MODELLING INFLUENZA INCIDENCE IN RELATION TO METEOROLOGICAL PARAMETERS IN KENYA

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Modelling Influenza incidence in relation to meteorological parameters in Kenya

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A project submitted in partial fulfillment for a degree of Master of Science in Applied Mathematics

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Declaration

I the undersigned declare that this project report is my original work and to the best of my knowledge has not been presented for the award of a degree in any other University.

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Declaration by the supervisor

This project report has been submitted for examination with my approval as the supervisor.

Signature:.....

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Statement

This dissertation has been submitted in partial fulfillment of requirement for a Master of Science degree at the University of Nairobi and is deposited in the University Library to be made available to the borrowers under the rules of the Library

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Dedication

I dedicate this work to my wife Sophia Achieng and my two children Brantone Juma and Cheryl Juma

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Abstract

Meteorological parameters are believed to play a role in the influenza seasonality; influenza activities occurs sporadically all year round in the tropical regions with some peaks coinciding with rainy season and cold months. In this study, Influenza is modelled as a 5-dimensional deterministic system of ODEs with a variable transmission rate expressed as an exponential function of the meteorological parameters.

We analysed the model and established local and global stability of disease free and endemic equilibrium points, the equations are solved numerically in matlab using ODE23 solver

The findings show that an increase in rainfall leads to an increase in influenza infections in the following month and a decrease in temperature leads to an increase in the influenza infections. The transmission rate was approximated from the data and we found that the peaks in the reproduction number and influenza infections occurs almost simultaneously and similarly when the reproduction number decreases, influenza infections also decreases.

CHAPTER 1

Introduction

1.1 Influenza

1.1.1 Classification and causes of influenza

Influenza is a major cause of acute respiratory disease among humans and is associated with global pandemics and annual epidemics, it is commonly referred to as 'flu'. It is highly infectious and is caused by the influenza viruses. These are the RNA viruses that make up three of the five viruses of the family orthomyxoviridae[1].

The disease causes mild to severe illness, those at high risk being the elderly people, children and people with other health complications[2]. Epidemics kills approximately 250,000-500,000 people around the world annually[2], while millions are killed during the pandemic years when the genetic reassortment of influenza virus results in the new novel strain. This disrupts global economic, social and public health systems.

Influenza virus is divided into three types: Influenza A, B and C. Of these types, Influenza A is the most virulent and has greatest potential to cause pandemic[3].

Influenza A has several subtypes, which are identified by the copies of hemagglutinin and neuraminidase glycoproteins found on the surface of the virus membrane. Hemagglutinin acts to recognise target cells by binding to the cell's receptors and

then allows entry to the target cells by fusion of the cell membrane with the viral membrane. Neuraminidase helps viruses to be released by the host cell[4].

There are 16 known subtypes of hemagglutinin and 9 known subtypes of neuraminidase and the strain of influenza A is determined by their combinations, examples of the subtypes of influenza A are: *H1N1, H2N2, H3N2, H5N1, H7N7,H1N2, H9N2, H7N2, H7N3, H7N9, H10N9*[5]. In Kenya, the predominant influenza strain circulating is the seasonal H3N2 virus.

Human-to-human transmission is only possible for H1, H2 and H3 subtypes but it is no yet clear if the other subtypes of influenza virus A have the ability for transmission as well. Natural hosts for large variety of influenza A are wild aquatic birds[11]. Influenza B virus is less common and less virulent than Influenza A and it almost exclusively infects human beings[5]; the seal and the ferret are the other animals known to be susceptible to influenza B[6]. Influenza C virus is the less common of the subtypes and it infects humans, dogs and pigs. Sometimes it can cause severe illness and local epidemics[7].

Figure **??** shows an example of influenza virus with distinct parts shown

1.1.2 Strains

Subtypes of influenza A virus and Influenza B viruses are further subdivided into strains. There are many vast strains of influenza A subtypes and influenza B. These new strains appear and replace the existing strains. This occurs through antigenic drift. When a new strain of human influenza virus emerges, antibody protection that may have developed after infection or vaccination with an older strain may sometimes not provide protection against the new emerged strain. This is the reason influenza vaccine is updated on a yearly basis to keep up with the changes in influenza viruses.

1.1.3 Signs and symptoms of influenza

An influenza infection is initiated due the inhalation of droplets from an infected person. The droplets containing the virus particles first land on the mucus blanket lining the respiratory tract[8, 9]. In this case many virons are destroyed by non-specific clearance mechanism like mucus binding but the remaining virons escape the mucus and attach to the receptors of the surface of the target epithelial cells. Its infection results in the desquamation of the epithelial cells lining the nasal mucosa, larynx and the tracheobronchial tree. For uncomplicated influenza in human, infection involves only the upper respiratory tract and the upper division of the bronchi[10]. In severe cases, influenza spreads and affects the lungs.

Incubation period of influenza is approximately 48 hours but may vary from 24-96 hours[8]. The symptoms start appearing after the incubation period and they vary from mild to severe and those commonly observed are:

- High fever,
- Runny nose,
- Sore throat,
- Muscle pains,
- Head ache and
- Coughing

These symptoms appear two days after exposure to the virus particles(incubation period of influenza) and last for less than a week but the cough may last for more than two weeks.
Sometimes influenza infection may bring about other complications like:

✓ Viral pneumonia,

✓ Bacterial pneumonia, and

✓ Sinus infections.

In addition the disease also worsens previous health problems like *Asthma* and may lead to heart failure, hence modeling of influenza is crucial as its control may help control some worse diseases as mentioned above.
The disease can be controlled by several ways. i.e.

a) Frequent hand washing with soap, this is because the influenza viruses are inactivated by soap,

b) Wearing surgical masks when attending to the infected groups; this reduces contact to the viruses

c) Yearly vaccination against influenza among the risk groups as recommended by World Health Organisation (WHO)

d) Influenza may be treated by using the antiviral drugs such as the *Neuraminidase inhibitors oseltamivir*

1.1.4 Influenza pandemic

A disease pandemic is a world wide disease outbreak; it is determined by how the disease spreads and not the number of people it affects. An influenza pandemic occurs when strain of influenza subtype spreads in the human population from other animals.i.e pigs, chicken and ducks.

Influenza A virus can be transmitted from wild birds to other species. This causes outbreaks in domestic poultry and results into human influenza pandemic[11].

Four main influenza pandemic have already occurred throughout the history, they are: Spanish flu, Asian flu, Hong Kong flu and 2009 flu pandemic(Swine flu)

Spanish flu(1918-1920)

The Spanish flu which occurred between January 1918 and December 1920 is also called the 1918 flu pandemic. it was the first pandemic involving H1N1 the second one being the 2009 influenza pandemic[12].

The papers were only free to report the effects of the pandemic in the neutral Spain hence its nickname **Spanish flu**. This pandemic affected between 20% to 40% of the world population and caused close to 50 million deaths worldwide and nearly 675,000 deaths occurred in the United states. The pandemic also caused economic burden to the countries.

In Kenya during the Spanish flu pandemic, the principal cause of death was bacterial pneumonia after influenza infections[14].

Asian flu

Asian flu also called the 1957 flu pandemic was caused by by the H2N2 influenza type A. The pandemic originated in China in early 1956 and it lasted until 1958[13]. The death toll varied between 1-4 million depending on different sources but it was estimated by World Health Organisation(WHO) to be 2 million and the elderly people were the most highly affected.

Hong Kong Flu

The Hong Kong flu pandemic that occurred between 1968-1970 was a category two flu pandemic caused by H3N2 influenza A. The virus descended from H2N2 that caused the Asian flu pandemic via antigenic shift[15].

The pandemic killed approximately one million people world wide and it affected mainly the elderly people[16].

2009 flu (swine flu) pandemic

The 2009 flu pandemic is the most recent and the second pandemic involving H1N1 influenza A virus. On June 11, 2009, WHO announced that the world was at the start of 2009 influenza pandemic. The pandemic lasted between 2009 and 2010. At that time almost 30,000 confirmed cases had been reported in 74 Countries globally[17].

On August 10, 2010, WHO declared an end to the H1N1 pandemic[17]. In Kenya the first recognised case was reported on June 29, 2009 and by September of the same year, majority of influenza cases were caused by H1N1[18].

In the year 2012, there was a decline of pandemic H1N1 cases observed among surveillance sites in Kenya.

1.1.5 Antigenic Drift and Shift

Influenza Viruses are capable of evolving rapidly and they jump between distinct species such that the immune system of the host does not detect the new species. There are two processes involved in this evolution namely; The antigenic drift and shift, drift occurs more often than shift.

Antigenic Drift

An influenza virus which is an RNA virus is prone to errors every time a copy of its genome is made. If the changes are sufficient enough on its surface protein, then the reinfection is possible as the immunity produced against the older strain fails to act against the new strain. This process is called the **Antigenic drift**, it occurs in both influenza A and B viruses[19]. This process is best characterised by the influenza A virus and the new strain due to antigenic drift can cause an influenza pandemic[20]. The process of antigenic drift depends on the host immunity and the duration of the epidemic, antigenic drift is also known to occur in the HIV viruses.

Antigenic shift

An antigenic shift also called reassortment occurs when two influenza strains mix to form a new strain that has the capabilities of both the mothers strains. This process only occurs in influenza A virus because it infects many different species like mammals and birds[21]. For example the H3N2 influenza A that caused the Hong Kong pandemic in 1968 descended from H2N2 that caused Asian pandemic via an antigenic shift[13, 22].

1.2 Problem statement

Influenza is believed to be a winter disease in the temperate countries due to its persistent appearing during the winter months in the temperate countries. In tropical countries this occurs all year round with most activity happening during the cold

months and rainy season hence influenza seasonality may depend on the meteorological parameters since the influenza virus' survival depends on these factors. Therefore this study is of importance as it aims to model the influenza incidence in Kenya with relation to meteorological parameters.

1.3 Objectives of the study

The main objective of this study is to explore the connection between meteorological parameters and influenza seasonality in Kenya.

1.3.1 Specific objectives

The specific objectives are:

(i) Examine the deterministic model and analyse the stability of the equilibrium points,

(ii) Express the reproduction number in terms of the meteorological parameters and compute it based on climatic data,

(iii) Approximate the influenza transmission rate from the influenza data,

(iv) Determine the correlation between rainfall and temperature with the observed data on influenza,

(v) Determine the correlation between the reproduction number and the observed data on influenza,

(vi) Obtain the numerical solution of the deterministic model and compare results with the observed data.

CHAPTER 2

Literature review

2.1 Influenza seasonality

Influenza is a viral infectious disease that causes epidemics and pandemics[23]. In order to develop the effective preventive and control strategies, it is essential to understand the seasonal patterns of influenza.

In temperate regions, the seasonality of influenza is well documented[24]. In these regions, influenza activity occurs constantly during winter or early spring months i.e. In the Northern hemisphere, the influenza activity peaks between the months of November and March while it peaks between the months of May and September in the southern hemisphere[25].

Contrary to the temperate regions, influenza seasonality in the tropical and subtropical areas is not well studied and documented, in these regions the influenza activity occurs sporadically with influenza activity all year round with some peaks being observed during certain seasons of the year. Some tropical regions experience more than one peak per year.

Kenya is among the few developing countries with elaborate national epidemiosurveillance networks on influenza but it still remains a major cause of hospitalisation and deaths every year[26].

