MODELLING CHILDHOOD PNEUMONIA AND ITS IMPLICATIONS REGARDING ITS CONTROL USING KENYAN DATA

PhD THESIS

BY

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DECLARATION AND APPROVAL

DECLARATION BY THE CANDIDATE

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DEDICATION

To my wife Jane, sons: Socrates and Einstein, my mother and father, and also to my friends. Thank you for your total support.

To Isiolo Boys High School community, thank you for creating a conducive environment for my studies and research.

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ABSTRACT

Pneumonia is an infection of the lungs. It is caused by bacteria, viruses, fungi or parasites, among others. Despite childhood pneumonia of the under five years of age still accounting for about 16% death in Kenya, there was no reliable deterministic mathematical model which had incorporated data and/or parameters from UNICEF and Kenya Health Information System (KHIS) to qualitatively and/or quantitatively give more insights to the pneumonia dynamics. This study developed a deterministic model describing population dynamics of the pneumonia of under five years of age in Kenya and suggested possibly the best control strategies. The objectives were to: develop a model of pneumonia for the under the age five with Kenya specific attributes, determine model thresholds as well as perform analysis of stability, backward bifurcation and sensitivity so as to establish the conditions for the spread of disease, estimate numerical results of model using data and/or parameters from KHIS and UNICEF as well as evaluate normalized sensitivity index and perform numerical simulations to validate analytical results of the model and finally assess the effects of efficacy of the vaccination, environmental factors and therapeutic treatment drugs. Susceptible-Infected-Recovered-Susceptible (SIRS) infectious disease classical model was modified to develop a population based model flow chart. The study considered the status of pneumonia infection, status of vaccination and essential features of pneumonia when formulating the flow chart. Expression R_C was determined from the eigenvalues of the next generation matrix. Sensitivity analyses of various parameters were carried out using partial differentiation. Kenya secondary data and parameters from KHIS and UNICEF of the under five years of age for the years 2012 and 2013 were used in the developed model and also the prediction of the dynamics estimated model for a period of twenty years was determined using 2013 as the initial year. The first order nonlinear differential equations which described pneumonia dynamics were deduced from the flow chart. The algebraic expression of R_C was obtained as the spectral radius of next generation matrix and its estimated numerical value was obtained as 9.31808.The estimated model was obtained through using data and parameters from UNICEF and KHIS. The numerical sensitivity analysis of various parameters was carried out analytically and their estimated numerical results were shown graphically. The Kenya population data from UNICEF and KHIS was used to carry out numerical simulations of the estimated model with 2013 as initial condition. Numerical simulation was carried out for a period of twenty years in Kenya and results obtained graphically. The results of simulations showed that the number of outpatients and inpatients in twenty years' time were expected to vary from 353000 and 4279 in 2013 to about 240000 and 1000 in 2033 respectively. The obtained numerical value for R_C was very high because one infected child is likely to infect 9.31808 other susceptible children in presence of current interventions. The Government of Kenya should strive to attain critical treatment rates whose expressions are provided as it is not possible to attain 100% treatment rates. The sensitivity analysis showed that addressing overcrowding which increases contact rates and improving vaccination drug's efficacy among other factors would lower pneumonia burden. Further research should consider the effect of hospital acquired pneumonia as this study only considered community acquired pneumonia.

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ABBREVIATIONS

MDG 4	Millennium Development Goals number 4
GoK	Government of Kenya
PCV	Pneumococcal Conjugate Vaccines.
Hib b	Haemophilus influanzae type b vaccine
WHO	World Health Organization
UNDP	United Nations Development Programme
UNICEF	United Nations International Children's Emergency Fund
MoH	Ministry of Health, Kenya.
MoPHS	Ministry of Public Health and Sanitation, Kenya.
HIV	Human Immunodeficiency Virus
KNBS	Kenya National Bureau of Statistics
KHIS	Kenya Health Information System
AIDS	Acquired Immune Deficiency Syndrome
KEMRI	Kenya Medical Research Institute
NACOSTI	National Commission for Science, Technology and Innovation
GAVI	Global Alliance for Vaccines and immunization
DFE	Disease Free Equilibrium point
EEP	Endemic Equilibrium Point

DEFINITION OF TERMS, STATE VARIABLES AND PARAMETERS

Table 1: Description of the model parameters and variables.

Variables	Description
N(t)	Total population of the under five years of age in Kenya
S(t)	Population of the under five years of age in Kenya who are susceptible to pneumonia.
V(t)	Population of the under five years of age in Kenya who are vaccinated for pneumonia.
$I_M(t)$	Population of the under five years of age in Kenya who are severely infected with pneumonia.
$I_C(t)$	Population of the under five years of age in Kenya who are very severely infected with pneumonia.
$T_M(t)$	Population of the under five years of age in Kenya who are outpatient with pneumonia (outpatient).
$T_C(t)$	Population of the under five years of age in Kenya who are inpatient with pneumonia (inpatient).
R(t)	Population of the under five years of age in Kenya who have recovered from pneumonia.
Parameters	**Description**
β	Pneumonia per capita infection rate of the under five years of age in Kenya.
π	Recruitment rate of the under five years of age in Kenya (birth rate).
γ_1	Recovery rate of the under five years of age in Kenya from outpatient class.
γ_2	Recovery rate of the under five years of age in Kenya from inpatient class.
δ_1	Pneumonia induced death of the under five years of age in Kenya in very severely infected class.
δ_2	Pneumonia induced death of the under five years of age in Kenya in inpatient class.
μ	Constant natural death rate including exit rate from under five age bracket in Kenya.
ϵ	Pneumonia vaccination drug's efficacy administered to the under five years of age in Kenya
ρ	Waning rate of treatment drug after recovery of the under five years of age in Kenya.
θ_1	Progression rate of the under five years of age in Kenya from mildly infected children progresses to chronic infected class.

θ_2	Discharged rate of the under five years of age in Kenya from inpatient to outpatient.
τ_1	Rate at which the under five years of age in Kenya in mildly infected class seek treatment.
τ_2	Rate at which the under five years of age in Kenya in chronically infected class seek treatment.
K	Coefficient at which force of infection is accelerated due to environmental factors.
Φ	Proportion of born children who are vaccinated
P	Proportion of children who become mildly infected

Table 2: Definition of terms

Endemic	It is long term infection which stays in the population at least 10 to 20 years.
Susceptible population	Proportion of the children population who are free of infection but at risk of contracting the infection
Vaccinated population	Proportion of the children populations who are free of infection and vaccinated with pneumonia but are at a lower risk of contracting the infection.
Severely Infected population	Proportion of the children population with the disease causing pathogen and capable of transmitting the infection to other children on contact but are non-severely infected.
Very Severely Infected population	Proportion of the children population with the disease causing pathogen and capable of transmitting the infection to other children on contact but are severely infected.
Outpatient population	Proportion of the children population with the disease causing pathogen under treatment and capable of transmitting the infection to other children on contact. Mostly treated as outpatient in our health facilities
Inpatient population	Proportion of the children population with the disease causing pathogen under treatment and capable of transmitting the infection to other children on contact. Mostly treated as inpatient in our health facilities
Recovered population	Proportion of the children population who are free of infection after treatment. The effect of treatment drugs is still in their body and they are highly unlikely to contract the infection.

Infectious Disease	Diseases where individuals are infected by pathogen micro-organisms, for instance viruses, bacteria, fungi or other micro parasites.
Alveoli	Microscopic sacs in the lungs that absorb oxygen.
Morbidity	Impairments as a result of a disease
Mortality	Susceptibility to death
Virulence	The degree of pathogenicity of a microorganism as indicated by the severity of disease produced and the ability to invade the tissues of the host.
Efficacy	A measure of how efficient is the drug. If the efficiency is 0% then it is useless but if it is 100% then it is perfect.
MATLAB	It is a high performance language for technical computing software.
Mathematica	It is a symbolic mathematical computation program used in many scientific, engineering, mathematical and computing fields.
Etiology	The investigation of attribution of the cause or reason for something
Basic reproduction number($\mathbf{R_0}$)	The expected number of secondary cases produced by a single(typical) infection in a completely susceptible population.
Control reproduction number($\mathbf{R_C}$)	It is the average number of secondary cases due to each case in the presence of control measures such as vaccination
Effective reproduction number($\mathbf{R}$)	It is the actual average number of secondary cases per primary case observed in a population with an infective disease. Note $R = R_0 x$, where x is the fraction of population susceptible to the infection.
Herd immunity/effect	Also called community immunity or population immunity or social immunity. It is a form indirect protection from infectious disease that occurs when a large percentage of a population has become immune to an infection, thereby providing a measure of protection for individuals who are not immune especially through

vaccination.

Eigenvector A vector that when operated on by a given operator gives a scalar multiple of itself.

CHAPTER ONE

INTRODUCTION

1.1 Background

Pneumonia is a common infectious lung disease that is characterized by inflammation of air sacs. It can result in limited oxygenation, painful breathing, inadequacy of breath, and death (Izadnegahdar, Cohen, Klugman and Quazi, 2013). Pneumonia is airborne disease primarily caused by bacteria and viruses. The other causes are fungi, parasite or inhaling corrosive chemicals (WHO, 2006). When one breathes pneumonia-causing pathogens into the lungs, and the body immune system cannot prevent its entry, the organisms will settle in small air sacs called alveoli and multiply. The host body will send white blood cells to attack the infection. This will cause the air sacs to be filled with fluid and pus, causing pneumonia (WHO, 2006).

The most vulnerable people to pneumonia are babies or elderly and those with other diseases or impaired immune systems. Pneumonia symptoms include cough, crusty or green mucus coughed up from lungs, fever, fast breathing and shortness of breath, shaking chills, chest pain that usually worsens when taking a deep breath, fast heart-beat, fatigue and feeling very weak. The other symptoms include nausea, vomiting, diarrhoea, sweating, headache, muscle pain, confusion or delirium and dusky or purplish skin colour from poorly oxygenated blood (WHO, 2006).

Pneumonia can be spread through inhaling viruses and bacteria that are commonly found in a child's nose or throat. They may also spread via air-borne droplets from a cough or

sneeze, direct contact or through blood contact, especially during and shortly after birth (WHO, 2006).

Pneumonia can be prevented through adequate nutrition including breastfeeding and zinc intake, vaccination, treatment and addressing environmental factors like reducing indoor air pollution. Globally, more than fifty percent of pneumonia induced deaths among children under the age of five years are linked to household air pollution (WHO, 2006).

Streptococcus pneumonia is the most widely spread and common cause of bacterial pneumonia. It remains a substantial source of morbidity and mortality in both the developing and developed countries. Viral pneumonia is caused by adenoviruses, rhinovirus, influenza virus and/or parainfluenza virus. Viral pneumonia is treated by taking rest and plenty of fluids. Fungal pneumonia mainly occurs in individuals with weakened immune systems, which is usually treated with antifungal medications. The most common parasites causing pneumonia are toxoplasma gondii, strongyloidesstercoralis and ascariasis. These parasites typically enter the body through the skin or the mouth and then travel through the blood to the lungs (WHO, 2006).

In 2011, pneumonia was the leading killer of children under the age of five worldwide. It was responsible for nearly twenty percent of the global child deaths annually. More than 99 percent of deaths resulting from pneumonia occurred in the developing world, where access to healthcare care and treatment is inaccessible to many children (UNICEF, WHO and UN, 2012).

One of the millennium development goals (MDGs) was to reduce globally the mortality rate for children under the age of five years by two thirds between 1990 and 2015.

UNICEF indicated that Kenya is lagging behind in East Africa in attaining MDGs on reducing child mortality rates. Globally, the mortality rate for the children under the age of five dropped by almost half in 2012. The under-five years deaths were mainly caused by preventable diseases. The leading infectious diseases include pneumonia, diarrhoea and malaria. Sub-Saharan Africa continues to have the highest mortality rate in the world for children under the age of five years which was more than 16 times the average for developed regions (UNDP, 2014).

Kenya's Vision 2030 recognized research as one of the pillars to accelerate development. The Ministry of Health (MoH) was tasked to formulate policy which would focus on the preventive care, as opposed to curative care (Government of Kenya, 2007). According to UNICEF, many children in Kenya continue to die unnecessarily due to poor accessibility of the recommended treatments. In particular, the cases of diarrhoea and pneumonia still accounted for an estimated 20% and 16% of annual children deaths respectively, in 2011.

The Government of Kenya (GoK) initiated efforts to reduce child mortality. These include the introduction of new vaccines to prevent diarrhoea and pneumonia, but poor access to recommended treatments is still a challenge (MoPHS, 2011). By the year 2009, pneumococcal vaccines (PCV 7, PCV 10, PCV 13 and PCV 6A) were introduced in Kenya (Mudhune and Wamae, 2009) and after the introduction of the vaccine, it was assumed that effective treatment could avert the remainder of those deaths (MoPHS, 2011). Vaccination of pneumococcal and haemophilus type b is being administered in three doses that are given 6 weeks, 10 weeks and 14 weeks after birth.

Surveillance data on childhood pneumonia in East African region emphasized the existence of different strains of pneumonia (Mudhune and Wamae, 2009). The weak nature of the under the age of five immune system makes them vulnerable to pneumonia disease. Many signs and symptoms of fungal infections are similar to those caused by bacteria and viruses which make difficult it to isolate the strains without testing. The data available in KHIS indicated that isolation of pneumonia was not carried being out in the Kenya health facilities.

The research by (Hammitt, Kazungu, Morpeth, Gibson, Mvera, Brent, Mwarumba, Onyango, Bett, Akech, Murdoch, Nokes and Scott, 2012), conducted a case-control study of pneumonia etiology among children aged 1 to 59 months in rural Kenya. The study generally classified pneumonia into two broad categories that is severely infected and very severely infected. The Kenya Health information system (KHIS), which is available online keeps age structured data of the treated pneumonia in Kenya into two categories as outpatient and inpatient classes.

Many Mathematical models for the spread of infectious diseases in populations have been analysed, threshold theorems involving the basic reproduction number(R_0) determined and applied to specific diseases. Similar results with new expressions for (R_0) were obtained for various classical epidemiology models that are often based on the flow patterns between the compartments such as SEIR, SEIRS , MSEIR, SIR, SIRS, SEI, SEIS, , MSEIRS, SIS and SI endemic models with either or age Groups or continuous age (Hethcote, 2000).

There are various techniques of evaluating the basic reproduction number(R_0) namely; use of Survival Function, use of The Jacobian, use of Constant Term of the Characteristic Polynomial, Next-Generation Method and Graph-Theoretic Method among others. The various

Methods available for calculating R_0 rarely concur with each other. The survival function method is the more realistic but is too cumbersome for complex models. It is significantly easier to use than Jacobian-based methods such as Next Generation Method, since it only requires the infectious states and ignores all other states (Li, Blakeley and Smith, 2011).

1.2 Statement of the problem

According to UNICEF, pneumonia of children under five was still accounting for about 16% deaths in Kenya (UNICEF *et al.*, 2012). The various developed model for pneumonia have assumed that it was isolated in health facilities. The data available in KHIS by 2013 indicated that pneumonia is not isolated in Kenya health facilities. The Ministry of Health in Kenya was still relying on surveys obtained from KHIS to formulate policy regarding pneumonia of the under five years of age. The surveys have the following shortcomings: they do not qualitatively describe the dynamics of the pneumonia, cannot act as a predictive tool, are expensive due to the cost involved in technology and accessibility of some regions and finally are more of curative care. Despite those shortcomings, there was no reliable deterministic mathematical model capable of incorporating data and/or parameters from UNICEF and KHIS to qualitatively and/or quantitatively give more insights to the pneumonia dynamics. This research study sought to develop a general deterministic mathematical model of pneumonia for the

under five years of age to overcome the shortcoming of not isolated data analytically. The model analysis would also determine equilibrium points, reproduction numbers and sensitivity analysis as well as conduct normalized sensitivity indices and simulation for validation of the model.

1.3 Objectives

The general objective and specific objectives are provided in subsections below.

1.3.1 General Objective

The main objective of this study was to develop a deterministic model of under five years pneumonia incorporating treatment, vaccination, environmental factors and drug efficacy within a single model and also estimate thresholds using data and parameters from KHIS and UNICEF for a possible control of disease.

1.3.2 Specific Objectives

The specific objectives were to:

i. Develop a model of pneumonia for the under the age five with Kenya specific attributes.
ii. Determine model thresholds and perform stability analysis, sensitivity analysis and backward bifurcation analysis so as to establish the conditions for the spread of disease.
iii. Estimate numerical results of model using data and/or parameters from KHIS and UNICEF as well as evaluate normalized sensitivity index.

iv. Perform numerical simulations to validate analytical results of the model and assess the effects of efficacy of the vaccination, environmental factors and therapeutic treatment drugs.

1.4 Justification of Study

Globally, pneumonia was one of the leading killers of the under the age of five, there was a call for the research beyond vaccines and treatment to mitigate the burden of pneumonia and improve child survival (Izadnegahdar *et al*., 2013).

KHIS has been keeping observed data of pneumonia for inpatient, outpatient and pneumonia induced deaths since year 2009. This research study introduced a deterministic mathematical model which is vital to be used by the following groups.

i. Help policy makers understand the observed epidemiological patterns, and underlying mechanism which influences the spread of the disease and to supplement the ongoing research.
ii. Qualitatively give insight into effects of therapy intervention strategies like treatment, vaccination and efficacy of the vaccination drug to dynamics of pneumonia, which could be used by preventive care specialist.
iii. Determine optimal control strategies, to be used by health facility and administrators.
iv. Allow researchers to test for sensitivity analysis of control reproduction number, and possibly amend the model if needed to adequately represent the reality.

1.5 Scope of the study

The study developed a deterministic general model for the community acquired pneumonia focusing on Kenya specific attributes for the population of persons under the age of five years. To validate the model, secondary data and parameters from UNICEF and KHIS were used while the rest of unknown data and parameters were either estimated or assumed, they are summarized in the section 4.3.1.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

Most of the developed mathematical models concentrated on bacterial pneumonia, antibiotic resistance, and vaccination. The developed models assumed that pneumonia was isolated in a population, during treatment and in death. Viral, fungi and parasitic pneumonia are mostly ignored. This chapter begins with review of bacterial pneumonia, viral pneumonia, fungal pneumonia, pneumonia without isolation, pneumonia surveillance and finally focuses on current research.

2.2 Bacterial pneumonia

The pneumococcal pneumonia model by (Huang, Lipsitch and Finkelstein, 2005), sought to explain risk factors effects at both the individual and community levels, such as child-care center attendance. A transmission model was developed to evaluate whether the combined risks of attending care center and associating with playmates who attend care center attendance accounted for a large proportion of the variability in the prevalence of pneumococcal. The parameters for the model were based on data from a multi community study from sixteen Massachusetts communities. The results indicated that the proportion of children who attend care center accounted for a range of four to fifty six for every 100 in the prevalence of pneumococcal carriage across communities.

The streptococcus pneumonia model by (Lipsitch, Cohen, Colijn, Hanage and Fraser, 2009), considered an in host deterministic model which took into account the issue of coexistence of pneumonia serotypes in a population. The study assumed isolation was

carried out in hospitals. Using mode thresholds the findings stressed the importance of correct modeling and the possibility of a host being able to become simultaneously invaded with more than one strain, taking into account difficulties in obtaining a second strain if already colonized, and considering acquired immunity of new strains.

The study by (Brown, Nguipdop-Djomo, Zhao, Stanford, Spiller and Chalker, 2016) was collated by Public Health England for epidemiologic analysis based voluntary reports from regional laboratories and hospitals in England from year 1975 to 2015. They investigated patients in all age groups with suspected mycoplasma pneumonia infection in England from 1970's. The pathogen was found to have higher prevalence in children five to fourteen age brackets. The findings pointed that recurrent epidemic periods have occurred at four yearly intervals with seasonal peaks ranging from December to February.

The study by (Mochan, Swigon, Ermentrout, Lukens and Clermont, 2014), formulated a model of intra-host immune response model to bacterial pneumonia. The model considered bacterial population in the blood and lungs, the immigration and activation of phagocytes to the infected tissue as well as the cellular death caused by the infection. The virulence of pneumococcal pneumonia in mouse models was shown to depend both on murine strain and bacterial serotype. Their model was presented in terms of simple ordinary differential equation model of the intra host immune response to bacterial pneumonia that was capable of capturing diverse experimentally determined responses of various murine strains. The model demonstrated the significance of a strong immune response both by phagocytosis by the innate immunity and in blood.

The bacterial pneumonia model by (Ong'ala, Mugisha and Odhiambo, 2012), formulated four compartmental classes that is susceptible, carriers, infected and recovered on assumption that pneumonia was isolated in health facilities. Model was analyzed using the theory of dynamical systems and ordinary differential equations. The results of the model analysis showed that there existed a locally stable disease free steady state, when $R_0 < 1$ and a unique endemic steady when $R_0 > 1$. The findings on model threshold analysis stressed the importance of treatment and quarantine where possible.

The study by (Greenhalgh, Lamb and Robertson, 2011), presented a simple mathematical model with vaccination to describe the dynamics of streptococcus pneumonia on assumption that the transmission of the bacterium is determined by multi-locus sequence type. The model was designed to inspect what happens in a vaccinated population if multi-locus sequence type can exist as both non vaccine and vaccine serotypes with capsular switching possible from the latter to the former. The findings showed that in general there were only three equilibria, two carriage equilibria and the carriage-free equilibrium. If the effective reproduction number, $R_e \leq 1$, then the carriage would die out. If effective reproduction number was greater than one, then the carriage was expected to tend to the carriage equilibrium corresponding to the multi-locus sequence type with the largest transmission parameter. Simulations with realistic parameter values were used to validate the analytical results.

The study by (Farooqui, Jit, Heymann and Zodpey, 2015), sought to estimate the number of severe pneumonia episodes, pneumonia deaths in children as well as pneumococcal pneumonia episodes younger than 5 years in 2010 in India. The study parameterized and adapted a mathematical model based on the epidemiological concept of potential impact

fraction developed CHERG for this analysis. The vital parameters that determined the distribution of severe pneumonia episode from one state to another in India were state-specific prevalence, meta-estimates of relative risks for each of these risk factors and state-specific under five years population of selected definite pneumonia risk factors. Their study applied the fraction of risk factors and incidence estimates to population estimates for year 2010 of each Indian state as well as estimated the number of pneumococcal pneumonia cases by applying the vaccine probe methodology to an existing trial. The combined incidence estimates with case fatality ratios from multi-centric hospital-based studies were used to estimate mortality due to severe pneumonia and pneumococcal pneumonia. The findings pointed that in year 2010, 0.35 million (from 0.31 to 0.40 million) and 3.6 million (from 3.3 to 3.9 million) episodes of severe pneumonia all cause pneumonia deaths occurred in children of under five years of age in India. Further, 105 thousand (from 92 to 119 thousand) pneumococcal deaths occurred in India and 0.56 million (from 0.49 to 0.64 million) severe episodes of pneumococcal pneumonia were estimated. Our results stressed the need to increase coverage, improve access to care and equity of pneumonia preventing vaccines in states with high pneumonia burden.

