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Mathematical Modeling of the Effect of Vaccination on the Dynamics of Infectious Diseases

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Abstract: *The development of vaccines revolutionized the methods of controlling infectious diseases and has saved many lives. In this work, an SEIR epidemic model was designed to demonstrate the impact of vaccination on the control of epidemic diseases. The model was shown to possess positive solutions. The disease-free equilibrium and the endemic equilibrium of the model were derived and the stability properties of the two equilibriums were examined via stability theory of nonlinear differential equation. An important epidemic-controlled parameter, the reproduction number, was derived for the model and computed via simulation using parameter values from published data. The result of the simulation showed that vaccination was capable of inhibiting the outbreak of epidemic diseases whenever the numerical values for reproduction number are less than unity.*

Keywords: *Epidemic model, Vaccination, Equilibrium, Reproduction number, Simulation*

1. Introduction

Infectious diseases pose a serious threat to human existence because every unprotected individual can contract a disease. Besides, the frequent emergence and reemergence of infectious diseases are a source of worry globally. However, adequate understanding of mode of spread of infectious diseases induced by the existing and new pathogens may enhance development of prevention strategies. Prevention strategies against transmissions, including drugs and vaccines, are to be designed at a parallel rate to that of pathogens. Infectious diseases are transmitted by different microbes. Few of these pathogens are visible by naked eyes. The commonest pathogens are viruses, bacteria, fungi and protozoa. These pathogens are responsible for various diseases which are regarded as "infectious" because those pathogens can be transmitted from an infected individual to a non-infected individual [8]. The well-known example of infectious diseases could be influenza which is transmitted by certain species of viruses. Measles, mumps, rubella, HIV, and malaria are also infectious diseases which have responsible for thousands of deaths globally. [7,11]. A good number of these diseases are prevalent both at local and global scales and undermine public health [14].

Infectious diseases can propagate in various ways and microbes trigger infections by various means. Some infections may occur through direct contacts while other may occur through indirect contacts. Disease spread can also occur through carriers or vectors. For examples, west Nile, filariasis, malaria, chikungunya, dengue and some others are spread through mosquitoes [22]. Diseases transmission through air and sex are particularly serious. Many diseases, e.g. SARS, influenza are airborne diseases and can be spread through air. The airborne infection is transmitted from an infected individual to an uninfected individual through cough, sneeze and even through laugh [16].

On the other hand, a considerable number of diseases are sexually transmitted diseases (STDs) and they are also spread through contaminated semen and blood, breastfeeding, or during childbirth [27]. HIV is the most death causing STDs. Other STDs includes herpes, gonorrhea, syphilis, trichomoniasis and Chlamydia also trigger significant infection and mortality [28]. Of the infectious diseases, STDs are the most worrisome to public health management, as many of them, such as Herpes and AIDS, have no cure but last for whole life. This poses severe economic and social threat. Due to longer infectious period, infected persons with STDs may responsible for high number of infections thus remain a major obstacle in prevention of diseases [20].

Another feature of STDs is that the infected individual may not show any symptom and spread the disease unknowingly. Drug resistance is another challenge to fighting STDs globally [15]. All these issues are reflected in HIV. About 37 million of the world population lives with HIV infection at the moment and the disease has claimed nearly 34 million lives globally since its emergence [2]. HIV statistics indicates that about 1.2 million people died of AIDS-related cases and almost 2.0 million people were infected with the disease in 2014 [27]. HIV and AIDS exist worldwide. However, it is rampant in Sub-Saharan African countries. The region harbors 25.8 million HIV-infected individuals which accounts for about 70% of the global HIV infection [1].

Reproduction number is a non-dimensional quantity that measures the average number of susceptible individuals which an infectious person is able to infect when he gets into the population of completely susceptible individuals. Diekmann et al. [10] defines reproduction number as the average number of secondary infections triggered by a typical infectious individual during the period of his infectiousness. It is a threshold for the outbreak or otherwise of a disease. If the numerical value of the reproduction number is greater than one then the outbreak of the disease will take off otherwise the outbreak will be inhibited [3]. Generally, health institutions are set up to prevent outbreak of diseases but when there are outbreaks, they do everything to curtail the outbreaks by bringing the reproduction number below unity.

