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Master Project in Mathematics

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Research Report in Mathematics, Number 21, 2019

PRETTY CYNTHIA NYALALA

June 2019

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

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Master Thesis

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

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

Abstract

The aim of this project is to carry out a research on the effects of weather variables on the seasonality of influenza. For this purpose we formulate a compartmental model to represent influenza transmission dynamics. Influenza is modeled as a 5-dimensional deterministic system of ODE's with a variable transmission rate expressed as an exponential function of the weather variables.

The basic properties including the basic reproduction number are derived. The disease free and endemic equilibrium of the model are found and their stability analyzed. The disease free equilibrium point is found to be both locally and globally stable.

Influenza data was organized into seasons from December 2006 to November 2011. Graphs were drawn for all the four stations to determine the season with the most flu prevalence. It was established that, the 3rd season has the most flu prevalence while the 1st season had the least flu prevalence.

The mean values of the weather variables were retrieved from world weather website online and aggregated into seasonal values. The correlation coefficient of flu with the basic reproduction number, temperature, rainfall and humidity was calculated. In Nairobi station, we see that there is a positive correlation between flu and the basic reproduction number. In all the four stations, we can see that there is a negative correlation between flu and temperature and flu and rainfall. On the other hand, there is a positive correlation between flu and humidity.

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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.

Signature Date

PRETTY CYNTHIA NYALALA
Reg No. I56/8605/2017

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

Signature Date

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Dedication

I dedicate this project to the Almighty God and my beloved family.

Contents

Acknowledgments

First and foremost, I thank the Almighty God for giving me life and wisdom to enable me write this project.

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PRETTY CYNTHIA NYALALA

Nairobi, 2019.

1 Introduction

The aim of this thesis is to study the effect of temperature, rainfall and humidity in the seasonality of Influenza virus in Kenya.

This thesis has five chapters. Chapter one basically covers the introduction. It gives the general background of the disease, problem statement, objectives and the significance of the study. Chapter two highlights some existing literature on effects of weather variables on the seasonality of Influenza. Formulation and analysis of the deterministic model is covered in Chapter three. Chapter five contains numerical simulations for the model and finally, results, discussions and recommendations of the simulations are covered in Chapter 6.

1.1 Classification and Causes of Influenza

Influenza is an communicable viral infection. The virus can be classified into three main types namely; Influenza A,B and C.

Influenza A mutates a lot through antigenic shift and antigenic drift and it ends up forming new strains like H1N1 (Swine Flu) and H3N2 (Avian Flu (Urban M.A., 2009). Since Influenza A has the ability to mutate and form a different strain, it can easily cause widespread outbreak.

1.2 Antigenic Drift and Antigenic Shift

Influenza viruses mutate often such that the immune system of the host is not able to protect against the new strain. The two processes involved in the mutation are called; antigenic drift and antigenic shift.

- An influenza virus is prone to errors every time a copy of its genome is being formed. If the errors are sufficient enough, reinfection is possible as immunity produced against the previous strain might not be able to protect against the newly formed strain. This process is called antigenic drift.
- When two influenza strains mix to form a new strain that has the properties of both both mother strains, the process is called antigenic shift.

1.3 Transmission and Spread of Influenza

The influenza virus is airborne. It can be transmitted through direct contact with an infectious person or by coming into contact with a contaminated surface. When an infectious person coughs or sneezes, air droplets carrying the infection enter the respiratory system of someone in close range, this makes makes the transmission of the flu quite rapid in crowded places.

If you have the flu, you are contagious from at least a day before you begin to experience symptoms up through five days after your symptoms begin.

1.4 Signs and Symptoms

Influenza is usually characterized by a sudden inception of fever, headache, sore throat and runny nose. In high risk groups, influenza can cause severe illnesses such as sinus infection and pneumonia or even lead to death.

1.5 High Risk Groups

Influenza infections affect all populations. However, pregnant women, children between 5 to 59 months, the elderly, and individuals with underlying chronic illnesses are at a high risk of infection due to weakened immune system. Since health care workers constantly interact with patients, they are also at a high risk of infection.

1.6 Diagnosis,Treatment and Recovery

The Rapid Influenza Diagnostics Test is often used to determine if a patient is infectious. Occasionally, the disease can clear when the infected takes plenty of water and has enough rest, hence, patients with uncomplicated seasonal influenza are usually advised to stay home to minimize chances of spreading the disease. However, there are antiviral drugs which may be prescribed to help reduce the ability of the disease to spread and relieve some of the symptoms. The treatment period lasts about 5 days but can be prolonged until there is satisfactory improvement.

1.7 Prevention

The most effective way to prevent the flu is through annual vaccinations. At least each flu shot protects against three to four different influenza viruses within that year's flu season.

Alternative routines that can be used to prevent the spread of the disease include:

- Constant wash of hands with soap and clean water.
- Avoiding overcrowded places when sick.
- Cleaning and disinfecting objects and surfaces.
- Avoiding direct sneezes and coughs onto one's hand

1.8 Risk of Re-infection

When one gets sick from one strain of the influenza virus, his or her body develops immunity that will protect him or her from getting re-infected with the same strain. However, one can still be infected with a different strain as the antibodies formed from the first infection might not be able to provide protection against a different strain.
However, if an immunized individual re-encounters a virus in 3-4 weeks re-infection is likely to occur because by then, the primary antibody response has not matured. This is likely to occur during an extensive circulation of the influenza virus.

1.9 Cycles of Occurrence

Influenza occurs in distinct outbreaks of varying extents every year in Kenya. The epidemiological pattern reflects the changing nature of the antigenic properties of influenza viruses (Mwangangi, 2013).The subsequent spread depends upon multiple factors including transmissibility of the virus and susceptibility of the population.
Influenza is prevalent during cold months as the flu virus is believed to be steady and stays in the air longer during cold months. In winter, most people are also indoors and hence overcrowding and lack of vitamin D.

1.10 Public Concern

Influenza presents a year-round disease burden.It causes illnesses that range in severity. The illnesses not only maim leading to hospitalization and loss of productivity but can also lead to death.

The fact that the virus mutates a lot, is a great potential for a pandemic. Every year, a new vaccine is introduced so that it is effective to the circulating influenza virus. In temperate

climates, seasonal epidemics occur mainly during winter, while in tropical regions like Kenya, influenza may occur throughout the year. In sub-Saharan Africa, influenza is not properly documented making it hard to detect a new strain or clusters of human cases that could be associated with a pandemic(Gessner, 2011).Knowledge of disease burden is essential in informing policy decisions around treatment and prevention of the disease.

1.11 Past Pandemic

A pandemic is a global outbreak of a disease. So far, we have had four global outbreaks of the influenza virus.

- The Spanish Flu involving H1N1 sub type of Influenza A was the first global outbreak of Influenza which occurred between the years 1918 and 1920.As the name suggests, the pandemic originated in Spain. It caused upto 50 million deaths worldwide (Taubenberger and Morens, 2006).
- The Asian Flu which originated from China in the year 1956 caused about 2 million deaths according to WHO and it involved the H2N2 Influenza A sub-type.
- The Hong Kong Flu which occurred between the years 1968 and 1970 was caused by the H3N2 sub-type which was generated from the H2N2 sub-type through antigenic shift (Hong, 2006). The virus caused about one million deaths world wide (Mandel, 2009).
- The 2009 Swine Flu which involved the H1N1 Influenza A sub-type occurred between 2009 and 2010. It caused about 200,000 deaths globally according to WHO website (Mwangangi, 2013).

1.12 Problem Statement

Although various efforts against the disease have been made, influenza is still endemic due to lack of sufficient knowledge on its dynamics and proper application of cost effective control strategies. This disease is highly linked with weather variables as it is seen to have peaks during cold months. This study is intended to develop a mathematical model for the transmission dynamics of Influenza and use this mathematical model to quantify the role of seasonal weather variables in the transmission dynamics of the virus.

1.13 Objectives of the Study

The main objective of this study is to devise a mathematical model for the transmission dynamics of Influenza and determine the effects of seasonal temperature, rainfall and humidity.

1.13.1 Specific objectives

1. To establish and ascertain the stability of equilibrium points.

2. To express the reproduction number as a function of temperature, rainfall and humidity.
3. To estimate the transmission rate from the data.
4. To analyze and detect patterns in the seasonality of observed influenza data.
5. To analyze and detect patterns in the seasonality of observed influenza data.

2 Literature Review

2.1 Influenza Seasonality

In temperate regions, influenza occurs constantly during winter and early spring months (Lipsitch, 2009). Its seasonality is well studied and documented. In tropical regions influenza seasonality is not well studied and documented. However, influenza is seen to occur sporadically all year round in tropical regions with peaks observed during cold months. If peak influenza activity is an accurate measure, flu viruses prefer the weather either cold and dry or humid and rainy, according to an analysis of climate variables and flu patterns around the world (CIDRAP, 2013).

Several studies conducted have linked weather variables to the seasonality of Influenza. Weather variables not only affect virus survivor-ship but also the transmission efficiency of the disease. Inadequate vitamin D and melantonin due to changes of number of days with sunlight is believed to affect the susceptibility of the population.

By using weekly meteorological data and disease surveillance data of influenza in Shaoyang (Zhou et al, 2007) used a general additive model to investigate the effect of weather variables on Influenza activity. The study suggests that the risk of influenza is higher in cold and less humid conditions in China.

Lowen and Palese (2009) in their study showed that low temperature and humidity not only improve the viability of the influenza virus but also facilitate rapid spread of the virus by providing suitable circumstances for aerosol borne transmission.

Zhou (2009) study suggested that the seasonality of Influenza could depend on several factors such as weather variables and internal dynamic resonance. Some of the weather variables he examined in his study were precipitation, solar radiation and dew point. The results of his study suggest that;

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

He recommended that in depth knowledge on roles of weather variables in Influenza activity is critical for early interventions such as opportune vaccination and social distancing. He used the general growth model in his study and derived a formula for the transmission dynamics of influenza.

Chong (2005) conducted a study in a subtropical city Hong Kong fitted weather variables and Influenza mortality data in an SIR model to identify the weather variables effect on the seasonality of influenza virus transmission. The results of the study showed that, air temperature and rainfall played a significant role in the seasonality of the Influenza virus. Air temperature and rainfall were found to be the significant drivers of seasonality of the disease.

These studies suggest that periodicity of Influenza is caused by a less-than-straight forward interaction of many different factors. Recognition of this complexity is essential for continued examination and study of the seasonality of the virus.

2.2 Mathematical Modeling of Influenza

Mathematical modeling dates back to 1766 when the very first publication was made. In the seminal paper, Bernoulli developed a mathematical model to study deaths caused by small pox in England. In 1772 Lambert extended Bernoulli's model by incorporating age dependent parameters (Dietz, 1976).

In 1911 Ross made an extension which was like the benchmark of modern mathematical epidemiology. Following up the work of Ross, Kermack and McKendrick founded the deterministic model. In their papers, they addressed the mass action incident, suggesting that the probability of infection of susceptible is analogous to the number of its contacts with infected individuals (Dietz, 1976).

Over the years, mathematical models have been adapted in analysis of disease dynamics (Chowell, 2008) estimated the reproduction number over three decades in Australia, France and in the United States by applying an elementary epidemic model to the weekly values of influenza deaths. In his study, he divided the population into five classes, namely; susceptible, exposed, infectious, protected and dead.

Chong et al (2015) extended the model by Chowell in their research which was aimed at describing the dynamic system of seasonal influenza in Hong Kong. Their model was divided into four compartments; susceptible, infectious, recovered and dead. They used a time varying transmission rate to express the transmission rate as a function of the weather variables.

3 Model Formulation and Analysis

In this Chapter, a deterministic model describing the dynamics of influenza transmission is formulated. The model comprising of non linear differential equations is qualitatively analyzed to determine the existence of the steady states. The steady states are then analyzed to determine local and global stability.

