CHAPTER 1

1. INTRODUCTION

The basic question of how we acquire immunity has been investigated for a century or more. Even so, several concepts in immunology still remain unclear. For instance, it is known that the first exposure of an individual to an antigen elicits a primary response, the initial antigen response. The primary immune response combats the infection with the production of antibodies, which appears after a time lag of a few days. After recovering from an infection, the concentration of antibodies against the infectious agent gradually declines over time, but the individual is still protected against a secondary occurrence of the disease. That is, the person is immuned. When an individual is exposed to antigen for a second time, a much larger number of antibodies are produced quickly to combat the infection. This mechanism is possible because the primary immune response produces memory cells, which are specialized to mount an immune response against the same antigen.

Memory is, therefore, a central characteristic of immune response [1]. Its advantages discussed so far include protection from re-infection, control of chronic infection, and the transfer of immune function to the next generation [2]. The exact process by which immunological memory evolves is not fully known. When individuals are immunized, the vaccine induces their immune system to respond and produce antibodies against the 'virus' in the vaccine. These antibodies then destroys the vaccine virus, but the immune system 'remembers' the virus so that it can fight off infection if the individual is ever exposed to the natural virus (the ones that cause the disease). Because the virus in the

vaccine and the natural virus are very similar, the immune system responds to both. This means that if an immunized person is ever exposed to the circulating virus, the immune system responds immediately and large amounts of antibodies are produced to overcome the infection. The level of effectiveness varies with the different components of vaccines. Some people do not respond well and develop immunity against a disease as intended [3].

Vaccination is a mechanism that attempts to lower the degree of susceptibility of a healthy individual against a particular pathogenic agent. Since this decrease of susceptibility occurs in a population, the overall effect of vaccination is to decrease the proportion of contacts with infected individuals. Thus, an efficient vaccination campaign acts to reduce the number of infectious individuals below its critical level. At the population level, one wishes to identify the critical vaccination rate necessary to eradicate the disease or prevent infection (epidemic outbreak). Hence it is important to address the required level of intervention in order to eradicate the disease, that is, the threshold at which the disease dies out. In [4], a simpler model of infectious diseases with temporary immunity and linear incidence rate was investigated. A temporary immunity from an infectious disease such as influenza, Chlamydia trachomatis, salmonella, etc., means that a recovered individual moves into the susceptible class after a period of time [8]. In the 1960s, the world saw an improvement in sanitation, antibiotics, and vaccination programs. This created a confidence that infectious diseases would soon be eradicated [7, 10, 11]. But infectious diseases have over the past years continued to be a major cause of suffering and mortality in developing countries [12, 16]. At the same time there has been

a tendency for infectious disease agents to adapt and evolve, so that new infectious diseases have emerged and some existing diseases have reemerged [18, 19].

Mathematical models have become important tools in analyzing the spread and control of infectious diseases. The model formulation process clarifies assumptions, variables, and parameters. Moreover models provide conceptual results such as thresholds, basic reproduction numbers, contact numbers, and replacement numbers, some of which will be of concern to us in this project. Of the utmost importance in this study is the understanding of the transmission characteristics of infectious diseases in communities that can lead to a better approach to decrease the transmission of these diseases. Mathematical epidemiology seems to have grown exponentially, starting in the middle of the 20^{th} century (the first edition in 1957 of Bailey's book [13] is an important landmark), so that a tremendous variety of models have now been formulated, mathematically analysed, and applied to infectious diseases [14]. Reviews of literature [7, 17] show the rapid growth of epidemiology modeling. The recent models have involved aspects such as passive immunity, gradual loss of vaccine-and disease-acquired immunity, stage of infection, vertical transmission, disease vectors, macro-parasitic loads, age structure, social and sexual mixing groups, spatial spread, vaccination, quarantine, and chemotherapy. It is not always necessary to include all components in any particular model. The modeler is informed by the nature of the problem as to which components to include. In other words, the characteristics of the particular disease being modeled will dictate the choice of the relevant components. Several researchers have published articles depicting various variations / possibilities of the model in use. Li et al. [12] studied the SEIR (Susceptible Exposed Infectious Recovery) model, where the variations are the

nonlinear rate of new infections while the birth rate and the death rate are assumed to be equal, which consequently mean that the total population is at equilibrium. It has been recognized that the age structure of the population affects the dynamics of disease transmission. It is for this reason that Lu et al. [8], and many authors investigated various age-structured epidemic models. Most authors studied SIR (Susceptible Infectious Recovery) and SIS (Susceptible Infectious Susceptible) models, i.e. they subdivided the total population of the country in two or three compartments containing susceptible, infectives or immunes. It was assumed therefore that there is no latent class, so the person who catches the disease becomes infectious immediately. Moreover, the dynamic behaviour about the age structured epidemic model with the latent period and no random mixing (i.e. there is a no separable age-dependent transmission coefficient) are investigated in [17, 18].

In the following sections, the statement of the problem to be investigated in this dissertation, its significance as well as the computational technique employed in the study will be highlighted.

1.1 Statement of the problem

One of the aims of vaccination is to reduce the prevalence of an infectious disease and ultimately to eradicate it. However, the immunity acquired against many infectious diseases such as Influenza, Dengue, Chlamydia trachomatis, Salmonella, etc., after vaccination does wane with time (i.e. a recovered individual has temporary immunity against the disease and moves into the susceptible class after a period of time). Moreover, the degree of efficacy of many vaccines varies from disease to disease; this implies that a vaccinated individual may still be re-infected if the vaccine administered is not very

effective. Since vaccination is considered to be the most effective strategy against infectious diseases, the development of a theoretical framework that would predict the optimal vaccine coverage level needed to prevent the spread of these diseases is crucial. This epidemiological study is part of theoretical framework needed to address this issue.

1.2 Aim of the study

This study aims to investigate theoretically the transmission dynamics of infectious diseases within a given population in the presence of preventive and therapeutic vaccines with waning immunity.

Specific objectives of the study

- To develop a mathematical model for the transmission dynamics of infectious diseases with vaccination and temporary immunity.
- To develop a theoretical framework that would predict the optimal vaccine coverage level needed to prevent the spread of infectious diseases with waning immunity.
- To provide a numerical algorithm for solving a non-linear system of differential equations using the Adomian decomposition technique.

1.3 Significance of the study

Modeling the transmission dynamics of infectious diseases in the presence of preventive or therapeutic vaccines with waning immunity is extremely important for the following reasons:

- To describe patterns of infection and disease occurrence in populations.

- Identify outbreaks or unusual rates of disease occurrence.
- Facilitate laboratory-based efforts to identify infectious agents.
- Provide a population-based description of clinical illness to improve the specificity of diagnosis for individual diseases.
- Assist in the understanding of disease pathogenesis.
- Identify and characterise factors in the chain of infection that contribute to agent transmissions and the development of diseases.
- Develop and evaluate treatment protocols through clinical trails.
- Develop and evaluate primary, secondary and tertiary prevention and control measures for individuals.
- Describe and assess the use of prevention measures on a community-wide basis.

1.4 Definitions and Theorems [13, 14, 17]

The operational definitions and theorems of concepts relating to the transmission dynamics of infectious diseases are presented in this section.

1.4.1 Autonomous system: Suppose $x' = (x_1, x_2, \ldots, x_n)'$ is a system of differential equations describing the changes in the variables characterizing an epidemiological problem. The system is said to be autonomous if $(x_1, x_2, \ldots, x_n)$ does not depend on t explicitly, where t is the time variable.

1.4.2 Stability condition: These are the conditions that has to do with long-term behavior of the system which is disturbed, with regard to whether or not it will differ from the undisturbed behavior by an acceptably small amount.

1.4.3 Equilibrium Point: An equilibrium point x_0 of an autonomous system is

a point which simultaneously satisfies $x' = 0$.

1.4.4 Stable equilibrium point: A critical point (x_0, y_0) of a system of differential equations $x' = Ax$ is stable if given a number $\varepsilon > 0$, there is a number $\delta > 0$ such that every $x = \phi(t)$; $y = \psi(t)$ of the system at t=0, satisfies $\left[(\phi(0) - x_0)^2 + (\phi(0) - y_0)^2\right]^{1/2} < \delta$ and $\left[(\phi(t) - x_0)^2 + (\psi(t) - y_0)^2\right]^{1/2} < \varepsilon$ for all t > 0. This definition implies that all solutions that are sufficiently close to (x_0, y_0) stay close to (x_0, y_0).

1.4.5 Asymptotic stability: A critical point (x_0, y_0) is asymptotically stable if it is stable and if $\exists\ \delta_0$, such that $0 < \delta_0 < \delta$ and such that if a solution $x = \phi(t), y = \psi(t)$ satisfies $\left[(\phi(0) - x_0)^2 + (\psi(0) - y_0)^2\right]^{1/2} < \delta_0$, then $\lim \psi(t) = x_0$; $\lim \psi(t) = y_0$ as $t \to \infty$. This means that the solution curves that start sufficiently close to (x_0, y_0) must not only stay close, but must eventually approach (x_0, y_0) as $t \to \infty$.

1.4.6 Agent: A factor whose presence causes a disease or one whose absence causes disease.

1.4.7 Basic reproductive number: The average number of secondary infections produced when one infected individual is introduced in the whole population where everyone is susceptible; or threshold quantity that determines when an infection can invade and persist in a new host population.

1.4.8 Endemic disease: The habitual presence of a disease or infectious agent in a defined geographical area or population.

1.4.9 Epidemic: Rates of disease clearly in excess of normal or expected

frequency in a defined geographical area.