The study by (Russell, Sanderson, Temple and Mulholland , 2011), sought to determine whether the distribution of invasive pneumococcal disease (IPD), WHO radiographic, pneumococcal meningitis and hospitalized WHO clinical pneumonia in children aged 0 to 59 months varies significantly within and between regions as well as to estimate the impact of a different PCV schedules. Individual contacts were made and co-operation was requested to supply data on IPD, WHO radiographic, pneumococcal meningitis and

hospitalized WHO clinical pneumonia, finely stratified by age. A model was constructed to estimate the proportional risk by month for the period from 0 to 59 months of age for regions and selected countries. Using these curves as the basis, curves were overlaid to describe the impact of PCV. There was not convincing evidence of major differences within or between regions with respect to the age distribution of cases of invasive pneumococcal disease, pneumonia and pneumococcal meningitis.

2.3 Viral pneumonia

The review by (Hoa, 2014), summarized the current state of etiology, diagnosis, epidemiology and management of viral pneumonia in sub-Saharan Africa. The community acquired pneumonia was estimated to cause 131 million new cases every year. Following the emergence of sensitive molecular diagnostic test and others, viruses such as respiratory syncytial virus, parainfluenza and influenza virus among others were then recognized as significance causes of respiratory disease in adults and older children in Africa. The data suggested multiple viral, viral/ bacterial infections and high prevalence of viral pathogens in Africa.

The study by (Nokes, Ngama, Bett, Abwao, Munywoki, English , Scott , Cane and Medley, 2009), conducted prospective surveillance of severe and very severe and pneumonia in children aged under 5 years admitted from year 2002 through 2007 to Kilifi district hospital in coastal Kenya. They screened nasal specimens. Their findings were as follows: out of 25,149 hospital admissions, 7359 patients (29 for every 100) had severe or very severe pneumonia, of whom 6026 (82 for every) were enrolled. The stressed the importance low-income setting in transmission of pneumonia.

The study by (Beauchemin and Handel, 2011), investigated mathematical modeling of influenza infection spread at a different scale, that is occurring within a cell culture or an individual host. They reviewed the models that had been developed in the last decades and discussed their contributions to understanding of the dynamics of influenza infections. They suggested future modeling studies that could help in getting solutions for additional questions relevant to public health.

2.4 Fungal pneumonia

The study by (Klimko, Kozlova, Khostelidi, Shadrivova, Borzova, Burygina, Vasilieva and Denning, 2015), estimated the burden of fungal infections in Russia according to the methodology of the LIFE program. They found that total number of patients who had serious and chronic mycoses in Russia in 2011 was three million. Out of those 3 million patients, 2607 494 had superficial fungal infections (recurrent vulvo vaginal candidiasis, tinea capitis oral and oesophageal and candidiasis with HIV infection), 69 331 patients had chronic and invasive fungal infections (Pneumocystis pneumonia, invasive and chronic aspergillosis, cryptococcal, mucormycosis meningitis and invasive candidiasis) and 406 082 adult patients had severe asthma with fungal sensitization and allergic bronchopulmonary aspergillosis.

2.5 Pneumonia without isolation

The study by (Zhang, Zhang, Chen, Feng, Hongjie, Zhao and Zhang, 2016), used Negative binomial regression models to estimate the influenza-associated excess hospitalization rate and compared the hospitalization length and costs between pneumonia and influenza and other community-acquired diseases. The study collected hospital discharge data on pediatric patients' discharge diagnosis, length of hospital stay

and hospital costs in Suzhou. From October 2005 to September 2011, a total of 180 091 all-cause hospitalizations among children less than 5 years of age were identified. The rates of influenza-associated excess hospitalizations and pneumonia and influenza were highest 2010 to 2011 post-pandemic seasons and in the 2009 to 2010 pandemic. Infants less than six months of age had the highest the longest hospital stays (from seven to eight and half days), pneumonia and influenza hospitalization rates and the highest hospitalization costs for pneumonia and influenza. Compared with other community acquired diseases, children admitted for pneumonia and influenza had longer hospital stays and higher hospitalization costs. They concluded that influenza-associated pneumonia, influenza hospitalization rates and economic burden were high among children, therefore targeted influenza prevention and control strategies for young children in Suzhou that could reduce the influenza-associated hospitalizations in that age group.

The study by (Pitt, Roberts and Checchi, 2012), used a decision mathematical model to estimate the relative effectiveness of two alternative strategies, mobile clinics and fixed community-based health services and mobile clinics, for antibiotic treatment of childhood pneumonia to populations that live in areas that are hard-to-access. Markov cycle to compare the number of deaths from pneumonia in children aged from one to fifty nine months.The findings estimated median pneumonia-specific fewer than five mortality rates of 0.51 deaths per 10,000 child-days without treatment, 0.31 with in fixed health posts and 0.45 with weekly mobile clinics.

The study by (Rudan, O'Brien, Nair, Liu, Theodoratou, Qazi, Lukšić, Walker, Black and Campbell, 2013), conducted a series reviews to update previous estimates of the global, regional and national impact of childhood pneumonia incidence, mortality, severe

morbidity, risk factors and specific contributions of the most common pathogens: respiratory syncytial virus (RSV), Streptococcus pneumoniae(SP), Haemophilus influenzae type B (Hib) and influenza virus (flu). The incidence of community–acquired childhood pneumonia was estimated as 0.22 in middle and low income countries in the year 2010, using WHO's definition.

The general pneumonia model by (Emaline, Kgosimore and Marijani, 2012), formulated four compartmental classes that is vaccinated, susceptible, infected and treated. The study assumed treated class to be non-infective. Adults and children were assumed to have the same infection rates. Based on sensitivity analysis of reproduction numbers, simulations and thresholds, the results stressed the importance of drug efficacy in lowering the burden of pneumonia.

The deterministic co-infection model of malaria and pneumonia for the under five years of age by (Lawi, Mugisha and Omolo, 2013), analyzed the reproduction number by partial derivatives. Based on sensitivity analysis of reproduction numbers, simulations and thresholds, their result stressed the importance of increase in treatment rates to lower new disease incidences.

The general pneumonia model by (Ngari, Malonza and Muthuri, 2014), formulated a model with three compartmental classes that is susceptible, infected and treated. Their findings based on sensitivity analysis of reproduction numbers, simulations and thresholds, stressed importance of natural immunity and treatment in lowering the burden of pneumonia.

2.6 Pneumonia surveillance

The study by (Yamazaki and Kenri, 2016) conducted surveillance of M. pneumoniae as part of the National Epidemiological Surveillance of Infectious Diseases (NESID) program in Japan starting in 1981. Significant increases in the numbers of M. pneumoniae patients were noted in years 1984, 1988, 2006, 2010, 2011, 2012 and 2015. The studies on genotyping based on the p1 gene sequence pointed that the p1 gene type 1 lineage had been dominant in Japan since 2003. Macrolide-resistant M. pneumoniae clinical isolates were estimated at 50–90% in Japan after 2000, dependent on the specific location. Their findings prompted Japanese societies issued guiding principles for treating M. pneumoniae pneumonia.

The study by (Sathian, De, Simkhada, Malla, Ghosh, Basnet, Roy, Banerjee, Supram and Devkota, 2015), collated information from existing data and charted out the trends of the incidence of pneumonia per every one thousand children less than five years of age in the future. A secondary data analysis of the incidence of Pneumonia per every one thousand children less than five years of age in Nepal was carried out between year 2005 to 2014. The data was analyzed using Statistical Package for the Social Sciences and data fitted in curve. The findings predicted 331 cases of pneumonia per every one thousand children less than five years of age in year 2020 in Nepal as well as increasing trend of incidences.

The research by (Mudhune and Wamae, 2009), carried out surveillance on childhood pneumonia especially streptococcus Pneumonia and Haemophilus pneumonia in East African Region. The results isolated 119 Haemophilus influenzae and 442 streptococcus pneumonia from children more than two years of age but less than five years of age.

A case-control study of pneumonia etiology among children aged 1–59 months in rural Kenya by (Hammitt *et al.* A., 2012), classified pneumonia in two categories as severe and very severe pneumonia. The result obtained indicated that very severe pneumonia cases constituted 29% of the 810 case patients.

2.7 Current research study

This study developed a general model to consider a possibility of all types of pneumonia in the population lack of isolation in health facilities. A compartment of vaccinated class was put in the model because pneumonia vaccination programme was already in place. The infected population of under the age of five in Kenya was classified in two categories in our model, that is, severe and very severe to implement a case-control study by (Hammitt *et al.*, 2012). Ministry of Health in Kenya Since pneumonia vaccination campaign programmes were focusing on coverage, this study besides coverage also considered the effect of vaccination efficacy. The two classes of available data for outpatient and inpatient from KHIS were considered when formulating treated classes in the model. The vital population dynamics of the under five years in Kenya from UNICEF were considered in the model. The Government of Kenya has been reporting about pneumonia based on surveys since 2009, this study introduced deterministic model approach which can be used to predict dynamics in absence of surveys. Although there is possibility co-infection of pneumonia with other diseases, there was no such empirical data in Kenya Health programmes, therefore this could not be analyzed.

CHAPTER THREE

METHODOLODY

3.1 Introduction

This chapter describes the methodology used in conducting this research to achieve the objectives in Section 1.3.2 namely to develop a model of pneumonia for the under the age five with Kenya specific attribute, to determine model thresholds and perform stability analysis, sensitivity analysis, backward bifurcation analysis so as to establish the conditions for the spread of disease, to estimate numerical results of model using data and/or parameters from KHIS and UNICEF as well as evaluate normalized sensitivity index and to perform numerical simulations to validate analytical results of the model and assess the effects of efficacy of the vaccination, environmental factors and therapeutic treatment drugs.

3.2 Model Development of pneumonia for the under the age five with Kenya specific attributes

The research by (Ledzewicz and Schattler, 2011) proposed that a standard epidemiology model should include the following five compartments that is M, S, E, I and R. In that model M represents infants with passive immunity, S represents the susceptible individuals, I stand for the class of infected individuals, R denotes the recovered class and E exposed individuals who are in the latent stage. Although M class was propose in the standard model, the study pointed out that maternal antibodies are cleared from the body relatively quickly and therefore infant enters the class S (Ledzewicz and Schattler, 2011). The most typical epidemiology model is of the type SIR in which class M and E are omitted (Hethcote, 2000). A classical endemic initial value problem of SIR includes three

classes. The flow chart in the Figure 1show a SIR model with vital dynamics of birth and death, the model equations are deduced from chart (Hethcote, 2000). The parameter μ is constant death rate, b is birth rate, γ is the recovery rate. The variables R(t), S(t) and I(t) are the numbers in these compartments, so that $R(t) + S(t) + I(t) = N$. The basic reproduction number(R_0) was obtained using Next Generation Matrix as $R_0 = \frac{\beta}{\gamma+\mu}$.

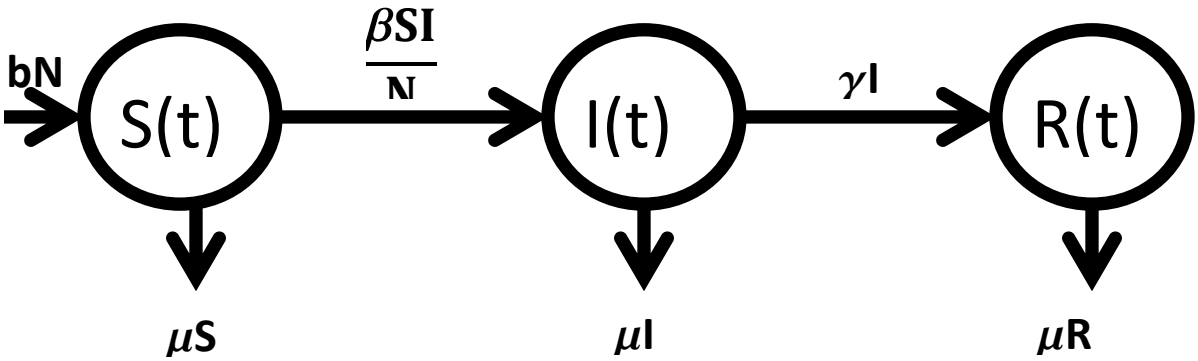
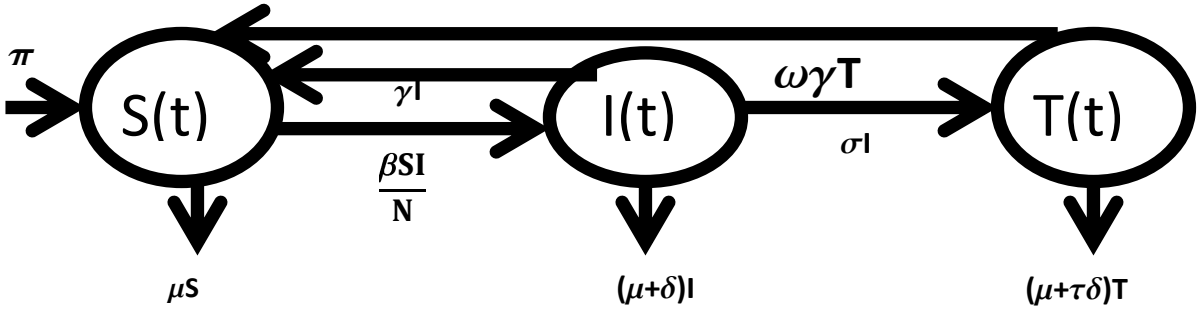


Figure 1: Flow chart diagram of classical endemic SIR model, (Adapted from Hethcote, 2011)

$$\frac{dS}{dt} = bN - \frac{\beta SI}{N} - \mu S, \qquad S(0) = S_0 > 0; \quad \frac{dI}{dt} = \frac{\beta SI}{N} - (\gamma + \mu)I, \qquad I(0) = I_0 > 0,$$

$$\frac{dR}{dt} = \gamma I - \mu R, \qquad R(0) = R_0 > 0,$$

Our research study was an extension of a general pneumonia model by (Emaline et al., 2012) and (Ngari et al., 2014), whose model flow charts and equation were as follows.



]Figure 2: Flow chart diagram of general pneumonia model, (Adapted from Emaline *et al.*, 2012)

The following ordinary differential equations were deduced from Figure 2,

$$\frac{dS}{dt} = \pi + \gamma I + \omega\gamma T - \frac{\beta SI}{N} - \mu S, \qquad S(0) = S_0 > 0,$$

$$\frac{dI}{dt} = \frac{\beta SI}{N} - \gamma I - (\mu + \sigma + \delta)I, \qquad I(0) = I_0 > 0,$$

$$\frac{dT}{dt} = \sigma I - (\mu + \tau\delta + \omega\gamma)T, \qquad T(0) = T_0 > 0,$$

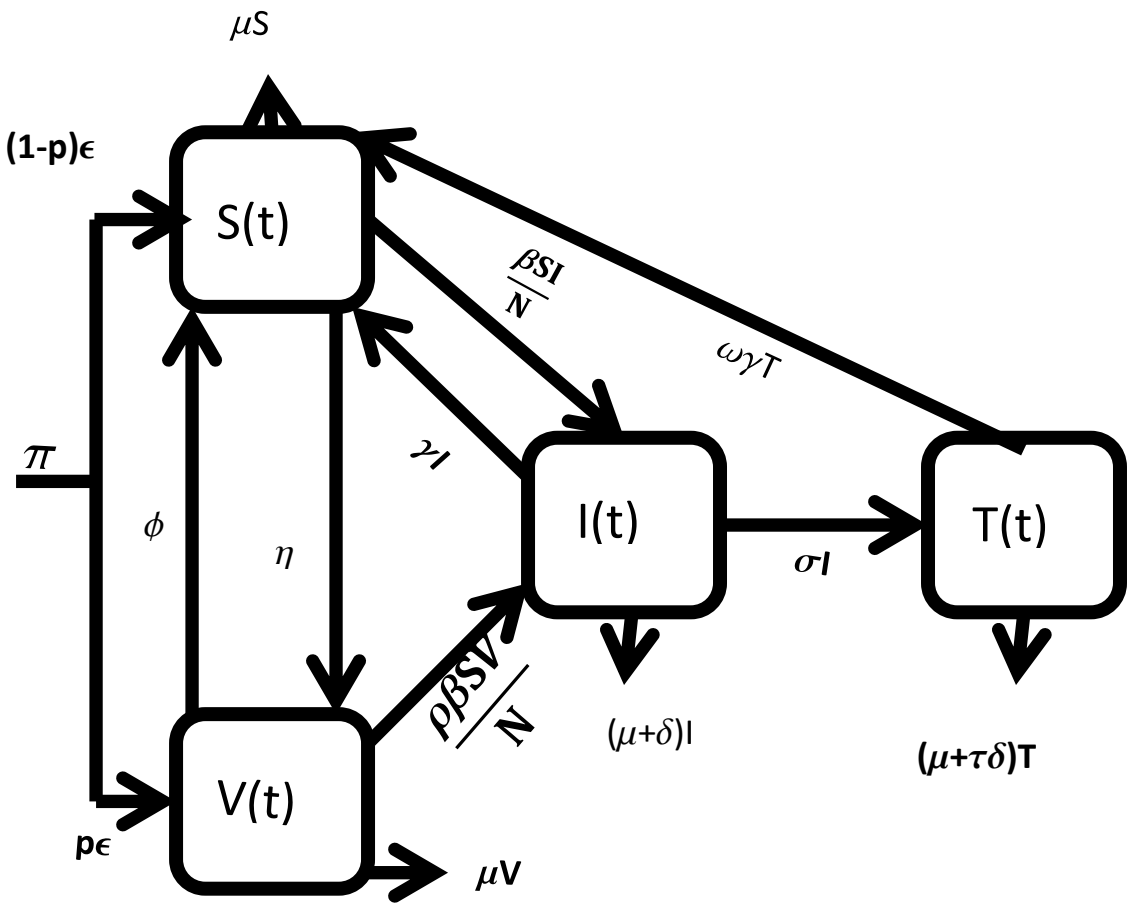


Figure 3: Flow chart model of general pneumonia, (Adapted from Emaline *et al.*, 2012)

The following ordinary differential equations were deduced from Figure 3,

$$\frac{dS}{dt} = (1 - P\epsilon)\pi + \phi V + \gamma I + \omega\gamma T - \eta V - \frac{\beta SI}{N} - \mu S, \qquad S(0) = S_0 > 0,$$

$\frac{dV}{dt} = P\epsilon\pi + \eta V - \phi V - \frac{\rho\beta SV}{N} - \mu V; \frac{dI}{dt} = \frac{\beta SI}{N} + \frac{\rho\beta SV}{N} - (\gamma + \mu + \sigma + \delta)I;$

$\frac{dT}{dt} = \sigma I - (\mu + \tau\delta + \omega\gamma)T;\ \ V(0) = V_0 > 0;\ \ I(0) = I_0 > 0;\ \ T(0) = T_0 > 0.$ From Figure 2 and Figure 3, S (t) represented the number of susceptible individuals, I(t) represented infectious individuals capable, V(t) represented the number of vaccinated individuals and T(t) represented the number of treated individuals. π was the birth rate, $\omega\gamma$ was the recovery rate after treatment, γ was the recovery rate through natural immunity, μ was constant natural death rate, σ was the rate at which infected individuals sought treatment, β was the infection rate for infected individuals, $\tau\delta$ was the rate of pneumonia induced death during treatment and δ was the rate of pneumonia induced death of infected individuals. The parameter ρ was drug efficacy, η was the rate of change from S(t) to V(t) and ϕ was the rate of change from V(t) to S(t). The expressions $(1 - P\epsilon)\pi$ and $P\epsilon\pi$ represented recruitment to S(t) and V(t) classes, where $0 \leq P \leq 1$. The modification parameters $\omega$and τ were such that $\omega \geq 1$ and $\tau \geq 1$. The R_0 and R_C for flow charts in Figure 2 and 3 were obtained using Next Generation Matrix as

$$R_0 = \frac{\beta}{\gamma + \sigma + \mu + \delta} \text{ and } R_C = \frac{\beta\pi(\mu - P\mu\epsilon + P\mu\epsilon\rho + \eta + \rho\phi)}{\mu(\mu + \eta + \phi)(\gamma + \sigma + \mu + \delta)}$$

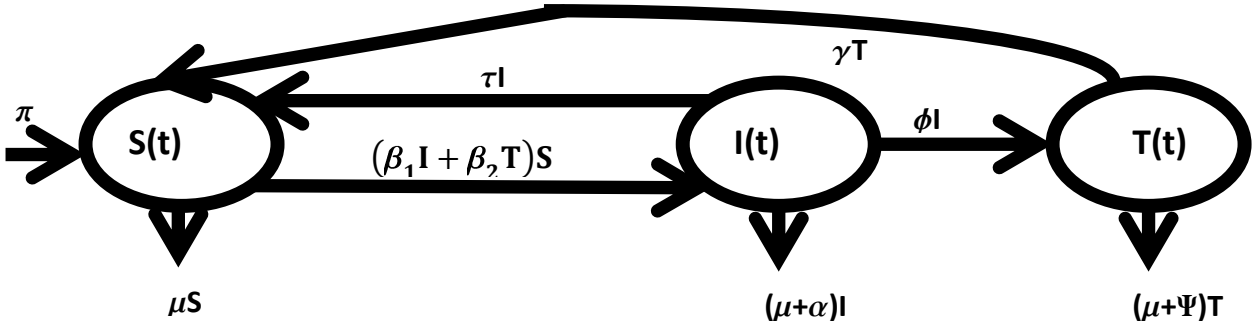


Figure 4: Flow chart diagram of pneumonia (Adapted from Ngari *et al*., 2014)

$\frac{dS}{dt} = \pi + \gamma T + \tau I - (\beta_1 I + \beta_2 T)S - \mu S, \qquad S(0) = S_0 > 0,$

$$\frac{dI}{dt} = (\beta_1 I + \beta_2 T)S - (\tau + \mu + \alpha + \phi)I, \qquad I(0) = I_0 > 0,$$

$$\frac{dT}{dt} = \phi I - (\mu + \Psi + \gamma)T, \qquad T(0) = T_0 > 0,$$

From Figure 4, S(t) represent susceptible individuals, I(t) represent infected individuals and T(t) represent individuals under treatment. π was the birth rate, γ was the recovery rate after treatment, τ was the recovery rate through natural immunity, μ was constant natural death rate, ϕ was the rate at which infected individuals sought treatment, β_1 and β_2 were infection rates for infected and treated individuals, Ψ was the rate of pneumonia induced death during treatment and α was the rate of pneumonia induced death of infected individuals. The basic reproduction number(R_0) and control reproduction number(R_C) for flow charts in Figure 4 were obtained using Next Generation Matrix as

$$R_0 = \frac{\beta_1 \pi}{\mu(\mu+\alpha+\delta)} \text{ and } R_C = \frac{\beta_1 \pi}{\mu(\tau+\mu+\alpha+\phi)} + \frac{\beta_2 \phi \pi}{\mu(\tau+\mu+\alpha+\phi)(\mu+\Psi+\gamma)}.$$

In our model, S class was subdivided into S (Susceptible individuals) and V (Vaccinated individuals), I class was subdivided into severely infected class (I_M) and very severely infected class (I_C), two compartments of individuals under treatment were introduced, that is, outpatients(T_M) and inpatients(T_C). Recovered(R) class was also introduced. The exit rate from under five years class was also integrated in constant death rate. Our model considered SIRS due to the fact that pneumonia does not confer permanent immunity after recovery.