3.1 Model Formulation

To come up with the model, we use the idea of the model formulated by Chowell (2010) and incorporate the idea of variable transmission rate by Chong (2015). To construct the SEIRD deterministic model, we divide the total population N into five epidemiological classes; the susceptible class (s); those who are not infected but are at a risk of getting the infection if exposed, the Exposed class (e); those who are infected but are not yet contagious , the Infected class (i); the group of people who already have the disease and are contagious, the Recovered class (r); the group of people who have been healed hence immune to the disease and the Dead class (d) consisting of those who die from the disease (Miller, 2007). Hence, the total population;

$$N = s + e + i + r + d.$$

The Susceptible become infected at a rate β_t. σ represents the rate at which one moves from the Exposed class to the Infected class, λ is the recovery rate and finally μ represents the rate of death due to the disease.

To analyze the system, we normalize it by dividing both sides of the equation by N. let $s/N = S$, $e/N = E$, $i/N = I$, $r/N = R$ and $d/N = D$.Hence S + E + I + R + D = 1.

3.2 Assumptions of the Model

- The population can be divided into a set of five classes depending on their experience with the disease.
- The population is homogeneous with the same probability of transmitting the disease.
- The population is constant at any given time. No natural births and deaths.This is because, influenza cycle is in days while deaths and births happen over years.
- The recovered assume permanent immunity.

- At the beginning , everyone in the population is assumed to be susceptible

Variable	Description
S	Susceptible
E	Exposed
I	Infected
R	Recovered
D	Dead

Parameter	Description
β_t	Transmission rate
σ	Infection rate
δ	Recovery rate
μ	Disease induced death rate

3.3 The Compartmental Model

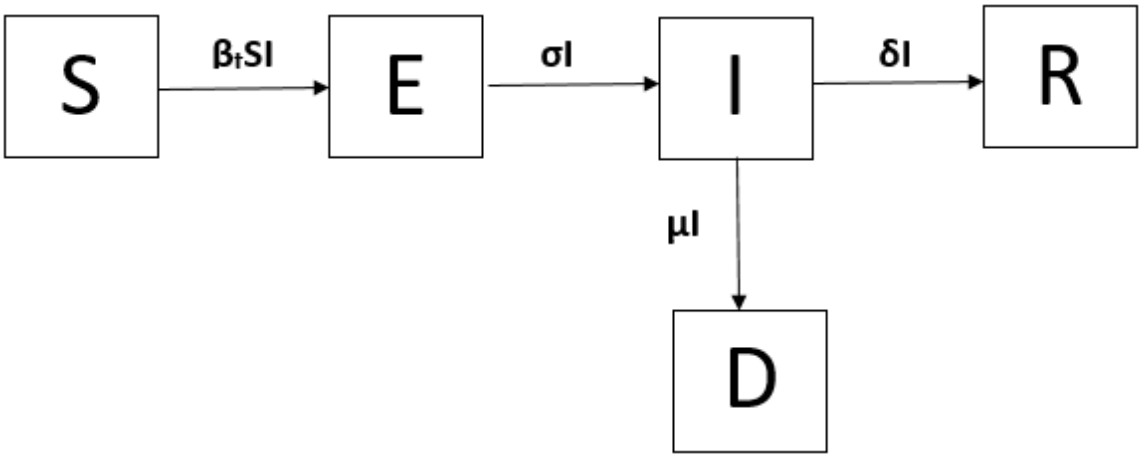

Figure 1. The Compartmental Model

3.4 The Model equations

From Figure 1 the following ordinary differential equations are obtained.

$$\begin{aligned} \frac{dS}{dt} &= -\beta_t SI, \\ \frac{dE}{dt} &= \beta_t SI - \sigma E, \\ \frac{dI}{dt} &= \sigma E - (\mu + \delta)I, \\ \frac{dR}{dt} &= \delta I, \\ \frac{dD}{dt} &= \mu I. \end{aligned} \tag{1}$$

3.5 Analysis of the Model

In this section qualitative analysis of the model is carried out in order to investigate the possibility of the existence and stability of equilibrium points.

3.5.1 Invariance of the region ,positivity and boundedness of the solution

To determine whether the model is biologically meaningful, it is tested for positivity and feasibility. To prove invariance, positivity and boundedness, it is imperative to show that the system is dissipative (Vibound, 2013). That is, all solutions are uniformly bounded in a proper subset $\Omega = R_+^4$ with non negative initial conditions.

$$\Omega = [(S,E,I,R) \in R_+^4 : N(t) \leq \frac{\Lambda}{\mu}] \tag{2}$$

3.5.2 Existence and Stability of the Equilibrium Points

The equilibrium points are found by setting model equation (1) to zero.

$$-\beta SI = 0, \tag{3}$$

$$\sigma E - (\mu + \delta)I = 0, \tag{4}$$

$$\delta I = 0, \tag{5}$$

$$\mu I = 0. \tag{6}$$

3.5.3 The Disease Free Equilibrium Point(D.F.E.P)

When there is no disease in the population, we have a D.F.E.P.

Stability of D.F.E.P is regarded as a case whereby the disease is totally eliminated from the population. When $R_0 \leq 1$ this can be achieved.

In the absence of the disease ; $E = I = R = 0$ hence, $S = N = 1$.

Hence;

$$E_0 = [1, 0, 0, 0]$$

3.5.4 Basic Reproduction Number

To analyze the stability of the disease free equilibrium point, the basic reproduction number R_0 for the model must be computed. The basic reproduction number R_0; is defined as the total number of secondary infections arising from one newly infected individual introduced into a totally susceptible population (May and Anderson, 1992). We calculate the basic reproduction number R_0 of the system using the next generation operator approach (Watmough, 2002). We define the model dynamics using;

$$\frac{dE}{dt} = \beta SI - \sigma E$$

$$\frac{dI}{dt} = \sigma E - (\mu + \delta)I$$

We define the vector valued function f as the rate of appearance of new infection in the disease compartments.

$$f = \begin{bmatrix} E_n \\ I_n \end{bmatrix}$$

Finding the Jacobian matrix of f at the disease free equilibrium gives,

$$F = \begin{bmatrix} 0 & \beta_t S^\star \\ 0 & 0 \end{bmatrix}$$

$$F = \begin{bmatrix} 0 & \beta_t(1) \\ 0 & 0 \end{bmatrix}$$

Calculating the difference between the rate of transfer of individuals out of the disease compartment and the rate of transfer of individuals into the disease compartment we get;

$$v = v^- - v^+$$

Where,v^- is the transfer of individuals out of the disease compartment.
v^+ is the transfer of individuals into the disease compartment. The transmission vector is given by;

$$v = \begin{bmatrix} \sigma E \\ (\mu+\delta)I - \sigma E \end{bmatrix}$$

$$V = \begin{bmatrix} \sigma & 0 \\ -\sigma & \mu+\delta \end{bmatrix}$$

$$V^{-1} = \frac{1}{(\sigma)(\mu+\delta)} \begin{bmatrix} \mu+\sigma & 0 \\ \sigma & \sigma \end{bmatrix}$$

$$= \begin{bmatrix} \frac{1}{\sigma} & 0 \\ \frac{1}{\delta+\mu} & \frac{1}{\delta+\mu} \end{bmatrix}$$

$$FV^-1 = \begin{bmatrix} 0 & \beta_t S \\ 0 & 0 \end{bmatrix} \begin{bmatrix} \frac{1}{\sigma} & 0 \\ \frac{1}{\delta+\mu} & \frac{1}{\delta+\mu} \end{bmatrix}$$

$$= \begin{bmatrix} \frac{\beta_t S}{\delta+\mu} & \frac{\beta_t S}{\delta+\mu} \\ 0 & 0 \end{bmatrix}$$

The basic Reproduction number R_0 is equal to the spectral radius(the greatest eigenvalue) of FV^{-1}

$$= \begin{vmatrix} \frac{\beta_t S}{\delta+\mu} - \lambda & \frac{\beta_t S}{\delta+\mu} \\ 0 & 0-\lambda \end{vmatrix}$$

$$(-\lambda)(\frac{\beta_t S}{\delta+\mu} - \lambda) = 0$$

Hence,

$$\lambda_1 = 0$$
$$\lambda_2 = \frac{\beta_t S}{\delta+\mu}$$

λ_2 is the greatest eigenvalue hence;

$$R_0 = \frac{\beta_t S\star}{\delta+\mu}$$

At the disease free equilibrium point, the value of E=O, I=0, R=0 and D=0 hence, the value of S is equal to the total population which is one; thus

$$R_0 = \frac{\beta_t}{\delta+\mu} \tag{7}$$

The terms in the basic reproduction number can be interpreted as follows;
$\frac{1}{\delta}$ = Mean Infectious Period
β_t = Transmission rate
$\frac{1}{\mu}$ = Life Expectancy of Human Population

It is clear that R_0 increases with increase in β. Therefore the transmission term increases the basic reproduction number R_0 . This means that more and more people get infected as more contacts are made by the susceptible population.

3.5.5 Local Stability of Disease Free Equilibrium Point

We analyze this by obtaining the Jacobian of the equation(1)and evaluating its eigenvalues. For the equilibrium to be locally asymptotically stable, $R0 < 1$.

From the equation (1) above, we have the Jacobian;

$$J(E) = \begin{bmatrix} -\beta_t I & 0 & -\beta_t S & 0 \\ \beta_t I & -\sigma & \beta_t S & 0 \\ 0 & \sigma & -(\delta+\mu) & 0 \\ 0 & 0 & \mu & 0 \end{bmatrix}$$

At the disease free equilibrium point, we know that: $[S,E,I,R,D] = [1,0,0,0,0]$. Hence, replacing the values of S and I in the matrix above, we get; The Jacobian matrix at the Disease Free Equilibrium Point;

$$J(E_0) = \begin{bmatrix} 0 & 0 & -\beta_t & 0 \\ 0 & -\sigma & \beta_t & 0 \\ 0 & \sigma & -(\delta+\mu) & 0 \\ 0 & 0 & \mu & 0 \end{bmatrix}$$

We now evaluate $J(E_0)$ to get it's eigenvalues

$$\begin{vmatrix} 0-\lambda & 0 & -\beta_t & 0 \\ 0 & -\sigma-\lambda & \beta_t & 0 \\ 0 & \sigma & -(\delta+\mu)-\lambda & 0 \\ 0 & 0 & \mu & 0-\lambda \end{vmatrix} = 0$$

$$\begin{vmatrix} \lambda & 0 & \beta_t & 0 \\ 0 & \sigma+\lambda & -\beta_t & 0 \\ 0 & -\sigma & (\delta+\mu)+\lambda & 0 \\ 0 & 0 & \mu & \lambda \end{vmatrix} = 0$$

$$\lambda \begin{vmatrix} \sigma+\lambda & -\beta_t & 0 \\ -\sigma & (\delta+\mu)+\lambda & 0 \\ 0 & \mu & \lambda \end{vmatrix} = 0$$

$$\lambda^2 \begin{vmatrix} \sigma+\lambda & -\beta_t \\ -\sigma & (\delta+\mu)+\lambda \end{vmatrix} = 0$$

$$\lambda^2[(\sigma+\lambda)(\delta+\mu)+\lambda)-\beta_t\sigma]=0$$

$$\lambda^2+\lambda(\delta+\mu+\sigma)+\sigma(\delta+\mu-\beta_t)=0$$

We use the Descartes rule of signs to analyze the signs of the eigenvalues. For all values of $\frac{1}{R_0}>1$, we have no sign change and hence, all the eigenvalues will be negative. This condition makes the disease free equilibrium point locally asymptotically stable. Any state initiated near E_0 tends to E_0 as time increases.