1.4.10 Horizontal transmission: Transmission that typically occurs through direct or indirect physical contact with infectious hosts or through disease vectors such as mosquitoes, ticks, or other biting insects.

1.4.11 Host: The individual human in whom an agent produces disease.

1.4.12 Immunization: Administration of a living modified agent, a suspension of killed organisms, or an inactivated toxin to protect susceptible individuals from infectious diseases.

1.4.13 Infection: The entry and establishment of an infectious agent in a host.

1.4.14 Infectious diseases: A disease that is able to spread by air, water, human body contact, etc.

1.4.15 Prevalence: Measure of the number of cases of a given disease in a specified population at a designated time; usually a rate measured at a point in time.

1.4.16 Susceptible: The susceptible consists of those who are not infected, but who are capable of catching the disease and become infective if exposed.

1.4.17 Infective: The infective consists of those individuals who are capable of transmitting the disease to others.

1.4.17 Threshold theorem [13, 17]: This states that an epidemic will occur only if the number of people who are susceptible to the disease exceeds a certain threshold value. It has to do with a situation where a small group of people having an infectious disease is inserted into a large population that is capable of catching the disease. The question is: What happens as time evolves? Will the disease die out rapidly, or will an epidemic occur? How many people will ultimately catch the disease? To answer this question a

system of differential equations, which govern the spread of infectious diseases within a population is derived, and the behaviour of its solution is analyzed.

1.4.18 Theorem (Lasella-Lyapunov Theorem) [17]**:** A function $V(z)$ is Positive definite for $|z| \leq k$ if V>0 for all $z \neq 0$.

(i) Let $V(z)$ be positive definite and $\frac{dV}{dt}$ be negative semi-definite for $|z| \leq k$, then the zero solution of non-linear system is uniformly stable.

(ii) Let $V(z)$ be positive definite and $\frac{dV}{dt}$ be negative definite for $|z| \leq k$, then the zero solution of non-linear system is uniformly and asymptotically stable.

Remark: This is an alternative approach to the investigation of Stability of fully non-linear systems. Here we seek a scalar function, which can be regarded as a measure of energy of the system and the seeks to demonstrate that either this energy decreases as $t \to \infty$, indicating stability or it increases indicating instability.

1.4.19 Theorem (Routh-Hurwitz Criterion)[17]: The roots of $P(\mu)$ have strictly negative real parts if and only if $\det M_K > 0$ for all k, where

$P(\mu) = \mu^n + a_{n-1}\mu^{n-1} + ... + a_1\mu + a_0$ define the matrices $M_1, ...M_n$ by

$$M_1 = (a_{N-1}),\ M_2 = \begin{pmatrix} a_{n-1} & a_{n-3} \\ 1 & a_{n-2} \end{pmatrix},\ M_3 = \begin{pmatrix} a_{n-1} & a_{n-3} & a_{n-5} \\ 1 & a_{n-2} & a_{n-4} \\ 0 & a_{n-1} & a_{n-3} \end{pmatrix},$$

$$M_4 = \begin{pmatrix} a_{n-1} & a_{n-3} & a_{n-5} & a_{n-7} \\ 1 & a_{n-2} & a_{n-4} & a_{n-6} \\ 0 & a_{n-1} & a_{n-3} & a_{n-5} \\ 0 & 1 & a_{n-2} & a_{n-4} \end{pmatrix}, \; M_n = \begin{pmatrix} a_{n-1} & a_{n-3} & a_{n-5} & . & . & . & . & . & a_{-n+1} \\ 1 & a_{n-2} & a_{n-4} & . & . & . & . & . & a_{-n+2} \\ 0 & a_{n-1} & a_{n-3} & . & . & . & . & . & a_{-n+3} \\ 0 & 1 & a_{n-2} & . & . & . & . & . & a_{-n+4} \\ 0 & 0 & a_{n-1} & . & . & . & . & . & a_{-n+5} \\ . & . & . & . & . & . & . & . & . \\ . & . & . & . & . & . & . & . & . \\ . & . & . & . & . & . & . & . & . \\ 0 & 0 & 0 & . & . & . & . & . & a_{-1} \\ 0 & 0 & 0 & . & . & . & . & . & a_0 \end{pmatrix}$$

where a_j is defined to be 0 if $j < 0$.

1.5 COMPUTATIONAL APPROACH

In the beginning of the 1980s, a new method for exactly solving nonlinear functional equations has been proposed by Adomian, the so called Adomian_s decomposition method [5, 21, 22]. Over these years, this method has been applied to solve a wide range of problems arising from physics, biology and engineering. This method uses a decomposition of the nonlinear operator as a series function [6]. To illustrate the method, let us consider a system of differential equations such as the following :

$$\frac{du}{dt} = N(u) + g(t) \text{ with u(0) = a,} \qquad (1.5.1)$$

where N is a nonlinear function. Let L(u) and $L^{-1}(u)$ represent both a linear operator and its inverse defined as

$$L = \frac{d}{dt} \quad \text{and} \quad L^{-1} = \int_0^t (.)dt \; . \qquad (1.5.2)$$

Equation (1.5.2) operates on (1.5.1) to give

$$u = a + L^{-1}(N(u)) + L^{-1}(g(t)). \tag{1.5.3}$$

As usual in Adomian decomposition method, the solution of equation (1.5.3) is considered to be the sum of the following series

$$u = \sum_{n=0}^{\infty} u_n \,, \tag{1.5.4}$$

the nonlinear term in the system is approximated as follows:

$$N(u) = \sum_{n=0}^{\infty} A_n \,, \tag{1.5.5}$$

where

$$A_n = \frac{1}{n!}\left[\frac{d^n\left(\sum_{k=0}^{\infty} N_k(u)\lambda^k\right)}{d\lambda^n}\right]_{\lambda=0}, \tag{1.5.6}$$

are called Adomian polynomials which can be easily obtained using computer symbolic algebra package like MAPLE. Moreover, the differential equations describing the transmission dynamics of infectious diseases constitute a nonlinear problem. Several numerical approaches have been developed in the last few decades, e.g. finite differences, spectral method, etc. to tackle this problem. More recently, the ideas of classical analytical methods have experienced a revival, in connection with the proposition of novel hybrid numerical-analytical schemes for nonlinear differential equations. One such trend is related to the Adomian decomposition approach [21, 22]. This approach, over the last few years, has proved itself as a powerful tool and a potential alternative to traditional numerical techniques in various applications in sciences and engineering. This semi-numerical approach is also extremely useful in the validation of purely numerical schemes. One of the objectives of this study is to construct an approximate solution for

the system of differential equations modeling the transmission dynamics of infection diseases with vaccination and temporary immunity. Our work stems mainly from the Adomian decomposition method. The chief merit of the method is that it is capable of greatly reducing the size of computation work while still maintaining high accuracy of the numerical solution [5]. The convergence of the decomposition scheme has been proved by many authors [20]. Further convergence of the resulting decomposition series can be achieved using the Padé approximation technique [6]. Both numerical and graphical results will be presented and discussed quantitatively with respect to various parameters embedded in the problem.

CHAPTER TWO

Dynamics of infectious diseases with vaccine induced temporary immunity

2.0 SUMMARY

In this chapter, a three compartmental mathematical model that describes the dynamics of re-infection under the assumption that the vaccine is effective and induced immune protection that may wane over time is presented. It is assumed that infection can only invade the susceptible class. The qualitative analysis reveals that the disease eradication depends on vaccination coverage as well as on vaccine efficacy. Using an appropriate Lyapunov function, we established that the disease free equilibrium is globally asymptotically stable if the vaccination coverage level exceeds a certain threshold value. Numerical algorithm based on Adomian's decomposition method coupled with Padé approximation technique implemented in MAPLE [23] is also developed to approximate the solution of the governing non-linear systems. Numerical simulations support our analytical conclusions and illustrate possible behaviour scenarios of the model.

2. 1 Introduction

One of the aim of vaccination programmes is to reduce the prevalence of an infectious disease and ultimately to eradicate it. In other words, the vaccination is a mechanism that attempts to lower the degree of susceptibility of healthy individuals against a particular pathogenic agent. Since this decrease of susceptibility occur in a population, the overall

effect of vaccination is to decrease the proportion of contacts with infected individuals. Thus, an efficient vaccination campaign acts to reduce the number of infectious individuals below its critical level. At the population level, one wishes to identify the critical vaccination rate necessary to eradicate the disease or prevent infection (epidemic outbreak). Hence, it is important to address the required level of intervention in order to eradicate disease, that is, the threshold at which the disease dies out. However, studies have shown that the immunity induced by the preventive vaccines against some infectious diseases may wane over time [3, 8, 9]. This means that after recovery an individual has a temporary immunity against a disease, and, therefore, it moves into the susceptible class after some period of time. This can be observed in the case of influenza, when after recovery there is a long (but not lifelong) immunity to the same strain of the disease but no immunity against other strains. Other cases of temporary immunity include *Chlamydia trachomatis* with very short temporal immunity and very high rates of reinfection; *Salmonella* infection with partial immunity; non-plague yersiniosis where the actual time of the immunity is unclear; respiratory syncytial virus after which immunity is incomplete and short-lived [15]. Since vaccination is considered to be the most effective strategy against infectious diseases, the development of a framework that would predict the optimal vaccine coverage level needed to prevent the spread of these diseases is crucial [14]. Theoretically speaking, it is well known that this type of problem can be easily modelled using a Susceptible-Infective-Susceptible (*SIS*) framework [4].