Kenya specific attributes mentioned in Section 2.6 such as categorizing pneumonia of under the age of five in two broad categories, introducing vaccinated individuals,

concentrating on the vulnerable class in Kenya(under the age of five) among others were considered when formulating a general population deterministic model based on Susceptible-Vaccinated-Infected-Treated-Recovered-Susceptible compartments (SVITRS). Seven nonlinear first order ordinary differential equations that govern the dynamics of pneumonia disease for the children under the age of five years in Kenya were deduced from the flow chart.

3.3 Determination of model thresholds and analysis of stability, sensitivity and backward bifurcation.

This involved the nine steps described as follows.

3.3.1 Investigate the positivity and boundedness of the solution

This established that the system of equations developed in Section 3.1 lied in the feasible region. The upper bound of population for the children under the age of five years in Kenya was determined.

3.3.2 Determine disease free equilibrium point (DFE)

The expressions of susceptible and vaccinated population were determined at infection free equilibrium point.

3.3.3 Determine the basic reproduction number$(\mathbf{R_0})$ and the control reproduction number$(\mathbf{R_C})$.

The reproduction numbers of the system were determined using the Next Generation Matrix method, whereby the Jacobi matrix of the system of equations was evaluated at DFE. Eigenvalues of the Next Generation Matrix were determined using Mathematica software. The R_C was obtained as spectral radius (Li *et al.*, 2011).

3.3.4 Investigate the existence of the endemic equilibrium point

The condition necessary for the force of infection to be positive was evaluated at endemic equilibrium point. This was used to predict the presence of positive endemic equilibrium point.

3.3.5 Carry out bifurcation analysis.

The Centre Manifold theorem was stated and then used to predict nonexistence of backward bifurcation in the system.

3.3.6 Investigate the local stability of the disease free equilibrium point

The Jacobi matrix of the reduced system of equations describing the model for pneumonia was determined. The matrix was then evaluated at disease free equilibrium point. Finally the signs of the eigenvalues of that matrix was used to determine the condition necessary for the local asymptotically stability of the disease free equilibrium point.

3.3.7 Investigate the global stability of the disease free equilibrium point

A Lyapunov criterion for stability was used to determine the condition necessary for the global asymptotic stability of the disease free equilibrium point. We determined conditions necessary for the derivative of Lyapunov function to be negative definite to ascertain global asymptotic stability.

3.3.8 Global stability of the endemic equilibrium point

A Lyapunov criterion for stability was used to determine the condition necessary for stability of the endemic equilibrium point. Our study proposed logarithmic function which was positive definite at endemic equilibrium point. We determined conditions

necessary for the derivative of Lyapunov function to be negative definite to ascertain global asymptotic stability.

3.3.9 Carry out analytical sensitivity analysis of control reproduction number and also determine epidemiological thresholds as well as their biological interpretations

Analytical sensitivity of the reproduction number was determined using partial differentiation with respect to: the rate of susceptible children under the age of five years who sought vaccination, vaccination drug's efficacy, rate of mild infected children under the age of five years who sought treatment and rate of chronic infected children under the age of five years who sought treatment. Critical treatment was determined. Equilibrium points and threshold were investigated and their biological meaning provided.

3.4 Estimation of numerical results of model using data and/or parameters from KHIS and UNICEF as well as evaluation of normalized sensitivity analysis

This involved the following three steps.

3.4.1 Estimation of unknown parameters using MATLAB software

The study used the available secondary data and/or parameters for the years 2012 and 2013 from KHIS, literature and UNICEF to estimate the unknown parameters using MATLAB software.

3.4.2 Estimation of numerical results reproduction numbers

The estimated numerical value for the control reproduction number(R_C), basic reproduction number(R_0), the reproduction number($R_{\epsilon=1}$), herd immunity and the

reproduction number(R_T) were obtained by substituting numerical value of the estimated parameters.

3.4.3 Evaluation of normalized sensitivity index

The study by (Nakul *et al.*, 2008), described sensitive index as a measure of the relative change in a state variable when a parameter changes. It also described normalized forward sensitivity index of a variable to a parameter as the ratio of the relative change in the variable to the relative change in the parameter.

Definition

The normalized forward sensitivity index of a variable, χ, that depends differentiability on a parameter, Ψ, is defined as (Nakul *et al.*, 2008):

$$R_{\Psi}^{\chi} = \frac{\partial \chi}{\partial \Psi} \times \frac{\Psi}{\chi}$$

The above was definition was used to evaluate the normalized sensitivity analysis of the control reproduction number(R_C).

3.5 Numerical simulations for validation of analytical results such as assessment the effects the of the efficacy of the vaccination drugs, environmental factors and therapeutic treatment drugs

This involved using the following two steps.

3.5.1 Carry out numerical simulations

Numerical simulation using MATLAB software was used to predict the dynamics of the estimated model.

3.5.2 Carry out numerical sensitivity analysis of the reproduction number

Sensitivity analysis of the reproduction number with various parameters was determined using MATLAB software and the results presented graphically.

CHAPTER FOUR

RESULTS AND DISCUSSION

4.1 Introduction

This chapter explains how each of the specific objectives in Section 1.3.2 was achieved namely development of a model of pneumonia for the under the age five with Kenya specific attribute, determination of model thresholds and perform stability analysis, sensitivity analysis, backward bifurcation analysis so as to establish the conditions for the spread of disease, estimation of numerical results of model using data and/or parameters from KHIS and UNICEF as well as evaluate normalized sensitivity index and performing numerical simulations to validate analytical results of the model and assess the effects of efficacy of the vaccination, environmental factors and therapeutic treatment drugs.

4.2 Outcomes of model development of pneumonia for the under the age five with Kenya specific attributes.

This section describes the model, list assumptions considered when formulating the model and deduced model equations from the flow chart. Our study considered community acquired pneumonia. The summary of the definition of terms, description of the variables and parameters are also provided in Page xiv.

4.2.1 Model description

Let N (t) be the total population of the under five years children which is divided into seven sub-classes as follows: susceptible to pneumonia class [S (t)], vaccinated against pneumonia class [V (t)], severely infected pneumonia class [$I_M(t)$], very severe infected pneumonia class[$I_C(t)$], class of inpatient[$T_C(t)$], class of outpatient [$T_m(t)$] and class of individuals recovered from pneumonia [R (t)] after treatment.

The rates at which $I_M(t)$ and $I_C(t)$ seeks treatment is given by $\tau_1$and τ_2 respectively, the recruitment rate (birth rate) is given by π, pneumonia induced deaths occur at a rate δ_1 and δ_2 in $I_C(t)$ and $T_C(t)$ respectively, μ is the constant natural death rate including exit rate from under age five bracket, β is the per capita infection rate , ϕ is the proportion of children vaccinated with available pneumonia vaccines (either streptococcus vaccines or haemophilus type b vaccine or both) at birth, ρ is the rate of waning of treatment drugs after recovery, $\lambda(t)$ is the force of infection, ϵ is the drug efficacy ($\epsilon = 1$ when the drug is 100% efficient and $\epsilon = 0$ when the drug is useless), θ_1 is the rate at which children under the age of five in class $I_M(t)$ progresses to $I_C(t)$ and θ_2 is the rate at which children under the age of five in class $T_C(t)$ are discharged to $T_M(t)$. The recovery rates after treatment are $\gamma_1$and γ_2 for $T_M(t)$ and $T_C(t)$ respectively.

4.2.2 Model assumptions

The following twelve assumptions were made when formulating the model.

i. Homogeneous mixing of the children under the age of five years in Kenya.
ii. The recovery from natural immunity not significant.
iii. Temporary immunity to pneumonia after treatment.
iv. Hospital acquired pneumonia and ventilator acquired pneumonia assumed to be not significant in this study.
v. The decreasing order of infectivity is; severely infected, very severely infected, outpatient and inpatients.
vi. Constant natural death rate in all classes.

vii. Disease induced death is assumed to be higher in very severely infected children than children in inpatient class($\delta_1 > \delta_2$). Treatment reduces likelihood of dying significantly.

viii. Modification parameter k is such that $k \geq 1$, implying that the environmental factors increase force of infection.

ix. Once vaccinated child contract pneumonia, the vaccination drug is assumed to be useless.

x. The effects of transmission of pneumonia by the ages beyond five years of age are assumed to be not significant in this study.

xi. The pneumonia of the under five years is assumed to be transmitted after effective contact between susceptible and/or vaccinated persons under the age of five years with infectious classes (severe and very severe) and/or treated classes (outpatients and inpatients).

xii. The weak nature of child's immune system was assumed to be vulnerable to all types of pneumonia as long as they exist in population.

4.2.3 Flow chart diagram and the model equations

Model descriptions in section 4.1.1 and model assumptions listed in section 4.1.2 were represented as flow chart diagram.

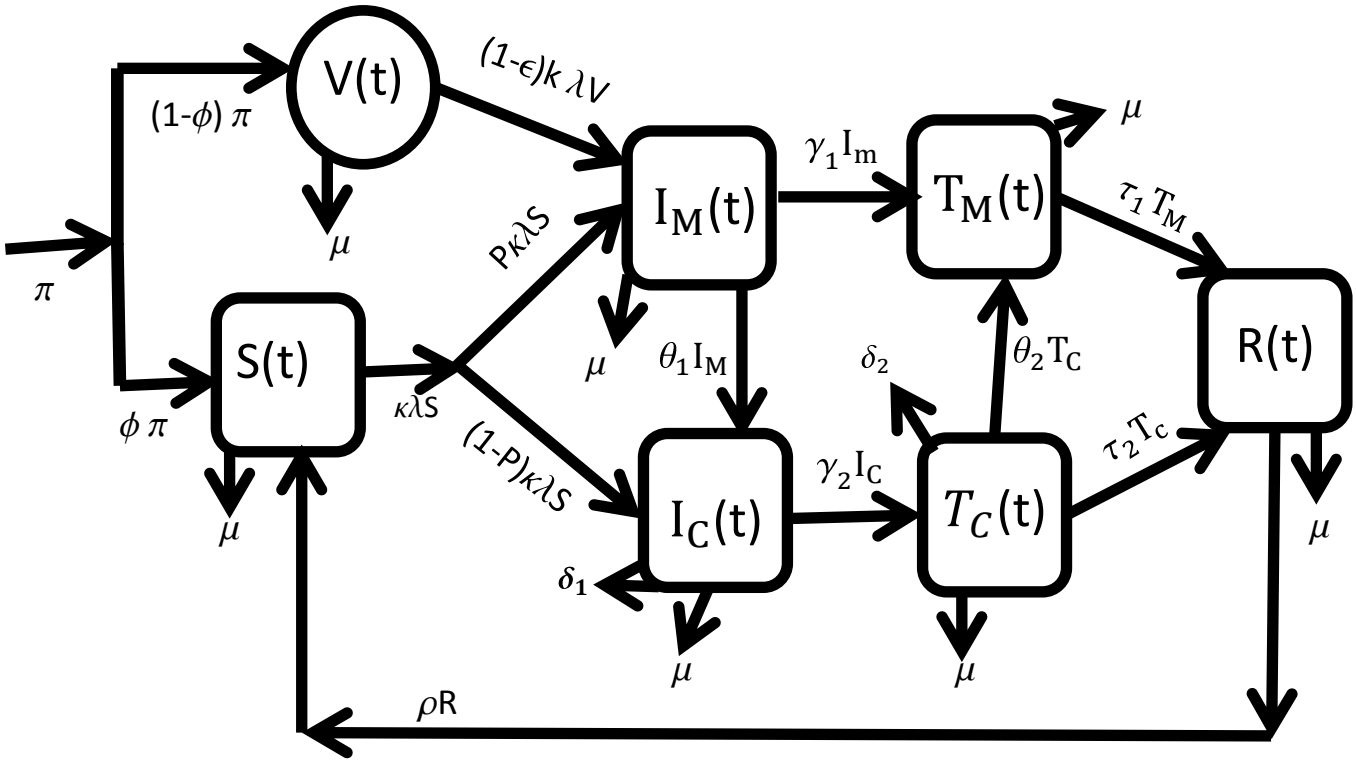


Figure 5: Flow chart diagram (Author, 2017).

From the flow chart, we obtained the following systems of equations representing the population dynamics of pneumonia for the under-five of years.

$$\frac{dS}{dt} = \phi\pi + \rho R - (k\lambda + \mu)S \quad (1),$$

$$\frac{dV}{dt} = (1-\phi)\pi - (1-\epsilon)k\lambda V - \mu V \quad (2),$$

$$\frac{dI_M}{dt} = PK\lambda S + (1-\epsilon)k\lambda V - \omega_1 I_M \quad (3),$$

$$\frac{dI_C}{dt} = (1-P)k\lambda S + \theta_1 I_M - \omega_2 I_C \quad (4),$$

$$\frac{dT_M}{dt} = \tau_1 I_M + \theta_2 T_C - \omega_3 T_M \quad (5),$$

$$\frac{dT_C}{dt} = \tau_2 I_C - \omega_4 T_C \qquad (6),$$

$$\frac{dR}{dt} = \gamma_1 T_m + \gamma_2 T_C - \omega_5 R \qquad (7),$$

where,

$N(t) = S(t) + V(t) + I_M(t) + I_C(t) + T_M(t) + T_C(t) + R(t)$; $\omega_1 = \theta_1 + \mu + \tau_1$; $\omega_2 = \mu + \delta_1 + \tau_2$; $\omega_3 = \gamma_1 + \mu$; $\omega_4 = \gamma_2 + \mu + \theta_2 + \delta_2$; $\omega_5 = \mu + \rho$; $0 \leq P, \epsilon, \phi \leq 1$. The initial conditions of the model are $S(0) = S_0, V(0) = V_0, I_M(0) = (I_M)_0, I_C(0) = (I_C)_0, T_M(0) = (T_M)_0, T_C(0) = (T_C)_0$ and $R(0) = R_{00}$. The force of infection denoted by $\lambda(t)$ was given by $\lambda(t) = \beta(I_M + \xi_1 I_C + \xi_2 T_M + \xi_3 T_C)$, where, $0 < \xi_3 < \xi_2 < \xi_1 < 1$. Rate of change of total population of under the age of five years was obtained by the total sum of equations (1) to (7) as,

$$\frac{dN}{dt} = \pi - \mu N - \delta_1 I_C - \delta_2 T_C.$$

4.3 Outcomes of the model thresholds and analysis of stability, sensitivity and backward bifurcation.

The model is analyzed by proving various theorems and carrying out algebraic computation dealing with different attributes.

4.3.1. Positivity and boundedness of the solutions

We prove positivity and boundedness by stating and proving the theorem below.

Theorem1. The region Q, given by

$$Q = \left\{S(t), V(t), I_M(t), I_C(t), T_M(t), T_C(t), R(t) \epsilon R_+^7 ; N \leq \frac{\pi}{\mu}\right\}$$

is positively invariant and attracting with respect to model system$[(1) - (7)]$,

Proof.

Let $S(t), V(t), I_M(t), I_C(t), T_M(t), T_C(t)$and $R(t)$ be any solutions of the system with non-negative initial conditions $S(0) \geq 0, V(0) \geq 0, I_M(0) \geq 0, I_C \geq 0, T_M \geq 0, T_C \geq 0, R(0) \geq 0.$

Since, $\frac{dS}{dt} = \phi\pi + \rho R - (k\lambda + \mu)S$, it follows that $\frac{dS}{dt} \geq -(k\lambda + \mu)S$. On integration, we obtain $\frac{dS}{dt} \geq \frac{d}{dt}[S(0)e^{\int_o^t -[k\lambda(s)+\mu]ds}] \geq 0$. Clearly, $S(0)e^{\int_o^t -[k\lambda(s)+\mu]ds}$ is a non-negative function of t, thus S (t) stays positive.

The positivity of $V(t), I_M(t), I_C, (t), T_M(t), T_C(t)$ and $R(t)$ are proved along the same lines as follows:

$$\frac{dV}{dt} = (1 - \phi)\pi S - [(1 - \epsilon)k\lambda + \mu]V,$$

$$\frac{dV}{dt} \geq -[(1 - \epsilon)k\lambda + \mu]V,$$

$$\frac{dV}{V} \geq -[(1 - \epsilon)k\lambda + \mu]dt,$$

$$V(t) \geq C_1 e^{-[(1-\epsilon)k\lambda(s)+\mu]dt},$$

where C_1 is a constant of integration, applying initial condition at $t = 0$,

$$C_1 = V(0),$$

$$V(t) \geq V(0)e^{-[(1-\epsilon)k\lambda(s)+\mu]t},$$

$$V(t) \geq V(0)e^{-[(1-\epsilon)k\lambda(s)+\mu]t} \geq 0.$$

Similarly,

$$I_M(t) \geq I_M(0)e^{-\omega_1 t} \geq 0,$$

$$I_C(t) \geq I_C(0)e^{-\omega_2 t} \geq 0,$$

$$T_M(t) \geq T_M(0)e^{-\omega_3 t} \geq 0,$$

$$T_C(t) \geq T_C(0)e^{-\omega_4 t} \geq 0,$$

$$R(t) \geq R(0)e^{-\omega_5 t} \geq 0.$$

Taking the time derivative of our total population along its solution path gives:

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dV}{dt} + \frac{dI_M}{dt} + \frac{dI_C}{dt} + \frac{dT_M}{dt} + \frac{dT_C}{dt} + \frac{dR}{dt}$$

$$\frac{dN}{dt} = \pi - \mu N - \delta_1 I_C - \delta_2 T_C$$

Therefore,

$$\frac{dN}{dt} + \mu N \leq \pi,$$

This implies that

$$N(t) \leq \frac{\pi}{\mu} + c_2 e^{-\mu t},$$

where c_2 is the constant of integration.

Hence,

$$\lim_{t\to\infty} N(t) \leq \frac{\pi}{\mu}.$$

This proves the boundedness of the solutions inside Q. This implies that all the solutions of our system$[(1) - (7)]$, starting in Q and will remains in Q for all $t \geq 0$. Thus Q is positively invariant and attracting, and hence it is sufficient to consider the dynamics of our system in Q. This completes the proof.

4.3.2 Disease free equilibrium point (DFE)

The disease free equilibrium point (DFE) of the system$[(1)-(7)]$ is obtained by setting all the infectious classes, recovered class and treatment classes to zero. We obtain

$$\phi\pi - \mu S^0 = 0;\ (1-\phi)\pi - \mu V^0 = 0,$$

which yields,

$$S^0 = \frac{\phi\pi}{\mu};\ V^0 = \frac{(1-\phi)\pi}{\mu}$$

The DFE point for our system is given by,

$$E^0 = (S^0, V^0, I_C^0, I_M^0, T_M^0, T_C^0, R^0) = \left(\frac{\phi\pi}{\mu}, \frac{(1-\phi)\pi}{\mu}, 0,0,0,0,0\right).$$

The DFE point (E^0) is the infection free equilibrium point of the system$[(1)-(7)]$, which indicates that in absence of pneumonia, the system$[(1)-(7)]$ will consist of two compartment classes (susceptible and vaccinated).

