non-AIDS HIV infection and with AIDS; the multipliers they estimated fall between the values obtained in two other studies of HIV-infected individuals (Owens et al. 1997, Tsevat et al. 1996). Bayoumi and Redelmeier (1999) estimated a quality-adjustment multiplier of 0.80 for HIV-infected individuals without AIDS who know their infection status; we estimated that half of HIV-infected individuals without AIDS know their status, and we assumed that the quality adjustment is 1.0 for those who do not know they are HIV-infected, leading to a multiplier of 0.90 for individuals in HIV-infected, non-AIDS compartments. Bayoumi and Redelmeier (1999) estimated quality-adjustment multipliers of 0.64 for individuals with "minor AIDS" and 0.42 for individuals with "major AIDS"; we used the average value, leading to a multiplier of 0.53 for individuals with AIDS. We assumed that the combined effect of HIV infection and injection drug use status on quality of life was multiplicative. Thus, for example, an HIV-infected injection drug user without AIDS was assigned a quality-adjustment multiplier of 0.72, which is the product of the multiplier for HIV

Table 2 Quality-of-Life Multipliers

Group	Infection Status		
	Uninfected	Infected, without AIDS	AIDS
IDUs not in methadone maintenance	0.80	0.72	0.42
IDUs in methadone maintenance	0.90	0.81	0.48
Non-IDUs	1.00	0.90	0.53

Table 3 Annual Per Person Health-Care and Methadone Maintenance Costs (in 1998 Dollars)

Group	Infection Status		
	Uninfected	Infected without AIDS	AIDS
IDUs not in methadone maintenance			
Non-HIV health care	3,850	3,850	3,850
HIV care	0	4,803	32,551
Methadone maintenance	0	0	0
Total	3,850	8,653	36,401
IDUs in methadone maintenance			
Non-HIV health care	3,011	3,011	3,011
HIV care	0	10,545	32,551
Methadone maintenance	5,250	5,250	5,250
Total	8,261	18,806	40,812
Non-IDUs			
Non-HIV health care	1,210	1,210	1,210
HIV care	0	4,803	32,551
Methadone maintenance	0	0	0
Total	1,210	6,013	33,761

without AIDS (0.9) and the multiplier for untreated injection drug use (0.8).

Incremental costs were measured for individuals in each compartment over each year in the time horizon. The annual costs per person in each compartment (in 1988 dollars) are shown in Table 3. Non-HIV health-care costs for an uninfected non-IDU were calculated from U.S. statistical data (U.S. Bureau of the Census 1997); the non-HIV care costs for IDUs not in MMT, and IDUs in MMT, include an additional amount of \$2,640 and \$1,801, respectively, reflecting the additional health-care costs associated with injection drug use (Gerstein et al. 1994). HIV-care costs were calculated using data on costs incurred by infected individuals in different stages of infection and data on the fraction of infected individuals who receive different types of treatment for HIV (no treatment, monotherapy, two-drug therapy, or combination therapy) (Gable et al. 1996, Holtgrave and Pinkerton 1997, McNaghten 1998); details are shown in the Appendix. For HIV-infected individuals without AIDS (middle column of Table 3), HIV-care costs are higher for individuals in MMT than for those not in MMT

because individuals in MMT are more likely to receive HIV care; many MMT programs offer screening to IDUs when they enter MMT. The cost of MMT was obtained from Barnett and Rodgers (1998). We inflated published cost data to 1998 dollars using the general Consumer Price Index for all urban consumers (U.S. Bureau of Labor Statistics 1998).

4. Results

We considered the cost-effectiveness of expanding current MMT programs by 10% (so that 16.5% of IDUs are in MMT, in contrast to 15% of IDUs in MMT in the base case). We assumed that the incremental MMT slots have the same cost and effectiveness in reducing risky behavior as current slots. Results are shown in Table 4. For all four populations, expanding current MMT programs is cost-effective: Cost per life year gained ranges from \$9,700 to \$17,200, and cost per QALY gained ranges from \$6,300 to \$10,900. Medical interventions that cost less than \$50,000 per life year or QALY gained are generally considered acceptable (Owens 1998). The values shown in Table 4 are well within that range.

Consideration of quality of life makes expansion of current MMT programs appear to be more cost-effective than when only life years are considered. This occurs because the increase in treatment capacity not only increases the number of life years lived, but also increases their quality. Expansion of treatment program size allows more IDUs to enter treatment and, in our model, for each HIV-infection state, a year of life lived by an IDU in treatment has higher quality than a year of life

lived by an untreated IDU. Furthermore, a few IDUs who undergo MMT stop injection drug use altogether, and in our model the quality of life for non-IDUs is higher than the quality of life for IDUs. Additionally, expanding MMT reduces HIV cases among IDUs and non-IDUs, and life years lived uninfected are of higher quality than life years lived with HIV or AIDS.

