Austin Journal of HIV/AIDS Research

Open Access

Austin Publishing Group

Research Article

Dynamics of the HIV Epidemics among Male Injecting Drug Users Using Agent-Based Modeling

Le TT[1], Shojaati N[2] and Lim HJ[1]*

[1]Department of Community Health and Epidemiology, College of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan, Canada

[2]Department of Computer Science, College of Arts & Sciences University of Saskatchewan, Saskatoon, Saskatchewan, Canada

***Corresponding author:** Hyun Ja Lim, Department of Community Health and Epidemiology, College of Medicine, University of Saskatchewan, 104 Clinic Place, Saskatoon, SK, S7N 5E5, Canada

Received: March 17, 2021; **Accepted:** April 09, 2021; **Published:** April 16, 2021

Abstract

Background: Although Injecting Drug Users (IDUs) carry a disproportionate burden of HIV, little is known about the dynamics of the HIV epidemics among IDUs.

Objective: This study aimed to characterize the dynamics of the HIV epidemic among IDUs and the effects of alternative HIV prevention intervention strategies using Agent-Based Modeling (ABM).

Methods: ABM was constructed using key behavioral risks. The HIV/STI Surveillance study was utilized to create datasets for simulation. Different intervention scenarios were simulated and compared.

Results: Lowering needle sharing level among IDUs resulted in the largest reductions in both HIV prevalence and the cumulative number of HIV infections over time in all simulated populations. The majority of the reductions occurred when needle sharing declined from the baseline level to 40% and 30%, respectively.

Conclusion: ABM may well complement traditional epidemiological regression-based analysis in providing important insights into the complex dynamics of the HIV epidemics among IDUs.

Keywords: HIV/AIDS; HIV dynamics; Injecting Drug Users (IDU); Agent-Based Model (ABM)

Introduction

There were an estimated 15.9 million people who might inject drugs worldwide, with nearly three-quarters of these individuals being from low- and middle-income countries [1,2]. Injecting drug use has made a substantial contribution to the HIV epidemic globally [3]. Although IDUs account for an estimated 0.2-0.5% of the world's population, they make up approximately 5-10% of people living with HIV globally [4]. In many parts of the world, the direct sharing of needles, syringes, and other injection equipment among IDUs has driven the HIV epidemic [2,4]. People who inject drugs have as 22 times higher the rate of HIV infection as the general population [5]. All regions report high HIV prevalence among IDU population, although the severity varies [2]. The HIV prevalence among IDUs ranged from 5% in Eastern Europe to 28% in Asia [2].

Despite the significant burden of HIV among IDUs, little is known about the dynamics of the HIV epidemics in this population. The majority of existing HIV research and analysis primarily rely on statistical regression-based models [6]. The key motivation for the use of regression-based approach has been the desire to estimate the effect of independent risk factors on a particular outcome, after statistically controlling for individual-level attributes which could simultaneously be related to both the risk factors and the outcome [6]. However, with the efforts to isolate the effect of changing a single factor while controlling for all other factors in the model, regression modeling approach might be ill-equipped to investigate the processes embedded in complex systems characterized by dynamic interactions among heterogeneous individuals, and between individuals and their environment [6]. Regression-based models thus present challenges which are associated with the incapacity of examining the dynamic and often reciprocal processes from which the HIV epidemic emerges [6].

There is increasing recognition that advanced computational modeling, which simulates the real world as it might be in a variety of circumstances, may address some of the challenges faced by traditional statistical regression-based methods [6,7]. Agent Based-Modeling (ABM) is a computational simulation method that defines the behavior of a population of heterogeneous individuals within an environment in which characteristics of the population are driven by the interactions of the individuals with each other and with the environment [8]. Compared with other types of HIV models which are built using mathematical or statistical equations, agent-based approach is advantageous in allowing understandings of heterogeneous individuals' behaviors and interactions between individuals, representation of the environment with which individuals interact, and a natural correspondence to real life situation that enhances model transparency for stakeholders [7,9]. ABM simulation also allows experimentation with the model by answering 'what-if' types of questions such as 'What if certain quantitative assumptions are altered'? 'Does the model reflect the real system that it represents'? and 'How will the model behave after a certain period of time'? [9] By experimentation with the model, ABMs can provide insights into the impact of behavioral feedbacks that may occur during the epidemic [8,9]. They further allow policy makers to understand multi-

Citation: Le TT, Shojaati N and Lim HJ. Dynamics of the HIV Epidemics among Male Injecting Drug Users Using Agent-Based Modeling. Austin J HIV/AIDS Res. 2021; 7(1): 1048.

Table 1: List of key parameters used in the Agent-Based Model.

