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A Vaccination Model For Seasonal Influenza Infection Dynamics

Research Report in Mathematics, Number 9, 2021

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July 2021

Submitted to the School of Mathematics in partial fulfilment for a degree in Master of Science in Applied Mathematics

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Master Thesis

Submitted to the School of Mathematics in partial fulfilment for a degree in Master of Science in Applied Mathematics

Submitted to: The Graduate School, University of Nairobi, Kenya

Abstract

The goal of this project, is to study using Mathematical Modelling, the impact of immunization with a partially effective vaccine on the transmission dynamics of influenza infection. To determine condition under which an epidemic occur. If it occur, what fraction of a even-mixed population get infected. To predict future spread of disease. To come up with plan for containment and eradication.

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Declaration and Approval

I the undersigned declare that this dissertation is my original work and to the best of my knowledge, it has not been submitted in support of an award of a degree in any other university or institution of learning.

25/July/2021

Signature Date

ANTONY MURIMI
Reg No. I56/11463/2018

In my capacity as a supervisor of the candidate's dissertation, I certify that this dissertation has my approval for submission.

04/08/2021

Signature Date

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Dedication

This project is dedicated to me. My dear brother Gedion (Kanunga High). My students, colleagues and friends in the field of Mathematics.

Contents

Acknowledgments

First, I thank my supervisor Dr. Victor Ogesa Juma for being there for me in any help and support I needed. I want to recognize Dr. Were for his professional teaching methodology to deliver content and thoroughly covering the syllabus. I want to acknowledge Dr. Nyandwi for professional and parental advice, and more so supporting Mathematics as a career to be respected and recognized. I want also to salute Professor Pokharial with his commitment and support on matters relating to studies. I want to acknowledge our former director Professor Weke with his humor, undiscriminating and encouragement to us as a department. ....

Antony Murimi

Nairobi, 2020.

1 Introduction

1.1 Influenza

1.1.1 Definition and meaning of INFLUENZA

Influenza, also called **flu** or **grippe**, an acute viral infection of the upper or lower respiratory track that is marked by fever, chills, and a generalized feeling of weakness and pain in the muscles, together with varying degrees of soreness in the head and abdomen. The most common symptoms include: high fever, runny nose, sore throat, muscle and joint pain, headache, coughing, and feeling tired[5]. These symptoms typically manifest two days after exposure to the virus and at most last less than a week. The cough, however, may last for more than two weeks[5]. In children, there may be **diarrhea** and vomiting, but not common in adults[6]. Diarrhea and vomiting occur commonly in gastroenteritis, which is an unrelated disease and sometimes inaccurately referred to as "stomach flu" or the "24-hour flu"[6].

1.1.2 Signs and Symptoms

Seasonal influenza is manifested by a sudden fever, headache, dry coughing, muscle and joint pain, severe malaise, sore throat and a runny nose. The cough can last at least 14 days. Majority recuperate within seven days without requiring medical attention. This disease can lead to illness or death especially in people at high risk. Illnesses range from mild to severe and to even death. High risk groups has high chance of getting infected and die. The annual epidemics are approximated to result about 3 to 5 million cases of severe illness, and about 290 000 to 650 000 respiratory deaths. Most deaths caused by influenza happens among people age 65 or older[5]. Epidemics leads to worker/school absenteeism and loss in productivity. Health facilities are overwhelmed greatly.
Research conduct estimated 99% of fatality is among the children under 5 years with influenza related lower respiratory tract infections are found in developing countries[7]. The effects of seasonal influenza epidemics in developing countries are not fully known

1.1.3 The Pathogen (Causes and Types)

Influenza is caused by viruses and transmitted through air.Influenza A and B viruses circulate and are responsible for seasonal epidemics of disease.[7], [8]

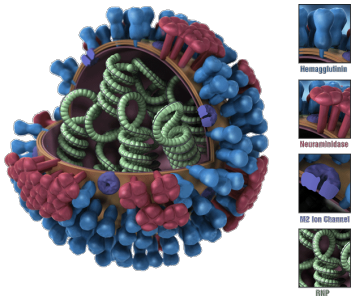

Figure 1. FLU VIRUS

- Influenza A viruses are classified into subtypes on the basis of two surface antigens (foreign proteins) combinations — hemagglutinin (HA) and the neuraminidase (NA), the proteins on the surface of the virus. Currently circulating in humans are subtype A(H1N1) and A(H3N2) influenza viruses known to have caused pandemics. Influenza A virus can be transmitted from wild birds to other species. This causes outbreaks in domestic poultry which spread into human influenza pandemic.
- Influenza B viruses are not classified into subtypes, but can be broken down into lineages. Currently circulating influenza type B viruses belong to either B/Yamagata or B/Victoria lineage.
- Influenza D viruses primarily affect cattle and are not known to infect or cause illness in people.

1.1.4 Global effect of influenza

Social impacts include intangible costs such as, domestic violence, behavoiral change, social interaction, pain, depression, suffering and impaired quality of life. Locally, misdiagnosis of influenza viruses and other respiratory viruses contributes to misuse of antimalarial and an, behavoiral change, social interaction, pain, depression, suffering and impaired quality of life. Locally, misdiagnosis of influenza viruses and other respiratory viruses contributes to misuse of antimalarial and antibiotic drugs. Europe and America research shows that if immunization programs target children under two years and the elderly over 65 years, the cost of influenza infection could be reduced by over 50%.

1.2 Influenza pandemics

Influenza pandemics are approximated to occur in intervals of half milenium. Epidemics are more frequent, and occurs in most parts of the world per year. Pandemic affecting the world can happen within a matter of months due to an antigenic shift. The influenza virus has led to repeated epidemics of great febrile syndrome every 1 to 4 years during the recent centuries. The initial epidemic report of an influenza-like illness was experienced in 1173–74, [**?**] but the first definite epidemic was reported in 1694 [9].

1.2.1 Case Study

The following list discussed but not least, shows some of the pandemics experienced in history.

The Spanish flu pandemic of 1918 – 19.

This was the most severe outbreak of the 20th century with greatest numbers of mortality, among the devastating pandemics in human history. This affected mostly children and elderly with low immunity. This killed approximate 40–50 million deaths according to recent research.

The Asian flu pandemic of 1957

This outbreak of influenza was first identified in February 1957 in East Asia and that in sequence spread to countries worldwide. It was the second major influenza pandemic to occur in the 20th century. The 1957 outbreak was caused by influenza A subtype H2N2, or Asian flu virus [1, 3]. Research has indicated that this virus was a reassortant strain, originating from strains of avian influenza and human influenza viruses. In the 1960s the human H2N2 strain underwent a series of minor genetic modifications, a process known as antigenic drift. The little alterations produced occasional epidemics. Months later, several cases of infection were reported, especially in young children, the elderly, and pregnant women as a results of second pandemic wave of illness that struck the Northern Hemisphere in November 1957 and was also already widespread in the United Kingdom. By December a total of some 3,550 deaths had been reported in England and Wales. The second wave was particularly devastating, and by March 1958 an estimated 69,800 deaths had occurred in the United States[1, 2, 4].

Table 1 refers to the AntigenShift and the Pandemics involved.

Year	Designation	Viral Strain	Death Toll
1189		H3N2	—
1918	Spanish flu Pandemic	H1N1 (A/Brevig Mission/1/18; A/South Carolina/1/18; and A/New York/1/18)	50 - 100 million
1957	Asian flu Pandemic	H2N2 (A/Singapore/1/57)	1 million
1968	Hong Kong flu Pandemic H3N2	H3N2 (A/NT/60/68; and A/Hong Kong/1/68)	1 million
1977	Pandemic in children and young adults (Russian flu)	H1N1 (A/USSR/90/77)	–
2001-2002	USA, Canada, Singapore, Malaysia, Egypt, Europe.	H1N2 (A/New Caledonia/20/99 H1 and A/Moscow/10/99 N2)	–
2001-2002	Northern Italy	Influenza B (B/Victoria/2/87)	—
2001-2002	St. Elisabeth Hospital, Tilburg	H3N2 (A/Sydney/5/97)	–
2003	Poultry Farm in Netherlands	H7N7 (Avian Influenza A)	–
2003-2004	USA, Canada, Europe, Japan	H3N2 (A/Fujian/411/2002)	–

Table 1. Antigen Shift and Pandemics

1.3 Vaccination

1.3.1 Meaning

This is the vaccine inoculation to protect from a particular strain of disease. It is dependent on the immune status of the recipient. The ideal way to protect people from influenza is to administer vaccinations annually.