The fraction of the population comprising IDUs varies across the four base cases: The lowest fraction occurs in the population with 5% base HIV prevalence among IDUs and the highest fraction occurs in the population with 40% base HIV prevalence among IDUs. Because we assumed that 15% of IDUs are in treatment in each population, each population has a different number of base treatment slots. Thus, a given percentage increase in the number of treatment slots generates a different absolute number of new treatment slots in each population.

To compare the effects of the same investment in treatment slots in the four populations, we considered expansion by the same number of slots in each population. Table 5 provides details of the economic costs and savings and the health benefits generated by expanding current MMT programs by 100 slots in each population. The cost of 100 additional MMT slots is \$525,800 per year over the 10-year time horizon, which has a net present value of \$4,538,000. The 100-slot expansion moves additional IDUs into treatment, which increases MMT costs and other health-care costs for those IDUs, including the cost of antiretroviral drugs for infected IDUs who enter MMT, but the additional treatment slots also lead to reduced HIV transmission among IDUs and among non-IDUs, which reduces HIV-care costs for all individuals who avoid infection. Table 5 shows that the cost of the additional MMT slots is partially offset (by about one-third to one-half) by reductions in the cost of HIV care and other health care.

The majority of the cost savings generated by the additional treatment slots are savings in HIV-care costs. Methadone maintenance reduces risky needle-sharing and sexual behavior among treated IDUs, and this reduces the risk of HIV infection for IDUs and for sex partners of IDUs. In all four populations, the cost of HIV care for IDUs and non-IDUs is reduced.

Table 4 Cost per Life Year Gained and Cost per QALY Gained by a Ten Percent Expansion of Current Methadone Maintenance Programs*

Base HIV Prevalence Among IDUs	Cost per Life Year Gained	Cost per QALY Gained
5%	\$17,200	\$10,900
10%	\$13,200	\$ 8,400
20%	\$ 9,700	\$ 6,300
40%	\$12,100	\$ 8,200

* All numbers are rounded to the nearest \$100.

Table 5 Costs and Benefits of Adding 100 Slots to Current Methadone Maintenance Programs*

	Base HIV Prevalence Among IDUs			
	5%	10%	20%	40%
Discounted Incremental Costs and Savings (in \$1000's)				
Methadone maintenance	4,538.5	4,538.5	4,538.5	4,538.5
HIV care—IDUs	-539.7	-872.2	-1,268.6	-968.9
HIV care—Non-IDUs	-323.3	-545.9	-684.5	-320.8
Other health care—IDUs	-795.9	-747.9	-667.6	-568.4
Other health care—Non-IDUs	241.8	248.1	252.4	241.3
Total incremental cost	3,121.4	2,620.6	2,170.7	2,663.8
Discounted HIV Infections Averted**				
HIV infections averted—IDUs	20.4	32.1	48.8	50.8
HIV infections averted—Non-IDUs	11.5	19.2	25.4	19.4
Total HIV infections averted	31.9	51.3	74.2	70.2
Discounted Life Years Gained				
Life years gained—IDUs	-18.3	-5.9	15.1	40.8
Life years gained—Non-IDUs				
Former IDUs	46.0	45.8	42.1	29.2
Never IDUs	153.7	159.2	166.4	170.1
Total among non-IDUs	199.7	205.0	208.5	199.3
Total life years gained	181.4	199.1	223.6	240.1
Discounted QALYs Gained				
QALYs gained—IDUs	81.3	97.6	123.7	148.7
QALYs gained—Non-IDUs				
Former IDUs	45.9	45.5	41.4	27.5
Never IDUs	159.6	169.2	179.3	177.8
Total among non-IDUs	205.5	214.7	220.7	205.3
Total QALYs gained	286.8	312.3	344.4	354.0
Absolute Change in HIV Prevalence After 10 Years				
Among IDUs	-0.240%	-0.390%	-0.427%	-0.167%
Among Non-IDUs	-0.001%	-0.002%	-0.002%	-0.002%
Overall	-0.003%	-0.005%	-0.007%	-0.006%

* The base cases assume different fractions of the population who are IDUs, so the 100-slot expansion corresponds to an expansion of current methadone maintenance programs by approximately 10%, 10%, 7.5%, and 2.7%, respectively, in the populations with 5%, 10%, 20%, and 40% base HIV prevalence among IDUs.

