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Submission date: 24-Aug-2021 05:39PM (UTC+0800)
Submission ID: 1635225525
File name: cal_model_of_the_spread_of_HIV_amongst_drug_users_who_inject.pdf (159.81K)
Word count: 4070
Character count: 18376

Available online at http://scik.org
Commun. Math. Biol. Neurosci. 2020, 2020:92
https://doi.org/10.28919/cmbn/5118
ISSN: 2052-2541

ON THE DYNAMIC AND APPLICATION OF A MATHEMATICAL MODEL OF THE SPREAD OF HIV AMONGST DRUG USERS WHO INJECT

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Abstract. Kaplan developed the early deterministic mathematical model of the spread of HIV spread amongst IDUs (injecting drug users). This was followed by Greenhalgh and Hay, who extended the Kaplan model by considering some realistic assumptions. The models detailed the dynamic of probability of exposure to HIV of an IDU after they had used contaminated needles, and the dynamic of the IDU fraction subject to HIV infection. The model from Greenhalgh and Hay has two equilibria (fixed points), namely the HIV-free equilibrium and the HIV-endemic equilibrium. Greenhalgh and Hay demonstrated the global stability of the fixed points for some specific conditions. If the specific condition was not satisfied, Greenhalgh and Hay left it as an open problem. In this paper, we show that the dynamics of HIV spread among injecting drug users completely results from the basic reproduction number by constructing suitable Lyapunov functions, which resolves the open problem. We also apply the model to describe HIV/AIDS spread in a real case. The predicted result agrees with the data.

Keywords: HIV; injecting drug users; global stability; basic reproduction number; parameter estimation.

2010 AMS Subject Classification: 34D20, 34D23, 93A30.

1. INTRODUCTION

The retrovirus HIV (Human Immunodeficiency Virus) causes AIDS (Acquired Immune Deficiency Syndrome), a disease caused by damage to the immune system. HIV only lives in

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Received October 16, 2020

cells or live media. HIV is found in bodily fluids which contain white blood cells, e.g. blood, placental fluid, semen, spinal fluid, vaginal fluid, breast milk, and cerebrospinal fluid. HIV is transmitted when bodily fluids which contain HIV mix, for instance during sexual intercourse with someone with the infection, if contaminated needles and piercing tools are shared (for example those used for tattoos, piercings, and shaving), or through blood products containing HIV, i.e. transfusions. Pregnant women living with HIV could transmit the virus to her fetus or baby. According to the UNAIDS report, there were 37.9 million (32.7-44.0 million) people living with HIV worldwide at the end of 2018 [1].

There are a number of mathematical models which describe the spread of HIV, including HIV transmission in NSW prison [2], HIV spread because of heterosexual contact [3, 4], and HIV spread amongst injecting drug users [5, 6, 9]. Kaplan constructed an early HIV mathematical model amongst IDUs [5, 6]. Kaplan made the assumption that populations in which HIV/AIDS spread consisted of constant people. Kaplan assumed that the IDU populations were homogeneous and only injected drugs in places such as "shooting galleries". A shooting gallery is where drug users can gather to inject and share drug injection equipment. Kaplan's model is deterministic. The model consisted of two ordinary differential equations. The differential equation described the fraction of injecting drug user population with HIV infection at time t (the prevalence of HIV infection) and the probability that an injecting drug user will be exposed to HIV as a result of using contaminated equipment. This probability could be considered as the proportion of infected (contaminated) needles.

Using some assumptions, Kaplan suggested the following mathematical model [5, 6]:

$$\frac{dx}{dt} = \lambda\gamma y - \lambda\gamma x\left[1-(1-y)(1-\theta)\right], \tag{1}$$

$$\frac{dy}{dt} = \lambda\alpha x(1-y) - \mu y. \tag{2}$$

Here $x(t)$ and $y(t)$ are the proportion of infected (contaminated) needles and the fraction of infected, injecting drug users at time t, respectively. In eq. (1) and eq. (2), γ is the gallery ratio (ratio between a number of IDU and number of shooting galleries), λ is the injecting rate of IDU, θ is the probability of a contaminated needle becoming an uncontaminated needle after use by an uninfected IDU. In this model, α is the probability of an uninfected addict becoming

infected because of using a contaminated needle. The 'birth' rate and the 'death' rate of IDUs were assumed to have the same value μ.