For example Kenya is a tropical country with influenza activity present all year

round with the activity being highest during a broad wave mostly corresponding to the southern hemisphere winter. It experiences influenza peaks the rainy season (March-April and October- November) and the cold month of July[27].

Several studies have been conducted to determine the causes of seasonality in influenza activities. Its seasonality has been associated with several factors like meteorological determinants, changes in the susceptibility of the population, changes in vitamin D and melatonin due to changes in the number of days with sunlight.

It has been shown that meteorological factors affect the virus survivorship, host susceptibility and the transmission efficiency:

♣ **Virus survivorship**: It is affected by temperature, humidity and solar radiation; all these factors vary inversely with the virus survivorship.

♣ **Transmission efficiency**: It is affected by: humidity, vapour pressure, rainfall, air travels/holidays and temperature. Temperature, vapour pressure and humidity vary inversely with the transmission efficiency while rainfall and air travels/holidays are proportional to the transmission.

♣ **Host susceptibility**: It varies inversely with sunlight.

The studies presented here illustrate the relationship between influenza activities and the meteorological factors:

Zhou[28] suggested that the seasonality of influenza could depend on several factors: internal dynamic resonance and variation of meteorological elements (solar radiation, precipitation and dew point). In his study, he found the following:

- Influenza activity is proportional to the exponential of the number of days with precipitation and to the negative exponential of quarter power of sunny hours in all climate regions,
- Influenza activity is a negative exponential function of dew point in temperate and arctic regions,
- In tropical region, influenza activity is an exponential function of an absolute deviation of dew point from its annual mean.

He suggested that understanding the roles of meteorological factors on the influenza activity would be crucial for early intervention such as; social distancing and opportune vaccination. In his study of the factors affecting the influenza activity, he used general reproduction (GR) model and found out that transmission follows the exponential law($e^{\alpha(\bar{t}).t}$).

Vam Noort et al.[29] fitted an influenza transmission model to a time series data of influenza-like illness (ILI) monitored from 2003 to 2010 in the three European cities; Netherlands, Belgium and Portugal. They found a significant correlation between temperature and absolute humidity with influenza activities at the time of infection and the proportion of the infected persons fulfilling the ILI factor.

Mahamat et al.[30] used a time series analysis to investigate the relationship between the ILI and climatic parameters in the tropical French Guiana which lies between the latitude 2^0N and 6^0N. They observed a marked seasonality in the circulation of influenza virus in the pre-pandemic period and then year round activity in the post-pandemic period with peaks coinciding with the rainy season. They concluded that influenza activity in the tropical regions is country specific. i.e. The factors affecting influenza seasonality in (sub)tropical regions is country specific.

Chong et al.[31] Fitted meteorological data and influenza mortality data in the SIR model to identify the meteorological drivers of influenza seasonality in a subtropical city, Hong Kong. Air temperature and rainfall were found to be the significant drivers of seasonal influenza though the results of rainfall was found to be less robust.

2.2 Mathematical modeling of influenza

The history of epidemiological modeling is traced back to the modeling framework developed by Kermack and Mckendrick[32] in the year 1927. They developed the standard SIR model where the population is divided into three compartments namely: Susceptible(S); Infectious individuals(I) and those who recover from the disease(R). Their model assumes a homogeneous mixing of the population with no births or deaths. They assume that each individual has the same chance of infecting other individuals in the population which is assumed to be constant at the outbreak of the epidemic.

The model equations are:

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \alpha I \\ \frac{dR}{dt} &= \alpha I \end{aligned} \tag{2.2.1}$$

Following the development of SIR model by Kermack and Mckendrick, other physicians contributed to modern epidemiology by extending the basic SIR model with more classes such as SIER model[33]. With reference to influenza and seasonality, some models have been developed to explain seasonality by expressing the transmission rate as a sinusoidal function[34] while the model of Fergurson et al.[49] incorporates seasonality by assuming a harmonic forcing of the transmission rate.

Chowell et al.[41] applied a simple epidemic model to weekly indicators of influenza mortality to estimate the reproduction numbers of seasonal influenza epidemics spanning three decades in the United States, France, and Australia. In the study they found similar distributions of reproduction number estimates in the three countries, with mean value 1.3 and important year-to-year variability in the interval 0.9-2.1. They assumed that the population is completely susceptible at the beginning of each influenza season prior to the first epidemic week, which is defined as the first week with non-zero influenza-related deaths. Their model equations are:

$$\begin{aligned}
\frac{dS}{dt} &= -\beta SI/N \\
\frac{dE}{dt} &= \beta SI/N - \kappa E \\
\frac{dI}{dt} &= \kappa E - (\gamma + \delta)I \\
\frac{dP}{dt} &= \gamma I \\
\frac{dD}{dt} &= \delta I
\end{aligned} \tag{2.2.2}$$

Chowell et al.[36] developed a mathematical model to determine the reproduction number of seasonal influenza epidemics in Brazil by dividing the population into: Susceptible (S), Exposed (E), Infectious (I), recovered/ protected (P) and dead (D). The model equations are:

$$\begin{aligned}
\frac{dS}{dt} &= -\beta SI/N \\
\frac{dE}{dt} &= \beta SI/N - \kappa E \\
\frac{dI}{dt} &= \kappa E - (\gamma + \delta)I \\
\frac{dP}{dt} &= \gamma I \\
\frac{dD}{dt} &= \delta I
\end{aligned} \tag{2.2.3}$$

This model was extended by Chong et al. [31] in their research to describe the dynamic system of seasonal influenza in a subtropical city-Hong Kong. Their model comprise four compartments namely: Susceptible (S), Infectious (I), Recovered (R) and Dead (D). They used a time varying transmission rate β_t given by:

$$\beta_t = b_0 + b_1 Z_t^1 + b_2 Z_t^2 + ... + b_n Z_t^n \quad \text{where} \quad Z_t^i, i = 1, 2, ...n$$

are the transformed meteorological variables. Their model equations are:

$$\begin{aligned}
\frac{dS}{dt} &= -\beta_t SI \\
\frac{dI}{dt} &= \beta_t SI - (\gamma + \delta)I \\
\frac{dR}{dt} &= \gamma I \\
\frac{dD}{dt} &= \delta I
\end{aligned} \tag{2.2.4}$$

CHAPTER 3

Model description and Analysis

3.1 Model formulation

In this project we use the exposed class from the model formulated by Chowell et al.[36, 41] and use the idea of variable transmission rate from the model formulated by Chong et al[31]. Here the population is divided into five compartments namely: Susceptible (S), Exposed but not infectious (E), Infectious individuals(I), Recovered individuals (R) and those who die from the disease (D). We assume a homogeneous mixing in which each individual has the same probability of transmitting the disease to other individuals who are susceptible to the disease. 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 figure 3.1 shows the compartmental model

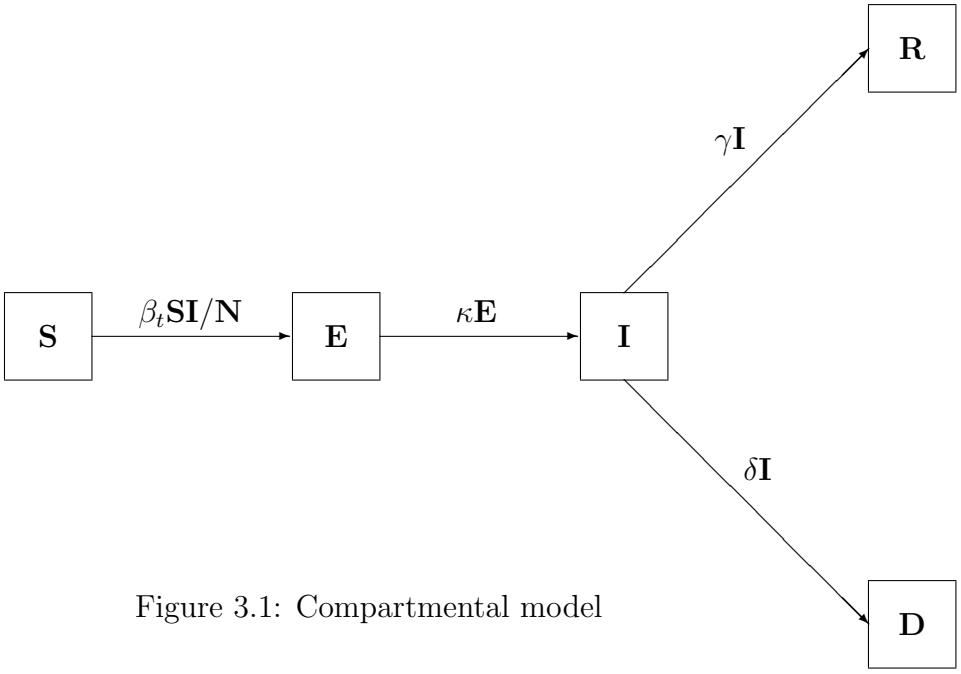

Figure 3.1: Compartmental model

In our model we use a time varying transmission rate β_t such that it depends on the meteorological parameters as discussed in the literatures[28, 29, 30, 31]. The model is described as a system of 5-dimensional system of ODE given by:

$$\begin{aligned} \frac{dS}{dt} &= -\beta_t SI/N \\ \frac{dE}{dt} &= \beta_t SI/N - \kappa E \\ \frac{dI}{dt} &= \kappa E - (\gamma + \delta)I \\ \frac{dR}{dt} &= \gamma I \\ \frac{dD}{dt} &= \delta \end{aligned} \tag{3.1.1}$$

Where

$$\beta_t = \beta_0 \exp(\alpha_1 T + \alpha_2 R + \alpha_3 S^{\frac{1}{4}} + \alpha_4 |T_d|)$$

and the values:

T is the monthly mean temperature,

R is the number of days with precipitation,

S is the number of hours with sunlight and,

$|T_d|$ is the absolute deviation of the dew point from its annual mean.

$S + E + I + R + D = N$ where N is the total population.

Table 3.1 shows the state variables of influenza model and their definitions while table 3.2 shows the definition of model parameters

Table 3.1: State variables for the influenza model

S	Susceptible individuals
E	Exposed individuals who are not infectious
I	Infectious individuals
R	Recovered individuals
D	Individuals who die from the disease

Table 3.2: Model parameter definitions

β_t	The time varying transmission rate
κ	The rate at which the exposed individuals move to infectious class
γ	The recovery rate
δ	The death rate due to the disease

3.2 Model Analysis

To analyse the system, we first normalise it by defining the new variables $S_n = S/N$,$E_n = E/N$,$I_n = I/N$,$R_n = R/N$ and $D_n = D/N$ so that

$$S_n + E_n + I_n + R_n + D_n = \frac{S + E + I + R + D}{N} = 1$$

since $S + E + I + R + D = N$ and so here the total population is taken to be 1 after the system has been normalised.
The normalised system becomes:

$$\frac{dS_n}{dt} = -\beta_t S_n I_n \tag{3.2.2}$$

$$\frac{dE_n}{dt} = \beta_t S_n I_n - \kappa E_n \tag{3.2.3}$$

$$\frac{dI_n}{dt} = \kappa E_n - (\gamma + \delta) I_n \tag{3.2.4}$$

$$\frac{dR_n}{dt} = \gamma I_n \tag{3.2.5}$$

$$\frac{dD_n}{dt} = \delta I_n \tag{3.2.6}$$

With $\beta_t = \beta_0 e^{(\alpha_1 R + \alpha_2 S^{1/4} + \alpha_3 N + \alpha_4 |T|)}$ and

$$S_n + E_n + I_n + R_n + D_n = 1$$

Hence we can now carry out the stability analysis from the normalised system of equations by computing the steady/equilibrium points and the reproduction number R_0.

