

# A Modeling Approach for Assessing the Spread of Tuberculosis and Human Immunodeficiency Virus Co-Infections in Thailand

Kornkanok Bunwong<sup>1,3</sup>, Wichuta Sae-jie<sup>2,3,\*</sup> and Natdanai Boonsri<sup>1,3</sup>

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## ABSTRACT

Mathematical models were formulated to describe the transmission dynamics of tuberculosis (TB) and human immunodeficiency virus (HIV) and the relationship between them. For TB infections, the population was separated into: 1) a susceptible non-infected group, 2) a latent asymptomatic infected group and 3) an active symptomatic infected group. For HIV infections, it was assumed that each of the three TB groups could be: 1) not infected with HIV or 2) actively infected with HIV. The model was used to study the spread of TB through the non-HIV and HIV groups. Formulas for the basic reproduction numbers and threshold criteria for the spread of TB through the two HIV groups were derived using the next generation method. Using population statistics (number of population, birth rate, and death rate) and health statistics (death by leading cause group, and number of persons affected with tuberculosis and acquired immune deficiency syndrome) reported by the Ministry of Interior, the Ministry of Public Health, and the World Health Organization, parameter values and estimate values were obtained for the basic reproduction numbers for the spread of TB. Numerical simulations confirmed the threshold criteria for the existence of a stable, disease-free equilibrium point and of a stable, endemic equilibrium point.

**Keywords:** basic reproduction number, epidemic model, tuberculosis (TB) and human immunodeficiency virus (HIV) co-infection, transmission dynamics

## INTRODUCTION

Detailed information on the tuberculosis disease and worldwide tuberculosis infection has been given in a recent report (World Health Organization, 2014a). Tuberculosis (TB) is an airborne infectious disease caused by bacteria (*Mycobacterium tuberculosis*). Pulmonary TB is the most common type of TB infection. Once a person with pulmonary TB coughs, sneezes, speaks or sings, TB germs are released to the

air. They can survive in the air for a period of time, depending on moisture and temperature conditions. Consequently, susceptible individuals have a chance to inhale TB germs and become a TB reservoir. Approximately, one-third of the world's human population has latent TB and additionally, people with a latent TB infection have a lifetime risk of 10% of falling ill with an active TB infection (World Health Organization, 2014a).

Field investigators face considerable

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<sup>1</sup> Department of Mathematics, Faculty of Science, Mahidol University, Bangkok 10400, Thailand.

<sup>2</sup> Department of Applied Mathematics and informatics, Faculty of Science and Industrial Technology, Prince of Songkla University, Suratthani 84000, Thailand.

<sup>3</sup> Centre of Excellence in Mathematics, CHE, Si Ayutthaya Road, Bangkok 10400, Thailand.

\* Corresponding author: e-mail: wichuta.sa@psu.ac.th

difficulties in collecting reliable data on the number of people with latent and active TB infections. Consequently, the approximation of the spread of TB using mathematical models is necessary. Porco and Blower (1998) developed a model of the intrinsic transmission dynamics of tuberculosis in the form of a flow diagram. Castillo-Chavez and Song (2004) introduced the slow-fast model for TB transmission and also modeled the number of new cases of TB per year in the the United States from 1953 to 2000. Fortunately, most TB patients can be treated so the number of new cases is decreasing (World Health Organization, 2014a).

Detailed information on human immunodeficiency virus (HIV) and worldwide HIV infection has also been given in a recent report by the World Health Organization (World Health Organization, 2014b). At the present time, there is no known cure for HIV infection. The most advanced stage of HIV infection is acquired immune deficiency syndrome (AIDS). There are many transmission routes such as having sex or sharing needles with someone who has HIV as well as receiving an HIV-contaminated blood transfusion. Moreover, infants may acquire HIV at delivery or through breast feeding if the mother is HIV-positive. Once infected, individuals may have latent infection and not appear clinically ill. Of course, since most HIV-infected people feel depressed and want to keep their status secret, there can be difficulty in obtaining reliable information on HIV infection. Again mathematical models can be used to understand the AIDS epidemic (Hyman and Stanley, 1988).

Due to medical advances, there are now effective treatments and therapies to prolong the life of an HIV-infected individual. Unfortunately, HIV weakens the immune system and therefore, HIV-infected people usually suffer from other diseases. TB is one of the leading causes of death in an HIV-infected population. On the other hand, the number of HIV-infected people carrying TB bacteria can be greater than in the non HIV-infected

population; therefore, understanding TB-HIV co-epidemics has become increasingly important. Long *et al.* (2008) have constructed and analyzed TB-HIV co-infection dynamics. Their parameter values were based on information from India. Bacaër *et al.* (2008) proposed a system of ordinary differential equations with six compartments, combining two states for HIV (HIV- and HIV+) with three states for TB infection (susceptible, latent TB and active TB). System parameters were obtained by either reviewing the medical literature or approximating from data from South Africa. Finally, they studied the impact of various control methods on these epidemics.

