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Cost-Effectiveness of Alternative Strategies for Provision of HIV Pre-Exposure Prophylaxis for People Who Inject Drugs

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Abstract

Background—Oral HIV pre-exposure prophylaxis (PrEP) has been recommended as a means of HIV prevention among people who inject drugs (PWID) but, at current prices, is unlikely to be cost-effective for all PWID.

Objective—To determine the cost-effectiveness of alternative strategies for enrolling PWID in PrEP.

Design—Dynamic network model that captures HIV transmission and progression among PWID in a representative US urban center.

Outcome Measures—HIV infections averted, discounted costs and quality-adjusted life-years (QALYs), and incremental cost-effectiveness ratios (ICERs).

Intervention—We assume 25% PrEP coverage and investigate four strategies: 1) random PWID are enrolled (Unselected Enrollment); 2) individuals are randomly selected and enrolled together with their partners (Enroll Partners); 3) individuals with the highest number of sexual and needle-sharing partnerships are enrolled (Most Partners); 4) individuals with the greatest number of infected partners are enrolled (Most Positive Partners).

Results—PrEP can achieve significant health benefits: compared to the status quo of no PrEP, the strategies gain 1114 QALYs (Unselected Enrollment), 2194 QALYs (Enroll Partners), 2481 QALYs (Most Partners), and 3046 QALYs (Most Positive Partners) over 20 years in a population of approximately 8500 people. The ICER of each strategy compared to the status quo (cost per QALY gained) is \$272,000 (Unselected Enrollment), \$158,000 (Enroll Partners), \$124,000 (Most Partners), and \$101,000 (Most Positive Partners). All strategies except Unselected Enrollment are cost-effective according to WHO criteria.

Conclusions—Selection of high risk PWID for PrEP can improve the cost-effectiveness of PrEP for PWID.

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Keywords

Cost-Benefit Analysis; HIV Infections/epidemiology; HIV Infections/prevention & control; Pre-Exposure Prophylaxis; United States/epidemiology

INTRODUCTION

HIV causes a substantial health burden in the US, with a disproportionate impact among people who inject drugs (PWID). HIV prevalence among US PWID is approximately 25 times that of the general population [1]. Enhancing HIV prevention programs to reach PWID may greatly reduce morbidity and mortality, thus protecting the health of a vulnerable population [2].

A number of interventions have been proposed for controlling drug injection and its associated harms, including oral HIV pre-exposure prophylaxis (PrEP). The Centers for Disease Control and Prevention (CDC) recommend PrEP use for uninfected adults who report injection of unprescribed drugs in past 6 months, and in addition have shared injection equipment, enrolled in a drug treatment program, or had risk of sexual HIV acquisition [3]. In prior work, we found that PrEP for PWID in the US is not cost-effective at current prices and would likely be unaffordable in terms of aggregate expenditures (including the cost of the drug plus ongoing care and monitoring) [4]. We also found that PrEP is not likely to be cost effective as part of a portfolio of preventive interventions that includes opioid agonist therapy, needle and syringe exchange, and intensive testing and treatment for HIV [5].

In this study, we evaluate the cost-effectiveness of various strategies for selecting high-risk PWID for PrEP. We adopt a healthcare sector perspective [6] and, for each strategy, we estimate costs, quality-adjusted life years (QALYs) gained, incremental cost per QALY gained and HIV infections averted compared to the status quo of no PrEP.

METHODS

Overview

We model the PWID population in a representative US urban center (i.e., a city with a relatively high population density and approximately 10% HIV prevalence among PWID), using a model of the form developed by Fu *et al.* [7] (Figure 1). We capture two types of risky contacts – sexual and needle-sharing – that are the primary routes of HIV transmission among PWID. We use a network model to represent sexual and needle-sharing partnerships [7]. The model is instantiated to reflect sexual and needle-sharing data of enrollees in a needle/syringe program operated by Community Outreach Intervention Projects (COIP) at the University of Illinois at Chicago [8]. The mean age of participants in that study was 40 years old. We obtained the joint sexual and needle-sharing partner distribution for male and female PWIDs in the population, and we simulated a network reflecting this distribution. The contact network evolves dynamically over time as individuals initiate or quit injection drug use, and partnerships form or dissolve. We assumed a constant population size and a steady partnership distribution over time.