4.3.3. The basic reproduction number $(\mathbf{R_0})$ and control reproduction number $(\mathbf{R_C})$

We use the Next Generation Matrix method to determine the control reproduction number (R_c) of the model (Chavez *et al.*, 2001). Using the notation f for a matrix of new infections terms and v for the matrix of the remaining transfer of infection terms in our system, we got,

$$f = \begin{pmatrix} Pk\lambda S + (1-\epsilon)k\lambda V \\ (1-P)k\lambda S \\ 0 \\ 0 \end{pmatrix}, v = \begin{pmatrix} \omega_1 I_M \\ -\theta_1 I_M + \omega_2 I_C \\ -\tau_1 I_M - \theta_2 T_C + \omega_3 T_M \\ -\tau_2 I_C + \omega_4 T_C \end{pmatrix}.$$

Let

$$F_1 = Pk\lambda S + (1-\epsilon)k\lambda V, \qquad F_2 = (1-P)k\lambda S, \qquad F_3 = 0,\ F_4 = 0,$$

$$F_5 = \omega_1 I_M, \qquad F_6 = -\theta_1 I_M + \omega_2 I_C,$$

$$F_7 = -\tau_1 I_M - \theta_2 T_C + \omega_3 T_M,\ F_4 = -\tau_2 I_C + \omega_4 T_C$$

We obtain the matrices F and V by finding the Jacobian matrices of f and v evaluated at DFE respectively to obtain,

$$F = \beta k \begin{pmatrix} R_1 & \xi_1 R_1 & \xi_2 R_1 & \xi_3 R_1 \\ R_2 & \xi_1 R_2 & \xi_2 R_2 & \xi_3 R_2 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix};\ V = \begin{pmatrix} \omega_1 & 0 & 0 & 0 \\ -\theta_1 & \omega_2 & 0 & 0 \\ -\tau_1 & 0 & \omega_3 & -\theta_2 \\ 0 & -\tau_2 & 0 & \omega_4 \end{pmatrix},$$

where, $R_1 = PS^0 + (1-\epsilon)V^0$ and $R_2 = (1-P)S^0$. We obtain V^{-1} as,

$$V^{-1} = \begin{pmatrix} \frac{1}{\omega_1} & 0 & 0 & 0 \\ \frac{\theta_1}{\omega_1\omega_2} & \frac{1}{\omega_2} & 0 & 0 \\ \frac{\theta_1\tau_2\theta_2 + \omega_2\omega_4\tau_1}{\omega_1\omega_2\omega_3\omega_4} & \frac{\theta_2\tau_2}{\omega_2\omega_3\omega_4} & \frac{1}{\omega_3} & \frac{\theta_2}{\omega_4\omega_3} \\ \frac{\theta_1\tau_2}{\omega_1\omega_2\omega_4} & \frac{\tau_2}{\omega_2\omega_4} & 0 & \frac{1}{\omega_4} \end{pmatrix}.$$

Multiplying the matrices F and V^{-1} we obtain,

$$FV^{-1} = \begin{pmatrix} T_1 & T_2 \\ T_3 & T_4 \end{pmatrix},$$

where,

T_1

$$= \beta k \begin{bmatrix} \frac{R_1}{\omega_1} + \frac{R_1\theta_1\xi_1}{\omega_1\omega_2} + \frac{R_1\xi_2(\theta_1\theta_2\tau_2 + \tau_1\omega_2\omega_4)}{\omega_1\omega_2\omega_3\omega_4} + \frac{R_1\theta_1\xi_3\tau_2}{\omega_1\omega_2\omega_4} & \frac{R_1\xi_1}{\omega_2} + \frac{R_1\theta_2\xi_2\tau_2}{\omega_2\omega_3\omega_4} + \frac{R_1\xi_3\tau_2}{\omega_2\omega_4} \\ \frac{R_2}{\omega_1} + \frac{R_2\theta_1\xi_1}{\omega_1\omega_2} + \frac{R_2\xi_2(\theta_1\theta_2\tau_2 + \tau_1\omega_2\omega_4)}{\omega_1\omega_2\omega_3\omega_4} + \frac{R_2\theta_1\xi_3\tau_2}{\omega_1\omega_2\omega_4} & \frac{R_2\xi_1}{\omega_2} + \frac{R_2\theta_2\xi_2\tau_2}{\omega_2\omega_3\omega_4} + \frac{R_2\xi_3\tau_2}{\omega_2\omega_4} \end{bmatrix},$$

$$T_2 = \beta k \begin{bmatrix} \frac{R_1\xi_2}{\omega_3} & \frac{R_1\theta_2\xi_2}{\omega_3\omega_4} + \frac{R_1\xi_3}{\omega_4} \\ \frac{R_2\xi_2}{\omega_3} & \frac{R_2\theta_2\xi_2}{\omega_3\omega_4} + \frac{R_2\xi_3}{\omega_4} \end{bmatrix}, T_3 = T_4 = \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix}.$$

Using Mathematica software we obtain the eigenvalues $\{q(i), i = 1, 2, 3, 4\}$ of the matrix (FV^{-1}) as,

$q(1) = q(2) = q(3) = 0,$

$$q(4) = \frac{\beta k}{\omega_1\omega_2\omega_3\omega_4}\{R_1\omega_2\omega_3\omega_4 + \xi_1(R_1\theta_1\omega_3\omega_4 + R_2\omega_1\omega_3\omega_4) + \xi_2(R_1\theta_1\theta_2\tau_2 + R_2\theta_2\tau_2\omega_1 + R_1\tau_1\omega_2\omega_4) + \xi_3(R_1\theta_1\tau_2\omega_3 + R_2\tau_2\omega_1\omega_3)\}.$$

The control reproduction number(R_C) is given by the spectral radius ζ (the dominant eigenvalue) of the matrix FV^{-1}, denoted by $\zeta(FV^{-1})$ which is;

$$R_C = \frac{\beta k}{\omega_1\omega_2\omega_3\omega_4}\{R_1\omega_2\omega_3\omega_4 + \xi_1(R_1\theta_1\omega_3\omega_4 + R_2\omega_1\omega_3\omega_4) + \xi_2(R_1\theta_1\theta_2\tau_2 + R_2\theta_2\tau_2\omega_1 + R_1\tau_1\omega_2\omega_4) + \xi_3(R_1\theta_1\tau_2\omega_3 + R_2\tau_2\omega_1\omega_3)\}.$$

The control reproduction number(R_C) is the average number of susceptible children under the age of five years, one infectious child (severely infected, very severely infected, outpatient or inpatient) can infect when combined interventions of vaccination and treatment are put in place.

The reproduction number($R_{\epsilon=1}$) when the vaccination drug efficacy is 100%, that is $\epsilon = 1$ is obtained by setting $\epsilon = 1$ in R_C

$$R_{\epsilon=1} = \frac{\beta k S^0}{\omega_1\omega_2\omega_3\omega_4}\{P\omega_2\omega_3\omega_4 + \xi_1(P\theta_1\omega_3\omega_4 + (1-P)\omega_1\omega_3\omega_4) + \xi_2(P\theta_1\theta_2\tau_2 + (1-P)\theta_2\tau_2\omega_1 + P\tau_1\omega_2\omega_4) + \xi_3(P\theta_1\tau_2\omega_3 + (1-P)\tau_2\omega_1\omega_3)\}.$$

The reproduction number(R_T) when the rate at which severely and very severely infected children are treated are equal to zero. We set $\tau_1 = 0$ and $\tau_2 = 0$ in R_C to obtain

$$R_T = \frac{\beta k}{(\omega_1 - \tau_1)(\omega_2 - \tau_1)}\{R_1(\omega_2 - \tau_1) + \xi_1\langle R_1\theta_1 + R_2(\omega_1 - \tau_1)\rangle\}.$$

The basic reproduction number(R_0) in absence of interventions is given by;

$$R_0 = \frac{\beta k S^0(P(\mu + \delta_1) + (\mu(1 - P) + \theta_1)\xi_1)}{(\mu + \delta_1)(\mu + \theta_1)}.$$

The basic reproduction number(R_0) is the average number susceptible children under the age of five years, one infectious child (severely infected or very severely infected or outpatient or inpatient) can infect in absence of interventions of treatment and vaccination.

The basic reproduction number(R_0) was used to determine herd immunity(q_c) using the expression below (Holland and Zachary, 2014)

$$q_c = 1 - \frac{1}{R_0}.$$

4.3.4. Existence of Endemic Equilibrium Point for the model (EEP).

We state and prove the following theorem.

Theorem 2

A positive endemic equilibrium exists and is locally asymptotically stable whenever $R_C^* > 1$.

Proof

Let $A(t) = I_M(t) + I_C(t) + T_M(t) + T_C(t)$. The time derivative of A is given by. $\frac{dA}{dt} = \frac{dI_M}{dt} + \frac{dI_C}{dt} + \frac{dT_M}{dt} + \frac{dT_C}{dt} = \frac{dN}{dt} - \frac{dS}{dt} - \frac{dV}{dt}$.

Since, $\{S(t), V(t), I_M(t), I_C(t), T_M(t), T_C(t), R(t)\} \epsilon R_+^7$, it also follows that $A(t) \epsilon R_+^7$. At endemic equilibrium point $A^* = I_M^* + I_C^* + T_M^* + T_C^*$. The system of equations $[(1) - (7)]$ reduces to,

$$\frac{dS}{dt} = \phi\pi + \rho R - (k\lambda + \mu + \phi\pi)S \qquad (8),$$

$$\frac{dV}{dt} = (1 - \phi)\pi - k(1 - \epsilon)\lambda V - \mu V \qquad (9),$$

$$\frac{dA}{dt} = -(\mu + \Omega)A - \delta_1 I_C - \delta_2 T_C + k\lambda S + k(1 - \epsilon)\lambda V - \gamma_1 T_m - \gamma_2 T_C \qquad (10),$$

$$\frac{dR}{dt} = \gamma_1 T_m + \gamma_2 T_C - \omega_5 R \qquad (11).$$

Since the following parameters $\gamma_1, \gamma_2, \delta_1, \delta_2, \mu, \xi_1, \xi_2$ and ξ_3 are less or equal to one but greater or equal to zero, it follows that,

$$I_M^* \le A^*;\ \xi_1 I_C^* \le A^*;\ \xi_2 T_M^* \le A^*;\ \xi_3 T_C^* \le A^*; \gamma_1 T_m \le A; \gamma_2 T_C \le A; \delta_1 I_C \le A;\ \delta_2 T_C \le A;$$

$$\mu A \le A; \xi_1 I_C \le A, \xi_2 T_M \le A; \xi_3 T_C \le A\ ; I_M^* + \xi_1 I_C^* + \xi_2 T_M^* + \xi_3 T_C^* \le A^*;$$

$$\left(\delta_1 I_C + \delta_2 T_C + \gamma_1 T_m + \gamma_2 T_C\right) \le A;\ ;\left(I_M + \xi_1 I_C + \xi_2 T_M + \xi_3 T_C\right) \le A.$$

Let $\gamma_1 T_m + \gamma_2 T_C = \Omega_2 A,\ \delta_1 I_C + \delta_2 T_C + \gamma_1 T_m + \gamma_2 T_C = \Omega_1 A,\ I_M + \xi_1 I_C + \xi_2 T_M + \xi_3 T_C = \Omega_3 A$ and $I_M^* + \xi_1 I_C^* + \xi_2 T_M^* + \xi_3 T_C^* = \Omega_4 A^*$.

After the change of variables, the system of equations $[(8) - (11)]$ becomes,

$$\frac{dS}{dt} = \phi\pi + \rho R - (k\lambda + \mu)S \qquad (12),$$

$$\frac{dV}{dt} = (1-\phi)\pi - k(1-\epsilon)\lambda V - \mu V \qquad (13),$$

$$\frac{dA}{dt} = k\lambda S + k(1-\epsilon)\lambda V \ - \Omega_1 A \qquad (14),$$

$$\frac{dR}{dt} = \Omega_2 A - \omega_5 R \qquad (15).$$

The control reproduction number (R_C^*) of the system $[(12)-(15)]$ determined using the Next Generation Matrix. The compartment A (t) is the only infectious class, let $q_1 = (k\lambda S + k(1-\epsilon)\lambda V\ )$ be a matrix of new infection and $q_2 = \Omega_1 A$ then the Jacobian of matrices q_1 and q_2 are $\beta k\Omega_3 H_1$ and Ω_1 respectively. The inverse of matrix Ω_1 is $\frac{1}{\Omega_1}$ the spectral radius of the matrix obtained by multiplying $\beta k\Omega_3 H_1$ is

$$R_C^* = \frac{\beta k\Omega_3 H_1}{\Omega_1},$$

where, $H_1 = S^0 + (1-\epsilon)V^0$.

After the change of variables, the force of infection at endemic equilibrium point $E^{**} = (S^{**}, V^{**}, A^{**}, R^{**})$ of the system $[(12)-(15)]$ was given by $\lambda^{**} = \beta\Omega_3 A^{**}$. The endemic equilibrium point, $E^{**} = (S^{**}, V^{**}, A^{**}, R^{**}$of the system $[(12)-(15)]$, is obtained by equating the system to zero to obtain;

$$\phi\pi + \rho R^{**} - (k\lambda^{**} + \mu)S^{**} = 0;\ (1-\phi)\pi - (1-\epsilon)k\lambda^{**}V^{**} - \mu V^{**} = 0;$$

$$k\lambda^{**}S^{**} + k(1-\epsilon)\lambda^{**}V^{**} - \Omega_1 A^{**} = 0;\ \Omega_2 A^{**} - \omega_5 R^{**} = 0.$$

After solving the system of equation above (i) to (iv)in terms of λ^{**} using Mathematica software we obtain;

$$S^{**} = \frac{\phi\pi + \rho R^{**}}{k\lambda^{**} + \mu},$$

$$V^{**} = \frac{(1-\phi)\pi}{k\lambda^{**}(1-\epsilon) + \mu},$$

$$A^{**} = \frac{k\pi\lambda^{**}((-1+\epsilon)(k\lambda^{**} + \mu) - \epsilon\mu\phi)\omega_5}{(k(-1+\epsilon) - \mu)((k\lambda^{**} + \mu)\omega_5\Omega_1 - k\lambda^{**}\rho\Omega_2)},$$

$$R^{*} = \frac{\Omega_2 A^{**}}{\omega_5}.$$

Substituting A^{**} then solve the equation below we obtain two cases

$$\lambda^{**} - \beta\Omega_3 A^{**} = 0,$$

Case 1; $\lambda^{**} = 0$, which correspond to the disease free equilibrium point(E^{00}) of the system $[(12) - (15)]$ given by;

$$E^{00} = (S^{00}, V^{00}, A^{00}, R^{00}) = (\frac{\phi\pi}{\mu}, \frac{(1-\phi)\pi}{\mu}, 0, 0)$$

Case 2; the value(s) of λ^{**} obtained by the quadratic equations below corresponded to endemic equilibrium point.

$$a(\lambda^{**})^2 + b\lambda^{**} + c = 0,$$

Using Mathematica software; a, b and c are obtained as follows,

$$a = k^2(-1+\epsilon)(\omega_5\Omega_1 - \rho\Omega_2) < 0,$$

$$b = k\left((-2+\epsilon)\mu - \left(\frac{\pi(-1+\epsilon)R_C^*}{H_1}\right)\omega_5\Omega_1 + \mu\rho\Omega_2\right),$$

$$c = \mu\left\{-\mu + \frac{\pi\left(1+\epsilon(-1+\phi)\right)R_C^*}{H_1}\right\}\omega_5\Omega_1.$$

For real λ^{**}, $b^2 \geq 4ac$. Since $a < 0$, it followed that $\lambda^{**} > 0$ if and only if $c > 0$ or $c < 0$, i. e

$$-\mu + \frac{\pi\left(1 + \epsilon(-1 + \phi)\right)R_C^*}{H_1} > 0 \text{ or } -\mu + \frac{\pi\left(1 + \epsilon(-1 + \phi)\right)R_C^*}{H_1} < 0$$

After algebraic manipulation it follows that the conditions necessary and sufficient for $\lambda^{**} > 0$ is $R_C^* > 1$ or $R_C^* < 1$. Epidemiologically the condition $R_C^* < 1$ correspond to global asymptotic stability of disease free equilibrium point pointed in Section 4.2.7 hence the necessary condition for the existence of endemic equilibrium point is $R_C^* > 1$. This completed the proof. This result show that pneumonia would persist whenever $R_C^* > 1$.

4.3.5 Bifurcation analysis.

According to study (Braurer, 2004), Mathematical models with vaccination often undergo bifurcation which makes the control of the infectious diseases difficult. This bifurcation can be explored using the Centre Manifold theory (Liu and Zhang, 2011). The change of variables is made first for simplicity. Let $S = y_1, V = y_2, A = y_3$ and $R = y_4$, so that, $N = y_1 + y_2 + y_3 + y_4$. Further, by using vector notation, $y = (y_1, y_2, y_3, y_4)^T$, the pneumonia model$[(12) - (15)]$ was written in the form $\frac{dy}{dt} = F(y)$, with $F = (p_1, p_2, p_3, p_4)^T$, as follows:

$$\dot{y_1} = p_1 = \phi\pi - (k\beta\Omega_3 y_3 + \mu)y_1 + \rho y_4, \qquad (16),$$

$$\dot{y_2} = p_2 = (1 - \phi)\pi - (1 - \epsilon)k\beta\Omega_3 y_3 y_2 - \mu y_2 \qquad (17),$$

$$\dot{y_3} = p_3 = k\beta\Omega_3 y_3 y_1 + k(1 - \epsilon)\beta\Omega_3 y_3 y_2 - \Omega_1 y_3 \qquad (18),$$

$$\dot{y_4} = p_4 = \Omega_2 y_3 - \omega_5 y_4 \qquad (19),$$

where, $\lambda^{***} = \beta\Omega_3 y_3$.

The method entails evaluating the Jacobian of the system $[(16)-(19)]$ at the disease free equilibrium point, $E_*^0 = (S_*^0, V_*^0, A_*^0, R_*^0) = (\frac{\phi\pi}{\mu}, \frac{(1-\phi)\pi}{\mu}, 0, 0)$, denoted by $J(E_*^0)$. We obtain:

$$J(E_*^0). = \begin{pmatrix} -\mu & 0 & -k\beta^*\Omega_3 S^0 & \rho \\ 0 & -\mu & -k(1-\epsilon)\beta^*\Omega_3 V^0 & 0 \\ 0 & 0 & k\beta^*\Omega_3 H_1 - \Omega_1 & 0 \\ 0 & 0 & \Omega_2 & -\omega_5 \end{pmatrix}, \qquad \text{where } H_1 = S^0 + (1-\epsilon)V^0.$$

We consider the case where $R_C^* = 1$. Suppose $\beta = \beta^*$ is chosen as a bifurcation parameter, then solving for β^* from $R_C^* = 1$ gives $\beta^* = \frac{\Omega_1}{k\Omega_3 H_1}$. The Jacobian of $\frac{dy}{dt} = F(y)$ at the disease free equilibrium point, with $\beta = \beta^*$, denoted by $J(E_*^0)$, has eigenvalues $(-\mu, -\mu, -\omega_5 \text{ and } 0)$. We obtain one zero eigenvalue and three negative eigenvalues, hence the Centre Manifold theory is used to analyze the dynamics of the model (Liu and Zhang, 2011). The theorem stated below is used to analyze the dynamics of the (*Okaka et al.*, 2013).

The theorem by (Chavez et al., 2001), considered the following general system of ordinary differential equations with a parameter β^*

$$\frac{dy}{dt} = f(y, \beta^*), f: R^n \times R \to R^n \text{ and } f \in C^2(R^n \times R),$$

where 0 is an equilibrium point of the system (that is, $f(y, \beta^*) \equiv 0$ for all β^*) and

1) $A = D_y f(0,0) = \left(\frac{\delta p_i}{\delta y_j}(0,0)\right)$, is the linearization matrix of the system around the equilibrium 0 with β^* evaluated at 0;
2) Zero is a simple eigenvalue of A and all other eigenvalues of A have negative real parts;

3) Matrix A has a right eigenvector u and a left eigenvector v corresponding to the zero eigenvalue. Let $p_k$be the kth component of p and

$$a = \sum_{k,ij=1}^{n} v_k u_i u_j \frac{\partial^2 p_k}{\partial y_i \, \partial y_j}(0,0),$$

$$b = \sum_{k,ij=1}^{n} v_k u_i \frac{\partial^2 p_k}{\partial y_i \, \partial \beta^*}(0,0),$$

then the local dynamics of the system around the equilibrium point (0,0) is totally determined by the signs of a and b.

Particularly when:

i. $a > 0$ and $b > 0$, when $\beta^* < 0$ with$|\beta^*| \ll 1, (0,0)$, is locally asymptotically stable and there exists a positive unstable equilibrium; when $0 < \beta^* \ll 1, (0,0)$ is unstable and there exists a negative and locally asymptotically stable equilibrium.

ii. $a < 0$ and $b < 0$, when $\beta^* < 0$ with $|\beta^*| \ll 1, (0,0)$ is unstable; when $0 < \beta^* \ll 1, (0,0)$ is asymptotically stable and there exists a positive unstable equilibrium.

iii. $a < 0$ and $b > 0$, when $\beta^* < 0$ with $|\beta^*| \ll 1, (0,0)$is unstable, and there exists a negative and locally asymptotically stable equilibrium; when $0 < \beta^* \ll 1, (0,0)$ is stable and there exists a positive unstable equilibrium.

iv. $a > 0$ and $b < 0$, when β^*changes from negative to positive, $(0,0)$ changes its stability from stable to unstable. Correspondingly a negative equilibrium becomes positive and locally asymptotically stable.

If a > 0 and b > 0, then a backward bifurcation occurs at $\beta^* = 0$ (Okaka *et al.*, 2013).

Eigenvectors ofJ_{β^*}: For the case, when $R_C^* = 1$, it can be shown that the Jacobian$[J(E_*^0)]$at $\beta = \beta^*$(denoted by J_{β^*}) has a right eigenvector given by $u = [u_1, u_2, u_3, u_4]^T$, where,

Let $u_3 = u_3 > 0$, then

$$u_1 = \frac{-k\beta\Omega_3 S^0 u_3 + \rho u_4}{\mu} = \frac{-k\omega_5\beta\Omega_3 S^0 u_3 + \rho\Omega_2 u_3}{\mu\omega_5} < 0,$$

$$u_2 = \frac{-k(1-\epsilon)\beta\Omega_3 V^0 u_3}{\mu} < 0,$$

$$u_4 = \frac{\Omega_2 u_3}{\omega_5} > 0.$$

Further, J_{β^*} has a left eigenvectors $v = [v_1, v_2, v_3, v_4]^T$, where,

Let $v_3 = v_3 > 0$, then $v_1 = 0, v_2 = 0$ and $v_4 = 0$.