Parameters	Values	Data Sources
Percentage of drug injection among SSWs	7.30%	2009 IBBS data
Percentage of drug injection among VSWs	2.40%	2009 IBBS data
Percentage of needle sharing among IDUs	50%	2009 IBBS data
Percentage of consistent condom use with FSWs by male IDUs	61%	2009 IBBS data
Percentage of consistent condom use with clients by SSWs	61%	2009 IBBS data
Percentage of consistent condom use with clients by SSWs	63%	2009 IBBS data
Number of sexual partners of SSWs per month: mean (min, max)	27.0 (18.0, 300.0)	2009 IBBS data
Number of sexual partners of VSWs per month: mean (min, max)	19.0 (14.0, 221.0)	2009 IBBS data
Number of sexual partners of male IDUs per month: mean (min, max)	2.0 (0.0, 92.0)	2009 IBBS data
Number of FSWs that male IDUs visited per month: mean (min, max)	1.0 (0.0, 92.0)	2009 IBBS data
IDU network size: mean (min, max)	9.0 (6.0, 600.0)	2009 IBBS data
Frequency of drug injection among IDUs	52% of IDU population injected at least twice per day	2009 IBBS data
Probability of HIV transmission through injecting drug use	0.002 - 0.004	Public Health Agency of Canada, 2012 [25]
Probability of HIV transmission through single needle stick	0.007 - 0.008	Public Health Agency of Canada, 2012 [25]
Probability of HIV transmission via receptive vaginal intercourse (i.e., male to female)	0.01 - 0.002	Public Health Agency of Canada, 2012 [25]
Probability of HIV transmission via insertive vaginal intercourse (i.e., female to male)	0.0005 - 0.001	Public Health Agency of Canada, 2012 [25]
Time to progress from primary HIV infection to acute HIV infection: mean (min, max)	21 days (14, 28)	U.S. Department of Health and Human Services, 2017 [26]
Time to progress from acute HIV infection to latent HIV infection: mean (min, max)	21 days (7, 28)	Canadian Foundation for AIDS Research, 2017 [27]
Time to progress from latent HIV infection to AIDS: mean (min, max)	9 years (1, 20)	Nadler, 2005 [28] O'Brien, 2004 [29] U.S Department of Health and Human Services, 2017 [26]
Time to progress from AIDS to death: mean (min, max)	3 years (1, 10)	Nadler, 2005 [28] O'Brien, 2004 [29] U.S Department of Health and Human Services, 2017 [26]

level determinants of HIV infection and to design and assess the effectiveness of HIV intervention policies [10]. Agent-based modeling has increasingly been employed in population health research, such as drug and alcohol health behavioral research, obesity, physical activity, and infectious diseases [11-16]. In recent years, agent-based approach has also been applied in HIV epidemic modeling [7-9,17-19]. However, to the best of our knowledge, there has not been any research using ABM to simulate HIV future trends among IDUs and to assess the effectiveness of HIV prevention interventions targeting this high-risk population. The aims of this study are (i) to characterize the dynamics of the HIV epidemic among IDUs and (ii) to explore the effects of alternative HIV prevention intervention strategies.

Materials and Methods

In this study, key behavioral data from the '2009 HIV/STI Integrated Biological and Behavioral Surveillance' (IBBS) study in Vietnam was utilized for constructing ABM to examine the relevance of agent-based approach in studying the dynamics of the HIV epidemic among IDUs and to explore the effects of various intervention strategies. The IBBS study is the first systematically community-based surveillance survey in Vietnam. More detailed descriptions of the IBBS study have been published elsewhere [20,21]. Briefly, the study was jointly conducted by the Vietnam Ministry of Health and Family Health International (FHI 360) since 2005 to provide estimates of HIV and Sexually Transmitted Infection (STI) prevalence as well as risk behaviors among HIV high-risk populations, including male IDUs and Female Sex Workers (FSWs) and men who have sex with men.

Model description

Model population: Model population size was set as 100,000 individual agents, taking into account the trade-off between the sizes of the population simulated, the sophistication of the model, and the model run time. An agent was drawn from a common population and changed its state (status) over the course of simulated time in the model, depending on its current risk behaviors (Figure 1). Given the intertwining of the drug injection-related epidemic and the heterosexual epidemic in Vietnam [22,23], relevant data on FSW population and HIV risk behaviors were also incorporated to build the model. To achieve close estimates of the proportion of IDUs and FSWs in the population, the model used assumptions from the Asian Epidemic Model developed by Brown and Peerapatanapokin that male IDUs account for 2.0% of adult male population while FSWs account for 1.0% of adult female population. FSW population is consisted of Street-Based Sex Workers (SSWs) (accounting for 30%) and Venue-Based Sex Workers (VSWs) (accounting for 70% of the overall sex worker population) [24]. The Male/Female (M/F) ratio set in this model closely reflected the actual M/F ratio in which males account for 51% and females account for 49% of the population. The population simulated was an open population with birth rate and death rate integrated into the model to capture population inflow and outflow.

Model parameters: An ABM that is simple but includes requisite mechanisms was constructed to maximize learning regarding the origin of emergent patterns observed in epidemiological data, and to understand the implications of existing intervention theories. The ABM therefore used only selected socio-demographic factors (i.e., sex and age), and drug injection-related behaviors (i.e., prevalence of drug injection, frequency of drug injection, prevalence of needle sharing among IDUs, and size of IDU network). In this model, a number of parameters related to HIV transmission and risk behaviors were created, with their values being set based upon IBBS data, past epidemiological research and prior knowledge (Table 1).

Statecharts capturing the dynamics of the HIV epidemics among injecting drug users: The dynamics of the HIV epidemics among IDUs was captured via the construction of four statecharts, including: i) HIV infection statechart; ii) Mortality statechart; iii) Drug use statechart; and iv) Sex work statechart as depicted in Figure 1. These four statecharts each maintained a separate focus but interlinked with each other in many different ways to represent the overlap and intertwinement between IDUs and FSWs as well as between these two high-risk populations and other low-risk populations.

The HIV infection statechart (HIV_Infection_StateChart) (Figure 1) was constructed to capture the natural progression of HIV infection. Upon creation, a not-yet-infected individual started in the 'Susceptible' state.

Upon initiation of either of needle sharing behavior or unsafe sex, the not-yet-infected individual would either get infected and progress to the 'Primary HIV' state or remain uninfected in the 'Susceptible' state, depending on a pre-specified probability. Once an infected individual was in the 'Primary HIV' state, it would progress to subsequent states representing HIV progression. An individual was removed from the population when it reached the 'Death' state. The residence times for an individual's residence in different HIV states are presented in Table 1.

