MATHEMATICAL MODELLING OF SYPHILIS IN A HETEROGENEOUS SETTING WITH COMPLICATIONS

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ABSTRACT. A non linear mathematical model is used to study the dynamics of spread of syphilis in a heterogeneous settings with two stages of infection. The existence and uniqueness of the system of equation is established using lipchitz condition. The disease free equilibrium(DFE) and endemic equilibrium(EE) were determined. The Disease Free Equilibrium is locally stable whenever $Ro < 1$ and unstable otherwise. The stability of the Endemic Equilibrium is also analyzed using Bellman and Cooke's theorem. Numerical simulations are carried out, results obtained are discussed and also graphically presented.

1. INTRODUCTION

Sexually transmitted diseases (STDs) are a group of infectious or communicable diseases in which the primary mode of transmission is through sexual contact [1] and are among the major causes of illnesses in the world especially in the developing countries [2] and [3]. The diseases caused by (STDs) are classified according to the type of organism causing the infection, which could be bacterial, fungal, viral or of parasitic origin. Some of the common sexually transmitted diseases include: Bacterial vaginosis, herpes, Chlamydia, trichomoniasis, gonorrhea, Hepatitis B virus, and syphilis [4]. More than 25 infectious organisms are transmitted primarily through sexual activity and studies reveal that STDs are among the many related factors that affect the broad continuum of reproductive health [5] and [6].

Mathematical model of (STDs) transmission were first developed in 1970s [7]; [8], in response to concern over the dramatic increases in the number of reported gonorrhea cases in the USA

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during the 1960s and 1970s.After there model, researchers developed mathematical models to simulate the spread of a wide range of (STDs),such as syphilis, HIV/AIDS, gonorrhea, Hepatitis B virus [4].This section is to provide an overview of themes that have been most commonly tackled in syphilis/ other infectious diseases and a commentary on the approaches that have must frequently been adopted.

Syphilis is a multistage disease that progresses, when untreated, from primary to secondary, latent and finally, to tertiary infection. The primary stage symptoms of syphilis involves the presents of a single chancre(a firm,painless, non-itchy ulceration). Secondary syphilis with a diffuse rash which involves the palms of the hands and soles of the feet. latent syphilis with a little to no symptoms and the tertiary syphilis with gummas, neurological or cardiac symptoms. Partial immunity is acquired in both treated and untreated syphilis. It is a disease of a considerable public health importance because, if not treated, it can lead to various cardiovascular and neurological diseases as well as to adverse pregnancy outcomes,such as stillbirth and congenital syphilis. [10] studied a syphilis model which include partial immunity and vaccination in which the model suggests that a backward bifurcation very likely to occurs for the real -life estimated epidemiological parameters syphilis which may explain d resurgence of syphilis after mass treatment. [11] studied a syphilis model using a mathematical model that include all stages of the disease.They assumed that infected individuals acquire temporary immunity only after recovery from the latent and tertiary infections.

In this paper, we propose a model for the transmission of syphilis, which is an extension of the existing mathematical models of syphilis. The extension of the model includes two susceptible classes, two infected classes with complications and treated class inclusive.

2. MODEL FORMULATION

The model sub-divides the total human population at time t denoted by $N(t)$, into six compartments of Susceptible male $S_m(t)$, Susceptible female $S_f(t)$, Infected male $I_m(t)$, Infected female $I_f(t)$, Complications $C(t)$ and Treated $T(t)$, where $N(t)$ is given as

$$N(t) = S_m(t) + S_f(t) + I_m(t) + I_f(t) + C(t) + T(t)$$

The susceptible male are individuals that have not contact syphilis but may be infected through sexual contacts with infected female,

while Susceptible female are individuals that have not contact syphilis but may be infected through sexual contacts with infected male. The Infected male are individual that have syphilis and are able to transmit to susceptible female,while Infected female are individual that have syphilis and are able to transmit to susceptible male.The complications are individual in the population with syphilis at the latent stage that leads to other diseases or death.Treated are people that have recovered from syphilis. The model equation is given as:

