Implementation of Syringe Services Programs to Prevent Rapid Human Immunodeficiency Virus Transmission in Rural Counties in the United States: A Modeling Study

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Background. Syringe services programs (SSPs) are effective venues for delivering harm-reduction services to people who inject drugs (PWID). However, SSPs often face significant barriers to implementation, particularly in the absence of known human immunodeficiency virus (HIV) outbreaks.

Methods. Using an agent-based model, we simulated HIV transmission in Scott County, Indiana, a rural county with a 1.7% prevalence of injection drug use. We compared outcomes arising in the absence of an SSP, in the presence of a pre-existing SSP, and with implementation of an SSP after the detection of an HIV outbreak among PWID over 5 years following the introduction of a single infection into the network.

Results. In the absence of an SSP, the model predicted an average of 176 infections among PWID over 5 years or an incidence rate of 12.1/100 person-years. Proactive implementation averted 154 infections and decreased incidence by 90.3%. With reactive implementation beginning operations 10 months after the first infection, an SSP would prevent 107 infections and decrease incidence by 60.8%. Reductions in incidence were also observed among people who did not inject drugs.

Conclusions. Based on model predictions, proactive implementation of an SSP in Scott County had the potential to avert more HIV infections than reactive implementation after the detection of an outbreak. The predicted impact of reactive SSP implementation was highly dependent on timely implementation after detecting the earliest infections. Consequently, there is a need for expanded proactive SSP implementation in the context of enhanced monitoring of outbreak vulnerability in Scott County and similar rural contexts.

Keywords. HIV; agent-based modeling; injection drug use; syringe services; rural health.

There are an estimated 3 million people who inject drugs (PWID) living with human immunodeficiency virus (HIV) worldwide [1]. While there have been great successes in reducing HIV transmission in some settings, there have been outbreaks in recent years [2]. Several factors have been associated with rapid HIV transmission among PWID, including limited access to sterile injection equipment and other harm-reduction services, including syringe services programs (SSPs) [2]. However, predicting where these outbreaks may occur is difficult.

In 2015, Indiana's Scott County experienced the largest HIV outbreak among PWIDs in a nonurban setting in the United States [3]. In 1 year, 181 people were diagnosed with

HIV in a rural community of approximately 24 000 residents [3]. The outbreak, driven mainly by high-frequency injection of oxycodone, elicited a multifaceted emergency response, supported, in part, by the declaration of a public health emergency [3]. Although syringe exchange itself was not explicitly criminalized in Indiana, sterile syringe access was limited by drug paraphernalia laws [4], leading to the operation of underground SSPs. The first legal SSP in Indiana was opened within 1 week of the declaration [3]. The SSP continues to offer needs-based syringe exchange alongside on-site HIV testing and referral to local providers to ensure timely access to substance use and HIV treatment [5]. Recent estimates have suggested that at least 80% of all infections that would eventually be diagnosed had occurred by the time the emergency was declared and the SSP began operation, suggesting that it likely had little impact on the trajectory of the outbreak [6].

It has been suggested that the outbreak in Scott County was entirely preventable had essential harm-reduction resources been available [7]. However, others have claimed that "[the] response in Scott County cannot be compared easily to what has been done

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in urban, less conservative settings” [8]. Using a compartmental model, Gonsalves and Crawford [9] found that early and robust surveillance efforts and case finding alone could reduce nascent epidemics, but this requires facilities like SSPs that can regularly engage vulnerable individuals with services. Nonetheless, despite significant vulnerability to rapid HIV transmission in rural areas of the United States [10], few SSPs exist in these communities [11, 12]. In addition to facilitating the use of sterile needles and syringes and reducing the number of injections with unsterile or used equipment, SSPs serve as an important point of entry for PWIDs to other health and social services, which they might otherwise be reluctant to use [13]. In the United States and many other contexts, operation of SSPs is met with political opposition and other barriers [4], particularly in the absence of a known outbreak, leaving emergency “reactive” implementation (ie, following the detection of an outbreak) as one of the only legal opportunities to bring essential harm-reduction services to these communities. In the current study, we used an agent-based model to estimate the relative benefits of pre-existing and reactive SSP implementation on HIV transmission within a virtual population representative of a rural county in the United States.