The mortality statechart (Mortality_StateChart) (located on top of Figure 1 and connects with the HIV infection statechart) was constructed to specify mortality rates for different individuals

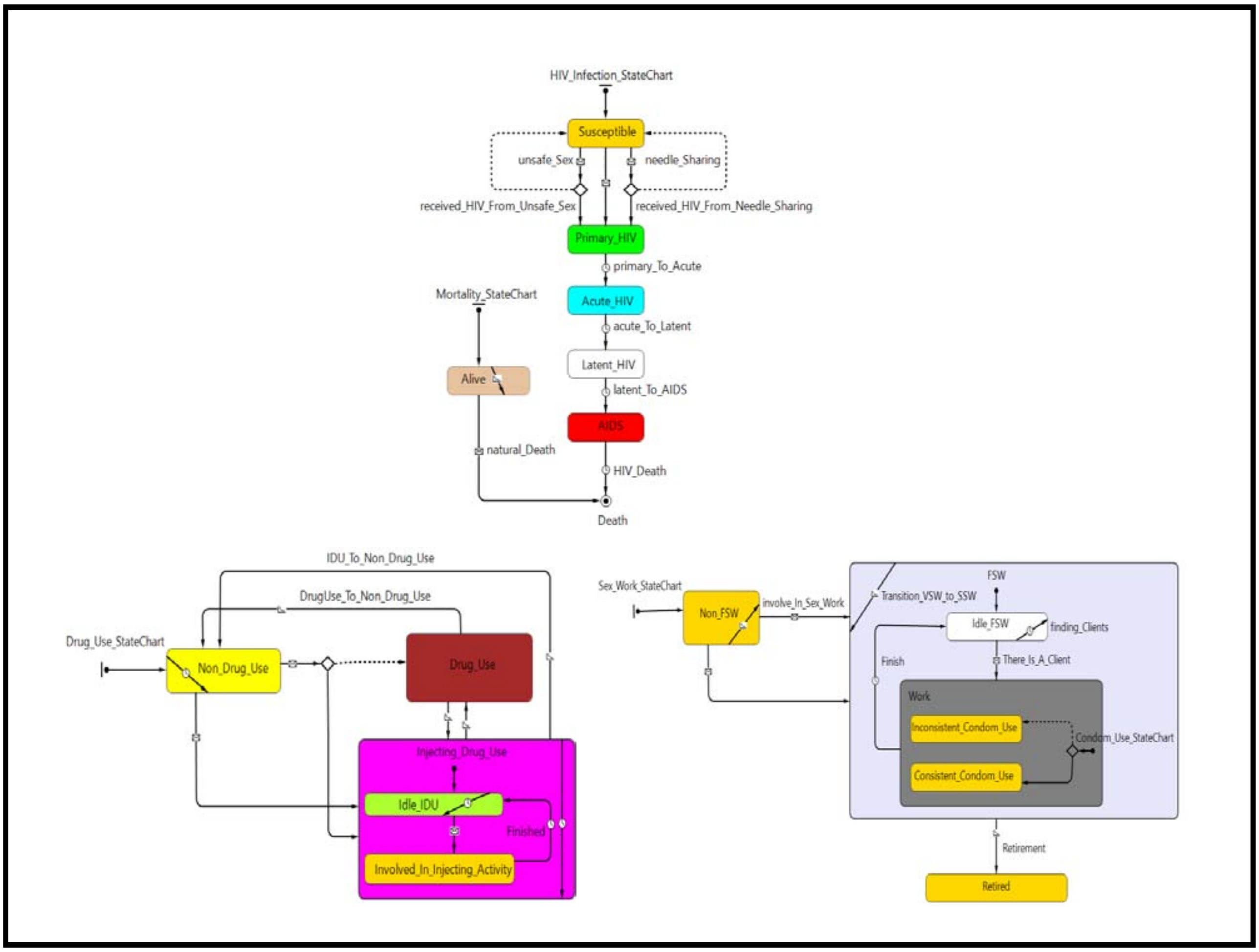

Figure 1: Statecharts representing the dynamics of the HIV epidemics among injecting drug users: HIV Infection Statechart and Mortality Statechart (Top), Drug Use Statechart (Bottom left), and Sex Work Statechart (Bottom right).

in the model. The mortality statechart was also linked with the HIV infection statechart to capture HIV/AIDS related-mortality. Calculation of a mortality rate for a specific agent took into account various characteristics of an agent, including age, sex, and current HIV infection status and risk behaviors.

The drug use statechart (Drug_Use_StateChart) (located at the bottom left of Figure 1) captured drug injection-related behaviors of an individual. Every individual started as a non-drug user as the model started. At a pre-specified rate per year, a proportion of the general population became involved in drug use. An individual could either injected immediately upon initiating drug use or first became a user of other drugs (ODU) and then subsequently switched from an ODU to an IDU. Once an agent became an ODU in the 'Drug Use' state, it could move back and forth between the 'Drug Use' and 'Injecting Drug Use' state. The likelihood of transiting from the 'Drug Use' state to the 'Injecting Drug Use' state was set at a higher value than the transition from 'Injecting Drug Use' to 'Drug Use' state in order to capture the real situation where the majority of ODUs switched to become IDUs after a period of time. However, once they have injected drugs, there is only a small chance that IDUs abandon it for recreational drug use. Similarly, there were transitions from 'Drug Use' and 'Injecting Drug Use' to 'Non Drug Use' state respectively to capture the probability that a proportion of the ODU or IDU population quit drug use and move back to the non-drug use population, either by their own decision or via drug use prevention interventions such as Methadone Maintenance Therapy, drug rehabilitation programs, and behavioral change interventions. Given the plausibility of quitting recreational drug use over quitting drug injection, the rate to transit from the 'Drug Use' to 'Non Drug Use' state was often higher than the one from the 'Injecting Drug Use' to the 'Non Drug Use' state.