In 1997, Greenhalgh and Hay altered the Kaplan model by adding some more realistic assumptions. Greenhalgh and Hay suggested the following mathematical model [6]:

$$\frac{dx}{dt} = (\sigma - \tau x)\, y - \rho x(1-y), \tag{3}$$

$$\frac{dy}{dt} = \upsilon x(1-y) - \mu y, \tag{4}$$

where $(x, y) \in \Omega = [0,1] \times [0,1]$. All parameters σ, τ, ρ, ν, μ are positive and $\sigma \leq \tau$. Two equilibria form the model: the HIV-free equilibrium $E_1 = (0,0)$ and the HIV-endemic equilibrium $E_2 = (x_2, y_2)$ where x_2 and y_2 were given by

$$x_2 = \frac{\sigma\upsilon - \rho\mu}{\tau\upsilon}, \quad y_2 = \frac{\sigma\upsilon - \rho\mu}{\sigma\upsilon - \rho\mu + \tau\mu}. \tag{5}$$

The HIV-endemic equilibrium E_2 exists when the basic reproduction number $R_0 := \frac{\sigma\upsilon}{\rho\mu} > 1$. A dynamical model's basic reproduction number can be determined by a Next-Generation Operator [7, 8]. Greenhalgh and Hay found that the HIV-free equilibrium E_1 was asymptotically, locally stable whenever $R_0 < 1$ and it was unstable whenever $R_0 > 1$. Also, the HIV-endemic equilibrium E_2 was asymptotically, locally stable whenever $R_0 > 1$. Moreover, Greenhalgh and Hay proved that the HIV-free equilibrium E_1 and the endemic equilibrium E_2 are asymptotically, globally stable for specific conditions. The following theorem came from Greenhalgh and Hay [6].

Theorem 1.1. *The HIV-free equilibrium E_1 is globally asymptotically stable if (a) $R_0 < 1$, or (b) $R_0 = 1$ and $\tau > \rho$.*

Theorem 1.2. *The endemic equilibrium E_2 is globally asymptotically stable if $R_0 > 1$ and $\tau > \rho$.*

For $\rho \geq \tau$, Greenhalgh and Hay left it as an open problem. Case $\rho > \tau$ could occur when the proportion of those infected who were aware of their infection (p) is higher than the probability of a contaminated needle becoming an uncontaminated needle after use by an infected addict (θ). In this paper, we demonstrated that Greenhalgh & Hay's HIV-free equilibrium model is asymptotically, globally stable whenever $R0 \leq 1$ and $\tau \leq \rho$. We also demonstrate that the

endemic equilibrium is asymptotically, globally stable whenever $R_0 > 1$ (no matter whether either $\tau > \rho$ or $\tau \leq \rho$).

This rest of this article is organized thus: Section 2 presents Greenhalgh and Hay's model of global stability of the HIV-free equilibrium by using a suitable Lyapunov function. Next, the global stability of the HIV-endemic equilibrium of Greenhalgh and Hay model is presented in Section 3. Applying the Greenhalgh and Hay model to HIV/AIDS spread data is shown in Section 4. Finally, the last section features the conclusion.

2. Global Stability of the HIV-Free Equilibrium

Here we shall show the global stability of the disease-free equilibrium for the case $R_0 \leq 1$. We start by presenting the following Lemma.