One of the best methods to contain infections is to limit contacts. However, in the modern day with growing interactions among individuals, the method is not easy to come by. Since social distance is difficult to maintain, vaccines become prevention tools that are widely used to control diseases and reduce transmissions. A vaccine is applied to enhance immune system against specific microbes. A vaccine contains substances which have related properties to those of a microbe. Generally, a vaccine can be regarded as a fake pathogen which has no power to replicate and to trigger infections. It can be produced to weak or eradicate pathogens. As vaccine is similar to pathogenic microorganism, it can stimulate the immune system and build up antibodies against the microbes to identify them as foreigners. Thus, whenever a microorganism is come upon, the immune system terminates it. This phenomenon is termed immunity. Thus, the availability of a vaccine for a disease is an ideal way of protecting a population from the disease [17].

After Edward Jenner's cowpox vaccines, regarded as the first vaccine in history, several successful campaigns had been launched against numerous infectious diseases [24]. In fact, millions of lives have been saved by vaccines. Before the introduction of the first vaccine for measles in 1963, nearly 400 000 measles cases used to be recorded in the US every year [18]. Polio, mumps, rubella and other childhood diseases used to trigger significant morbidity and mortality before the invention of vaccines. With the introduction of vaccines, these diseases and infections are no longer epidemic [25]. Vaccine has also had a successful record against the spread of influenza, the most notable infectious disease in the world. Before the implementation of flu vaccines, curtailing an influenza pandemic was a serious task. It was recorded that around 20-50 million people died globally in the Spanish flu outbreak of 1918-19. The global death toll after a century for the 2009-10 flu pandemic was around 300 000 [22]. The remarkable

reduction in the casualty rate was attributed to the implementation of vaccines. Influenza vaccination has now become a routine program. It is now recommended that an individual receives an updated flu-vaccine before flu-season advances with fresh strains of flu viruses.

Mathematical models have been applied to examine the dynamics of epidemic diseases for years. The applications of mathematics in epidemiology have grown tremendously in recent years. By estimating model variables, reproduction number, transmission rate and other parameters, a model can forecast whether a disease will die out or spread through the population. A model can also estimate the effect of an intervention and provide necessary guidelines to public health administrators for further efforts needed to eradicate diseases. It is on this note that we formulate a mathematical model to study the effect of vaccination on the reproduction number of an epidemic model.

2. Model Formulation

The *SEIR* is partitioned into compartments *S(t), E(t), I(t)* and *R(t)* where *S(t)* is used to represent the population of individuals who have not been infected with the disease at time *t* but are capable of being infected; *E(t)* denotes the population of the exposed which stands for the population of individuals who have been infected with the disease but do not still have any disease symptoms; *I(t)* denotes the population of individuals who have not only been infected with the disease but are infectious; *R(t)* is the compartment used for those individuals who are either temporarily immune to the disease due to vaccination or have been cured of the infection.

In the model, π is the recruitment rate into the *S(t)* which was as a result of birth or loss of acquired immunity, υ is the rate of vaccination, ρ is the rate of death from disease related cases while μ is the rate of death from causes unrelated to the infection, β is the rate of transmission of the disease, σ is the rate of moving from exposed stage to infectious stage though death due to the disease during the latent stage is neglected. γ is the recovery rate which is due to treatment via vaccination (treatment may be in form of vaccination) while ω is the rate of losing immunity which is the rate at which recovered individuals becomes susceptible again. The flow between the compartments is depicted in Figure 1