Key drug injection-related behaviors, including frequency of drug injection, needle sharing, and the IDU's egocentric network size (defined as the number of other IDUs who an IDU knew and met in the last month) were all captured in a nested statechart within the 'Injecting Drug Use' state. The rationale for creating a nested statechart within the 'Injecting Drug Use state was to reflect the need to represent drug injection-related behavior. Since needle sharing is by definition an activity involving at least two people (often concurrently), capturing the interaction between these people is important in understanding how HIV spreads among the IDU population. In the 'Idle IDU' state, an agent was assumed to stay away from drug injection. We assumed that IDU inject at least twice per day and at a specific time of each day, in which case they would move to the 'Involved in Injecting Activity' state. This is the place where most of the drug injection-related behaviors occurred (e.g., organizing 'parties' for drug injection, meeting other drug injecting partners in a 'drug party', and needle sharing). Any IDU in a drug party could share needles and syringes with IDUs of their choice. As long as one needle/syringe was infected, HIV would have a chance to spread within the specific network of those who shared that infected needle/syringe. The model was set so that drug parties took place where there was needle sharing among IDUs members and also where there was no needle sharing. An IDU agent could randomly go to one type of drug party or the other. It is worth mentioning that the percentage of drug parties with needle sharing attributes (i.e., those where needle sharing activities occurred) could be varied in the model to chart the impact of behavioral changes on the level of HIV infection. Once the injecting activity was completed, the agent moved back from the 'Involved in Injecting Activity' to the 'Idle IDU' state and a new cycle started again at a different point in time.

The sex work statechart (Sex_Work_StateChart) (located at the bottom right of Figure 1) captured sexual risk behaviors (including condom use practice) of both IDUs and FSWs. The reason to include FSW component in the model capturing the HIV epidemics in IDUs is because of the intertwinement in sexual risk behaviors between IDUs and FSWs. A part of the IDU population engaged in commercial sexual relationships with FSWs and condom use was not widely practiced in these populations, particularly IDUs. Within the sex work statechart, every FSW started as a general woman in the population. At a pre-specified rate per year, a proportion of the general female population initiated involvement in the sex work industry and became FSWs. A FSW remained in the sex industry for a certain period of time before they retired from sex work, with the retirement rate depended on the current age of the FSWs. Two predominant sexual behaviors risk factors of FSWs: number of clients and condom use practice were represented via the two nested statecharts within the 'FSW' state. A FSW agent was in the 'Idle FSW' state when she did not have any clients to serve. Once she found a client, the FSW moved from the 'Idle FSW' to the 'Work' state where the sexual transaction occurred. When the transaction completed, she returned to 'Idle FSW' and a new cycle of client seeking began. Condom use practice among FSWs and IDUs was both represented in the 'Condom Use StateChart' as the branch with two conditional transitions, each of which applies at time of initiation of commercial sex work: the solid transition to 'Consistent Condom Use' state represented a situation in which the FSW or IDU would adhere to consistent condom use, while the dashed transition to 'Inconsistent Condom Use' state represented prevalence situation in which the FSW or IDU would maintain inconsistent condom use.

Time horizon: The time unit for this model was a 'year'. The time horizon specified was 50 years and the model was continuous in time, meaning that the model ran for 50 years from its start with events occurring as finely or coarsely as required, rather than having time divided into discrete time steps.

Monte Carlo sensitive analysis

Monte Carlo sensitivity analysis, with each simulation being run for 100 realizations, was performed to examine the effects of stochastic variability on model outputs, since this might shed light on the degree to which the model explains the variability seen in the empirical IBBS data.

Experimentation with different intervention scenarios

Once the logic of the ABM was confirmed, different HIV prevention intervention scenarios based upon different levels of risk behaviors were simulated and compared with a baseline scenario to examine which intervention scenario(s) reduce HIV infection the most in each simulated population (Table 2). The baseline scenario served as the reference scenario, having incorporated levels of risk behaviors drawn from the IBBS study. The experimentation included: (i) five scenarios investigating the impact of lowering the needle sharing level to a level in the range (40% - 0%) from the baseline level

Table 2: List of experimental scenarios.