Since$(v_1 = v_2 = v_4 = 0)$, we only need to compute the partial derivatives of p_3 (at the disease free equilibrium point). For the system $[(16) - (19)]$ the associated non-zero partial derivative of p_3 (at the disease free equilibrium) is given by

$$\frac{\partial^2 p_3}{\partial y_1 \partial y_3} = \frac{\partial^2 p_3}{\partial p_3 \partial y_1} = k\beta^*\Omega_3, \qquad \frac{\partial^2 p_3}{\partial y_2 \partial y_3} = \frac{\partial^2 p_3}{\partial y_3 \partial y_2} = (1-\epsilon)k\beta^*\Omega_3.$$

It implies,

$$a = v_3 \sum_{i,j=1}^{4} u_i u_j \frac{\partial^2 p_k}{\partial x_i \partial x_j},$$

$$a = 2v_3 \left\{ u_1 u_3 \frac{\partial^2 p_3}{\partial y_1 \partial y_3} + u_2 u_3 \frac{\partial^2 p_3}{\partial y_2 \partial y_3} \right\}.$$

Since u_1 and u_2 are less than zero, it follows that,

$$a = 2v_3\{u_1 u_3 k\beta^*\Omega_3 + u_2 u_3(1-\epsilon)k\beta^*\Omega_3\} < 0.$$

Also,

$$\frac{\partial^2 p_3}{\partial y_3 \, \partial \beta^*} = k\beta\Omega_3 S^0 + k(1-\epsilon)\beta\Omega_3 V^0,$$

$$b = v_3 \sum_{i=1}^{4} u_i \frac{\partial^2 p_k}{\partial y_i \, \partial \beta^*} + v_4 \sum_{i=1}^{4} u_i \frac{\partial^2 p_k}{\partial y_i \, \partial \beta^*},$$

$$b = v_3 \left\{ u_3 \frac{\partial^2 p_3}{\partial y_3 \, \partial \beta^*} \right\}.$$

Since v_3 and u_3 were greater than zero it followed that,

$$b = v_3 u_3 \{k\beta\Omega_3 S^0 + k(1-\epsilon)\beta\Omega_3 V^0\} > 0.$$

Hence, it followed (from Theorem 3 above) that when $\beta^* < 0$ with $|\beta^*| \ll 1, (0,0)$ is unstable, and there exists a negative and locally asymptotically stable equilibrium; when $0 < \beta^* \ll 1, (0,0)$ is stable and there exists a positive unstable equilibrium. Absence of backward bifurcation show that it is possible to eradicate pneumonia whenever $R_C^* < 1$.

4.3.6. Local Stability of the disease free equilibrium point (DFE)

To determine the local stability of the disease free equilibrium point we stated and proved the following theorem.

Theorem 4.

The DFE of the system $[(12)-(15)]$ is locally asymptotically stable whenever $R_C^* < 1$ and unstable otherwise.

Proof

To establish the local stability of the system$[(12)-(15)]$, we used the Jacobian of the model evaluated at E_*^0. Stability of this steady state was then determined based on the signs of eigenvalues of the corresponding Jacobian which were functions of the model parameters. We let

$$P_1 = \phi\pi - (k\lambda + \mu)S \quad + \rho R,$$

$$P_2 = (1-\phi)\pi - (1-\epsilon)k\lambda V - \mu V,$$

$$P_3 = k\lambda S + k(1-\epsilon)\lambda V \quad - \Omega_1 A,$$

$$P_4 = \Omega_2 A - \omega_5 R.$$

The Jacobian matrix evaluated at disease free equilibrium point E_*^0 is obtained as

$$J(E^0) = \begin{pmatrix} -\mu & 0 & -k\beta\Omega_3 S^0 & \rho \\ 0 & -\mu & -k(1-\epsilon)\beta\Omega_3 V^0 & 0 \\ 0 & 0 & k\beta\Omega_3 H_1 \quad -\Omega_1 & 0 \\ 0 & 0 & \Omega_2 & -\omega_5 \end{pmatrix}, \text{where } H_1 = S^0 + (1-\epsilon)V^0.$$

Solving the equation

$$|J(E^0) - q(i)I| = 0,$$

where I is the identity matrix and , $i = 1,2,3,4$ are eigenvalues. We obtain the following eigenvalues

$q(1) = q(2) = -\mu, q(3) = -\omega_5$ and $q(4) = -\Omega_1 + k\beta\Omega_3 H_1$.

Clearly three eigenvalues are negative but the conditions necessary and sufficient for $q(4)$ is

$$-\Omega_1 + k\beta\Omega_3 H_1 < 0,$$

$$R_C^* < 1.$$

This completed the proof. If the initial conditions of the disease dynamics begin in the neighbourhood of DFE, this result show that pneumonia would die out whenever $R_C^* < 1$.

4.3.7. Global stability of the disease free point

To prove the global stability, we state and prove the following theorem.

Theorem 5

The DFE is globally asymptotically stable in Lyapunov sense whenever $R_C^* < 1$ unstable otherwise.

Proof

We propose the following Lyapunov function for the system $[(12)-(15)]$

$$L(S,V,A,R) = S - S^0 - S^0 \mathrm{Ln}\frac{S}{S^0} + X_1\left(V - V^0 - V^0 \mathrm{Ln}\frac{V}{V^0}\right) + X_2 A + X_3 R,$$

where $X_1, X_2 \text{and} X_3$ were positive constants to be determined at DFE point.

$L(S,V,A,R)$ is positive definite and satisfies the conditions;

$$L(S^0,V^0,A^0,R^0) = 0 \text{ and } L(S,V,A,R) > 0.$$

For $\frac{dL(S,V,A,R)}{dt}$ to be negative definite, it must satisfy

$$\frac{dL(S^0,V^0,A^0,R^0)}{dt} = 0 \text{ and } \frac{dL(S,V,A,R)}{dt} < 0.$$

At $E_*^0 = (S^0,V^0,A^0,R^0)$ the system$[(12)-(15)]$ satisfy,

$$\phi\pi = \mu S^0,$$

$$(1-\phi)\pi = \mu V^0.$$

The time derivative of the Lyapunov function is obtained as,

$$\frac{dL(S,V,A,R)}{dt} = \left(1 - \frac{S^0}{S}\right)\frac{dS}{dt} + X_1\left(1 - \frac{V^0}{V}\right)\frac{dV}{dt} + X_2\frac{dA}{dt} + X_3\frac{dR}{dt},$$

Substituting $\frac{dS}{dt}, \frac{dV}{dt}, \frac{dA}{dt}$ and $\frac{dR}{dt}$ to obtain;

$$\frac{dL(S,V,A,R)}{dt} = \left(1 - \frac{S^0}{S}\right)\{\phi\pi - (k\lambda + \mu)S \ + \rho R\}$$

$$+ X_1\left(1 - \frac{V^0}{V}\right)\{(1-\phi)\pi - k(1-\epsilon)\lambda V - \mu V\}$$

$$+ X_2\{k\lambda S + k(1-\epsilon)\lambda V \ - \Omega_1 A\} + X_3\{\Omega_2 A - \omega_5 R\}.$$

Substituting $\phi\pi$ and $(1-\phi)\pi$ to obtain;

$$\frac{dL(S,V,A,R)}{dt} = \left(1 - \frac{S^0}{S}\right)\{\mu S^0 - (k\beta\Omega_3 A + \mu)S \ + \rho R\}$$

$$+ X_1\left(1 - \frac{V^0}{V}\right)\{\mu V^0 - k(1-\epsilon)\beta\Omega_3 AV - \mu V\}$$

$$+ X_2\{k\Omega_3 AS + k(1-\epsilon)\Omega_3 AV \ - \Omega_1 A\} + X_3\{\Omega_2 A - \omega_5 R\},$$

$$\frac{dL(S,V,A,R)}{dt} = -\mu\frac{(S-S^0)^2}{S} - \mu\frac{(V-V^0)^2}{V}$$

$$+ \{-X_2\Omega_1 + X_3\Omega_2 + k\beta\Omega_3 S^0 + X_1 k\beta(1-\epsilon)\Omega_3 V^0\}A$$

$$+ \{X_2 - 1\}k\beta\Omega_3 AS + \{X_2 - X_1\}k\beta(1-\epsilon)\Omega_3 AV + \left\{\rho - X_3\omega_5 - \rho\frac{S^0}{S}\right\}R.$$

Setting AS, AV and A to zero we obtain the following equation,

$$X_2 - 1 = 0,$$

$$X_2 - X_1 = 0,$$

$$-X_2\Omega_1 + X_3\Omega_2 + k\beta\Omega_3 S^0 + X_1 k\beta(1-\epsilon)\Omega_3 V^0 = 0.$$

Solving the above equation we obtain;

$X_1 = X_2 = 1,$

$X_3 = \frac{\Omega_1}{\Omega_2} - \frac{k\beta\Omega_3 H_1}{\Omega_2} = \frac{\Omega_1}{\Omega_2}(1 - R_C^*)$, where, $H_1 = S^0 + (1-\epsilon)V^0$.

The derivative of the Lyapunov function reduces to;

$$\frac{\mathrm{dL(S,V,A,R)}}{\mathrm{dt}} = -\mu\frac{(\mathrm{S}-\mathrm{S}^0)^2}{\mathrm{S}} - \mu\frac{(\mathrm{V}-\mathrm{V}^0)^2}{\mathrm{V}} + \rho\left(1-\frac{\mathrm{S}^0}{\mathrm{S}}\right)\mathrm{R} - \frac{\Omega_1}{\Omega_2}(1-\mathrm{R}_\mathrm{C}^*)\omega_5\mathrm{R}$$

Since $\left(1-\frac{S^0}{S}\right) \leq 0$, the conditions necessary and sufficient for $\frac{dL(S,V,A,R)}{dt} < 0$ was $(1-R_C^*) > 0$. This implied that disease free equilibrium point was globally stable if and only if $R_C^* < 1$ and unstable otherwise. This completed the proof. This result show that pneumonia would die out whenever $R_C^* < 1$ irrespective of the initial conditions.

4.3.8. Global stability of the Endemic Equilibrium point (EEP)

To determine global asymptotic stability we stated and proved the following theorem.

Theorem 6

The EEP is globally asymptotic stable in Lyapunov sense whenever $P > Q$ and unstable otherwise, where

$$\mathrm{P} = \mu\frac{(\mathrm{S}-\mathrm{S}^{***})^2}{\mathrm{S}} + \mu\frac{(\mathrm{V}-\mathrm{V}^{***})^2}{\mathrm{V}} + \frac{\Omega_1}{\Omega_2}\mu\mathrm{R} \quad + \mathrm{k}\beta\Omega_3\mathrm{A}^{***}\mathrm{S}^{***}\frac{\mathrm{S}^{***}}{\mathrm{S}}$$

$$+ \mathrm{k}(1-\epsilon)\beta\Omega_3\mathrm{A}^{***}\mathrm{V}^{***}\frac{\mathrm{V}^{***}}{\mathrm{V}} + 2\{\mathrm{k}\beta\Omega_3\mathrm{A}^{***}\mathrm{S} + \mathrm{k}(1-\epsilon)\beta\Omega_3\mathrm{A}^{***}\mathrm{V}\ \}$$

$$+ \Omega_1\mathrm{A}\frac{\mathrm{R}^{***}}{\mathrm{R}} + \frac{\mathrm{R}_\mathrm{C}^{**}\{(1-\epsilon)\mathrm{V}^{***} + \mathrm{S}^{***}\}\mu\mathrm{R}^{***}}{\mathrm{H}_1},$$

$$\mathrm{Q} = \frac{\mathrm{R}_\mathrm{C}^{**}\{(1-\epsilon)\mathrm{V}^{***} + \mathrm{S}^{***}\}\Omega_2\mathrm{A}}{\mathrm{H}_1}\frac{\mathrm{R}^{***}}{\mathrm{R}} + \frac{\mathrm{R}_\mathrm{C}^{**}\{(1-\epsilon)\mathrm{V}^{***} + \mathrm{S}^{***}\}}{\mathrm{H}_1}\mu\mathrm{R} + 3\Omega_1 A^{***}$$

Proof

For the system $[(12)-(15)]$ to be tractable mathematically we considered a special case where the waning due to drugs was zero i.e $\rho = 0$ to obtain (Liu and Zhang, 2011),

$$\frac{dS}{dt} = \phi\pi - (k\lambda + \mu)S \qquad (16),$$

$$\frac{dV}{dt} = (1-\phi)\pi - k(1-\epsilon)\lambda V - \mu V \qquad (17),$$

$$\frac{dA}{dt} = k\lambda S + k(1-\epsilon)\lambda V \ - \Omega_1 A \qquad (18),$$

$$\frac{dR}{dt} = \Omega_2 A - \mu R \qquad (19).$$

The control reproduction number(R_C^{**}), the force of infection(λ^{***}), disease free equilibrium point $E^{00} = (S^0, V^0, A^{00}, R^{00}) = (\frac{\phi\pi}{\mu}, \frac{(1-\phi)\pi}{\mu}, 0,0)$ and endemic equilibrium point $E^{***} = (S^{***}, V^{***}, A^{***}, R^{***})$ of the system $[(16) - (19)]$ were given by

$$R_C^{**} = \frac{\beta k \Omega_3 H_1}{\Omega_1};\ \lambda^{***} = \beta\Omega_3 A^{***}$$

$$S^{***} = \frac{\phi\pi}{k\lambda^{***} + \mu},$$

$$V^{***} = \frac{(1-\phi)\pi}{k\lambda^{***}(1-\epsilon) + \mu},$$

$$A^{***} = \frac{\frac{\pi(-1+\epsilon)\lambda^{***}(-1+\phi)}{k(-1+\epsilon)\lambda^{***} - \mu} - \frac{k\pi\lambda^{***}\phi}{k\lambda^{***} + \mu}}{-\Omega_1},$$

$R^{***} = \frac{\Omega_2 A^{***}}{\mu}$. Where, $H_1 = S^0 + (1-\epsilon)V^0$.

We proposed the following Lyapunov function,

$$K(S,V,A,R) = S - S^{***} - S^{***}\mathrm{Ln}\frac{S}{S^{*}} + Y_1\left(V - V^{***} - V^{***}\mathrm{Ln}\frac{V}{V^{**}}\right)$$

$$+ Y_2\left(A - A^{*} - A^{*}\mathrm{Ln}\frac{A}{A^{*}}\right) + Y_3\left(R - R^{***} - R^{*}\mathrm{Ln}\frac{R}{R^{***}}\right),$$

where, Y_1, Y_2 and Y_3 were positive constants to be determined. The Lyapunov function $K(S,V,A,R)$ satisfies the conditions,

$K(S^{***},V^{***},A^{***},R^{***}) = 0$ and $K(S,V,A,R) > 0$, hence it is positive definite. For $\frac{dK(S,V,A,R)}{dt}$ to be negative definite, it must satisfy,

$$\frac{dK(S^{*},V^{*},A^{*},R^{*})}{dt} = 0 \quad \text{and} \quad \frac{dK(S,V,A,R)}{dt} < 0.$$

The endemic equilibrium point $E^{*}_{**} = (S^{***}, V^{*}, A^{*}, R^{*})$ for the system satisfies,

$\phi\pi = (k\beta\Omega_3 A^{***} + \mu)S^{***}$,

$(1-\phi)\pi = k(1-\epsilon)\beta\Omega_3 A^{***}V^{*} + \mu V^{***}$,

$\Omega_2 A^{***} = \mu R^{***}$,

$k\beta\Omega_3 A^{***}(S^{***} + (1-\epsilon)V^{***}) = \Omega_1 A^{***}$.

Determining the time derivative of the lyapunov function we obtain,

$$\frac{dK(S,V,A,R)}{dt} = \left(1 - \frac{S^{***}}{S}\right)\frac{dS}{dt} + X_1\left(1 - \frac{V^{***}}{V}\right)\frac{dV}{dt} + X_2\left(1 - \frac{A^{***}}{A}\right)\frac{dA}{dt}$$

$$+ X_3\left(1 - \frac{R^{***}}{R}\right)\frac{dR}{dt},$$

Substituting for $\frac{dS}{dt}, \frac{dV}{dt}, \frac{dA}{dt}$ and $\frac{dR}{dt}$ in the above equation to obtain,

$$\frac{dK(S,V,A,R)}{dt} = \left(1 - \frac{S^{***}}{S}\right)\{\phi\pi - (k\beta\Omega_3 A + \mu)S\ \}$$

$$+ X_1\left(1 - \frac{V^{***}}{V}\right)\{(1-\phi)\pi - k(1-\epsilon)\beta\Omega_3 AV - \mu V\}$$

$$+ X_2\left(1 - \frac{A^{***}}{A}\right)\{k\beta\Omega_3 AS + k(1-\epsilon)\beta\Omega_3 AV\ - \Omega_1 A\}$$

$$+ X_3\left(1 - \frac{R^{***}}{R}\right)\{\Omega_2 A - \mu R\},$$

$$\frac{dK(S,V,A,R)}{dt} = \left(1 - \frac{S^{*}}{S}\right)\{(k\beta\Omega_3 A^{***} + \mu)S^{***}\ - (k\beta\Omega_3 A + \mu)S\ \}$$

$$+ X_1\left(1 - \frac{V^{***}}{V}\right)\{k(1-\epsilon)\beta\Omega_3 A^{***}V^{***} + \mu V^{***} - k(1-\epsilon)\beta\Omega_3 AV - \mu V\}$$

$$+ X_2\left(1 - \frac{A^{***}}{A}\right)\{k\beta\Omega_3 AS + k(1-\epsilon)\beta\Omega_3 AV\ - \Omega_1 A\}$$

$$+ X_3\left(1 - \frac{R^{***}}{R}\right)\{\Omega_2 A - \mu R\},$$

$$\frac{dK(S,V,A,R)}{dt} = -\mu\frac{(S - S^{***})^2}{S} - \mu\frac{(V - V^{***})^2}{V}$$

$$+ \{X_3\Omega_2 - X_1\Omega_1 + X_1 k(1-\epsilon)\beta\Omega_3 V^{*} + k\beta\Omega_3 S^{***}\}A$$

$$+ \{X_2 - 1\}k\beta\Omega_3 AS + \{X_2 - X_1\}k\beta(1-\epsilon)\Omega_3 AV + -X_3\mu R$$

$$+ \left(-\frac{S^{***}}{S}\right)\{k\beta\Omega_3 A^{***}S^{***}\} + X_1\left(-\frac{V^{***}}{V}\right)\{k(1-\epsilon)\beta\Omega_3 A^{***}V^{***}\}$$

$$+ X_2\left(-\frac{A^{***}}{A}\right)\{k\beta\Omega_3 AS + k(1-\epsilon)\beta\Omega_3 AV\ - \Omega_1 A\}$$

$$+ X_3\left(-\frac{R^{***}}{R}\right)\{\Omega_2 A - X_3\mu R\} + k\beta\Omega_3 A^{*}S^{*}\ \ + X_1\{k(1-\epsilon)\beta\Omega_3 A^{***}V^{***}\}.$$

Setting AS, AV and A to zero we obtained the following equation,

$$X_2 - 1 = 0,$$

$$X_2 - X_1 = 0,$$

$$X_3\Omega_2 - X_1\Omega_1 + X_1 k(1-\epsilon)\beta\Omega_3 V^{***} + k\beta\Omega_3 S^{***} = 0.$$

Solving the above equations to obtain,

$$X_1 = X_2 = 1,$$

$$X_3 = \frac{\Omega_1}{\Omega_2} - \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}}{H_1}.$$

The equation reduces to,

$$\begin{aligned}\frac{dK(S,V,A,R)}{dt} = &-\mu\frac{(S-S^{***})^2}{S} - \mu\frac{(V-V^{***})^2}{V} - \frac{\Omega_1}{\Omega_2}\mu R \quad - k\beta\Omega_3 A^{***}S^{***}\frac{S^{***}}{S} \\ &- k(1-\epsilon)\beta\Omega_3 A^{***}V^{***}\frac{V^{***}}{V} - \{k\beta\Omega_3 AS + k(1-\epsilon)\beta\Omega_3 AV\ \}\frac{A^{***}}{A} \\ &- \{k\beta\Omega_3 AS + k(1-\epsilon)\beta\Omega_3 AV\ \}\frac{A^{***}}{A} - \Omega_1 A\frac{R^{***}}{R} \\ &- \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}\mu R^{***}}{H_1} + \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}\Omega_2 A}{H_1}\frac{R^{***}}{R} \\ &+ \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}}{H_1}\mu R + \frac{\Omega_1\mu R^{***}}{\Omega_2} + 2\Omega_1 A^{***}.\end{aligned}$$

$$\frac{dK(S,V,A,R)}{dt} = -\mu\frac{(S-S^{***})^2}{S} - \mu\frac{(V-V^{***})^2}{V} - \frac{\Omega_1}{\Omega_2}\mu R \quad - k\beta\Omega_3 A^{***}S^{***}\frac{S^{***}}{S}$$

$$- k(1-\epsilon)\beta\Omega_3 A^{***}V^{***}\frac{V^{***}}{V} - 2\{k\beta\Omega_3 A^{***}S + k(1-\epsilon)\beta\Omega_3 A^{***}V\ \}$$

$$- \Omega_1 A\frac{R^{***}}{R} - \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}\mu R^{***}}{H_1}$$

$$+ \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}\Omega_2 A}{H_1}\frac{R^{***}}{R} + \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}}{H_1}\mu R$$

$$+ 3\Omega_1 A^{***}$$

Let

$$P = \mu\frac{(S-S^{***})^2}{S} + \mu\frac{(V-V^{***})^2}{V} + \frac{\Omega_1}{\Omega_2}\mu R \quad + k\beta\Omega_3 A^{***}S^{***}\frac{S^{***}}{S}$$

$$+ k(1-\epsilon)\beta\Omega_3 A^{***}V^{***}\frac{V^{***}}{V} + 2\{k\beta\Omega_3 A^{***}S + k(1-\epsilon)\beta\Omega_3 A^{***}V\ \}$$

$$+ \Omega_1 A\frac{R^{***}}{R} + \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}\mu R^{***}}{H_1},$$

$$Q = \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}\Omega_2 A}{H_1}\frac{R^{***}}{R} + \frac{R_C^{**}\{(1-\epsilon)V^{***} + S^{***}\}}{H_1}\mu R + 3\Omega_1 A^{***},$$

Then $\frac{dK}{dt} = 0$ holds only when($S = S^{***}, V = V^{***}, A = A^{***}$ and $R = R^{***}$): So the maximal compact invariant set in $\{(S;\ E;\ I) \in \Pi: \frac{dV}{dt} = 0\}$ is the singleton $\{E_*^{**}\}$ using Lasalle's invariance principle $\frac{dL(S,I,A,R)}{dt} < 0$, if and only if $P > Q$ (Mukandavire *et al.*,2010). This result show that pneumonia would persist whenever $P > Q$ irrespective of the initial conditions.

4.3.9 Analytical sensitivity analysis of control reproduction number, epidemiological thresholds and their biological interpretations

This involves steps to: determine epidemiological thresholds, sensitivity analysis of reproduction number, provide biological interpretation, herd immunity, estimate numerical results and carry out simulation.