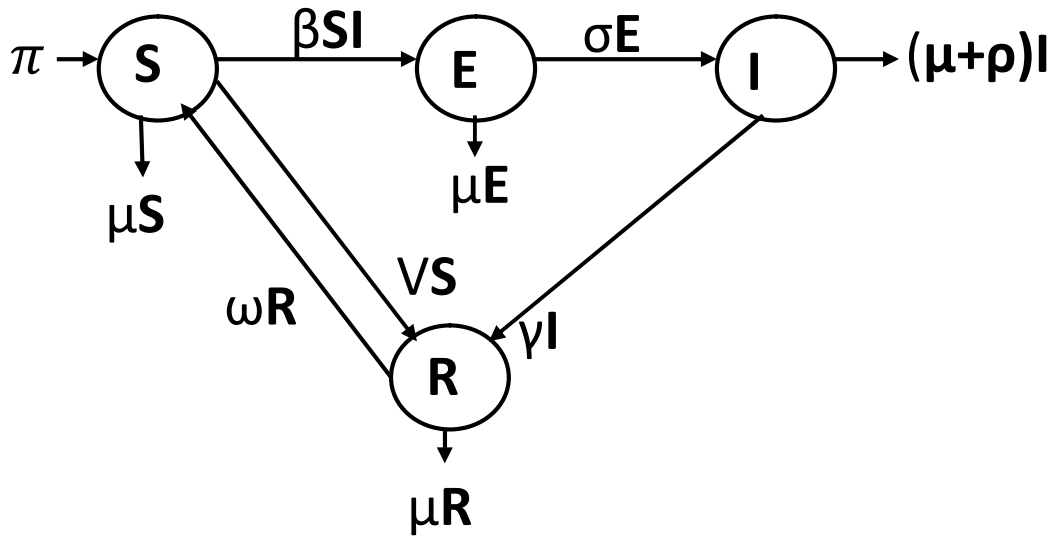

Figure 1*: Dynamics of the disease between the compartments*

The flow chart showed that those who were successfully vaccinated would receive immunity and moved straight to the recovered class though some of them would die naturally. Besides, some of those who were not vaccinated or not successfully vaccinated would also die naturally. The remaining people who were not vaccinated or not successfully vaccinated would contract the disease and become exposed. As a result of the fact that the exposed individuals were totally ignorant of their status, some of them would die

naturally while the remaining people would become infectious. Some of the infectious individuals would die either naturally or as a result of the infection while the remaining individuals would be cured of the disease and moved to the recovered class at a rate γ. Some of those who recovered from the disease would die naturally while the remaining people would become susceptible again and the flow would go like that.

Going by the above assumptions and transfer diagram, the following set of first order ordinary differential equations is obtained.

$$\frac{dS}{dt} = \pi - \beta SI - \mu S - \upsilon S + \omega R \quad (1)$$

$$\frac{dE}{dt} = \beta SI - \sigma E - \mu E \quad (2)$$

$$\frac{dI}{dt} = \sigma E - \mu I - \rho I - \gamma I \quad (3)$$

$$\frac{dR}{dt} = \upsilon S + \gamma I - \omega R - \mu R \quad (4)$$

The numerical values assigned to the parameters to conduct the simulations are presented in Table 1.

Table 1: ***Parameters Description and Values***

Parameter	Interpretation	Value	Source
β	Transmission rate	0.091	[4]
σ	Latent period	0.125	[3]
μ	Natural death rate	0.005	[3]
π	Recruitment rate	0.45	[3]
ω	Rate of losing immunity	0.36	[3]
ρ	Disease induced death	0.009	[3]
γ	Recovery rate	0.6	[3]
ν	Rate of vaccination	0.02	Assumed

The region of feasibility for the model can be established. Let $N(t)$ denotes the total population at time t then $N(t) = S(t) + E(t) + I(t) + R(t)$ so that

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dE}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = \pi - \mu N(t) - \rho I$$
$$\leq \pi - \mu N(t).$$

Following [30], $N(t) \leq \frac{\pi}{\mu} + \left(N(0) - \frac{\pi}{\mu}\right) e^{-\mu t}$.

$N(0) \Rightarrow N(t) = N(0)$ at $t = 0$.

Therefore, $N(t) \to \frac{\pi}{\mu}$ as $t \to \infty$. Hence, $N(t)$ is bounded as $0 \leq N(t) \leq \frac{\pi}{\mu}$. Therefore, the invariant region or the region of feasibility Ω for the model is defined as $\Omega = \left\{(S, E, I, R) \in \mathbb{R}_+^4 : N(t) \leq \frac{\pi}{\mu}\right\}$.

2.1 Positivity of solutions

Since epidemic models monitor human and animal populations, it is assumed that the solutions to the models are positive. We shall therefore verify whether our model preserves positive solutions before it is used to conduct the study.

Suppose $\{S(t), E(t), I(t), R(t)\}$ are the solutions to the model for all $t \geq 0$ with positive initial conditions$\{S(0) > 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0\}$. Then, from equation (1),

$$\frac{dS}{dt} \geq -\mu S. \quad (5)$$

$$\Longrightarrow \ln S \geq \mu t + k, \quad (6)$$

$\Longrightarrow \mathrm{S(t)} \geq S(0)e^{-\mu t} > 0.$ (7)

Following the same process,

$\Longrightarrow \mathrm{E(t)} \geq E(0)e^{-(\mu+\sigma)t} > 0,$ (8)

$\Longrightarrow \mathrm{I(t)} \geq I(0)e^{-(\rho+\mu+\gamma)t} > 0\,,$ (9)

$\Longrightarrow \mathrm{R(t)} \geq R(0)e^{-(\omega+\mu)t} > 0.$ (10)

Hence, the solutions of the model remain positive as long as the initial conditions of the state variables are positive because e^p is positive for all real values of p. Since the model preserves positive solutions then it is suitable to conduct the study.