HIV prevention intervention scenarios	Needle sharing levels	Consistent condom use levels
Baseline scenario	50% among IDUs	61% among IDUs 61% among SSWs 63% among VSWs
Scenarios lowering needle sharing levels among IDUs		
Scenario 1 (NS_40%)	40% among IDUs	61% among IDUs 61% among SSWs 63% among VSWs
Scenario 2 (NS_30%)	30% among IDUs	61% among male IDUs 61% among SSWs 63% among VSWs
Scenario 3 (NS_20%)	20% among IDUs	61% among IDUs 61% among SSWs 63% among VSWs
Scenario 4 (NS_10%)	10% among IDUs	61% among IDUs 61% among SSWs 63% among VSWs
Scenario 5 (NS_0%)	0% among IDUs	61% among IDUs 61% among SSWs 63% among VSWs
Scenarios increasing consistent condom use levels among IDUs and FSWs		
Scenario 1 (CU_70%)	50% among IDUs	70% among IDUs, SSWs, VSWs
Scenario 2 (CU_80%)	50% among IDUs	80% among IDUs, SSWs, VSWs
Scenario 3 (CU_90%)	50% among IDUs	90% among IDUs, SSWs, VSWs
Scenario 4 (CU_100%)	50% among IDUs	100% among IDUs, SSWs, VSWs
Combined scenarios of lowering needle sharing levels among IDUs and increasing consistent condom use levels among IDUs and FSWs		
Scenario 1 (NS_40% & CU_70%)	40% among IDUs	70% among IDUs, SSWs, VSWs
Scenario 2 (NS_30% & CU_70%)	30% among IDUs	70% among IDUs, SSWs, VSWs
Scenario 3 (NS_30% & CU_80%)	30% among IDUs	80% among IDUs, SSWs, VSWs
Scenario 4 (NS_20% & CU_80%)	20% among IDUs	80% among IDUs, SSWs, VSWs
Scenario 5 (NS_10% & CU_90%)	10% among IDUs	90% among IDUs, SSWs, VSWs

of 50% among IDUs while retaining the level of consistent condom use as in the baseline scenario; (ii) four scenarios of increasing consistent condom use level (positing adherence of 70% - 100%) from the baseline level of 61% among male IDUs, 61% among SSWs and 63% among VSWs, while retaining the level of needle sharing among IDUs as in the baseline scenario; and (iii) five combined intervention scenarios of lowering the needle sharing level to a value in the range (40% - 0%) among IDUs while simultaneously increasing consistent condom use level to a value in the range (70% - 90%) among male IDUs and FSWs.

Software

AnyLogic 7.1.2 Professional Edition was used as a platform to construct and simulate the ABM.

Results

Baseline scenario

If risk behaviors of IDUs remained at the levels as observed in the IBBS study, HIV prevalence among IDUs kept increasing from almost zero percent as the model started to reach 36.1% at year 50 (Figure 2A, blue line). The HIV prevalence also increased in the overall population, from almost zero percent to 0.5% at year 50 (Figure 2B, blue line). There was a cumulative count of 1,383 HIV cases among male IDUs and 1,699 cases among the overall population over 50 years (data now shown).

Intervention scenarios involving lowering needle sharing level among IDUs

Lowering needle sharing level among IDUs reduced both the prevalence and the cumulative number of HIV infections. For male IDUs, HIV prevalence reduced from 36.1% at baseline to 23.2% in NS_40%, 6.8% in NS_30%, and to less than 1% in other three scenarios at year 50 (Figure 2A). There was a 35% reduction in cumulative HIV cases among male IDUs in NS_40%, 80% reduction in NS_30%, 97% reduction in NS_20%, and almost 100% reduction in the remaining two intervention scenarios over 50 years (data not shown). The same pattern of reduction was observed among the overall population (Figure 2B). In all simulated populations, the largest reductions in both HIV prevalence and the number of HIV cumulative cases at year 50 were observed when needle sharing level was lowered from 40% to 30%.

Intervention scenarios of increasing consistent condom use level among male IDUs and FSWs

Increasing consistent condom use did not appear to have a significant impact on the reduction of HIV among IDUs or amongst the overall population. A slight decrease in HIV prevalence - from

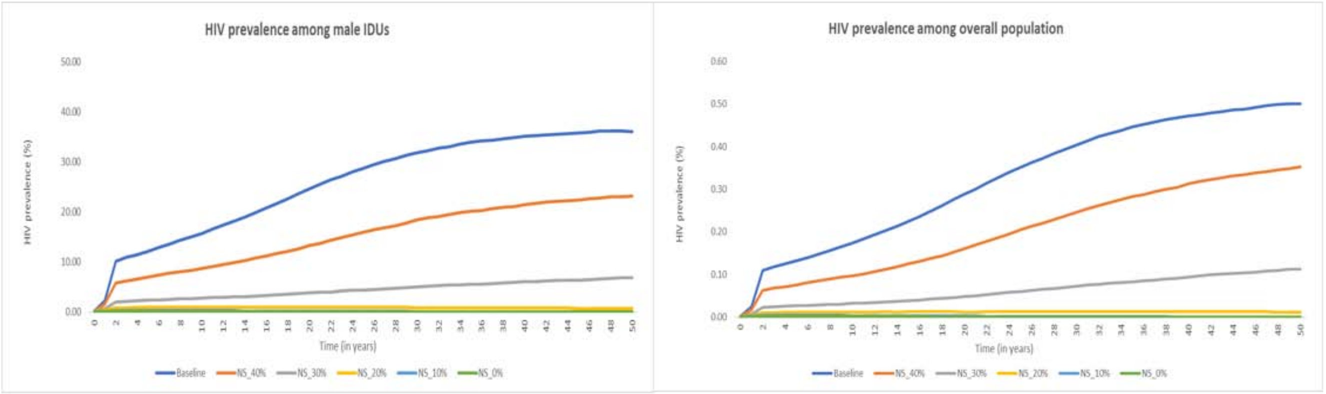

Figure 2: Comparisons between baseline scenario and five intervention scenarios of lowering needle sharing level among IDUs. Top: HIV prevalence among IDUs. Bottom: HIV prevalence among the overall population.