3.5.6 Global Stability of the Disease Free Equilibrium point

The disease free equilibrium point E_0 is said to be globally stable if all solutions of the model that start out anywhere in the feasible region stay near the point E_0 at all times. The global stability of the disease free equilibrium point will be analyzed using a Lyapunov function.
If L(x) is a Lyapunov function, then we have;

1. $L(x)>0$ and $L=0$ only at $x=x^\star$
2. $L'(x)<0$ and $L'(x)=0$ at $x=x^\star$

Let $L=E+I$

$$L'=\frac{dE}{dt}+\frac{dI}{dt}$$

$$L'=\beta_t SI-\sigma E+\sigma E-\delta I-\mu I$$

$$=\beta_t SI-[\delta+\mu]I$$

$$=[\delta+\mu][\frac{\beta SI}{\delta+\mu}-I]$$

$$= [\delta + \mu]I[SR_0 - 1]$$

for $R_0 < 1$, the disease can be controlled but, for $R_0 > 1$, the disease perseveres.

3.5.7 Existence of the Endemic Equilibrium point

For Influenza to persist in the population, it means $R_0 > 1$ and $S(t) \neq 0, E(t) \neq 0, I(t) \neq 0, R(t) \neq 0$. An endemic equilibrium point is a steady state that exists when there is disease in the population.

Stability of an endemic equilibrium point represents a situation in which a disease establishes itself within a community. In epidemiological modeling, this is possible when $R0 > 1$.

Then the model has an endemic equilibrium point at S = 0. This implies that, E is also equal to zero, hence, we have $I + R = 1$.

3.5.8 Local Stability of the Endemic Equilibrium point

We determine the stability of the endemic equilibrium point by eigenvalue analysis where the Jacobian matrix is computed and evaluated at the endemic equilibrium point.

$$J(E) = \begin{bmatrix} -\beta_t I & 0 & -\beta_t S & 0 \\ \beta_t I & -\sigma & \beta_t S & 0 \\ 0 & \sigma & -(\delta + \mu) & 0 \\ 0 & 0 & \mu & 0 \end{bmatrix}$$

At the endemic equilibrium point, we have

$$J(E^\star) = \begin{bmatrix} -\beta_t I^\star & 0 & -\beta_t S & 0 \\ \beta_t I^\star & -\sigma & \beta_t S & 0 \\ 0 & \sigma & -(\delta + \mu) & 0 \\ 0 & 0 & \mu & 0 \end{bmatrix}$$

We find the eigenvalues of the Jacobian matrix at the endemic equilibrium point.

$$\begin{vmatrix} -\beta_t I^\star - \lambda & 0 & -\beta_t S & 0 \\ \beta_t I^\star & -\sigma - \lambda & \beta_t S & 0 \\ 0 & \sigma & -(\delta+\mu) - \lambda & 0 \\ 0 & 0 & \mu & 0 - \lambda \end{vmatrix} = 0$$

$$[-\beta_t I^\star - \lambda] \begin{vmatrix} -\sigma - \lambda & \beta_t S & 0 \\ \sigma & -(\delta+\mu) - \lambda & 0 \\ 0 & \mu & 0 - \lambda \end{vmatrix} = 0$$

$$[-\beta_t I^\star - \lambda][-\sigma - \lambda] \begin{vmatrix} -(\delta+\mu) - \lambda & 0 \\ \mu & 0 - \lambda \end{vmatrix} = 0$$

$$[-\beta_t I^\star - \lambda][-\sigma - \lambda][\lambda(\delta+\mu) + \lambda^2] = 0$$

Using the Descartes rule of signs, we find that all the eigenvalues will be negative, hence, the endemic equilibrium point is locally asymptotically stable.

4 Numerical Analysis of the Model

In this Chapter, we verify the model equations by solving them numerically and also establish the relationship between Influenza with the different weather variables and the basic reproduction number for each station.

Using the least square method, we obtained the transmission rate for the four stations. The true values of some of the parameters used in the simulations are not well known since they required extensive field work. Therefore, their values were extracted from literature. The differential equations are solved using the MATLAB in-built function ode-45 and the numerical results are plotted to ease interpretation.

The influenza data was acquired from a University of Nairobi alumnus (Juma V., 2015), who carried out a related study in 2015.The influenza data provided for different stations was given in months from 2006 to 2011. We organized the data into seasons from December of 2006 to November 2011 in order to have a general idea of flu prevalence for the different seasons.

In terms of weather conditions calendar seasons in Kenya are reversed in relation to Northern Hemisphere. So at Spring months in Kenya, there is local Autumn. Yet average temperature is $29^{\circ C}$ more like at summer.

4.1 R_0 as a function of meteorological parameters

From equation (7)

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

Station	Name
1	Nairobi
2	Nyanza
3	Malindi
4	Isiolo

Table 1. Stations under consideration

Season	Period
$D-F$	December of the previous year to February
$M-M$	March to May
$J-A$	June to August
$S-N$	September to November

Table 2. Seasons and their interpretation

This model was extended by Chong et al in their research. They used a time varying transmission rate β_t given by $\beta_t = \beta_0 e^{(\alpha_1 T+\alpha_2 R+\alpha_3 H)}$ (Chong et al, 2015).

$$R_0 = \frac{\beta_0 e^{(\alpha_1 T+\alpha_2 R+\alpha_3 H)}}{\delta+\mu} \tag{8}$$

The transmission rate has been expressed as a function of the meteorological parameters. T represents the transformed value of temperature, R represents the transformed value of Rainfall and H represents the transformed value of Humidity.

The transformation

$$Z_i = \frac{x_i - \bar{x_i}}{\sigma x_i} \tag{9}$$

is used to evaluate the different values of the weather variables.

4.2 Parameter Estimation

The parameters β_0, α_0, α_1 and α_2 are estimated using the least squares method. The rest of the parameters, σ, δ and μ are retrieved from literature.We assume the values of the variables S(0)= 100, E(0)= 9, I(0)= 9 , R(0)= 0 for all the stations under consideration.

4.3 Least Squares Method

We transform the meteorological parameters to make the model coefficients more comparable to each other. Taking x_i as one of the weather variables, $\bar{x_i}$ as the the mean of the sample and σx_i as the standard deviation of the sampling period. The transformation

$$Z_i = \frac{x_i - \bar{x_i}}{\sigma x_i} \tag{10}$$

where Z_i stands for the transformed weather variables ($\hat{T}$, $\hat{R}$ and $\hat{H}$) is used to evaluate the different values of the weather variables.

1	December 2006 to February 2007
2	2007 March to May 2007
3	2007 June to August 2007
4	2007 September to November 2007
5	2007 December to February 2008
6	2008 March to May 2008
7	2008 June to August 2008
8	2008 September to November 2008
9	2008 December to February 2009
10	2009 March to May 2009
11	2009 June to August 2009
12	2009 September to November 2009
13	2009 December to February 2010
14	2010 March to May 2010
15	2010 June to August 2010
16	2010 September to November 2010
17	2010 December to February 2011
18	2011 March to May 2011
18	2011 June to August 2011
20	2011 September to November 2011

Table 3. Season labels from 2006 to 2011

Parameter	Description	Value	Referencce
σ	Infection rate	1/1.9 days	Lipsitch, 2004
δ	Recovery rate	1/4.1 days	Lipsitch, 2004
CFP	Case Fatality Proportion	0.2 percent	Lipsitch, 2004
μ	Death rate due to the disease	δ[CFP/(1-CFP)]	Chowell et al, 2008b

Table 4. Parameter description and their values

$$\beta_t = \beta_0 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})} \tag{11}$$

We linearize the equation to get:

$$ln\beta_t = ln\beta_0 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})}$$

$$ln\beta_t = ln\beta_0 + lne^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})}$$

$$ln\beta_t = ln\beta_0 + (\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})$$

By letting $ln\beta_t = \hat{y}, ln\beta_0 = \alpha_0$, we obtain a multiple linear regression equation

$$y_i = \alpha_0 + \alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H} \tag{12}$$

If we assume y is the approximate value corresponding to the value y_i then, the Error Sum of Squares(SSE) is given by:

$$SSE = \sum_{i=1}^{4} e_i^2$$

$$= \sum_{i=1}^{4} (\bar{y}_i - y_i)^2)$$

$$= \sum_{i=1}^{4} (\alpha_0 + \alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H} - y_i)^2$$

We need to find the values of α_0, α_1 ,α_2 and α_3 so that the error is minimum.

$$\frac{\partial S}{\partial \alpha_0} = 2 \sum_{i=1}^{4} (\alpha_0 + \alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H} - y_i)(1) = 0$$

$$\frac{\partial S}{\partial \alpha_1} = 2 \sum_{i=1}^{4} (\alpha_0 + \alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H} - y_i)(\hat{T}) = 0$$

$$\frac{\partial S}{\partial \alpha_2} = 2 \sum_{i=1}^{4} (\alpha_0 + \alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H} - y_i)(\hat{R}) = 0$$

$$\frac{\partial S}{\partial \alpha_3} = 2 \sum_{i=1}^{4} (\alpha_0 + \alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H} - y_i)(\hat{H}) = 0$$

$$= \alpha_0 + \alpha_1 \sum_{n=1}^{4} \hat{T} + \alpha_2 \sum_{i=1}^{4} \hat{R} + \alpha_3 \sum_{i=1}^{4} \hat{H} = \sum_{i=1}^{4} y_i \tag{13}$$

$$= \alpha_0 \sum_{i=1}^{4} \hat{T} + \alpha_1 \sum_{i=1}^{4} \hat{T}^2 + \alpha_2 \sum_{i=1}^{4} \hat{H}\hat{T} = \sum_{i=1}^{4} y_i \hat{T} \tag{14}$$

$$= \alpha_0 \sum_{i=1}^{4} \hat{R} + \alpha_1 \sum_{i=1}^{4} \hat{T}\hat{R} + \alpha_2 \sum_{i=1}^{4} \hat{R}^2 + \alpha_3 \sum_{i=1}^{4} \hat{H}\hat{R} = \sum_{i=1}^{4} y_i \hat{R} \tag{15}$$

$$= \alpha_0 \sum_{i=1}^{4} \hat{H} + \alpha_1 \sum_{i=1}^{4} \hat{T}\hat{H} + \alpha_2 \sum_{i=1}^{4} \hat{R}\hat{H} + \alpha_3 \sum_{i=1}^{4} \hat{H}^2 = \sum_{i=1}^{4} y_i H_i \tag{16}$$

For each station, we shall substitute the values of the weather variables $(\hat{T}, \hat{R}, \hat{H})$ then evaluate the system of equations using MATLAB to obtain α_0, α_1,α_2 and α_3.

4.4 Results and Discussions

To evaluate the behavior of the model over time, we assume the values of the variables S(0)= 100, E(0)= 9, I(0)= 9 , R(0)= 0. We used the transmission rate evaluated above with respect to the meteorological parameters and the rest of the parameters are gotten from literature.

4.4.1 Nairobi Station

$$\hat{T} = 0.851$$

$$\hat{R} = 0.0774$$

$$\hat{H} = 0.72$$

$$y_i = 0.440901$$

$\alpha_0 = 3.807078$, $\alpha_1 = -0.000$, $\alpha_2 = -0.000$ and $\alpha_3 = -5.2885$.