1.3.2 Types of vaccines

Each is designed to train the immune system how to combat certain types of germs — and the serious effects they cause. Depending on a list of factors, researchers chose the kind of vaccine they will produce. The main types of vaccines:

- Live-attenuated vaccines.
- Inactivated vaccines.
- Subunit, recombinant, polysaccharide, and conjugate vaccines.
- Toxoid vaccines 2.

1.4 Epidemiology and Target Group

Influenza is easily spread, mainly in areas with many people including institutions and nursing places. Frequent hand washing, covering mouth and nose with face masks can prevent transmission. **Seasonal epidemics** spread mainly during winter in temperate climate, and throughout the year in tropical regions, leading to irregular outbreaks.

1.4.1 Expectant mothers

This is the group with high risk of contaminating with the disease. They require immunization to avoid the negative impact to the unborn. They are also very weak at this season hence exposing them into high risk of getting sick. Conclusion: Expectant mothers should be frequently checked and immunized regularly. This is to protect the mother and the infants.

1.4.2 Children

Young children are susceptible to disease infections leading to burden associated with influenza with frequent clinic visits, hospitalizations and deaths compared to non-elderly adults. The vaccine effectiveness among children varies. Inactivated vaccines are the best

vaccination programs below two years old. Those older than two years, best suit for either inactivated vaccine (IV) or live-attenuated vaccine (LAIV).

1.4.3 Elderly People

Influenza is a primary cause to high deaths among the elderly. High income countries have lower risk for elderly deaths than low income countries. The risk of morbidity and mortality in the elderly can be reduced with the use of inactivated vaccines. However the effectiveness reduces with ageing and among those with underlying medical conditions.

1.4.4 People with special health conditions

People with unhealthy conditions, such as cardiac disease, morbid obesity, chronic respiratory and compromised immune status, are more prone to develop fatal sickness due to influenza infection than healthy people of the same age group. Influenza vaccine effectiveness has been demonstrated among individuals with underlying health conditions in a number of settings. This group has been targeted for influenza vaccination, and continue to be an appropriate targeted group for vaccination. Identification of individuals is difficult due to stigma related issues.

1.4.5 HealthCare Workers

This group suffers high risk due to exposure, compared to the general population. Vaccinating this group is ideal and effective and increases work attendance. Healthcare workers vaccination not only protects the individual, but also sustain healthcare services during epidemics and protection of vulnerable patients.

1.5 Aim of the Project/objectives

Vaccination being as an effective strategy against infection, does not guarantee due to different immune status of individual. Seasonal drift in the viral genome, annual vaccination against the influenza virus strains anticipated to be in circulation during the upcoming season is necessary to prevent new infections and subsequent outbreaks. Failures: present influenza vaccine to protect all vaccine recipient warrant the determination.
Aim

- To unveil through Mathematical Modelling, the influence of a partially effective vaccine on the influenza infection transmission dynamics.
- To determine condition under which an epidemic happen.
- If it occur, what fraction of a uniform population get ill.

- Disease spreading forecasting.
- For strategic development to control and elimination.

This address question whether such vaccine can permanently terminate the disease spread. While Mathematical Model establish the strength of imperfect vaccine to tame influenza, having several models suggested for transmission dynamics of influenza, the impact of an imperfect vaccine hasn't been fully analyzed. The model aim to recruit susceptible individuals and infected individuals into the population.

2 LITERATURE REVIEW

2.1 LITERATURE REVIEW

The probability of recurrent flu pandemic has emerged. This will be a result of high pathogenic avian influenza A (HPAI) subtype H5N1 virus in Southeast Asia, the Middle East of Africa and other countries around the world [13] Currently it's still in question whether there is human-to-human transmission of H5N1. If it really occurs and there is no preparedness against the pandemic, H5N1 would spread worldwide through the global transportation network. Due to the fear that a mutant avian influenza may occur, interest in the study of pandemic H5N1 flu has increased significantly. Thus in many nations, preparedness against the pandemic H5N1 flu has become a high priority public health issue. To have the pandemic preparedness plans that maximize realism, generality and precision, the design of such plans and the effects of different intervention strategies, such as quarantine and vaccination, need to be investigated. To curb the outbreak of H5N1 in the beginning it was to isolate humans infected with mutant avian influenza, in order to reduce transmission to susceptible group. Once the disease has occurred, vaccine can be developed. To curb the spread of H5N1 effectively, understanding the behavioral patterns of the disease spreading is paramount. Recently, epidemic models plays an important role for the pandemic readness plans because it allows one to predict and compare the effects of different intervention strategies. However, it has been recognized that the uncertainty in predictions of the epidemic model cause the uncertainty in prediction of disease spread and public health responses.

Over the last two decades, a number of epidemic models for predicting the spread of influenza through human population have been proposed based on either the classical susceptible-infected-removed (SIR) model [14, 15, 16] developed by Kermack and McKendrick [23] or the classical susceptible-exposed-infected-removed (SEIR) model [17, 18, 19, 20, 21] developed by Rvachev and Longini [22]. It has long been recognized that using any epidemic model having inaccurate values of the parameters in the model will lead to wrong predictions of the spread of the disease and therefore to inappropriate public health responses.

Many disease modelings make assumption of constant or asymptotically constant total population. The following are the examples of models used before.

2.1.1 The SI Model

This categorize people as either susceptible or infective (SI). Assumption in the model is that people under the study are well mixed up, with equal probability of contacting with every other person. The transfer diagram and its differential equation is as follow;

$$\frac{dI}{dt} = \beta\ SI \tag{1}$$

where β is the probability that an infective person infect a random susceptible person.

2.1.2 The SIR Model

The SIR model developed by Kermack and McKendrick is more general and include a closed population, without considering immigrants during the plague. The assumption made was constant population with exemption to demographic process. By extending the model of ordinary differential equations [23] to fluctuating population (with birth and death) Anderson and May (1979) [24] brought the Kermack-McKendrick model back to prominence after decades of neglect.

The **SIR** Model is comprised of three groups:
Susceptible (S),
Infected (I) and
recovered (usually) with lifelong immunity (R) Model Assumptions.

The differential equations are;

$$s' = -\beta si \tag{2a}$$
$$d' = \beta si - vi \tag{2b}$$
$$r' = vi \tag{2c}$$

where, $s = \frac{S}{N}, i = \frac{I}{N}, r = \frac{R}{N}$
β effective contact rate.

2.1.3 A SEIQR MODEL FOR PANDEMIC INFLUENZA

In this research, first proposes a pandemic influenza susceptible (S), exposed(E),infected(I), quarantined (Q) and recovered (R) (SEIQR) model and analyze the model properties.

Mathematical model.

$$S' = A - \frac{\beta S(E+I)}{N} - dS \tag{3a}$$
$$E' = \frac{\beta S(E+I)}{N} - (d+\alpha+\kappa)E \tag{3b}$$
$$I' = \alpha E - (d+\delta+\gamma)I \tag{3c}$$
$$Q' = \delta I - (d+\varepsilon)Q \tag{3d}$$
$$R' = \kappa E + \gamma I + \varepsilon Q - dR \tag{3e}$$

The recruitment-death demographic structure in model (1) is such that;

$$N' = A - dN(t) \tag{4}$$

2.1.4 The SIRV model.

The practical strategies in disease models is important for public health authority intervention accessibility. The two major types of control curtails the infectious diseases extends: Pharmaceutical intervention (drugs, vaccine) and non-pharmaceutical interventions (social distancing, quarantine).