4.3.9.1 Epidemiological thresholds

We determined treatment thresholds and impact of treatment using control reproduction number and basic reproduction number. Treatment thresholds for severely infected(I_M) and very severely infected(I_C) were determined using the control reproduction number. According to (Ngari *et al.*, 2014), the treatment threshold was determined when R_C was equated to one and solving for ${\tau_1}^C$(critical treatment for severely infected children(I_M) to obtain,

$$\tau_1{}^{\mathrm{C}} = \frac{\omega_1\omega_3}{\beta \mathrm{k}\xi_2 \mathrm{R}_1} - \{\mathrm{R}_1\omega_2\omega_3\omega_4 + \xi_1(\mathrm{R}_1\theta_1\omega_3\omega_4 + \mathrm{R}_2\omega_1\omega_3\omega_4) + \xi_2(\mathrm{R}_1\theta_1\theta_2\tau_2 + \mathrm{R}_2\theta_2\tau_2\omega_1) + \xi_3(\mathrm{R}_1\theta_1\tau_2\omega_3 + \mathrm{R}_2\tau_2\omega_1\omega_3)\}.$$

The inpatient treatment threshold was determined when $\mathrm{R_C}$ is equated to one and solving for $\tau_2{}^{\mathrm{C}}$, that is, critical treatment for very severely infected children($\mathrm{I_C}$) to obtain,

$$\tau_2{}^{\mathrm{C}} = \{\xi_2(\mathrm{R}_1\theta_1\theta_2 + \mathrm{R}_2\theta_2\omega_1) + \xi_3(\mathrm{R}_1\theta_1\omega_3 + \mathrm{R}_2\omega_1\omega_3)\}\langle\frac{\omega_1\omega_2\omega_3\omega_4}{\beta \mathrm{k}} - \{\mathrm{R}_1\omega_2\omega_3\omega_4 + \xi_1(\mathrm{R}_1\theta_1\omega_3\omega_4 + \mathrm{R}_2\omega_1\omega_3\omega_4) + \xi_2(\mathrm{R}_1\tau_1\omega_2\omega_4)\}\rangle.$$

The study by(Clean and Blower, 1993), defined measure of treatment impact based on the reproduction numbers can be defined as,

$$(\mathrm{U}) = 1 - \frac{\mathrm{R_C}}{\mathrm{R_0}},$$

$$(\mathrm{U}) = 1 + ((\mu + \delta_1)(\mu + \theta_1)\Big((1 - \mathrm{P})\mathrm{S}^0(\mu + \theta_1 + \tau_1)\left(\theta_1\xi_2\tau_2 + \omega_3\left(\xi_3\tau_2 + \xi_1\omega_4\right)\right)$$

$$+ (\mathrm{PS}^0 + (1 - \epsilon)\mathrm{V}^0)\Big((\mu + \delta_1 + \tau_2)\left(\xi_2\tau_1 + \omega_3\right)\omega_4$$

$$+ \theta_1\left(\theta_2\xi_2\tau_2 + \omega_3\left(\xi_3\tau_2 + \xi_1\omega_4\right)\right)\Big)\Big))$$

$$/(\mathrm{S}^0\left(-\mathrm{P}(\mu + \delta_1) + \left((-1 + \mathrm{P})\mu - \theta_1\right)\xi_1\right)(\mu + \theta_1 + \tau_1)(\mu + \delta_1$$

$$+ \tau_2)\omega_3\omega_4.$$

4.3.9.2 Sensitivity analysis of the control reproduction number$(\mathbf{R_C})$

Impacts of intervention strategies are vital in lowering burden of pneumonia. We investigated the sensitivity of R_C to: the rate at which severely and very severely infected children sought treatment($\tau_1$and τ_2), with respect to vaccination drug efficacy ϵ and effects of environmental factors (k). We determine partial derivatives of R_C with respect to;

i. effect of environment (k) .

$$\frac{\mathrm{dR_C}}{\mathrm{dk}} = \frac{\beta}{\omega_1\omega_2\omega_3\omega_4}\{\mathrm{R}_1\omega_2\omega_3\omega_4 + \xi_1(\mathrm{R}_1\theta_1\omega_3\omega_4 + \mathrm{R}_2\omega_1\omega_3\omega_4)$$

$$+ \xi_2(\mathrm{R}_1\theta_1\theta_2\tau_2 + \mathrm{R}_2\theta_2\tau_2\omega_1 + \mathrm{R}_1\tau_1\omega_2\omega_4) + \xi_3(\mathrm{R}_1\theta_1\tau_2\omega_3 + \mathrm{R}_2\tau_2\omega_1\omega_3)\}$$

$$> 0,$$

ii. rate at which mild infected children sought treatmentτ_1.

$$\frac{\mathrm{dR_C}}{\mathrm{d}\tau_1} = -\frac{\beta \mathrm{k}}{{\omega_1}^2\omega_2\omega_3\omega_4}\{\mathrm{R}_1\omega_2\omega_3\omega_4 + \xi_1(\mathrm{R}_1\theta_1\omega_3\omega_4 + \mathrm{R}_2\omega_1\omega_3\omega_4)$$

$$+ \xi_2(\mathrm{R}_1\theta_1\theta_2\tau_2 + \mathrm{R}_2\theta_2\tau_2\omega_1 + \mathrm{R}_1\tau_1\omega_2\omega_4) + \xi_3(\mathrm{R}_1\theta_1\tau_2\omega_3 + \mathrm{R}_2\tau_2\omega_1\omega_3)\}$$

$$+ \frac{\beta \mathrm{k}}{\omega_1\omega_2\omega_3\omega_4}\{\xi_1\mathrm{R}_2\omega_3\omega_4 + \xi_2(\mathrm{R}_2\theta_2\tau_2 + \mathrm{R}_1\omega_2\omega_4) + \xi_3\mathrm{R}_2\tau_2\omega_3\} < 0,$$

iii. rate at which mild infected children sought treatment τ_2.

$$\frac{\mathrm{dR_C}}{\mathrm{d}\tau_2} = -\frac{\beta \mathrm{k}}{\omega_1{\omega_2}^2\omega_3\omega_4}\{\mathrm{R}_1\omega_2\omega_3\omega_4 + \xi_1(\mathrm{R}_1\theta_1\omega_3\omega_4 + \mathrm{R}_2\omega_1\omega_3\omega_4)$$

$$+ \xi_2(\mathrm{R}_1\theta_1\theta_2\tau_2 + \mathrm{R}_2\theta_2\tau_2\omega_1 + \mathrm{R}_1\tau_1\omega_2\omega_4) + \xi_3(\mathrm{R}_1\theta_1\tau_2\omega_3 + \mathrm{R}_2\tau_2\omega_1\omega_3)\}$$

$$+ \frac{\beta \mathrm{k}}{\omega_1\omega_2\omega_3\omega_4}\{\mathrm{R}_1\omega_3\omega_4 + \xi_2(\mathrm{R}_1\theta_1\theta_2 + \mathrm{R}_2\theta_2\omega_1 + \mathrm{R}_1\tau_1\omega_4)$$

$$+ \xi_3(\mathrm{R}_1\theta_1\omega_3 + \mathrm{R}_2\omega_1\omega_3)\} < 0.$$

iv. With respect to vaccinated (V) drug efficacy(ϵ).

$$\frac{\mathrm{dR_C}}{\mathrm{d}\,\epsilon} = -\frac{\beta \mathrm{k} \mathrm{V}^0}{\omega_1\omega_2\omega_3\omega_4}\{\omega_2\omega_3\omega_4 + \xi_1\theta_1\omega_3\omega_4 + \xi_2(\theta_1\theta_2\tau_2 + \tau_1\omega_2\omega_4) + \xi_3\theta_1\tau_2\omega_3\} < 0.$$

4.3. 9.4 The expression for herd immunity

The herd immunity threshold/ critical vaccination threshold is determined by, $q_c = 1 - \frac{1}{\mathrm{R}_0}$, where $\mathrm{q_c}$ is the critical vaccination threshold (Holland and Zachary, 2014). Substituting for basic reproduction number(R_0), we obtain,

$$\mathrm{q_c} = 1 - \frac{(\mu + \delta_1)(\mu + \theta_1)}{\beta \mathrm{k} \mathrm{S}^0(\mathrm{P}(\mu + \delta_1) + (\mu(1 - \mathrm{P}) + \theta_1)\xi_1)}.$$

4.3. 9.5 Discussion of the first objective

Our research study emphasized on the importance of treatment in lowering the burden of pneumonia in agreement with research findings of (Ngari *et al.*, 2014), (Ong'ala *et al.*,

2012) and (Lawi *et al.*, 2013). In contrast to studies by (Ngari *et al.*, 2014), (Ong'ala *et al.*, 2012) and (Lawi *et al.*, 2013), this research study detemined the minimum critical treatment thresholds, incorporated kenya data to estimate numerical results and predicted the dynamics of pneumonia under the age of five years which had not been taken into account in previous pneumonia studies. In concurrent with (Hammitt *et al.*, 2012), this research study classified pneumonia as severe and very severe when formulating the mathematical model.

Although study by (Emaline *et al.*, 2012) studied effect vaccination, their research study never: determined the herd immunity, considered the effects enviromental factors and also assumed contribution of the treated classes to the dynamics of childhood pneumonia.

4.4 Outcomes of the estimation of numerical results of model using data and/or parameters from KHIS and UNICEF

This involves step to estimate unknown parameters and carryout sensitivity analysis

4.4.1 Estimation of unknown parameters using MATLAB software

The study used the available secondary data and/or parameters from KHIS, literature and UNICEF to estimate the unknown parameters using MATLAB software.

The following assumptions are made for the model;

i. The upper bound of the 0 to 4 age bracket is 4.5 years. The progression rate to next age bracket is computed as reciprocal of 4.5 years that is $0.\dot{2}$. According to study by (Health, Kenya fact sheet of Health statistics 2010, 2012), death of the under five years due to other causes constituted an average of 84% of the total

under five mortality. The actual progression rate/ constant death rate (μ) is computed as $0.\dot{2}$ added death rate due other causes.

ii. According to Ministry of health in Kenya, Coast province recorded the highest childhood pneumonia prevalence rate at 13% and the lowest was Eastern & Western at 6%, (Health, Monitoring and evaluation plan, 2013). The estimation adopted in this study estimated pneumonia prevalence rate in Kenya at 11.26% and 13.695% for 2012 and 2013 respectively. It is assumed the difference was as a result of unreported cases.

The table below shows of summary of data, variables and parameter available in Literature

Table 3 : Summary of the data and/or parameters available in literature

Class\Year/ Estimates	2012	2013	Total	Source
Total population	6,956,000	7,048,020	14,004,020	(UNICEF, State of the world's children 2015 country statistical information, 2014 and 2015)
Susceptible	120,613	444,367	564,980	[Assumed]
Vaccinated	5,703,920	5,286,015	10,989,935	[Estimated at 82% and 75% respectively]
Severely Infected	196,022	277,357	473,379	[Estimated from treated by 100%/56%]
Very severely Infected	330,135	330,601	660,736	[Estimated from the as assumption i]
Outpatient	249,482	353,000	602,482	[Estimated as proportional to inpatient]
Inpatient	8,028	4,279	12,307	Kenya Health information system

Recovered	347,800	352,401	700,201	Assumed to be 5% of total population
Birth(π)	1,535,000	1,550,000	3,085,000	(UNICEF, State of the world's children 2015 country statistical information, 2014 and 2015)
Percent of pneumonia death for under five years of age in %	-	-	16	(Health, Kenya fact sheet of Health statistics 2010, 2012)
Total outpatient pneumonia cases for all ages in Kenya.(Not classified)	535,024	576,703	1,111,727	KHIS
Total inpatient pneumonia cases for all ages in Kenya.	13,528	6,991	20,519	KHIS
Pneumonia induced death during inpatient treatment	410	225	635	KHIS
Pneumonia induced death during very severely infected stage	16870	17383	34253	Assumed to 16% of total death less pneumonia induced death during inpatient treatment
Under five mortality	108,000	110,050	218,050	(UNICEF, State of the world's children 2015 country statistical information, 2014 and 2015)
Under five deaths due to other causes	90,720	92442	183,162	Assumed to 84% of total under five years annual death
Immunization against pneumococcal(PCV),(Φ)	0.18	0.25	0.25	(UNICEF, State of the world's children 2015 country statistical information, 2014 and 2015)
Immunization against Haemophilus type b influenza(Φ)	0.17	0.17	0.25	(UNICEF, State of the world's children 2015 country statistical information, 2014 and 2015)

Pneumonia care seeking children		0.56		(UNICEF, State of the world's children 2015 country statistical information, 2014 and 2015)
Antibiotic treatment for pneumonia		0.50		(UNICEF, State of the world's children 2015 country statistical information, 2014 and 2015)
Percent of the under-five in total pneumonia inpatient cases (%)	46.63	61.21		
Under five mortality rate	0.015526	0.015614	0.0155705	Proportion of the under-five death to total population.
Pneumonia induced death rate during inpatient treatment(δ_2)	0.0510713	0.0525824	0.0515967	Proportion of the under-five death due to pneumonia to total inpatient
Pneumonia induced death rate during very severely infected class(δ_1)	0.0511003	0.05258	0.05184	Proportion of the under-five death due to pneumonia to total estimated infected.
Under five years death rates due to other causes	0.013042	0.013116	0.013079	
Pneumonia prevalence rate (%)	11.27	13.695%		[Estimated as sum of infected divided by total population of the under five years]
Infection rate(β)	-	-	1-10	(Emaline et al., 2012)
Natural death rate/progression rate(μ)	0.235264	0.235338	0.235301	[Estimated from assumption i]
Pneumococcal vaccine efficacy(ϵ).	-	-	0.37	(Andersen et al., 1994)
Proportion of chronic pneumonia in Kenya population (P)	0.71	-	0.71	(Hammitt *et al.*, 2012)

The summary of data and parameters in the Table 4 was obtained through fitting data and parameters in Table 3 to the developed model $[(1)-(7)]$ using MATLAB software.

Table 4: Summary of the parameters obtained from MATLAB and/or assumption

Parameters	ξ_1	ξ_2	ξ_3	τ_1	τ_2	ρ	θ_1	θ_2	k	γ_1	γ_2
Value	0.3	0.15	0.05	0.0131	0.0456	0.00113	0.00452	0.23688	1	0.167	0.1432
Source	A	A	A	M	M	M	M	M	A	M	M

where, A represents assumed parameters and M represent estimate from MATLAB software.

4.4.2 Estimated numerical results of the reproduction numbers using data and/or parameters from KHIS and UNICEF

The estimated numerical result is obtained by substituting the parameters in the analytical results of the model. The control reproduction number(R_C) was obtained as 9.31808 and the basic reproduction number(R_0) was obtained as 22.5914, the reproduction number($R_{\epsilon=1}$) as 3.7578 and the reproduction number(R_T) as 10.1174. The herd immunity($1-\frac{1}{R_0}$) was obtained as 95.57% and impact of treatment($1-\frac{R_C}{R_0}$) was obtained as 0.5881. The upper bound of the under five years population in Kenya which was obtained analytically in Section 4.3.1 as $N \leq \frac{\pi}{\mu}$, was estimated numerically as $N \leq$ 6,585,210.369.

4.4.3 Outcomes of the normalized sensitivity analysis

The normalized sensitivity analysis was evaluated using the definition in Section 3.4.3 by substituting parameters in Section 4.4.1. The following values were obtained.

Positive values:

$\beta = k = \pi = 1;\ \Phi = 0.255561; P = 0.150148;\ \xi_1 = 0.0864632;\ \xi_2 = 0.0817084;\ \xi_3 = 0.000757944;\ \theta_1 = 0.000350308$

Negative values: $\mu = -1.39958;\ \epsilon = -0.950668;\ \tau_1 = -0.518997;\ \delta_1 = -0.0137083;$

$\tau_2 = -0.0105333; \theta_1 = -0.0025002;\ \gamma_1 = -0.0543327;\ \gamma_2 = -0.00060364;\ \delta_2 = -0.0000907513$

Zero value: $\rho = 0$

The parameters with negative values are inversely proportional to R_C while those with positive values are directly proportional to it. Therefore, increase in parameters with negative values and decrease in parameters with positive values hold great promise in lowering burden of childhood pneumonia.

4.4.5 Limitations of the second objective

The study faced the following challenges:

i. To obtain estimate of population data for under five years of age from kenya bureau of statistics beyond 2009.

ii. To obtain valid and reliable efficacy value of pneumonia vaccines in Kenya, our efficacy value was obtained in reference to artice for year 1994 from study by (Andersen *et al*., 1994).

iii. To estimate the viable infection rate of pneumonia, our study assumed β=0.00000012.

iv. It was impossible to fit non linear model to the data because our study obtained only two reliable data points, these were data for years 2012 and 2013.

v. To obtain sufficient previous studies targetting pneumonia of under five years of age for the whole country.

4.5 Outcomes of the numerical simulations, validation of analytical results and assessment of the effects of efficacy of the vaccination drugs, environmental factors and therapeutic treatment drugs

This section involved steps to carryout numerical simulations and numerical sensitivity analysis.

4.5.1 Numerical simulations

Our research study used the parameters in Section 4.4 and the population data for the years 2013 as initial conditions of the initial value problem.

$S(0) = 444367,$ the population data of the susceptible children in year 2013.

$V(0) = 5286015,$ the population data of the vaccinated children in year 2013.

$I_M(0) = 277357,$

the population data of the severely infected children in year 2013.

$I_C(0) = 330601,$

the population data of the very severely infected children in year 2013.

$T_M(0) = 353000,$ the population data of the outpatient children in year 2013.

$T_C(0) = 4279$, the population data of the inpatient children in year 2013.

$R(0) = 352401,$ the population data of the recovered children in year 2013.

$N(0) = 7{,}048{,}020$, the total population data of the children in year 2013.

The model was simulated using the MATLAB ordinary differential equation inbuilt solver. The value for infection rate(β) was assumed to be 0.00000012 in the simulations. The simulations are summarized in the graphs below.

Graphs

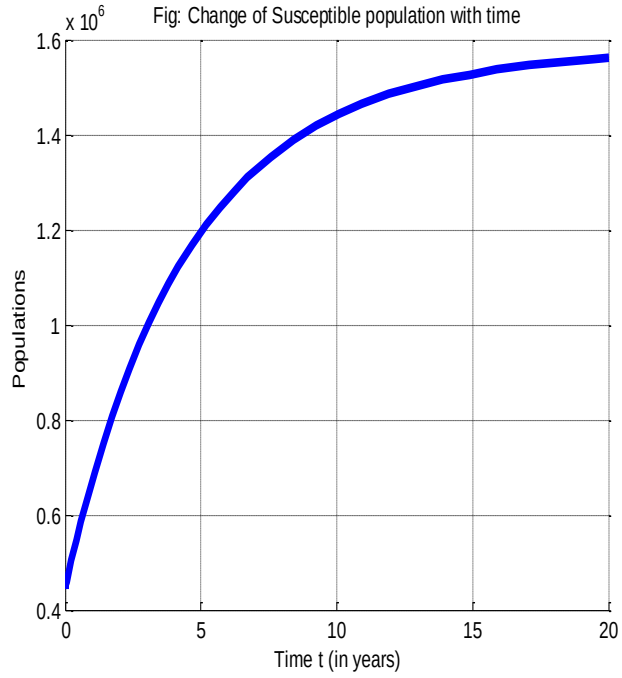


Figure 6: Numerical simulation of the susceptible population with time (Author, 2017).

Description

The simulation obtained whenever $R_C > 1$ indicated that the number of susceptible children increased over time up to a maximum of about 1,550,000 in twenty years' time.

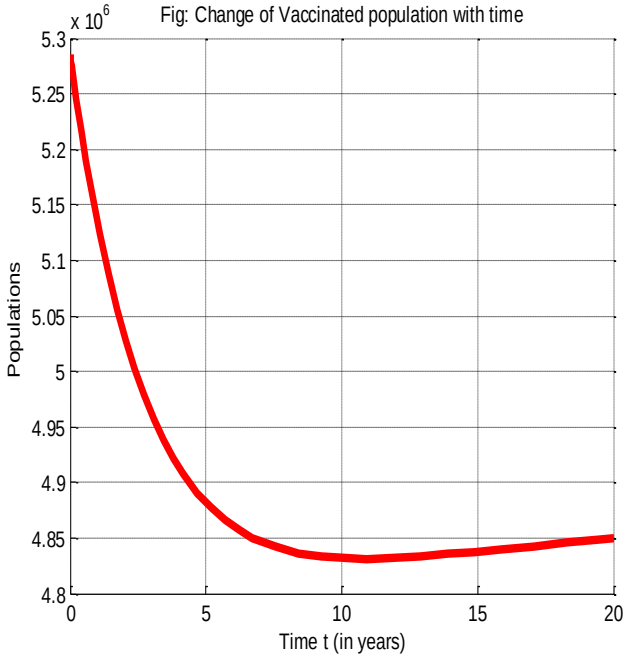


Figure 7: Numerical simulation of the vaccinated population with time (Author, 2017).

The simulation obtained whenever $R_C > 1$ indicated that the number of the vaccinated children under the age of five years decreased to about 25000 in ten years' time and then rises steadily to about 4850000 by twenty years' time.

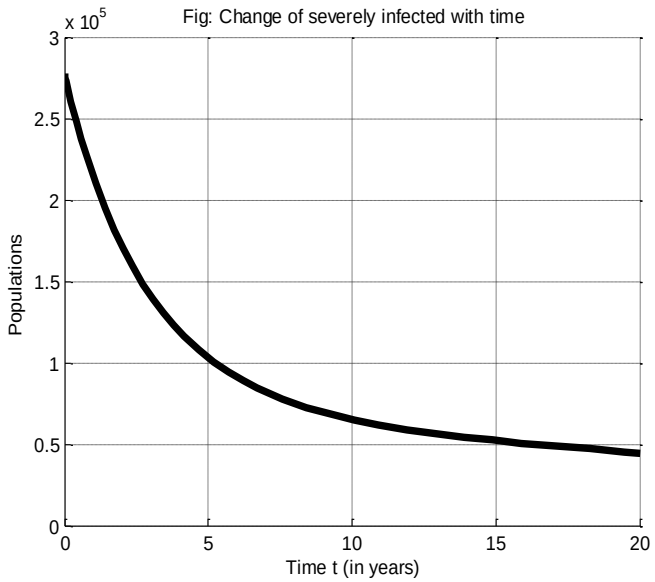


Figure 8: Numerical simulation of the mildly infected with time (Author, 2017).

The simulation obtained whenever $R_C > 1$ indicated that the number of the severely infected decreased to about 50000 in twenty years' time.

