The role of syringe sharing in the spread of HIV/AIDS among injectable drug users

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Abstract

Containment syringe sharing among individuals is considered to be the most contributing factor to human immunodeficiency virus (HIV). It's well recognized that sharing syringes significantly contributes to the transmission of diseases amongst individuals. This study examines how syringe sharing may contribute to HIV infection and spread among injectable drug users. Sharing syringes greatly aids in the spread of infections among people, as is widely acknowledged. The model was calibrated using data from Malaysia from 2000 to 2011 on the incidence of HIV among drug injectors. Through the use of the Markov chain Monte Carlo simulation approach, the parameters are estimated using Bayesian inference. The basic reproduction number for HIV disease suggests that the disease-free equilibrium was stable during the 12 years. This is a good indicator from the public health point of view since the goal is to stabilize the infection rate. Our findings emphasized the potential involvement of syringe sharing in the transmission of HIV among injectable drug users and the need for more research into this infection rate in order to improve strategies for reducing the incidence of individual HIV cases among people who inject drugs.

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Abstract

Containment syringe sharing among individuals is considered to be the most contributing factor to human immunodeficiency virus (HIV). It's well recognized that sharing syringes significantly contributes to the transmission of diseases amongst individuals. This study examines how syringe sharing may contribute to HIV infection and spread among injectable drug users. Sharing syringes greatly aids in the spread of infections among people, as is widely acknowledged. The model was calibrated using data from Malaysia from 2000 to 2011 on the incidence of HIV among drug injectors. Through the use of the Markov chain Monte

Carlo simulation approach, the parameters are estimated using Bayesian inference. The basic reproduction number for HIV disease suggests that the disease-free equilibrium was stable during the 12 years. This is a good indicator from the public health point of view since the goal is to stabilize the infection rate. Our findings emphasized the potential involvement of syringe sharing in the transmission of HIV among injectable drug users and the need for more research into this infection rate in order to improve strategies for reducing the incidence of individual HIV cases among people who inject drugs.

Keywords: Basic reproduction number, HIV among PWID, Mathematical transmission modelling, Markov chain Monte Carlo simulation.

Introduction

The World Health Organization (WHO) estimates that 16 million people who inject drugs (PWID) globally. Out of this, 3 million of them live with the human immunodeficiency virus (HIV). Thus, two of ten new HIV infections are caused by injected drug use. Consequently, PWID is at high risk of HIV, hepatitis B and C, and many other socially related diseases such as an individual's physical and mental health. The number of PWID in India who are HIV positive is estimated to be 177,000 (7.4%) of the total population. PWID experiences high mortality and morbidity rates, often from drug overdose users. The situation is not different in Malaysia, where it is estimated that there are about 170,000 (67%) PWID. Since the emergence of HIV, PWID has been the leading cause of epidemic disease spread, ranging from 70-80% of all reported cases. The statistical analysis gives evidence that sharing contaminated syringe injecting equipment by PWID is responsible for increasing HIV infections in Malaysia. Due to the usage of injectable drugs, Malaysia is struggling with an HIV epidemic that has contributed to one of the highest rates of HIV infection in Southern Asia.

Several studies have used compartment models in order to simulate the spread of HIV and AIDS in different countries. For instance, De Gruttola and Mayer assessed how to implement an extension of the SIRmodel to fit the spread of the HIV epidemic of heterosexuals in the US. Nishiura studied predictions of AIDS incidences in the United States and Japan, while Nyabadza and colleagues presented a mathematical model to predict the HIV/AIDS epidemic trend in South Africa. Other studies have focused on how to minimise the spread in terms of intervention. For example, a study by Murray, Law, Gao, and Kaldor shows the impact of behavioural changes on the prevalence of HIV and hepatitis C among injecting drug users, with the purpose to determine how to reduce the spread of HIV infection among PWID. Recently, the use of Markov chain Monte Carlo (MCMC) has been put to advantageous for obtaining information about distributions, particularly for estimating posterior distributions in Bayesian inference. The computational intractability of the model formulated in this paper will be addressed using MCMC methods. The study aim is to formulate a model to analyze the role of syringe sharing in the spread of HIV/AIDS among injectable drug users in Malaysia. Incidence case data from the Ministry of Health (MOH) in Malaysia will be used to provide insights into the nature of the epidemic of HIV-infected people in relation to the use of syringes. The estimated parameters will be used to calculate the basic reproduction number R_0 for HIV/AIDS among PWID.