In this model SIRV stand for S-Susceptible, I-Infected and R is the number of individual who have recovered.

The system of differential equations derived are;

$$S' = bN - \frac{\beta IS}{N} - (d+\phi)S + \theta V \tag{5a}$$
$$I' = \frac{\beta IS}{N} + \frac{\sigma\beta IV}{N} - (\gamma+\mu+d)I \tag{5b}$$
$$V' = \phi S - \frac{\delta\beta IV}{N} - (d+\theta)V \tag{5c}$$
$$R' = \gamma I - dR \tag{5d}$$

The entire population $N=S+I+R+V$ is ruled by

$$N' = (b-d)N - \mu I \tag{6}$$

this is obtained on adding equations (5).

According to Murray Alexander of The University of Winnipeg, Arthur Randolph Summers of National Research Council Canada and Abba B. Gumel of Arizona State University, USA, the SIRV model recognizes that the recruitment is from a common population with some being Susceptible and others already infected individuals ($\prod$ - Recruitment rate of individuals).
The general transfer diagram is shown below:

Their system of differential equations are:

$$\tilde{S}' = (1-\varepsilon)\Pi + \tilde{\omega}\,\tilde{V} + \tilde{\delta}\tilde{R} - \tilde{\beta}\tilde{S}\tilde{I} - \tilde{\xi}\,\tilde{S} - \mu\tilde{S} \tag{7a}$$

$$\tilde{V}' = \tilde{\xi}\tilde{S} - (1-\sigma)\tilde{\beta}\tilde{V}\tilde{I} - (\tilde{\omega}+\mu)\tilde{V} \tag{7b}$$

$$\tilde{I}' = \varepsilon\Pi + \tilde{\beta}\tilde{S}\tilde{I} + (1-\sigma)\tilde{\beta}\,\tilde{V}\tilde{I} - (\tilde{\alpha}+\mu)\tilde{I} \tag{7c}$$

$$\tilde{R}' = \tilde{\alpha}\tilde{I} - (\mu+\tilde{\delta})\tilde{R} \tag{7d}$$

2.1.5 The SEIRD Model

This was developed by Chowell et al. [11, 12] and use the idea of variable transmission rate from the model formulated by Chong et al.[10]. The total population is divided into five groups namely: Susceptible (S), Exposed (E), Infectious (I), Recovered (R) and those who die from the disease (D). We assume a homogeneous mixing. We also assume a constant population with no natural births or deaths; this is because the influenza parameters occurs in days while death and birth parameters occurs in years hence they have little effect on the disease and can be ignored.

The system of differential equations are:

$$S'(t) = -\frac{\beta_1 SI}{N} - \frac{\beta_D SD}{N} \tag{8a}$$

$$E'(t) = \frac{\beta_1 SI}{N} + \frac{\beta_D SD}{N} - \frac{E}{T_E} \tag{8b}$$

$$I'(t) = \frac{E}{T_E} - \frac{I}{T_I} \tag{8c}$$

$$R'(t) = (1-f)\frac{I}{T_I} \tag{8d}$$

$$D'(t) = f\frac{I}{T_I} - \frac{D}{T_D} \tag{8e}$$

2

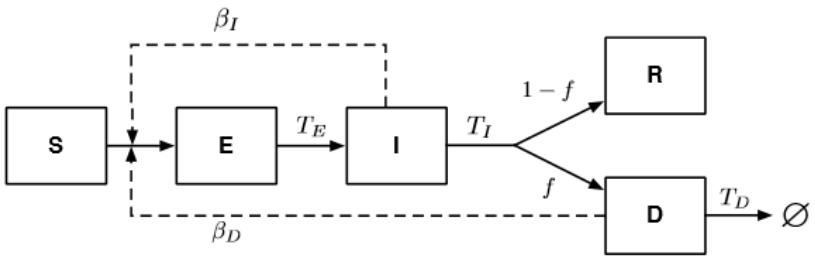

Figure 2. SEIRD

Chapter 3

3 DISCUSSION OF MODEL AND ASSUMPTION

3.1 FORMATION OF MODEL

To derive mathematical modeling equations, let total population be N. We partition the total population N into four compartments based on individual epidemiological status:

The Susceptible individuals are drawn or recruited from the closed population within a geographical region through immigration or by birth. These are individuals who have never been sick from Influenza before. The group can also increase from vaccinated group.This group declines through vaccination and then enters to vaccinated group. It also reduce through infection hence entering the infected one, and by normal death.

The vaccinated group is recruited through vaccination of susceptible one at the rate of ω. This group can decline in number as a result of vaccine losing efficacy and therefore enters infected stage or group. The vaccinated individual however, get infected at a lower rate $\xi\eta\frac{VI}{N}$ due to vaccine induced immunity. Also reduces through natural death dV. It declines through members entering the susceptible group.

The infected group accumulates from susceptible who get infected by the influenza virus $\xi\frac{SI}{N}$. Also it gains from vaccinated people whose immune has wane strength at a lower rate. The population decline through natural death dI and death due to infections δ I. This group can also reduce through recovery of infected at the rate of γ. Hence transiting to group R.

The recovered group increases from infected individuals as a result of gaining natural immunity and at the same time decline through natural death dR.

The individuals recruited are from a closed population. The newly recruited susceptible individuals is either by birth or/and immigration $A = bS_0$, where b represent natural birth and S_0 represent the initial susceptible value. The identified susceptible must undergo testing to isolate for treatment as infected individuals (I) or group them for vaccination class (V). Therefore, all recruited individuals are considered susceptible until after testing anybody can be considered infected.

The vaccination class gains through testing of susceptible who turns out negative. The group reduces by moving to infected class due to waning of vaccine and also as a results

of natural death and emigration **dV**. The vaccinated individual as their vaccine induced immunity fails may pass to susceptible class .

The number of infected individuals is gained through testing of individuals from susceptible class and vaccinated individuals at a low rate due to waning of vaccine. The individuals are treated and moved to recovery (R) class as they've acquired natural immunity through infection. This group can also reduce through natural death **dI** or death due to influenza infection δI. The parameter **d** represent emigration and natural death due to age, accidents or other infections while δ represent the rate of death due to influenza.

Individual contaminate an average of ψ other individuals per unit time.

The total number of people contacted by effective per unit time is ψI. Proportion ν of contacts are effective in transmitting disease. The recovery group is gained from treated infected individuals. It reduces through natural death **dR**.

Induced immunity by infection is assumed to confer total cross immunity in all strains. The vaccine protects against a fraction of infections of other strains, but at much lower infection.

The total population N change as a results of natural birth in addition to disease induced death or other deaths. This creates instability in the increase and reduction of a specified population and it will vary with time.

The susceptible or vaccinated rate of infection is $\xi \frac{IS}{N}$ ($\xi \frac{IV}{N}$) where the transmission coefficient is ξ = V Ψ

Susceptible are vaccinated at the rate of ω Vaccinated become infected at low rate of η ξ and 1-η ε [0, 1] describe the efficacy of the vaccine.

When η=0 the vaccine is effective perfectly. When η=1 the vaccine is not effective.

Vaccination effectiveness is assumed to decline at the rate of α Vaccinated individuals are protected at the average of $\frac{1}{\alpha}$ time units. λ is decrease recovery rate from infected.