** The undiscounted total number of infections averted in the four populations is, respectively, 37.9, 60.6, 87.1, and 81.4. Since the population size is approximately 1 million people (the population at the beginning of the time horizon is 1 million people, but decreases slightly in future years due to deaths), these numbers translate to an approximate average annual reduction in HIV incidence of 3.8, 6.1, 8.7, and 8.1 per million people in the four populations, respectively.

Table 5 shows that approximately one-third of the HIV infections averted as a result of the treatment program expansion are among non-IDUs. The non-IDU group includes individuals who never used injection drugs, as well as former IDUs who stopped injection drug use as a result of MMT. To estimate how many of the life years and QALYs gained accrue to former IDUs versus individuals who were never IDUs, we estimated the number of former IDUs in non-IDU compartments. We did so by counting entry

into and exit from non-IDU compartments each period by IDUs (from untreated injection drug use and from MMT). We estimated the number of former IDUs who leave to return to injection drug use by assuming that they are ten times as likely to take up injection drug use as individuals who were never IDUs, and we estimated the number who leave due to deaths and maturation out of the population by assuming that former IDUs have the same death and maturation rates as never-IDUs. (To get an idea of the magnitude

of the numbers, at any point in time, the populations comprise more than 95% non-IDUs, of which we estimate that fewer than 0.1% are former IDUs.)

Table 5 shows that the majority of life years gained are among individuals who have never been IDUs. In the populations with 5% and 10% base HIV prevalence among IDUs, although HIV infections are averted in the IDU population as a result of the 100 additional MMT slots, life years are *lost* in the IDU population because of migration of treated IDUs into the non-IDU population. However, the total number of life years gained among current and former IDUs is a positive quantity in all of the populations.

The benefits of treatment are greater when years of survival are quality adjusted. Quality adjustment increases the total measured benefit by approximately 50%. Table 5 shows that quality adjustment has a much greater effect on the measured benefit in the IDU population than in the non-IDU population. In the non-IDU population, the increased quality of life stems from reduced HIV infection: The 100 additional treatment slots lead to a small decrease in HIV prevalence among non-IDUs. Quality adjustment to life years in the non-IDU population increases the measured benefit slightly. In the populations of current and former IDUs, quality of life increases due to reduced HIV prevalence: The addition of 100 treatment slots reduces HIV prevalence among IDUs by approximately 0.2%–0.4%. Additionally, quality of life increases for IDUs who enter MMT. These two effects create a significant increase in the total measured benefit among current and former IDUs when quality adjustment is made.

Our analysis assigned the same quality-adjustment multiplier to all individuals in any given non-IDU compartment (Table 2). It is plausible that the value of a life year lived by a former IDU lies somewhere between the value for an IDU in MMT and a non-IDU. The incorporation of a different quality adjustment for “former IDUs” versus “never IDUs” would not change the results in any significant way: Quality adjustment still increases the value of life years lived because MMT directly increases quality of life for IDUs in treatment and indirectly increases quality of life when IDUs avoid HIV infection and when IDUs

cease injection drug use. If one assigned a slightly lower quality of life to years lived by the former IDUs, the number of QALYs gained would decrease only slightly because only 3.5% of IDUs in MMT successfully “graduate” each year to become former IDUs.

We performed extensive one-way sensitivity analyses to determine the effect of changes in all model parameters. We varied each model parameter over a wide range of possible values to account for uncertainty about parameter values and to account for possible variability of parameter values in different populations. Over a wide range of assumptions about each model parameter, the cost per life year gained by an expansion of current MMT programs was less than \$25,000 and cost per QALY gained was less than \$20,000 in all four populations. Further details are provided in Zaric et al. (2000).

Changes in factors relating to sexual behavior had only a small impact on our cost-effectiveness estimates. Factors relating to risky drug injection—number of injections per IDU per year and fraction of injections that are shared—had a larger effect on our cost-effectiveness estimates. The base case analyses assumed that IDUs in MMT inject only 20% as often as IDUs not in MMT (an 80% reduction in frequency) and share 30% as often as IDUs not in MMT (a 70% reduction in sharing), leading to a 94% reduction in risky injections among IDUs in MMT ($20\% \times 30\% = 6\%$ as many risky injections). These estimates were based on studies that suggest that the percentage reduction in injection frequency among IDUs in MMT versus IDUs not in treatment may be 60% (Meandzija et al. 1994), 71% (U.S. General Accounting Office 1990a), 75% (U.S. General Accounting Office 1990a), or 84% (U.S. General Accounting Office 1990b), and studies of needle sharing among IDUs in MMT which have found the reduction in needle sharing by IDUs in MMT to be 50% (Caplehorn and Ross 1995), 72% (Martin et al. 1990), and 81% (U.S. General Accounting Office 1990a) (further details are in the data appendix which can be obtained from the authors). If the reduction in injection frequency due to MMT is only 50%, then the cost per QALY gained is \$11,300 in the population with 5% HIV prevalence among IDUs, and \$9,500 in the population with 40% prevalence. If MMT

causes no reduction in needle sharing (but causes an 80% reduction in injection frequency), then the cost per QALY gained in the two populations is \$11,500 and \$10,300, respectively.