METHODS

Model Setting

Agent-based modeling is an individual-based simulation approach used to understand how microlevel interactions generate and influence macrolevel phenomena [14]. Our model simulated HIV transmission for 5 years within a population of 24 110 residents of a rural county in the United States. Detailed information regarding parameter values, calibration, key assumptions, and data sources is shown in the [Supplementary Appendix](#). Parameters were informed by data from Scott County, where possible, as well as by estimates from the existing literature as needed (see [Table 1](#)). This model simulated a population of adults in steady state, where individuals left the population at death or due to aging out at 65 years old. The model progressed in a series of time steps, each representing 1 calendar month. The model simulates the full population. Consequently, it encompasses the heterogeneity of risk of HIV infection present in Scott County during the outbreak [6] and conveys an understanding of the potential spillover effects that SSP implementation might have on HIV transmission among people who do not inject drugs.

Agent Behavior and Network Formation

Injection Behavior and Injection Network Formation

The prevalence of injection drug use within the population was estimated to be 1.7% [3]. An individual engaging in injection drug use was assigned a target number of injection partners per year, drawn from a negative binomial distribution with a mean of 5 partners [6], as well as a target number of injection events per month, drawn from a Poisson distribution with a mean of

Table 1. Key Input Parameter Values for an Agent-based Model Simulating HIV Transmission in a Virtual Population Representative of a Rural County in the United States

Parameter	Value	Source
Sexual behavior		
Number of sex partners per year (mean)	1	[6]
Number of condomless vaginal intercourse acts per month (mean)	13	[16]
Injection behavior		
Proportion of population engaging in injection drug use, %	1.7	[3]
Number of injection partners per year (mean)	5	[6]
Number of injection acts per month (mean)	150	[17]
Probability of syringe sharing (per injection event)		
Among clients of syringe services program, %	2.0	[17]
Among all other people who inject drugs, %	34.0	[17]
HIV transmission		
Per-act risk of HIV transmission, %		
Insertive vaginal intercourse	0.04	[22]
Receptive vaginal intercourse	0.11	[22]
Syringe sharing	0.63	[22]
HIV testing, %		
Proportion of population ever tested for HIV infection	53.6	[5]
Proportion of population tested for HIV infection per year	20.4	[18]
HIV treatment, %		
Antiretroviral treatment use (among people diagnosed with HIV infection)	60.3	[3]
Achievement of viral suppression (among people diagnosed with HIV infection)	42.8	[20]
Reduction in per-act risk of HIV transmission, %		
With antiretroviral treatment use, with viral suppression	94.0	[21]
With antiretroviral treatment use, without viral suppression	17.0	[21]

Abbreviation: HIV, human immunodeficiency virus.

150 injection events [17]. Syringe sharing occurred in 34% of all injection events [17]. We assumed that undiagnosed HIV-infected individuals would be equally likely to share syringes as HIV-uninfected individuals and that injection behavior (eg, number of injection partners and events) did not change following diagnosis [15]. The probability that both sexual and injection behaviors occurred within a dyad of 2 PWIDs in a 12-month period was 12.9% [6].

Sexual Behavior and Sexual Network Formation

We assumed that all individuals in the model were able to engage in sexual behavior. An individual engaging in sexual behavior was assigned a target number of sex partners per year, drawn from a negative binomial distribution with a mean of 1 partner [6], as well as a number of condomless vaginal intercourse acts per month, drawn from a Poisson distribution with a mean of 13 acts [16]. Sexual behaviors protected by condom use were assumed to have little or no risk of HIV transmission and were therefore not explicitly simulated. We assumed that undiagnosed HIV-infected individuals would be equally likely

to engage in condomless vaginal intercourse as HIV-uninfected individuals, but that diagnosed individuals would engage in 27% fewer condomless sex acts each month [15].