$\beta_0 = e^{\alpha_0} = 45.0187$

Since $\beta_t = \beta_0 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})}$

The transmission rate for Nairobi station; $\beta_t = 45.0187 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})} = 0.998$. The corresponding R_0 for this particular station is

$$R_0 = \frac{45.0187 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})}}{\delta + \mu} = 0.799 \tag{17}$$

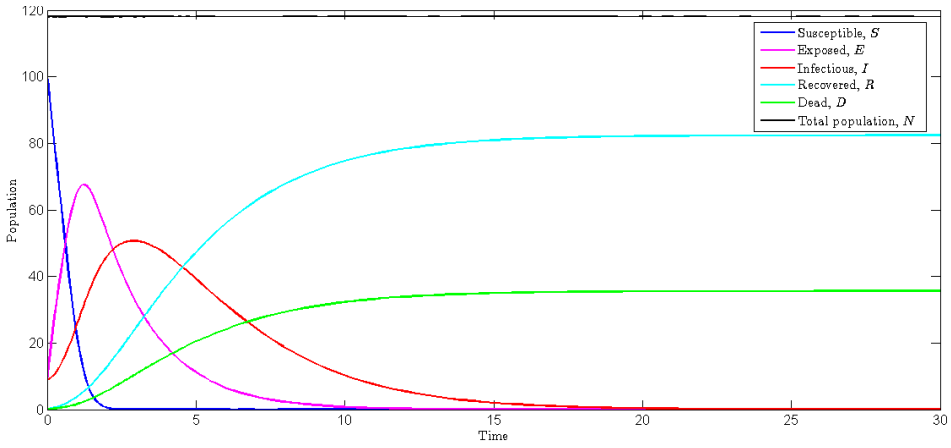

Figure 2. A Numerical Simulation for Nairobi Station

4.4.2 Nyanza Station

$$\hat{T} = 0.9426$$

$$\hat{R} = 0.35$$

$$\hat{H} = 0.71$$

$$y_i = 0.3728814$$

$\alpha_0 = 0.0371$, $\alpha_1 = 0.0000$, $\alpha_2 = 7.4219$ and $\alpha_3 = -3.7110$.

$\beta_0 = e^{\alpha_0} = 1.0377968$

Since $\beta_t = \beta_0 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})}$ The transmission rate for Nyanza station; $\beta_t = 1.0377968 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})} = 14.98$. The corresponding R_0 for this particular station is

$$R_0 = \frac{1.0377968 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H}}}{\delta + \mu} = 0.812 \tag{18}$$

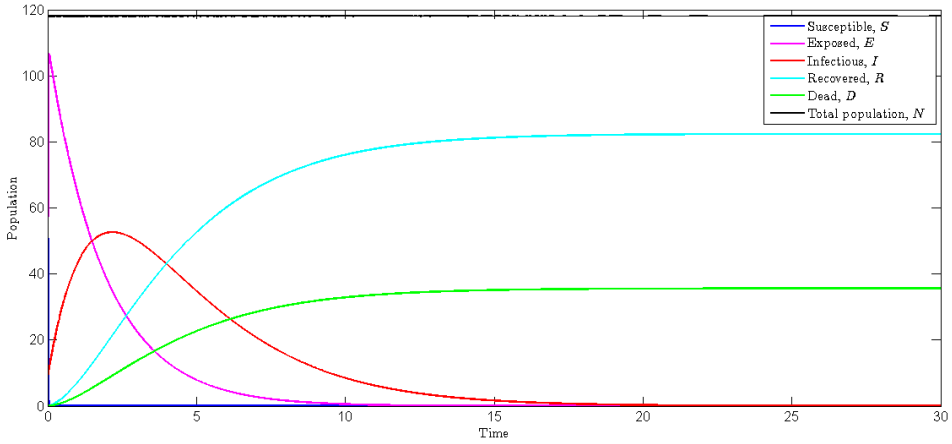

Figure 3. A Numerical Simulation for Nyanza Station

4.4.3 Malindi Station

$$\hat{T} = 0.8648$$

$$\hat{R} = 0.4273$$

$$\hat{H} = 0.81$$

$$y_i = 0.437247$$

$\alpha_0 = -0.1559$, $\alpha_1 = 4.9559$, $\alpha_2 = 2.2724$ and $\alpha_3 = -5.7576$

$\beta_0 = e^{\alpha_0} = 0.8556448$

Since $\beta_t = \beta_0 e^{(\alpha_1 T + \alpha_2 R + \alpha_3 H)}$

The transmission rate for Malindi station; $\beta_t = 0.8556448 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})} = 0.018623$. The corresponding R_0 for this particular station is

$$R_0 = \frac{0.018623 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H}}}{\delta + \mu} = 1.45 \tag{19}$$

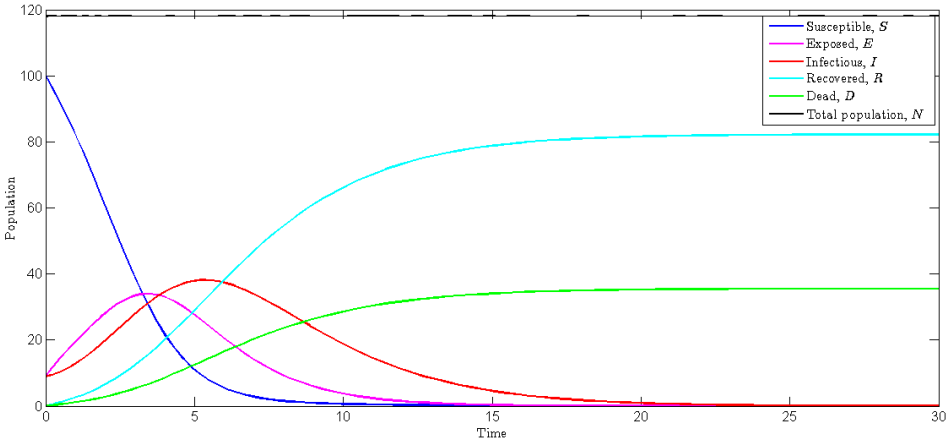

Figure 4. A Numerical Simulation for Malindi Station

4.4.4 Isiolo Station

$$\hat{T} = 0.8510$$
$$\hat{R} = 0.1943$$
$$\hat{H} = 0.72$$
$$y_i = 0.2393822$$

$\alpha_0 = -1.6986$, $\alpha_1 = 1.4214$, $\alpha_2 = -0.0288$ and $\alpha_3 = 0.6870$.

$\beta_0 = e^{\alpha_0} = 0.18294$

Since $\beta_t = \beta_0 e^{(\alpha_1 \hat{T} + \alpha_2 \hat{R} + \alpha_3 \hat{H})}$

The transmission rate for Isiolo station; $\beta_t = 0.18294 e^{(\alpha_1 T + \alpha_2 R + \alpha_3 H)} = 1.000056$. The corresponding R_0 for this particular station is

$$R_0 = \frac{1.000056e^{(\alpha_1\hat{T}+\alpha_2\hat{R}+\alpha_3\hat{H})}}{\delta+\mu} = 0.39 \tag{20}$$

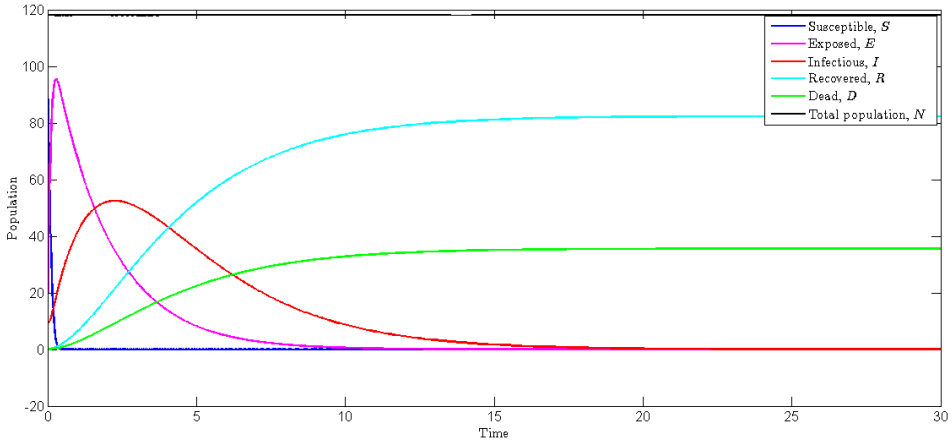

Figure 5. A Numerical Simulation for Isiolo Station

From Fig. 2 - 4 and 5, we notice that when the transmission rate is high as in the case of Nyanza station, the line representing the Susceptible drops almost immediately, meaning more people become exposed and hence infected faster.

The death rate for all the stations is maintained above 20 percent. A study done in 2015 by a university of Nairobi student Dr. Juma showed the death rate being slightly above 10 percent.However, he only considered two weather variables that is temperature and rainfall.

Fig. 6 shows a graph of percentage Flu against seasons over the years. This graph was plotted using the aggregated seasonal values for Nairobi station. The graph clearly shows the fluctuation status of each flu type per season over the years.

We notice that at the beginning of 2007, only the seasonal H1N1 is dominant with noticeable fluctuations. When the pandemic H1N1 starts dominating, the seasonal H1N1 decreases and eventually fades away, as seen in Fig. 7.