The cost-effectiveness estimates were most affected by the cost of MMT and the costs of HIV care and non-HIV health care. For example, if an incremental MMT slot costs only \$2,000, the cost per QALY gained is \$1,300 in the population with 5% base HIV prevalence among IDUs, and \$300 in the population with 40% prevalence; conversely, if an incremental MMT slot costs \$10,000, the cost per QALY gained is \$25,400 and \$19,800, respectively. As another example, if the non-HIV health-care costs for IDUs in MMT are \$3,000 more than the non-HIV health-care costs for IDUs not in MMT (the increment in the base case was \$800), then the cost per QALY gained is \$4,500 and \$3,200 in the two populations, respectively. If non-HIV health-care costs are the same for IDUs in and out of MMT, then the cost per QALY gained is \$13,700 and \$10,200, respectively. We also considered different expansion sizes (up to doubling of current program sizes), assuming that new slots have the same cost and effectiveness as current slots. The calculated cost-effectiveness ratios were very similar to those in Table 4.

Our base-case analyses assumed that quality of life for an untreated IDU is equal to 80% of the quality of life for a comparable non-IDU (one with the same HIV infection status), and that quality of life for an IDU in treatment is equal to 90% of the quality of life for a comparable non-IDU. The base-case analyses thus assume that quality of life for individuals in MMT is 12.5% higher than quality of life for untreated IDUs. In sensitivity analysis, we considered the case in which quality of life for individuals in MMT is the same as for untreated IDUs: Then, the cost per QALY gained is \$15,500 in the population with 5% base HIV prevalence among IDUs and \$10,600 in the population with 40% prevalence.

Some may argue that life years lived by IDUs should be assigned even lower values relative to life years lived by non-IDUs. Opioid addicts are likely to have psychiatric comorbidities (von Limbeek et al. 1992) and medical comorbidities such as hepatitis, soft-tissue infections, and other diseases (Contoreggi

et al. 1998). These comorbidities may significantly diminish quality of life. In sensitivity analysis, we considered lower values for the quality-adjustment multipliers assigned to life years lived by IDUs. Even in the extreme case when all life years lived by IDUs are assigned a quality-adjustment multiplier of zero, expansion of existing MMT programs is still cost-effective: The net cost per QALY gained ranges from \$15,200 in the population with 5% base HIV prevalence among IDUs to \$14,100 in the population with 40% prevalence.

We performed two-way sensitivity analysis on the effectiveness of MMT in reducing risky behavior and the "graduation" rate from MMT. In the population with 5% base HIV prevalence among IDUs, the cost-effectiveness of expanding MMT would be about the same as estimated in Table 4 if MMT was only half as effective in reducing risky behavior as we originally assumed and the MMT graduation rate was 5% (as opposed to the 3.5% we assumed in our analyses). If the risk reduction remained the same and the graduation rate increased to 5%, the cost per QALY gained would decrease to approximately \$10,000. In the population with 40% base HIV prevalence among IDUs, the cost-effectiveness of expanding MMT would be about the same as estimated in Table 4 if MMT was only half as effective in reducing risky behavior as we originally assumed and the MMT graduation rate was 8%. If the risk reduction remained the same and the graduation rate increased to 8%, the cost per QALY gained would decrease to approximately \$5,000.

Our analyses indicated that expansion of current MMT programs is cost-effective in all four of the IDU populations we considered and over all expansion amounts we considered. If a new MMT program is *less* expensive and *more* effective in reducing risky behavior than current MMT programs, then it will be even more cost-effective. However, it is possible that a new treatment program, or incremental treatment slots associated with an existing treatment program, might be more expensive and/or less effective in reducing risky behavior than current MMT programs. This might occur, for example, if the IDUs reached when treatment

Table 6 Cost-Effectiveness of a Ten Percent Expansion in Methadone Maintenance Slots: Effects of Lower Treatment Effectiveness and Higher Cost

	Base HIV Prevalence Among IDUs			
	5%	10%	20%	40%
Incremental treatment slots with the same cost, but half the effectiveness, of current methadone maintenance slots				
Cost per life year gained	\$25,200	\$23,200	\$22,600	\$28,800
Cost per QALY gained	\$16,700	\$15,400	\$15,300	\$20,200
Incremental treatment slots with the same effectiveness, but twice the cost, of current methadone maintenance slots				
Cost per life year gained	\$42,200	\$36,000	\$30,000	\$31,000
Cost per QALY gained	\$26,700	\$22,900	\$19,500	\$21,000
Incremental treatment slots with half the effectiveness and twice the cost of current methadone maintenance slots				
Cost per life year gained	\$54,600	\$51,000	\$48,700	\$54,300
Cost per QALY gained	\$36,100	\$33,900	\$32,900	\$38,300

programs expand are harder to reach and more resistant to change than IDUs currently in MMT.