2.2 Mathematical model

In this present study, a vaccinated class V with temporary vaccine-induced immunity that wanes over time at the rate δ is added to the classic *SIS* model. The proposed model

assumes that the natural death rates μ in the classes remain unequal to births, so that the population size N is realistically not constant. Citizens are born into the population at a constant birth rate π with extremely very low childhood disease mortality rate. We denote the fraction of citizens vaccinated at birth each year as P (with $0 < P < 1$) and assume the rest are susceptible. A susceptible individual will move into the infected group through contact with an infected individual, approximated by an average contact rate β. An infected individual recovers through effective treatment at a rate γ, and enters vaccinated-treated group with temporary immunity. The differential equations for the model are

$$\frac{dS}{dt} = (1-P)\pi N - \beta\frac{SI}{N} + \delta V - \mu S\,, \tag{2.2.1}$$

$$\frac{dI}{dt} = \beta\frac{SI}{N} - (\gamma+\mu)I\,, \tag{2.2.2}$$

$$\frac{dV}{dt} = P\pi N + \gamma I - (\delta+\mu)V\,. \tag{2.2.3}$$

We also have the relationship $N=S+I+V$ and assume μ, π, β, γ, μ, δ are all positive constant parameters. Adding equations (2.2.1) to (2.2.3), we obtain

$$\frac{dN}{dt} = (\pi-\mu)N\,, \tag{2.2.4}$$

so that we are now dealing with a varying total population [7]. A summary of the process is drawn in a flow chart in Fig. 2.2.1 below:

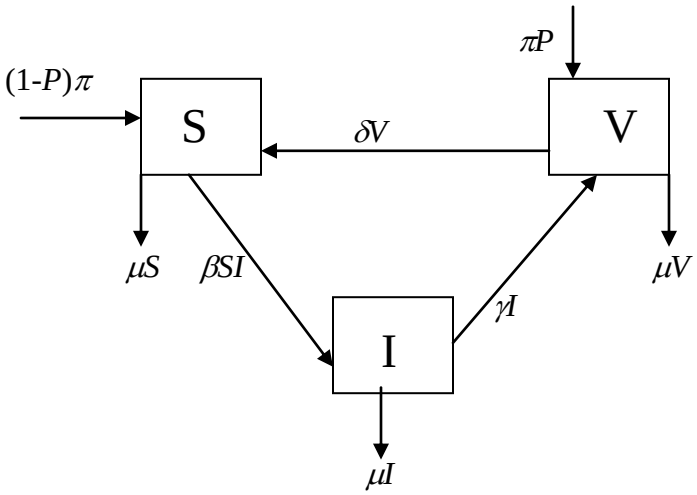

Figure 2.2.1: Flow chart for the model

The groups can be scaled by population N using the new variables, $s=S/N$, $i=I/N$, and $v=V/N$. The population is now normalised, meaning $s+i+v=1$, and we have the new system,

$$\frac{ds}{dt} = (1-P)\pi - \beta si + \delta v - \pi s, \tag{2.2.5}$$

$$\frac{di}{dt} = \beta si - (\gamma + \pi)i, \tag{2.2.6}$$

$$\frac{dv}{dt} = P\pi + \gamma i - (\delta + \pi)v. \tag{2.2.7}$$

2.3 Qualitative analysis

A qualitative investigation of the system described by equations (2.2.5)-(2.2.7) reveals that the long-term behaviour, falls into two categories: endemic or die out. The appropriate Jacobian matrix to equations (2.2.5)-(2.2.7) is given as

$$J(s,i,v)=\begin{bmatrix} -\beta i-\pi & -\beta s & \delta \\ \beta i & \beta s-\gamma-\pi & 0 \\ 0 & \gamma & -\delta-\pi \end{bmatrix}. \qquad (2.3.1)$$

When the disease dies out, the solution asymptotically approaches a disease free equilibrium E_0 of the form,

$$E_0=\left(\frac{\delta P+(1-P)(\pi+\delta)}{\pi+\delta},0,\frac{P\pi}{\pi+\delta}\right), \qquad (2.3.2)$$

The threshold that determines the stability of this equilibrium is obtain from the eigenvalues of the Jacobian matrix evaluated at E_0 and the vaccination reproduction number given by

$$R_v=\frac{\beta\delta P+\beta(1-P)(\pi+\delta)}{(\pi+\delta)(\pi+\gamma)}. \qquad (2.3.3)$$

Proposition 2.3.1: The disease free equilibrium is locally asymptotically stable if $R_v<1$, i.e. the disease will be eradicated from the community if the initial sizes of the three state variables are within the vicinity of R_v. All eigenvalues at E_0 will be negative if $R_v<1$, and E_0 will be a locally asymptotically stable node.

Furthermore, equation (2.3.3) also reveals that there is a critical vaccination proportion $P_c=(\pi+\delta)(\beta-\gamma-\pi)/\beta\pi$ above which the disease free equilibrium is stable i.e. $P>P_c$.

Thus, in order to successfully prevent disease, the vaccination proportion should be large enough.

Proposition2.3.2: The disease free equilibrium is gobally asymptotically stable if R_v<1. Using Lasalle-Lyapunov theorem [14, 17], consider a feasible region of the model defined as

$$\Gamma = \left\{ (s,i,v) \in \Re_+^3 \middle| s \le \frac{\delta P + (1-P)(\pi+\delta)}{\pi+\delta}, v \le \frac{P\pi}{\pi+\delta} \right\}. \tag{2.3.4}$$

For $R_v < 1$, let $G = (\pi+\delta)i$ be a given Lyapunov function, then

$$\begin{aligned} \frac{dG}{dt} &= (\pi+\delta)\frac{di}{dt} \\ &= (\pi+\delta)\left[\beta s - (\pi+\gamma)\right]i \\ &\le \left[\beta P\delta - \beta(1-P)(\pi+\delta) - (\pi+\delta)(\pi+\gamma)\right]i \\ &= (\pi+\delta)(\pi+\gamma)(R_v - 1)i \le 0. \end{aligned} \tag{2.3.5}$$

Clearly, dG/dt =0 if and only if i = 0. Equation (2.3.5) confirms the Lyapunov argument for the global asymptotic stability of disease free equilibrium. Hence, every solution that starts within the region Γ approaches E_0 as $t \to \infty$. Therefore, if the model parameters are selected such that R_v < 1, then the disease will be totally eradicated from the community.

Proposition 2.3.3: The endemic equilibrium is locally asymptotically stable if R_v > 1. When the disease free equilibrium is unstable, there exists an endemic equilibrium E_u =(s*, i*, v*), where

$$s^* = \frac{\gamma + \pi}{\beta}, \quad i^* = \frac{(R_v - 1)(\delta + \pi)(\gamma + \pi)}{\beta(\delta + \gamma + \pi)}, \quad v^* = \frac{P\pi}{\delta + \pi} + \frac{\gamma(\gamma + \pi)(R_v - 1)}{\beta(\gamma + \delta + \pi)}. \quad (2.3.6)$$

From equation (2.3.6) it is very obvious that the condition $R_v > 1$ ensures existence of the positive endemic equilibrium state E_u, since i^* will assume a negative value for $R_v<1$ which is biologically not feasible. The characteristic polynomial for the eigenvalues of Jacobian matrix evaluated at the endemic equilibrium E_u gives:

$$H(\lambda) = \lambda^3 + b_2\lambda^2 + b_1\lambda + b_0, \quad (2.3.7)$$

where

$$b_2 = 3\pi + \delta + \beta i^* - \beta s^* + \gamma$$
$$b_1 = (\delta + \pi)(2\pi + \beta i^* - \beta s^* + \gamma) + \beta^2 s^* i^* - (\beta i^* + \pi)(\beta s^* - \gamma - \pi)$$
$$b_0 = -\gamma\beta\delta i^* + (\delta + \pi)(\beta^2 s^* i^* - (\beta i^* + \pi)(\beta s^* - \gamma - \pi)).$$

Thus by Routh-Hurwitz criterion [13], the endemic equilibrium E_u is locally asymptotically stable with $R_v > 1$ as it can be seen clearly that $b_2 > 0, b_1 > 0, b_0 > 0$ and $b_2 b_1 - b_0 > 0$.

2.4 Computational method

In order to explicitly construct approximate non-perturbative solutions of the system described by equations (2.2.5)-(2.2.7), Adomian decomposition method well addressed in [1-3] is employed and implemented in MAPLE (a symbolic algebra packaged). The advantage of this method is that it provides a direct scheme for solving the problem, i.e., without the need for linearization, perturbation, massive computation and any transformation.