Disease transmission is restricted by the contact network, and disease progression is simulated separately for each individual in the model. Our model includes HIV testing, antiretroviral therapy (ART) and opioid agonist therapy (OAT; e.g., methadone or buprenorphine maintenance) to reflect the current scale of HIV prevention programs targeted to PWID. Table 1 lists values and sources for key model parameters, as well as ranges considered in sensitivity analysis; Table S1 shows values and sources for all parameters. We calibrate the model to the proportion of the population who know they are HIV-infected (infection awareness), ART enrollment, and HIV prevalence trends [1, 9, 10]. We simulate the model over a 20-year time horizon in monthly time steps and calculate all healthcare costs incurred and QALYs experienced.

Population

Our model follows the drug injecting population in a representative US urban center. Reflecting data from COIP [8], we model a population of 5000 male and 3503 female PWID [7]. We assume 9.8% baseline HIV prevalence [1]. We assume an open population: individuals enter the population at a monthly rate of 0.1%, and exit following non-HIV or HIV-related mortality.

Network model

The network model captures sexual and needle-sharing contacts. We divide sexual partnerships into two types – regular and casual – since they differ significantly in terms of duration, frequency of sexual acts, and consistency of condom use. Similarly, we divide needle-sharing partnerships into long-term and one-time partnerships. Long-term partners share injection equipment on a regular basis, while one-time partners share once. It is worth noting that the sexual and needle-sharing networks are correlated, since sexual partners are likely to share needles, and vice versa [8].

To generate a simulated network that reflects the joint degree distribution of the COIP PWID network, we use behavioral data collected by COIP to infer values for the parameters that govern network structure: we obtained data on the proportion of PWID having a regular sex partner, the concurrent sexual partnership distribution, and the distribution of long-term needle-sharing partnerships [8]. We adjust these values in model calibration to account for the fact that PWID who enroll in a needle/syringe exchange program (such as that in COIP) are potentially more risk-aware and less prone to risky behaviors than those who do not [7]. We account for the dynamics of the contact network: each existing partnership dissolves at a rate reciprocal to the average duration of that particular type of partnership. We compute the rates at which new partnerships form so that the joint degree distribution of the network remains steady over time [7].

HIV progression and Treatment

Upon acquiring HIV, an individual enters an acute phase marked by high viral load and high infectivity, and then progresses through an asymptomatic phase (CD4 count 500–1,200 cells/mm³), a symptomatic phase (200–500 cells/mm³) and finally AIDS (< 200 cells/mm³). ART suppresses the HIV virus and slows the progression of HIV disease, leading to decreased infectivity and prolonged average duration of the symptomatic and AIDS stages.

HIV transmission

The network model captures the two key routes of HIV transmission among PWID – sexual contact and injection equipment sharing. This allows us to model disease acquisition on an individual basis over time. Each sexual partnership is associated with a frequency of sexual behavior and a binary variable indicating consistency of condom use. These two parameters, together with the HIV stage and ART status of the infected partner, and possible PrEP use by the uninfected partner, determine the HIV transmission risk in each sexual partnership. Transmission risks are not constant over time: for example, if the infected partner progresses from asymptomatic to symptomatic HIV infection, his or her viral load rises, thereby increasing the risk of transmission to the uninfected partner.

Each needle-sharing partnership is associated with a frequency of sharing behavior. We assumed three levels of needle-sharing frequency with long-term partners: once per month (in 38% of long-term needle-sharing partnerships), once per week (45% of partnerships), and once per day (17%) [11]. We assume that needle-sharing partners are equally likely to inject with a used needle (“receptive sharing”); that is, if two partners are sharing a clean needle, there is an equal likelihood of each person being the first to use the needle (a clean needle) or the second to use the needle (a used needle). Transmission risk via each needle-sharing partnership is determined by the number of times a needle is shared with the uninfected partner, the HIV stage and ART status of the infected partner, as well as the uninfected partner’s use of PrEP.

At each time step, we simulate disease transmission for every sero-discordant partnership in the network. A susceptible person becomes infected if HIV transmission occurs via any of his or her risky relationships.