3.3 A compact positively invariant set

Theorem 3.3.1. *The set*

$$D = \{(S_n, E_n, I_n, R_n) \in \mathbb{R}^4_+ : S_n \geq 0, E_n \geq 0, I_n \geq 0, R_n \geq 0,$$
$$S_n + E_n + I_n + R_n + D_n \leq 1\}$$

is compact positively invariant with respect to the model.

Proof. By using Barriers theorem, Since the system is Lipschitz, it is sufficient to check that the vector field induced by the system is either tangent or entering D on the boundary D[42]. Clearly we have:

1) By using equation(3.2.2) $S_n = 0 \Rightarrow \dot{S}_n = 0$ and if we assume $S_n \geq 1 \Rightarrow \dot{S}_n \leq 0$,

2) $E_n = 0 \Rightarrow \dot{E}_n \geq 0$ from equation(3.2.3)

3) $I_n = 0 \Rightarrow \dot{I}_n \geq 0$ from equation(3.2.4)

4) $R_n = 0 \Rightarrow \dot{R}_n \geq 0$ from equation(3.2.5)

5) Since $S_n + E_n + I_n + R_n \leq 1$, we have that $\dot{E}_n \leq 0, \dot{I}_n \leq 0$ and $\dot{R}_n \leq 0$

Hence the above relations prove that all the trajectories tends to D hence the set D is positively invariant with respect to the model □

3.4 Basic reproduction number

The basic reproduction number is defined as the mean number of secondary infections produced by a typical infective individual into a completely susceptible (naive) host population[33, 37, 38]. This is a measure of the potential for the disease spread within the population. If $R_0 < 1$ then the infected individuals introduced into the susceptible population will on average fail to replace themselves hence the disease will not spread into the population, but on the other hand if $R_0 > 1$ then the number of infected individuals will increase in each generation hence the disease will spread into the population.

The basic reproduction number is a threshold parameter for the invasion of the disease organism into a completely naive population. Once the disease has spread into the population, this number may no longer be a good measure of the disease transmission. To obtain the reproduction number we use the next generation matrix. The system has a unique disease free equilibrium $(1, 0, 0, 0, 0)$. Here the infected compartments are E_n and I_n hence the infectious class is given by the vector

$$\begin{pmatrix} E_n \\ I_n \end{pmatrix}$$

The new infections are given by the matrix:

$$\mathcal{F} = \begin{pmatrix} \beta_t S_n I_n \\ 0 \end{pmatrix} \tag{3.4.7}$$

And the transition vector is given by

$$\mathcal{V} = \begin{pmatrix} \kappa E_n \\ (\gamma+\delta)I_n - \kappa E_N \end{pmatrix} \tag{3.4.8}$$

Finding the Jacobian of $\mathcal{F}$ we obtain

$$\mathbf{F} = \begin{bmatrix} 0 & \beta_t S_n \\ 0 & 0 \end{bmatrix} \tag{3.4.9}$$

At the disease free equilibrium i.e at the point $(1, 0, 0, 0, 0)$ we have

$$\mathbf{F} = \begin{bmatrix} 0 & \beta_t \\ 0 & 0 \end{bmatrix} \tag{3.4.10}$$

Also the Jacobian of $\mathcal{V}$ is given by:

$$\mathbf{V} = \begin{bmatrix} \kappa & 0 \\ -\kappa & \gamma+\delta \end{bmatrix} \tag{3.4.11}$$

and at the disease free equilibrium we obtain

$$\mathbf{V} = \begin{bmatrix} \kappa & 0 \\ -\kappa & \gamma+\delta \end{bmatrix} \tag{3.4.12}$$

The next generation matrix K is given by $K = FV^{-1}$ and the reproduction number by $\rho(\mathbf{FV^{-1}})$

Here

$$\mathbf{V^{-1}} = \frac{1}{\kappa(\gamma+\delta)} \begin{bmatrix} \gamma+\delta & 0 \\ \kappa & \kappa \end{bmatrix} = \begin{bmatrix} \frac{1}{\kappa} & 0 \\ \frac{1}{\gamma+\delta} & \frac{1}{\gamma+\delta} \end{bmatrix} \tag{3.4.13}$$

Therefore

$$K = \mathbf{FV^{-1}} = \begin{bmatrix} \frac{\beta_t}{\gamma+\delta} & \frac{\beta_t}{\gamma+\delta} \\ 0 & 0 \end{bmatrix} \tag{3.4.14}$$

The basic reproduction number denoted by R_0 is given by the spectral radius(eigenvalue of the largest magnitude) of the next generation matrix, K i.e. $R_0 = \rho(\mathbf{FV^{-1}})$

The eigenvalues of K are 0 and $\frac{\beta_t}{\gamma+\delta}$.

The entries of K represent the expected number of secondary infections produced by the infection hence R_0 is given by

$$R_0 = \frac{\beta_t}{\gamma+\delta} \tag{3.4.15}$$

The basic reproduction number provides the necessary condition for the eradication of an epidemic. If $R_0 < 1$, then the disease dies out but if $R_0 > 1$, the disease remains in the population.

Since R_0 is a function of β_t, it also depends on the meteorological parameters for the seasonal epidemic, hence any measures put in place to control the disease has to put into consideration these meteorological factors. Now since

$$\beta_t = \beta_0 \exp(\alpha_1 T + \alpha_2 R + \alpha_3 S^{\frac{1}{4}} + \alpha_4 |T_d|).$$

R_0 may be expressed as:

$$R_0 = \frac{\beta_0 \exp(\alpha_1 T + \alpha_2 R + \alpha_3 S^{\frac{1}{4}} + \alpha_4 |T_d|)}{\gamma + \delta} \tag{3.4.16}$$

3.5 Stability Analysis

3.5.1 Equilibrium states

To obtain the equilibrium states, the derivatives with respect to time are equated to zero. Here the unknowns are S_N E_N I_N and R_N. The equations are given as

$$\begin{aligned} -\beta_t S_N I_N &= 0 && (3.5.1)\\ \beta_t S_N I_N - \kappa E_N &= 0 && (3.5.2)\\ \kappa E_N - (\gamma + \delta) I_N &= 0 && (3.5.3)\\ \gamma I_N &= 0 && (3.5.4) \end{aligned}$$

From the equation (3.5.1), either $S_N = 0$ or $I_N = 0$ hence the system has two equilibrium points; i.e. $I_N = 0$ for the disease free equilibrium and $S_N = 0$ for the endemic equilibrium.

Here we want to establish both local and global stability of the disease free and endemic equilibria points.

3.5.2 Disease free equilibrium (DFE)

The disease free equilibrium point is obtained by setting $I_N = 0$ from equation (3.5.1) hence we also obtain $E_N = 0$ from equation (3.5.2)and $R_N = c$ by equation (3.2.5) hence we take the initial value $R(0) = 0$ therefore $R_N = 0$. Now since the total population is 1, we obtain that $S_N = 1$ for the disease free equilibrium, thus the disease free equilibrium is $E_0 = (1, 0, 0, 0)$

Local stability analysis of DFE

To analyse the local stability of the DFE equilibrium, we linearise the system at the equilibrium point. The Jacobian of the system is given by:

$$\mathbf{J_0} = \begin{bmatrix} -\beta_t I_N & 0 & -\beta_t S_N & 0 \\ \beta_t I_N & -\kappa & \beta_t S_N & 0 \\ 0 & \kappa & -(\gamma+\delta) & 0 \\ 0 & 0 & \delta & 0 \end{bmatrix} \tag{3.5.1}$$

At the disease free equilibrium, the Jacobian simplifies to:

$$\mathbf{J}(\mathbf{E_0}) = \begin{bmatrix} 0 & 0 & -\beta_t & 0 \\ 0 & -\kappa & \beta_t & 0 \\ 0 & \kappa & -(\gamma+\delta) & 0 \\ 0 & 0 & \delta & 0 \end{bmatrix} \tag{3.5.2}$$

The eigenvalues of $J(E_0)$ are:

$$\lambda_{1,2} = 0$$

and

$$\lambda_{3,4} = -(\gamma+\delta+\kappa) \pm \sqrt{(\gamma+\delta+\kappa)^2 - 4\kappa(\gamma+\delta-\beta_t)}$$

or

$$\lambda_{3,4} = -(\gamma+\delta+\kappa) \pm \sqrt{(\gamma+\delta+\kappa)^2 - 4\kappa(1-R_0)}$$

If $R_0 < 1$ then the eigenvalues have none positive real parts and if $R_0 > 1$, there is an eigenvalue with positive real part, hence we conclude that the DFE is locally stable if $R_0 < 1$ and and unstable if $R_0 > 1$.

Global stability analysis of DFE

Theorem 3.5.1. *The disease free equilibrium is globally asymptotically stable if* $R_0 \leq 1$ *and unstable if* $R_0 > 1$

Proof. Here we consider the following Lyapunov function

$$L = I_N + E_N \tag{3.5.3}$$

Its derivative along the trajectories of the solution to the system is,

$$V' = I'_N + E'_N \tag{3.5.4}$$
$$= [\kappa E_N - (\gamma + \delta)I_N] + [\beta_t S_N I_N - \kappa E_N] \tag{3.5.5}$$
$$= \beta_t S_N I_N - (\gamma + \delta)I_N \tag{3.5.6}$$
$$= (\gamma + \delta)\left[\frac{\beta}{(\gamma + \delta)} S_N I_N - I_N\right] \tag{3.5.7}$$
$$= (\gamma + \delta)I_N[S_N R_0 - 1] \tag{3.5.8}$$

Now since $S_N \leq 1$, then we have that $V' \leq 0$ if $R_0 \leq 1$ and the equality holds when $R_0 = 0$ and $S_N = 1$ or $I_N = 0$, therefore by using the Lasalle's principle, all paths in D approach the largest positive invariant subset of the set where $V' = 0$ i.e. the set $\{(S_N, E_N, I_N, R_N) \in D : V' = 0\}$. If $E_N = I_N = R_N = 0$, we have that $\frac{dS_N}{dt} = 0$ hence solving we get that $S_N = C$, C a constant or precisely since the total population is 1, we get $S_N = 1$ therefore as $t \to \infty$ then $S_N = 1$. Thus all solutions in D approach the disease free equilibrium point. This completes the proof

□

3.5.3 Endemic equilibrium

For the endemic equilibrium E_1, we have that $S^*_N = 0$ hence implying that $E^*_N = 0$, therefore we get that $I^*_N + R^*_N = 1$ therefore the endemic equilibrium is $E_1 = (0, 0, I^*_N, 1 - I^*_N)$.