The equivalent canonical form of this system is as follows:

$$s(t) = s(0) + (1-P)\pi t - \beta\int_0^t sidt + \delta\int_0^t vdt - \pi\int_0^t sdt\,, \tag{2.4.1}$$

$$i(t) = i(0) + \beta\int_0^t sidt - (\gamma+\pi)\int_0^t idt\,, \tag{2.4.2}$$

$$v(t) = v(0) + P\pi t + \gamma\int_0^t idt - (\delta+\pi)\int_0^t vdt\,. \tag{2.4.3}$$

As usual in Adomian decomposition method the solutions of equations (2.4.1)-(2.4.3) are considered to be as the sum of the following series

$$s = \sum_{n=0}^{\infty} s_n\,, \qquad i = \sum_{n=0}^{\infty} i_n\,, \qquad v = \sum_{n=0}^{\infty} v_n\,. \tag{2.4.4}$$

Then we approximate the nonlinear terms in the system as follows:

$$si = \sum_{n=0}^{\infty} F_n(s_0,...,s_n,i_0,...,i_n)\,, \tag{2.4.5}$$

where

$$F_n = \frac{1}{n!}\left[\frac{d^n\left(\sum_{k=0}^{\infty} s_k\lambda^k\right)\left(\sum_{k=0}^{\infty} i_k\lambda^k\right)}{d\lambda^n}\right]_{\lambda=0}. \tag{2.4.6}$$

The nonlinear functions F_n are called Adomian's polynomials. Substituting (2.4.4)-(2.4.6) into (2.4.1)- (2.4.3), we get:

$$\sum_{n=0}^{\infty} s_n = s(0) + (1-P)\pi t - \beta\int_0^t \sum_{n=0}^{\infty} F_n dt + \delta\int_0^t \sum_{n=0}^{\infty} v_n dt - \pi\int_0^t \sum_{n=0}^{\infty} s_n dt\,, \tag{2.4.7}$$

$$\sum_{n=0}^{\infty} i_n = i(0) + \beta\int_0^t \sum_{n=0}^{\infty} F_n dt - (\gamma+\pi)\int_0^t \sum_{n=0}^{\infty} i_n dt\,, \tag{2.4.8}$$

$$\sum_{n=0}^{\infty} v_n = v(0) + P\pi t + \gamma\int_0^t \sum_{n=0}^{\infty} i_n dt - (\delta+\pi)\int_0^t \sum_{n=0}^{\infty} v_n dt\,. \tag{2.4.9}$$

From equations (2.4.7)-(2.4.9) we define the following scheme:

$$s_0 = s(0) + (1-P)\pi t\,,\ i_0 = i(0), v_0 = v(0) + P\pi t \tag{2.4.10}$$

$$s_{n+1} = -\beta\int_0^t F_n dt + \delta\int_0^t v_n dt - \pi\int_0^t s_n dt\,, \qquad (\text{for } n \geq 0), \tag{2.4.11}$$

$$i_{n+1} = \beta\int_0^t F_n dt - (\gamma+\pi)\int_0^t i_n dt\,, \quad (\text{for } n \geq 0), \tag{2.4.12}$$

$$v_{n+1} = \gamma\int_0^t i_n dt - (\delta+\pi)\int_0^t v_n dt\,, \quad (\text{for } n \geq 0). \tag{2.4.13}$$

Using equation (2.4.6), we compute some of the Adomian polynomials as follows:

$$F_0 = s_0 i_0\,,\ F_1 = s_0 i_1 + s_1 i_0,\ F_2 = s_0 i_2 + s_1 i_1 + s_2 i_0,\ F_3 = s_0 i_3 + s_1 i_2 + s_2 i_1 + s_3 i_0\,,$$

$$F_4 = s_0 i_4 + s_1 i_3 + s_2 i_2 + s_3 i_1 + s_4 i_0, F_5 = s_0 i_5 + s_1 i_4 + s_2 i_3 + s_3 i_2 + s_4 i_1 + s_5 i_0, \ldots$$

(2.4.14)

Substituting equations (2.4.10)-(2.4.14) into equations (2.4.7)-(2.4.9), and using MAPLE we obtained a few terms approximation to the solutions as

$$s_N = \sum_{n=0}^{N} s_n\,, \qquad i_N = \sum_{n=0}^{N} i_n\,, \qquad v_N = \sum_{n=0}^{N} v_n\,, \tag{2.4.15}$$

where

$$s(t) = \lim_{N\to\infty}(s_N)\,, \quad i(t) = \lim_{N\to\infty}(i_N)\,, \quad v(t) = \lim_{N\to\infty}(v_N)\,. \tag{2.4.16}$$

Usually, the decomposition method yields rapidly convergent series solutions by using a few iterations for the nonlinear deterministic equations [20]. However, in this particular problem the convergence of the decomposition series partial sum in equation (2.4.15) can be further enhanced using Padé approximation technique [6]. For instance, the series in equation (2.4.15) is transformed as follows,

$$s_N = \frac{\sum_{n=0}^{M} a_n t^n}{\sum_{n=0}^{M} b_n t^n}, \quad i_N = \frac{\sum_{n=0}^{M} c_n t^n}{\sum_{n=0}^{M} d_n t^n}, v_N = \frac{\sum_{n=0}^{M} e_n t^n}{\sum_{n=0}^{M} h_n t^n}, \tag{2.4.17}$$

where $N = M + M$ is the order of the series required for each approximant.

2.5 Numerical experiment

In this section, we monitor the effect of vaccination on the dynamics of an infectious disease with waning immunity described by the model in Eqs. (2.2.5)-(2.2.7). For illustration purposes as well as the numerical validation of the qualitative results obtained in Eqs. (2.3.2)-(2.3.6), the parameter values in Table 2.5.1 below are used:

Table 2.5.1: Effect of vaccination coverage and waning immunity for various parameter values

Case	*s(0)*	*i(0)*	*v(0)*	β	γ	π	δ	P	R_v	Comments
1	0.8	0.2	0.0	0.7	0.04	0.3	0.05	0.9	0.47058	E_0 stable (disease eradication)
2	0.8	0.2	0.0	0.7	0.04	0.3	0.01	0.8	0.46489	E_0 stable (disease eradication)
3	0.8	0.2	0.0	0.7	0.04	0.3	0.05	0.3	1.52941	E_u stable (no eradication)
4	0.8	0.2	0.0	0.7	0.04	0.3	0.01	0.2	1.66034	E_u stable (no eradication)

We transformed the decomposition series partial sum shown in the appendix for cases 1-4 into diagonal Padé approximants [M/M] as given by Eq. (2.4.17) in order to enhance their convergence. Figures 2.5.1-2.5.2 depict cases 1-2 in the Table 2.5.1 and illustrate the impact of high vaccination coverage on the initial population groups with low level of infective group. The populations of the susceptible and infective groups decrease with time while that of the vaccinated-treated group gradually increases and the disease outbreak ends. In both cases, it is very interesting to note that the effect of waning immunity is strongly dominated by the vaccination coverage level that exceeds a certain threshold (P_c) and the entire population generally becomes disease free with time.

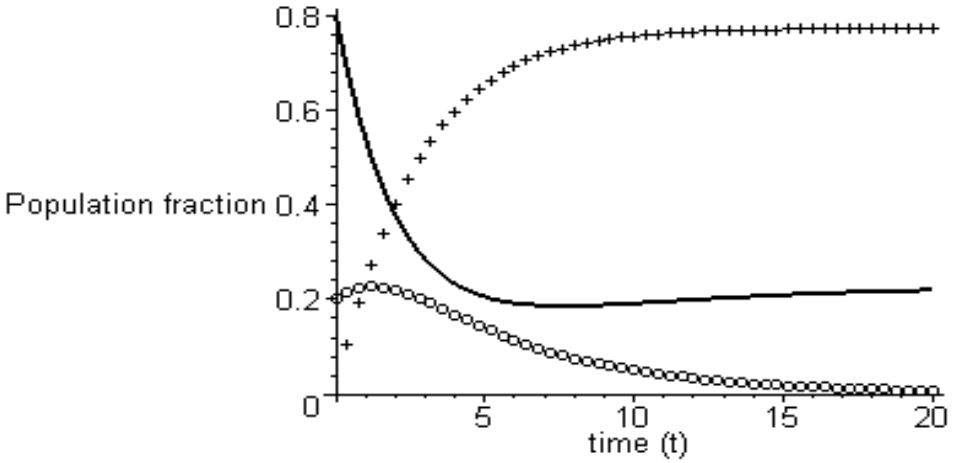

Figure 2.5.1: Population fraction versus time for case 1: *P*=0.9;_____Susceptible fraction; oooooInfectives fraction; ++++++Vaccinated-treated fraction

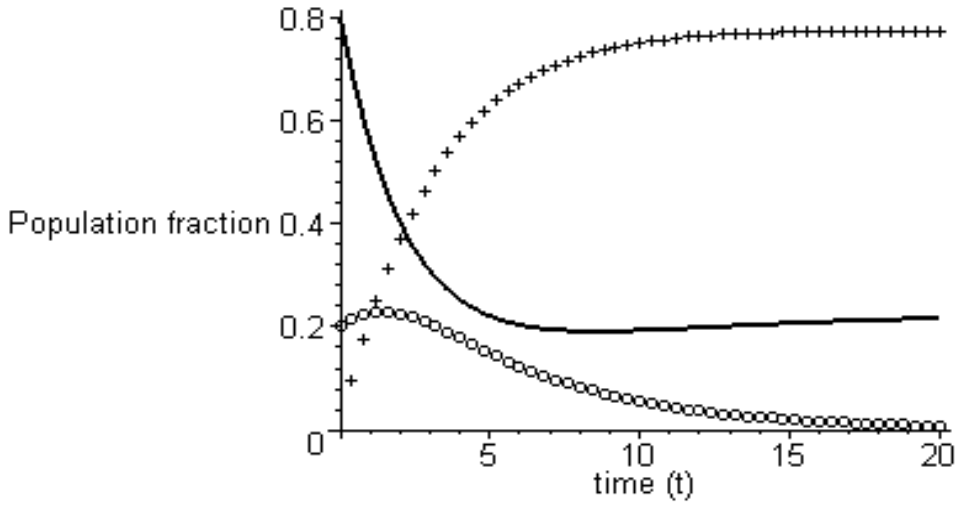

Figure 2.5.2: Population fraction versus time for case 2: *P*=0.8;_____Susceptible fraction; oooooInfectives fraction; ++++++Vaccinated-treated fraction.