To address this possibility, we used our model to analyze the cost-effectiveness of additional treatment slots with lower effectiveness in reducing risky behavior and higher cost than current MMT slots (Table 6). In these analyses, treatment program "effectiveness" was defined as the rate at which IDUs leaving treatment enter the non-IDU population (the program's "graduation" rate) and the extent to which IDUs in treatment reduce their risky needle-sharing behavior. These factors were varied simultaneously: Thus, a 10% decrease in program effectiveness was modeled as a 10% decrease in the graduation rate for the incremental treatment slots (from 3.5% in the base cases to 3.15%) as well as a 10% decrease in the reduction in risky needle-sharing episodes for IDUs in the incremental treatment slots relative to IDUs not in treatment (from a reduction of 94% in the base cases to a reduction of 84%). Table 6 shows that even if the additional treatment slots are half as effective and twice as expensive as current MMT slots, the incremental cost-effectiveness ratio will still be less than about \$50,000 per QALY gained in all four of the IDU populations we considered.

5. Discussion

The use of a dynamic model of methadone maintenance treatment and the spread of HIV in a population of IDUs and non-IDUs enabled us to assess the cost-effectiveness of expanding existing MMT programs, and the cost-effectiveness of new treatment slots that may be less effective and/or more expensive than current MMT slots. Health benefits of such programs, measured in years of life lived, are the result of reductions in risky drug injection and risky sexual behavior by IDUs in treatment, and from cessation of drug injection by a relatively small number of successfully rehabilitated IDUs. The measured benefit increases when quality of life is considered. The cost savings from MMT mirror the health benefits: Although IDUs in treatment incur higher health-care costs than untreated IDUs, MMT reduces the spread of HIV, thus lowering HIV-care costs, and reduces drug injection, thus lowering non-HIV health-care costs.

Our analysis has shown that expanding existing MMT programs is a cost-effective health-care intervention, and that such expansion is cost-effective in populations with high HIV prevalence among IDUs (40%), as well as in populations with low HIV prevalence among IDUs (5%). The analysis showed that the

net incremental cost of an additional MMT slot is approximately one-third less than the incremental cost of the slot itself, due to savings in HIV-care and other health-care costs. The majority of health-care cost savings are savings in the cost of HIV care.

Medical interventions that cost less than \$50,000 per QALY gained are generally considered acceptable (Owens 1998). For example, administration of zidovudine to HIV-infected individuals, a standard treatment before the introduction of newer antiviral drugs, was shown to have a cost-effectiveness ratio of approximately \$43,000 per QALY gained (Moore et al. 1994). As another example, the Centers for Disease Control and Prevention currently recommend that acute-care hospitals and associated clinics offer voluntary screening to patients aged 15 to 54 years if the HIV prevalence in the patient population is 1% or greater (CDC 1993). Owens et al. (1996) have shown that the cost per QALY gained of such a screening program is approximately \$55,000. Our analyses show that, over a wide range of assumptions, the cost per life year gained by expansion of existing MMT programs is less than \$25,000, and the cost per QALY gained is less than \$20,000.

Additionally, although methadone maintenance treatment is provided to IDUs, significant benefits accrue to non-IDU members of the population. Our analysis showed that half or more of the life years and QALYs gained are among individuals who have never been IDUs. The analysis highlights the health benefits to society as a whole that are generated by MMT programs.

Our estimate of the \$5,250 annual cost of methadone maintenance was obtained from analysis of data provided by some 600 methadone maintenance programs to the U.S. National Drug and Alcohol Treatment Unit Survey (Barnett and Rodgers 1998). Controlling for the amount of other types of treatment the programs provided, they estimated that methadone maintenance treatment costs \$5,414 per year (in 1998 dollars). French et al. (1997) reported detailed data for eight methadone maintenance programs. The mean weekly cost of these programs was \$83.38 (in 1994 dollars). When adjusted to 1998 dollars, the average is \$91.70 per week, or \$4,768 per year. Our use of the higher figure for the cost of MMT makes our cost-effectiveness estimates conservative.