Local stability analysis of the endemic equilibrium

The Jacobian of the system is:

$$\mathbf{J_1} = \begin{bmatrix} -\beta_t I_N & 0 & -\beta_t S_N & 0 \\ \beta_t I_N & -\kappa & \beta_t S_N & 0 \\ 0 & \kappa & -(\gamma + \delta) & 0 \\ 0 & 0 & \delta & 0 \end{bmatrix} \tag{3.5.1}$$

At the equilibrium point it is given by:

$$\mathbf{J(E_1)} = \begin{bmatrix} -\beta_t I^*_N & 0 & 0 & 0 \\ \beta_t I^*_N & -\kappa & 0 & 0 \\ 0 & \kappa & -(\gamma + \delta) & 0 \\ 0 & 0 & \delta & 0 \end{bmatrix} \tag{3.5.2}$$

The eigenvalues are:

$$\lambda_1 = 0$$
$$\lambda_2 = -\beta_t I_N^*$$
$$\lambda_{3,4} = -(\gamma + \delta + \kappa) \pm \sqrt{(\gamma + \delta + \kappa)^2 - 4\kappa(\gamma + \delta)}$$

Here since the eigenvalues are not functions of R_0, they have negative real parts for any values of R_0. Thus there exist a unique endemic equilibrium which is locally asymptotically stable.

CHAPTER 4

Numerical Analysis of the model

4.1 Numerical simulations

In this chapter we present the numerical analysis of the model. We run the numerical simulations to illustrate the relationship between the influenza activities and the meteorological parameters and also its relation to the reproduction number.

We also determine the correlation coefficient between the influenza infections and the rainfall, temperature and the reproduction number. The analysis are done using Mat lab and Excel.

The influenza data was obtained from the Kenya Medical Research Institute (KEMRI) while the meteorological data was obtained from the Kenya Meteorological Department

4.2 R_0 as a function of meteorological parameters

From equation (3.4.15), the reproduction number R_0 is given by

$$R_0 = \frac{\beta_t}{\gamma + \delta}$$

where β_t is the daily transmission rate per individual, γ is the recovery rate and δ is the death rate.

From equation (3.4.16) by assuming that the transmission rate depends on only rainfall and temperature we get

$$\beta_t = \beta_0 \exp(\alpha_1 T + \alpha_2 R). \tag{4.2.1}$$

Substituting for β_t we get

$$R_0 = \frac{\beta_0 \exp(\alpha_1 T + \alpha_2 R)}{\gamma + \delta},$$

Hence R_0 is a function of rainfall and temperature.

4.3 Parameter estimation

We assume a 0.2% average case fatality proportion(CFP)[39, 40], the parameters β_0, α_0 and α_1 are estimated by least squares fitting to the model. We used monthly data therefore the time t is measured in months. Table 4.1 shows parameters and their approximations

Table 4.1: Parameter definitions and their approximations

Parameter	**Definition**	**estimate**	**Source**
$1/\kappa$	latent period	1.9 days	[40]
$1/\gamma$	recovery period	4.1 days	[40]
CFP	Case Fatality proportion	0.2%	[40]
δ	mortality rate	γ[CFP/(1 − CFP)]	[41]

Table 4.2: Definition of terms

ZONE	**REGION**
Zone 1	Lake region and its environs
Zone 4	Nairobi region and its environs

Here we run some simulations to illustrate the dependency of influenza activities on the meteorological parameters. We use data for the two regions, i.e. Zone 1 and Zone 4 from January, 2009 to October, 2011. Here we illustrate the results using only the temperature and rainfall. We also approximate the transmission rate, β_t by using the averaged seasonal values in both Zone 1 and Zone 4 and hence estimated the coefficients β_0, α_1 and α_2 using the least squares method. Here since the values doesn't differ by far, we approximated the transmission rate by combining the values in both zones so that we just come up with just one transmission rate function to use rather than using different transmission rates for each zone.

4.3.1 Least squares method

Given the transmission rate:

$$\beta_t = \beta_0 \exp(\alpha_1 T + \alpha_2 R) \tag{4.3.1}$$

We linearise the equation (4.3.1). Finding ln on both sides of the equation we obtain

$$\ln \beta_t = \ln \beta_0 + \alpha_1 T + \alpha_2 R.$$

Letting $y = \ln \beta_t$ and $\ln \beta_0 = \alpha_0$ we obtain a multiple linear regression equation

$$y_i = \alpha_0 + \alpha_1 T_i + \alpha_2 R_i \tag{4.3.2}$$

If we assume $\bar{y}_i$ is the approximate value corresponding to the value y_i and if $e_i = y_i - \bar{y}_i$ is the error Let

$$S = \sum_{i=1}^{n} e_i^2 \tag{4.3.3}$$

$$= \sum_{i=1}^{n} (\bar{y}_i - y_i)^2 \tag{4.3.4}$$

$$= \sum_{i=1}^{n} [\alpha_0 + \alpha_1 T_i + \alpha_2 R_i - y_i]^2 \tag{4.3.5}$$

The objective is to determine α_0, α_1 and α_2 so that the error is minimum

$$\text{i.e.} \quad \frac{\partial S}{\partial \alpha_0} = 0, \frac{\partial S}{\partial \alpha_1} = 0, \frac{\partial S}{\partial \alpha_2} = 0$$

Therefore we obtain the normal equations:

$$\begin{aligned} &\alpha_0 + \alpha_1 \textstyle\sum T_i + \alpha_2 \sum R_i = \sum y_i \\ &\alpha_0 \textstyle\sum T_i + \alpha_1 \sum T_i^2 + \alpha_2 \sum T - iR_i = \sum T_i y_i \\ &\alpha_0 \textstyle\sum R_i + \alpha_1 \sum T_i R_i + \alpha_2 \sum R_i^2 = \sum R_i y_i \end{aligned} \tag{4.3.6}$$

We substitute the meteorological data for each zone into the normal equations (4.3.6). For zone 4 we obtain

$$\alpha_0 = 5.1745, \alpha_1 = -0.3233 \quad \text{and} \quad \alpha_2 = -0.1113$$

and hence obtain $\beta_0 = \exp(\alpha_0) = 239.7$. Substituting these values in equation (4.2.1) we obtain the transmission rate as

$$\beta_t = 176.7 \exp(-0.3233T - 0.1113R)$$

Hence the reproduction number for Zone 4 is given by:

$$R_0 = \frac{176.7 \exp(-0.3233T - 0.1113R)}{\gamma + \delta} \tag{4.3.7}$$

Similarly for Zone 1 we obtain

$$\alpha_0 = 17.1162, \alpha_1 = -0.7445 \quad \text{and} \quad \alpha_2 = -0.5647$$

and hence obtain $\beta_0 = \exp(\alpha_0) = 27.13 \times 10^6$. Substituting these values in equation (4.2.1) we obtain the transmission rate as

$$\beta_t = 27.13 \times 10^6 \exp(-0.7445T - 0.5647R)$$

Hence the reproduction number for Zone 1 is given by:

$$R_0 = \frac{27.13 \times 10^6 \exp(-0.7445T - 0.5647R)}{\gamma + \delta} \tag{4.3.8}$$

We also find the correlation coefficient between different meteorological parameters with the positive number of influenza and also the correlation coefficient between the reproduction number, R_0 with the influenza positives.

In the numerical solution we use the initial infected people as the first season with non-zero number of infected individuals, i.e the value in the second season of Zone 1 since in the first season we have zero infected individuals in Zone 4 and used the same information for both zones so that solutions could be comparable in Zones 1 and 4. We assume that $I(0) = E(0) \quad \text{and} \quad R(0) = 0$

- $D(0) = 0$
- $R(0) = D(0)/CFP - D(0)$
- I(0)=E(0)=5%
- S(0)=1-I(0)-E(0)-R(0)-D(0)=90%

4.4 Discussion and results

We normalised the equations by finding the proportions of individuals to the constant total population, from the normalised system we reduced the system to a 4-dimensional system of ODEs from which we carried out the stability analysis, we derived the reproduction number and expressed it as a function of the meteorological parameters: rainfall, temperature, sunlight and the absolute deviation. We conducted the stability analysis and found that the DFE is locally asymptotically stable when $R_0 < 1$ and unstable when $R_0 > 1$ and globally asymptotically stable when $R_0 \leq 1$, we also found that when $R_0 > 1$, then there exist and endemic equilibrium which is locally asymptotically stable, this result was also found by the numerical solution of the model.

We simulated the values by using the data from Zone 1 and Zone 4 as provided by the KEMRI institute and the meteorological department , the data represents two zones 1 and 4.

Figures 4.1 and 4.2 represents a numerical simulation of the normalised Influenza model equations (3.2.2) to (3.2.6) using the normalised system variables which was conducted using Matlab's ODE23. The solution represents the simulation of data in Zone 4 and Zone 1 respectively.

ZONE 4

In the numerical solution of the model For Zone 4 we use annual average temperature for the three years i.e. $19.8°C$ and annual average rainfall of 2.1mm/day. In the figure 4.1 we observe that the Susceptible proportion decreases and reaches zero at around the first month and remains zero throughout, exposed individuals start by increasing and reaches its peak which is approximately 70% in the First month and finally decrease to zero in the 10^{th} month, similarly the infectious individuals increases and attains its peak approximately 46% in the 4^{th} month and finally decreases to zero in 20^{th} month. Finally the recovered and the dead proportions increase and attain their maximum values 82% and 18% in the 20^{th} and 15^{th} months respectively.

ZONE 1

In Zone 1 we used average temperature $22.7°C$ average rainfall 4.5mm/day, the simulation is as shown in figure 4.2. In this figure we observe that the Susceptible proportion decreases and vanishes in the 3^{rd} month, exposed individuals increases up to the peaks value 53% in the 3^{rd} month and and finally decreases and reaches zero in the 10^{th} month. Similarly the infectious individuals increases to a maximum value 45% in the 5^{th} month and finally decreases and vanish in the 20^{th} month. Lastly the recovered and the dead proportions increase and attains their peak values 82% and 18% in the 20^{th} and 15^{th} months respectively

In the two graphs 4.1 and 4.2, we notice some differences in different classes; for example we observe that the Susceptible class vanishes after one month in Zone 4 while it varnishes after three months in Zone 1, Exposed class also attains different peaks in the two Zones 1 nd 4 and at different months, similar observations are made with the infectious class. We notice that stability of all the classes except the Susceptible in figure 4.1 are attained at the same point as in figure 4.2.

To understand better the effects of temperature and rainfall on influenza seasonality, we plotted graphs of temperature and rainfall against influenza and also the reproduction number against influenza time both seasonally and monthly. We also determined the correlation coefficient between temperature, rainfall and the reproduction number number with influenza.

From figure 4.3 we observe that as rainfall peaks influenza also peaks and as rainfall decreases influenza also decreases. The peaks of the influenza appears lagged after the rainfall has peaked and the decrease influenza also appears after some time when rainfall has decreased, this may be due to the fact that the effects of increase and decrease in rainfall are felt after some time. Similar patterns are observed when we plotted seasonal values as seen in figure 4.4. The graphs were plotted using values from Zone 4

Similar patterns are observed when we plot values from Zone 1 as shown in graphs 4.9 and 4.10.

We also plotted influenza data and temperature from Zone 4 both monthly and seasonal as shown in the figures 4.5 and 4.6. We observe that an increase in temperature corresponds to a decrease in influenza while a decrease in temperature correspond to an increase in influenza. We observe similar observations when we use values from Zone 1 as shown in graphs 4.11 and 4.12.