$$\frac{dS_m}{dt} = \pi_m - \alpha_1 I_f S_m - \mu S_m \tag{2.1}$$

$$\frac{dS_f}{dt} = \pi_f - \alpha_2 I_m S_f - \mu S_f \tag{2.2}$$

$$\frac{dI_m}{dt} = \alpha_1 I_f S_m - (r_1 + \beta_1 + \mu) I_m \tag{2.3}$$

$$\frac{dI_f}{dt} = \alpha_2 I_m S_f - (r_2 + \beta_2 + \mu) I_f \tag{2.4}$$

$$\frac{dC}{dt} = \beta_1 I_m + \beta_2 I_f - (\nu + \mu + \delta) C \tag{2.5}$$

$$\frac{dT}{dt} = r_1 I_m + r_2 I_f + \nu C - \mu T \tag{2.6}$$

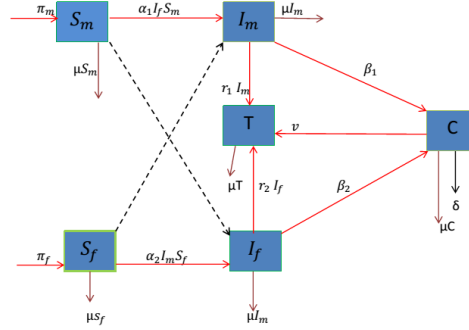

FIGURE 1. Flow Chart

Model Assumption.

1. No homosexuality in the population e.g anal sex.

2. Constant per capital death rate for all Compartments.
3. Individuals in the Complications class are assumed to be sexually inactive.
4. No permanent immunity after treated.
5. Syphilis induced death occurs at complications compartment only.
6. The population is heterogeneous i.e in a broad sense, diversity, variety.

The Existence and Uniqueness of Solution For The Model.
Theorem 1 [12]: Let D' denote the region $|t-t_0| \leq a, \quad ||x-x_0|| \leq b, \quad : x = (x_{10}, x_{20}, \cdots, x_{n0})$ and suppose that $f(t, x)$ satisfies the Lipschitz condition $||f(t, x_1) - f(t, x_2)|| \leq k||x_1 - x_2||$. Whenever the pairs (t, x_1) and (t, x_2) belong to D', where k is a positive constant, then, there is a constant $\delta > 0$ such that there exists a unique continuous vector solution $x(t)$ of the system in the interval $t - t_0 \leq \delta$. It is important to note that the condition is satisfied by requirement that $\frac{\partial f_i}{\partial x_j}, i = 1, 2 \cdots$, be continuous and bounded in D'.
Theorem 2: Let D' denote the region $0 \leq \alpha \leq \mathcal{R}$. Then the system of equations have a unique solution, if $\frac{\partial f_i}{\partial x_j}, i, j = 1 - 6$ are continuous and bounded in D'. Using the Lipchitz condition to verify the existence and uniqueness of the of the systems of equation in 2.1-2.6. Let

$$f_1 = \pi_m - \alpha_1 I_f S_m - \mu S_m$$
$$f_2 = \pi_f - \alpha_2 I_m S_f - \mu S_f$$
$$f_3 = \alpha_1 I_f S_m - (r_1 + \beta_1 + \mu)I_m$$
$$f_4 = \alpha_2 I_m S_f - (r_2 + \beta_2 + \mu)I_f$$
$$f_5 = \beta_1 I_m + \beta_2 I_f - (\nu + \mu + \delta)C$$
$$f_6 = r_1 I_m + r_2 I_f + \nu C - \mu T$$

The partial derivative of f_1 yield:

$$\left|\frac{\partial f_1}{\partial S_m}\right| = |-\alpha_1 I_f - \mu| \leq \infty; \left|\frac{\partial f_1}{\partial S_f}\right| = 0 \leq \infty; \left|\frac{\partial f_1}{\partial I_m}\right| = 0 \leq \infty$$

$$\left|\frac{\partial f_1}{\partial I_f}\right| = |-\alpha_1 S_m| \leq \infty; \left|\frac{\partial f_1}{\partial C}\right| = 0 \leq \infty; \left|\frac{\partial f_1}{\partial T}\right| = 0 \leq \infty \quad (2.7)$$

As clearly shown above, the partial derivatives of the whole system of equations exist, they are finite and bounded. Hence by theorem 1, the model system has a unique solution.

Disease Free Equilibrium. We want to study how the population changes when there is no disease.At the disease free,we assume the absence of syphilis; therefore we equate $I_m = I_f = C = 0$

The disease free equilibrium is given as:

$$\left(S_m^*, S_f^*, I_m^*, I_f^*, C^*, T^*\right) = \left(\frac{\pi_m}{\mu}, \frac{\pi_f}{\mu}, 0, 0, 0, 0\right)$$

In the absence of syphilis, the susceptible male and susceptible female changes in proportion to the ratio of their recruitment rates to the death rate.