Current methadone maintenance programs do not induce complete cessation of drug injection among IDUs in treatment, and only about 3.5% of IDUs per year successfully “graduate” (and stop injection drug use). Despite this, our analysis shows that such programs are a cost-effective means of slowing the spread of HIV: Even a temporary reduction in risky behavior leads to reduced HIV infection, reduced mortality, and increased quality of life—and these changes are sufficient to make methadone maintenance cost effective. Other HIV prevention programs that change risky behavior only partially have also been shown to be cost-effective (e.g., see Kaplan and Abramson 1989, Owens et al. 1998).

Clients in methadone maintenance do not completely stop injecting drugs, so much work has been done to attempt to improve the effectiveness of MMT programs. However, our analysis suggests that rather than investing resources to improve the effectiveness of current MMT programs, a better use of public-health resources is to expand existing MMT programs since they are already highly cost-effective. In addition, expanded MMT programs that reach additional IDUs without reducing the number of IDUs in current types of treatment are likely to be cost-effective over a broad range of values for treatment cost and effectiveness. Sensitivity analysis indicates that incremental MMT slots are likely to be cost-effective even if they cost twice as much and are half as effective in reducing risky behavior as current MMT programs.

Our analysis has several limitations. We limited our analysis to a population of individuals aged 18 to 44. We did not consider transmission of HIV from others to their newborns. Consideration of vertical HIV transmission would make methadone maintenance appear more cost effective.

We did not include the effect of abuse of cocaine by injection. Little information exists on the prevalence of cocaine injection in the United States, but this practice is clearly a risk factor for HIV (Schoenbaum et al. 1989). Injection cocaine users are more likely than those who inject only opiates to share injection equipment and engage in other high-risk behaviors (Chaisson et al. 1989, Meandzija et al. 1994). The risks associated with injection cocaine use extend to individuals in MMT (Bux et al.

1995, Joe and Simpson 1995). Evidence about the effect of methadone maintenance on cocaine use is mixed: Some individuals increase cocaine use after entering MMT, but the overall effect may be a reduction in injection cocaine use (Chaisson et al. 1989, Meandzija et al. 1994). The exclusion of cocaine injection practices from our model may have overstated the benefit of methadone maintenance.

Our analysis is based on a compartmental model that uses matrices to describe mixing patterns between members of various compartments. This approach is similar to other analyses of the spread of HIV and other diseases (e.g., Hethcote 1976, Hethcote and Yorke 1984) and the cost and effectiveness of HIV prevention programs (e.g., Brandeau et al. 1992, Brandeau et al. 1993, Edwards et al. 1998). The matrices may specify preferences between groups (e.g., individuals in high-risk groups prefer to mix with other individuals in high-risk groups), but once the risk groups involved in a contact have been specified, the mixing is random. The random mixing assumption greatly simplifies the analysis, but may not be realistic.

A more sophisticated compartmental model (e.g., Blower et al. 1991) could incorporate more risk groups (e.g., "core" and "noncore" IDU groups) and thus incorporate preferential mixing within risk groups. However, little data is available on mixing patterns among IDUs. Furthermore, the incorporation of non-random mixing patterns among IDUs may not change the measured cost-effectiveness of incremental MMT slots by much: Our estimates of incremental costs incurred and QALYs gained are measured relative to a base case that also assumes a random mixing pattern for individuals within each compartment. Under a nonrandom mixing scenario, if one also assumes that IDUs from any compartment who flow into other compartments are a random sample of IDUs from that compartment (regardless of what their mixing pattern might be), then the difference between the incremental MMT slot case and the base case, assuming nonrandom mixing, is likely to be about the same as the difference (i.e., the measured cost-effectiveness) when random mixing is assumed.

An alternative approach uses models of social networks to examine disease transmission by considering

how individuals form and break social connections within a network (e.g., Kretzschmar and Wiessing 1998, Morris and Kretzschmar 1995). Studies comparing randomly generated networks to highly structured social networks with preferential mixing have shown that: For low levels of infectivity the two network patterns produce equal numbers of infections; the trends in number of new infections are the same in both network structures; and, except for a few cases, the magnitude of the change in number of infections resulting from a given change in infectivity is also the same (Watts and Strogatz 1998, Watts 1999). Kaplan and Lee (1990) showed that random mixing models generate numbers of new infections that are very close to the worst-case bounds for modest levels of infectivity. These results suggest that a random mixing model like ours may overestimate the number of infections that occur both with and without the extra MMT slots, but that the trend in infections is identical to what would be observed if a true network model were used, and for many values of infectivity change, the change in number of infections would also be very similar.