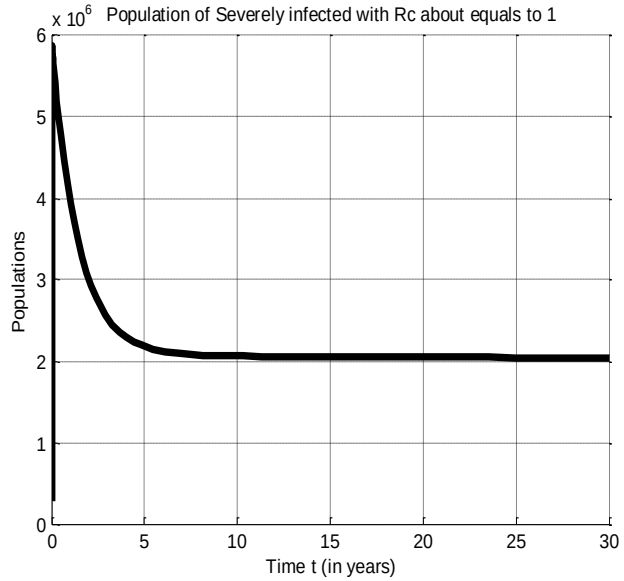


Figure 9: Simulation of the severely infected individuals with Rc approximately equal to one (Author, 2017).

The simulation obtained whenever $R_C \cong 1$ showed that the number of the severely infected would rise abruptly and then decrease to equilibrium in ten years' time.

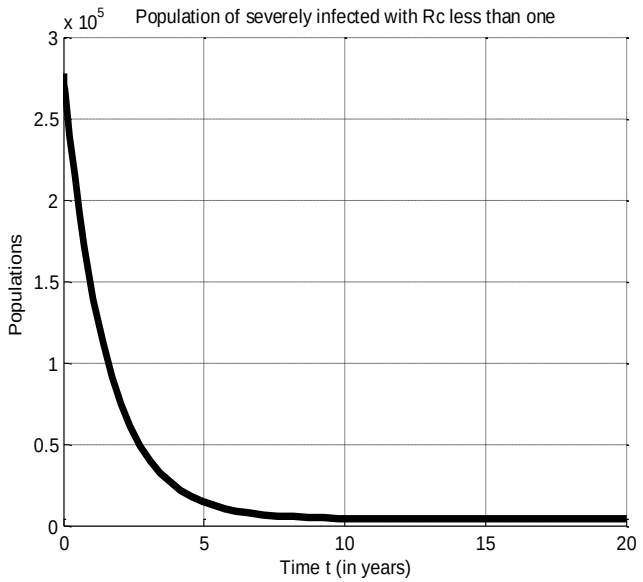


Figure 10: Simulation of the severely infected with Rc less than one (Author, 2017)

The simulation obtained whenever $R_C < 1$ showed that the number of the severely infected would decrease to zero in twenty years' time.

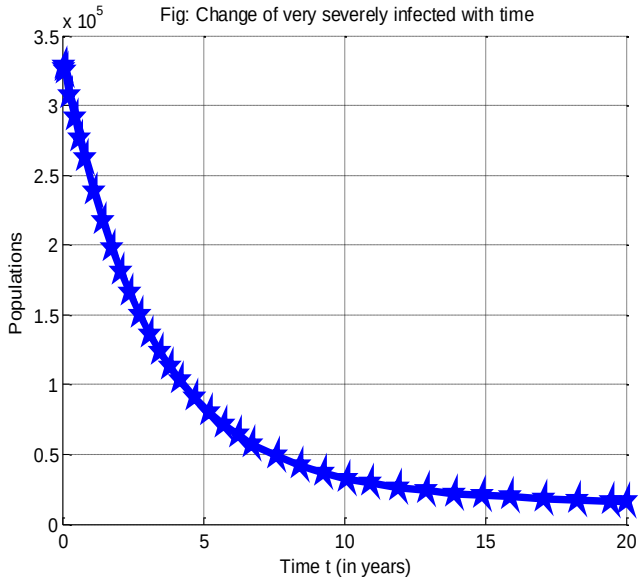


Figure 11: Numerical simulation of chronically infected population with time (Author, 2017).

The simulation obtained whenever $R_C > 1$ showed that the number of the severely infected decreased to about 25000 in twenty years' time.

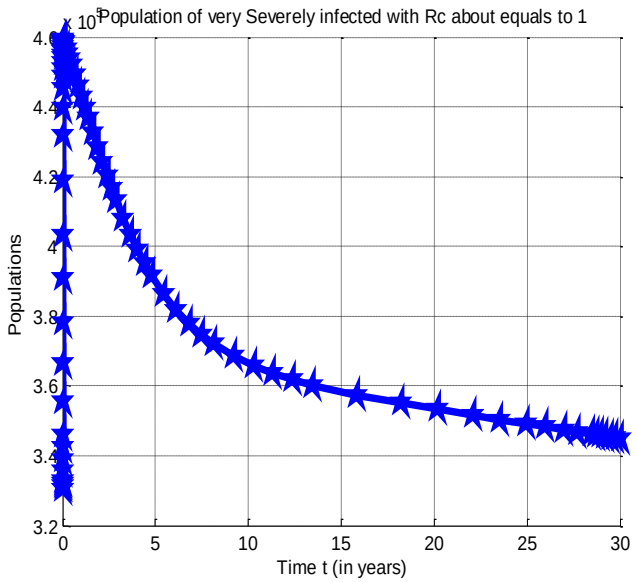


Figure 12: Simulation of very severely infected with Rc approximately equal to one (Author, 2017).

The simulation obtained whenever $R_C \cong 1$ showed that the number of the severely infected would rise abruptly and then decrease to equilibrium in thirty years' time.

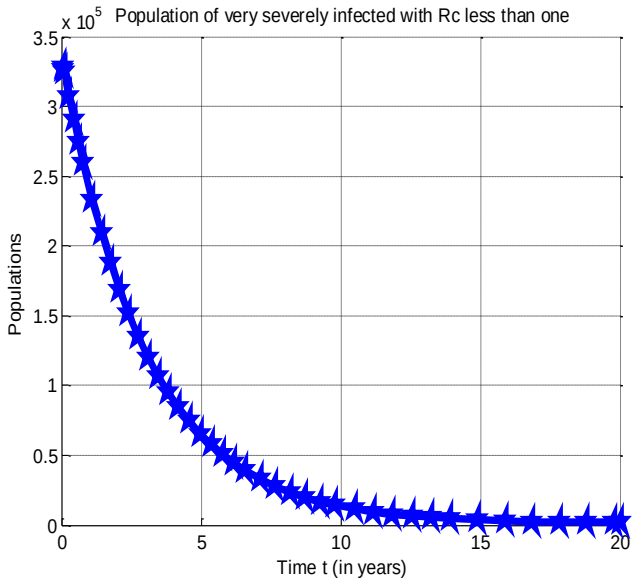


Figure 13: Simulation of very severely infected with Rc less than one (Author, 2017).

The simulation obtained whenever $R_C < 1$ showed that the number of the severely infected would rise abruptly and then decrease to zero in twenty years' time.

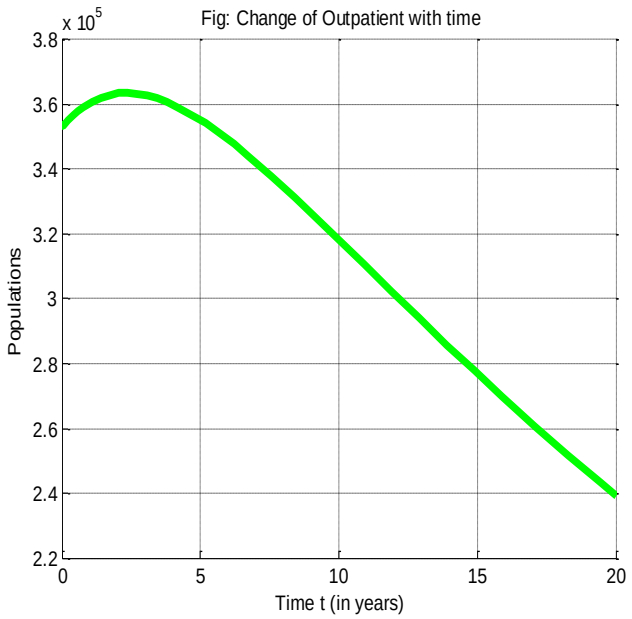


Figure 14: Numerical simulation of mildly treated population with time (Author, 2017).

The simulation obtained whenever $R_C > 1$ showed that the number of the outpatient children to about 36000 in 2.5 years the decreased to about 230000.

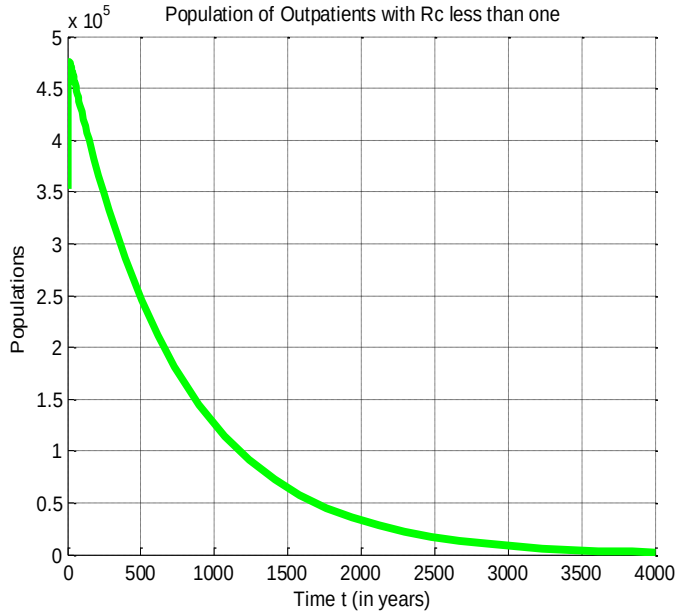


Figure 15: Simulation of outpatient with Rc less than one (Author, 2017)

The simulation obtained whenever $R_C < 1$ showed that the number of the outpatient children would decrease to zero in 3500 years' time.

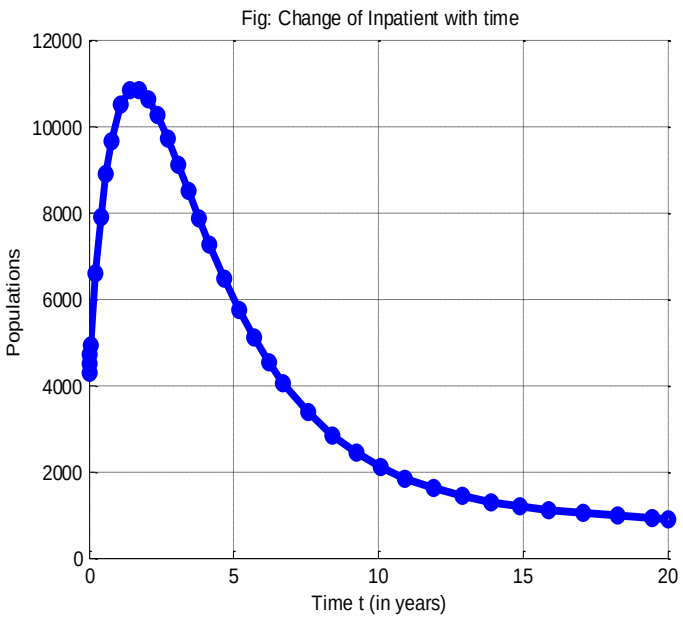


Figure 16: Numerical simulation of the inpatient population with time (Author, 2017).

The simulation obtained whenever $R_C > 1$ showed that the number of the inpatient children increases to about 11000 in about 2.5 years' time and then decreases to about 1000 in twenty years' time.

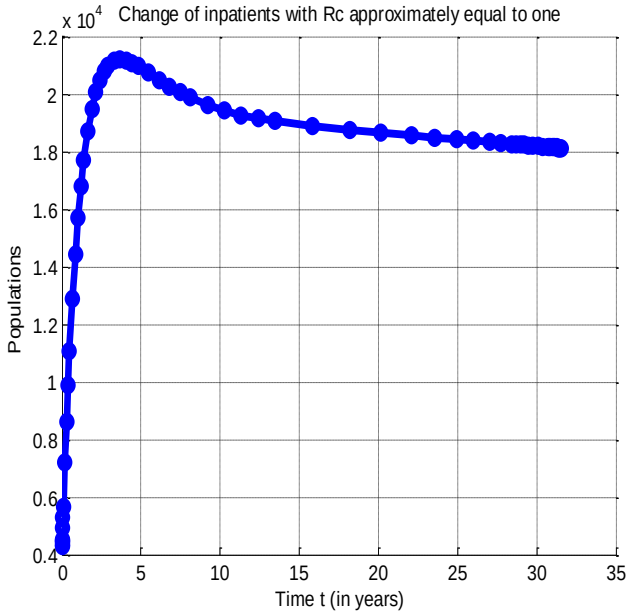


Figure 17: Simulation of inpatient population with Rc approximately equal to one (Author, 2017).

The simulation obtained whenever $R_C \cong 1$ showed that the number of the severely infected would rise abruptly and then decrease to equilibrium in twenty five years' time.

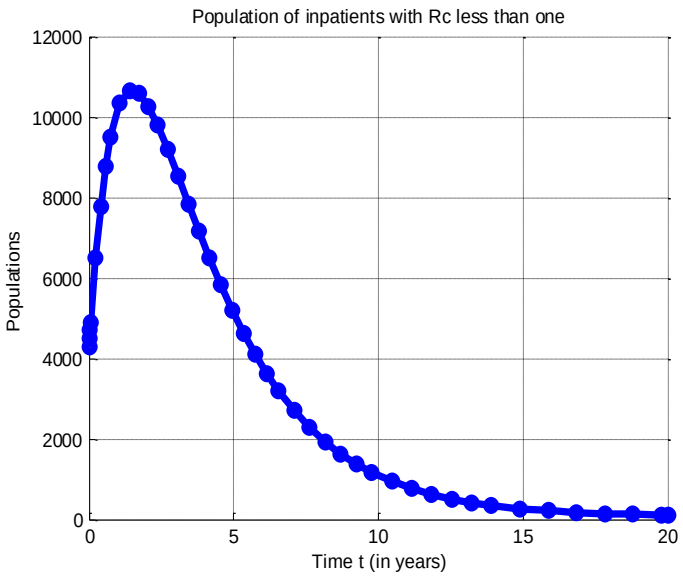


Figure 18: Simulation of inpatient population with Rc less than one (Author, 2017).

The simulation obtained whenever $R_C < 1$ indicated that the number of the inpatient children would decrease to zero in twenty years' time.

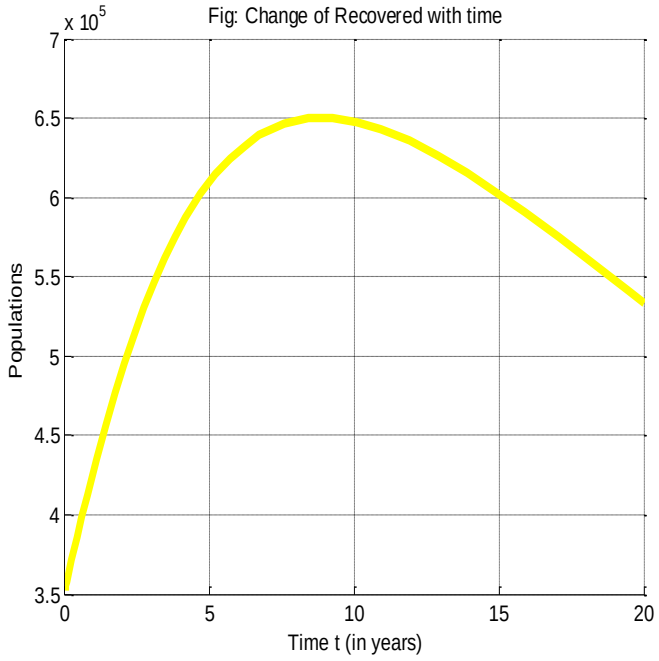


Figure 19: Numerical simulation of the recovered population with time (Author, 2017).

The simulation obtained whenever $R_C > 1$ indicated that the number of the recovered children under the age of five years increases steadily up to 600000 in 10 years' time then decreases to slightly above 500000 in twenty years' time.

4.5.2 Numerical sensitivity analysis of the reproduction number

Sensitivity analysis of the reproduction number with various parameters was determined graphically using MATLAB software. The description is summarized in the tables below;

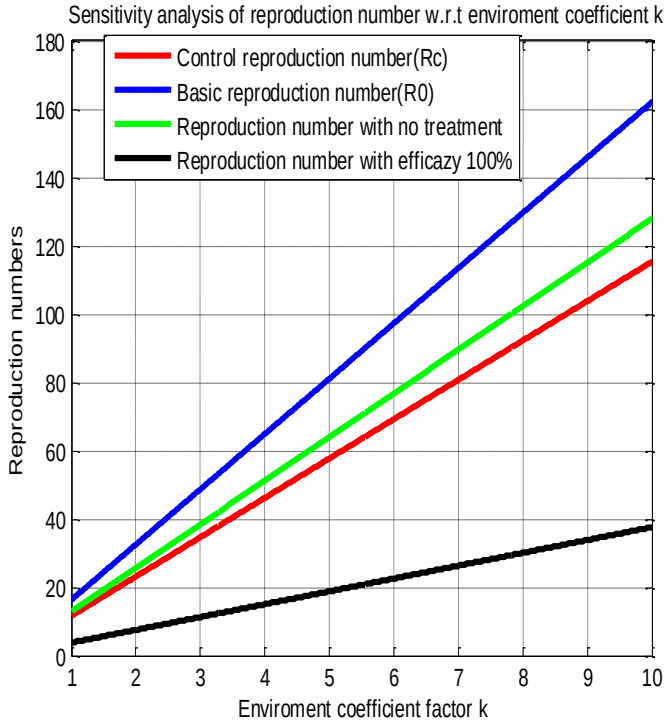
Graphs	Description
	The environmental coefficient k varies directly with the reproduction numbers. The R_0 was the most sensitive while the reproduction number with 100% was the least sensitive. Low effects of the environmental factors hold great promise in lowering the reproduction numbers.

Figure 20: Sensitivity analysis of Rc w.r.t environmental coefficient k (Author, 2017).

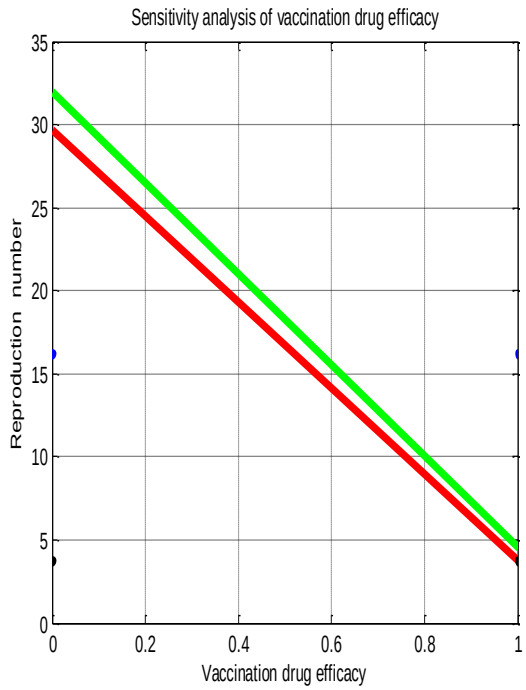


Figure 21: Sensitivity analysis of Rc w.r.t drug efficacy parameter (Author, 2017).

Control reproduction number(R_C) and reproduction number with no treatment(R_T) were sensitive to change in drug efficacy. The graph indicates that very high vaccination drug efficacy holds great promise in lowering the reproduction numbers.

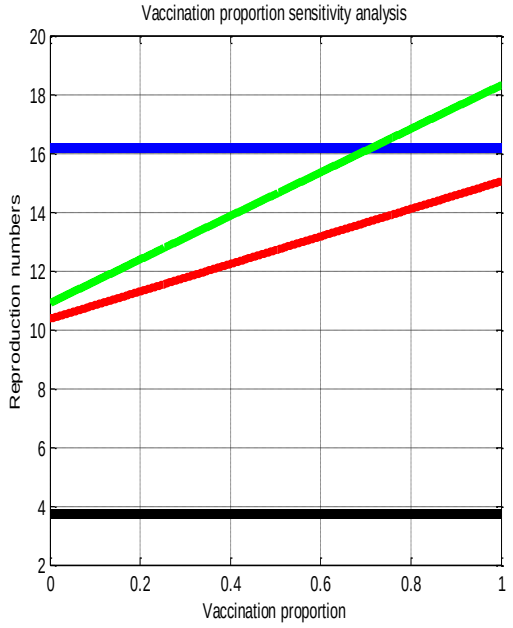


Figure 22: Sensitivity analysis of Rc w.r.t to vaccination parameter (Author, 2017).

Control reproduction number(R_C) and reproduction number with no treatment(R_T) were sensitive to change in vaccination rates. Very High vaccination rate holds great promise in lowering the reproduction numbers.

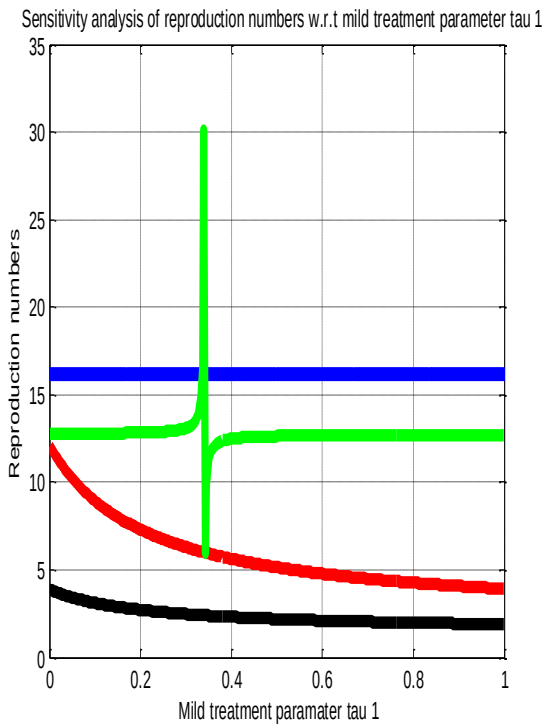


Figure 23: Sensitivity analysis of Rc w.r.t to mild treatment parameter (Author, 2017).