Material and Methods

Figure 1 presents the simplest HIV/AIDS model with treatment without considering the sexual behaviour of HIV/AIDS among PWID.

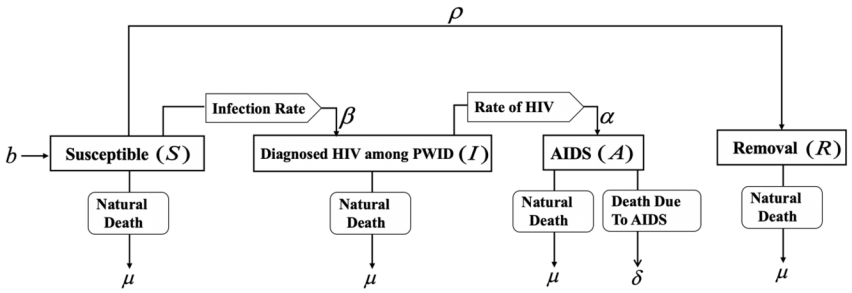

Figure 1. Flow diagram of HIV transmission among PWID: The HIV/AIDS disease is based on the assumption that once an individual becomes infected, the individual remains infectious for life. The total population N has been subdivided into the following: i) The entire population is one susceptible to infection $S(t)$. We wish to model a populace, population at risk of acquiring HIV/AIDS among PWID. However, the susceptible compartment has a natural birth rate independent of vertical transmission, which makes it unstable and assumed to be susceptible. Therefore the natural death μ is constant across all compartments. ii) Infection is classified in the model into two categories for those infected and diagnosed with HIV among PWID$I(t)$, and those who are infected and diagnosed with AIDS, $A(t)$. iii) $R(t)$ represents the people with safe habits of sharing syringes and maintaining the habits for the rest of their lives.ρ is the rate at which susceptible individuals change their habits of sharing syringes per unit of time. iv) The rate of infected HIV individuals progresses at a rate α into the AIDS compartment. v) It is assumed that β is the probability of susceptible and HIV as $\beta\frac{I}{N}S$. vi) It is assumed that AIDS individuals are given an additional disease-induced mortality rate,$\delta > 0$ for $A(t)$.

With the assumptions (i-vi), the model is represented by the following equations:

$$\frac{\mathrm{dS}}{\mathrm{dt}} = b - \beta\frac{I}{N}S - (\mu + \rho)\, S \tag{1}$$

$$\frac{\mathrm{dI}}{\mathrm{dt}} = \beta\frac{I}{N}S - (\alpha + \mu)\, I \tag{2}$$

$$\frac{\mathrm{dA}}{\mathrm{dt}} = \alpha I - (\delta + \mu)\, A \tag{3}$$

$$\frac{\mathrm{dR}}{\mathrm{dt}} = \rho S - \mu R \tag{4}$$

The total population at time t, denoted by $N(t)$ is:$N(t) = S(t) + I(t) + A(t) + R(t)$. In the absence of disease equilibrium (1) will become

$$S^* = \tfrac{b}{\rho+\mu} \tag{5}$$

Analysis of the basic reproduction number $\mathbf{R_0}$

The average number of secondary infections caused by a single infected individual in a completely susceptible population is the reproduction number, R_0. When $R_0 < 1$, it indicates that the disease-free state is stable, and the disease is expected to eventually become extinct, while $R_0 > 1$ indicates that the disease-free state is unstable, and the disease is able to invade a population to spread the disease. Using the next-generation matrices adopting the approach by van den Driessche et al., and Diekmann et al. , we calculated the R_0. We write the Jacobian matrices of (1)-(4) as$A$ and B with the following equations:

$$A = \begin{bmatrix} \beta\frac{S^*}{N} & amp;0 \\ 0 & amp;0 \end{bmatrix} \tag{6}$$

$$B = \begin{bmatrix} \alpha + \mu & amp;0 \\ -\alpha & amp;\mu + \delta \end{bmatrix} \tag{7}$$

By small expression and simplification, (6) and (7) are given by:

$$A \times B^{-1} = \frac{\beta S^*}{N(\alpha+\mu)} \tag{8}$$

By substituting (5) into (8). The basic reproduction number of the system is obtained as the spectral radius of the matrix$A \times B^{-1} =$ $\underline{\acute{\beta}\beta}$

englishN$(\alpha + \mu)\,(\rho + \mu)$.