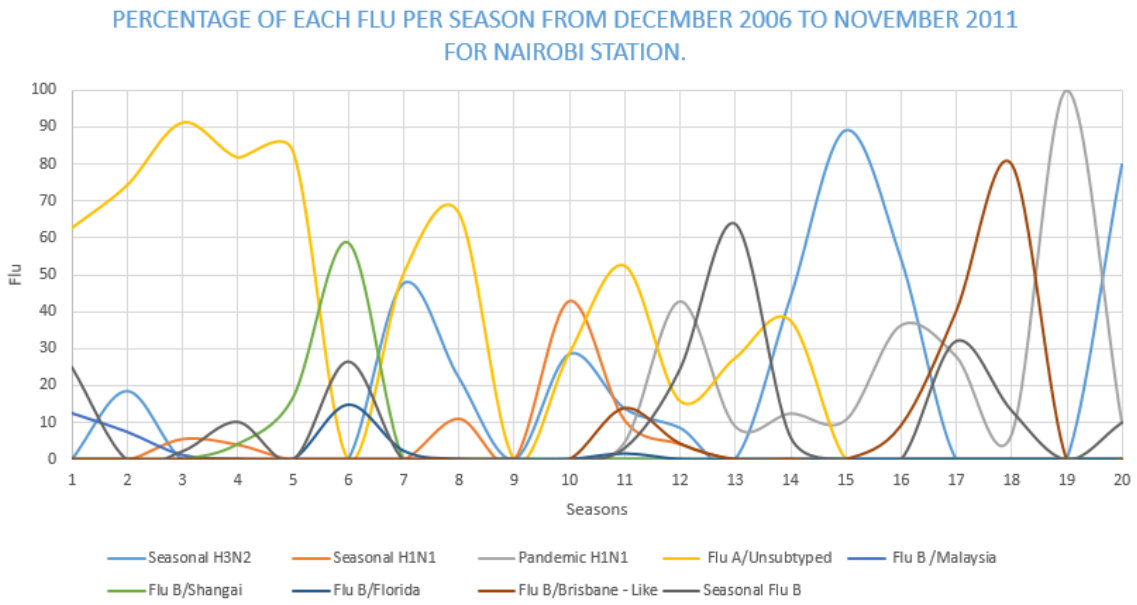

Figure 6

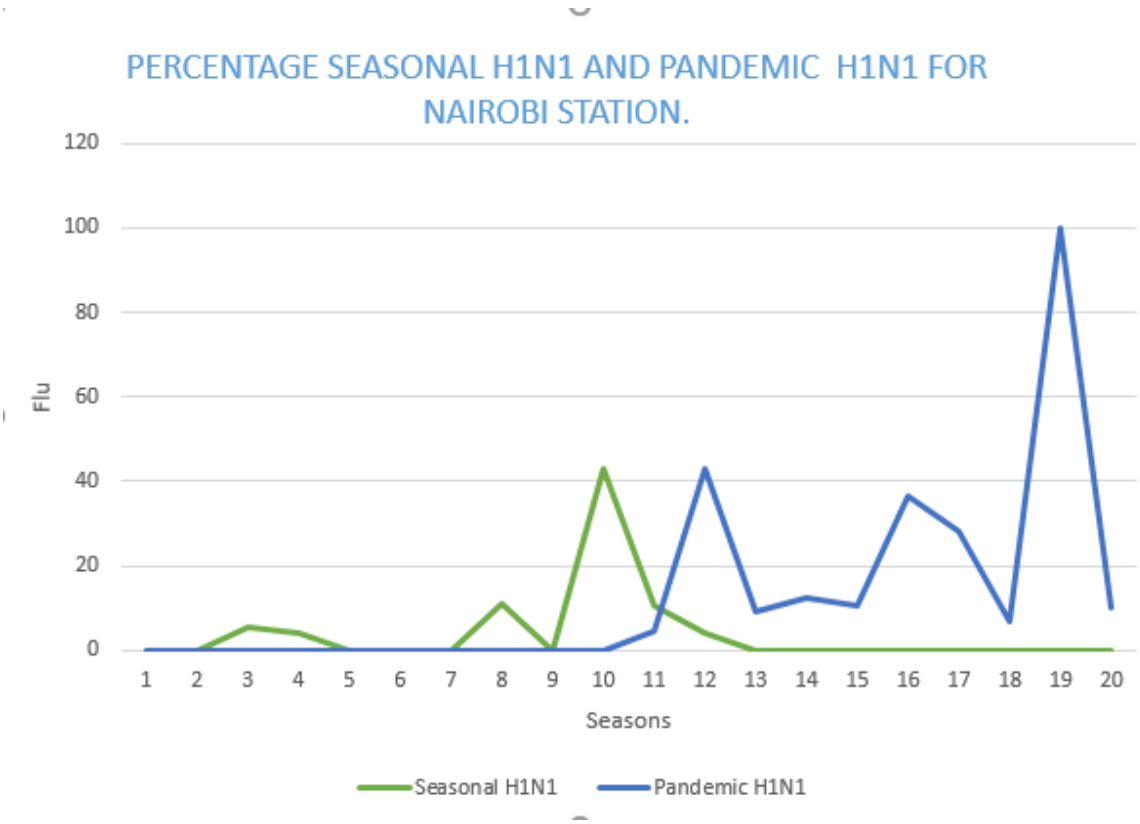

Figure 7

As depicted in Fig. 8 - 11 there is an inverse relationship between Flu A and Flu B over the years. As Flu a increases, Flu B tends to decrease and vice versa.

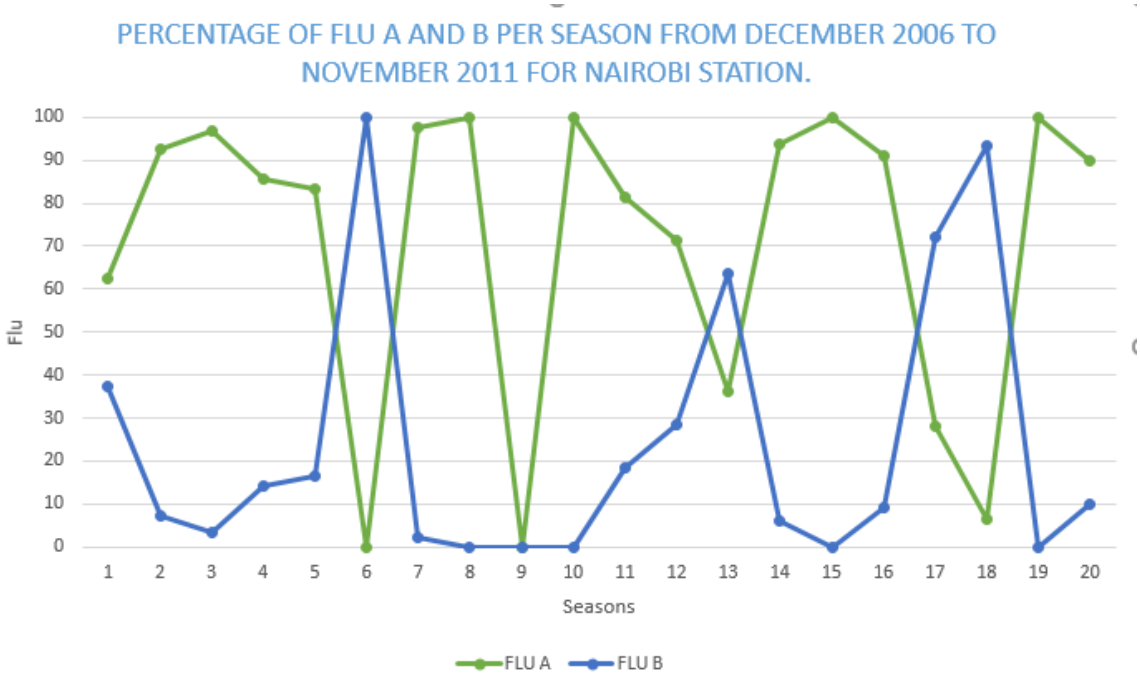

Figure 8

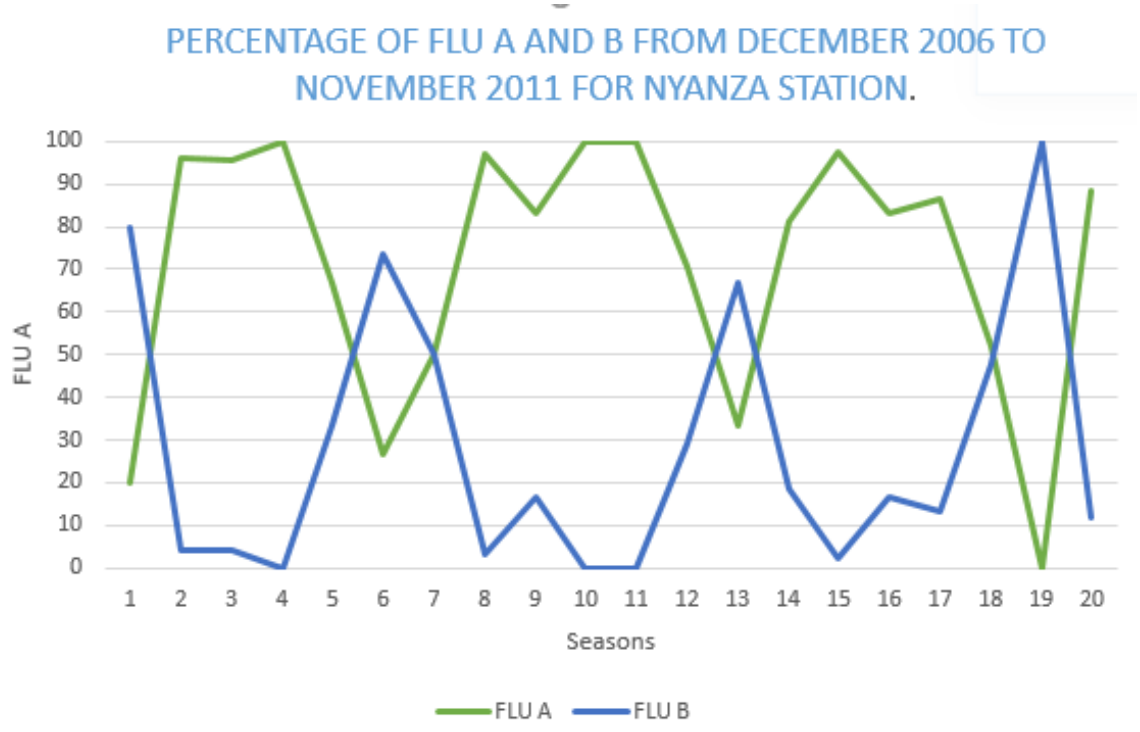

Figure 9

Flu A is seen to be dominant in the 3rd season(June - August), while Flu B dominates in the 2nd season(March - May) in all the stations apart from Nairobi station where it dominates in the 1st season(December - February).This is clearly illustrated in Fig. 12 - 15.