In epidemiology, the basic reproduction number ( $R_0$ ) is one of the most important quantities used to predict invasion of a disease into a population. The basic reproduction number is defined as the expected number of secondary cases produced, in a completely susceptible population, by a typical infected individual during their entire period of infectiousness. Moreover, the threshold criterion states “The disease can invade if  $R_0 > 1$  whereas it cannot if  $R_0 < 1$ ” (Diekmann *et al.*, 1990; Diekmann *et al.*, 2010), that is, a disease-free equilibrium point is locally stable if  $R_0 < 1$  and unstable if  $R_0 > 1$ .  $R_0$  can be observed in the field or calculated from mathematical models. A classical method for calculating the stability of a disease-free equilibrium point or an endemic equilibrium point is to calculate the eigenvalues of the Jacobian matrix of the linearized system about the equilibrium point. Alternative approaches for testing local stability are finding an intrinsic growth rate, a survivor function, or the next generation matrix (Heffernan *et al.*, 2005). Thus the basic reproduction numbers from different models and different approaches are unable to be compared.

The objective of the current study was to compute and compare the basic reproduction numbers for the spread of TB through the two HIV groups derived using the next generation method.

## MATERIALS AND METHODS

### Model formulation

The motivation for this study came from demographic statistics reported by the Thai Ministry of Interior and epidemiological information reported by the Thai Ministry of Public Health (Ousvapoom *et al.*, 2013; Official Statistics Registration Systems, 2015). These data provide sufficient TB and HIV information to construct a TB-HIV co-infection model. The main aim of the model is to compare the spread of TB through a population that is not infected with HIV and through a population that is infected with HIV. A compartment model was considered consisting of six populations classified either as infected or not infected with HIV and either as being TB susceptible (not having TB) or as having either a latent or active TB infection as shown in Figure 1.

The notations for the populations in Figure 1 are as follows.

$S_N$  Number of people who are HIV susceptible and TB susceptible

$E_N$  Number of people who are HIV susceptible and have latent TB infection

$I_N$  Number of people who are HIV susceptible and have active TB infection

$S_H$  Number of people who have HIV infection and are TB susceptible

$E_H$  Number of people who have HIV infection and latent TB infection

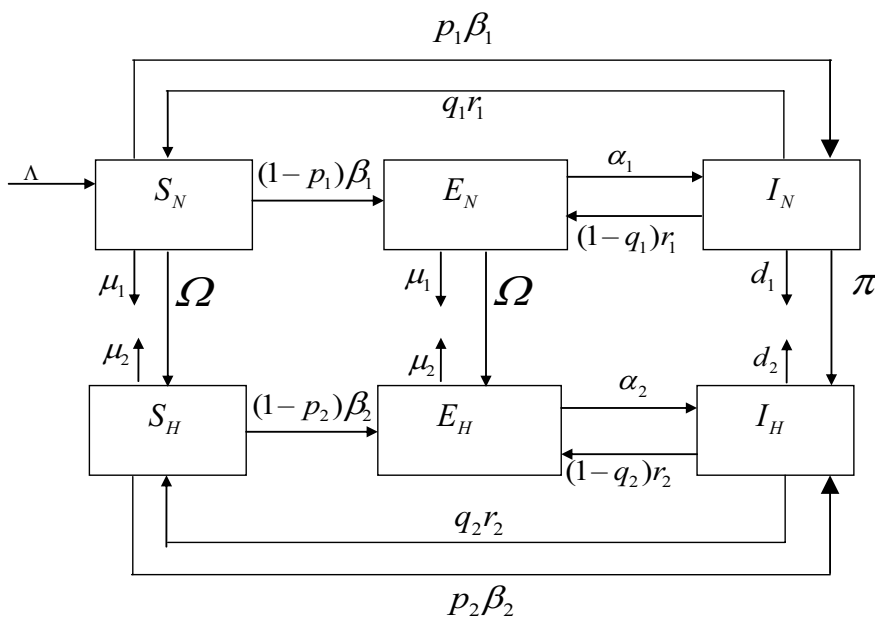
$I_H$  Number of people who have HIV infection and active TB infection

Clearly,  $S_N$ ,  $E_N$ ,  $I_N$  are subgroups of the non-HIV group and  $S_H$ ,  $E_H$ ,  $I_H$  are subgroups of the HIV group. Thus, Figure 1 can be translated into the differential equations as follows.

Equation 1 is assumed to describe the rate of change of the population who are HIV and TB susceptible.

$$\frac{dS_N}{dt} = \Lambda + q_1 r_1 I_N - \beta_1 S_N I_N - \mu_1 S_N - \Omega S_N. \quad (1)$$

where  $\Lambda$  represents the natural birth rate,  $q_1 r_1 I_N$  represents the rate of recovery from active TB infection due to successful treatment,  $\beta_1 S_N I_N$  represents the rate at which the TB susceptible



**Figure 1** Flow diagram of tuberculosis (TB) and human immunodeficiency virus (HIV) model (see Table 1 for definition of terms).

population becomes infected with either latent TB or active TB due to contact with the actively infected TB population,  $\mu_1 S_N$  represents the natural death rate and  $\Omega S_N$  represents an HIV infection rate.

Equation 2 is assumed to describe the rate of change of the population who are HIV susceptible and have a latent TB infection.

$$\frac{dE_N}{dt} = (1-p_1)\beta_1 S_N I_N + (1-q_1)r_1 I_N - (\alpha_1 + \mu_1 + \Omega)E_N. \quad (2)$$

where  $(1-p_1)\beta_1 S_N I_N$  represents the rate at which the population of TB and HIV susceptible people become infected with latent TB due to contact with the actively infected population,  $(1-q_1)r_1 I_N$  represents the rate at which the non-HIV population with active TB is partially cured and reverts to a state of latent TB infection,  $(\alpha_1 + \mu_1 + \Omega)E_N$  represents a decrease in the non-HIV, latent TB population due to transition to an active TB infection at rate  $\alpha_1 E_N$ , dying at death rate  $\mu_1 E_N$  or becoming HIV-infected at rate  $\Omega E_N$ . In practice, it is difficult to identify a person with a latent TB infection and therefore it is difficult for them to receive proper treatment.