Endemic Equilibrium. Calculating the endemic point, where $I_m \neq 0$ $I_f \neq 0$ $C \neq 0$ we have,

$$I_f^{**} = \frac{\pi_m - \mu S_m^{**}}{\alpha_1 S_m^{**}} \quad S_m^{**} > 0$$

$$I_m^{**} = \frac{\pi_f - \mu S_f^{**}}{\alpha_2 S_f^{**}} \quad S_f^{**} > 0$$

$$C^{**} = \frac{\alpha_1 \beta_1 S_m^{**}(\pi_f - \mu S_f^{**}) + \alpha_2 \beta_2 S_f^{**}(\pi_m - \mu S_m^{**})}{\alpha_1 \alpha_2 S_m^{**} S_f^{**}(\nu + \mu + \delta)}$$

$$T^{**} = \frac{(\nu + \mu + \delta)(K_1 + K_2) + K_3 + K_4}{\mu \alpha_1 \alpha_2 S_m^{**} S_f^{**}(\nu + \mu + \delta)} \tag{2.8}$$

where

$$K_1 = \alpha_1 r_1 S_m(\pi_f - \mu S_f)$$
$$K_2 = \alpha_2 r_2 S_f(\pi_m - \mu S_m)$$
$$K_3 = \alpha_1 \beta_1 S_m(\pi_f - \mu S_f)$$
$$K_4 = \alpha_1 \beta_2 S_f(\pi_f - \mu S_f)$$

At endemic equilibrium point we have $S_m^{**} > 0, S_f^{**} > 0$ and the values of $I_m^{**}, I_f^{**}, C^{**}, T^{**}$ depending on both $S_m^{**} > 0, S_f^{**} > 0$.

Basic Reproduction Number/ Basic Reproduction Ratio. Basic reproduction number (R_0) can be defined as the average number of secondary infections that occur when one infection is introduced into a complete susceptible host population[13].For this research work the method of next generation matrix by [14] was used.Considering the next generation matrix G. $G = FV^{-1}$

Applying the method of next generation matrix to the model. There are three infected classes,the infected male (I_m), infected

female (I_f), and the complications class (C) i.e $m = 3$ .Choosing F and V from the infected classes we have;

$$F = \begin{pmatrix} \alpha_1 I_f S_m \\ \alpha_2 I_m S_f \\ \beta_1 I_m + \beta_2 I_f \end{pmatrix}, V = \begin{pmatrix} (r_1 + \beta_1 + \mu)I_m \\ (r_2 + \beta_2 + \mu)I_f \\ (\nu + \mu + \delta)C \end{pmatrix}$$

At disease free equilibrium

$$\left(S_m^*, S_f^*, I_m^*, I_f^*, C^*, T^*\right) = \left(\frac{\pi_m}{\mu}, \frac{\pi_f}{\mu}, 0, 0, 0, 0\right)$$

The reproduction number of the given system of equations is:

$$R_0 = \rho(FV^{-1}) = \frac{\sqrt{(\mu + \beta_2 + r_2)(\mu + \beta_1 + r_1)\,\alpha_2 \pi_f \alpha_1 \pi_m}}{(\mu + \beta_2 + r_2)(\mu + \beta_1 + r_1)\,\mu} \quad (2.9)$$

3. Stability Analysis of The Model

At disease free equilibrium

$$\left(S_m^*, S_f^*, I_m^*, I_f^*, C^*, T^*\right) = \left(\frac{\pi_m}{\mu}, \frac{\pi_f}{\mu}, 0, 0, 0, 0\right)$$

Inserting the value of $S_m^*, S_f^*, I_m^*, I_f^*, C^*, T^*$ into the jacobian matrix we have;

$$J = \begin{pmatrix} \mu & 0 & 0 & -\alpha_1 \frac{\pi_m}{\mu} & 0 & 0 \\ 0 & -\mu & -\alpha_2 \frac{\pi_f}{\mu} & 0 & 0 & 0 \\ 0 & 0 & -(r_1 + \beta_1 + \mu + \delta) & \alpha_1 \frac{\pi_m}{\mu} & 0 & 0 \\ 0 & 0 & \alpha_2 \frac{\pi}{\mu} & -(r_2 + \beta_2 + \mu + \delta) & 0 & 0 \\ 0 & 0 & \beta_1 & \beta_2 & -(\nu + \mu + \delta) & 0 \\ 0 & 0 & r_1 & r_2 & \nu & -\mu \end{pmatrix}$$