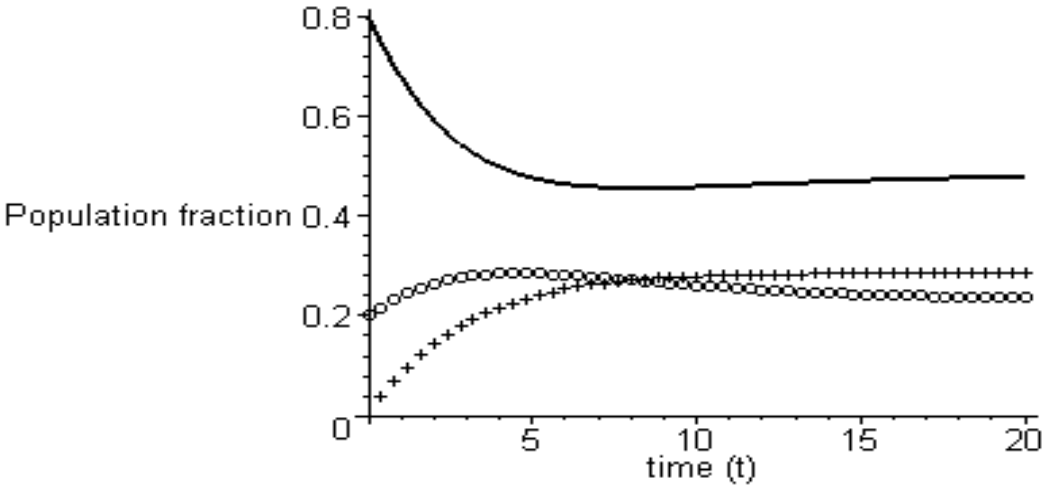

Figure 2.5.3: Population fraction versus time for case 3: *P*=0.3;_____Susceptible fraction; oooooInfectives fraction; ++++++Vaccinated-treated fraction.

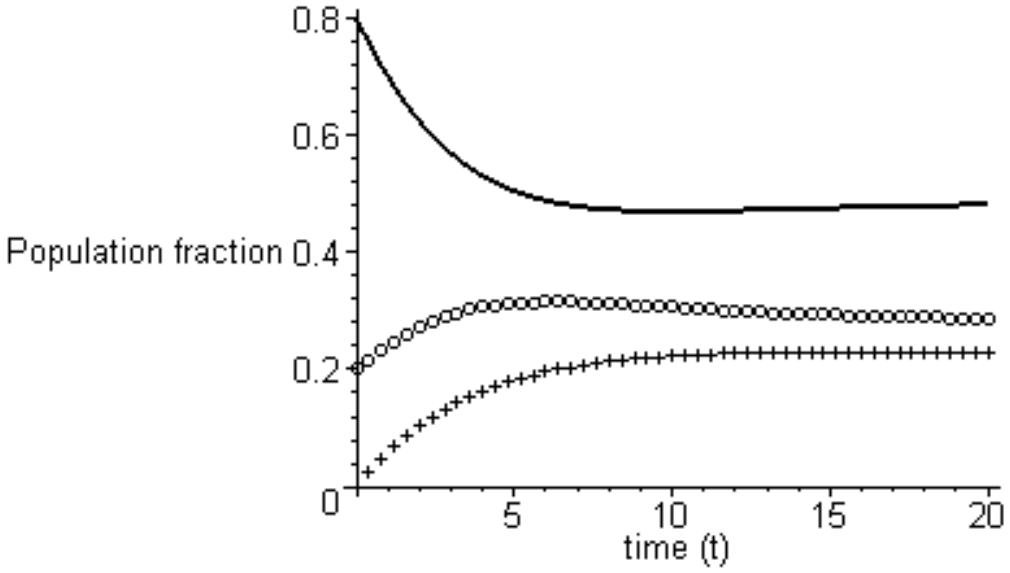

Figure 2.5.4: Population fraction versus time for case 4: *P*=0.2;_____Susceptible fraction; oooooInfectives fraction; ++++++Vaccinated-treated fraction.

Cases 3-4 in the Table 2.5.1 are represented in Figures 2.5.3-2.5.4 and illustrate the effect of very low vaccination coverage on the initial population groups with low levels of infective group. The population of the susceptible group temporally decreases while that of vaccinated-treated group gradually increases with time until they attain their equilibrium levels. However, it is noteworthy that the population of infective group will never disappear with time and the endemic situation persists. This confirmed that a disease free equilibrium could not be achieved once the vaccination coverage level is lower than a certain threshold (P_c) and the endemic equilibrium remains stable.

CHAPTER THREE

Effect of ineffective vaccine on dynamics of infectious diseases with temporary immunity

3.0 SUMMARY

In this chapter, we extend the three compartmental mathematical model discussed in Chapter 2 to include the effect of totally ineffective vaccine on the transmission dynamics of re-infection under the assumption that the vaccine induced immune protection may wane over time. Here, infection can invade both the susceptible or vaccinated classes. The qualitative analysis reveals that the disease eradication depends on vaccination coverage as well as on vaccine efficacy. Using an appropriate Lyapunov function, we established that the disease free equilibrium is globally asymptotically stable if the vaccination coverage level exceeds a certain threshold value. Numerical experiment is performed on the governing nonlinear system using the Runge–Kutta integration scheme in order to validate our analytical conclusions and illustrate possible behaviour scenarios of the model.

3. 1 Introduction

When individuals are immunized by vaccine, the vaccine induces their immune system to respond and produce antibodies against the ‘virus’ in the vaccine. These antibodies then destroy the vaccine virus, but the immune system ‘remembers’ the virus so that it can fight off infection if the individual is ever exposed to the natural virus (the ones that

cause the disease). Because the virus in the vaccine and the natural virus are very similar, the immune system responds to both. This means that if an immunized person is ever exposed to the circulating virus, the immune system responds immediately and large amounts of antibodies are produced to overcome the infection. However, the level of vaccine effectiveness varies which account to why some people do not respond well and develop immunity against a disease as intended. Furthermore, some diseases, such as gonorrhea, do not confer immunity and can be modelled using a Susceptible-Infective-Susceptible (SIS) framework [4]. The SIS model is the core of any disease transmission model and serves as a basic template to be expanded for special cases. Thus a full understanding of a simple SIS model is essential regardless of how well any particular disease can be forced into its framework. The use of control measures, such as the use of condoms (for example, in the case of gonorrhea), can be interpreted as a partially effective "vaccine." Hence, a vaccinated class is added to the classic SIS model in a population. "Vaccine" efficacy is a function of the disease e.g., influenza vaccines have a 70% to 90% efficacy rate among healthy young adults but only 30% to 40% among the elderly [7]. Other cases of temporary immunity include *Chlamydia trachomatis* with very short temporal immunity and very high rates of reinfection; *Salmonella* infection with partial immunity; non-plague yersiniosis where the actual time of the immunity is unclear; respiratory syncytial virus after which immunity is incomplete and short-lived.

The use of mathematical modelling influences the theory and practice of disease management and control. This is because they can help in figuring out decisions that are of significant importance on the outcomes and provide comprehensive examinations that enter into decisions in a way that human reasoning and debate cannot. One of the main

issues in the study of behaviour of epidemics is the analysis of steady states of the model and their stability. Generally, a model contains a disease-free equilibrium and one or more endemic equilibria. The stability of a disease-free steady state as well as the existence of other non-trivial equilibria can be determined using the so-called basic reproduction ratio, which quantifies how many secondary infections appear from a single infected put in a population of susceptibles [9, 15]. When the basic reproduction number is less than unity, the disease-free equilibrium is locally asymptotically stable, and, therefore, the disease dies out after some period of time. Similarly, when the endemic equilibrium is a global attractor, epidemiologically this means that the disease will prevail and persist in a population.

In the model presented here, it is assumed that the ineffective vaccine induce only temporary immunity to the disease. Hence, both susceptible and vaccinated individuals will never become permanently immuned, since they are at risk of reinfection. But this re-infection in vaccinated group will occur at a lower rate of infectiousness than those of the susceptible individuals who never have been either vaccinated or infected.

3.2 Mathematical model

Here, a vaccinated class V with temporary vaccine-induced immunity that wanes over time at the rate δ is added to the classic *SIS* model. The propose model assumes that the natural death rates μ in the classes remain unequal to births, so that the population size N is realistically not constant. Citizens are born into the population at a constant birth rate π with extremely very low childhood disease mortality rate. We denote the fraction of citizens vaccinated at birth each year as P (with $0 < P < 1$) and assume the rest are susceptible. Both susceptible and vaccinated individual will move into the infected group

through contact with an infected individual, approximated by an average contact rate β_1 and β_2 respectively, where ($\beta_1 > \beta_2$). An infected individual recovers through effective treatment at a rate γ, and enters vaccinated-treated group with temporary immunity. The differential equations for the model are

$$\frac{dS}{dt} = (1-P)\pi N - \beta_1 \frac{SI}{N} + \delta V - \mu S , \tag{3.2.1}$$

$$\frac{dI}{dt} = \beta_1 \frac{SI}{N} + \beta_2 \frac{VI}{N} - (\gamma + \mu) I , \tag{3.2.2}$$

$$\frac{dV}{dt} = P\pi N + \gamma I - \beta_2 \frac{VI}{N} - (\delta + \mu) V . \tag{3.2.3}$$

We also have the relationship $N=S+I+V$ and assume μ, π, β_1, β_2, γ, μ, δ are all positive constant parameters. Adding equations (3.2.1) to (3.2.3), we obtain

$$\frac{dN}{dt} = (\pi - \mu) N , \tag{2.2.4}$$

so that we are now dealing with a varying total population [10]. A summary of the process is drawn in a flow chart in Fig. 3.2.1 below:

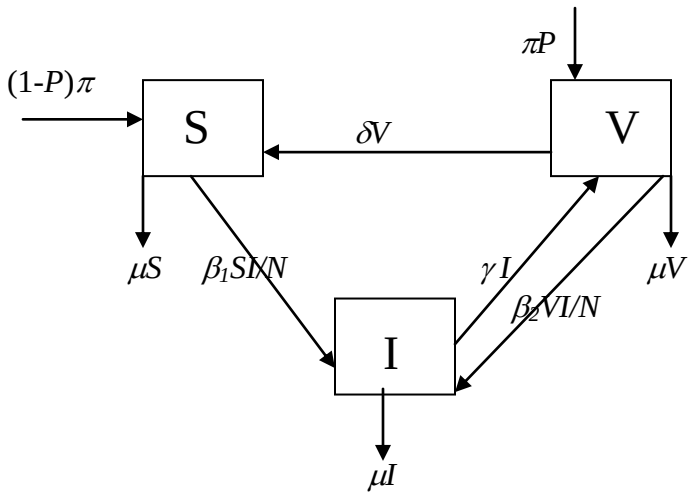

Figure 3.2.1: Flow chart for the model

The groups can be scaled by population N using the new variables, $s=S/N$, $i=I/N$, and $v=V/N$. The population is now normalised, meaning $s+i+v=1$, and we have the new system,

$$\frac{ds}{dt} = (1-p)\pi - \beta_1 si + \delta v - s\pi \tag{3.2.5}$$

$$\frac{di}{dt} = (\beta_1 s + \beta_2 v - \gamma - \pi)i \tag{3.2.6}$$

$$\frac{dv}{dt} = (p-v)\pi + i(\gamma - \beta_2 v) - \delta v \tag{3.2.7}$$

3.3 Qualitative analysis

A qualitative investigation of the system described by equations (3.2.5)-(3.2.7) reveals that the long-term behaviour, falls into two categories: endemic or die out. The appropriate Jacobian matrix to equations (3.2.5)-(3.2.7) is given as

$$J(s,i,v) = \begin{pmatrix} -\beta_1 i - \pi & -\beta_1 s & \delta \\ \beta_1 i & \beta_1 s + \beta_2 v - \gamma - \pi & \beta_2 i \\ 0 & \gamma - \beta_2 v & -\beta_2 i - \delta - \pi \end{pmatrix}. \tag{3.3.1}$$

When the disease dies out, the solution asymptotically approaches a disease free equilibrium E_0 of the form,

$$E_0 = \left((1-p) + \frac{\delta p}{\pi + \delta}; 0; \frac{p\pi}{\pi + \delta} \right), \tag{3.3.2}$$

The threshold that determines the stability of this equilibrium is obtain from the eigenvalues of the Jacobian matrix evaluated at E_0 and the vaccination reproduction number given by

$$R_{v0} = \frac{\beta_1(\pi - p\pi + \delta)}{(\gamma + \pi)(\pi + \delta)} + \frac{p\pi\beta_2}{(\gamma + \pi)(\pi + \delta)} = R_1 + R_2 . \qquad (3.3.3)$$

Remark: R_2 is the contribution to the vaccination reproduction number by the re-infection rate of the vaccinated individual due to the vaccine ineffectiveness and $R_{v0} \to R_v$ as $R_2 \to 0$ which is the case studied in chapter 2.

Proposition 3.3.1: The disease free equilibrium is locally asymptotically stable if $R_{v0} < 1$, i.e. the disease will be eradicated from the community if the initial sizes of the three state variables are within the vicinity of R_v. All the eigenvalues at E_0 will be negative if $R_{v0} < 1$, and E_0 will be locally asymptotically stable node.

Furthermore, equation (3.3.3) also reveals that there is a critical vaccination proportion $P_c = [\beta_1(\pi + \delta) - (\pi + \gamma)(\pi + \delta)] / \pi(\beta_1 - \beta_2)$ and $\beta_1 > \beta_2$ above which the disease free equilibrium is stable i.e. $P > P_c$. Thus, in order to successfully prevent disease, the vaccination proportion should be large enough.

Proposition 3.3.2: The disease free equilibrium is globally asymptotically stable if $R_v<1$. Using Lasalle-Lyapunov theorem [13, 17], consider a feasible region of the model defined as

$$\Gamma = \left\{ (s, i, v) \in \Re_+^3 \middle| s \le \frac{\delta P + (1 - P)(\pi + \delta)}{\pi + \delta}, v \le \frac{P\pi}{\pi + \delta} \right\}. \qquad (3.3.4)$$

For $R_v < 1$, let $G = (\pi+\delta)i$ be a given Lyapunov function, then

$$\begin{aligned}\frac{dG}{dt} &= (\pi+\delta)\frac{di}{dt}\\ &= (\pi+\delta)\left[\beta_1 s+\beta_2 v-(\pi+\gamma)\right]i\\ &\le (\pi+\delta)(\pi+\gamma)\left[\frac{\beta_1(\pi+\delta)-p\pi(\beta_1-\beta_2)}{(\gamma+\pi)(\pi+\delta)}-1\right]i\\ &= (\pi+\delta)(\pi+\gamma)(R_{v0}-1)i\le 0.\end{aligned} \tag{3.3.5}$$

Clearly, dG/dt =0 if and only if i = 0. Equation (3.3.5) confirms the Lyapunov argument for the global asymptotic stability of disease free equilibrium. Hence, every solution that starts within the region Γ approaches E_0 as $t \to \infty$. Therefore, if the model parameters are selected such that R_{v0} < 1, then the disease will be totally eliminated from the community.

Proposition 3.3.3: The endemic equilibrium is locally asymptotically stable if R_v > 1. When the disease free equilibrium is unstable, there exists an endemic equilibrium E_u =(s*, i*, v*), where

$$s^* = \frac{\pi+\gamma}{\beta_1}-\frac{\beta_2}{\beta_1}\left(\frac{p\pi+i^*\gamma}{\delta+\beta_2 i^*+\pi}\right),\ v^* = \frac{p\pi+i^*\gamma}{\delta+\beta_2 i^*+\pi}, \tag{3.3.6}$$

and F(i*) = 0, where

$$\begin{aligned}F(i^*) &= \beta_1\beta_2 i^{*2}+(\beta_2\pi-\beta_1\beta_2+\beta_1\pi+\gamma\beta_1+\delta\beta_1)i^*+(\pi p\beta_1-\delta\beta_1-\pi\beta_2 p-\pi\beta_1+\pi\delta+\pi^2+\gamma\delta+\gamma\pi).\\ &= \beta_1\beta_2 i^{*2}+(\beta_2\pi-\beta_1\beta_2+\beta_1\pi+\gamma\beta_1+\delta\beta_1)i^*+(1-R_{v0})(\gamma+\pi)(\pi+\delta)\end{aligned}$$

It is important to show that if i* exists (that is real and positive), then s* and v* exist and R_{v0} > 1. Solving for i* in the quadratic equation F(i*) = 0, we obtain

$$i^* = \frac{M\pm\sqrt{M^2-4(1-R_{v0})\beta_1\beta_2(\gamma+\pi)(\pi+\delta)}}{2(\beta_1\beta_2)} \tag{3.3.7}$$

where $M=(\beta_1\beta_2-\beta_2\pi-\beta_1\pi-\gamma\beta_1-\delta\beta_1)$.

Thus, for i^* to be real and positive in Eq. (3.3.7)

$$M^2 - 4(1 - R_{v0})\beta_1\beta_2(\gamma + \pi)(\pi + \delta) > 0 \qquad (3.3.8)$$

From equation (3.3.8) it very obvious that the condition $R_{v0} > 1$ ensures the existence of the positive endemic equilibrium state E_u, since i^* will assume a complex value for $R_{v0} < 1$ which is biologically not feasible.

3.4 Numerical experiment

In this section, we monitor the effect of ineffective vaccine on the dynamics of an infectious disease with waning immunity described by the model in Eqs. (3.2.5)-(3.2.7). For illustration purposes, the numerical experiment is performed using the Runge–Kutta integration scheme implemented in MAPLE programming language [23] in order to validate the qualitative results obtained in Eqs. (3.3.2)-(3.3.6), the parameter values in Table 3.4.1 below are used:

Table 3.4.1: Effect of ineffective vaccine and waning immunity on infectious disease transmission.

Case	*s(0)*	*i(0)*	*v(0)*	β_1	β_2	γ	π	δ	*P*	R_{v0}	Comments
1	0.8	0.2	0.0	0.3	0.1	0.04	0.4	0.05	0.9	0.22726	E_0 stable (disease eradication)
2	0.8	0.2	0.0	0.3	0.1	0.04	0.4	0.01	0.8	0.32704	E_0 stable (disease eradication)
3	0.8	0.2	0.0	0.3	0.1	0.04	0.2	0.01	0.1	1.17063	E_u stable (no eradication)
4	0.8	0.2	0.0	0.3	0.1	0.04	0.2	0.07	0.1	1.18827	E_u stable (no eradication)

Figures 3.4.1-3.4.2 depict cases 1-2 in the Table (3.4.1) and illustrate the impact of high vaccination coverage on the initial population groups with low level of infective group in

the presence of ineffective vaccine. The populations of the susceptible and infective groups decrease with time while that of the vaccinated-treated group gradually increases and the disease outbreak ends. In both cases, it is very interesting to note that the combined effect of low vaccine efficacy and waning immunity is strongly dominated by the vaccination coverage level that exceeds a certain threshold (P_c) and the entire population generally becomes disease free with time.