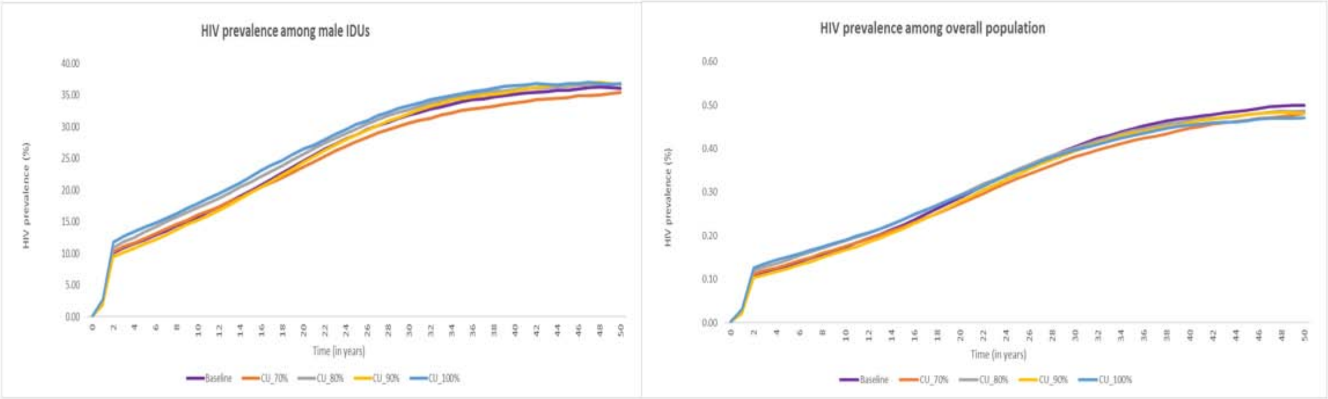

Figure 3: Comparisons between baseline scenario and four intervention scenarios involving increasing consistent condom use level among male IDUs and FSWs. Top: HIV prevalence among IDUs. Bottom: HIV prevalence among the overall population.

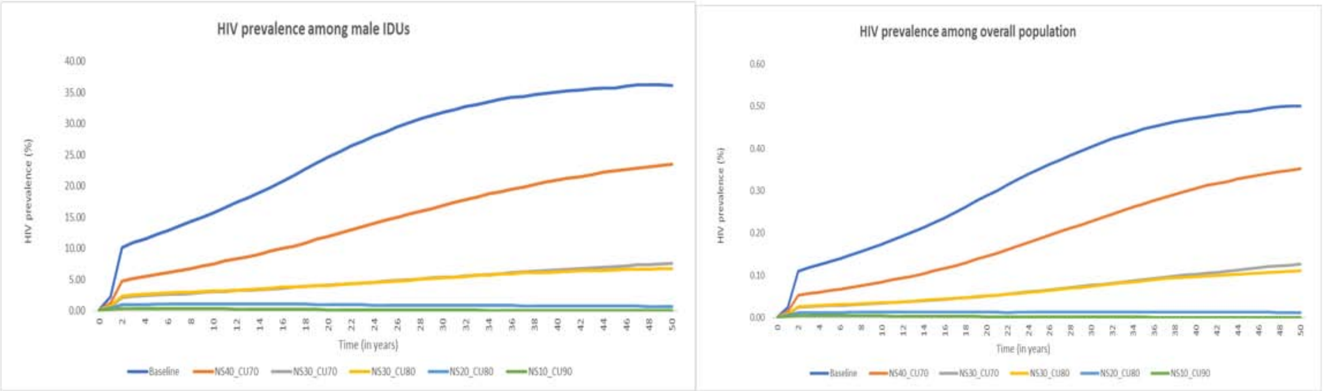

Figure 4: Comparisons between baseline scenario and different intervention scenarios investigating the impact of lowering needle-sharing level among IDUs while increasing consistent condom use level among male IDUs and FSWs. Top: HIV prevalence among IDUs. Bottom: HIV prevalence among the overall population.

36.1% to 35.4% - among IDUs was only observed when consistent condom use increased from the baseline level to 70% (p-value=0.02) (Figure 3A). The HIV prevalence among the overall population was slightly lower in four intervention scenarios (0.47% - 0.49%) than in the baseline scenario (0.5%) (Figure 3B). Slight reductions in the cumulative number of HIV infections over 50 years were observed in CU_70%, CU_90%, and CU_100% (data not shown).

Combined intervention scenarios of lowering needle sharing levels among IDUs and increasing consistent condom use levels among male IDUs and FSWs

The patterns of HIV reduction in combined intervention scenarios were relatively similar to those observed in intervention scenarios of solely lowering the needle sharing level among IDUs. The most noticeable reductions in HIV infection were observed in the first two intervention scenario, NS_40% & CU_70% and NS_30% & CU_70%. For example, HIV prevalence among male IDUs at year 50 decreased from 36.1% at baseline to 23.5% in NS_40% & CU_70%, and to 7.6% in NS_30% & CU_70%. When needle sharing level was lowered to 30%, increasing consistent condom use from 70% to 80% resulted in a decrease in the HIV prevalence from 7.6% to 6.8% at year 50 (Figure 4A) and a 4% reduction in cumulative HIV cases among male IDUs over 50 years (data not shown). The reductions in HIV infection among the overall population also followed the same patterns as those among IDUs (Figure 4B). Compared with the intervention scenario lowering the needle sharing level to 40%, the combined intervention scenario of lowering needle sharing level to 40% while simultaneously increasing consistent condom use level to 70% contributed to an additional 3% reduction in cumulative HIV cases among the overall population (data not shown).

Discussion

The ABM presented in this study provides a showcase for the relevance of using ABM approach in modeling the HIV epidemic among high-risk populations such and IDUs. The application of ABM to simulate HIV trends add to understanding of the burden of the HIV epidemic among high-risk populations and serve as a useful guide for prevention intervention efforts.