Lemma 2.1. *Suppose $R_0 \leq 1$. Then the following statements hold:*

(a) $x\dot{x} = -[\rho(1-y)+\tau y]x^2 + \sigma xy.$

(b) $y\dot{y} = -[\upsilon x+\mu]y^2 + \upsilon xy.$

(c) $\dot{x} + \frac{\sigma}{\mu}\dot{y} = -\rho(1-R_0)x(1-y) - \tau xy.$

Proof:

(a) By performing algebraic manipulation for $\dot{x}$, we found that

$$\dot{x} = -[\rho(1-y)+\tau y]x + \sigma y.$$

This yields

$$x\dot{x} = -[\rho(1-y)+\tau y]x^2 + \sigma xy.$$

(b) By performing algebraic manipulation for $\dot{y}$, we found that

$$\dot{y} = -(\nu x+\mu)y + \nu x.$$

Hence we find

$$y\dot{y} = -[\upsilon x+\mu]y^2 + \upsilon xy.$$

(c) Suppose $R_0 \leq 1$. Then

$$\dot{x} + \frac{\sigma}{\mu}\dot{y} = \sigma y + (\rho x - \tau x)y - \rho x - \frac{\sigma}{\mu}(\upsilon x(1-y) - \mu y)$$

$$= -\left(\rho - \frac{\sigma\upsilon}{\mu}\right)x + \left(\rho - \frac{\sigma\upsilon}{\mu}\right)xy - \tau xy$$

$$= -\rho\,(1-R_0)\,x\,(1-y) - \tau xy.$$

The disease-free equilibrium E_1 global stability is shown in the following theorem.

Theorem 2.2. *Suppose* $R_0 \leq 1$. *Thus, the HIV-free equilibrium* $E_1 = (0,0)$ *is asymptotically, globally stable in* Ω.

Proof: We have defined a Lyapunov function $U:\ \Omega \to R$ by

$$U\,(x,y) = \frac{\tau}{4\sigma}x^2 + \frac{\tau}{4\nu}y^2 + x + \frac{\sigma}{\mu}y.$$

Then U is in the C^{∞} class function on the domain Ω. The HIV-free equilibrium (E_1) is the global minimum of U. Moreover, U is a definite positive function around E_1 where for every $(x,y) \in \Omega\backslash\{E_1\},\quad U\,(x,y) > U\,(E_1) = 0$. The time derivative of U computed alongside the mathematical model solutions in (3)-(4), is given by the following expression

$$\frac{dU}{dt} = \frac{\tau}{2\sigma}x\dot{x} + \frac{\tau}{2\nu}y\dot{y} + \dot{x} + \frac{\sigma}{\mu}\dot{y}.$$

By using Lemma 2.1, we found that

$$\frac{dU}{dt} = -\frac{\tau}{2\sigma}\left[\rho\,(1-y) + \tau y\right]x^2 - \frac{\tau}{2\nu}\left(\upsilon x + \mu\right)y^2 - \rho\,(1-R_0)\,x\,(1-y).$$

Since all model parameters are positive, and every variable is non-negative, therefore $\frac{dU}{dt} \leq 0$ for $R_0 \leq 1$. Also, $\frac{dU}{dt} = 0$ if and only if $(x,y) = E_1$. Thus, the greatest compact invariant set in $\left\{(x,y) \in \Omega : \frac{dU}{dt} = 0\right\}$ is the singleton $\{E_1\}$. By LaSalle's invariance principle [10] then implies that the disease free equilibrium E_1 is asymptotically, globally stable in Ω. □

Remarks: Any functions $U\,(x,y) = mx^2 + ny^2 + x + \frac{\sigma}{\mu}y$ where $m \geq 0,\ n \geq 0,\ \ m\sigma + n\upsilon = \tau$ are also Lyapunov functions for proving the disease's global stability of free equilibrium E_1.

3. Global Stability of Endemic Equilibrium

Here, we demonstrate endemic equilibrium's global stability for the case $R_0 > 1$ using Dulac criterion and a Lyapunov function.

Theorem 3.1. *If $R_0 > 1$ then the endemic equilibrium E_2 is globally asymptotically stable in $\Omega \backslash \{E_1\}$.*

Proof: Suppose $f(x,y) = \dot{x}$ and $g(x,y) = \dot{y}$. We found that

$$\frac{\partial f}{\partial x} + \frac{\partial g}{\partial y} = -[\rho(1-y) + \tau y] - (\nu x + \mu) < 0. \tag{6}$$

Therefore, the mathematical model in equations (3)-(4) does not have any periodic solution in Ω [11, 12, 13]. Since E_2 is asymptotically, locally stable whenever $R_0 > 1$, then by applying the classical Poincare-Bendixson theorem, the endemic equilibrium E_2 is asymptotically, globally stable in $\Omega \backslash \{E_1\}$. □

Now, we show the endemic equilibrium's global stability whenever it exists by using a Lyapunov function. We present the following lemma.