Equation 3 is assumed to describe the rate of change of the non-HIV, active TB population.

$$\frac{dI_N}{dt} = p_1 \beta_1 S_N I_N + \alpha_1 E_N - (r_1 + d_1 + \pi)I_N. \quad (3)$$

where  $p_1 \beta_1 S_N I_N$  represent the rate at which the non-HIV, TB susceptible population becomes actively infected with TB due to contact with the actively infected population,  $\alpha_1 E_N$  represents the rate at which the latent TB of the non-HIV population changes to the active form of TB,  $(r_1 + d_1 + \pi)I_N$  represents the rate of decrease of the non-HIV, active TB population due either to: total cure to the susceptible TB population or partial cure to the latent TB population at rate  $r_1 I_N$ , dying at death rate  $d_1 I_N$ , or becoming infected with HIV at rate  $\Omega I_N$ . It is assumed that the rates of change of the HIV-infected populations ( $S_H$ ,  $E_H$ ,  $I_H$ ) for the susceptible, latent and active TB states can be

described by equations similar to Equations 1–3. Consequently, Equations 4–6 are:

$$\frac{dS_H}{dt} = \Omega S_N + q_2 r_2 I_H - \beta_2 S_H I_H - \mu_2 S_H \quad (4)$$

$$\frac{dE_H}{dt} = (1-p_2)\beta_2 S_H I_H + (1-q_2)r_2 I_H + \Omega E_N - (\alpha_2 + \mu_2)E_H \quad (5)$$

$$\frac{dI_H}{dt} = p_2 \beta_2 S_H I_H + \alpha_2 E_H + \pi I_N - (r_2 + d_2)I_H. \quad (6)$$

In these equations, the meanings of the parameters  $d_2$ ,  $p_2$ ,  $q_2$ ,  $r_2$ ,  $\alpha_2$ ,  $\beta_2$  and  $\mu_2$  for the HIV infected populations are the same as the meanings of the parameters  $d_1$ ,  $p_1$ ,  $q_1$ ,  $r_1$ ,  $\alpha_1$ ,  $\beta_1$  and  $\mu_1$  for the non-HIV populations.

### Basic reproduction number

The basic reproduction number  $R_0$  for a disease is defined so that a disease-free equilibrium point for a population is locally asymptotically stable if  $R_0 < 1$  and unstable if  $R_0 > 1$ . This can also be interpreted to mean that if one infected individual enters a population that is disease free, then  $R_0$  is the average number of secondary infections that will occur.

### TB-only model

The TB-only model in Equations 1–3 has two infected states ( $E_N$ ,  $I_N$ ) and one uninfected state ( $S_N$ ). At the TB-infection-free equilibrium point  $E_N = I_N = 0$  and hence the equilibrium population for  $S_N$  is  $S_N^* = \frac{\Lambda}{\mu_1}$ . The appearance of  $S_N$  in Equations 1–3 can now be replaced by  $\frac{\Lambda}{\mu_1}$ . For small ( $E_N$ ,  $I_N$ ), the following linearized system is obtained about the TB infection-free equilibrium point:

$$\frac{dE_N}{dt} = (1-p_1)\beta_1 \frac{\Lambda}{\mu_1} I_N + (1-q_1)r_1 I_N - (\alpha_1 + \mu_1)E_N \quad (7)$$

$$\frac{dI_N}{dt} = p_1 \beta_1 \frac{\Lambda}{\mu_1} I_N + \alpha_1 E_N - (r_1 + d_1)I_N. \quad (8)$$

$R_0$  can be calculated from these equations by using the next generation method as described by Diekmann *et al.* (2010). Let  $X = (E_N, I_N)'$

where the prime denotes transpose. Following Diekmann's recipe, the linearized infection subsystem can be rewritten in the form:

$$\dot{X} = (T + \Sigma)X \quad (9)$$

where the matrix  $T$  corresponds to transmissions:

$$T_{TB} = \begin{pmatrix} 0 & (1-p_1)\frac{\beta_1\Lambda}{\mu_1} \\ 0 & \frac{p_1\beta_1\Lambda}{\mu_1} \end{pmatrix} \quad (10)$$

and the matrix  $\Sigma$  corresponds to transitions:

$$\Sigma_{TB} = \begin{pmatrix} -(\alpha_1 + \mu_1) & (1-q_1)r_1 \\ \alpha_1 & -(r_1 + d_1) \end{pmatrix}. \quad (11)$$

Hence, the next generation matrix (NGM) with large domain is two-dimensional and given by

$$K_L^{TB} = -T_{TB}\Sigma_{TB}^{-1} \quad (12)$$

$$K_L^{TB} = \frac{1}{A} \begin{pmatrix} (1-p_1)\frac{\alpha_1\beta_1\Lambda}{\mu_1} & (1-p_1)\frac{\beta_1\Lambda}{\mu_1}(\alpha_1 + \mu_1) \\ \frac{\alpha_1 p_1 \beta_1 \Lambda}{\mu_1} & \frac{\beta_1 \Lambda p_1}{\mu_1}(\alpha_1 + \mu_1) \end{pmatrix} \quad (13)$$

where  $A = \det \Sigma_{TB} = (\alpha_1 + \mu_1)(r_1 + d_1) - \alpha_1 r_1(1 - q_1)$ .