HIV Transmission, Treatment, and Progression

The base per-act probabilities of transmission associated with all injection and sexual risk behaviors were derived from a recent meta-analysis [22]. To improve computational efficiency, only behaviors occurring within serodiscordant dyads were explicitly simulated. After seroconversion, an individual experienced a period of increased infectiousness lasting 2 time steps, representing acute-stage infection, where the base probabilities of transmission were increased 5-fold [23]. All HIV-infected individuals experienced a monthly probability of progression to AIDS based on their use of antiretroviral treatment and their achievement of viral suppression [18].

At model initialization, we assumed that 53.6% of all individuals had ever been tested for HIV in their lifetime [17], with a monthly probability of testing of 1.7% [19]. To represent testing activities that may occur during a contact-tracing investigation, after 10 newly diagnosed infections an individual was tested with a probability of 87.3% in the time step immediately following the diagnosis of a partner [3].

Upon diagnosis, an individual initiated antiretroviral treatment in the next time step with a probability of 60.8% [3] and achieved viral suppression with a probability of 42.8% [19]. Upon initiating treatment, the base probabilities of transmission were reduced by 94% among individuals with viral suppression and by 17% among individual without viral suppression [21]. In the base case scenario, postdiagnosis changes in sexual behavior, access to HIV testing, and reduced probabilities of transmission with the provision of antiretroviral treatment represent the only interventions taken to reduce transmission.

Syringe Services Program Access and Utilization

As was observed during the outbreak in Scott County, we assumed that, in scenarios where the SSP was implemented, an estimated 55% of all PWIDs utilized its services [17]. Individuals enrolled in the SSP were less likely to share syringes with their partners (ie, 2% of injection events involved syringe sharing among clients of the SSP versus 34% among all other PWIDs) [17]. There were no changes to the number of injection partners or the frequency of injection among clients of the SSP [17].

Model Scenarios

The model simulated HIV transmission over 5 years. At model initialization, a single HIV-infected individual without viral suppression was introduced into the injection network. In the base case scenario, this initial infection was introduced and the SSP never became available. In 2 counterfactual scenarios, the SSP became available after a threshold of 10 newly diagnosed infections was met (representing reactive implementation) or

became available at model initialization without any required threshold (representing an existing SSP). All scenarios were simulated for 1000 iterations.

Outcome Measures

The primary comparison measure was HIV incidence (expressed as the number of new infections per 100 person-years) and the associated percent reduction relative to the base case scenario. All measures were stratified by engagement in injection drug use.

Sensitivity Analyses

Sensitivity analyses were conducted to examine the robustness of the primary analyses to uncertain model parameters that might impact the observed effect of SSP implementation, including the diagnosis-based threshold for reactive implementation of the SSP and the coverage of the SSP upon implementation.

RESULTS

In the absence of an SSP, the model predicted 210 incident infections (95% simulation interval [SI], 206–214 infections) in the entire population over 5 years (Figure 1), corresponding to an incidence of 0.18 infections per 100 person-years (95% SI, 1.07–1.13 infections) and resulting in a prevalence of 0.96% (95% SI, 0.94–0.98%) after 5 years. The vast majority of these infections were among PWID, who accounted for between 1.5% and 2.1% of the population in each iteration. Among PWID, the model predicted 176 incident infections (95% SI, 173–180 infections) in 5 years, corresponding to an incidence of 12.1 infections per 100 person-years (95% SI, 11.8–12.4 infections) (Figure 2) and resulting in a prevalence of 43.5% (95% SI, 42.6–44.4%) (Figure 3) after 5 years. Few infections occurred among people who do not inject drugs, with 34 incident infections (95% SI, 33–35 infections) in 5 years, corresponding to an incidence of 0.03 infections per 100 person-years (95% SI, 0.03–0.03 infections) (Figure 2) and resulting in a prevalence of 0.22% (95% SI, 0.22–0.23%) (Figure 3) after 5 years.