Sensitivity analysis of the model parameters

Sensitivity analysis is performed to determine the relative impact of each parameter on disease transmission and prevalence. In terms of the model parameters, we calculate the sensitivity indices of the R_0. The index measures the relative change in R_0 in relation to the relative change in the parameters. The analysis could aid in determining which parameter causes the greatest decrease in R_0, and such a parameter could be targeted at keeping the prevalence level low enough to be an appropriate measure. The normalized forward sensitivity index of a variable, Z, that depends differentially on a parameter, x, is given by$\psi_x = \frac{x}{Z}\frac{\partial Z}{\partial x}$. The R_0sensitivity indices in terms of the model parameters are calculated as follows:

$\psi_\beta = \frac{\beta}{R_0}\frac{\partial R_0}{\partial \beta} = 1$

$\psi_b = \frac{b}{R_0}\frac{\partial R_0}{\partial b} = 1$

$$\psi_\alpha = \frac{\alpha}{R_0}\frac{\partial R_0}{\partial \mu} = -\alpha(\mu + \rho)$$

$\psi_\rho = \frac{\rho}{R_0}\frac{\partial R_0}{\partial \rho} = -\rho(\mu + \alpha)$(9)

$$\psi_\mu = \frac{\mu}{R_0}\frac{\partial R_0}{\partial \mu} = -\mu(2\mu + \alpha + \rho)$$

$$\psi_b = \frac{b}{R_0}\frac{\partial R_0}{\partial b} = 0$$

Data

The model is calibrated using HIV incidence epidemiological data obtained from the Ministry of Health, Malaysia. The epidemiological model (see chapter 2.1) incorporated the reported infected HIV among PWID per year in the period 2000-2011. For instance, in 2000, 3815 of 23,420,751 Malaysian individuals were infected with HIV among PWID, which represents the initially infected $I(0)$ compartment (HIV cases among PWID), while 23,416,936 individuals can be assigned in the susceptible $S(0)$ class.

Model Calibration

The model is calibrated to nationally represent individuals diagnosed with HIV among PWID incidence data, described in chapter 2.1. Parameters relating to syringe sharing, the start time of the epidemic, the magnitude of syringe sharing behaviour which may change with time, and the rate of the existing supply of syringe and methadone maintenance therapy programs were estimated by using a Bayesian Markov chain Monte Carlo. Let θ represent the epidemiological parameters that will be estimated using the Flexible Modelling Environment (FME) package in R-software. It is also assumed that θ is the additive and independent Gaussian prior. Let ϕ be the error when fitting epidemiological data from the model in Figure 1 (for details see).

Then$\phi \sim N(0, \sigma^2)$ The posterior distribution of the model unknown variable θ is generated using the Delayed Rejection Adaptive Metropolis algorithm (for details see).

Results and discussion

To determine the uncertainty in the estimated parameters, the formulated model is linearized to obtain the best-fit based on Bayesian Markov chain Monte Carlo simulations. The estimated parameters from the formulated model fitted to HIV incidence among PWID data are given in Table 1. The data is insufficient in the number of data points to independently assess all parameters.