Evaluating $|J - \lambda I| = 0$ The determinant equation reduces to;

$$(-\mu - \lambda)(-(\nu + \mu + \delta - \lambda))(-\mu - \lambda)(-\mu - \lambda)bfX$$

$$\begin{vmatrix} -(r_1 + \beta_1 + \mu) - \lambda & \alpha_1 \frac{\pi_m}{\mu} \\ \alpha_2 \frac{\pi_f}{\mu} & -(r_2 + \beta_2 + \mu) - \lambda \end{vmatrix} = 0$$

The first four eigenvalues of the equation are given as:

$$\lambda_1 = -\mu, \lambda_2 = -(\nu + \mu + \delta), \lambda_3 = -\mu, \lambda_4 = -\mu$$

The last two eigenvalues are obtained from the determinant of the 2 x 2 matrix:

$$(r_1 + \beta_1 + \mu + \lambda)(r_2 + \beta_2 + \mu + \lambda) - \frac{\alpha_1 \alpha_2 \pi_m \pi_f}{\mu^2} = 0$$

Which simplify to

$$\lambda^2 + \lambda(r_1 + \beta_1 + r_2 + \beta_2 2\mu + 2\delta) + (r_1 + \beta_1 + \mu + \delta)(r_2 + \beta_2 + \mu + \delta)$$

$$-\frac{\alpha_1\alpha_2\pi_m\pi_f}{\mu^2} = 0$$

Evaluating the above equation using the Rourth-Hurwitz stability criteria for a quadratic function.

Theorem: The roots of the characteristics equation of a quadratic equation

$a_2\lambda^2 + a_1\lambda + a_0 = 0$ all have negative roots, if and only if all the coefficient satisfy $a_n > 0$. by Rourth-Hurwitz stability criteria we have;

$$\frac{\alpha_1\alpha_2\pi_m\pi_f}{\mu^2(r_1 + \beta_1 + \mu)(r_2 + \beta_2 + \mu)} < 1 \tag{3.1}$$

from the value of R_0 obtained from the next generation matrix i.e

$$R_0^2 < 1$$

which implies

$$R_0 < 1$$

Therefore the system of equations is locally asymptotically stable at the (DFE) point.

4. Numerical Simulation and Discussion

Numerical Simulations were performed with values and units of the model parameters given in the table below.These values are for the purpose of illustrating the outcome of the model transmission of syphilis in a heterogeneous setting with compartments.

| Parameters	values	Source
π_m	0.3	Hypothetical
π_f	0.45	Hypothetical
μ	0.1	Hypothetical
δ	0.01	Hypothetical
α_1	0.2	Hypothetical
α_2	0.5	Hypothetical
ν	0.2	Hypothetical
r_1	0.1	Hypothetical
r_2	0.1	Hypothetical
β_1	0.5	Hypothetical
β_2	0.5	Hypothetical