3. Model Analysis

The equilibrium and stability analyses shall be discussed in this section. Also, the reproduction number of the model shall be derived.

3.1 Equilibria and reproduction number

Emphasis shall be placed on two equilibria – infection-free equilibrium (DFE) and the endemic equilibrium. Infection-free equilibrium exists when infection agents are virtually non-existence in the population such that nobody is exposed, infected or recovered, i.e., $E = I = R = 0$. Hence, the infection-free equilibrium (DFE) for the system is given as

$$E_0 = \{S_0, E_0, I_0, R_0\} = \left\{\frac{\pi}{\mu+\nu}, 0, 0, 0\right\} \tag{11}$$

In epidemiology, the reproduction number is a non-dimensional quantity that measures the average number of secondary infection produced when an infectious agent gets into the population of completely susceptible individuals. The quantity is usually denoted by R_0. If $R_0 > 1$ then the infectious agent is able to infect at least one susceptible individual who will cause the disease to spread in the population but if $R_0 < 1$ then the infectious agent is unable to infect a single individual and the outbreak will not take off in the population. Following the approach in [26], the reproduction number for our model is obtained as

$$R_0 = \frac{\pi\sigma\beta}{(\mu+\nu)(\mu+\sigma)(\mu+\rho+\gamma)} \tag{12}$$

At the endemic equilibrium, there exist infection agents in the population such that all the compartments co-exist for the solution of the model. Denoting the endemic state for the state variables as $S_*, E_*, I_*,\ R_*$, equating the RHS of equation (1) – equation (4) to zero and solving for the state variables to obtain

$$S_* = \frac{a_2 a_3}{\sigma\beta} \tag{13}$$

$$E_* = \frac{a_3}{\sigma\beta}\left[\frac{\pi\sigma\beta a_4 + \omega\nu a_2 a_3 - a_1 a_2 a_3 a_4}{a_2 a_3 a_4 - \omega\sigma\gamma}\right] \tag{14}$$

$$I_* = \frac{\pi\sigma\beta a_4 + \omega\nu a_2 a_3 - a_1 a_2 a_3 a_4}{\beta a_2 a_3 a_4 - \omega\sigma\beta\gamma} \tag{15}$$

$$R_* = \frac{\nu a_2 a_3}{\sigma\beta a_4} + \frac{\gamma}{a_4}\left[\frac{\pi\sigma\beta a_4 + \omega\nu a_1 a_3 - a_1 a_2 a_3 a_4}{\beta a_2 a_3 a_4 - \omega\sigma\beta\gamma}\right] \tag{16}$$

Where,

$a_1 = \mu+\nu$, $a_2 = \mu+\sigma$, $a_3 = \mu+\rho+\gamma$, and $a_4 = \mu+\omega$

3.2 Stability of Equilibria

To verify the stability property of the model at the infection-free equilibrium state E_0, the variational matrix of the model is derived as

$$J(E_0)=\begin{pmatrix} -(\beta \mathrm{I}+a_1) & 0 & -\beta S & \omega \\ 0 & -a_2 & \beta S & 0 \\ 0 & \sigma & -a_3 & 0 \\ \nu & 0 & \gamma & -a_4 \end{pmatrix} \tag{17}$$

Since there is no transmission of infection at the infection-free equilibrium then the transmission parameter β is reduced to zero in equation (17) and equation. (17) becomes

$$J(E_0)=\begin{pmatrix} -a_1 & 0 & 0 & \omega \\ 0 & -a_2 & 0 & 0 \\ 0 & \sigma & -a_3 & 0 \\ \nu & 0 & \gamma & -a_4 \end{pmatrix} \tag{18}$$