Table 1: Model parameter, definition, and parameter estimated

Parameters	Definition	Estimate (lower and upper CI)
β	Contact rate	$5.463\text{x}10^{-1}$ ($5.458\text{x}10^{-1}$ - $5.468\text{x}10^{-1}$)
α	The rate of HIV individuals progressing to AIDS	$1.974\text{x}10^{-1}$ ($1.973\text{x}10^{-1}$ - $1.974\text{x}10^{-1}$)
ρ	Susceptible individuals who change their habits of sharing syringes	$4.890\text{x}10^{-1}$ ($4.877\text{x}10^{-1}$ - $4.902\text{x}10^{-1}$)
μ	Natural death rate	$5.929\text{x}10^{-3}$ ($5.856\text{x}10^{-3}$ - $6.002\text{x}10^{-3}$)
δ	The disease-induced mortality rate of AIDS	$1.044\text{x}10^{-9}$ ($-1.225\text{x}10^{-8}$ - $1.434\text{x}10^{-8}$)
b	Natural birth rate	$1.434\text{x}10^{-4}$ ($1.233\text{x}10^{-4}$ - $1.438\text{x}10^{-4}$)

The plot of the data and the best-fit model for yearly reported incidence cases of tested HIV positive among PWID is shown in Figure 2. In general, the reported HIV incidence data are calibrated and validated well during the 12 years observation period. The HIV incidence cases among PWID peaked at three years. There was an intervention at the time of three years which shows a decrease in the spread of HIV among PWID.

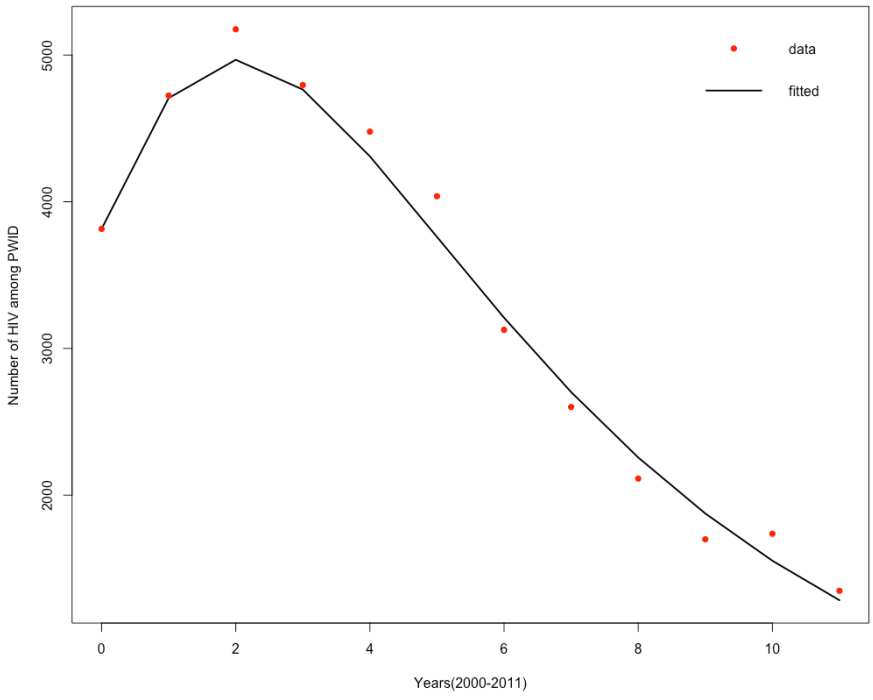

Figure 2: Fitted model for HIV incidence among PWID

Figure 3 shows yearly reported HIV-positive users among PWID-reported cases based on parameter distribution as generated with the MCMC application of calibration for the period. The high variances are observed

in the following compartment order: $I > S > A > R$. The large number for variance is due to either the uncertainties in the model or noise in data collection and the model fits the noisy data reasonably well.