Proactive implementation of an SSP reduced the size of the outbreak. In this scenario, the model predicted 32 incident infections (95% SI, 31–33 infections) over 5 years (Figure 1), corresponding to an incidence of 0.03 infections per 100 person-years (95% SI, 0.02–0.03 infections) and resulting in a prevalence of 0.22% (95% SI, 0.22–0.23%) after 5 years. Among PWID, 154 infections (95% SI, 152–155 infections) were averted, decreasing the incidence by 90.3% to 1.17 infections per 100 person-years (95% SI, 1.11–1.23 infections) (Figure 2). The average prevalence among PWID after 5 years decreased by 86.0% to 6.1% (95% SI, 5.8–6.4%) (Figure 3). People who did not inject drugs also benefitted in this scenario (Figures 2 and 3).

Reactive implementation of the SSP following the diagnosis of 10 infections was able to reduce the size of the outbreak.

Figure 1. Cumulative number of incident HIV infections in a rural county in the United States over a 5-year period following the introduction of a single infection when an SSP was never implemented (A), when an SSP was existing at initialization (B), and when an SSP was implemented after 10 incident HIV infections were diagnosed (C). Abbreviations: HIV, human immunodeficiency virus; SSP, syringe services program.

In the scenarios where the diagnosis-based threshold of 10 infections was met ($n = 992$), the SSP was implemented an average of 10 months after model initialization. The model predicted an average of 91 incident infections (95% SI, 89–94 infections) over 5 years (Figure 1), corresponding to an incidence of 0.08 infections per 100 person-years (95% SI, 0.07–0.08 infections) and resulting in a prevalence of 0.47% (95% SI, 0.46–0.48%) after 5 years. The largest reductions were observed among PWID with 107 infections (95% SI, 105–109 infections) averted, decreasing the incidence by 60.8% to 4.0 infections per 100 person-years (95% SI, 3.9–4.1 infections) (Figure 2). The average prevalence among PWID after 5 years decreased by 58.4% to 18.1% (95% SI, 17.6–18.6%) (Figure 3). People who did not inject drugs also benefitted (see Figures 2 and 3).

Sensitivity Analyses

The impact of reactive SSP implementation on transmission was sensitive to the diagnosis-based threshold used to trigger its implementation, with larger reductions in incidence observed with a lower threshold and smaller reductions observed with a higher threshold (Supplementary Figure 1). These results were also sensitive to the coverage of the SSP upon implementation, with larger reductions with higher coverage and smaller reductions with lower coverage (Supplementary Figure 2).

DISCUSSION

To our knowledge, this study is the first to model the relative benefits of reactive and proactive implementation of SSPs in reducing HIV transmission among PWID. In the absence

of an SSP, the model predicted large outbreaks among PWID following the introduction of HIV into the network, with incidence rates reaching levels observed among PWID in many urban settings in the United States in the early 1990s before the advent of antiretroviral treatment [24, 25]. The eventual size of the outbreak could be reduced if an SSP was implemented proactively before the introduction of HIV into the network. Our model also suggests that SSP implementation may have spillover effects. In averting infections occurring via injection drug use, we are likely also averting transmission between PWID and their partners who do not inject drugs.

Our simulations suggest that the introduction of an SSP after the identification of 10 new infections attributable to injection drug use has the potential to substantially reduce the eventual size of an outbreak if timely detection of the earliest infections is possible. The occurrence of a large outbreak in Scott County, Indiana, in 2015, alongside other recent injection-related outbreaks in Greece, Ireland, and Israel, has raised concerns regarding the vulnerability of similar communities to the rapid spread of HIV among PWIDs [2, 10]. However, it is difficult to predict when and where such outbreaks may occur. Since the outbreak in Scott County, at least 120 HIV infections have been diagnosed as part of an outbreak related to the injection of fentanyl, a potent synthetic opioid, in 2 counties in Massachusetts. Although 220 US counties were recently identified as vulnerable to rapid HIV transmission among PWID [10], these 2 counties were not included in this list, emphasizing a continued need to improve access to SSPs regardless of the potential for an outbreak and highlighting a need for improved monitoring of outbreak vulnerability.