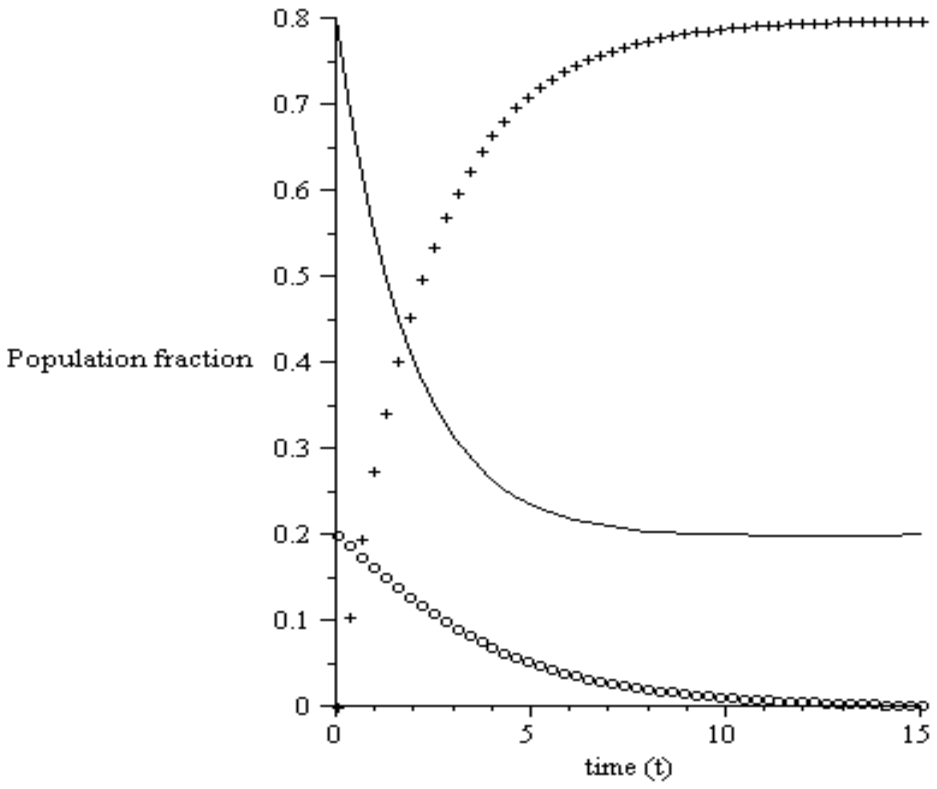

Figure 3.4.1: Population fraction versus time for the case 1; _____*s*; oooooo*i*; +++++*v*

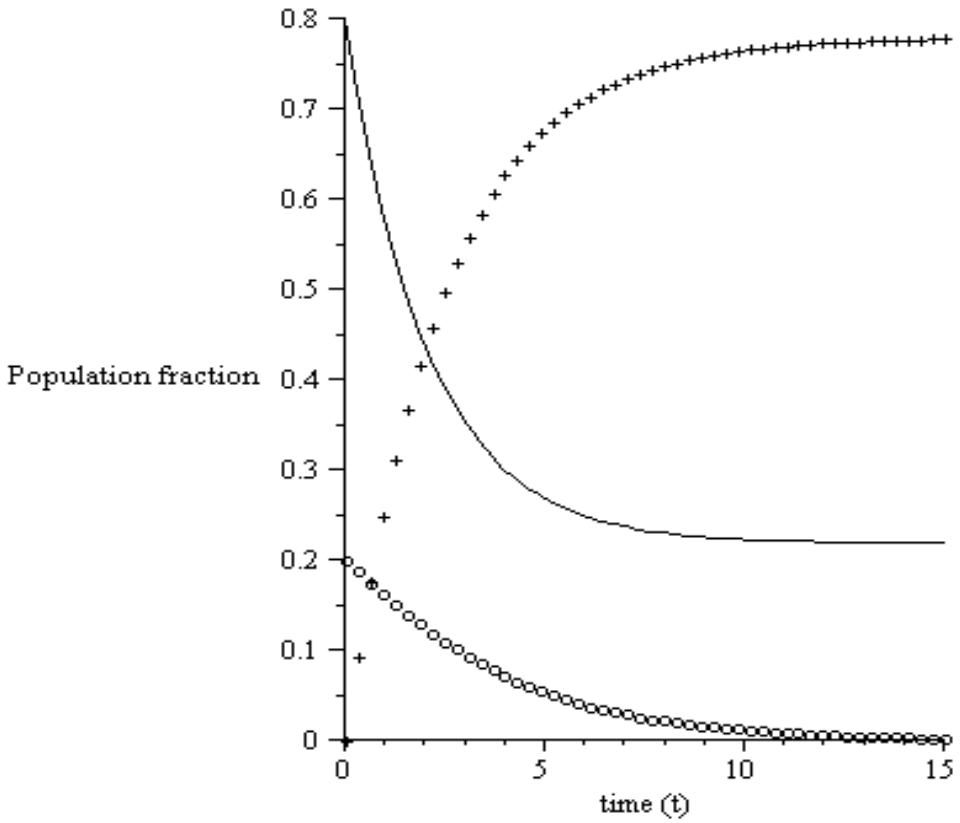

Figure 3.4.2: Population fraction versus time for the case 2; _____*s*; ooooooo*i*; +++++*v*

Cases 3-4 in the Table (3.4.1) are represented in Figures 3.4.3-3.4.4 and illustrate the effect of very low vaccination coverage on the initial population groups with low levels of infective group in the presence of ineffective vaccine. The population of the susceptible group temporally decreases while that of vaccinated-treated group gradually increases with time until they attain their equilibrium levels. However, it is noteworthy that the population of infective group also increases until it attains its equilibrium level and never disappears with time and the endemic situation persists. This can be attributed to the combined effect of low vaccine efficacy and waning immunity in the presence of very low vaccination coverage. Hence, a disease free equilibrium could not be achieved once the vaccination coverage and the endemic equilibrium remain stable.

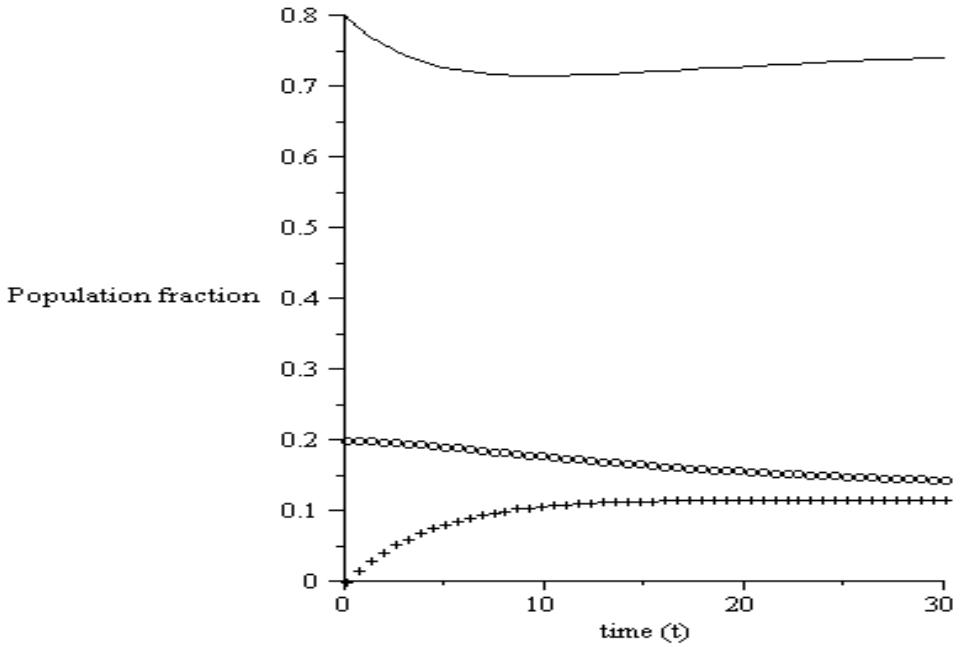

Figure 3.4.3: Population fraction versus time for the case 3; _____*s*; oooooo*i*; +++++*v*

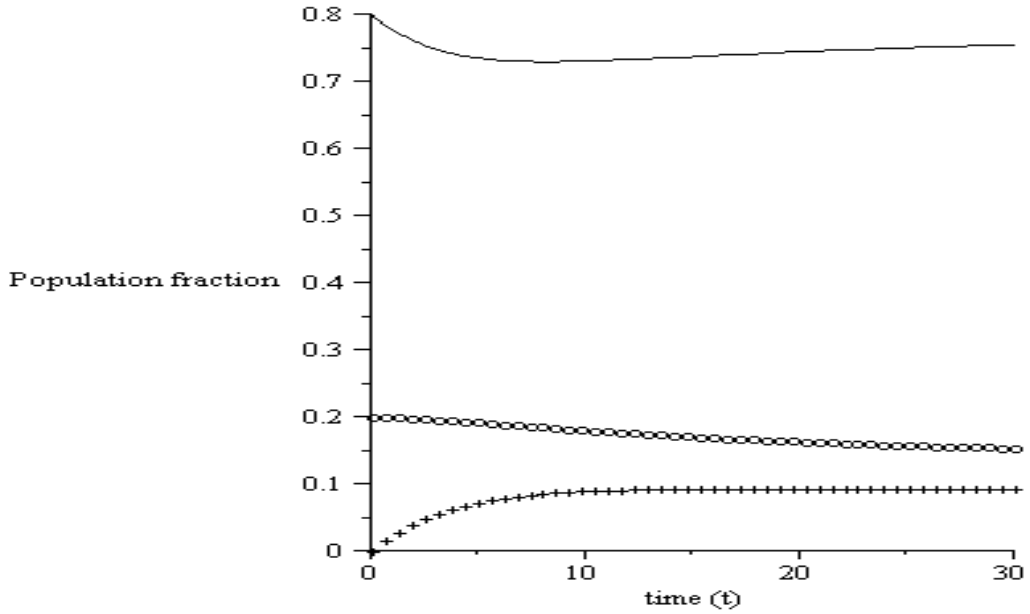

Figure 3.4.4: Population fraction versus time for the case 4; _____*s*; oooooo*i*; +++++*v*

Figure 3.4.5 illustrates the impact of ineffective vaccine on the vaccination reproductive number. For $\beta_2 > 0$, it is interesting to note that the tendency for $R_{v0} > 1$ is extremely high even in the presence of high vaccination coverage on the initial population groups with low level of infective group.