Lemma 3.2. *Suppose $R_0 > 1$. Then the following statement are hold:*

(a) $\dot{x} = -[\rho(1-y) + \tau y](x - x_2) + \rho \frac{x_2}{y_2}(y - y_2)$.

(b) $\dot{x} = -\sigma \frac{y_2}{x_2}(x - x_2) + (\sigma - \tau x + \rho x)(y - y_2)$.

(c) $\dot{y} = \mu \frac{y_2}{x_2}(x - x_2) - (\nu x + \mu)(y - y_2)$.

(d) $\dot{y} = \nu(1-y)(x - x_2) - \nu \frac{x_2}{y_2}(y - y_2)$.

(e) Let $F = \left[x - x_2 + \frac{\sigma}{\mu}(y - y_2)\right]\left(\dot{x} + \frac{\sigma}{\mu}\dot{y}\right)$. *Then*

$$\begin{aligned} F \quad = & -[-\rho(R_0 - 1)(1-y) + \tau y](x - x_2)^2 - \frac{\sigma}{\mu}[\rho(R_0 - 1)x + \tau x](y - y_2)^2 \\ & -\rho(R_0 - 1)\frac{x_2}{y_2}(x - x_2)(y - y_2). \end{aligned}$$

Proof: Let $R_0 > 1$. Then, the endemic equilibrium E_2 given in (5) is exist. Moreover suppose $f(x,y) = \dot{x}$ and $g(x,y) = \dot{y}$.

(a) By using Taylor theorem, $\dot{x} = f(x,y)$ could be represented as

$$f(x,y) = f_x(x - x_2) + f_y(y - y_2) + \frac{1}{2}f_{xx}(x - x_2)^2 + f_{xy}(x - x_2)(y - y_2) + \frac{1}{2}f_{yy}(y - y_2)^2,$$

where all partial derivatives of are evaluated at E_2. By direct calculation, we found that

$$f_x = -[\rho(1-y) + \tau y],\ f_y = \sigma - \tau x + \rho x, f_{xx} = 0,\ f_{xy} = \rho - \tau, f_{yy} = 0.$$

Hence $\dot{x}$ could be represented as

$$\dot{x} = -\left[\rho\left(1-y_2\right)+\tau y_2\right]\left(x-x_2\right)+\left(\sigma-\tau x_2+\rho x_2\right)\left(y-y_2\right)+\left(\rho-\tau\right)\left(x-x_2\right)\left(y-y_2\right).$$

From equilibrium condition, $\sigma-\tau x_2+\rho x_2=\rho\frac{x_2}{y_2}$. Hence we found

$$\dot{x} = -\left[\rho\left(1-y\right)+\tau y\right]\left(x-x_2\right)+\rho\frac{x_2}{y_2}\left(y-y_2\right).$$

(b) From Lemma 3.2.(a), we found that

$$\begin{aligned}\dot{x} &= -\left[\rho\left(1-y_2\right)+\tau y_2\right]\left(x-x_2\right)+\left(\sigma-\tau x_2+\rho x_2\right)\left(y-y_2\right)+\left(\rho-\tau\right)\left(x-x_2\right)\left(y-y_2\right)\\ &= -\left[\rho\left(1-y_2\right)+\tau y_2\right]\left(x-x_2\right)+\left(\sigma-\tau x+\rho x\right)\left(y-y_2\right).\end{aligned}$$

From equilibrium condition, $\rho\left(1-y_2\right)+\tau y_2=\sigma\frac{y_2}{x_2}$. Hence we found

$$\dot{x} = -\sigma\frac{y_2}{x_2}\left(x-x_2\right)+\left(\sigma-\tau x+\rho x\right)\left(y-y_2\right).$$