Awareness of HIV status

Infected individuals become aware of their status through HIV testing. We assume that 69.9% of HIV-infected PWID are aware of their infection [1, 9]. Unaware patients receive testing at a rate that depends on their disease stage (e.g., individuals with AIDS are more likely to be diagnosed than those with asymptomatic HIV) and OAT status (individuals are screened for HIV upon enrollment in OAT), and whether they are on PrEP (in which case they are screened every three months). We calibrate the screening rates for individuals not on PrEP so that at any given time, approximately 69.9% of HIV-infected PWID are aware of their status.

Following a positive diagnosis, some PWID immediately initiate ART and adhere to the treatment for life. This probability of ART uptake is higher for individuals in later HIV stages as they have greater need for sustained medical care, and is calibrated to reflect the current ART enrollment level. Awareness of disease status leads to reduced needle-sharing (to a lower level of the three assumed frequencies, if not already at the once per month sharing level) and increased condom use.

Opioid agonist therapy

Opioid agonist therapy (OAT) reduces the number of risky injections and the overdose mortality risk. In our base-case analysis, we assume that 25% of PWID receive OAT, and the annual entrance and exit rates are balanced to maintain a steady OAT enrollment level. We also assume that PWID who quit OAT resume their risk behavior at the level prior to receiving treatment [12].

PrEP strategies

A recent analysis [13] showed that PrEP is most effective when accompanied by a package of clinical care that includes HIV screening every 3 months and increased provision of ART given a positive diagnosis, as recommended by the CDC [4]. We assume a similar program (25% PrEP coverage, HIV screening every three months for those enrolled in PrEP, and access to ART for 50% of newly diagnosed PWID) and consider different strategies for enrolling PWID at high risk of HIV acquisition with the hope of improving the cost-effectiveness of the program. We investigate four strategies: 1) random PWID are enrolled (Unselected Enrollment); 2) individuals are randomly selected and enrolled together with their partners (Enroll Partners); 3) individuals with the highest number of sexual and needle-sharing partnerships are enrolled (Most Partners); 4) individuals with the greatest number of infected partners are enrolled (Most Positive Partners). The last three strategies depend on information about sexual and needle-sharing partnerships: the Enroll Partners strategy relies on the partnership information possessed by each individual, while the Most Partners and Most Positive Partners strategies are idealized strategies that require knowledge of every individual's number of risky contacts and, for the Most Positive Partners strategy, the infection status of every individual in the drug injecting population. Located partners who are found to be HIV-infected receive ART at rates consistent with the rest of PWID population.

To initialize the model, we select a group of PWID according to our enrollment strategy and screen them for HIV infection. Individuals with a negative test result are enrolled in PrEP, while those who are found to have HIV become aware of their infection and receive ART with a given probability depending on HIV stage [4]. We repeat this process until 25% of PWID are enrolled. As the simulation progresses, some enrollees die from non-HIV causes. Additionally, some enrollees become HIV infected since PrEP does not completely eliminate the chance of HIV acquisition; these individuals continue on PrEP until they are diagnosed by screening that accompanies PrEP. New enrollees are selected every 6 months to sustain the 25% enrollment level.

Given the evolution of the contact network as well as the disease status of PWID over time, the high-risk groups reached by the three network-based enrollment strategies also vary over time. To address this variation, we reselect PWID according to our enrollment strategy every 6 simulated months. PWID who are no longer enrolled are assumed to stop PrEP intake.

Health outcomes and costs

We adopted QALY and cost frameworks from previous HIV studies [13–15]. Each simulated month, QALYs and costs accrue to individuals depending on their HIV disease stage,

treatment status, and enrollment in OAT and PrEP programs. We also included future health benefits and costs of individuals still alive at the end of the 20-year time horizon using estimates from published literature [4]. We discounted all values to the present at 3% annually [16]. Using WHO criteria, a strategy is considered to be very cost-effective with an incremental cost-effectiveness ratio (ICER) less than the national annual GDP per capita (\$57,466 in 2016), and cost-effective with an ICER less than three times the per capita GDP [17]. Thus, the cost-effectiveness threshold adopted for this study is \$170,000 (an approximation of \$172,398) per QALY gained.

For the Unselected Enrollment strategy, we assume no additional cost to identify and enroll PWID in PrEP; this assumption is natural since PWID are assumed to be randomly recruited and any one-time enrollment costs are negligible compared to the drug cost of \$10,000 per year [14, 18–20].