The spectral radius of a matrix  $A$  is defined by  $\rho(A) := \sup\{|\lambda| : \lambda \in \sigma(A)\}$ , where  $\sigma(A)$  denotes the spectrum of  $A$ . By definition, the basic reproduction number is the largest eigenvalue of the NGM. Thus,  $R_0 = \rho(K)$ . Consequently,

$$R_0^{TB} = \rho(K_L^{TB}) = \frac{1}{2} \left( \text{trace}(K_L^{TB}) + \sqrt{\text{trace}(K_L^{TB})^2 - 4 \det(K_L^{TB})} \right) \quad (14)$$

Finally, the reproductive number for the TB only model is

$$R_0^{TB} = \left( (1-p_1)\alpha_1 + p_1(\alpha_1 + \mu_1) \right) \frac{\beta_1\Lambda}{A\mu_1}. \quad (15)$$

Here some parameters have superscripts or subscripts to indicate the model they belong to. For example,  $R_0^{TB}$  is the basic reproduction number

for the TB-only model.

### HIV-only model

From Equations 1 and 4–6, this system has two infected states ( $E_H, I_H$ ) and two uninfected states ( $S_N, S_H$ ). At the TB-infection-free equilibrium point  $E_H = I_H = 0$ . Hence,

$$S_N^* = \frac{\Lambda}{\mu_1 + \Omega} \text{ and } S_H^* = \frac{\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right). \quad (16)$$

For small ( $E_H, I_H$ ), the following linearized system is obtained:

$$\frac{dE_H}{dt} = (1-p_2)\beta_2 \frac{\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) I_H + (1-q_2)r_2 I_H - (\alpha_2 + \mu_2)E_H \quad (17)$$

$$\frac{dI_H}{dt} = \frac{p_2\beta_2\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) I_H + \alpha_2 E_H - (r_2 + d_2)I_H \quad (18)$$

Let  $X = (E_H, I_H)'$ . Then the following results are obtained:

$$T_{HIV} = \begin{pmatrix} 0 & \frac{(1-p_2)\beta_2\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) \\ 0 & \frac{p_2\beta_2\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) \end{pmatrix} \quad (19)$$

$$\Sigma_{HIV} = \begin{pmatrix} -(\alpha_2 + \mu_2) & (1-q_2)r_2 \\ \alpha_2 & -(r_2 + d_2) \end{pmatrix} \quad (20)$$

$$K_L^{HIV} = \frac{1}{B} \begin{pmatrix} \frac{(1-p_2)\alpha_2\beta_2\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) & \frac{(1-p_2)\beta_2\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) (\alpha_2 + \mu_2) \\ \frac{p_2\alpha_2\beta_2\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) & \frac{p_2\beta_2\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) (\alpha_2 + \mu_2) \end{pmatrix} \quad (21)$$

where  $B = \det \Sigma_{HIV} = (\alpha_2 + \mu_2)(r_2 + d_2) - \alpha_2(1 - q_2)r_2$ .

Therefore, the basic reproductive number for the HIV-only model is  $R_0 = \rho(K_L^{HIV})$ .

$$R_0^{HIV} = \frac{(1-p_2)\alpha_2\beta_2\Omega}{B\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) + \frac{p_2\beta_2\Omega}{B\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) (\alpha_2 + \mu_2) \quad (22)$$

### TB and HIV co-epidemic model

From Equations 1–6, this system has four infected states ( $E_N, E_H, I_N, I_H$ ) and two uninfected states ( $S_N, S_H$ ). At the TB infection free equilibrium point  $E_N = I_N = E_H = I_H = 0$ . Hence,

$$S_N^* = \frac{\Lambda}{\mu_1 + \pi} \text{ and } S_H^* = \frac{\Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right). \quad (23)$$

For small  $(E_N, E_H, I_N, I_H)$ , the following linearized system is obtained:

$$\frac{dE_N}{dt} = (1-p_1) \frac{\beta_1 \Lambda}{\mu_1 + \Omega} I_N + (1-q_1) r_1 I_N - (\alpha_1 + \mu_1 + \Omega) E_N \quad (24)$$

$$\frac{dE_H}{dt} = (1-p_2) \frac{\beta_2 \Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) I_H + (1-q_2) r_2 I_H + \Omega E_N - (\alpha_2 + \mu_2) E_H \quad (25)$$

$$\frac{dI_N}{dt} = \frac{p_1 \beta_1 \Lambda}{\mu_1 + \Omega} I_N + \alpha_1 E_N - (r_1 + d_1 + \pi) I_N \quad (26)$$

$$\frac{dI_H}{dt} = \frac{p_2 \beta_2 \Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) I_H + \alpha_2 E_H + \pi I_N - (r_2 + d_2) I_H \quad (27)$$