The table was used to draw the graph of each compartment against time(days) using maple 18 computational software.The initial values are $S_m = 80$, $S_f = 90$, $I_m = 5$, $I_f = 8$, $C = 3$, $T = 0$ (Assumed values).
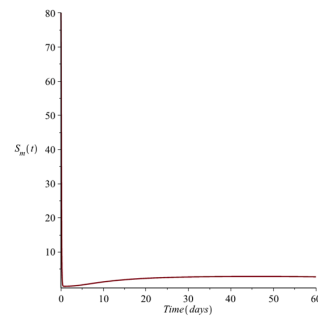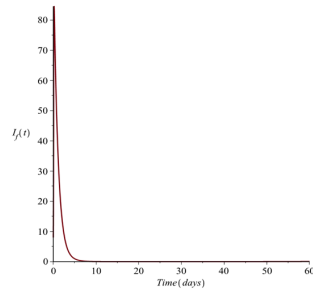
(A) Graph of Susceptible male with time
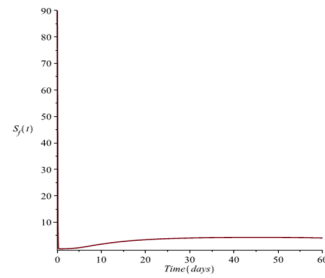
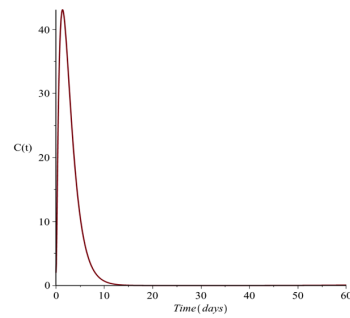(B) Graph of Susceptible female with time
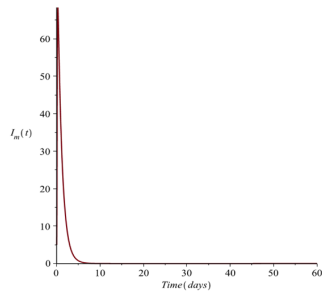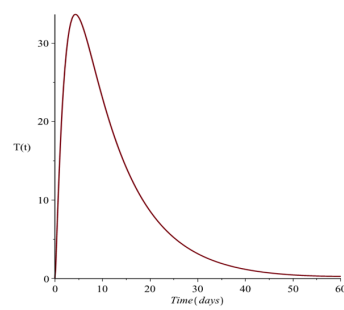

(C) Graph of Infected male with time

(D) Graph of Infected female with time

(E) Graph of Complications with time

(F) Graph of Treated with time.

From Fig.1, in a highly sexually active environment the number of susceptible male would drop drastically as people get infected with syphilis. An equilibrium is reached after about 20 days as recovered people become susceptible again in the absence of treatment.

From Fig.2, similarly, in a highly sexually active environment the number of susceptible female would drop drastically as people get infected with syphilis. An equilibrium is reached after about 20 days as recovered people become susceptible again in the absence of treatment.

In Fig.3,there is a sharp rise in the number of infected male, when untreated infected male develop complications. From

Fig.4, there is also a sharp rise in the number of infected female, when untreated infected female develop complications. From

Fig.5,as people continue to get infected without treatment,cases of complications increases and drop gradually when they are treated.

In Fig.6, the number of treated individuals will steadily rise to it peak and gradually reduce.People get reinfected due to their life style or eventually become susceptible to syphilis again.

Table 4.1: First Simulation Table.

π_m	π_f	μ	α_1	α_2	β_1	β_2	r_1	r_2	R_0(DFE)	Remarks
0.3	0.45	0.1	0.1	0.1	0.5	0.5	0.5	0.6	0.3198010	Stable
0.3	0.45	0.1	0.1	0.15	0.5	0.5	0.5	0.6	0.3916747	Stable
0.3	0.45	0.1	0.15	0.2	0.5	0.5	0.5	0.6	0.5539117	Stable
0.3	0.45	0.1	0.2	0.25	0.5	0.5	0.5	0.6	0.7150969	Stable
0.3	0.45	0.1	0.25	0.3	0.5	0.5	0.5	0.6	0.8758113	Stable
0.3	0.45	0.1	0.3	0.35	0.5	0.5	0.5	0.6	1.0362739	Unstable
0.3	0.45	0.1	0.35	0.4	0.5	0.5	0.5	0.6	1.1965860	Unstable

Table 4.1 Varying the contact rate of susceptible male and susceptible female while other parameters used are kept constant.

Table 4.2: Second Simulation Table.

π_m	π_f	μ	α_1	α_2	β_1	β_2	r_1	r_2	R_0(DFE)	Remarks
0.3	0.45	0.1	0.2	0.5	0.5	0.6	0.2	0.3	1.36930639	Unstable
0.3	0.45	0.1	0.2	0.5	0.6	0.65	0.3	0.4	1.22474487	Unstable
0.3	0.45	0.1	0.2	0.5	0.6	0.7	0.4	0.5	1.10782342	Unstable
0.3	0.45	0.1	0.2	0.5	0.6	0.7	0.5	0.6	1.01129979	Unstable
0.3	0.45	0.1	0.2	0.5	0.6	0.7	0.6	0.7	0.93026051	Stable
0.3	0.45	0.1	0.2	0.5	0.8	0.8	0.7	0.8	0.86125388	Stable
0.3	0.45	0.1	0.2	0.5	0.8	0.8	0.8	0.9	0.80178373	stable

Varying the recovery rate of infected male and infected female while other parameters used are kept constant.