For the Most Partners and Most Positive Partners strategies, obtaining the partnership information of the entire PWID population incurs extra cost. Estimation of such cost is difficult, since it depends on the size of the population, the accessibility of PWID (due to the illicit nature of drug use, PWID may be difficult to reach), the amount of information possessed by each individual (a person may be unaware of the disease status of his/her risky contacts), and a variety of other factors. In our baseline analysis we assumed no enrollment cost; in sensitivity analysis we calculated the maximal cost we would be willing to spend on collecting information to make these two strategies still cost-effective.

The Enroll Partners strategy requires health workers to elicit identifying information on the sexual or needle-sharing partners of enrolled PWID, then seek to locate these partners and enroll them in the PrEP program. The cost of contact tracing depends on the cost of collecting and managing identifying information, the cost of physically tracking the identified partners, and the level of incentive offered. The success rate of locating and enrolling partners also affects the cost-effectiveness of such programs. We obtained estimates of the cost and success rate for contact tracing from the Santa Clara County (California) Public Health Department which operates an HIV partner notification service using a team of social workers. They estimate that the cost to track a partner is \$400, and that 30% of those they attempt to track can be located [21]. Thus, we assumed in the baseline analysis that the contact tracing cost for the Enroll Partners strategy would be \$400 per person, with a 30% success rate. We varied these values widely in sensitivity analysis.

Model calibration

We calibrated the model so that projected HIV prevalence matches observed trends, and the proportion of HIV-infected PWID aware of infection/receiving treatment as well as OAT enrollment levels remain steady.

Sensitivity analyses

We performed sensitivity analysis on parameters relating to PrEP program cost, efficacy, and coverage, as well as OAT coverage (ranges in Table 1). Because we calibrated the model to match data from the COIP program [8], we did not vary demographic, behavioral, and epidemiological parameters in sensitivity analysis.

RESULTS

Baseline Results

Baseline results are shown in Figure 2 and Table 2. The least effective strategy is the Unselected Enrollment strategy which, over 20 years, averts 207 new HIV infections and gains 1114 QALYs compared to the status quo. The next most effective strategy, Enroll Partners, averts 435 HIV infections and gains 2087 QALYs compared to the status quo, followed by the Most Partners strategy, which averts 476 HIV infections and gains 2481 QALYs. The most effective strategy, Most Positive Partners, averts 581 HIV infections and gains 3046 QALYs. Costs of the four strategies over the 20-year time horizon are very similar, ranging from \$303 million for the Unselected Enrollment strategy to \$331 million for the Enroll Partners strategy.

The Most Positive Partners strategy is the most cost effective and dominates all other strategies. (The Most Positive Partners strategy strongly dominates the Most Partners strategy and the Enroll Partners strategy, as it costs less yet accrues more QALYs. It weakly dominates the Unselected Enrollment strategy since it has an incremental cost-effectiveness ratio that is less than that of Unselected Enrollment strategy). However, because all strategies may not be realistic in some settings, we also present the cost effectiveness of each strategy compared to no PrEP (Table 2). The Unselected Enrollment strategy costs \$272,000 per QALY gained compared to the status quo of no PrEP, and is thus not likely to be considered cost-effective. The ICER for the Enroll Partners strategy is approximately half as much, at \$158,000 per QALY gained compared to the status quo. This shows that even simple targeting can significantly improve the cost-effectiveness of PrEP. The ICER for the Most Partners strategy is further improved, at \$124,000 per QALY gained compared to the status quo. The ICER for the Most Positive Partners strategy is lowest, at \$101,000 per QALY gained compared to the status quo. All strategies, except the Unselected Enrollment strategy, are cost-effective.

Results of Sensitivity Analysis

Cost and success rate of tracking partners—The base case assumed that the cost to track a partner is \$400, with a 30% success rate in identifying and enrolling partners. We evaluated the Enroll Partners strategy over a wide range of costs and success rates (Figure 3), finding that the Enroll Partners strategy is still more favorable than Unselected Enrollment even if the cost per partner traced is \$1,000 and the success rate in locating partners is 10%. PrEP costs less than \$170,000/QALY gained when the contact tracing cost is no more than \$600 per partner traced and the success rate in locating and enrolling partners is at least 20%. The ICER did not change much as the contact tracing cost and success rate varied (Figure 3). This can be explained by the fact that the cost to track partners is much smaller than cost of PrEP itself.