Let  $X = (E_N, E_H, I_N, I_H)'$ . Then the following results are obtained:

$$T_{TB-HIV} = \begin{pmatrix} 0 & 0 & (1-p_1) \frac{\beta_1 \Lambda}{\mu_1 + \Omega} & 0 \\ 0 & 0 & 0 & (1-p_2) \frac{\beta_2 \Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) \\ 0 & 0 & \frac{p_1 \beta_1 \Lambda}{\mu_1 + \Omega} & 0 \\ 0 & 0 & 0 & \frac{p_2 \beta_2 \Omega}{\mu_2} \left( \frac{\Lambda}{\mu_1 + \Omega} \right) \end{pmatrix} \quad (28)$$

$$\Sigma_{TB-HIV} = \begin{pmatrix} -(\alpha_1 + \mu_1 + \Omega) & 0 & (1-q_1) r_1 & 0 \\ \Omega & -(\alpha_2 + \mu_2) & 0 & (1-q_2) r_2 \\ \alpha_1 & 0 & -(r_1 + d_1 + \pi) & 0 \\ 0 & \alpha_2 & \pi & -(r_2 + d_2) \end{pmatrix} \quad (29)$$

and  $K_L^{TB-HIV} = -T_{TB-HIV} \Sigma_{TB-HIV}^{-1}$ . Since  $\det K_L^{TB-HIV} = 0$ , the high dimensional matrix can be reduced to the NGM with small domain which is given by  $K_L^{TB-HIV} = -T_{TB-HIV} \Sigma_{TB-HIV}^{-1}$  where

$$R = \begin{pmatrix} 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \quad (30)$$

$$C = \begin{pmatrix} \frac{(1-p_1) \beta_1 \Lambda}{\mu_1 + \Omega} & 0 \\ 0 & \frac{(1-p_2) \beta_2 \Omega \Lambda}{\mu_2 (\mu_1 + \Omega)} \\ \frac{p_1 \beta_1 \Lambda}{\mu_1 + \Omega} & 0 \\ 0 & \frac{p_2 \beta_2 \Omega \Lambda}{\mu_2 (\mu_1 + \Omega)} \end{pmatrix} \quad (31)$$

Therefore, the basic reproductive number for TB-HIV co-epidemic model can be obtained easily from the trace and the determinant of the corresponding two-dimensional matrix.

$$R_0 = \rho(K_S) = \frac{1}{2} \left( \text{trace}(K_S) + \sqrt{\text{trace}(K_S)^2 - 4 \det(K_S)} \right). \quad (32)$$

It is difficult to show the long expression of the basic reproductive number, so the numerical value of  $R_0$  will be presented in the next section instead.

## RESULTS AND DISCUSSION

In 2010, the Registration Administration Bureau, Department Local Administration, Ministry of Interior reported that the Thai population size was approximately 63,701,703 and the number of births and deaths were 766,370 and 414,888, respectively (Official Statistics Registration Systems, 2015). Additional information from Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, provided insight into the causes of death. However, the current study is concerned with TB and HIV only. The numbers of deaths-by-cause groups were 4,460 cases of TB and 3,631 cases of HIV (Ousvapoom *et al.*, 2013). The death rate for HIV-infected TB patients was about 14%. From clinical data in 2010, there were 62,365 TB patients and 277,656 HIV patients. About 8,564 people or 16% of TB patients were detected HIV-positive (Bureau of Tuberculosis, 2014). Therefore, the correspondence between the information and the model are:

$$S_N + E_N + I_N + S_H + E_H + I_H = 63,701,703$$

$$S_H + E_H + I_H = 227,656$$

$$I_N + I_H = 62,365$$

$$16\% I_N = 8,564$$

As a result, in 2010, the Thai population can be classified into six compartments and the numbers in each compartment can be calculated step by step. Firstly,  $I_N = 53,525$  and  $I_H = 8,840$ .

National Tuberculosis Control Programme Guidelines, Thailand, (2013) also suggested that 90% of people who get infected with TB will develop latent TB. Otherwise, they become active TB (Nateniyom, 2013). To simplify the problem, this concept was used for the HIV group and non-HIV group separately. Therefore,

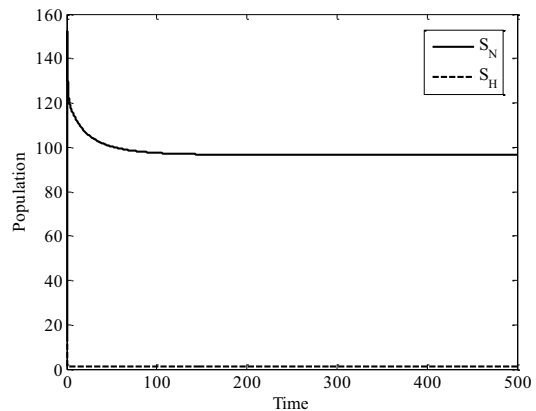
$$0.1(E_N + I_N) = I_N$$

$$0.1(E_H + I_H) = I_H$$

$$\text{Then } E_N = 481,725 \text{ and } E_H = 79,560.$$

Finally,  $S_H = 189,256$  and  $S_N = 62,888,797$ . Moreover, about one in ten latent TB will eventually progress to active TB. World Health Statistics reported that the incidence rate of TB in Thailand was 137 per 100,000 population per year (Ousvapoom *et al.*, 2013). It can be seen that many epidemiological quantities are reported in the form of rate per 100,000 individuals. Thus, the whole population is considered as 100,000 individuals and proportions are used for the remainder. Table 1 shows the meaning of parameters and their estimated values.