The infection-free equilibrium of the model is stable if all the eigen values of equation (18) are negative. To prove the theorem, the characteristic equation of equation (18) is obtained by software maple as

$$b_0\lambda^4 + b_1\lambda^3 + b_2\lambda^2 + b_3\lambda + b_4 = 0 \tag{19}$$

where

$$\left.\begin{aligned} b_0 &= 1, \\ b_1 &= a_1 + a_2 + a_3 + a_4, \\ b_2 &= a_1a_2 + (a_1 + a_2)(a_3 + a_4) + a_3a_4 - \omega\upsilon, \\ b_3 &= a_1a_2(a_3 + a_4) + a_3a_4(a_1 + a_2) - \omega\upsilon(a_2 + a_3), \\ b_4 &= a_2a_3(a_1a_4 - \omega\upsilon). \end{aligned}\right\} \tag{20}$$

Following Routh-Hurtwitz stability criteria in [19,5], the eigen values of equation (19) are all less than zero if

$$b_1 > 0, b_3 > 0, b_4 > 0 \quad \text{and} \quad b_1b_2b_3 > b_3^2 + b_1^2b_4 \tag{21}$$

Therefore, the *DFE* is stable if inequalities (21) are satisfied. The implication of stable *DFE* is that given a population described by our model, the emergence of an infectious individual in the population would not instigate disease outbreak if the initial size of the population is in the basin of attraction of E_0.

To examine the stability property of the endemic equilibrium, the variational matrix of the model is also obtained but at the endemic equilibrium state as

$$J(E_*)=\begin{pmatrix} -(\beta I_* + a_1) & 0 & -\beta S_* & \omega \\ \beta I_* & -a_2 & -\beta S_* & 0 \\ 0 & \sigma & -a_3 & 0 \\ \nu & 0 & \gamma & -a_4 \end{pmatrix} \tag{22}$$

As in *DFE,* the endemic equilibrium of the model is stable if all the eigen values of equation (22) have negative real parts. The condition is satisfied if $det\{J(E_*)\} > 0$ whenever $tr\{J(\mathrm{E}_*)\} < 0$ [21]. In equation (22),

$$|J(E_*)| = a_2a_3a_4\beta I_* + a_1a_2a_3a_4 + \beta S_*\omega\sigma\upsilon - a_1a_4\beta S_*\sigma - \beta I_*\gamma\omega\sigma - a_1a_2\omega\upsilon \tag{23}$$

The trace of matrix in equation (22) is already negative hence, the condition $tr\{J(\mathrm{E}_*)\} < 0$ is satisfied. This is only the necessary condition for the endemic equilibrium of the model to be stable. The sufficient

condition is for $a_2a_3a_4\beta I_* + a_1a_2a_3a_4 + \beta S_*\omega\sigma\upsilon - a_1a_4\beta S_*\sigma - \beta I_*\gamma\omega\sigma - a_1a_2\omega\upsilon$ in equation (23) to be greater than zero. Hence, the endemic equilibrium of the model is stable if

$a_2a_3a_4\beta I_* + a_1a_2a_3a_4 + \beta S_*\omega\sigma\upsilon - a_1a_4\beta S_*\sigma - \beta I_*\gamma\omega\sigma - a_1a_2\omega\upsilon > 0$.

4. Results and Discussion

The theoretical results for stability of equilibria in section 3 can be discussed in terms of the numerical values of the reproduction number R_0. If $R_0 < 1$ then the infection-free equilibrium of the model is stable whereas it is the endemic equilibrium of the model that is stable if $R_0 > 1$. It implies that if $R_0 < 1$, the introduction of vaccines is yielding results and the outbreak of disease is either prevented or eradicated but if $R_0 > 1$, the application of vaccines is not having any effect on disease prevention or eradication. To come about the numerical values for R_0, the parameter values in Table 1 are used to evaluate equation (12) and the result of R_0 in serial number one of Table 2 is achieved. The values of some the parameters are then varied to come about other results for R_0 in Table 2. The result in Table 2 is then illustrated graphically in Figure 2 – Figure 5 to show the trend of the susceptible, the exposed, the infected and the recovered populations. The plots in Figure 2 – Figure 5 are achieved by using the parameter values in Table 1.