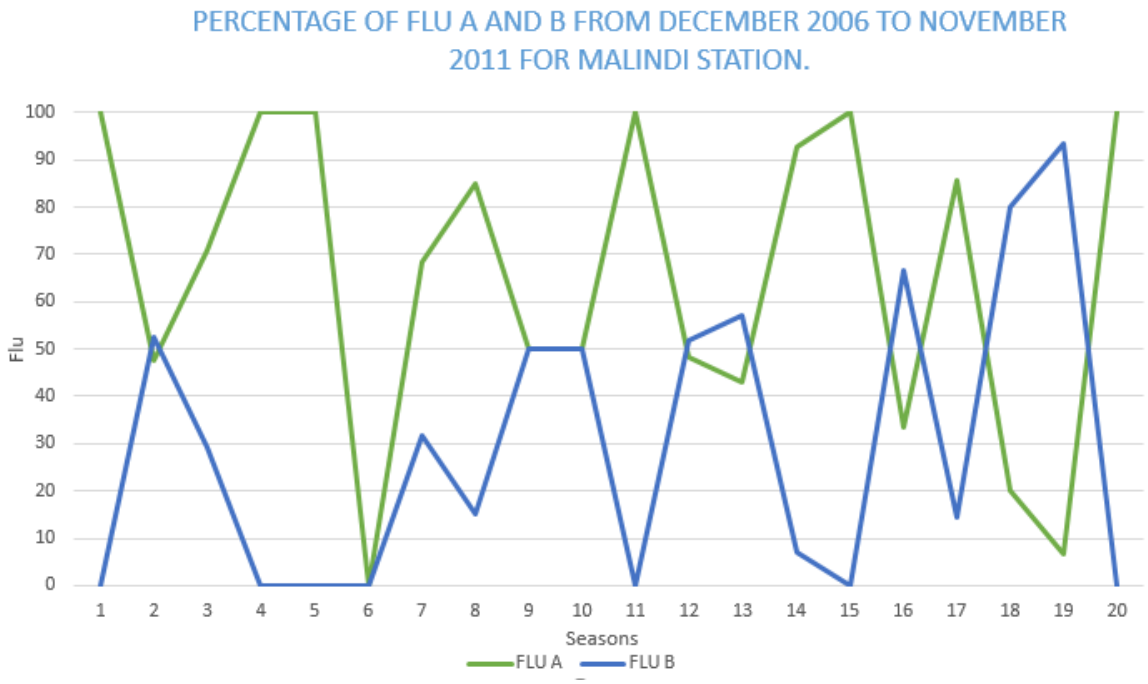

Figure 10

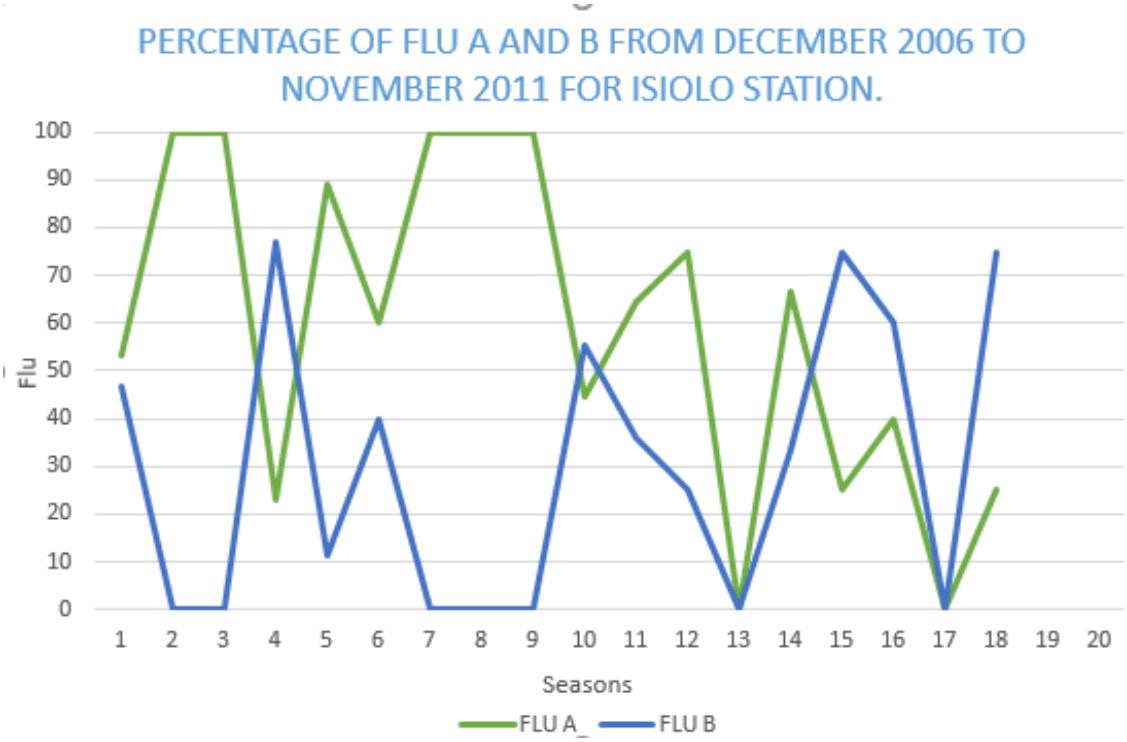

Figure 11

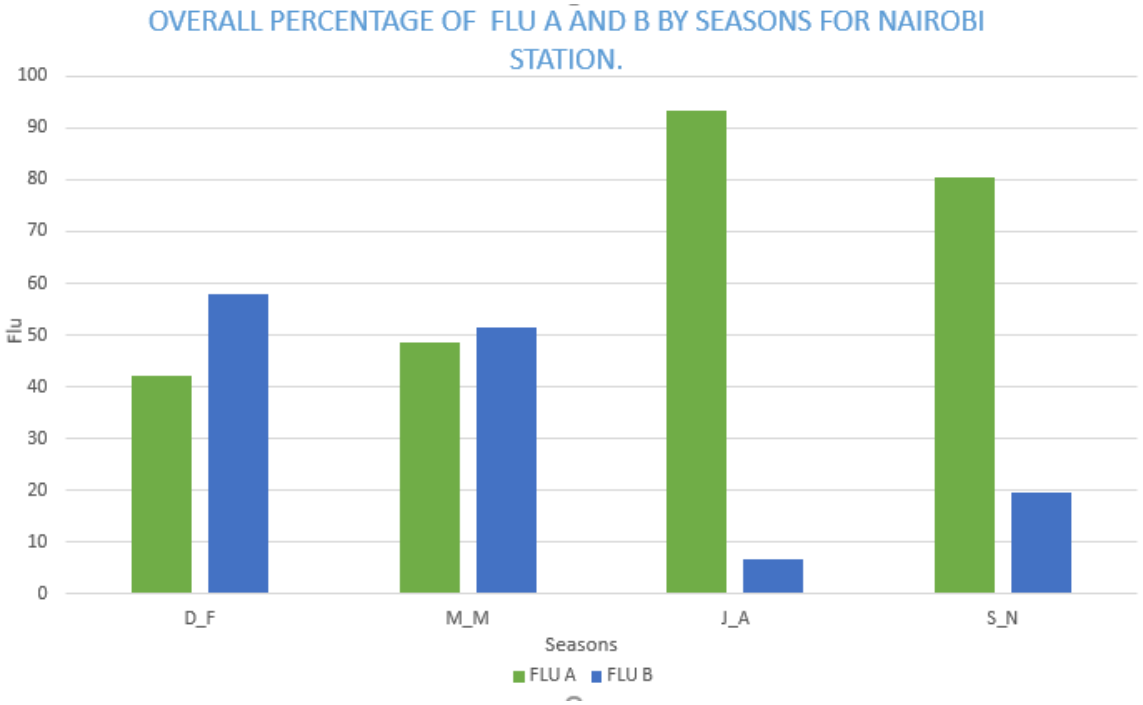

Figure 12

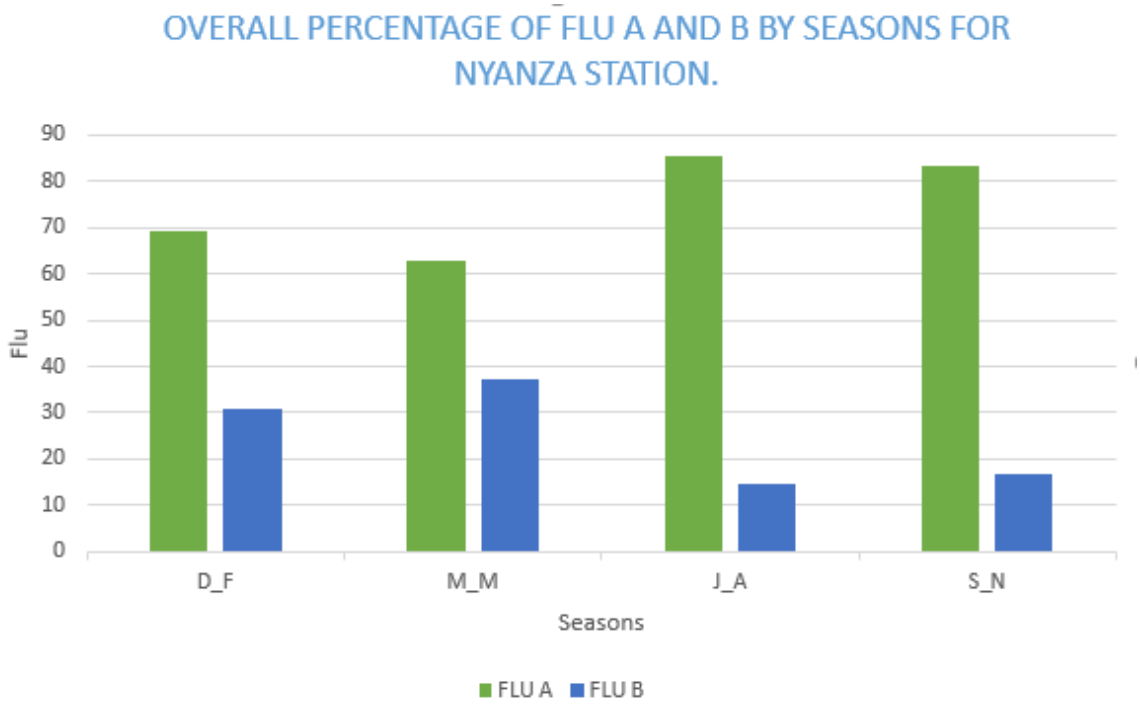

Figure 13

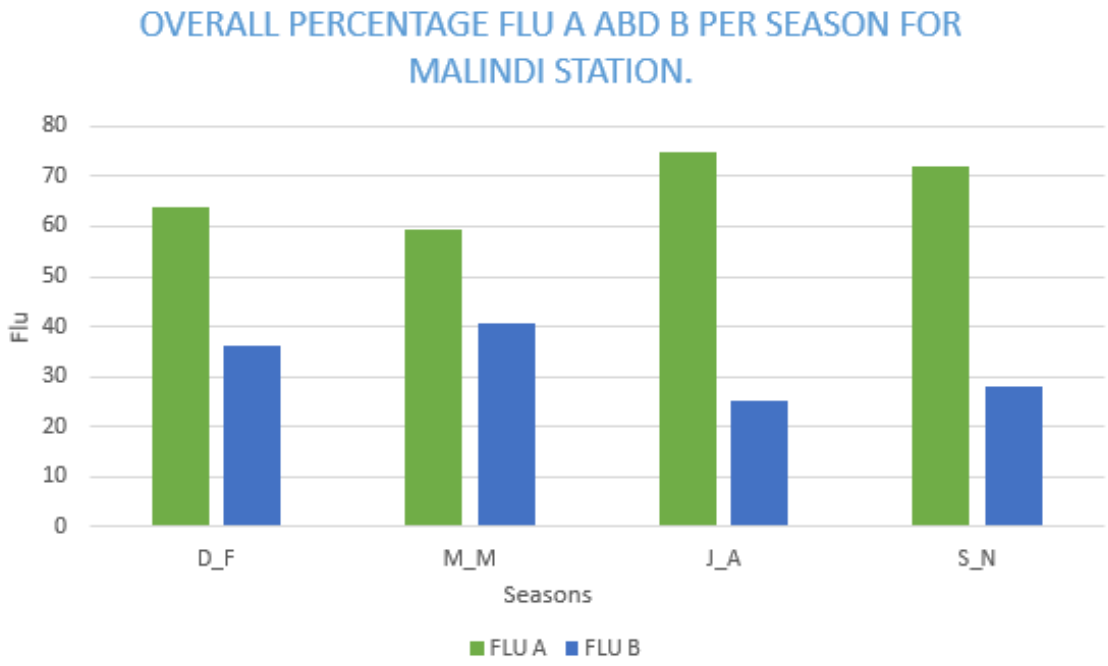

Figure 14

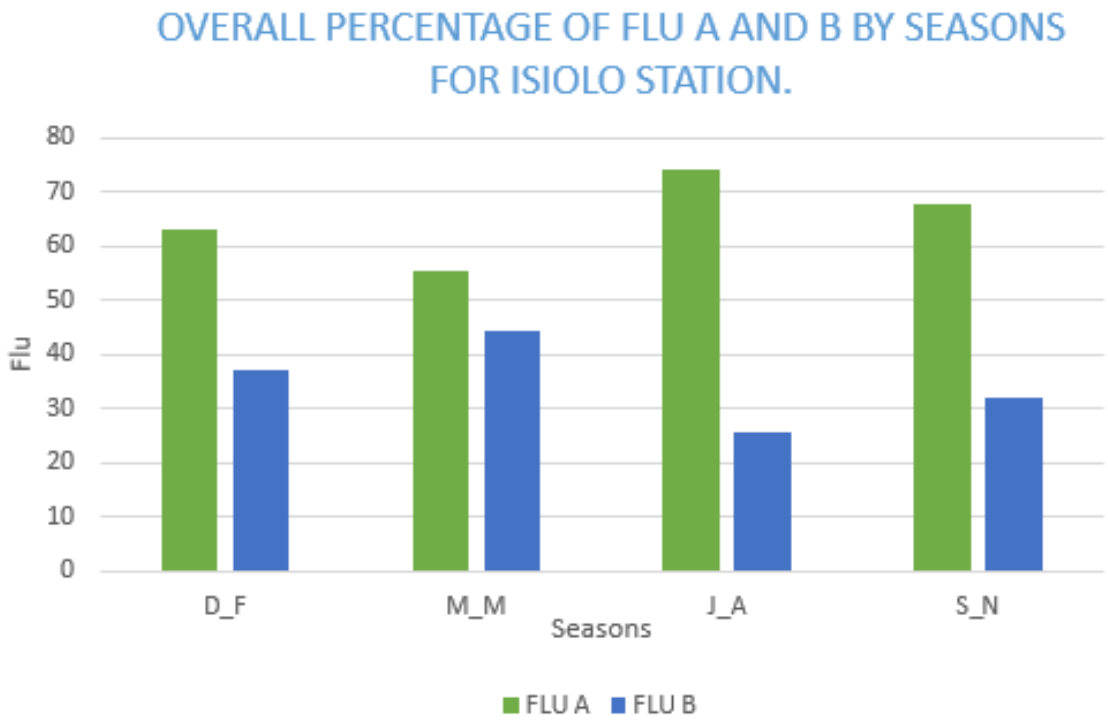

Figure 15

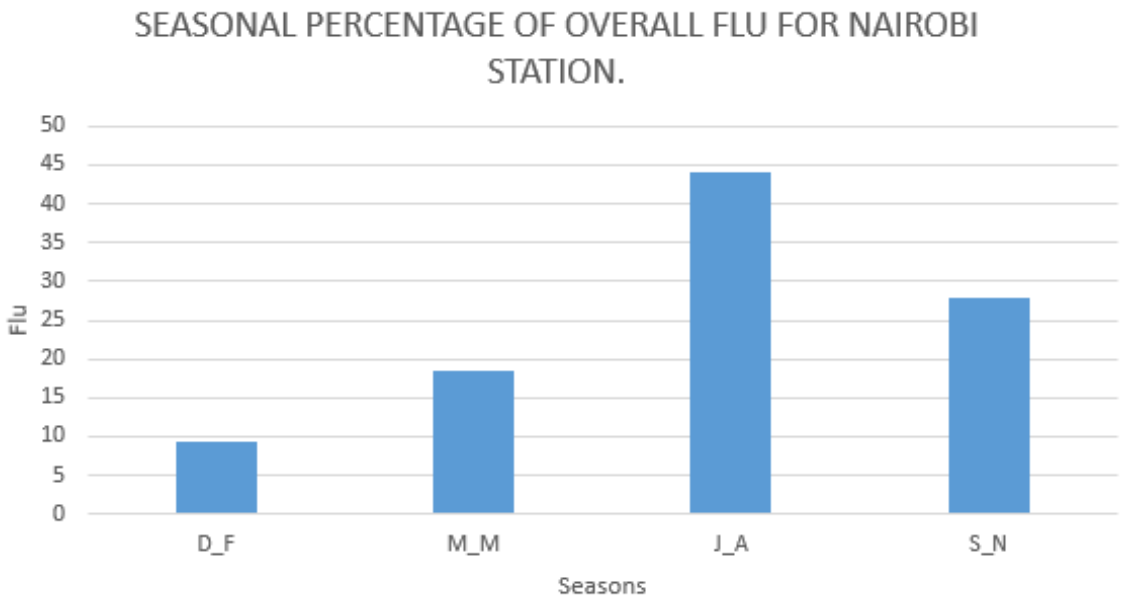

Figure 16

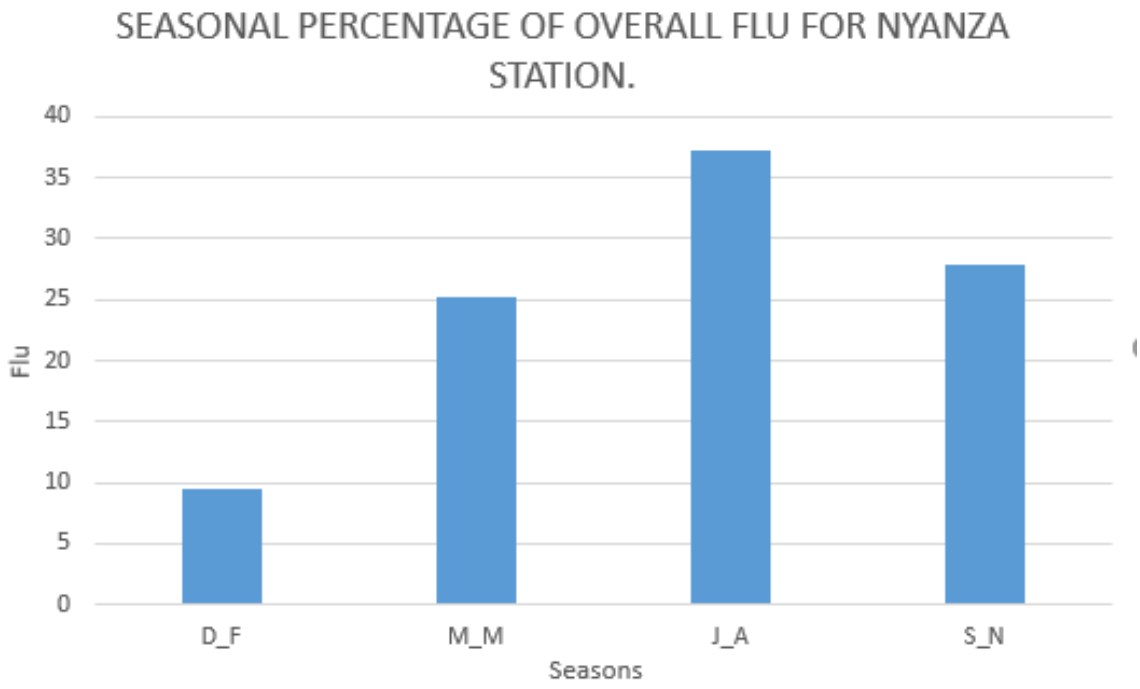

Figure 17

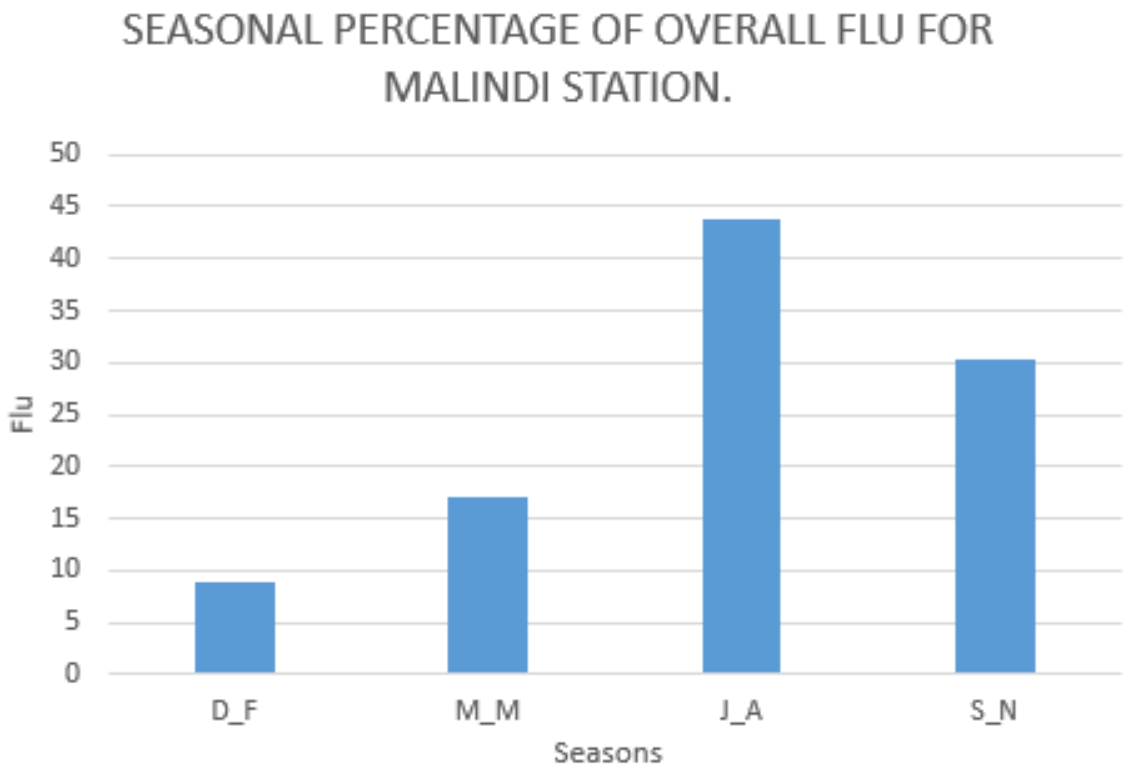

Figure 18

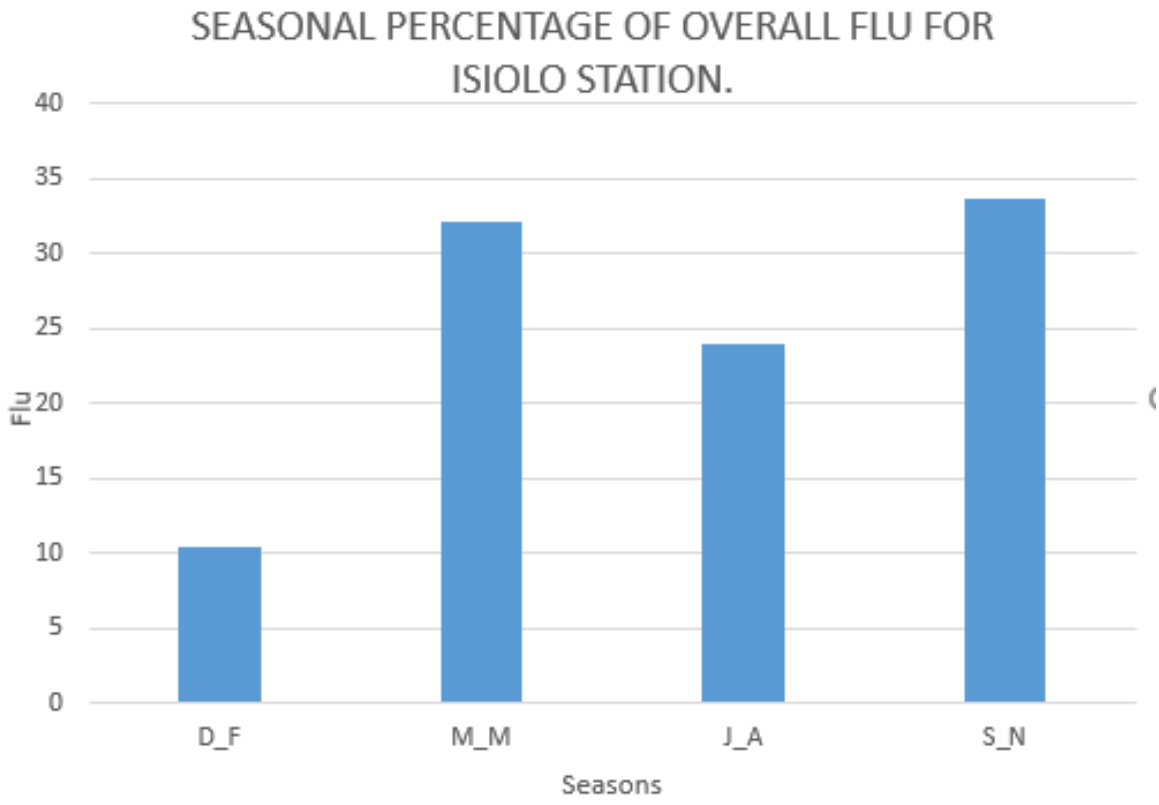

Figure 19

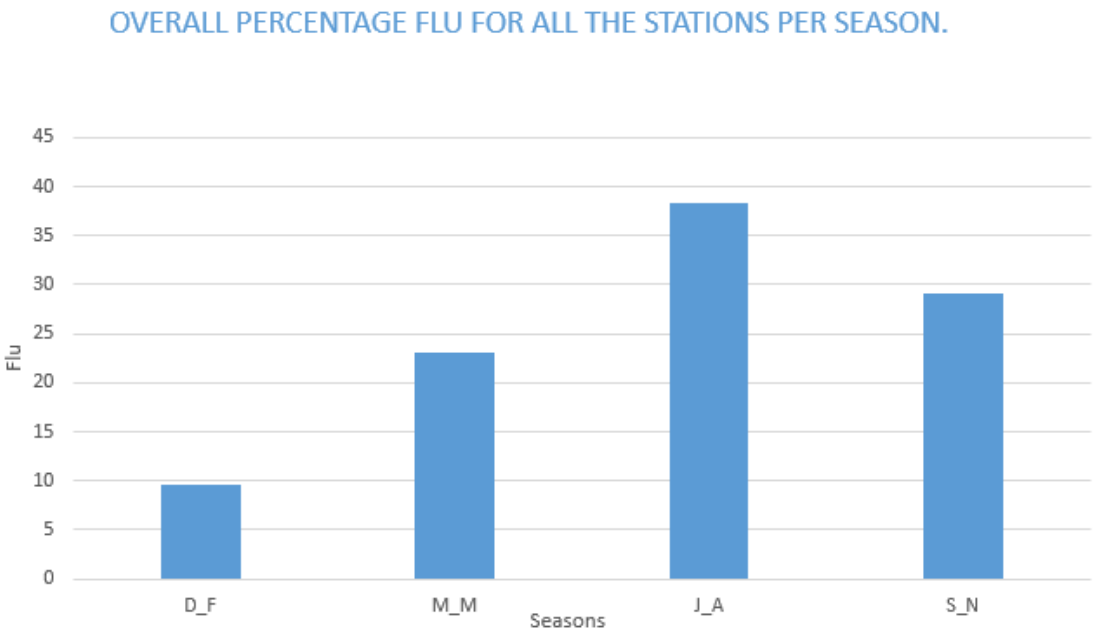

Figure 20

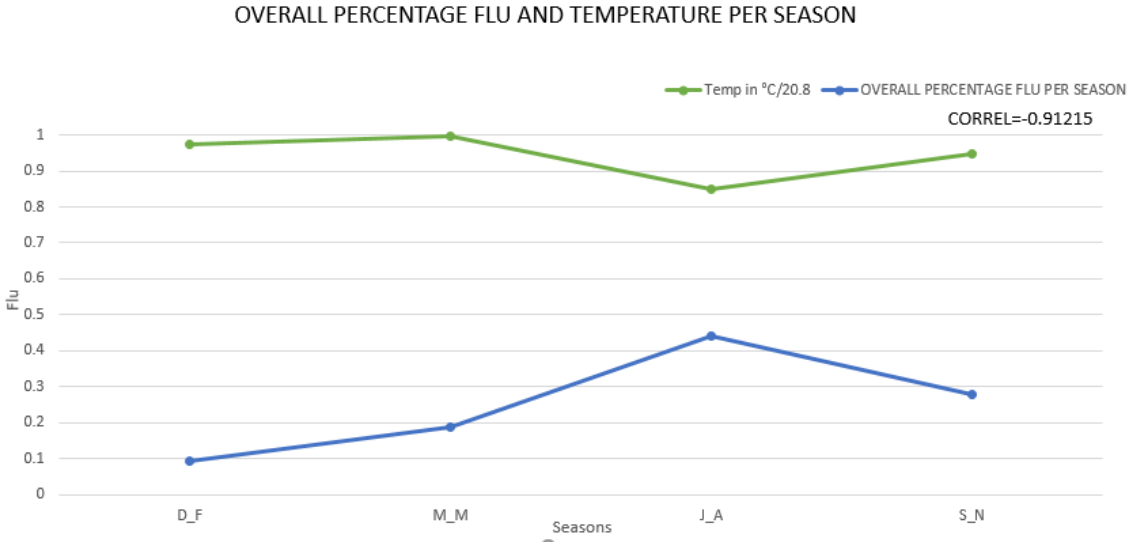

Figure 21

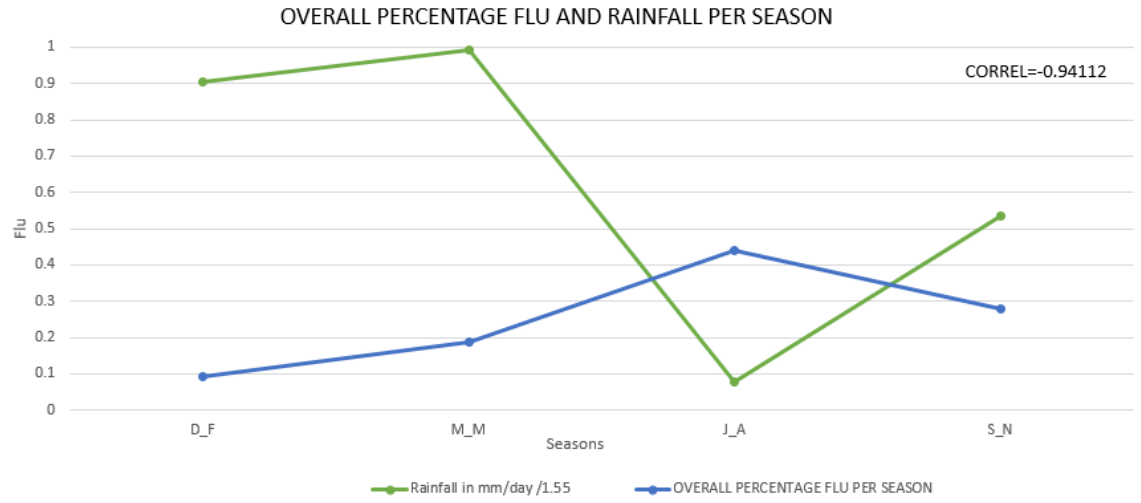

Figure 22

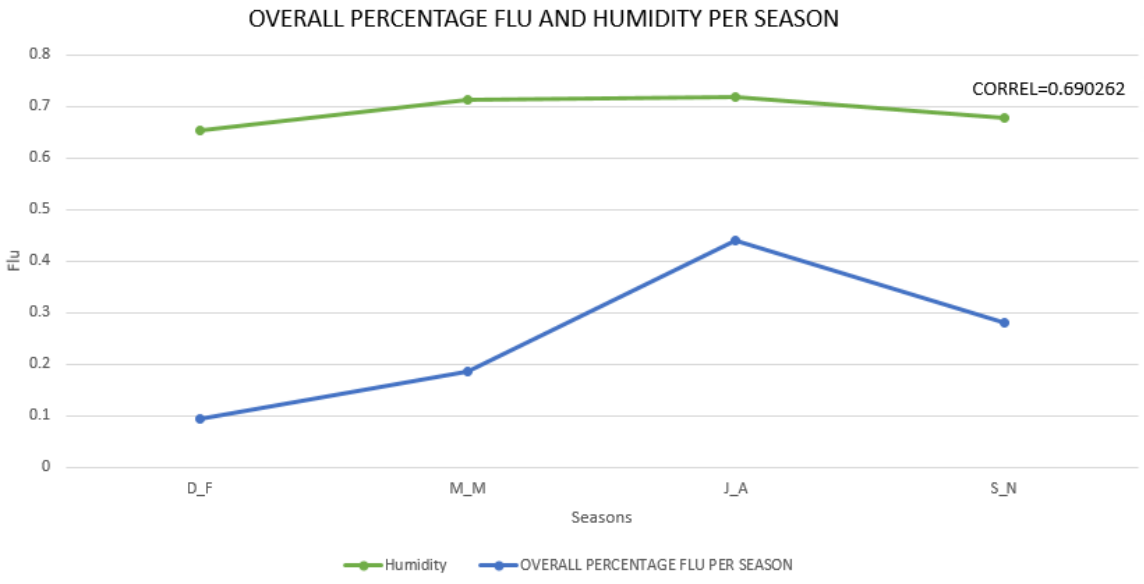

Figure 23

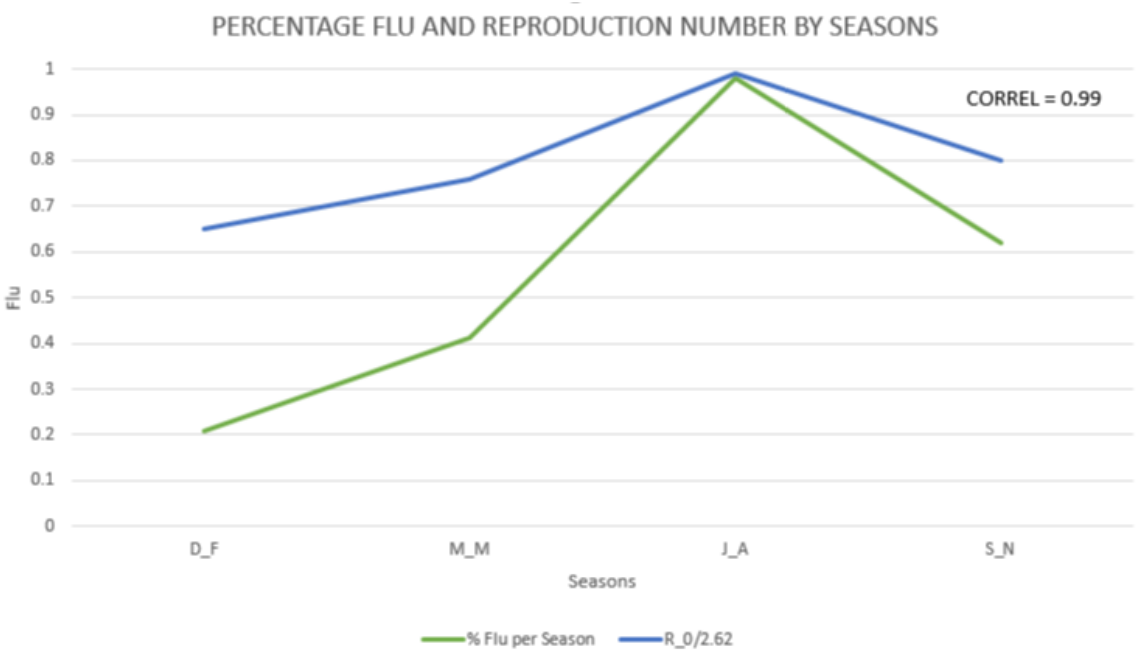
PERCENTAGE FLU AND REPRODUCTION NUMBER BY SEASONS
CORREL = 0.99
Flu
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
D_F
M_M
J_A
S_N
Seasons
% Flu per Season
R_0/2.62

Figure 24

5 Conclusion

5.1 Findings

Analysis of the model was carried out at Disease free and endemic equilibrium points. The basic reproduction number was computed using the next generation matrix. It was discovered that if R0 < 1, then the disease free equilibrium point is locally asymptotically stable and when R0 > 1, the endemic equilibrium emerge whose global stability was analyzed using the Lyapunov function.