Some contact tracing programs may consider paying small incentives to partners who enroll in PrEP. The value of such incentives under different assumptions about success in enrolling partners who receive an incentive can be assessed using the information in Figure 3.

Cost of partnership information—Our baseline analysis assumes no cost for obtaining information about the number of (infected) partners that each person has for the Most (Positive) Partners strategy. In sensitivity analysis we calculated the maximum amount of expenditure per person receiving PrEP to obtain network information such that the enrollment strategies that employ network information are at least as cost-effective as the Enroll Partners strategy. The Most Partners strategy is at least as cost-effective as the Enroll Partners strategy if the cost to obtain information about the number of partners of each individual is no more than \$251 per person in the population. The Most Positive Partners strategy is at least as cost-effective as the Enroll Partners strategy if the cost to obtain information about the number of infected partners of each individual is no more than \$518 per person in the population.

Cost of PrEP—We varied PrEP cost from \$4,000 to \$10,000. Figure 4 shows that drug cost critically determines cost-effectiveness. At current drug prices, the cost per QALY gained is below \$170,000 for all enrollment strategies except Unselected Enrollment. At a 60% price reduction, the Unselected Enrollment strategy becomes cost-effective, and the Most Partners and Most Positive Partners strategy very cost-effective.

PrEP efficacy—Previous studies suggest that PrEP's efficacy in reducing HIV acquisition depends strongly on adherence [22]. The Bangkok Tenofovir Study estimated a 49% reduction in risk of HIV acquisition (95% CI: 9.6 to 72.2), and a 74% risk reduction among high adherers (95% CI: 16.6 to 94.0) [23]. It is unclear what level of adherence would be achieved if 25% of PWID in the US received PrEP. To assess this uncertainty, we varied PrEP efficacy from 10% to 90%. Figure 4 shows that cost-effectiveness decreases significantly as efficacy (adherence) decreases, especially for the Unselected Enrollment strategy. When efficacy is below 20%, the cost per QALY gained remains above \$170,000 regardless of enrollment strategy. This suggests that insufficient adherence undermines the value of a PrEP program even if it reaches high-risk PWID.

PrEP Coverage—The baseline analysis assumes 25% PrEP coverage. In sensitivity analysis we varied coverage from 5% to 50% (Figure 4), and observed that cost per QALY gained increases as coverage increases, suggesting that PrEP delivers less marginal health benefit as coverage increases. This is probably because in our network model, which reflects data from a PWID network, a high proportion of uninfected PWID have no HIV-infected contacts; a higher coverage level means enrolling individuals who are not at risk of acquiring HIV, driving down the cost-effectiveness of the intervention. This might not be the case for well-connected PWID communities (with sexual and needle-sharing contacts between many individuals) or for PWID communities with high HIV prevalence.

OAT Coverage—We evaluated the influence of the level of OAT coverage on cost-effectiveness of PrEP program by varying it within the range of 25% to 60%. Figure 4 shows that scaling up OAT reduces the ICERs of Unselected Enrollment, Enroll Partners and Most Partners strategy, though the reduction of ICERs is in a diminishing manner. For the Most Positive Partners strategy, expanding OAT coverage increases the ICER. This suggests that

the marginal health benefit provided by expansion of OAT decreases as the PrEP enrollment strategy reaches individuals at higher risk of acquiring HIV infection.

DISCUSSION

Although PrEP for all PWID is likely not cost-effective at current drug prices [4], PrEP programs that can reach PWID who are at substantially higher than average risk of acquiring HIV infection may be cost-effective. We estimate that with Unselected Enrollment, PrEP for PWID would cost \$272,000/QALY compared to no PrEP; this is similar to the cost of \$253,000/QALY gained estimated in a recent study [4]. A program that enrolls random PWID and then their sexual and needle-sharing partners would be significantly more cost-effective, at \$158,000 per QALY gained relative to no PrEP. Although likely not feasible in practice, an idealized strategy that could enroll PWID who have the greatest number of HIV-infected sexual and needle-sharing partners would cost \$101,000 per QALY gained relative to no PrEP.