ABM results showed that needle sharing behavior and inconsistent condom use are confirmed as the major risk factors for HIV infection among IDUs, though needle sharing is recognized as a predominant risk behavior that fuels the HIV epidemic in many parts of the world [4,5]. Decreasing the needle sharing level among IDUs and/or increasing the level of consistent condom use among male IDUs and FSWs all contribute to the reduction of HIV infections in all simulated populations, yet the magnitude and speed of the reduction varies by the type of interventions implemented. Major implication from simulations were followed:

- Prevention interventions to increase consistent condom use among male IDUs and FSWs have minimal impact on the reduction of HIV infections in IDU population as well as among the overall population. By contrast, prevention interventions to lower the level of needle sharing among people who injected drugs resulted in a sizable reduction in HIV infection in all simulated populations. Such discrepancy in HIV reductions is likely due to the fact that there was observed an overlap between the IDU and FSW population when there was a proportion of FSWs who injected drugs and also a proportion of male clients of FSWs who are IDUs. Lowering needle sharing levels, therefore, reduced HIV spread not only among male IDUs themselves but also injecting FSWs, male clients of FSWs, which ultimately results in a large reduction in HIV infection among the overall population. In places where drug injection fuels the HIV epidemic, prevention interventions targeting major drug injection related behaviors such as the sharing of contaminated needles and syringes appear to result in larger HIV reduction than those targeting sexual practices.

- Interventions scenarios solely focusing on lowering needle sharing levels among IDUs resulted in the largest reduction in HIV infection in all simulated populations. These results are particularly useful for policy makers, program managers and stakeholders to set priorities for HIV prevention interventions. The combination of decreasing needle sharing behavior and increasing consistent condom use practice should be the ideal intervention strategies where resources are available. However, in resource constrained settings, where resources cannot be equally contributed to different HIV high-risk populations, intervention efforts to lower the needle sharing level should be prioritized in order to result in the largest reduction in HIV infections, not just among IDUs, but also among the overall population.

- The majority of the reductions in HIV infection in all populations occurred when needle sharing level was lowered from the baseline level to 40%, and then to 30%. Once needle sharing reached these levels, further decrease in needle sharing level, which probably requires significant efforts and resources to achieve, result in less obvious reductions, possibly because at this point the HIV prevalence among IDUs are already kept at low enough level that it is difficult to see any further significant reductions. Of equal importance, results from these scenarios also indicate that the achievement of any reduction, even several percent from the baseline's high level of needle sharing, could yield several times that big a proportional reduction in the prevalence of HIV infection.

The application of the agent-based approach in this study provides significant insights into the complex dynamics of the HIV epidemic. It has been shown from this study that ABM serves as an important tool that supplements the insufficiency of epidemiological research in addressing the underlying mechanisms of the HIV epidemic. The additional use of epidemiological data to fit ABM helps provide a consistent framework in which to knit together different lines of evidence, and aids in identifying the gaps between empirical data and model inputs of high sensitivity, which can inform prioritization of data collection. The discrepancies between epidemiological data and ABM outputs also help more quickly detect shortcomings in and aid refinement of the specific dynamic hypothesis captured within the model, help regenerate hypotheses as to future evolution of the situation, improve study designs and sampling strategies, and develop better proxy measures for the level of risk behaviors. When used in an iterative fashion – where identified gaps between model expectations and incoming empirical data are viewed not as failures of the model but as successes in learning via modeling - such a model can serve as a powerful tool for organizational learning. The experimentation with different "what-if" intervention scenarios makes ABM a useful modeling tool for policy makers to evaluate the effectiveness of different prevention intervention strategies in reducing HIV infection. Leveraging their natural representation of the situation, ABM models can also serve as an effective communication tool to help stakeholders at different levels identify areas of focus for prevention efforts and in setting proper targets for intervention strategies in order to achieve the greatest reduction in HIV infections.

The ABM presented in this study, however, has several important limitations. First, the relative small size of the population simulated might result in large variation in the results obtained. The sample size issue was also one among various reasons that probably explained the non-significant differences obtained from various intervention scenarios investigating the impact of increases in condom use. In addition, given the trade-off between the level of detail in the model and the time required to simulate the model behavior, the ABM constructed in this study was relatively simple and there was not a yet chance to examine other factors which have been recognized as important contributors to HIV infection, such as educational attainment, occupation, mobility, knowledge of HIV/AIDS, STIs, and Antiretroviral Therapy. However, for the factors that were included, the model does yield results that are relatively rich in the sense that they capture behaviors and change in clinical status, risk exposure and networks over time, which could be compared with richer epidemiological data sources.

Conclusion

While traditional epidemiological analysis promotes thinking about multilevel determinants of health, the exclusive use of regression-based approach may constrain the types of questions asked, the answers received, and the hypotheses and theoretical explanations that are developed [6]. By allowing users to explore dynamic, nonlinear, heterogeneous, reciprocal spatiotemporal processes, ABMs shed lights on the ways in which individuals interact with each other and with their environments and open up our thinking to new conceptualizations. Results from this study support Auchincloss and Diez Roux's contentions and suggest that the use of ABM can complement traditional epidemiologic regression-based analysis in gaining important insights into the complex dynamics of the HIV epidemic among high-risk populations [6]. Simulation results in our study could therefore serve as a guide for policy makers on setting proper targets for prevention interventions, given the availability of resources as well as the feasibility of target achievement.