Table 2: Numerical Simulation of the Reproduction Number (R_0)

S/No	π	β	σ	μ	γ	υ	ρ	R_0	Remark
1	0.45	0.091	0.125	0.005	0.60	0.02	0.009	2.565	Unstable
2	0.45	0.090	0.125	0.005	0.61	0.03	0.008	1.786	Unstable
3	0.45	0.080	0.125	0.005	0.62	0.04	0.007	1.217	Unstable
4	0.45	0.070	0.125	0.005	0.63	0.05	0.006	0.859	Stable
5	0.45	0.060	0.125	0.005	0.64	0.06	0.005	0.614	Stable
6	0.45	0.050	0.125	0.005	0.65	0.07	0.004	0.438	Stable
7	0.45	0.040	0.125	0.005	0.66	0.08	0.003	0.305	Stable
8	0.45	0.092	0.125	0.005	0.59	0.015	0.0091	3.295	Unstable
9	0.45	0.093	0.125	0.005	0.58	0.010	0.0092	4.515	Unstable

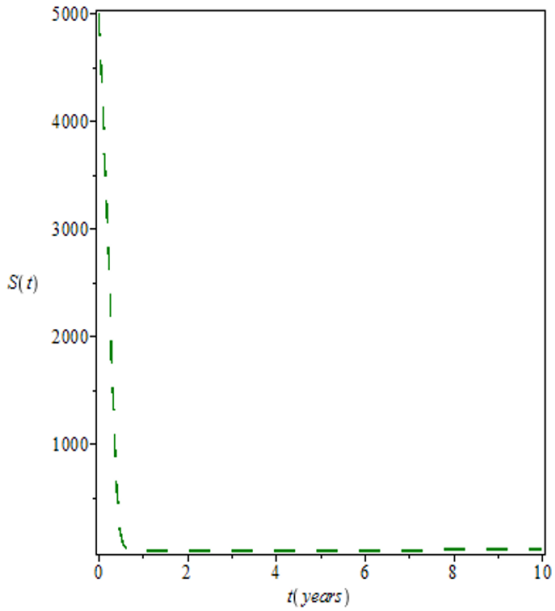

Figure 2 : Trend of susceptible population

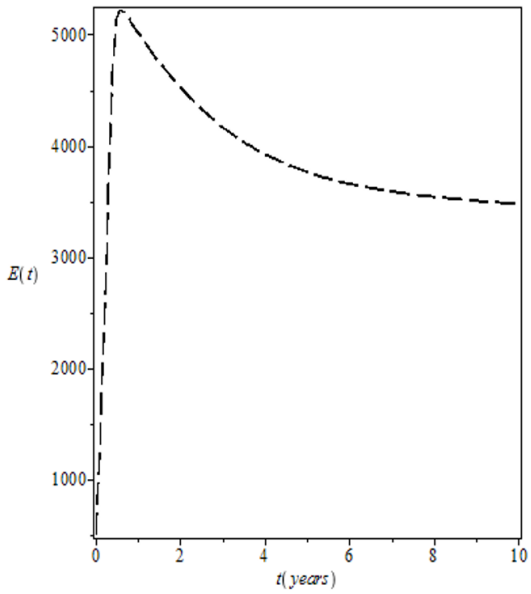

Figure 3: Trend of exposed population

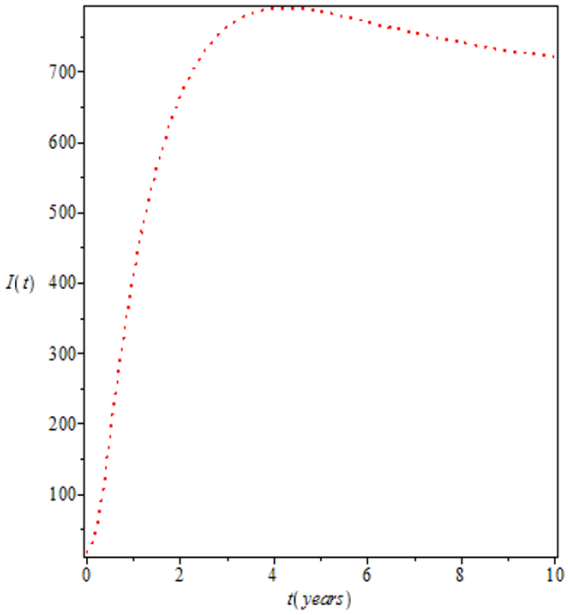

Figure 4: Trend of infectious population

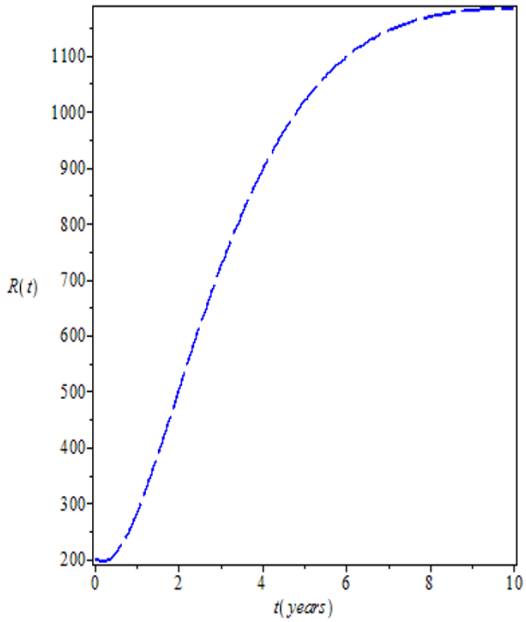

Figure 5: Trend of recovered population

Generally, an increase in vaccination rate as a form of disease prevention and control will increase recovery rate but reduce both disease transmission rate and disease-induced death rate. From the simulation Table 2, it is observed that an increase in vaccination rate up to serial number three leads to increase in the recovery rate γ but decrease in both disease transmission rate β and disease-induced death rate ρ. The infection-free equilibrium in this region is unstable as $R_0 > 1$ (S/No 1 – S/No 3 in Table 2). The instability of the infection-free equilibrium implies disease persistence in the population which is as a result of low coverage of vaccination. On the other hand, the infection-free equilibrium becomes stable in the region where the increase in vaccination rate attains 0.05 upwards as $R_0 < 1$ (S/No 4 – S/No 7 in Table 2). The stability of the infection-free equilibrium implies disease eradication in the population and it is achieved when vaccination coverage is sufficient. However, the infection-free equilibrium maintains instability with decrease in vaccination rate which reduces the recovery rate but increases both disease transmission rate and disease-induced death rate as $R_0 > 1$ (S/No 8 – S/No 9 in Table 2). The implication of the result in Table 2 is that to eradicate an infectious disease through vaccination, the rate of vaccination must exceed certain critical level. Vaccination as a tool to fight against the propagation of infectious diseases will not yield a desirable result if the coverage is low.