Studies in various U.S. cities have identified large social networks of IDUs and described network characteristics such as size, density, "centralness" of network members (e.g., Neaigus et al. 1996, Suh et al. 1997). A key conclusion of these studies is that prevention efforts are more effective if they target individuals who are centrally located in a network rather than individuals on the network's periphery. Thus, if increased MMT capacity is targeted to IDUs who are centrally located in IDU social networks, then expansion of MMT programs would likely be more cost-effective than we have estimated; if increased MMT capacity reaches IDUs located on the periphery of IDU social networks, then such expansion is likely to be less cost-effective than we have estimated.

The guidelines of the Federal Panel on Cost-Effectiveness in Health and Medicine recommend the use of a societal perspective (Gold et al. 1996). This suggests that the effect of methadone maintenance on the cost of operating public programs, such as the criminal justice and social service systems, should be included. We opted for a more restrictive viewpoint, that of the health-care payer,

and considered only the direct costs of methadone maintenance and its effect on health-care costs.

Other analyses have found that methadone maintenance reduces nonmedical costs (Gerstein et al. 1994, Harwood et al. 1995), although the magnitude of the savings is not precisely known. By excluding such savings, we made a conservative assumption about the benefit of methadone maintenance. It is possible that decision makers, such as employers and health insurers, may be unwilling to consider economic benefits that they do not realize, such as the reduced cost of criminal justice and social services agencies. The administrators of public health care programs may share this same perspective: For example, a state Medicaid program may not be able to finance the cost of treatment expansion from reduced costs of other state agencies.

Future analysts may wish to take the broader, societal view and include the effect of methadone maintenance treatment on the criminal justice system and social service agencies. They may also wish to take the special viewpoint of the "law abiding taxpayer" adopted by some analysts (e.g., Gerstein et al. 1994, Harwood et al. 1995) and also include the effects of property loss due to crime and welfare costs. These costs are not included in the societal perspective, which considers them to be transfer payments.

In the United States, injection drug use is a serious public-health problem that has contributed significantly to the spread of HIV. Our analysis shows that expansion of existing methadone maintenance programs is a cost-effective use of health-care resources that can reduce the spread of HIV and improve the length and quality of life for injection drug users, and that programs that are less effective and more expensive than current methadone maintenance programs may also be cost-effective. The analysis suggests that barriers to methadone maintenance are limiting access to a cost-effective health-care intervention.¹ ■

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Appendix²

Data for Compartmental Model

Initial Compartment Sizes

Total population size: 1,000,000

Fraction of population who are IDUs: 0.007 (Population 1); 0.007 (Population 2); 0.009 (Population 3); 0.025 (Population 4); assumes that all IDUs are aged 18 to 45.

HIV prevalence in overall population: 0.0017 (Population 1); 0.0026 (Population 2); 0.0061 (Population 3); 0.0301 (Population 4); assumes that the HIV epidemic is in steady state, mean time from infection to death is 9.5–11.5 years, and all cases occur in individuals aged 18 to 45.

HIV prevalence among IDUs: 5% (Population 1); 10% (Population 2); 20% (Population 3); 40% (Population 4)

Fraction of IDUs in MMT: 0.15

Fraction of HIV-infected individuals who have AIDS: 0.176

Initial compartment sizes: $X_i(0)$ were calculated by applying the above multipliers appropriately.

Rates of Maturation, Death, Disease Progression, and Transition Between Risk Groups

Maturation rates: $\rho = \mu_i = 0.0399$, $i = 1, \dots, 9$

Non-HIV death rates: $\delta_1 = \delta_2 = \delta_3 = 0.0300$; $\delta_4 = \delta_5 = \delta_6 = 0.0113$; $\delta_7 = \delta_8 = \delta_9 = 0.0014$

AIDS death rates: $\alpha_3 = \alpha_6 = \alpha_9 = .384$; we assumed that protease inhibitors lengthen life with AIDS by a factor of 1.5 beyond life without protease inhibitors; 95% of persons with AIDS receive HIV care; of those who receive HIV care, 55% receive protease inhibitors. Rate of AIDS development: $\theta_2 = \theta_8 = 0.087$; $\theta_5 = 0.082$; we assumed that protease inhibitors lengthen life with asymptomatic HIV by a factor of 1.5 beyond life without protease inhibitors; 39% of infected IDUs without AIDS who are not in methadone maintenance and 39% of infected non-IDUs without AIDS receive HIV care; 95% of infected IDUs without AIDS who are in methadone maintenance receive HIV care; of those who receive HIV care, 55% receive protease inhibitors.