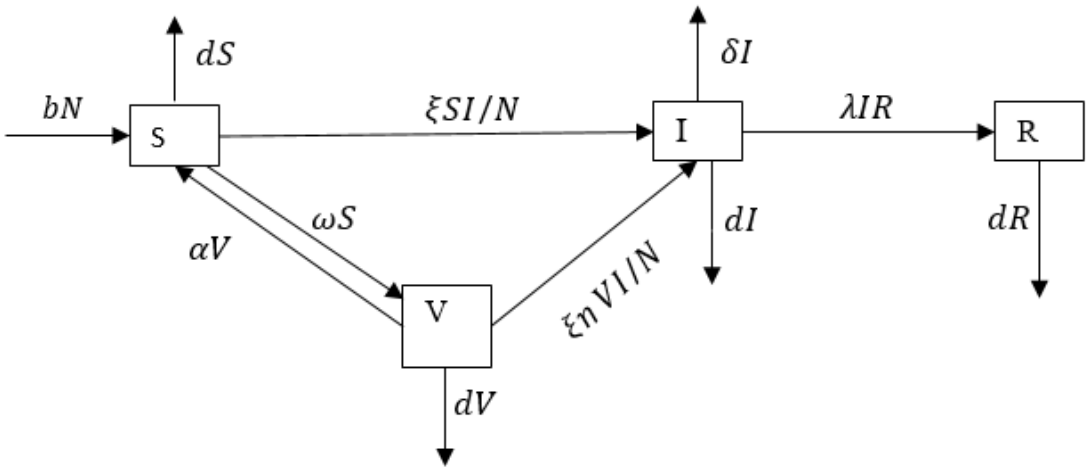

Figure 3. SVIR model showing the transfer of individuals from one group to another in a clossed population.

The system of differential equations are:

$$\frac{dS}{dt} = bN + \alpha V - \xi \frac{IS}{N} - \omega S - dS \tag{9a}$$

$$\frac{dI}{dt} = \xi \frac{IS}{N} + \xi \eta \frac{VI}{N} - \delta I - \lambda I - dI \tag{9b}$$

$$\frac{dV}{dt} = \omega S - \alpha V - dV - \xi \eta \frac{VI}{N} \tag{9c}$$

$$\frac{dR}{dt} = \lambda I - dR \tag{9d}$$

The total population N is N=I + S + V + R

$$\begin{aligned} \frac{dN}{dt} = bN + \alpha V - \xi \frac{IS}{N} - \omega S - dS + \xi \frac{IS}{N} + \xi \eta \frac{VI}{N} - \delta I - \lambda I \\ - dI + \omega S - \alpha V - dV - \xi \eta \frac{VI}{N} + \lambda I - dR \end{aligned} \tag{10}$$

$$\frac{dN}{dt} = bN - dS - \delta I - dI - dV - dR \tag{11}$$

$$\frac{dN}{dt} = bN - d(S+I+V+R) - \delta I \tag{12}$$

$$\frac{dN}{dt} = (b-d)N - \delta I \tag{13}$$

Table 2 refers to the parameters used, symbols, units and their meaning.

Parameters	Units	Meaning
ξ	Time	Rate at which Susceptible get infected
η	Time	Rate of infection as a result of loosing immunity
δ	Time	Rate of death caused by infection
ω	Time	Vaccination Rate of susceptible
α	Time	Rate at which vaccinated loose immunity and enter into susceptible class
λ	Time	Rate at which infected recover as a result of developing and acquiring natural immunity

Table 2. Parameters and their respective symbols.

Chapter 4

4 MATHEMATICAL MODEL ANALYSIS

4.1 Non-dimensionalization

From previous topic, I am going to analyze the system we normalize by defining new variable or parameters through dimensionless transformation.

$$S+V+I+R=N \tag{14}$$

Dividing all terms by N we see that;

$$\frac{S}{N}+\frac{V}{N}+\frac{I}{N}+\frac{R}{N}=1 \tag{15}$$

Let $\frac{S}{N}$ = s, $\frac{V}{N}$ = v, $\frac{I}{N}$ = i, $\frac{R}{N}$ = r, it shows that s + v + i + r=1
that is the total population N = 1.
The total birth is equal to deaths due to infection and natural death.

$$bN = dS+dV+dI+dR+\delta I \tag{16}$$

But N=S+V+I+R

$$b = d+\delta i \tag{17}$$

Consider $\frac{S}{N}$=s or S=sN equation(9) becomes;

$$N\frac{ds}{dt} = bN+\alpha V-\xi\frac{IS}{N}-\omega S-dS \tag{18}$$

Dividing each term by N we obtain;

$$\frac{ds}{dt} = b+\alpha v-\xi is-\omega s-ds \tag{19}$$

But since d=b-δ i we substitute d for b above.

$$\frac{ds}{dt} = b+\alpha v-\xi si-(\omega+b)s+\delta is \tag{20}$$

Similarly, I=iN, taking derivative on both sides we can non-dimensionlize equation (9) to obtain;

$$N\frac{di}{dt} = \frac{dI}{dt} \tag{21a}$$

$$N\frac{di}{dt} = \xi\frac{IS}{N} + \xi\eta\frac{VI}{N} - \delta I - \lambda I - dI \tag{21b}$$

Dividing each term by N, we obtain:

$$\frac{di}{dt} = \xi is + \xi\eta vi - \delta i - \lambda i - di \tag{22}$$

But d=b-δ i, therefore the above expression will become

$$\frac{di}{dt} = \xi is + \xi\eta vi - \delta i - \lambda i - (b - \delta i)i \tag{23a}$$

$$\frac{di}{dt} = \xi is + \xi\eta vi - (\delta + b + \lambda)i + \delta i^2 \tag{23b}$$

We now non-dimensionalize equation (9) by considering V=vN.

$$N\frac{dv}{dt} = \frac{dV}{dt} \tag{24a}$$

$$N\frac{dv}{dt} = \omega S - \alpha V - dV - \xi\eta\frac{VI}{N} \tag{24b}$$

We divide all terms by N and at the same time substitute d for b in (4.1) to obtain;

$$\frac{dv}{dt} = \omega s - \alpha v - dv - \xi\eta vi \tag{25a}$$

$$\frac{dv}{dt} = \omega s - \alpha v - (b - \delta i)v - \xi\eta vi \tag{25b}$$

We now non-dimensionalize equation (9)
Since, Nr=R, then;

$$N\frac{dr}{dt} = \frac{dR}{dt} \tag{26a}$$

$$N\frac{dr}{dt} = \lambda I - dR \tag{26b}$$

Dividing all terms by N, we obtain;

$$\frac{dr}{dt} = \lambda i - dr \tag{27a}$$

$$\frac{dr}{dt} = \lambda i - (b - \delta i)r \tag{27b}$$

Hence, the s, v, i and r satisfies the normalized system below;

$$\frac{ds}{dt} = b + \alpha v - \xi si - (\omega + b)s + \delta is \tag{28a}$$

$$\frac{di}{dt} = \xi is + \xi \eta vi - (\delta + b + \lambda)i + \delta i^2 \tag{28b}$$

$$\frac{dv}{dt} = \omega s - \xi \eta vi - (\alpha + b)v + \delta iv \tag{28c}$$

$$\frac{dr}{dt} = \lambda i - br + \delta ir \tag{28d}$$

In the next section we analyse the asymptotic behavior of model (28)

4.2 The Positive Invariant Compact Set

Theorem 4.2.1. *The compact positive invariant set is given by* $\Omega = \{(s,v,i) \in \mathbb{R}^3_+ \mid 0 \leq s + v + i \leq 1, s \geq 0, v \geq 0, i \geq 0\}$

Where $\mathbb{R}^3_+$ *is non-negative with the variable.*

We can substitute **r** from the equation to study the remaining system.
That is $\frac{dr}{dt}$=λi - br + δir
r=1-s-i-v
The parameter $\partial\Omega$ is the boundary and $\mathring{\Omega}$ the interior of Ω in R^3_+ respectively.
The set Ω is positively invariant with respect to the model system;

$$\frac{ds}{dt} = b - \xi si - (b + \omega)s + \alpha v + \delta si \tag{29a}$$

$$\frac{di}{dt} = \xi si + \eta \xi iv - (b + \delta + \lambda)i + \delta i^2 \tag{29b}$$

$$\frac{dv}{dt} = \omega s - \eta \xi iv - (b + \alpha)v + \delta iv \tag{29c}$$

4.3 The Basic Reproductive Number

This is the mean number of secondary infections produced by a typical primary infective individual into a completely susceptible population. This measures potential for the disease spread within the population. It is denoted by R_o. It is computed from the equation of next generation.