(c) By using Taylor theorem, $\dot{y}=g\left(x,y\right)$ could be represented as

$$g\left(x,y\right)=g_x\left(x-x_2\right)+g_y\left(y-y_2\right)+\frac{1}{2}g_{xx}\left(x-x_2\right)^2+g_{xy}\left(x-x_2\right)\left(y-y_2\right)+\frac{1}{2}g_{yy}\left(y-y_2\right)^2,$$

where all partial derivatives of are evaluated at E_2. By direct calculation, we found that

$$g_x=\nu(1-y),\ g_y=-(\nu x+\mu),g_{xx}=0,\ g_{xy}=-\nu,g_{yy}=0.$$

Hence $\dot{y}$ could be represented as

$$\dot{y} = \nu(1-y_2)\left(x-x_2\right)-\left(\nu x_2+\mu\right)\left(y-y_2\right)-\nu\left(x-x_2\right)\left(y-y_2\right).$$

From equilibrium condition, $\nu(1-y_2)=\mu\frac{y_2}{x_2}$. Hence we found

$$\dot{y} = \mu\frac{y_2}{x_2}\left(x-x_2\right)-\left(\nu x+\mu\right)\left(y-y_2\right).$$

(d) From Lemma 3.2.(c), we found that

$$\begin{aligned}\dot{y} &= \nu(1-y_2)\left(x-x_2\right)-\left(\nu x_2+\mu\right)\left(y-y_2\right)-\nu\left(x-x_2\right)\left(y-y_2\right)\\ &= \nu(1-y)\left(x-x_2\right)-\left(\nu x_2+\mu\right)\left(y-y_2\right).\end{aligned}$$

From equilibrium condition, $\nu x_2+\mu=\nu\frac{x_2}{y_2}$. Hence we found

$$\dot{y} = \nu\left(1-y\right)\left(x-x_2\right)-\nu\frac{x_2}{y_2}\left(y-y_2\right).$$

(e) F could be decomposed as $F = F_1 + F_2 + F_3 + F_4$ where

$$F_1 = (x-x_2)\dot{x},\ F_2 = \frac{\sigma}{\mu}(x-x_2)\dot{y}, F_3 = \frac{\sigma}{\mu}(y-y_2)\dot{x},\ F_4 = \frac{\sigma^2}{\mu^2}(y-y_2)\dot{y}.$$

From Lemma 3.2(a)-(d), we found that

$$F_1 = -[\rho(1-y)+\tau y](x-x_2)^2 + \rho\frac{x_2}{y_2}(x-x_2)(y-y_2),$$

$$F_2 = \frac{\sigma\nu}{\mu}(1-y)(x-x_2)^2 - \frac{\sigma\nu}{\mu}\frac{x_2}{y_2}(x-x_2)(y-y_2),$$

$$F_3 = -\frac{\sigma^2}{\mu}\frac{y_2}{x_2}(x-x_2)(y-y_2) + \frac{\sigma}{\mu}(\sigma-\tau x+\rho x)(y-y_2)^2,$$

$$F_4 = \frac{\sigma^2}{\mu}\frac{y_2}{x_2}(x-x_2)(y-y_2) - \frac{\sigma^2}{\mu^2}(\nu x+\mu)(y-y_2)^2.$$

After cancelling identical terms with opposite signs, we found that

$$\begin{aligned} F &= -\left[\left(\rho-\frac{\sigma\nu}{\mu}\right)(1-y)+\tau y\right](x-x_2)^2 - \frac{\sigma}{\mu}\left(\frac{\sigma\nu}{\mu}x-\rho x+\tau x\right)(y-y_2)^2 \\ &\quad -\left(\frac{\sigma\nu}{\mu}-\rho\right)\frac{x_2}{y_2}(x-x_2)(y-y_2). \end{aligned}$$

Hence

$$\begin{aligned} F &= -[-\rho(R_0-1)(1-y)+\tau y](x-x_2)^2 - \frac{\sigma}{\mu}[\rho(R_0-1)x+\tau x](y-y_2)^2 \\ &\quad -\rho(R_0-1)\frac{x_2}{y_2}(x-x_2)(y-y_2). \square \end{aligned}$$

In the following theory, the endemic equilibrium E_2 global stability is shown by building a suitable Lyapunov function.