Though the Most Positive Partners enrollment strategy significantly improves the cost-effectiveness of PrEP, the knowledge of entire contact network that would enable such a strategy is generally unavailable. In contrast, the Enroll Partners strategy is likely to be feasible in a real-world setting. The idea is to start with unselected PWID, then enroll the sexual/needle-sharing partners of these PWID (first wave), then the risky contacts of those individuals (second wave), and so forth until program capacity is reached. Although not as cost-effective as the Most Positive Partners strategy, the Enroll Partners strategy nonetheless provides a significant improvement in cost-effectiveness compared to the Unselected Enrollment strategy, reducing the ICER to \$158,000/QALY gained. Our analysis highlights the value of targeting PrEP to PWID who are at increased risk of acquiring HIV.

Although we have shown that PrEP delivers greater population-level health benefits when delivered to PWID at highest HIV risk, we emphasize that other PWID who wish to enroll in PrEP should not be excluded.

Our study has several limitations. We exclude the non-PWID population even though PWID can spread the infection to their non-PWID sexual partners. This exclusion may lead to an underestimate of the cost-effectiveness of PrEP programs. For example, we estimate that the Unselected Enrollment strategy would cost \$272,000 per QALY gained compared to the status quo of no PrEP, while a study that also included non-PWID estimated that such a program would cost \$252,000 per QALY gained [4]. However, inclusion of only PWID in our network model does not undermine the conclusion of our study that targeted PrEP is more cost-effective; inclusion of non-PWID would make PrEP look even more favorable. Additionally, we do not include men who have sex with men or sex workers in our model though they constitute a non-negligible proportion of the PWID population [9]. They are often centrally located in the contact network, and selecting this population might make PrEP more cost-effective.

Our model makes several simplifying assumptions regarding needle sharing behavior. We assumed that, in a needle-sharing partnership, each partner is equally likely to inject with a

used needle (“receptive sharing”). A previous study shows that PWID with fewer resources to share are more often engaged in receptive sharing than distributive sharing [24]. Extending our model to assign a specific probability to each needle-sharing partnership of one partner injecting before another would require identifying the socioeconomic status of every PWID in the population and then estimating the probability of receptive and distributive sharing as a function of the difference between the socioeconomic status of two partners. We assumed that awareness of HIV disease status leads to reduced frequency of needle-sharing but the likelihood of receptive sharing is unaffected by the HIV status of the partners. Some studies report the rate of disclosure of HIV+ serostatus to injecting partners to be around 33–49%, and some PWID may adopt strategies to manage the risk, such as asking others to wash used equipment, and limiting the number of injecting partners [25–29]. We were unable to find studies that investigate the behavioral change of PWID who become aware of the HIV+ serostatus of their injecting partners. We also assumed that sharing behavior is unaffected by HCV status. In a serosurvey of out-of-treatment PWID, those who reported awareness of HCV infection engaged in fewer risky behaviors compared to those who were unaware [30]. Other studies, however, suggest that HCV awareness is insufficient to change injection risk behaviors [31, 32] and may even increase needle sharing [33].

Finally, although we performed extensive sensitivity analysis on factors such as PrEP efficacy and cost, and found that the relative cost-effectiveness of PrEP enrollment strategies was unchanged, we cannot address the effect of uncertainty in parameters that govern characteristics of the contact network. This is a common challenge in network models [34].

Our study is the first to evaluate the cost-effectiveness of PrEP for PWID under alternate strategies for enrolling high-risk PWID. Consistent with previous studies on PrEP for men who have sex with men (MSM) and heterosexuals [35–37], we find that PrEP is most valuable when delivered to individuals at highest risk of HIV acquisition. We find that strategies such as enrolling the sexual and needle-sharing partners of PWID enrolled in PrEP can improve the cost effectiveness of PrEP if the partners can be identified efficiently.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

RF, MLB, and DKO designed the study. RF collected data and built and ran the simulation model with advice from MLB. All authors contributed to analyzing the simulation results and writing the report.

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Figure 1. Model schematic

We consider an open population of male and female PWID. Each person is characterized by gender, disease status, awareness, treatment status, and OAT status. Individuals form heterosexual and needle-sharing relationships with each other, thus creating a contact network that spreads HIV among the PWID population. We further distinguish regular and casual sexual partnerships, and long-term and one-time needle-sharing relationships. The bi-layer contact network evolves over time, but we assume that its degree distribution is constant over the 20-year time horizon we simulate.