Figures 2–4 are the numerical simulations carried out in support of the analytical results with the same set of parameters and initial conditions. Parameter values are shown in Table 1. The initial condition is (15, 20,000, 1,000, 15, 20,000, 1,000).



**Figure 2** Time series of people with human immunodeficiency virus (HIV) susceptible and TB susceptible (solid curve) and people with HIV infected and TB susceptible (dashed curve).

**Table 1** Description of the parameters, their values (per year) and references with regard to human immunodeficiency virus (HIV) and tuberculosis (TB).

Model Description	Without HIV		With HIV	
	Parameter	value	Parameter	value
Mortality rate	$\mu_1$	0.64% <sup>e</sup>	$\mu_2$	0.88% <sup>e</sup>
TB mortality rate	$d_1$	5.95% <sup>e</sup>	$d_2$	14.00% <sup>d</sup>
TB detection rate	$\beta_1$	1.20% <sup>e</sup>	$\beta_2$	67.40% <sup>e</sup>
Proportion of active TB	$p_1$	0.10 <sup>b</sup>	$p_2$	0.10 <sup>b</sup>
TB recovery rate	$r_1$	89.00% <sup>a</sup>	$r_2$	89.00% <sup>a</sup>
TB successful treatment	$q_1$	0.97 <sup>a</sup>	$q_2$	0.97 <sup>a</sup>
TB activation rate	$\alpha_1$	10.00% <sup>b</sup>	$\alpha_1$	10.00% <sup>b</sup>
Model	Without infectious TB		With infectious TB	
Description	Parameter	value	Parameter	value
HIV detection rate	$\Omega$	0.16% <sup>e</sup>	$\pi$	16.00% <sup>a</sup>
Birth rate	$\Lambda$	1,200 per 100,000 individuals <sup>a,c</sup>		

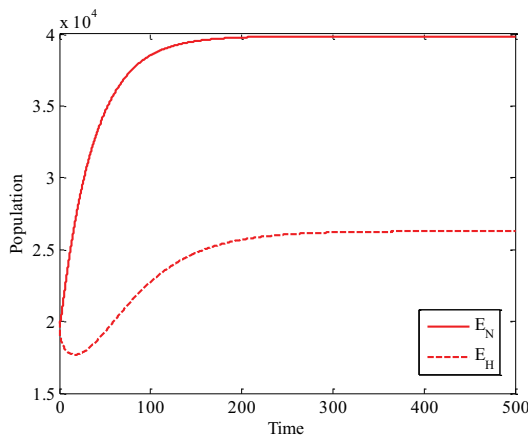
<sup>a</sup> = Bureau of Tuberculosis, Department of Disease Control, Ministry of Public Health, Thailand (2014).

<sup>b</sup> = Nateniyom S (2013).

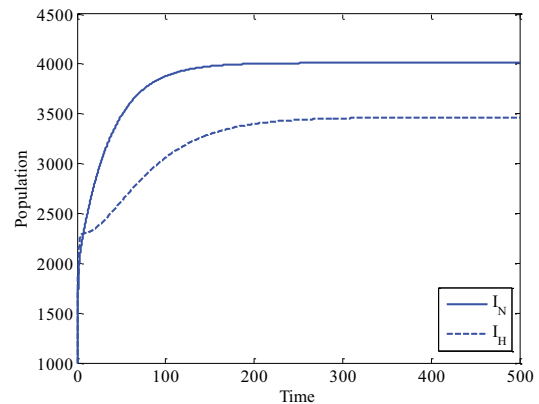
<sup>c</sup> = Official Statistics Registration Systems (2015).

<sup>d</sup> = Tuberculosis Center Region 12 (2015).

<sup>e</sup> = calculated from data of <sup>a</sup>, <sup>b</sup>, <sup>c</sup> and Official Statistics Registration Systems. 2015.



**Figure 3** Time series of people with human immunodeficiency virus (HIV) susceptible and latent tuberculosis (TB) infected (solid curve) and people with HIV infected and latent TB infected (dashed curve).



**Figure 4** Time series of people with human immunodeficiency virus (HIV) susceptible and active tuberculosis (TB) infected (solid curve) and people with HIV infected and active TB infected (dashed curve).

From Figures 2–4, the endemic equilibrium point  $((S_N^*, S_H^*, E_N^*, E_H^*, I_N^*, I_H^*) = (96.58, 1.28, 39,852.88, 26,279.39, 4,010.95, 3,463.67))$  clearly exists and is locally stable and is associated with the basic reproduction numbers:  $R_0^{TB} = 2,309.98$  and  $R_0^{HIV} = R_0^{TB-HIV} = 17,872.57$  which satisfy  $R_0 > 1$ . This implies that TB, HIV, and TB-HIV infections will remain in the system. Consequently, TB and HIV still spread in Thai society. These simulations confirm the theoretical result that the disease-free equilibrium is unstable. This model also reveals that birth rate plays an important role since more people lead to more chance to get infected. The detection rate ( $\Omega$ ) is also sensitive to  $R_0$ .