Theorem 3.3. *Assume that $R_0 > 1$. Thus, the endemic equilibrium $E_2 = (x_2, y_2)$ is asymptotically, globally stable in $\Omega\backslash\{E_1\}$.*

Proof: We have defined the Lyapunov function $V : \Omega \to R$ by

$$\mathrm{V}(\mathrm{x},\mathrm{y}) = \frac{1}{2}(R_0-1)(x-x_2)^2 + \frac{1}{2}\left[x-x_2+\frac{\sigma}{\mu}(y-y_2)\right]^2.$$

Then V is a member of C^∞ function set on the domain Ω. In addition, the endemic equilibrium E_2 is the global minimum of V on Ω. Moreover, V is definite positive function around E_2 where

for every $(x,y) \in \Omega \backslash E_2$, $V(x,y) > 0$. The time derivative of V computed along solutions of the mathematical model in (3)-(4), is given by the expression

$$\frac{dV}{dt} = (R_0 - 1)(x - x_2)\dot{x} + \left[(x - x_2) + \frac{\sigma}{\mu}(y - y_2)\right]\left(\dot{x} + \frac{\sigma}{\mu}\dot{y}\right).$$

By using Lemma 3.2, we found that

$$\begin{aligned}\frac{dV}{dt} &= -(R_0 - 1)[\rho(1 - y) + \tau y](x - x_2)^2 + (R_0 - 1)\rho\frac{x_2}{y_2}(x - x_2)(y - y_2) \\ &\quad + [(R_0 - 1)\rho(1 - y) - \tau y](x - x_2)^2 - \frac{\sigma}{\mu}[\rho(R_0 - 1)x + \tau x](y - y_2)^2 \\ &\quad - \rho(R_0 - 1)\frac{x_2}{y_2}(x - x_2)(y - y_2).\end{aligned}$$

Hence we found

$$\frac{dV}{dt} = -R_0\tau y(x - x_2)^2 - \frac{\sigma}{\mu}x(\rho(R_0 - 1) + \tau)(y - y_2)^2.$$

Since every parameter in the model is positive and every variable is non-negative, then $\frac{dV}{dt} \leq 0$ for $R_0 > 1$. Moreover, $\frac{dV}{dt} = 0$ if and only if $(x,y) = (0,0) = E_1$ or $(x,y) = (x_2,y_2) = E_2$. Thus, the greatest compact invariant set in $\left\{(x,y) \in \Omega \backslash \{E_1\} : \frac{dV}{dt} = 0\right\}$ is the singleton $\{E_2\}$. By LaSalle's invariance principle [10] then the implication is that endemic equilibrium E_2 is asymptotically, globally stable in $\Omega \backslash \{E_1\}$. □

4. Application of the Model

Here we applied the Greenhalgh and Hay mathematical model in eq. (3)-(4) for describing the spread of HIV/AIDS in Jawa Timur (East Java) province, Indonesia. To apply the model, HIV/AIDS spread in Jawa Timur province adheres to the following assumption:

(1) Number of injecting drug user is assumed to be constant.
(2) Number of the needle is assumed to be constant.
(3) HIV/AIDS spread could only be transmitted by sharing needles amongst injecting drug users.

The amount of cumulative HIV/AIDS case (z) at time t in Jawa Timur province is presented in Table 1, the data of which was compiled from the Health Profile of Jawa Timur 2011-2018 [14].

TABLE 1. Cumulative HIV/AIDS (z(t)) in Jawa Timur province

Year	2011	2012	2013	2014	2015	2016	2017	2018
t	0	1	2	3	4	5	6	7
z(t)	11585	15681	20030	26433	32646	36881	44949	53641

Here, our objective is to predict the basic reproductive ratio R_0 from the Table 1 data. Therefore, every parameter $(\sigma, \tau, \rho, \nu, \mu)$ in the Greenhalgh and Hay model in eq. (3)-(4) is estimated from the data. Unfortunately, the number of the injecting drug users (N) and dynamics of the needle are unknown. By defining $y(t) = \frac{z(t)}{N}$, then number of cumulative HIV/AIDS case in the Table 1 could be transformed into dimensionless variable $y(t)$. The parameters σ, τ, ρ, ν, μ and the initial values $x(0)$, $y(0)$ are estimated such that the mean average percentage error $(MAPE)$

$$MAPE = \frac{1}{8}\sum_{i=0}^{7}\left|\frac{z_i(t) - N\widehat{y_i(t)}}{z_i(t)}\right| * 100\%$$

is minimum. Here $\widehat{y_i}(t)$ is the proportion of HIV-infected IDUs (injecting drug users) at time i predicted from the model.