We define the dynamics of the model using equation (29) by obtaining the vector valued function f as the appearance rate of new infection in the disease groups.

$$\frac{di}{dt} = \xi si + \eta \xi iv - (b + \delta + \lambda)i + \delta i^2$$

$$\frac{dv}{dt} = \omega s - \eta\xi iv - (b+\alpha)v + \delta iv$$

$$f = \begin{bmatrix} I_n \\ V_n \end{bmatrix} \tag{30}$$

$$f = \begin{bmatrix} \xi si + \eta\xi iv - (b+\delta+\lambda)i + \delta i^2 \\ \omega s - \eta\xi iv - (b+\alpha)v + \delta iv \end{bmatrix} \tag{31}$$

At the disease free equilibrium, the computation of Jacobian matrix F is obtained as:

$$F = Jf = \begin{bmatrix} \frac{\partial f}{\partial i} & \frac{\partial f}{\partial v} \\ \frac{\partial f}{\partial i} & \frac{\partial f}{\partial v} \end{bmatrix} \tag{32}$$

$$F = Jf = \begin{bmatrix} \xi s + \eta\xi v + 2\delta i & \eta\xi i \\ \delta v & \delta i \end{bmatrix} \tag{33}$$

This jacobian matrix of f is at disease free equilibrium.

We now determine the transition vector V, given by;

$$v = \begin{bmatrix} (b+\delta+\lambda)i \\ (b+\alpha)v + \eta\xi iv - \omega s \end{bmatrix} \tag{34}$$

$$V = Jv = \begin{bmatrix} \frac{\partial v}{\partial i} & \frac{\partial v}{\partial v} \\ \frac{\partial v}{\partial i} & \frac{\partial v}{\partial v} \end{bmatrix} \tag{35}$$

$$V = \begin{bmatrix} b+\delta+\lambda & 0 \\ \xi\eta v & (b+\alpha)+\eta\xi i \end{bmatrix} \tag{36}$$

The next step is to determine th inverse of V i.e V^{-1}

$$V^{-1} = \frac{1}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} \begin{bmatrix} (b+\alpha)+\eta\xi i & 0 \\ -\eta\xi v & b+\delta+\lambda \end{bmatrix}$$

$$V^{-1} = \begin{bmatrix} \frac{(b+\alpha)+\eta\xi i}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} & 0 \\ \frac{-\eta\xi v}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} & \frac{b+\delta+\lambda}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} \end{bmatrix} \tag{37}$$

The next generation operator is given by FV^{-1}.

$$FV^{-1} = \begin{bmatrix} \xi s+\eta\xi v+2\delta i & \eta\xi i \\ \delta v & \delta i \end{bmatrix} \begin{bmatrix} \frac{(b+\alpha)+\eta\xi i}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} & 0 \\ \frac{-\eta\xi v}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} & \frac{b+\delta+\lambda}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} \end{bmatrix} \tag{38}$$

Thus R_o=J(FV^{-1}) and its;

$$R_o = J \begin{bmatrix} \xi s+\eta\xi v+2\delta i & \eta\xi i \\ \delta v & \delta i \end{bmatrix} \begin{bmatrix} \frac{(b+\alpha)+\eta\xi i}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} & 0 \\ \frac{-\eta\xi v}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} & \frac{b+\delta+\lambda}{[(b+\alpha)+\eta\xi][b+\delta+\lambda]} \end{bmatrix}$$

$$R_o = \frac{\xi s_o+\eta\xi v_o}{b+\lambda+\delta} = \frac{\xi(b+\alpha+\eta\omega)}{(b+\alpha+\delta)(b+\alpha+\omega)} \tag{39}$$

If R_o > 1, the endemic will occur, that is if an infected individual in an otherwise susceptible population will be in average infect more than one person. If R_o<1, there is no endemic and the disease is suppressed.

The R_o is the Threshold Parameter.

$$b-\xi si-(b+\omega)s+\alpha v+\delta si = 0 \tag{40a}$$
$$\xi si+\eta\xi iv-(b+\delta+\lambda)i+\delta i^2 = 0 \tag{40b}$$
$$\omega s-\eta\xi iv-(b+\alpha)v+\delta iv = 0 \tag{40c}$$

4.3.1 The Disease Free Equilibrium

Linearizing system at the equilibrium point e_o, we can determine the local stability .

$$J_o = \begin{bmatrix} \frac{\partial f_1}{\partial s} & \frac{\partial f_1}{\partial i} & \frac{\partial f_1}{\partial v} \\ \frac{\partial f_2}{\partial s} & \frac{\partial f_2}{\partial i} & \frac{\partial f_2}{\partial v} \\ \frac{\partial f_3}{\partial s} & \frac{\partial f_3}{\partial i} & \frac{\partial f_3}{\partial v} \end{bmatrix} = \begin{bmatrix} -(\xi-\delta)i-(b+\omega) & -\xi s+\delta s & \alpha \\ \xi i & \xi s+\eta\xi v+2\delta i & \eta\xi i \\ & -(b+\delta+\lambda)+\delta i & \\ \omega & -\eta\xi+\delta v & -\eta\xi i-(b+\alpha)+\delta i \end{bmatrix}$$

The cases of infections to be zero means the stabilty is;

$$J(e_o) = \begin{bmatrix} -(b+\omega) & -\xi s+\delta s & \alpha \\ 0 & \xi s+\eta\xi v-(b+\delta+\lambda) & 0 \\ \omega & -\eta\xi+\delta v & -(b+\alpha) \end{bmatrix}$$

When i=0 for free equilibrium for the disease is e_0 and it's given by;

$$e_0 := (s_0, i_0, v_0,) = (\frac{b+\alpha}{b+\alpha+\omega}, 0, \frac{\omega}{b+\alpha+\omega}) \tag{41}$$

This denote the disease free population, i=0. If $e_n := (s_n, v_n, i_n)$ is endemic equilibrium .

Therefore, $\frac{dr}{dt}$=λi - (b - δ i) r ; $\frac{dr}{dt}$ =0 ; λ i_n = r(b-δ i_n) > 0

This shows that 0<i_n<min {1, $\frac{b}{\delta}$}

Solving equations (29) gives;

$$s_n = \frac{b[(\eta\xi-\delta)i_n+b+\alpha]}{[(\eta\xi-\delta)i_n+b+\alpha][(\xi-\delta)i_n+b+\omega]-\omega\alpha} \tag{42}$$

$$v_n = \frac{b\omega}{[(\eta\xi-\delta)i_n+b+\alpha][(\xi-\delta)i_n+b+\omega]-\omega\alpha} \tag{43}$$

Therefore, i_n is a positive solution of the equation. The critical vaccination rate ω_c can be derived when R_o=1 in terms of ω

$$\omega_c = \frac{(b+\alpha)[\xi-(b+\delta+\lambda)]}{(b+\delta+\lambda)-\xi\eta} \tag{44}$$

4.3.2 THE GLOBAL DYNAMICS

The stability of desease free equilibrium globally jacobian matrix e_o is

$$J(e_o) = \begin{bmatrix} -(b+\omega) & -\xi s_o + \delta s_o & \alpha \\ 0 & \xi s_o + \eta \xi v_o - (b+\varepsilon-\delta) & 0 \\ \omega & -\eta \xi v_o + \delta v_o & -(b+\alpha) \end{bmatrix} \tag{45}$$

If R_o>1, there exist one eigen value (R_o - 1) and e_o is unstable. If again ω>ω_c all eigenvalues will be negative, implying that e_o is locally asymptotically stable. The solution of the set Ω is attracted to e_o when R_o<1

If $\xi \leq \delta$ or $\eta\ \xi \geq \delta$, i(t) converge at zero globally. The system for asymptotical for v(t), s(t) ;

$$\frac{ds}{dt} = b - (b+\omega)s + \alpha v \stackrel{\triangleright}{=} h_1(s,v) \tag{46}$$

$$\frac{dv}{dt} = \omega s - (b+\alpha)v \stackrel{\triangleright}{=} h_2(s,v) \tag{47}$$

Therefore, $\lim_{t\to\infty} s(t) = \frac{b+\alpha}{b+\alpha+\omega}$ $\lim_{t\to\infty} v(t) = \frac{\omega}{b+\alpha+\omega}$

Entire solution in Ω are attracted to e_o to get the following outcomes.