Figure 2. Results: incremental cost and QALYs

We evaluate a PrEP program under four delivery strategies: Unselected Enrollment, Enroll Partners, Most Partners, and Most Positive Partners. The x-axis shows incremental cost compared to the status quo of no PrEP; the y-axis shows incremental QALYs.

Figure 3. Two-way sensitivity analysis: cost to identify a partner and success rate in locating and enrolling partners for the Enroll Partners strategy

We perform a two-way sensitivity analysis by simultaneously varying the cost to identify a partner on the x-axis and the success rate in locating and enrolling the partner on the y-axis. The resulting ICER is indicated by the color in each grid square.

Figure 4. One-way sensitivity analysis: PrEP cost, efficacy, coverage, and OAT coverage
 For each strategy, we individually vary four parameters that may influence the cost-effectiveness of the PrEP program. Three variables are related to PrEP – its cost, effectiveness, and coverage, and one variable is related to OAT – its coverage. The horizontal bars demonstrate the range of ICERs, and the dashed line represents the cost-effectiveness threshold (\$170,000 per QALY gained, which is approximately three times the US GDP per capita).

Table 1

Values and Sources for Key Model Parameters*

Parameter	Value	Range	Source
Initial HIV conditions			
HIV prevalence	9.8%	--	[1]
Fraction aware of HIV status	69.9%	--	[1, 9]
Initial ART enrollment given aware	40.9%	--	[38, 39]
Injecting behavior			
Long-term needle-sharing partnership duration	36 months	--	[40, 41]
Long-term partnership distribution			[8]
0 partners	64%	--	
1 partner	21%	--	
2 partners	11%	--	
3 partners	3%	--	
4 partners	1%	--	
Distribution of long-term sharing frequency			[11]
1 time per month	38%	--	
1 time per week	45%	--	
1 time per day	17%	--	
One-time sharing frequency	0.14 times/week	--	Estimated**
Sexual behavior			
Percent of male PWID having a regular sex partner	58%	--	[8]
Percent of female PWID having a regular sex partner	82%	--	Calculated
Partnership duration			
Regular sex partner	24 months	--	[42]
Casual sex partner	6 months	--	Estimated**
Concurrent sexual partnership distribution [§] , male and female			[8]
0 partners	26%, 15%	--	
1 partner	51%, 48%	--	
2 partners	17%, 12%	--	
3 partners	6%, 25%	--	
OAT program parameters			
Initial PWID enrollment	25%	25%–60%	[4, 9, 43]
Percent of PWID who quit annually	31.5%	--	[43]
PrEP program parameters			
Weekly infection reduction	48.9%	10%–90%	[23]
HIV screening frequency	3 months	--	[3]
PrEP coverage level (percent of eligible PWID)	25%	5%–50%	Assumed
Success rate of contact tracing	30%	10%–100%	[21]
Cost of contact tracing ^{§§}	400	0–1000	[21]
Annual cost of PrEP drug	10,000	4,000–10,000	[14, 18–20]

Parameter	Value	Range	Source
Annual cost of PrEP screening services	800	--	[14, 44]
Cost of partnership information, per person	0	0–600	Assumed

* ART = antiretroviral therapy; PWID = people who inject drugs

** Estimated through calibration

§ Defined as sexual partnerships a person is involved in at the same time

§§ All costs in 2016 US dollars

Table 2**Benefits and Costs of PrEP Program Over 20 Years**

Enrollment Strategy	HIV Infections Averted[*]	Percent Change in HIV Prevalence at 20 Years[*]	Incremental Costs[*] (\$ Millions)	Incremental QALYs[*]	ICER[†] (\$/QALY gained)	ICER[*] (\$/QALY gained)
Most Positive Partners	581	-28.1%	307	3045.7	101,000	101,000
Most Partners	476	-21.7%	308	2480.5	Dominated	124,000
Enroll Partners	435	-20.6%	331	2086.5	Dominated	158,000
Unselected Enrollment	207	-15.2%	303	1114.1	Dominated	272,000

^{*} Relative to the status quo of no PrEP

[†] Relative to the next most cost-effective strategy on the efficient frontier