Because the mathematical models in eq. (3)-(4) are nonlinear differential equations, the models' analytical solutions cannot be obtained. As such, a heuristic method, for example a genetic algorithm method can be used for estimating parameter values from the non-linear model differential equations. Here, we used continuous genetic algorithm, because the algorithm has a larger suitable mutation rate than the binary genetic algorithm [15, 16]. Table 2 shows the estimation results of parameters in the Greenhalgh and Hay mathematical model in Eq. (3)-(4) for various mutation rate (m) using a continuous genetic algorithm .

The Table 2 results are the best values from seven times implementation of continuous genetic algorithm. It can be seen from the table that the minimum value of normalized residual sum of square is attained when the mutation rate is 0.5. Therefore, we obtain the parameter values of the mathematical model in equations. (3)-(4) are $x(0) = 0.088779$, $y(0) = 0.073013$, $\sigma = 3.2430$, $\tau = 8.8956$, $\rho = 4.0158$, $\nu = 0.4332$ and $\mu = 0.0125$. Hence, we found that the basic reproductive ratio of HIV/AIDS spread in Jawa Timur province predicted from the model is $R_0 = \frac{\sigma\nu}{\rho\mu} = 27.985$. In addition, by assuming that number of injecting drug users (IDUs) is

constant, we could predict the number of the injecting drug users (N). Here we found that $N = \frac{z(0)}{\hat{y}(0)} = 158671$ IDUs.

TABLE 2. Predicted parameter values

m	$x(0)$	$y(0)$	σ	τ	ρ	υ	μ	*MAPE*
0.1	0.118593	0.086516	2.3790	4.7432	1.2892	0.2773	0.0193	1.764 %
0.2	0.119980	0.079262	3.4187	6.0882	3.3441	0.3379	0.0141	1.723 %
0.3	0.123532	0.071872	4.4768	8.7402	4.4420	0.3310	0.0125	1.738 %
0.4	0.091608	0.101401	2.5473	5.9607	3.9028	0.5549	0.0127	1.768 %
0.5	0.088779	0.073013	3.2430	8.8956	4.0158	0.4332	0.0125	1.722 %

Figure 1 presents the dynamic of infected IDUs predicted from the model. As previously predicted by the analytical result, the dynamic of infected IDUs tends towards the endemic equilibrium when the basic reproductive ratio is more than one. From a practical point of view, harm reduction programs e.g. methadone therapy or needle exchange programs should be used to control and reduce the spread of HIV/AIDS among injecting drug users.