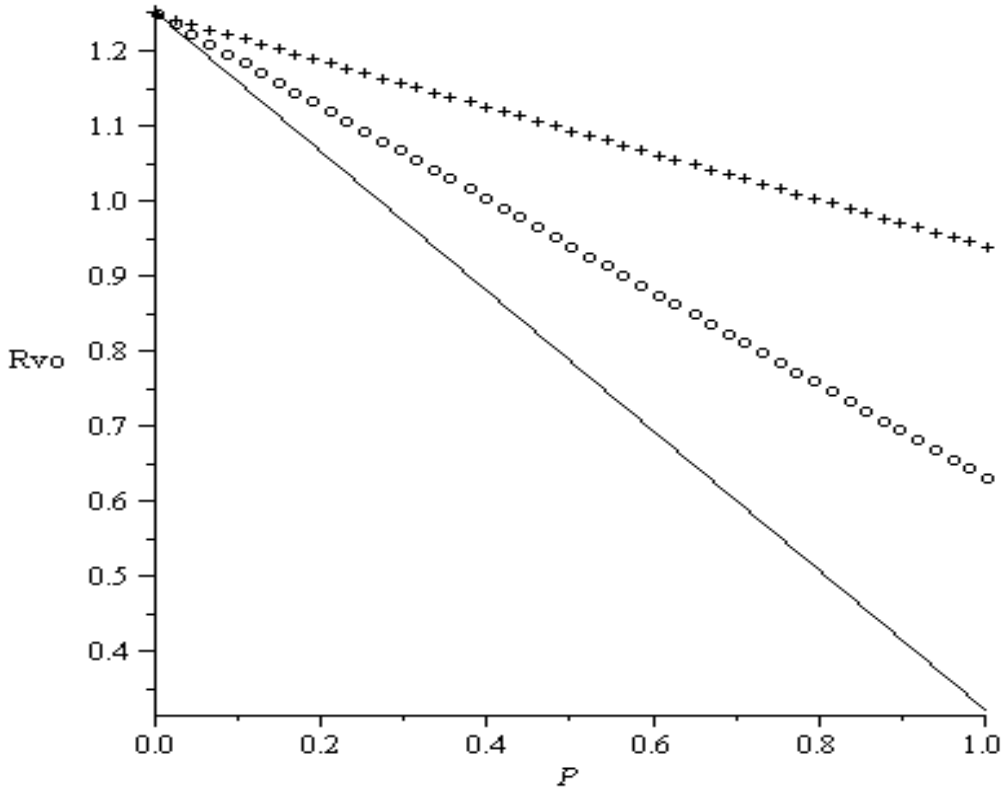

Figure 3.4.5: Variation in vaccination reproductive number for β_1 =0.3; π=0.2; γ=0.04; δ=0.07; _____β_2 =0, oooooβ_2 =0.1, +++++β_2 =0.2

APPENDIX

Appendix 1: According to the values introduced in table (2.5.1) of chapter 2 the following approximate solutions are derived;

Case1.

$$s(t) \approx .8 - .32200\,t + .065470\,t^2 - .0037885\,t^3 - .00080121\,t^4 + .000037663\,t^5 - .000021298\,t^6 + .75941\,10^{-7}\,t^7 + .80714\,10^{-8}\,t^8 + .26119\,10^{-11}\,t^9 - .21271\,10^{-12}\,t^{10}$$

$$i(t) \approx .2 + .044000\,t - .017700\,t^2 - .0015486\,t^3 + .0012837\,t^4 - .000081710\,t^5 + .000022264\,t^6 - .65680\,10^{-7}\,t^7 - .80860\,10^{-8}\,t^8 - .30621\,10^{-11}\,t^9 + .21271\,10^{-12}\,t^{10}$$

$$v(t) \approx .27800\,t - .047770\,t^2 + .0053372\,t^3 - .00048248\,t^4 + .000044043\,t^5 - .19782\,10^{-5}\,t^6 - .10258\,10^{-7}\,t^7 + .14663\,10^{-10}\,t^8 + .45016\,10^{-12}\,t^9$$

Case 2.

$$s(t) \approx .8 - .29200\,t + .053160\,t^2 - .0020121\,t^3 - .00074345\,t^4 + .8412\,10^{-5}\,t^5 - .000034049\,t^6 - .13371\,10^{-5}\,t^7 + .38988\,10^{-7}\,t^8 + .92776\,10^{-9}\,t^9 - .68065\,10^{-11}\,t^{10}$$

$$i(t) \approx .2 + .044000\,t - .015600\,t^2 - .0016611\,t^3 + .0010447\,t^4 - .000035445\,t^5 + .000033624\,t^6 + .13689\,10^{-5}\,t^7 - .38481\,10^{-7}\,t^8 - .93496\,10^{-9}\,t^9 + .68065\,10^{-11}\,t^{10}$$

$$v(t) \approx .24800\,t - .037560\,t^2 + .0036732\,t^3 - .00030128\,t^4 + .000027037\,t^5 - .58733\,10^{-6}\,t^6 - .31877\,10^{-7}\,t^7 - .50668\,10^{-9}\,t^8 + .72028\,10^{-11}\,t^9$$

Case 3.

$$s(t) \approx .8 - .14200\,t + .021370\,t^2 - .0009955\,t^3 - .0000420\,t^4 - .000016750\,t^5 - .000076663\,t^6 - .000014433\,t^7 + .14208\,10^{-5}\,t^8 + .14524\,10^{-6}\,t^9 - .35752\,10^{-8}\,t^{10}$$

$$i(t) \approx .2 + .044000\,t - .005100\,t^2 - .0008346\,t^3 + .0002104\,t^4 + .329\,10^{-5}\,t^5 + .000075279\,t^6 + .000014760\,t^7 - .13974\,10^{-5}\,t^8 - .14632\,10^{-6}\,t^9 + .35752\,10^{-8}\,t^{10}$$

$$v(t) \approx .098000\,t - .016270\,t^2 + .0018302\,t^3 - .00016848\,t^4 + .000013477\,t^5 + .37140\,10^{-6}\,t^6 - .32556\,10^{-6}\,t^7 - .23331\,10^{-7}\,t^8 + .10809\,10^{-8}\,t^9$$

Case 4.

$$s(t) \approx .8 - .11200\,t + .012660\,t^2 - .0001791\,t^3 - .0000252\,t^4 - .000015737\,t^5 - .000079964\,t^6 - .000018866\,t^7 + .19366\,10^{-5}\,t^8 + .25825\,10^{-6}\,t^9 - .69703\,10^{-8}\,t^{10}$$

$$i(t) \approx .2 + .044000t - .003000t^2 - .0007791t^3 + .0001072t^4 + .979\,10^{-5}\,t^5 + .000078145t^6 + .000019273t^7 - .1900510^{-5}\,t^8 - .2600910^{-6}\,t^9 + .6970310^{-8}\,t^{10}$$

$$v(t) \approx .068000\,t - .0096600\,t^2 + .00095820\,t^3 - .000082052\,t^4 + .5945\,10^{-5}\,t^5 + .80401\,10^{-6}\,t^6 - .40698\,10^{-6}\,t^7 - .36133\,10^{-7}\,t^8 + .18440\,10^{-8}\,t^9$$

Appendix 2: MAPLE program used in chapter 3 problem.

```
# Note that L = Pi, r = P, b1 = beta1, b2 = beta2, g = gamma, d1 = delta
# s(t) represents proportion of susceptible group (_______)
# i(t) represents proportion of infected group (ooooooo)
# v(t) represents proportion of vaccinated treated group(++++++)
#Please kindly change the parameters according to the four cases in the attached table and
#plot the graph, then write a note to explain each graph.
```

```
with(plots):
L:= 0.4: d1:= 0.05: b1:= 0.3: b2:= 0.1: r:= 0.9: g:= 0.04:
fcns:={s(t),i(t),v(t)}:
sys:=diff(s(t),t)=(1-r)*L-b1*s(t)*i(t)+d1*v(t)-L*s(t),diff(i(t),t)=(b1*s(t)+b2*v(t)-g -
L)*i(t),diff(v(t),t)=(r-v(t))*L+(g-b2*v(t))*i(t)-d1*v(t):
p:= dsolve({sys,s(0)=0.9,i(0)=0.1,v(0)=0},fcns,type=numeric):
p1:=odeplot(p,[t,s(t)],0..30,numpoints=50,labels=["time (t)","Population
fraction"],title=(`Diseases transmission model`),style=line,color=black):
p2:=odeplot(p,[t,i(t)],0..30,numpoints=50,labels=["time (t)","Population
fraction"],title=(`Diseases transmission model`),style=point,symbol=circle,color=black):
p3:=odeplot(p,[t,v(t)],0..30,numpoints=50,labels=["time (t)","Population
fraction"],title=(`Diseases transmission model`),style=point,symbol=cross,color=black):
plots[display]({p1,p2,p3});
```

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