Transition rates between risk groups: $\phi_{71}(t) = \phi_{82}(t) = 0.00057$ (Populations 1 and 2), 0.0009 (Population 3), 0.0030 (Population 4); $\phi_{41}(t) = \phi_{32}(t) = \phi_{63}(t) = 0.315$; $\phi_{47}(t) = \phi_{38}(t) = \phi_{69}(t) = 0.035$; $\phi_{17}(t) = \phi_{28}(t) = \phi_{39}(t) = 0.0102$; $\phi_{93}(t) = 0$; $\phi_{14}(t)$, $\phi_{25}(t)$ and $\phi_{36}(t)$ are calculated dynamically using Equations (10) and (11).

Transmission Risk Factors

Average number of injections per year: $I_1 = I_2 = 200$; $I_3 = 50$; $I_4 = I_5 = 40$; $I_6 = 10$ (Populations 1, 2 and 3); $I_1 = I_2 = 225$; $I_3 = 56.25$; $I_4 = I_5 = 45$; $I_6 = 11.25$ (Population 4); assumes that persons with AIDS have a 75% reduction in risky injection behavior.

² Sources for all parameter values are provided in Zaric et al. (2000). A detailed data appendix, showing data from all sources considered and relevant calculations, is available from the authors.

Fraction of injections that are shared: $s_1 = s_2 = s_3 = .2$; $s_4 = s_5 = s_6 = 0.06$
 Chance of HIV transmission to a person in compartment i ($i = 1, 4$) per risky injection: $\tau_{ij}^i = 0.005$, $j = 2, 3, 5, 6$; $\tau_{ij}^i = 0$, $j = 1, 4$

Average number of new sexual partnerships per year: $P_1 = P_2 = P_4 = P_5 = 3.50$; $P_3 = P_6 = 0.875$; $P_7 = P_8 = 1.20$; $P_9 = 0.30$; we assumed a three-fourths reduction in risky behavior among persons with AIDS.

Chance of HIV transmission to a person in compartment i ($i = 1, 4, 7$) per unprotected sexual partnership with a person in compartment j : $\tau_{ij}^s = 0$, $j = 1, 4, 7$; $\tau_{ij}^s = 0.05$, $j = 2, 5, 8$; $\tau_{ij}^s = 0.11$, $j = 3, 6, 9$

Condom usage rate: $d_1 = \dots = d_6 = 0.20$; $d_7 = d_8 = d_9 = 0.30$

Condom effectiveness in preventing HIV transmission: $ce = 0.9$

Proportion of sexual partnerships of IDUs that are with other IDUs: For $i = 1, \dots, 6$: $G_i = 0.1$ (Populations 1 and 2); $G_i = 0.25$ (Population 3); $G_i = 0.5$ (Population 4)

Calculation of HIV-Care Costs

HIV-care costs were estimated for each of the four CDC-defined stages of HIV infection. The cost of each type of treatment was estimated based on data in Gable et al. (1996) and Holtgrave and Pinkerton (1997). The fraction of individuals receiving each type of treatment was estimated based on data in McNaghten (1998). Costs were calculated using:

	Stage 1	Stage 2	Stage 3	Stage 4
Annual cost to treat opportunistic infections (for those with no HIV care)	\$74	\$512	\$2,434	\$16,872
Annual Drug Cost				
Monotherapy	\$2,082	\$6,476	\$9,723	\$27,170
Two-drug therapy	\$3,864	\$8,258	\$11,505	\$28,952
Triple therapy	\$14,450	\$15,363	\$19,050	\$37,159
Fraction receiving care who receive				
Monotherapy	0.05	0.05	0.05	0.05
Two-drug therapy	0.40	0.40	0.40	0.40
Triple therapy	0.55	0.55	0.55	0.55
Average HIV-care cost (for those who receive HIV care)	\$9,597	\$12,077	\$15,565	\$33,377
Fraction who receive HIV care				
Non-IDUs and IDUs not in MMT	0.25	0.50	0.75	0.95
IDUs in MMT	0.95	0.95	0.95	0.95
Average HIV-care cost				
Non-IDUs and IDUs not in MMT	\$2,455	\$6,295	\$12,283	\$32,551
IDUs in MMT	\$9,121	\$11,499	\$14,908	\$32,551

HIV-care cost for infected individuals without AIDS is calculated as an average of the HIV-care costs for Stages 1, 2, and 3, weighted by the fraction of infected individuals without AIDS who are in each stage (estimated as 0.544, 0.356, and 0.100, respectively, based on information in Gable et al. (1996)). This yields:

Average HIV-care cost for infected individuals without AIDS:
 Non-IDUs and IDUs not in MMT: \$4,803
 IDUs in MMT: \$10,545

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