The higher the transmission rate, the higher the rate of infection. Different stations have different transmission rates the highest being the one for Nyanza which saw a rapid fall in the Susceptible population almost immediately as depicted in Fig. 3.

The death rate in all the stations is maintained at slightly above 20 percent which is in accordance with other literature.

In all the stations, it is observed that Influenza tends to peak during the third season apart from Isiolo station where the flu is prevalent in the 2nd and 4th seasons. As seen in Fig. 16 - 20, the 3rd season has the most flu prevalence while the 1st season depicts the least flu in Nairobi station, Nyanza station, Malindi station and also across all the stations. Isiolo station however exhibits a rather different pattern. It has it's peak in the 4th season and the 1st season is still the one withe the least flu prevalence just like the other stations.

From Nairobi station, we see that there is a high positive correlation between flu and the reproduction number.Hence, when the basic reproduction number increases, the flu also increases.

In all the four stations, we can see that there is a positive correlation between flu and humidity.This is in line with recent studies which have demonstrated that climatic factors account for a proportion of seasonality.

In this study we found a negative correlation coefficient of temperature and overall flu. This implies that,a decrease in temperature indicates an increase in influenza while an increase in temperature will indicate a decrease in influenza. This may be due to the fact that, a decrease in temperature could enhance crowding and indoor activities which would eventually increase the contact.

5.2 Recommendations

Basing on the results of the study, it is paramount to pay attention to the following recommendations:

- Appropriate data for both flu and weather variables for the different stations should be availed to enable extensive analysis.
- The use of as many meteorological drivers of seasonality as possible in the simulation. This could provide a better approximations than only using three of the meteorological parameters.
- other demographics such as age, social mixing should be considered in future as they can be a great limitation to attaining realism.

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