The result in Table 2 is corroborated in Figure 2 – Figure 5. The number of susceptible individuals falls continuously and tends to zero after first year due to the presence prevention parameter vaccination which is introduced to equation (1). However, the populations of both the exposed and the infected individuals firstly rise but begin to fall at a point in Figure 3 and Figure 4. The reason is that no control measure is introduced to equation (2) and equation (3) but in reality, when the symptom of a disease is manifested in an individual, treatment is inevitable. Besides, some of the exposed individuals may be aware of their status through medical checkup, get themselves treated and recovered from the illness even at the exposed stage. These possibilities account for the falling trends in Figure 3 and Figure 4. In Figure 5, the population of the recovered individuals increases continuously due to the influx from the susceptible and the infectious compartments as a result of immunity induced by prophylaxis vaccination and treatment respectively.

5. Conclusion

Vaccination is a well-known and an indispensable tool to prevent and check the menace of infectious diseases. The invention of vaccines has been beneficial to mankind for it has brought about the

eradication smallpox in 1979, two years after the last case in Somalia. It has also instigated the eradication of some other diseases like rinderpest. In this work, attempts have been made to analyze the effect of vaccination on the spread and propagation of infectious diseases. Going by the theory of reproduction number due to [10], we were able to establish the regions of eradication and persistence for infectious diseases in terms of the application of vaccination. Based on the results of the study, vaccination of the population before the outbreak of epidemic known as pre-exposure prophylaxis is capable of reducing transmission rate (β) if an infectious individual eventually gets into the population of susceptible individuals while vaccination of the population after the outbreak of the epidemic known as post-exposure prophylaxis is capable of increasing recovery rate (γ) which affirms some recent results [4,9,29,12]. The ongoing COVID-19 pandemic was able to spread like the harmattan fire and claimed many lives at onset due to unavailability of pre-exposure prophylaxis [13,6,31,32]. The world was able to subdue the spread and fatality of COVID-19 when the COVID-19 vaccines were developed. Therefore, since prevention is better than cure, adequate pre-exposure prophylaxis is recommended in an area where a particular infectious disease is endemic. A good example is periodic administration of Shanchol in cholera *hotspots* to forestall frequent outbreak of the disease.

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