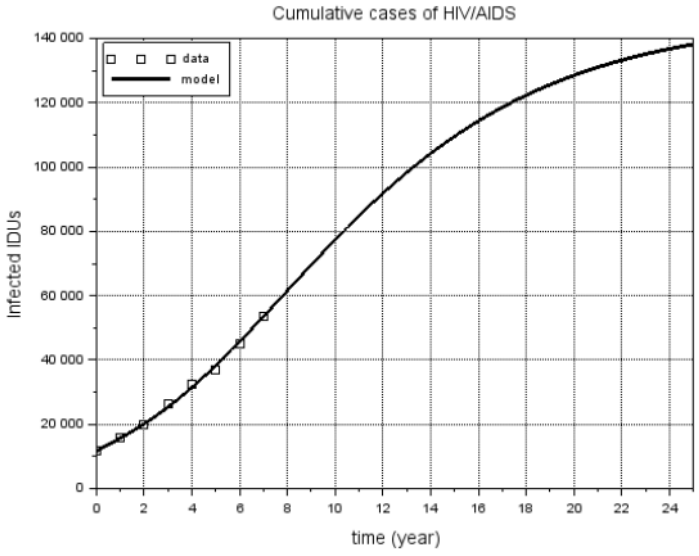

FIGURE 1. The dynamics of infected IDUs predicted from the model

5. Conclusion

We have proved the global stability of equilibria in a mathematical model of the spread of HIV spread amongst injecting drug users. We have shown that the mathematical model's global stability was completely determined by the basic reproduction number, which is either equal or less than one, the disease-free equilibrium is asymptotically, globally stable in the feasible region. The proof is completed by constructing a suitable Lyapunov function. Furthermore, if the basic reproduction number is more than one, then the endemic equilibrium is asymptotically, globally stable in the feasible region, provided that the initial value is not located at the disease-free equilibrium. This was proved by the construction of a suitable Lyapunov function and combination of Dulac function and Poincare-Bendixon theorem. We also applied the model to describe HIV/AIDS spread in a real case. The predicted model result agrees with the data.

6. Acknowledgement

This research was part funded by the Ministry of Research, Technology and Higher Education Republic Indonesia through "Penelitian Unggulan Perguruan Tinggi (PUPT)" project.

Conflict of Interests

The author(s) declare that there is no conflict of interests.

References

[1] UNAIDS Fact sheet 2019, [Accessed on 5 July 2020] Available at: https://www.unaids.org/en/resources/fact-sheet

[2] K. Dolan, A. Wodak, W. Hall, and E. Kaplan, A Mathematical model of HIV transmission in NSW prisons, Drug Alcohol Depend. 50 (1998), 197–202.

[3] Windarto, Model Matematika Penyebaran HIV (A mathematical model for HIV spread), Media Matematika dan Ilmu Pengetahuan Alam. 10 (2007), 1.

[4] A. Sani, D.P. Kroese, and P.K. Pollett, Stochastic models for the spread of HIV in a mobile heterosexual population, Math. Biosci. 208 (2007), 98–124.

[5] E. H. Kaplan, Needles that kill Modelling human immunodeficiency virus transmission via shared drug injection equipment in shooting galleries, Rev. Infect. Dis. 11 (1989), 289 - 298.

[6] D. Greenhalgh and G. Hay, Mathematical Modeling of the Spread of HIV/AIDS amongst Injecting Drug Users, IMA J. Math. Appl. Med. Biol. 14 (1997), 11 - 38.

[7] C. Castillo-Chaves, Z. Feng, and W. Huang, On the computational of R_0 and its role of global stability, in Mathematical approaches for emerging and reemerging infectious diseases: models, methods and theory, Editors: C. Castillo-Chavez, S. Blower, P. van den Driessche, D. Kirschner, and A.A. Yakubu, Springer, (2002).

[8] P. van den Driessche and J. Watmough, Reproduction numbers and subthreshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (2002), 29-48.

[9] N. Nuraini, R. Irawan, Zulkifly and E. Soewono, Mathematical Modeling of HIV/AIDS Transmission among Injecting Drug Users with Methadone Therapy, Asian Trans. Basic Appl. Sci. 1 (5) (2011), 11-15.

[10] J. P. LaSalle, The stability of dynamical systems, SIAM, Philadelphia, (1976).

[11] J. K. Hale, Ordinary differential equation, Krieger Publishing Company, Florida, (1980).

[12] S. Wiggins, Introduction to applied nonlinear dynamical systems and chaos, Springer, Florida, (2003).

[13] G. Teschl, Ordinary Differential Equations and Dynamical Systems, American Mathematical Society, (2011).

[14] Dinas Kesehatan Provinsi Jawa Timur, Profil Kesehatan Provinsi Jawa Timur 2011-2018 (Text in Indonesian), available online at www.kemkes.go.id/resources/download/profil/ (accessed on 7 March 2020)

[15] Windarto, S. W. Indratno, N. Nuraini and E. Soewono, A comparison of binary and continuous genetic algorithm in parameter estimation of a logistic growth model, AIP Conf. Proc. 1587 (2014), 139.

[16] Windarto, An implementation of continuous genetic algorithm in parameter estimation of predator-prey model, AIP Conf. Proc. 1718 (2016), 110005.

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