We also graphed the reproduction number and influenza in both Zones 1 and 4 using monthly and seasonal data. This is shown in the graphs 4.7, 4.8, 4.13 and 4.14. The peaks in both flu and reproduction number peaks simultaneously and they also decrease simultaneously.

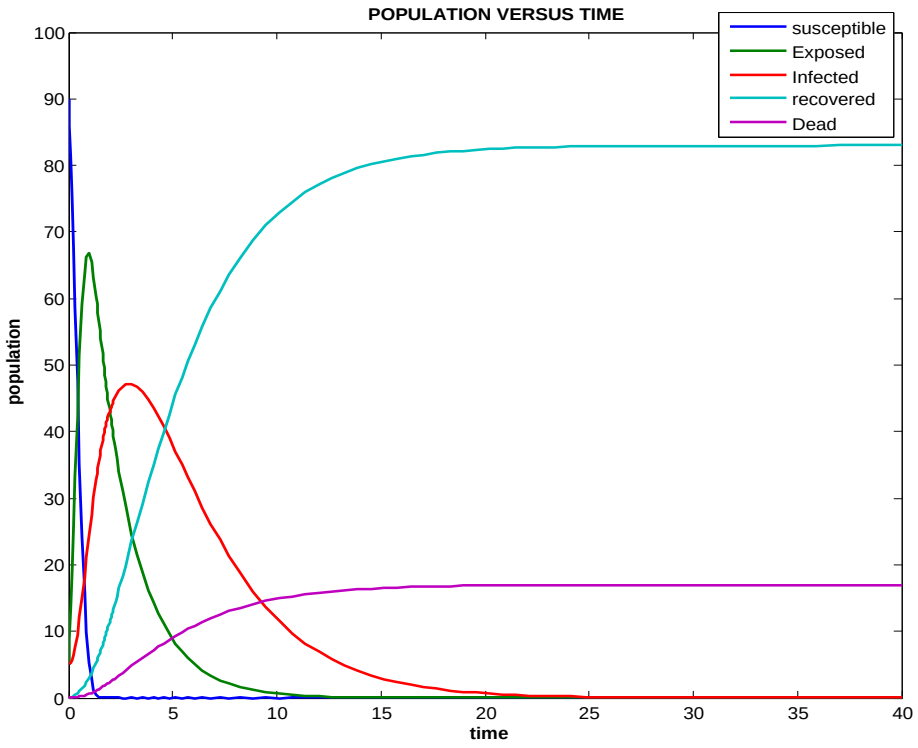

Figure 4.1: A numerical simulation of the influenza model for Zone 4

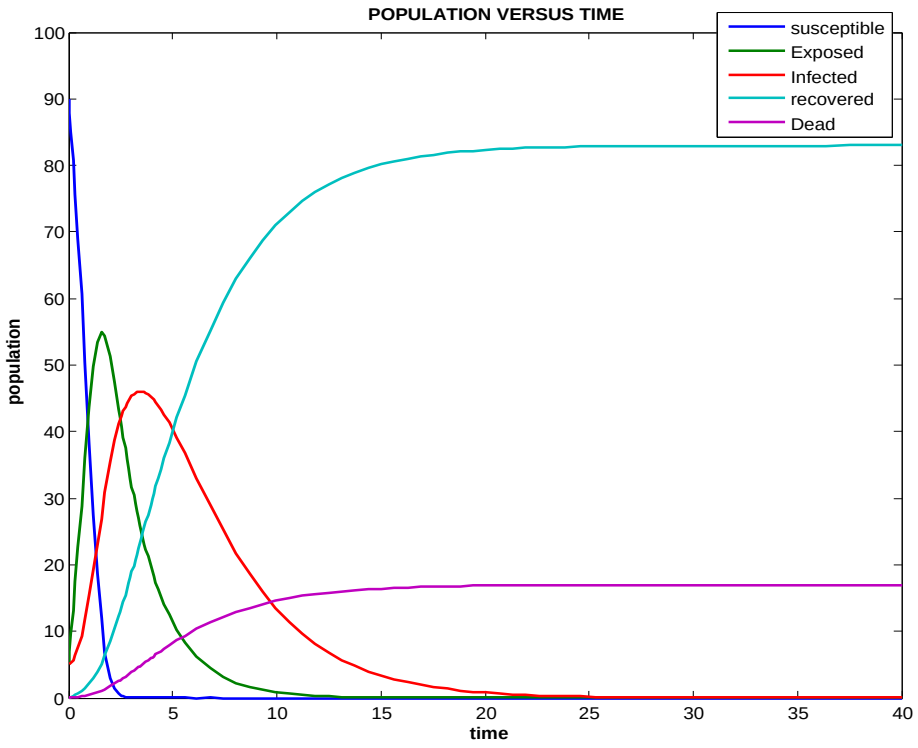

Figure 4.2: A numerical simulation of the influenza model for Zone 1

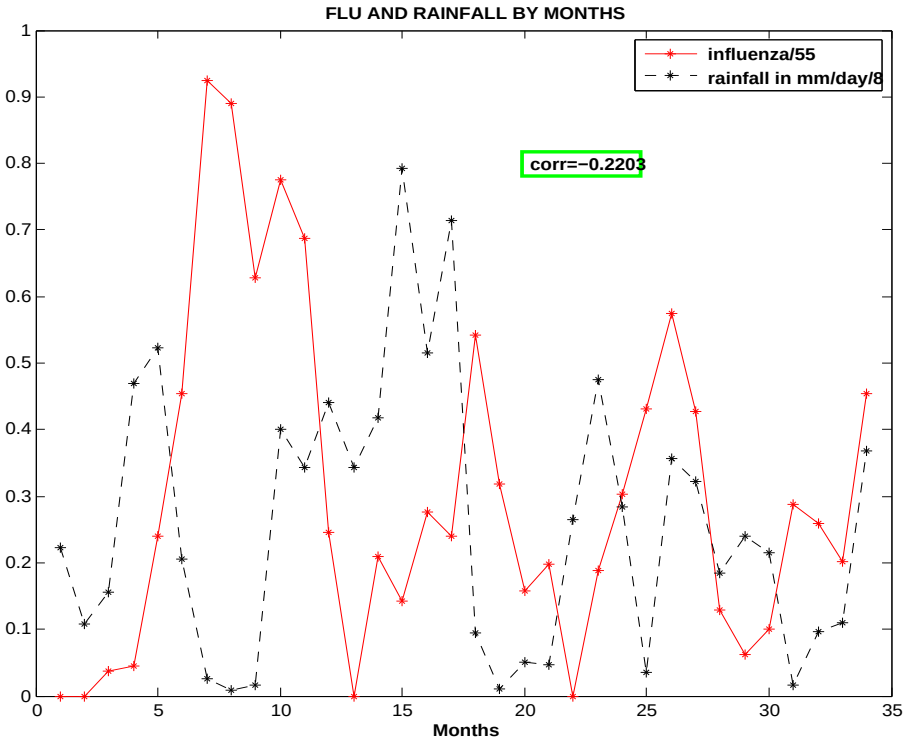

Figure 4.3: Graph of monthly Rainfall and Flu in Zone 4

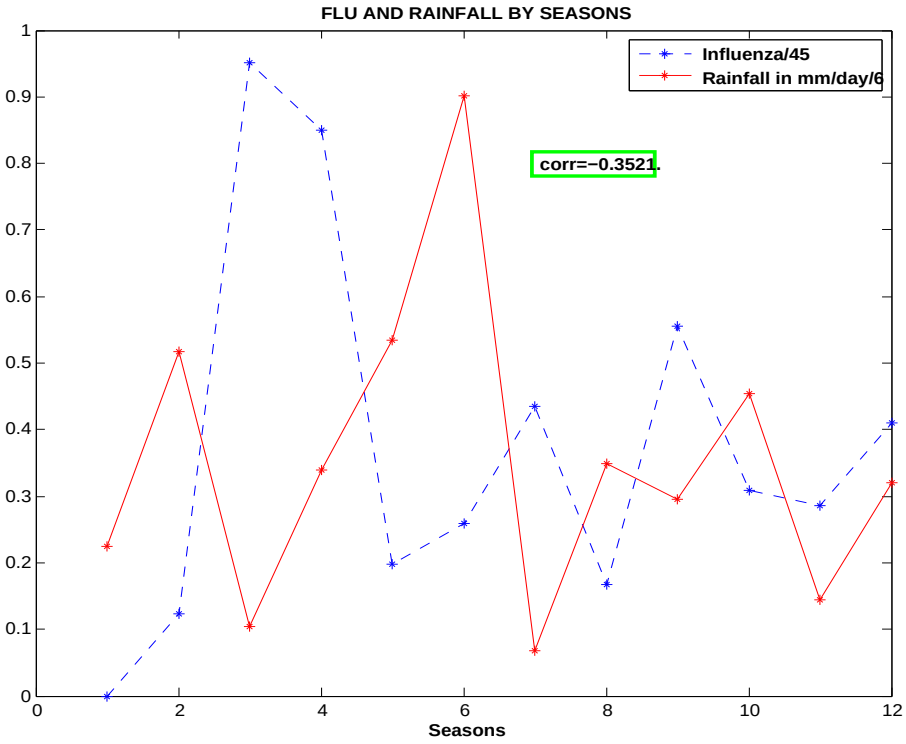

Figure 4.4: Graph of Seasonal Rainfall and Flu in Zone 4

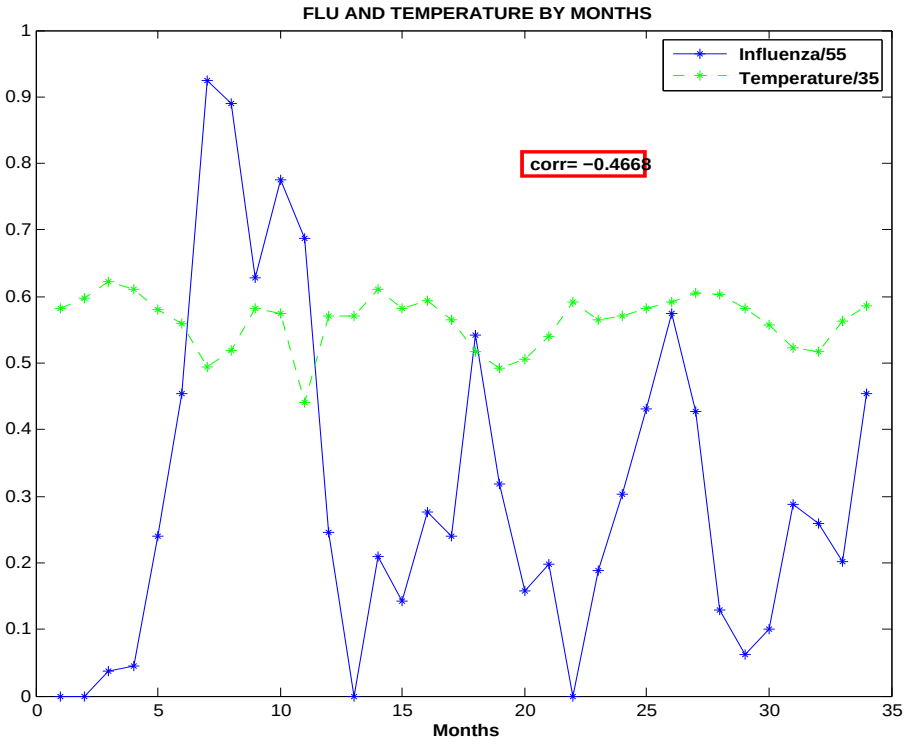

Figure 4.5: Graph Monthly Temperature and Flu in Zone 4

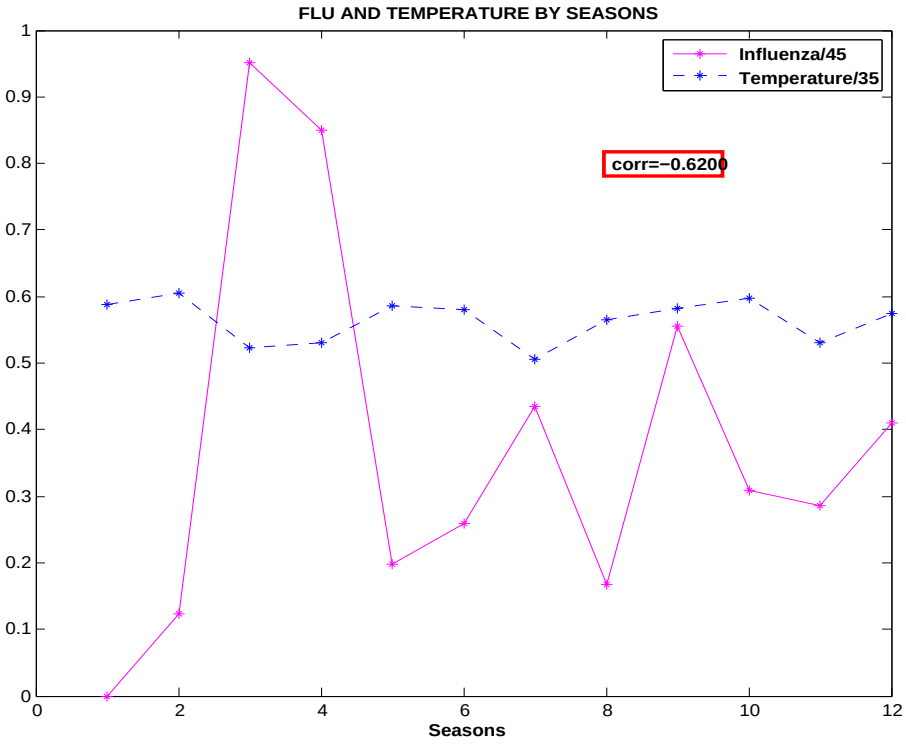

Figure 4.6: Graph of Seasonal Temperature and Flu in Zone 4

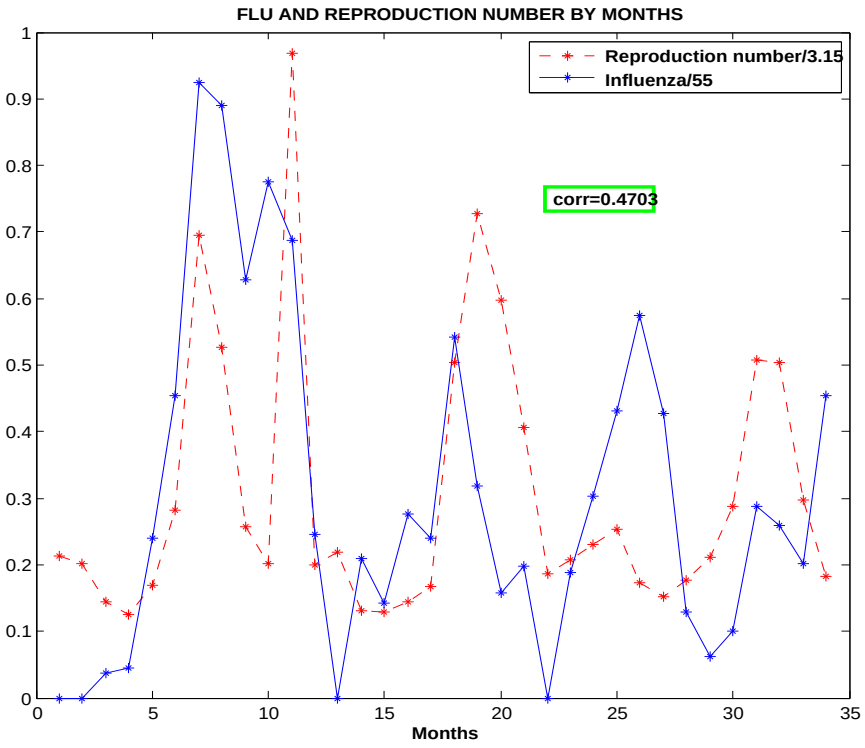

Figure 4.7: Graph of Monthly Reproduction number and Flu in Zone 4

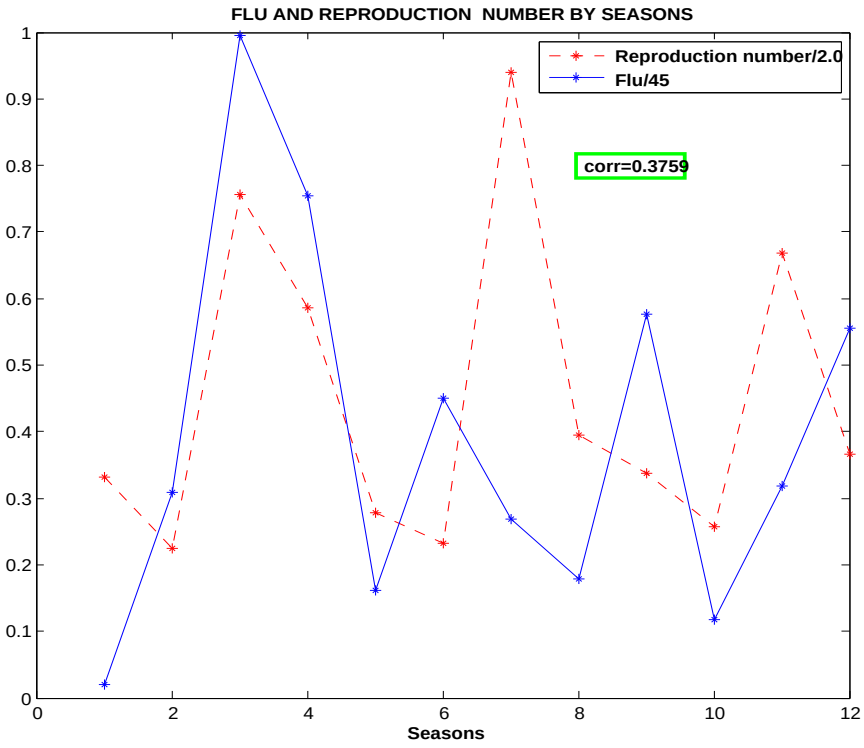

Figure 4.8: Graph of Seasonal Reproduction number and Flu in Zone 4

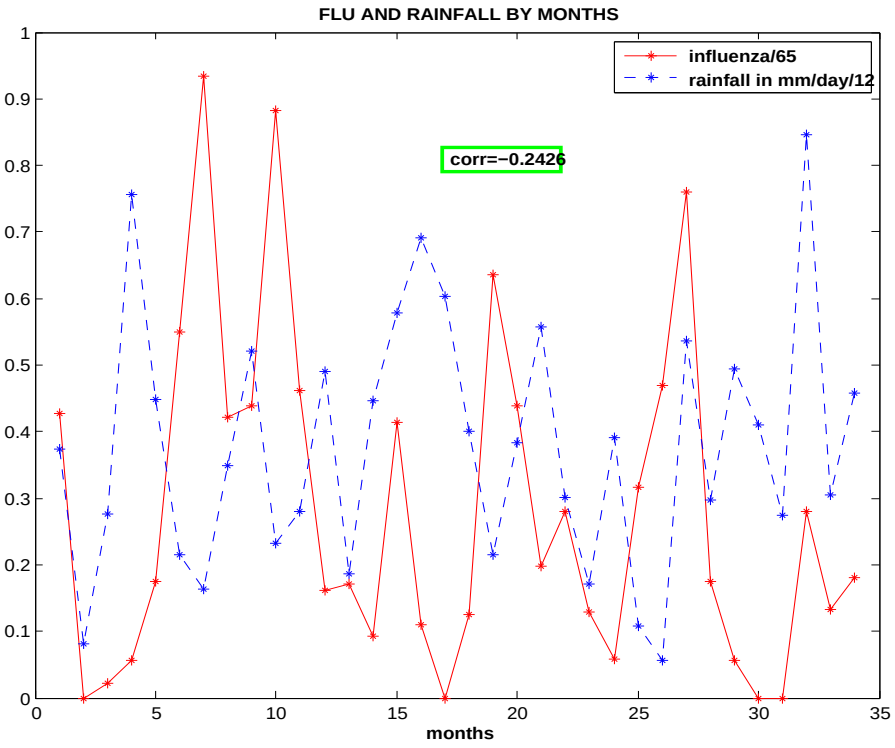

Figure 4.9: Graph of monthly rainfall and Flu in Zone 1

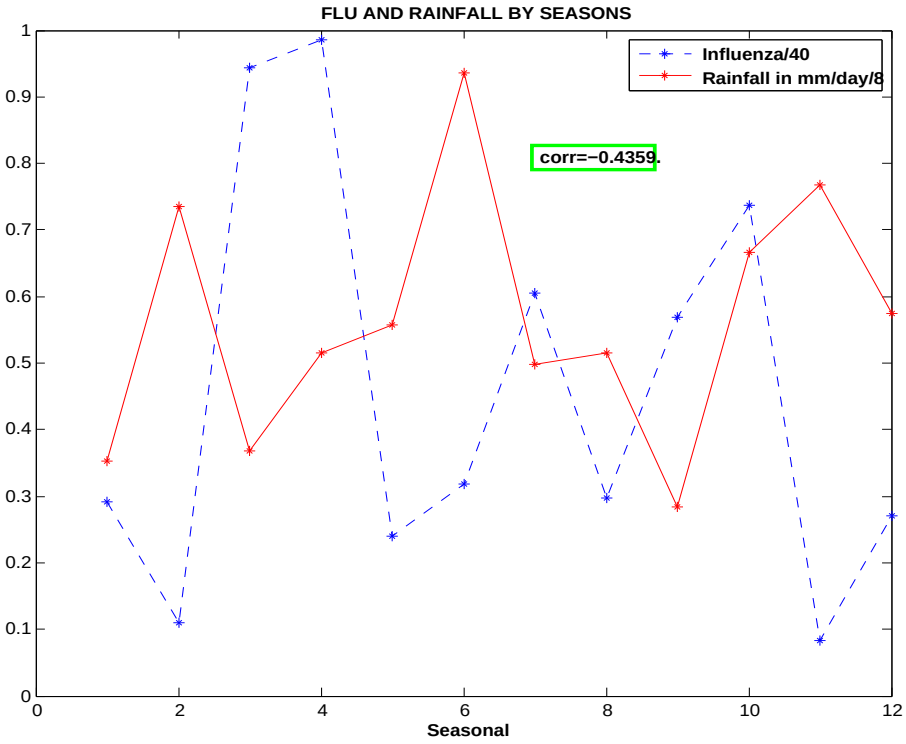

Figure 4.10: Graph of Seasonal rainfall and Flu in Zone 1

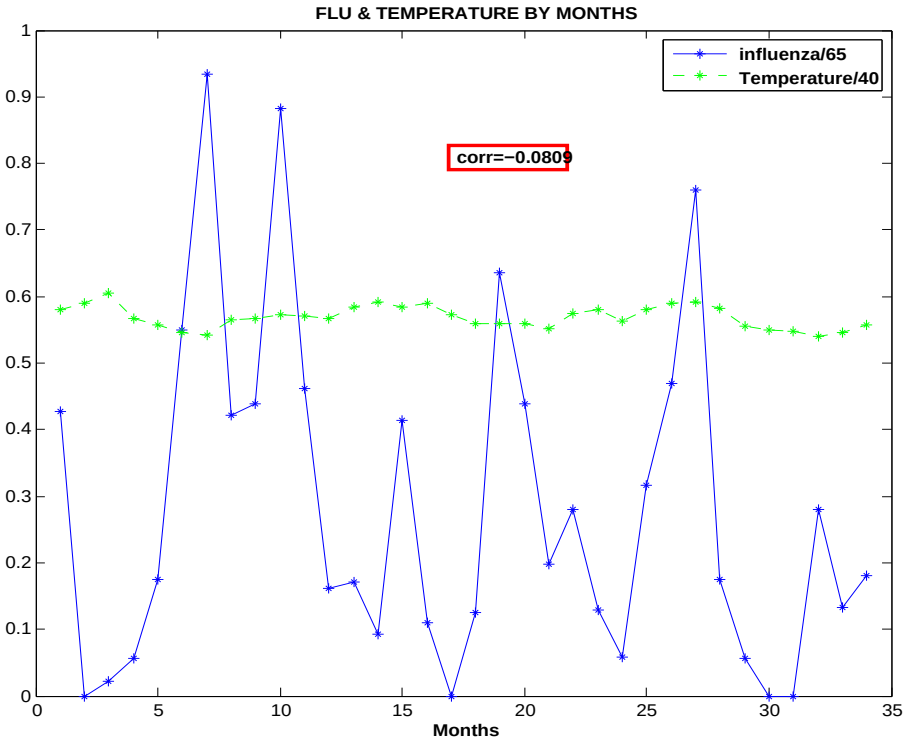

Figure 4.11: Graph of monthly Temperature and Flu in Zone 1

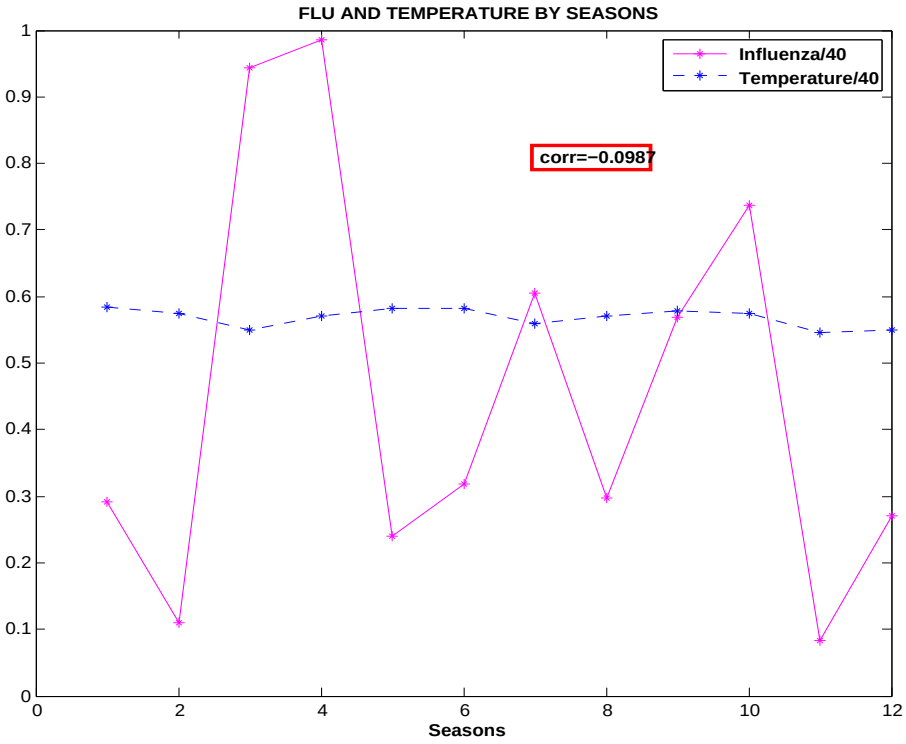

Figure 4.12: Graph of Seasonal Temperature and Flu in Zone 1

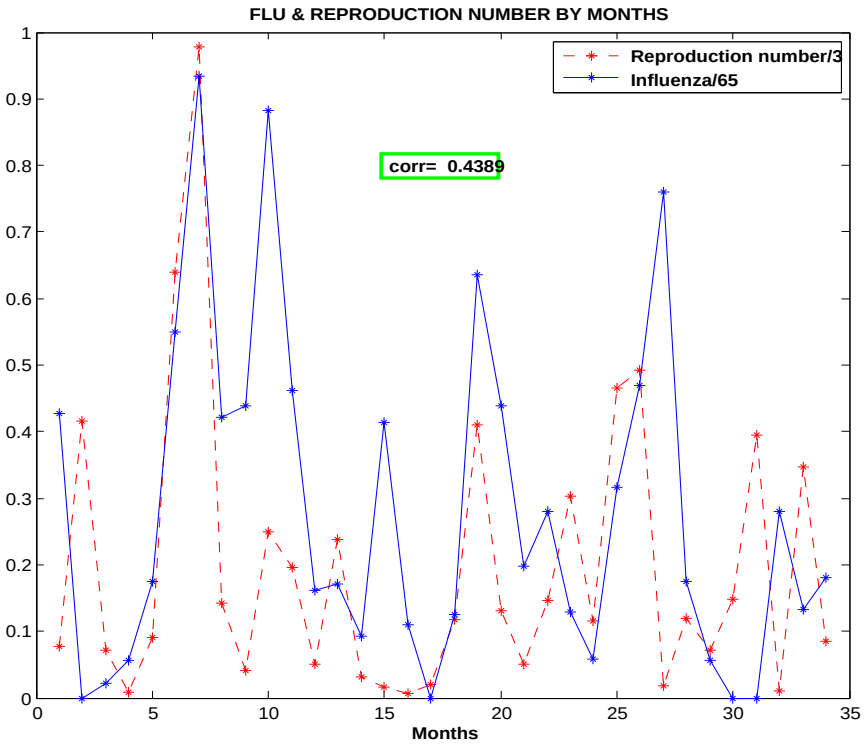