New numerical results with the previous parameter values except with the birth rate changed to  $\Lambda = 0.12\%$  show that the disease-free equilibrium point  $((S_N^*, S_H^*, E_N^*, E_H^*, I_N^*, I_H^*) = (0.15, 0.03, 0, 0, 0, 0))$  is locally stable associated with the basic reproduction numbers:  $R_0^{TB} = 0.0023$  and  $R_0^{HIV} = R_0^{TB-HIV} = 0.0179$ , satisfied  $R_0 < 1$ . It implies that the numbers of people with TB and HIV decline and the infections have a strong

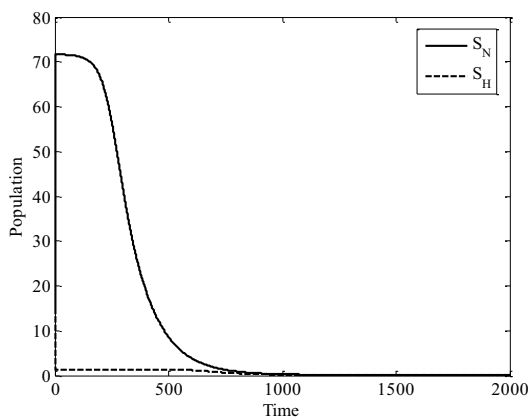
tendency to disappear from the system as shown in Figures 5–7.

After running several numerical calculations to investigate the trends of the basic reproduction number  $R_0^{TB-HIV}$  when a related parameter changes, only four parameters ( $\beta_1, \beta_2, p_2, \Lambda$ ) could provide the threshold of  $R_0^{TB-HIV} = 1$ . Among them, TB detection rates ( $\beta_1, \beta_2$ ) could be used to compare the spread of TB in two groups. Figure 8 shows how the basic reproduction number  $R_0^{TB-HIV}$  varies with TB detection rates.

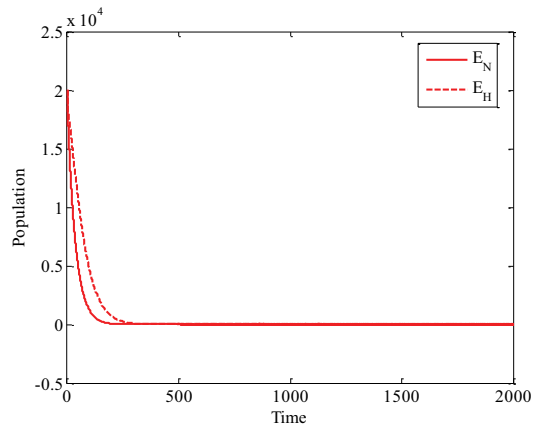
Clearly, the value of  $R_0^{TB-HIV}$  increases linearly as  $\beta_1$  or  $\beta_2$  increases. The thresholds of  $R_0^{TB-HIV} = 1$  for a non-HIV group and an HIV group occur at  $\beta_1 = 7.73$  and  $\beta_2 = 37.71$ , respectively. From Table 1,  $\beta_1 = 0.012$  and  $\beta_2 = 0.674$  imply that the number of people in the two groups of TB decline and the infections have a strong tendency to disappear from the system. Finally, the threshold parameter  $R_0^{TB-HIV}$  in the TB detection rate space is illustrated in Figure 9.

From the literature review, many researchers have studied TB-HIV. The current study was mainly focussed on the situation in Thailand.

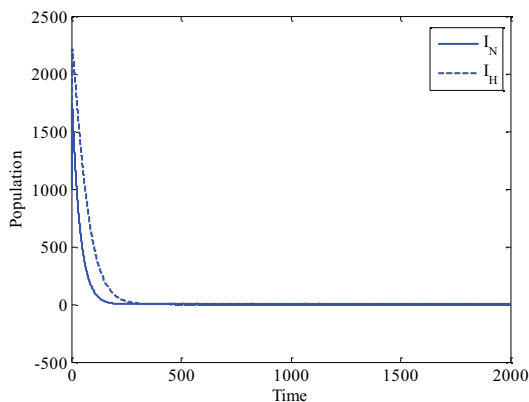




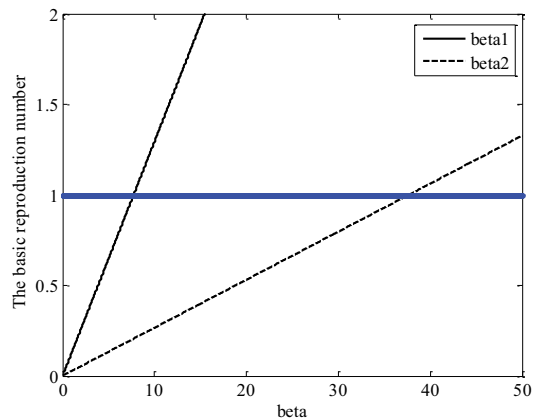
**Figure 5** Time series of people with human immunodeficiency virus (HIV) susceptible and tuberculosis (TB) susceptible (solid curve) and people with HIV infected and TB susceptible (dashed curve).



**Figure 6** Time series of people with human immunodeficiency virus (HIV) susceptible and latent tuberculosis (TB) infected (solid curve) and people with HIV infected and latent TB infected (dashed curve).