If R_o <1, the disease free equilibrium e_o is locally stable in Ω, if $\xi \leq \delta$ or $\eta\ \xi \geq \delta$, then e_o is globally asymptotically stable in Ω

4.3.3 ENDEMIC EQUILIBRIUM GLOBAL STABILITY

For the case e_n>1, the unique endemic equilibrium for global asymptotic stability can be determined. The Jacobian matrix for the system (29), at any point is;

$$J = \begin{bmatrix} \frac{\partial s'}{\partial s} & \frac{\partial s'}{\partial i} & \frac{\partial s'}{\partial v} \\ \frac{\partial i'}{\partial s} & \frac{\partial i'}{\partial i} & \frac{\partial i'}{\partial v} \\ \frac{\partial v'}{\partial s} & \frac{\partial v'}{\partial i} & \frac{\partial v'}{\partial v} \end{bmatrix} = \begin{bmatrix} -(\xi-\delta)i - b - \omega & -(\xi-\delta)s & \alpha \\ \xi i & \xi s + \eta\xi v + 2\delta i - b - \delta - \lambda & \eta\xi i \\ \omega & -(\eta\xi-\delta)v & -\eta\xi) + \delta i \end{bmatrix}$$

$$J^{(2)} = \begin{bmatrix} \xi s + \eta\xi v - \xi i & \eta\xi i & -\alpha \\ -(2b+\delta+\varepsilon+\omega)+3\delta i & & \\ -(\eta\xi-\delta)v & -\xi i - \eta\xi i + 2\delta i & -(\xi-\delta)s \\ & -(2b+\alpha+\omega) & \\ -\omega & \xi i & \xi s + \eta\xi v - \eta\xi i \\ & & -(2b+\delta+\lambda+\alpha)+3\delta i \end{bmatrix}$$

We therefore, take M=$\frac{1}{i}$ I_3, and $M_f\ M^{-1}$=[(b+δ+λ)-ξs-$\eta\xi$v-δi]I_3. I_3 is identity matrix of 3 by 3 and $M_f$is the directional vector of the system(29).

$$N = M_f M^{-1} + M J^{(2)} M^{-1} = \begin{bmatrix} -\xi i - (b+\omega) & \eta\xi i & -\alpha \\ +2\delta i & & \\ -\eta\xi v + \delta v & -\xi i - \eta\xi i + \delta i - \xi s - \eta\xi v & -\xi s + \delta s \\ & -(b+\alpha+\omega)+\delta+\lambda & \\ -\omega & \xi i & \eta\xi i - (b+\alpha) \\ & & +2\delta i \end{bmatrix}$$

If the linear homogeneous system $\frac{d\Sigma}{dt}$=NΣ, where Σ=(Σ_1, Σ_2, Σ_3) is the solution.

$$\frac{d\Sigma_1}{dt} = -\xi i + 2\delta i - (b+\omega)\Sigma_1 + \eta\xi i\Sigma_2 - \alpha\Sigma_3 \tag{48}$$

$$\frac{d\Sigma_2}{dt} = [-\xi i - \eta\xi i + \delta i - \xi s\eta\xi V + \delta + \lambda - (b+\alpha+\omega)]\Sigma_2 + (-\eta\xi V + \delta V)\Sigma_1 + (-\xi s + \delta s)\Sigma_3 \tag{49}$$

$$\frac{d\Sigma_3}{dt} = -\omega\Sigma_1 + \xi i\Sigma_2 + [-\eta\xi i + 2\delta i - (b+\alpha)]\Sigma_3 \tag{50}$$

Hence from equation (28) it proves that

$$\frac{s'(t)}{s} = \frac{b}{s} + \frac{\alpha v}{s} - \xi i - (\omega + b) + \delta i \tag{51a}$$

$$\frac{i'(t)}{i} = \xi s + \xi \eta v - (\delta + b + \lambda) + \delta i \tag{51b}$$

$$\frac{v'(t)}{v} = \frac{\omega s}{v} - \xi \eta i - (\alpha + b) + \delta i \tag{51c}$$

$$\frac{r'(t)}{r} = \frac{\lambda i}{r} - br + \delta i \tag{51d}$$

$$\delta i - b = \frac{r\prime}{r} - \frac{\lambda i}{r}\xi s - \eta \xi v = \frac{-i\prime}{i} + \delta i - (b + \lambda + \delta)$$

Thus $\eta\xi \geqslant \delta$ and ξ > b+δ+λ, to obtain

$$D_+\|Z\| \leqslant [-(b+\lambda)i + \frac{r\prime}{r} - \frac{\lambda i}{r}]|Z_1| + (\frac{r\prime}{r} - \frac{\lambda i}{r})|Z_3| + [\frac{-i\prime}{i} - 2(\frac{r\prime}{r} - \frac{\lambda i}{r}) - (\alpha + \omega)]|Z_2|$$

$$\leqslant max\{\ -(b+\lambda)i + \frac{r\prime}{r} - \frac{\lambda i}{r}, \frac{r\prime}{r} - \frac{\lambda i}{r} - \frac{i\prime}{i} + 2(\frac{r\prime}{r} - \frac{\lambda i}{r}) - (\alpha + \omega)\}\ \|Z\|$$

If φ is a sample closed orbit in Ω we have

$$\int_\varphi [-(b+\lambda)i + \frac{r\prime}{r} - \frac{\lambda i}{r}]dl \leq -\varpi$$

$$\int_\varphi (\frac{r\prime}{r} - \frac{\lambda i}{r})dl \leq -\varpi$$

$$\int_\varphi (\frac{-i\prime}{i} + 2(\frac{r\prime}{r} - \frac{\lambda i}{r}) - (\alpha + \omega)]dl \leq -2\varpi - A$$

where

$$\varpi = \int_\varphi \frac{\lambda i}{r})dl > 0$$

and

$$A = \int_\varphi (\alpha + \omega)dl > 0$$

Thus $\int_{\varphi} D_{+} \| Z \| dl \leq -\lambda \varpi < 0$

This proves existence of closed curve in Ω as a solution system of differential equation among periodic orbits, hormoclonic orbits and also heteroclinic cycle.

Chapter 5

5 NUMERICAL SIMULATION AND DISCUSSION

5.1 Numerical Simulation

The simulation of variables and numerical parameters of the systems of ODE's from chapter 3, indicates that the pandemic vanishes when the modified vaccination rate ω_i is below the normal vaccination rate $\omega_i<\omega$ and the disease persist at an endemic state when $\omega_i>\omega$ as the condition $\delta+\lambda<b+\alpha$ is satisfied.

The $\delta>\min\{ \lambda, b+\omega, b+\alpha-\lambda \}$ when the modified vaccination rate is greater than general vaccination ω.

The varied initial conditions for s,i and v indicates that numerically the disease can be still be endemic.

The global asymptotic stability at e_2 has a weaken conditions. When modified $\omega<\omega_i$ the system of ODE's results different dynamics.

The disease free equilibrium for global asymptotic stability doesn't acertain disease elimination. For global stabily $\omega<\omega_i$ a unique endemic equilibrium the diseasenmay vanish.