The simulation results presented above established the positivity solutions of the model.Table 4.1 shows the value of R_0 when the contact rate of susceptible male and susceptible female are varied, when the contact rate is low the Reproduction number is less than one(Syphilis will die out), when $\alpha_1 = 0.3$ and $\alpha_2 = 0.35$ syphilis becomes endemic(disease spread out within the population due to high contact rate) which may lead to complications. Table 4.2 shows the value of R_0 when the recovery rate of infected male, infected female is varied within a heterogeneous setting,in which at low recovery rate the value of the Reproduction number R_0 is greater than one(syphilis become endemic), when $r_1 = 0.6$ and $r_2 = 0.7$ the value of $R_0 < 1$ which indicate that, due to strong treatment at initial stages of syphilis, the disease will die out of the population and this would result to no cases of complications.

4. CONCLUSION

In this paper, we derived and analyzed a deterministic model for the transmission of syphilis in a heterogeneous setting with complications. We carried out the stability of the disease free equilibrium (DFE) and endemic equilibrium (EE) in which the (DFE) is said to be locally asymptotically stable when $R0 < 1$, at endemic equilibrium the system is found to be stable. Syphilis at initial stages should be treated properly because at the complications stage, no amount of treatment will reverse the damage causes to the body. Despite much progress in understanding the transmission dynamics of the syphilis, we still have a long way to go before the disease and other sexual transmitted diseases (STDs) are conquered due to the increase in the practice of homosexuality in some countries. Hence, proper educational campaign for use of correct and effective medicines and use of condom among sexual workers to reduce the disease and other (STDs) should be done.

REFERENCES

[1] R. Gilson and A. Mindel, *Infectious and Communicable Diseases and Mode of Transmission*, British Medical Journal, 1160-1164,(322), 2009.

[2] World Health Organization(WHO), *WHO Website: http: //www. who. int /publishers / en .html*, Geneva, 2001.

[3] V. U. Usanga, B. L. Abia , I. E. Efoh, P. C. Udoh, E. Archibong and F. Ani, *Incidence of N. gonorrhoeae among pregnant woman in calabar, Nigeria*, The International of Gynecology and Obstetrics, 2010.

[4] World Health Organization (WHO), *WHO Technical Report Series No 810* ,Geneva, 2006.

[5] I. O. Okonko, P. O. Okerentugba ,A. O. Adejuwon and C. C. Onoch, *Prevalence of sexually Transmitted Infectious(STIS)* ,Archives of Applied Science Research, 980-987, 4(2), 2012.

[6] M. Shafer and A. Moscicki, *Sexually Transmitted Infectious* ,website:www.biomed-experts .com/Profile.bme/Mary-Ann Shafer, 1-8, 2006.

[7] J. A. Yorke and H. W. Hethcote, *Gonorrhea Transmission Dynamics and Control* ,Biometrical Journal, (28), 1984.

[8] J. A. Yorke and H. W. Hethcote, *Dynamics and Control of the transmission of gonorrhea* , 1973.

[9] B. A. Mohammed ,Y. Abu Hassan and F. A. Abdullahi, *A mathematical model of malaria and the effectiveness of Drugs*,Applied Mathematical Science,3079-3095 (7), 2013.

[10] F. A. Milner and R. Zhao, *A New Mathematical model of syphilis*,Arizonal State University, 2010.

[11] G. P. Garnett, S. O. Aral, D. V. Hoyle , W. Cates and R. M. Anderson, *The natural history of syphilis:Implication for the transmission dynamics and control of infection,Sex Transmission Disease.*,Department of zoology , Oxford University, 185-200, (24)1997.

[12] Derrick, N.R and Grossman, S.L, *Differential Equations with Applications*,Addison Wesley Publishing Company, Inc Philippines, 1976.

[13] O. Diekmann, J.A.P Heesterbeek and J. A. J Metz, *On the definition and the computation of the basic reproduction ratio RO in the models of infectious diseases in heterogeneous populations*,J.Math Biol.,365-382, (28) 1990.

[14] Hefferman , J. R. Smith and L. Wahl, *Perspectives on the basic Reproduction ratio*,Journal of the Royal Society Interface 2 USA, 2005.

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