Figure 2. Density plot of HIV incidence (per 1000 person-years) in a rural county in the United States over a 5-year period following the introduction of single infection when an SSP was never implemented (purple shading), when an SSP was implemented after 10 incident HIV infections are diagnosed (blue shading), and when an SSP was existing at initialization (red shading), stratified by injection drug use. Abbreviations: HIV, human immunodeficiency virus; SSP, syringe services program.

In the model, syringe exchange was not modeled as an explicit process, but rather, accessing an SSP was implied in the reduced probability of syringe sharing among SSP clients. Current best-practices guidelines for SSP operation recommend that SSPs be low threshold, easy to enroll in, and harm-reduction oriented and that they actively attract clients to services [13]. However, utilization of SSPs and the associated behavior change among their clients may vary based on syringe exchange policy. In Scott County, the SSP offers needs-based syringe exchange, placing no limits on the number of syringes a client can receive regardless of the number of used syringes returned [17]. In other contexts, policies are more restrictive, placing arbitrary limits of the number of syringes a client may receive or restricting distribution to a “one-for-one” basis. Previous research has shown that more restrictive policies are associated with lower SSP utilization [26, 27]. High population-level coverage of an SSP is crucial to realize the full preventive benefits associated with these programs. The modeled impact of SSP implementation on HIV incidence was sensitive to its population-level coverage, where higher incidence was observed among PWID upon reactive implementation

Figure 3. Distribution of HIV prevalence in a rural county in the United States at the end of a 5-year period following the introduction of a single infection when an SSP was never implemented, when an SSP was implemented after 10 incident HIV infections are diagnosed, and when an SSP was existing at initialization, stratified by injection drug use. Abbreviations: HIV, human immunodeficiency virus; SSP, syringe services program.

with lower-than-observed coverage and lower incidence was observed with higher-than-observed coverage.

In addition to providing sterile injection equipment, SSPs offer many additional harm-reduction services that improve the health of PWID. Current best-practices guidelines for SSP operation also recommend that syringe exchange be integrated with other services where possible and offer referrals to drug treatment, legal aid, family and housing advice, and safe consumption spaces where available [13]. A recent modeling study has suggested that the expansion of syringe exchange services in the United States alone would be cost-saving when considering costs saved on the treatment of averted HIV infections [28]. The provision of overdose education and naloxone distribution and coordination of linkage to treatment for substance use disorders through SSPs were also found to be cost-saving when considering reductions in medical care and mortality related to overdose [29]. As such, the current analyses may underestimate all of the potential benefits of reactive and proactive implementation of SSPs because our simulations focus on HIV transmission only.

Several limitations to our study demand further investigation. First, the implementation of the SSPs represented the only intervention explicitly introduced in addition to the preventive benefits of HIV testing and provision of antiretroviral treatment for people living with HIV to reduce transmission. The model does not account for the potential benefits that other harm-reduction services may have in altering injection behavior [29]. Second, the model does not account for heterogeneity in injection behavior by substances used. In Scott County, 92% of all PWID who were diagnosed during the outbreak reported injection of oxycodone [3]. Some substances may have longer or shorter durations of action, potentially resulting in varying injection and syringe-sharing frequencies and, subsequently, different opportunities for HIV transmission. The model does not account for transitions between injection and noninjection drug use that may result in a population of PWID of varying size over time [30]. Finally, local data were used to parameterize the model where possible, but as in many agent-based models, the input parameters were derived from multiple sources, which may introduce bias and adversely affect the representativeness of the model and the generalizability of its outputs [31]. However, given that the vast majority of parameters were derived from the outbreak investigation in Scott County, we are confident that the magnitude of this bias, if present, is minimal. It is unclear how representative Scott County is of other rural counties in the United States. As such, future research is needed to characterize the injection networks present in these settings to understand how the structure of these networks facilitates or impedes rapid transmission of HIV infection.

In conclusion, based on model predictions, proactive implementation of an SSP in Scott County had the potential to avert more HIV infections than reactive implementation after the detection of an outbreak. The predicted impact of reactive SSP implementation was highly dependent on the timely detection of the earliest infections. Consequently, there is a need for expanded proactive SSP implementation in the context of enhanced monitoring of outbreak vulnerability in Scott County and in similar rural contexts.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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