Figure 4.13: Graph of monthly Reproduction number and Flu in Zone 1

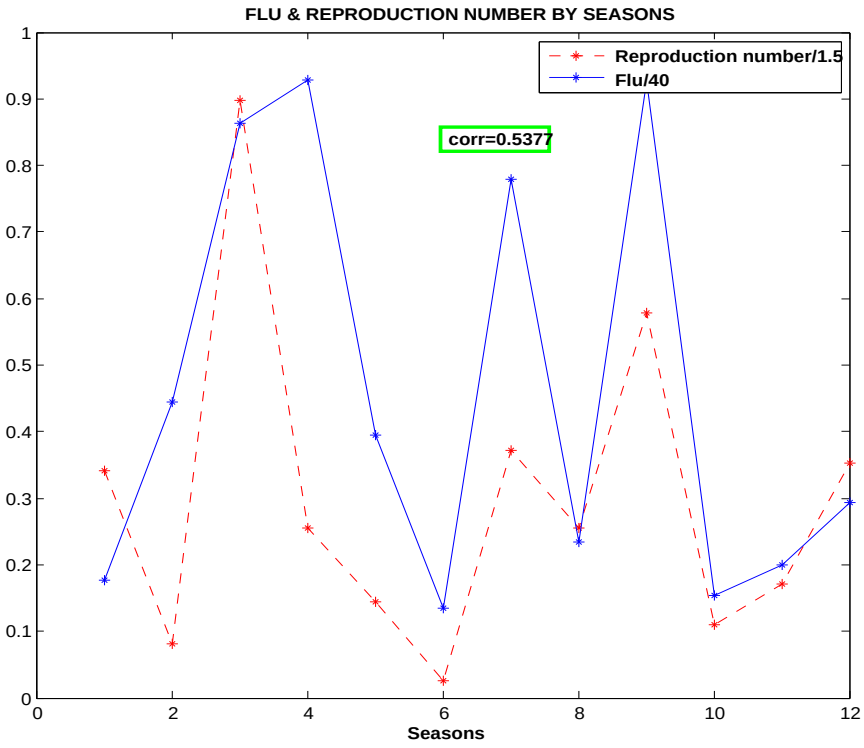

Figure 4.14: Graph of Seasonal Reproduction number and Flu in Zone 1

CHAPTER 5

Conclusion and Recommendations

Recent studies have demonstrated that environmental factors account for a proportion of seasonality, as well as infection oscillations of influenza in temperate regions[43]. Here we used a mathematical model to asses the relation between meteorological parameters and influenza activities in Kenya. We modelled Influenza as a 5-dimensional system of differential equations, through expressing transmission rate as a function of meteorological parameters, the seasonality of influenza incidences could be depicted.

This study shows the dependency of influenza seasonality in Kenya to meteorological parameters. Influenza infection was high in the cold seasons and and the season succeeding the rainy season. An accurate results would enable officials to take appropriate control measures for influenza epidemics, such as vaccination activities prior to the cold seasons and rainy seasons. Further laboratory and epidemiological studies are required to validate and justify the associations between influenza infections with rainfall and temperature

In the numerical solution of the model, i.e. figures 4.1 and 4.2, the values stabilize in the long run confirming that the endemic equilibrium is globally asymptotically stable. Since we have taken same initial values, the difference in the two zones 1 and 4 come as a result of different meteorological parameters, that is different average temperature and rainfall values. Therefore under same initial conditions, the influenza peak in the long run will depend on the temperature and rainfall under consideration but this does not affect the point at which the endemic equilibrium is attained.

It is observed that reproduction number and influenza appear to peak or decrease simultaneously. Therefore we use this as a qualitative index for future climatic changes where results which indicate an increase in the reproduction number during a given period will imply likely increase in influenza in the same period and results which indicate a decrease in reproduction number will imply likely decrease in influenza. This is just a qualitative conclusion and does not indicate the percentage by which a decrease or increase occurs.

In many laboratory tests and various studies on influenza seasonality, air temperature is often found to be associated with influenza transmissions, i.e. low temperatures increases influenza transmissions [44, 45, 47]. Lowen et al.[44] conducted an experimental study using a guinea pig model to demonstrate that cold temperature favored to the spread of the influenza virus. I this study we found that a decrease in temperature will likely indicate an increase in influenza in the same period while an increase in temperature will indicate likely decrease in influenza. This may be due to the fact that, a decrease in temperature could enhance crowding at indoor activities, and would thus increase the contact, aerosol and droplet transmission intensity.