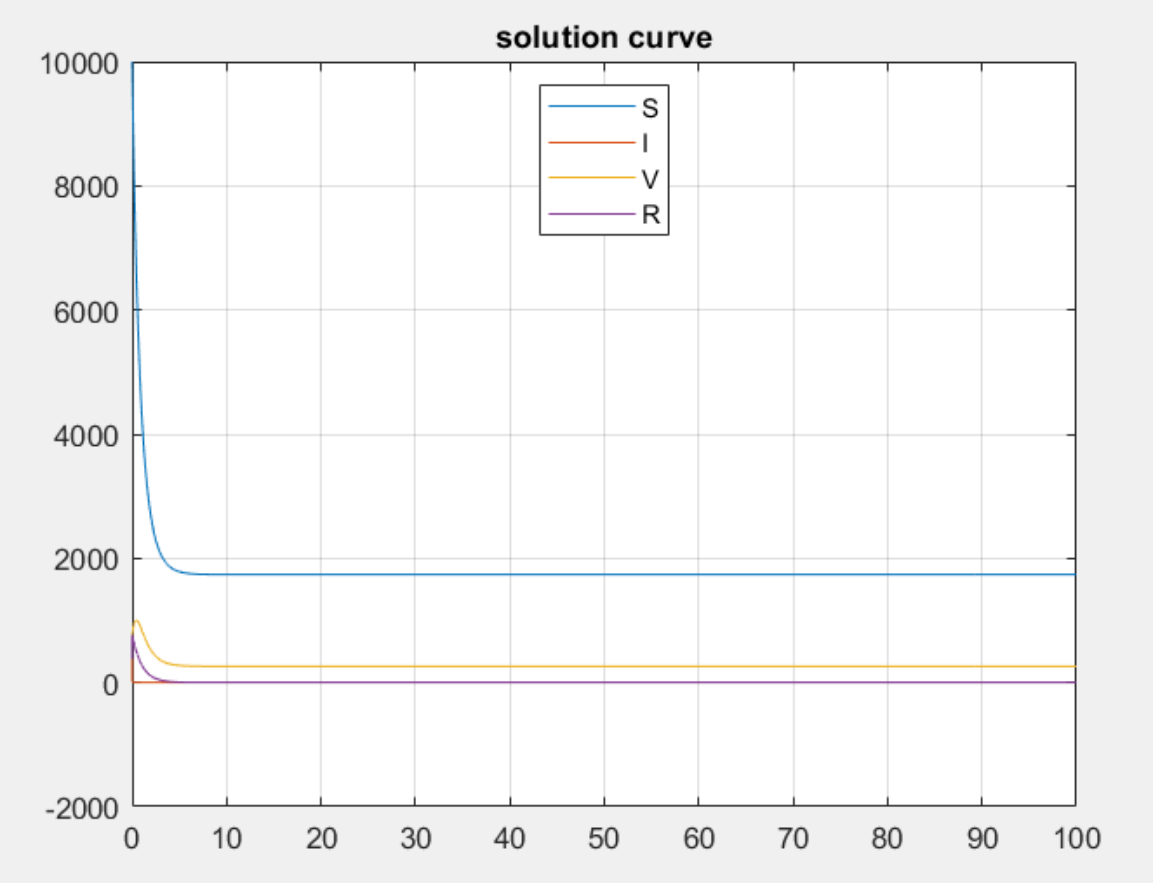

Figure 4. b=2 ξ=0.004, ω=0.300, α=1.00, λ=1.00, δ=0.500, η=0.100

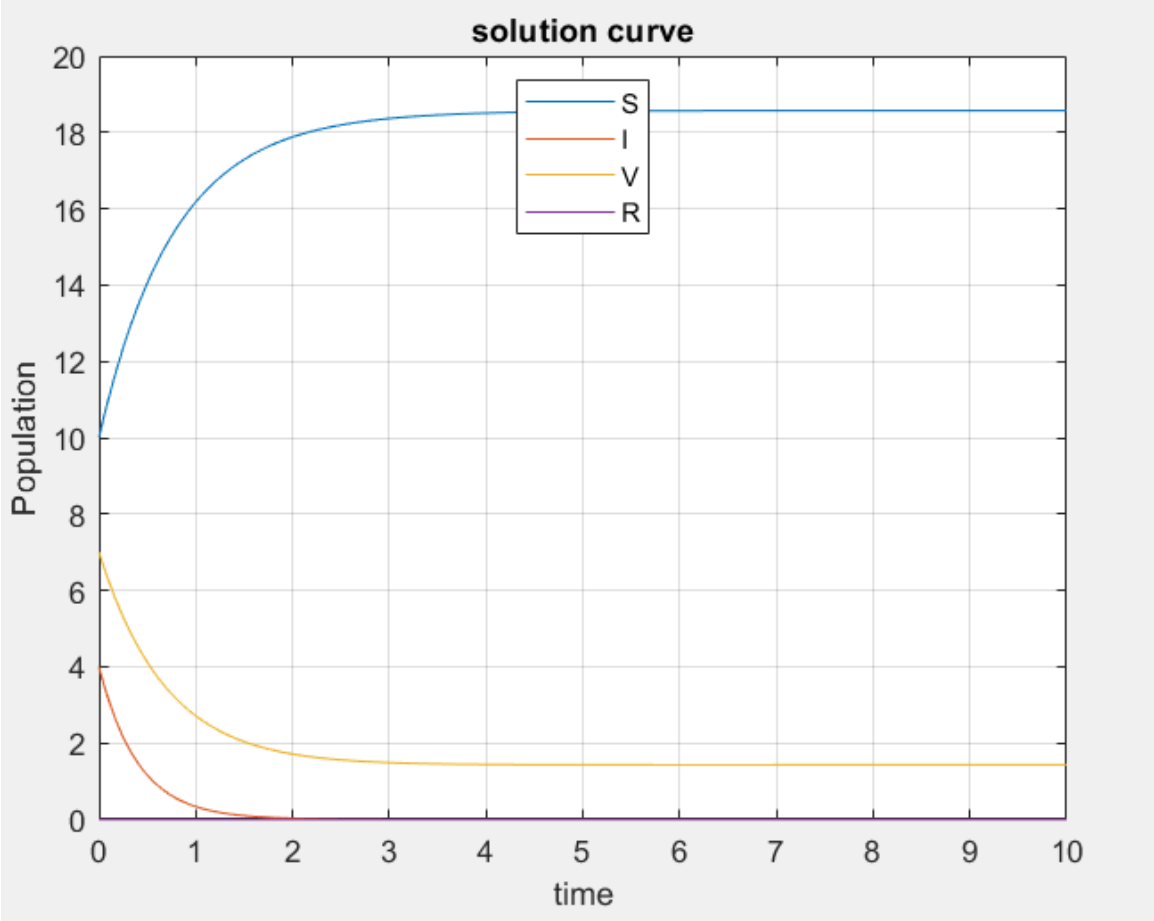

Figure 5. b=2 ξ=0.008, ω=0.100, α=0.300, λ=0.400, δ=1.500, η=0.500

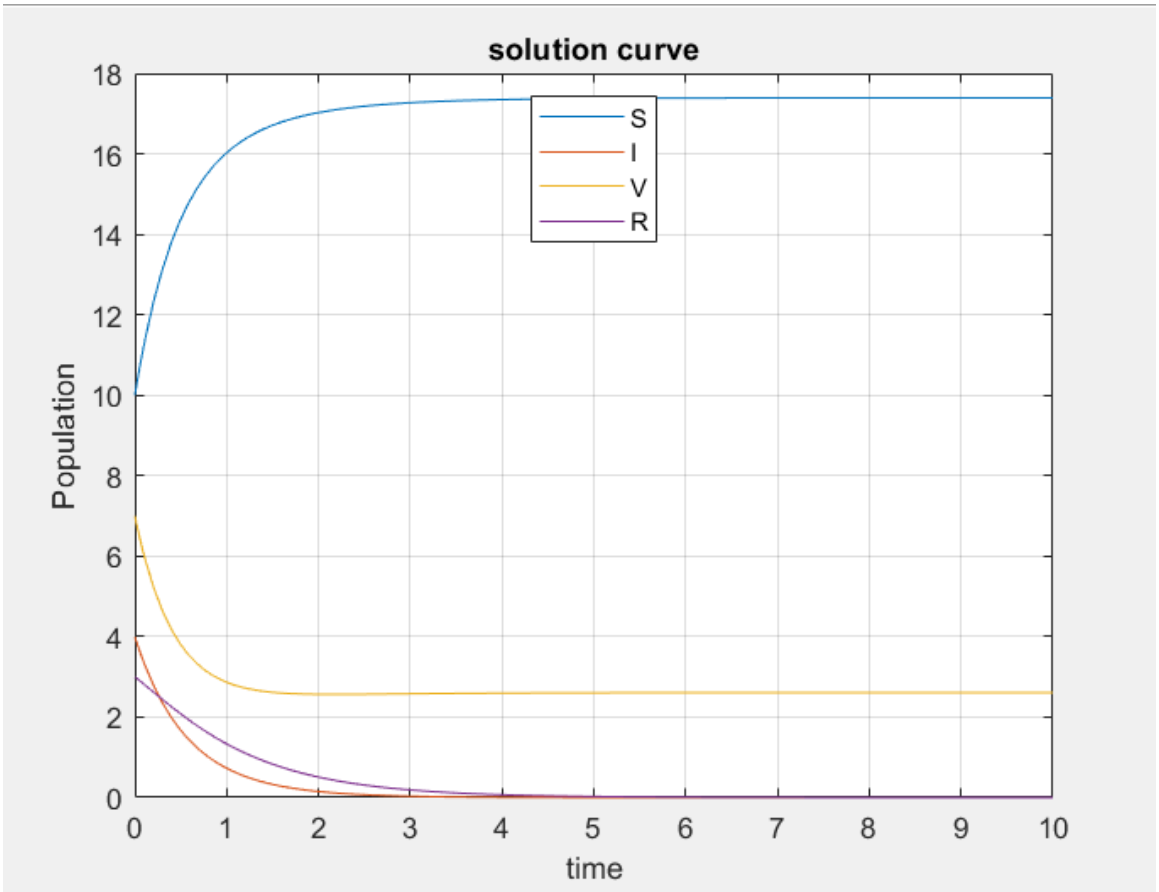

Figure 6. b=2 ξ=0.004, ω=0.300, α=1.00, λ=0.400, δ=0.500, η=0.100

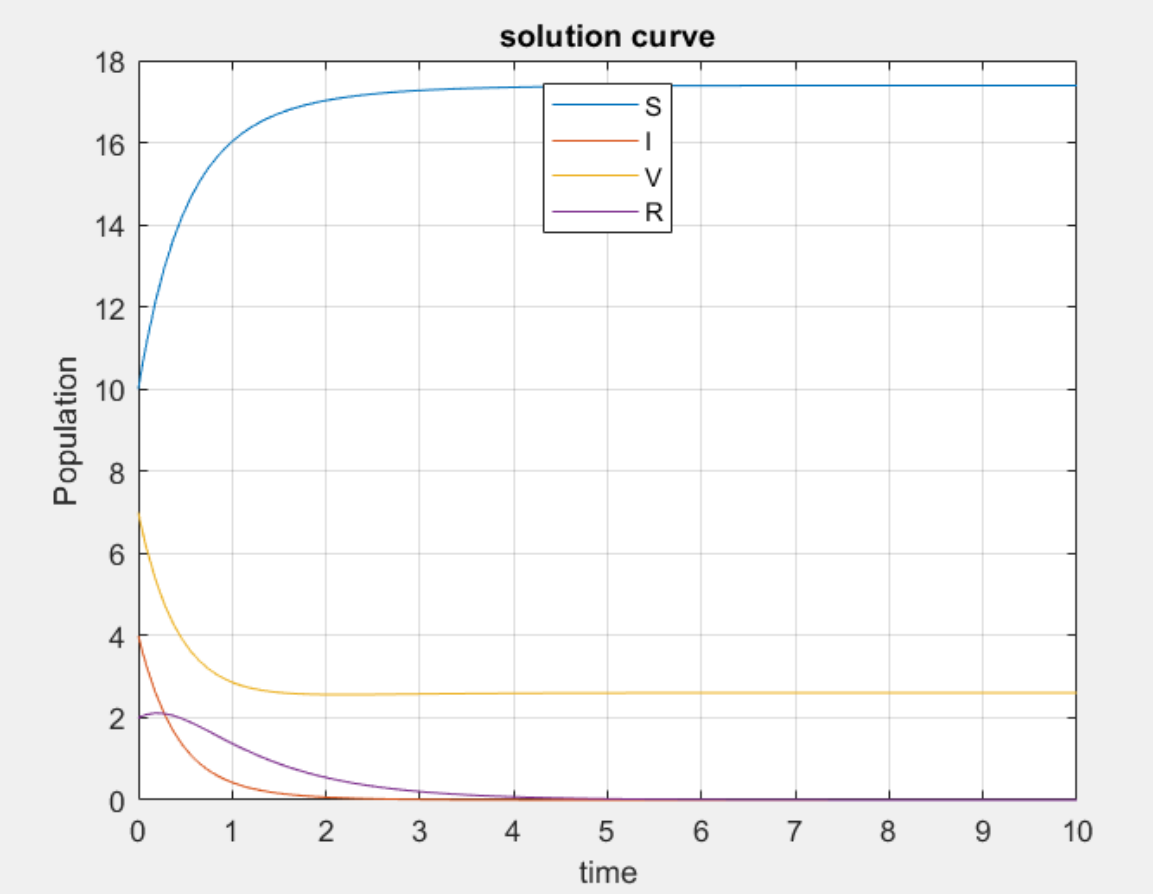

Figure 7. b=2 ξ=0.004, ω=0.300, α=1.00, λ=0.400, δ=0.500, η=0.100

6 DISCUSSION AND RECOMMENDATION

6.1 Discussion

The mathematical model was used to asses the relation between group parameters and influenza infections. The model of influenza as a 4-dimensional system of ordinary differential equations. The rate of infections reduces during hot seasons.

This study shows the dependency of influenza seasonality in Kenya to meteorological parameters. Influenza infection becomes high in the winter and during rainy season. An accurate data can help officials to facilitate best control measures for influenza epidemics, such as vaccination activities prior to the cold seasons and rainy seasons. Further studies are required to validate and justify the associations between influenza infections with rainfall and temperature in laboratory and epidemiology.

Thus confirming that the endemic equilibrium is globally asymptotically stable. Due to varying meteorological parameters, that is different average temperature and rainfall values. Therefore under same initial conditions, the influenza peak depend on temperature and rainfall of the region under consideration but this does not affect the point at which the endemic equilibrium is attained.

The reproduction number and influenza appear to increase or decrease simultaneously. This is a sure way of predicting for future climate change and rate of infections. The increase in Reproductive number indicate the increase in influenza infection. Also the infection reduces with reducing reproduction number.

Seasons can be used to predict the future infections and also helps in the preparedness for immunization. This helps the health workers and healthy facilities to be equipped in advance for control measure.

6.2 Recommendation

Seasons can be used to predict future infections. This can be used to plan and budget for the control measures and eradication of influenza.

The disease “fades out” for the reduced proportionate system when the vaccination rate exceeds critical point. Eradication of the disease needs increases effort in vaccination, else

the disease persist and spreading sporadically. Else, the flu will rapidly spread beyond the control in the long run.

Mathematical models should be applied to observe future outbreak and also for prediction of approximate number of infections for planning purposes.

These models can also be used to predict other disease outbreak in Kenya and Globally.

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