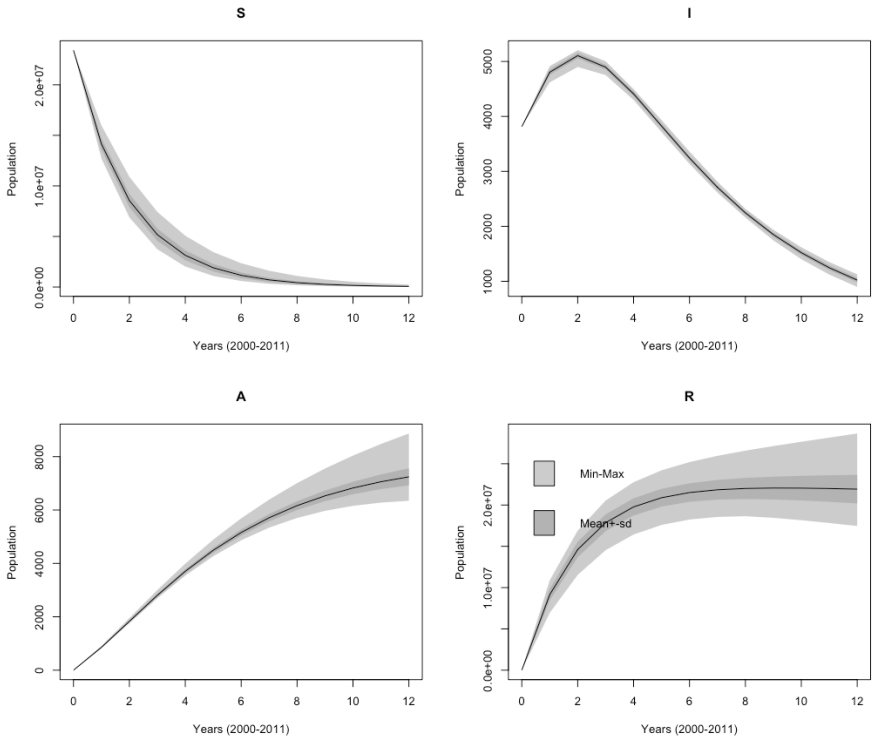

Figure 3: Predictive envelopes of the model showing the sensitivity range of yearly reported HIV incidence cases among PWID individuals. The light grey shade by Min−Max represents the minimum and maximum model response at each time step, whereas the dark grey shade by Mean±sd refers to the mean model response plus/minus one standard deviation.

From equation (9), we calculate the sensitivity indices based on the basic reproduction number, R_0. Table 2 indicated that the parameter β has more sensitivity indices value which shows that the behaviour of individual's syringe sharing is very high. Although, the natural birth rate b, is also more of a sensitivity index value which may due to the fact that individuals who are into this act of syringe sharing their birthrate is high and their new-born must test for HIV infection. These results indicated the need for intervention plans that target reducing the rate of contact among injecting drug users.

Table 2. Sensitivity indices of the six parameters involved in the model

Parameter	Definition	Sensitivity Index
β	Contact rate	1.000
α	The rate of HIV individuals progress to AIDS	-0.097
μ	Natural death rate	-0.004
ρ	Susceptible individuals who change their habits of sharing syringes	-0.099
δ	The disease-induced mortality rate of AIDS	0.000
b	Natural birth rate	1.000

Additionally, we investigate the impact of the contact rate for the individual among HIV incidence cases to

ascertain its effect. This was done by increasing and decreasing the baseline parameter β from 25% to 75%, while the remaining parameters are kept fixed. We notice the individuals of HIV among PWID incidence cases have the same effect as we increase or decrease β from the baseline. This illustrates how increasing the baseline will help to reduce the spread of the disease.