Previous studies have shown that rainfall could be used as a predictor for influenza infection for sub-tropical regions, but not in all temperate regions [46]. Here we have found that an increase in rainfall in a given period will most likely indicate an increase in influenza in the following period while a decrease in rainfall will likely indicate a decrease in influenza in the following period. However, there is no clear and lucid explanation for the mechanism of rainfall driving the influenza seasonality. Although low temperature and dry air have been proven to be favorable for survival of the influenza viral particles [47]. One possible mechanism is that rainfall could affect human social behaviors, such as indoor activities, and therefore increase the number of contacts and the risk of exposure to contaminated environments or infected individuals.

5.1 Recommendations

In this study we only used the percentage of infected individuals to simulate the results, it is recommended that for future research more data should be made available so that the mortality data is used to estimate the the recovered individuals and also the least squares fitting of the influenza mortality data to the model approximates the transmission rate as well as the initial number of infections, here we used the influenza infection in the preceding month as the initial number of infection in the current month.

One limitation of this study is that we only considered the meteorological parameters as a cause of influenza seasonality in Kenya and in simulation we only used the rainfall and the temperatures due to the availability of data, in future we recommend the use of as many meteorological drivers of seasonality as possible in the simulation, example: Sunlight, relative humidity, absolute humidity and absolute deviation of dew point from annual maean . This could provide a better approximations than

only using temperature and rainfall.

We also recommend the use of other factors like social distancing and air travels to model the influenza seasonality. According to some studies [43, 47], some seasonal changes of host behavior (e.g., international travel [48] and school holidays) might also affect the transmission dynamics of influenza. It has been shown that the closure of kindergartens and primary schools was able to reduce the disease transmission rate by around 25% for the 2009 influenza A/H1N1 pandemic.

We used a deterministic model to asses the influenza activity in relation to meteorological parameters, we used the reproduction number to illustrates the qualitative relationship with the influenza activities, We suggest that regression models should be used to explain the influenza seasonality in Kenya, this brings the quantitative relationship and is able to predict future incidences.

Bibliography

[1] M.A. Urban (2009) *Influenza. Viral infections: Merck Manual home edition.* Technical report.

[2] Media centre (2009-04-12).The World health organisation(WHO). Seasonal influenza fact sheets[E-B/OL]. http;www.who.int/media centre/factsheet/fs211/en/.

[3] N.J. Cox and K. Subbarao (2000) *Global epidemiology of Influenza*: Past and Present, Annu. Rev. Med.,**51**,407-421.

[4] A. Moscona (2005) *Neuraminidase inhibitors for Influenza*, N. Engl.J. Med., **353**, 1363-1373.

[5] A.J. Hay, V. Gregory , A.R. Douglass and Y.P. Lin (2001) *The evolution of human influenza virus. Philosophical Transcations of the Royal society B* : Biological, **356**, 1891-1870.

[6] K. J Jakeman, M. Tisdale, S. Russel, A. Leone, and C. Sweet (1994) *Efficacy of 2'-deoxy-2', Fluororibosides against influenza A and B virus in ferrets.* Antimicrobial Agents and chemotherapy, **38**, 1864-1867.

[7] J.K. Taubenberger and D.M. Morens (2008) *The pathology of influenza virus infections.* Annual Review of pathology, **3**, 499-522.

[8] C.W.Potter: (2004) *Influenza*, *In Principles and Practice of Clinical Virology.* Zuckerman AJ, Banatvala JE, Pattison JR, Griffiths PD, Schoub BD, John Wiley & Sons, Ltd., **5**, 271-297.

[9] F.M. Davenport (1961) *Pathogenesis of influenza.* Bacteriol Rev., **25**, 294-300.

[10] Sweet C, Smith H (1980) *pathogenicity of influenza virus* . Microbiol Rev, **44**, 303-330.

[11] T.C Meteinteitter and F. Sobrino (2008) *Anual Virus*. Molecular Biology. Caster academic press, 1edition.

[12] J.K. Taubenberger and D. Morens (2006) *1918 influenza*: *the mother of all pandemics*. EID journal, **12**, 15-22.

[13] J. Green (2006) *The Bird flu pandemic*: *can it happen? will it happen ? How to protect yourself and your family if it does*, St. Martin's Griffin, 1 edition.

[14] JF. Brundage, GD. Shanks (2008) *Deaths from Bacterial Pneumonia during 1918-19 Influenza Pandemic*. Emerg Infect Dis. Aug; **14**,(8):1193-9.

[15] H. Hong (2006) *Plague. SARS and the story of medicine in Hong Kong*. Hong University press, 1 edition

[16] M. Mandel (2009) *No need to panic*. Toronto sun.

[17] M. Chan (2009) *World now at the start of 2009 influenza pandemic*. Technical report, Worl Health Organisation,

[18] P.A Oria, W. Matini, I. Nelligan, G. Emukule, M. Scherzer, B.Oyier et al. (2010) *Are Kenyan healthcare workers willing to receive the pandemic influenza vaccine? Results from a cross-sectional survey of healthcare workers in Kenya about knowledge, attitudes and practices concerning infection with and vaccination against 2009 pandemic influenza A (H1N1)*. Vaccine. 2011 Apr 27;**29**,(19):3617-22.

[19] D. J. D. Earn, J. Dushoff and S.A. Levin (2002) *Ecology and evolution of flu, trends in ecology and evolution*. **17**, 334-340

[20] K. Rodgers (2007) *Flu shorts for everypne*. Technical report, encyclopedia Britannia, Inc, 2007

[21] J. Treanor (2004) *Influenza vaccine-outmaneuvering antigenic shift and Drift*. New England journal of medicine, **350**, 218-220.

[22] R.B. Belshe (2005) *The origin of pandemic influenza, lessons, demo the 1918 virus*.N. Engl. J.Med. **353**, 2207-11

[23] J. Lin, M. Kang, H. Zhong, X. Zhang, F. Yang, H. Ni, P. Huang, T. Hong, C. Ke, and H. jiefeng (2013) *Influenza seasonality and predominant subtypes of influenza virus in Guang dong, China 2004-2012*. J Thorac Dis2013: **5**,(52): 5109-5117. doi:10.3978/jissn.2072-1439.2013.08.09.

[24] M. Lipsitch, C. Viboud (2009) *Influenza sesonality*: *lifting the fog*. Proc Natt Acad Sci USA 2009:**106**, 3645-6.

[25] J.D. Tamerius, J. Shaman, W.J. Alonso, K.B. Feshback, C.K. Uejio, A. Comric, C. Viboud (2013) *Environmental predictors of seasonal influenza epidemics across temperate and tropical climates*. PLos pathog **9**, e1003194.

[26] B.D. Gessner, N. Shindo, S. Briand (2011) *Seasonal influenza epidemiology in sub saharan Africa*. A systemic review. Lancet infect Dis.2011 Mar; **11**,(3): 223-35.

[27] D.M. Matheka, J. Mokay and M. Maritim (2013) *Overview of influenza virus in Kenya*: past, present and future. Pan African medical journal.2013.14:138:doi10.11604/pamj.2013.14.138.2812.

[28] S.Z.Zhou (2009) *A seasonal influenza theory and mathematical model incorporating meteorological and socio-Behavioral factors*. Journal of tropical meteorology.2009: **5**, 001-12: doi: 10.3969/j.issn.1006-8775.2009.01.01

[29] S.P. Noort, R. Aguas, S. Ballestos, M.G. Gomes (2012) *The role of weather on the relation between influenza and influenza-like illness*: Journal of theoretical Biology **298**, 131-137.

[30] A. MAhamat, P. Dusaart, A. Barix, L. Carvalho, F. Eltges, S. Matheus. M.A. Miller, P. Querel and C. Viboud (2013) *Climatic drivers of seasonal influenza epidemics in French Guiana, 2006-2010*.jinfect.**67**,(2):14-147.doi: 10.1016/j.jinf.2013.03.08.

[31] K.C. Chong, W. Goggins, B.C Yingzee and M.H. Wang (2015) *Identifying meteorological drivers for the influenza variations of influenza infections in a subtropical city-Hong Kong*. int.j.Environ.Res.public Health, **12**, 1560-1576.doi:10.3390/ijerph120201560.

[32] W.O. Kermack and A.G Mckendrick (1927) *A contribution to the mathematical theory of epidemics*. Proceeding of the royal society, London A, **115**, 700-721

[33] Hethcote (2000) *The mathematics of infectious diseases*. SIAM Review. **42**,(4): 599-653.

[34] K. Dietz (1976) *The incidence of infectious diseases under the influence of seasonal fluctuations*, Lect. Notes Biomath. **11** 1-11.

[35] N. Fergurson, A. Garvani and R. Bush (2003) *Ecological and immunological determinants of influenza evolution*. Nature **422**, 428-433

[36] G. Chowell, C. Viboud, L. Simonsen, M. Miller and W.J. Alonso (2010) *The reproduction number of seasonal influenza epidemics in Brazil*, 1996-2006. Proc. R. Soc. B , **277**, 1857-1866.

[37] R. Anderson and R. May (1991) *Infectious Diseases of Humans: Dynamics and Control*, Oxford University Press.

[38] O. Diekmann and A.P. Heesterbeek (2000) *Mathematical epidemiology of infectious diseases*, Wiley series in mathematical and computational biology, John Wiley and Sons. West Sussex, England.

[39] F.C.K. Li, B.C.K. Choi, T. Sly, A.W.P. Pak (2008) *Finding the real case fatality rate of H5N1 avian influenza*. J. Epidemiol. Community Health, **62**, 555-559.

[40] C.E. Mills, S.M. Robins, M. Lipsitch (2004) *Transmillibility of 1918 pandemic influenza*. Nature; **432**, 895-906.

[41] G. Chowell, M. A. Miller and C. Viboud (2008b) *Seasonal influenza in the United States, France, and Australia*: transmission and prospects for control. Epidemiol. Infect. **136**, 852864.

[42] M. Quincampiox (1992) *Differential Inclusions and Target problems*. SIAM journal and control optmization, **30**, (2), 324-335.

[43] D.E. Te Beest, M. van Boven, M. Hooiveld, C. van den Dool, J. Wallinga (2013) *Driving factors of influenza transmission in the Netherlands*. Amer. J. Epidemiol. **178**, 14691477.

[44] A.C. Lowen, S. Mubareka, J. Steel, P. Palese (2007) *Influenza virus transmission is dependent on relative humidity and temperature*. PLoS Pathog., **3**, doi:10.1371/journal.ppat.0030151.

[45] P.K. Chan, H.Y. Mok, T.C. Lee, I.M. Chu, W.Y. Lam, J.J.Sung (2009) *Seasonal influenza activity in Hong Kong and its association with meteorological variations*. J. Med. Virol., **81**, 17971806.

[46] R.P. Soebiyanto, R.Kiang (2014) *Meteorological parameters as predictors for seasonal influenza*. Geocarto Int., **29**, 3947.

[47] E. Lofgren, N.Fefferman, Y.N. Naumov, J. Gorski, E.N. Naumova (2007) *Influenza seasonality: Underlying causes and modeling theories*. J. Virol. **81**, 54295436.

[48] K.C. Chong,B.C. Zee (2012) *Modeling the impact of air, sea, and land travel restrictions supplemented by other interventions on the emergence of a new influenza pandemic virus*. BMC Infect. Dis. **12**, doi:10.1186/1471-2334-12-309.

[49] N. M. Ferguson, A. P. Galvani and R. M. Bush, (2003) *Ecological and immunological determinants of influenza evolution*. Nature **422**, 428433. (doi:10.1038/nature01509)