Acknowledgements

The IBBS study was supported by the United States Agency for International Development (USAID) in Vietnam through the HIV/AIDS Prevention, Care, and Treatment project, Cooperative Agreement number 486-A-00-06-00009-00, and the Sustainable Management of the HIV/AIDS Response and Transition to Technical Assistance Project – or "SMART TA", Cooperative Agreement No. 486-A-11-00011, both managed by FHI 360, as part of the United States President's Emergency Plan for AIDS Relief (PEPFAR). The authors are indebted to FHI 360 Vietnam for their permission to use the IBBS dataset for this study.

We would like to thank Dr. Nathaniel Osgood from the Department of Computer Science, University of Saskatchewan who provided significant guidance throughout the modeling process and valuable comments and edits toward the completion of this manuscript. We also thank Drs. Quoc C Nguyen, Ha TT Tran, and Stephen Mills for leading the IBBS study.

Authors' Contributions

TL performed the simulation analysis and wrote the first draft of the manuscript. NS contributed simulation programing. HL conceived the original study idea and provided interpretation of the study results. All authors read and approved the final manuscript.

References

1. Strathdee SA, Stockman JK. Epidemiology of HIV among injecting and non-injecting drug users: current trends and implications for interventions. Curr HIV/AIDS Rep. 2010; 7: 99-106.
2. Vlahov D, Robertson AM, Strathdee SA. Prevention of HIV infection among injection drug users in resource-limited settings. Clin Infect Dis. 2010; 50: S114-S121.
3. Wodak A, Cooney A. Do needle syringe programs reduce HIV infection among injecting drug users: a comprehensive review of the international evidence. Subst Use Misuse. 2006; 41: 777-813.
4. UNAIDS. Global report: UNAIDS report on the global AIDS epidemic. Geneva. 2013.
5. Bergenstrom A, Andreeva V, Reddy A. Overview of epidemiology of injection drug use and HIV in Asia [Poster presentation]. Harm Reduction Conference. 2013; Lithuania.
6. Auchincloss A, Diez Roux A. A new tool for epidemiology: The usefulness of Dynamic-Agent Models in understanding place effects on health. Am J Epi. 2008; 168: 1-8.
7. Abuelezam NN, Rough K, Seage GR 3rd. Individual-based simulation models of HIV transmission: reporting quality and recommendations. PloS One. 2013; 8: e75624.
8. Rhee AJ. An agent-based approach to HIV/AIDS epidemic modeling: a case study of Papua New Guinea [master's thesis]: Massachusetts Institute of Technology. 2006; 133.
9. Teweldemedhin E, Marwala T, Mueller C. Agent-based modelling: a case study in HIV epidemic. 2005.
10. Hammond NA. Agent-based modeling and public health: progress and potential. 2014.
11. Yang Y, Diez-Roux AV. Using an agent-based model to simulate children's active travel to school. Int J Behav Nutr Phys Act. 2013; 10: 67.
12. Barrett CL, Eubank SG, Smith JP. If smallpox strikes Portland. Sci Am. 2005; 292: 42-49.
13. Epstein JM, Parker J, Cummings D, Hammond RA. Coupled contagion dynamics of fear and disease: mathematical and computational explorations. PLoS ONE. 2008; 3: e3955.
14. Ferguson NM, Cummings DAT, Fraser C, Cajka JC, Cooley PC, Burke DS. Strategies for mitigating an influenza pandemic. Nature. 2006; 442: 448-452.
15. Galea S, Hall C, Kaplan GA. Social epidemiology and complex system dynamic modelling as applied to health behaviour and drug use research. Int J Drug Policy. 2009; 20: 209-216.
16. Gorman DM, Mezic J, Mezic I, Gruenewald PJ. Agent-mased modeling of drinking behavior: a preliminary model and potential applications to theory and practice. Am J Public Health. 2006; 96: 2055-2060.
17. Alam SJ, Meyer R, Norling E. Using agent-based modeling to understand the impact of HIV/AIDS in the context of socioeconomic stressors. 2006.
18. Huang CY. An agent-based epidemic simulation of social behaviors affecting HIV transmission among Taiwanese homosexuals. Comput Math Method Med. 2015; 2015: 10.
19. Tully S, Cojocaru M, Bauch CT. Coevolution of risk perception, sexual behaviour, and HIV transmission in an agent-based model. J Theor Biol. 2013; 337: 125-132.
20. Le TTC, Nguyen CQ, Tran TTH, Mills S, Schwandt M, Lim HJ. HIV Prevalence and Correlates of needle sharing among male injecting drug users in Vietnam. J Epi Public Health Review. 2016; 16.
21. Le TTC, Nguyen CQ, Tran TTH, Schwandt M, Lim HJ. Correlates of HIV infection among street-based and venue-based sex workers in Vietnam. Int J STD/AIDS. 2015; 27: 1093-1103.
22. Vietnam Authority of HIV/AIDS Control. An annual update on the HIV epidemic in Vietnam. Hanoi (Vietnam). 2017.
23. Vietnam Ministry of Health. Sentinel surveillance survey data. Hanoi (Vietnam). 2014.
24. Brown T, Peerapatanapokin W. The Asian Epidemic Model: A process model

for exploring HIV policy and programme alternatives in Asia. BMJ. 2004; 80: 19-24.

25. Public Health Agency of Canada. HIV transmission risk: a summary of the evidence. 2012.
26. U.S. Department of Health and Human Services. The Stages of HIV Infection. 2017.
27. Canadian Foundation for AIDS Research. Stages of HIV Infection. 2017.
28. Nadler J. Pathophysiology of HIV infection. Florida/Caribbean AIDS Education and Training Center. 2005.
29. O’Brien SJ, Nelson GW. Human genes that limit AIDS. Nat Genet. 2004; 36: 565-574.