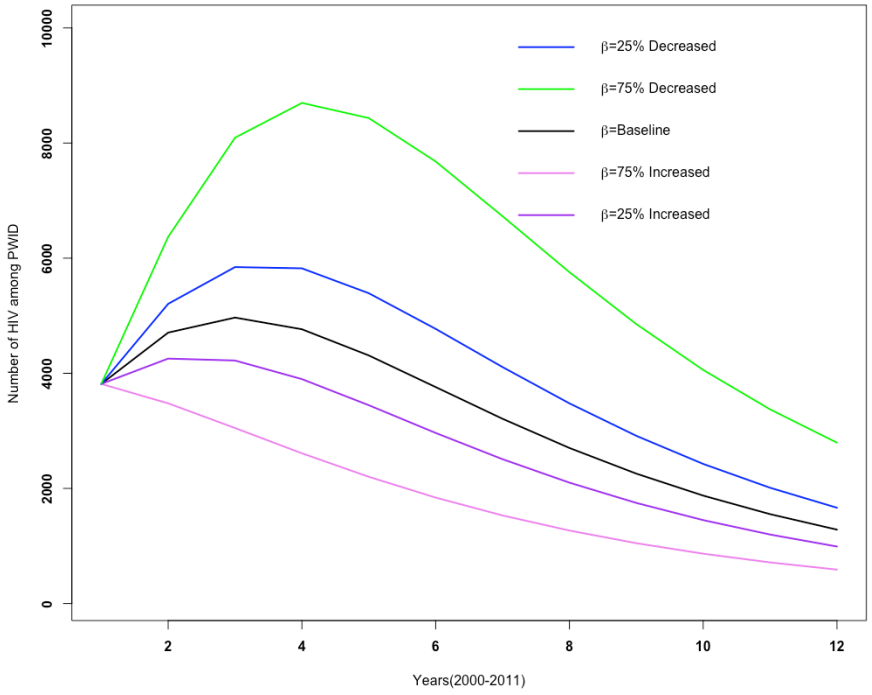

Figure 4: The impact of contact rate on HIV incidence among PWID cases.

Conclusion

The current study demonstrates that the numbers of HIV epidemic incidence cases are relatively low and steady in Malaysia, despite the presence of syringe sharing among PWID individuals. A combination of syringe sharing by those who are already infected and the relatively high incidence of injectable drug users in Malaysia keep the HIV epidemic at the current level and from declining further. Even though, due to the small number of injectable drug users, their comparatively harmless habit of syringe sharing and exchange can rapidly lead to significant increases in HIV among PWID. There are some limitations in our study. Firstly, the estimated parameter values that were used to calculate the basic reproduction number may alter depending on the quality of the data at the time the epidemic began. The outcomes of parameter estimates could be influenced by many variables during the data collection process. The developed sensitivity analysis in the present study can assist in the formulation of public health policy. As shown in Table 2, the sensitivity indices suggest that the contact rate of syringe sharing among injectable users has more impact on the spread of HIV with the PWID group. Whiles, the disease-induced mortality rate of AIDS does not contribute to the spread of HIV among PWID individuals. Secondly, the incidence cases of HIV among PWID were not enough which was 12 years of data points. Thirdly, in order to avoid parameterizing the model, five assumptions were made when formulating it. Finally, only AIDS cases were considered in the model's formulation, not HIV-related deaths among PWID. Our results further indicated a need for intervention plans that target reducing the rate of contact among injecting drug users. For instance, as shown in Table 1, the contact rate is very high due to the sharing of infected syringes between infected HIV and uninfected susceptible individuals. Due to the fact the rate at which individuals who are syringe sharing users is $5.463\text{x}10^{-1}$ ($5.458\text{x}10^{-1}$ - $5.468\text{x}10^{-1}$) which is (55%) significantly contributes to the spread

of HIV among PWID. Generally speaking, $R_0 < 1$ if then, the spread of disease will die out, and if $R_0 > 1$, then, the infection will survive and continue to spread. Our results show that the spread of disease among injectable drug users is stable The basic reproduction number was computed to be $3.324\text{x}10^{-11}$, implying that the disease-free equilibrium is stable. This is a good indicator from the public health point of view since the aim is to stabilize the infection at a disease-free equilibrium. As shown in Figure 4, we noticed that the 75% increase in the contact rateβ has a successful impact on the spread of HIV among PWID incidence cases. This shows that β, can only be decreasing in one direction in order to minimise or reduce the spread of HIV among PWID. The results should be used with caution due to assumptions for example the entire population is susceptible to infection made while estimating the model parameters. However, the findings from our theoretical and simulation studies represent the first critical step in determining the scope of Malaysia's syringe sharing practices among PWID. The study establishes the groundwork for further investigation into individuals who are and are not syringe sharing drug users, which could significantly lessen or eradicate the disease's persistence.

Author contributions

O.O.A. conceived and designed experiments and performed the experiments. O.O.A., H.N., and B.C. analyzed the data and contributed reagents/materials/analysis tools. O.O.A. wrote the first of the paper. O.O.A., H.N., L.A.N., L.M.B., B.C. formatted the manuscript according to journal requirements.

Data availability statement

Data supporting the results presented in this manuscript is available as stated above.

Disclosure statement

All authors declared that no competing interests exist.

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Reference