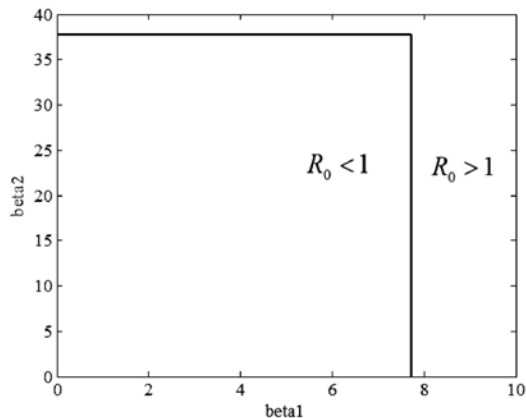
**Figure 7** Time series of people with human immunodeficiency virus (HIV) susceptible and active tuberculosis (TB) infected (solid curve) and people with HIV infected and active TB infected (dashed curve).



**Figure 8** Relationship between the basic reproduction number  $R_0^{TB-HIV}$  and tuberculosis detection rates.

Thus, most parameter values were obtained using information from the Epidemiological Information Section, Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand (Epidemiological Information Section, 2015). Unfortunately, the reported data is

secondary data which can be very difficult to obtain and complicated to interpret and use. Moreover, the long period of latent TB infection implies that new cases of infection are not clinically apparent. Therefore, they are unobserved for some time. To take this delay into consideration, it would be necessary to develop a time-delay differential equation model.



**Figure 9** Invasion analysis in the tuberculosis detection rate space.

### CONCLUSION

This model investigated the spread of TB through a non-HIV group and an HIV group. Each group consists of three compartments, namely TB susceptible, latent TB infected and active TB infected. The basic reproduction numbers predicting invasion of TB, HIV, and TB-HIV were determined by following Diekmann's recipe (Diekmann *et al.*, 2010). The useful information from related disease control departments led to parameter estimation. Several numerical results also illustrated the existence of a stable, disease-free equilibrium point and a stable, endemic equilibrium point. For Thailand, the infections still have a substantial effect on the Thai population because of the hidden TB-infected population.

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### LITERATURE CITED

- Bacaër, N., R. Ouifki, C. Pretorius, R. Wood and B. Williams. 2008. Modeling the joint epidemics of TB and HIV in a South African township. **J. Math. Biol.** 57: 557–593.
- Bureau of Tuberculosis, Department of Disease Control, Ministry of Public Health, Thailand 2014. [Available from: <http://tbthailand.org/images/present/pre-20140725042109-1.pdf>]. [Sourced: 9 February 2015].
- Castillo-Chavez, C. and B. Song. 2004. Dynamical models of tuberculosis and their applications. **Math. Biosci. Eng.** 1: 361–404.
- Diekmann, O., J.A.P. Heesterbeek and J.A.J. Metz. 1990. On the definition and the computation of the basic reproduction ratio  $R_0$  in models for infectious diseases in heterogeneous populations. **J. Math. Biol.** 28: 365–382.
- Diekmann, O., J.A.P. Heesterbeek and M.G. Roberts. 2010. The construction of next-generation matrices for compartmental epidemic models. **J. R. Soc. Interface.** 7: 873–885.
- Epidemiological Information Section. 2015. **Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Thailand.** [Available from: [http://www.boe.moph.go.th/files/report/20111206\\_35941163.pdf](http://www.boe.moph.go.th/files/report/20111206_35941163.pdf)]. [Sourced: 9 February 2015].
- Heffernan, J.M., R.J. Smith and L.M. Wahl. 2005. Perspectives on the basic reproductive ratio. **J. R. Soc. Interface.** 2: 281–293.
- Hyman, J.M. and E.A. Stanley. 1988. Using mathematical models to understand the AIDS epidemic. **Math. Biosci.** 90: 415–473.
- Long, E.F., N.K. Vaidya and M.L. Brandeau. 2008. Controlling co-epidemics: analysis of HIV and tuberculosis infection dynamics. **Oper. Res.** 56: 1366–1381.

- Nateniyom S. 2013. **National Tuberculosis Control Programme Guidelines**. The Agricultural Co-operative Federation of Thailand, Limited. Bangkok, Thailand. 182 pp.
- Official Statistics Registration Systems. 2015. **Department of Provincial Administration, Ministry of Interior**, Thailand. [Available from: <http://stat.bora.dopa.go.th/stat/statnew/statTDD>]. [Sourced: 28 October 2015].
- Ousvapoom, P, A. Suthiart, T. Aryukasam and S. Senpong. 2013. **Statistical Thailand 2013**. WVO Office of Printing Mill. Bangkok, Thailand. 180 pp.
- Porco, T.C. and S.M. Blower. 1998. Quantifying the intrinsic transmission dynamics of tuberculosis. **Theor. Popul. Biol.** 54: 117–132.
- Tuberculosis Center Region 12. 2015. **Tuberculosis Center Region 12**, Yala [Available from: [http://203.157.45.179/yala12/wpcontent/uploads/2014/06/1. Thailand-Tuberculosis-Situation\\_Feb2014\\_V4.pdf](http://203.157.45.179/yala12/wpcontent/uploads/2014/06/1. Thailand-Tuberculosis-Situation_Feb2014_V4.pdf) ]. [Sourced: 20 February 2015].
- World Health Organization. 2014a. **World Health Organization, Media Centre, Factsheets, Tuberculosis** [Available from: <http://www.who.int/mediacentre/factsheets/fs104/en/>]. [Sourced: 20 February 2015].
- World Health Organization. 2014b. **World Health Organization, Media Centre, Factsheets, HIV/AIDS** [Available from: <http://www.who.int/mediacentre/factsheets/fs360/en/>]. [Sourced: 20 February 2015].