Control reproduction number(R_C) and the reproduction number with vaccination efficacy at 100% were sensitive to rate of change of mild infected seeking treatment. Very high treatment rate to mild infected population of the under five years of age holds great promise in lowering the reproduction numbers.

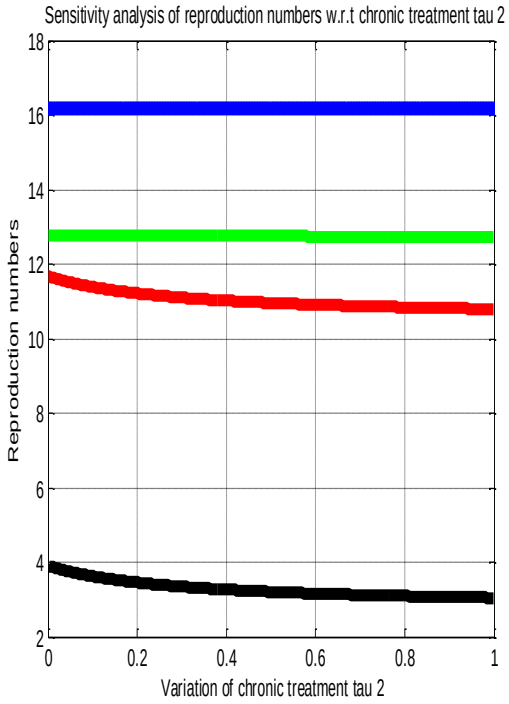


Figure 24: Sensitivity analysis of Rc w.r.t chronic treatment rate parameter (Author, 2017).

Control reproduction number(R_C) and the reproduction number with vaccination efficacy at 100% were sensitive to rate of the chronic infected seeking treatment. Very high treatment rate to chronic infected population of under five years of age holds great promise in lowering the reproduction numbers.

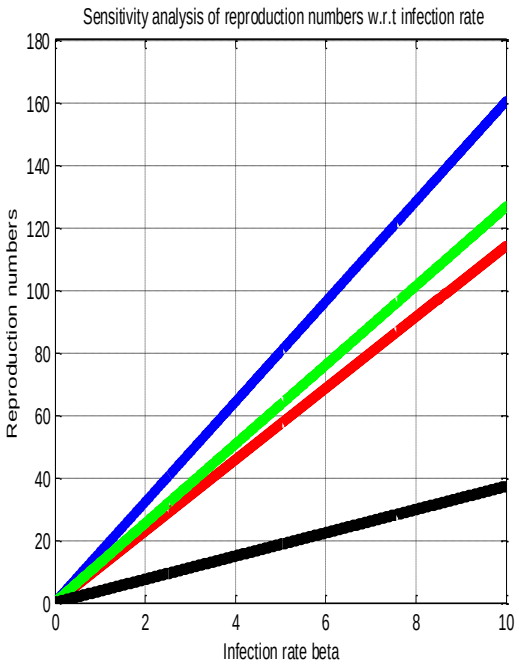


Figure 25: Sensitivity analysis of Rc w.r.t infection rate parameter (Author, 2017).

The infection rate (β) varies directly with the reproduction numbers. The basic reproduction number(R_0) was the most sensitive while the reproduction number with vaccination efficacy at 100% was the least sensitive. Low infection rate hold great promise in lowering the reproduction numbers.

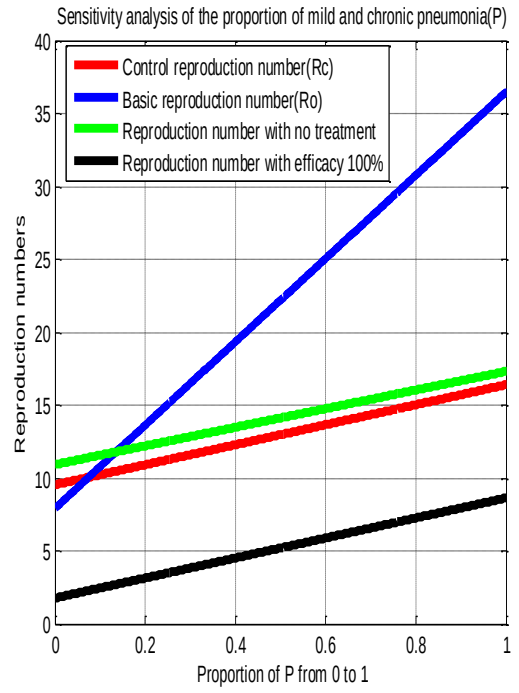


Figure 26: Sensitivity analysis of Rc w.r.t proportion of mild and chronic **(**Author, 2017).

The proportion of mild infected (P) varies directly with the reproduction numbers. Low proportion of mild infected in the population hold great promise in lowering the reproduction numbers.

CHAPTER FIVE

CONCLUSIONS AND RECOMMENDATIONS

5.1 Introduction

This chapter explains conclusions and recommendations arising out of each of the specific objectives in Section 1.3.2 namely development of a model of pneumonia for the under the age five with Kenya specific attribute, determination of model thresholds and perform stability analysis, sensitivity analysis, backward bifurcation analysis so as to establish the conditions for the spread of disease, estimation of numerical results of model using data and/or parameters from KHIS and UNICEF as well as evaluate normalized sensitivity index and performing numerical simulations to validate analytical results of the model and assess the effects of efficacy of the vaccination, environmental factors and therapeutic treatment drugs.

5.2 Model development of the pneumonia for the under the age five with Kenya specific attributes

The study sought to develop a deterministic model of the under five years of age pneumonia using Kenya specific attributes. Outpatient and inpatient classes were formulated in the model so as to incorporate the attribute of data which was available in KHIS. KHIS has been recording data for outpatient and inpatient since 2009.

This study considered general model because pneumonia is not isolated in Kenya. In Kenya the under five years are usually vaccinated with haemophilus type b and PCV. Vaccinated class was included in the model so as to incorporate the vaccinated population. This study considered pneumonia of under five years of age because it is

more burdensome in Kenya. The exit rate from the bracket of age of five years was incorporated in the model.

Our study incorporated the findings of study by (Hammitt *et al.*, 2012) which had classified infected pneumonia for children from 0 to 59 months in Kenya into two broad categories severe and very severe. The proportions of severe and very severe were considered when formulating the model. This study considered community acquired pneumonia (CAP), future studies should also consider the effect of hospital acquired pneumonia (HAP) and ventilator acquired pneumonia (VAP). This objective was achieved in Section 4.2 whereby the system of first order nonlinear differential equation describing the dynamics of pneumonia were deduced from the flow chart.

5.3 Model thresholds and analysis of stability, sensitivity and backward bifurcation.

The expression for control reproduction number(R_C) was obtained in Section 4.3.2 using Next Generation Method. The analytical expression of R_C threshold gives the estimate of secondary infections that can arise if one infectious individual is introduced in susceptible population. An equilibrium point is said to be locally asymptotically stable if all points in the neighborhood of the equilibrium point move towards it over time. An equilibrium point is globally asymptotically stable if all points move towards it over time.

The stability analysis of the DFE showed that the necessary and sufficient condition for local and global asymptotic stability of DFE was $R_C^* < 1$, this means interventions should strive to maintain control reproduction number less than one in order to avoid pneumonia persistence. The endemic equilibrium point of system $[(16) - (19)]$ was globally

asymptotically stable whenever $P < Q$ in Lyapunov sense and unstable otherwise, where expression of P and Q are provided in Section 4.3.8.

The result of bifurcation analysis in Section 4.3.5 indicated that system did not exhibit backward bifurcation hence it is possible to eradicate pneumonia in Kenya once the condition $R_C < 1$ is achieved.

The expressions of critical treatment threshold ${\tau_1}^C$ and ${\tau_2}^C$ are provided in section 4.2.9.1. When actual treatments ($\tau_1$and τ_2) are greater than critical treatment ${\tau_1}^C$ and ${\tau_2}^C$ respectively, it can ensure total eradication of pneumonia. The analytical expression for population-level impact of treatment impact was obtained in Section 4.3.9.1. Thus, population-level impact of treatment should always be positive. This condition is likely to be satisfied for treatment with effective drugs. The Ministry of Health should create public awareness through media or any other effective mean to parents and other stakeholders on symptoms of pneumonia. The Chief Officers in charge of health at county level should create awareness on the need for the infected children to visit hospitals for treatment when signs of pneumonia are suspected.

The results of analytical sensitivity analysis in Section 4.3.9.2 showed that R_C was directly proportional to k but inversely proportional to ϵ, τ_1 and τ_2. Therefore, higher value vaccination efficacy(ϵ), higher rates of severely and very severely infected children seeking treatment(τ_1 andτ_2) would decrease the control reproduction number and the intensity of the pneumonia endemic. Also, lower effect environmental factors (k) would decrease the control reproduction number (R_C). Therefore, County Governments and relevant authorities should address the environmental factors which increase children susceptibility to pneumonia like indoor air pollution, living in crowded homes and

parental smoking. This can be achieved through providing proper housing, upgrading slum areas and discouraging parental smoking through civic education. Medical research institutes like KEMRI should advice Government to ensure that the efficacy of the vaccination drug (ϵ) bought by Kenya is as high as possible.

The expression for critical vaccination threshold(q_c) was obtained in Section 4.3.9.4. Vaccination is a voluntary process therefore it is not possible to vaccinate all individuals in the population. The stakeholders should ensure that actual vaccination $(I-\Omega)\pi$ is greater than critical treatment (q_c) to ensure total eradication of pneumonia. This objective was sufficiently achieved.

5.4 Estimated numerical results of the model using data and/or parameters from KHIS and UNICEF as well as evaluated normalized sensitivity index.

To validate the results of Section 4.3.2 the numerical values of the reproduction numbers were obtained in Section 4.4.2. In particular, the numerical value for R_C was obtained as 9.31808 whose value too high. Every effort should be made to lower this value of R_C to less than one. The findings boundedness of the solution showed that if birth rate and natural would not vary significantly, the total population of the under five years will always be less or equal to 6,585,211.

The result indicated that reproduction number was lowest when vaccination drug efficacy is 100% and it was highest in absence of any intervention. The impact of treatment was found to be positive. The Government should target to vaccinate is 95.57% of new born. Vaccination campaigns carried out by Ministry of health and other agencies like GAVI

should ensure that over 95 children for every 100 of new birth are vaccinated in Kenya in order to achieve herd immunity.

The stakeholders and policy should formulate policies aimed at lowering parameters with positive values and increasing in parameters with negative values so as to control spread of pneumonia. Government should formulate policies on settlement because overcrowding increases contact rates (infection rate β) as well as increase pneumonia vaccine coverage. The result of the effect of environmental coefficient k was validated by normalized sensitivity index. The result in Section 4.4.3 indicates increases in vaccination drug efficacy holds the great promise lowering childhood pneumonia impact. Rates of treatment severely infected, treatment severely infected, progression of severely infected to very severely infected, recovery of outpatient and recovery of inpatient should also be also be increased in that order of preference to control childhood pneumonia. This objective was sufficiently achieved.

Future studies should consider fitting model to data because it was not feasible to fit it to 2012 and 2013 data points from KHIS.

5.5 Numerical simulations for validation of analytical results and also assessment of the effect of the efficacy of the vaccination drugs, environmental factors and therapeutic treatment drugs

The study validated the analytical sensitivity in Section 4.3.9.2 by carrying out numerical sensitivity analysis in Section 4.5.2 and upheld the conclusion explained in Section 5.3 above.

In long term, numerical simulation in Section 4.5.1 showed that the number of outpatients and inpatients in twenty years' time are expected to vary from 353000 and 4279 in 2013 to about 240000 and 1000 in 2033 respectively, a decrease of 113000 and 3279. The total population of children under the age of five is expected to vary from 7048020 in 2013 to 7253500 in 2033, an increase of 205,480. Simulated graphs indicated that maintaining $R_C < 1$ is a sufficient condition to eradicate childhood pneumonia.

In short term, numerical simulation in Section 4.5.1 showed that the number of outpatients and inpatients in five years' time are expected to vary from 4279 in 2013 to about 6000 in 2018 respectively, a decrease of 1529. The total population is expected to vary from 7048020 in 2013 to 7,342,750 in 2018, an increase of 294730. This population data is very important in policy formulation.

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APPENDIX

Appendix I: MATLAB codes

i) Codes for parameter estimation through fsolve command

```
function F = myfun(y)

%y(2)=0.3; y(3)=0.15;y(4)=0.05;
F = [0.83*1549500+2000*y(1)-0.1867*4302679-
1*0.0115*(144176+0.3*1748+0.15*576703+0.05*6991)*4302679;
        0.29*1*0.0115*(144176+0.3*1748+y(3)*576703+y(4)*6991)*4302679+(1-
0.37)*1*0.0115*(144176+0.3*1748+0.15*576703+0.05*6991)*1286085-
(y(7)+0.1867+y(5))*144176;
    (1-
0.29)*1*0.0115*(144176+0.3*1748+0.15*576703+0.05*6991)*4302679+y(7)*144176-
(0.1867+0.03976+y(6))*1748;
    y(5)*144176+y(4)*1748-(y(3)+0.1867)*144176;
    y(6)*1748-(y(2)+0.1867+y(4)+0.01988)*6991;
    y(3)*576703+y(2)*6991-(0.1867+y(1))*2000];
 % rho= y(1) **psi1=y(2)=0.3** **psi2=y(3)** **psi3=y(4)** tau1=y(5) tau2=y(6)
theta1=y(7) theta2=y(4) gamma1=y(3) UDMR5=0.071 % death due to pneumonia
16%=16%0f 0.071
 % constant= gamma2=y(2)
 % progression rate(mu)=1/duration of stay in under five=1/4.5-84%0f 0.071
 %P=0.29; k=1 beta=0.0115 from samsa  epil=0.37 mu=0.1867
 %delta1+delta2=84%0f 0.071 let delta1=2/3*84%0f 0.071=0.03976 delta2=1/3*84%0f
```

```
 %0.071=0.01988
 %(1-0.83)*1549500-(1-
0.37)*1*0.0115*(144176+0.3*1748+0.15*576703+0.05*6991)*1286085-
0.1867*1286085
 %0.1570  8.1956   0.0993  -8.1938   0.1987   0.0074   0.0000  -0.5641

y0 = [0.9;0.23;0.55;0.5;0.23;0.56];          % Make a starting guess at the solution
options=optimset('Display','iter');   % Option to display output
[y,fval] = fsolve(@myfun,y0,options)  % Call solver
% rho= y(1) psi1=y(2) psi2=y(3) psi3=y(4) tau1=y(5) tau2=y(6) theta1=y(8) theta2=y(9)
gamma1=y(10) UDMR5=0.071 % death due to pneumonia 16%=16%0f 0.071
 % constant= gamma2=y(11)
 % progression rate(mu)=1/duration of stay in under five=1/4.5-84%0f 0.071
 %P=0.29; k=1 beta=0.0115 from samsa  epil=0.37 mu=0.1867
 %delta1+delta2=84%0f 0.071 let delta1=2/3*84%0f 0.071=0.03976 delta2=1/3*84%0f
 %0.071=0.01988
```

ii) Codes for numerical sensitivity analysis

```
% t represent symbol for mild treatment tau 2%

t=0:0.003:1;
RC =10.5363+0.33577./(0.294243+t);
RO =16.1877;
RT =12.7305+0.0146418./(0.281143+t);
```

```
RE1 =2.79394+0.327561./(0.294243+t);

plot(t,RC,'r-',t,RO,'b-',t,RT,'g',t,RE1,'k-','linewidth',4)

grid on

% e represent symbol for efficazy%

e=[0 1];

RC = 0.000053773*(23343.6+0.0866145*(537312+5558400*(1-e)));

RO = 16.1877;

RT = 0.0000149883*(0.3*(429826+0.00452*(537312+5558400*(1-

e)))+0.326743*(537312+5558400*(1-e)));

RE1 = 3.7578;

plot(e,RC,'r-',e,RO,'b-',e,RT,'g',e,RE1,'k-')

grid on


% e represent symbol for enviroment%

k  = [1 10]

RC = 11.52*k;

RO = 16.1877*k;

RT = 12.7753*k;

RE1 = 3.7578*k;

plot(k,RC,'r-',k,RO,'b-',k,RT,'g',k,RE1,'k-')


% let b represent beta the force of infection%

b  = 0:0.01:10;
```

```
RC = (11.52*b)/1.01;

RO = (16.1877*b)/1.01;

RT = (12.7753*b)/1.01;

RE1 = (3.7578*b)/1.01;

plot(b,RC,'r-',b,RO,'b-',b,RT,'g',b,RE1,'k-')


% m represent symbol for mild treatment tau 1%

m=0:0.003:1;

RC =1./(0.213663+m).*(0.0000121937*(189982+75450.9.*m+102943.*(0.213663+m)));

RO =16.1877;

RT =1./(0.339843-m).*(4.89732*10^(-6)*(0.3*(9965.84+1.31549*10^6*(0.339843-

m))+2.20483*10^6.*(0.339843-m)));

RE1 =1.47947+0.5116642./(0.213663+m);

plot(m,RC,'r-',m,RO,'b-',m,RT,'g',m,RE1,'k-')

grid on


% P represent symbol for proportion of vaccinated%


P  = 0:0.001:1;

RC = 9.53448+6.86149*P;

RO = 7.90662+28.5556*P;

RT = 10.9224+6.38928*P;
```

```
RE1 = 1.76797+6.86149*P;
plot(P,RC,'r-',P,RO,'b-',P,RT,'g',P,RE1,'k-')


% V represent symbol for efficazy%
V=[0 1];
RC = 0.000053773*(93374.6*V+0.0866145*(2223360*(1-V)+2149250*V));
RO = 16.1877;
RT = 0.0000149883*(0.326743*(2223360*(1-
V)+2149250*V)+0.3*(1719310*V+0.00452*(222336*(1-V)+2149250*V)));
RE1 = 3.7578;
plot(V,RC,'r-',V,RO,'b-',V,RT,'g',V,RE1,'k-')
grid on
```

ii) Codes for numerical simulations

```
function dy = simulate(t,y)

dy = zeros(7,1);    % a column vector
phi=0.25; rho=0.00113; beta=0.00000012; mu=0.2353; k=1; psi1=0.3; psi2=0.15;
psi3=0.05;
epil=0.63;P=0.71;theta1=0.00452; tau1=0.456; delta1=0.05184;
tau2=0.0456;theta2=0.23688127; gamma1=0.467;
delta2=0.0515967;gamma2=0.3432; pi=1549500;
%dy(1) = phi*pi+rho*y(7)-mu*y(1)-
k*beta*(0.5*y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(1);
```

```
%dy(2) = (1-phi)*pi-(1-epil)*k*beta*(0.5*y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(2)-
mu*y(2);
%dy(3) = P*k*beta*(0.5*y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(1)+(1-
epil)*k*beta*(0.5*y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(2)-(theta1+mu+tau1)*y(3);
%dy(4) = (1-P)*k*beta*(0.5*y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(1)+theta1*y(3)-
(mu+delta1+tau2)*y(4);
%dy(5) = tau1*y(3)+theta2*y(4)-(gamma1+mu)*y(3);
%dy(6) = tau2*y(4)-(gamma2+mu+theta2+delta2)*y(6);
%dy(7) = gamma1*y(5)+gamma2*y(6)-(mu+rho)*y(7);
%pi=0.3198*(y(1)+y(2)+y(3)+y(4)+y(5)+y(6)+y(7));
dy(1) = phi*pi+rho*y(7)-mu*y(1)-k*beta*(y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(1);
dy(2) = (1-phi)*pi-(1-epil)*k*beta*(y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(2)-
mu*y(2);
dy(3) = P*k*beta*(y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(1)+(1-
epil)*k*beta*(y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(2)-(theta1+mu+tau1)*y(3);
dy(4) = (1-P)*k*be(ta*(y(3)+psi1*y(4)+psi2*y(5)+psi3*y(6))*y(1)+theta1*y(3)-
(mu+delta1+tau2)*y(4);
dy(5) = tau1*y(3)+theta2*y(4)-(gamma1+mu)*y(3);
dy(6) = tau2*y(4)-(gamma2+mu+theta2+delta2)*y(6);
dy(7) = gamma1*y(5)+gamma2*y(6)-(mu+rho)*y(7);
[T,Y] = ode15s(@simulate,[0 20],[4302679;1286085;144176;1748;576703;6991;2000]);
%plot(T,Y(:,1),'r',T,Y(:,2),'r',T,Y(:,3),'g',T,Y(:,4),'y',T,Y(:,5),'g',T,Y(:,6),'p',T,Y(:,7),'v')
%plot(T,Y(:,1),'b-',T,Y(:,2),'r-',T,Y(:,3),'*',T,Y(:,4),'y-',T,Y(:,5),'g',T,Y(:,6),'b',T,Y(:,7),'r')
```

```
hold on

plot(T,Y(:,1),'b-','LineWidth',4);

plot(T,Y(:,2),'r-','LineWidth',4);

plot(T,Y(:,3),'k-','LineWidth',4);

plot(T,Y(:,4),'p-','LineWidth',4);

plot(T,Y(:,5),'g-','LineWidth',4);

plot(T,Y(:,6),'o-','LineWidth',4);

plot(T,Y(:,7),'y-','LineWidth',4);

ylabel('Populations')

xlabel('Time t (in years)')

hold off

grid on
```

Appendix II: List of published papers and their link, and copies of abstracts.

Table 5: List of the published papers from the thesis.

Publications on Thesis	**Title of the original research published paper**	**Published in the Link**
1	Analytical model for childhood pneumonia, a case study of Kenya	http://sciencedomain.org/issue/1405
2	Estimated numerical results for the deterministic model of the under five years pneumonia in Kenya	http://www.ikpress.org/issue/647
3	Numerical simulation of the deterministic model of the under-five year's pneumonia in Kenya	http://www.ikpress.org/issue/648

i Snapshot of the first page of the first published paper

British Journal of Mathematics & Computer Science
12(2): 1-28, 2016, Article no.BJMCS.20180
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SCIENCEDOMAIN *international*
www.sciencedomain.org

Analytical Model for Childhood Pneumonia, a Case Study of Kenya

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Original Research Article

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Abstract

Pneumonia is an infection of the lungs that is caused by bacteria, viruses, fungi, or parasites. For a long time to the best of our knowledge there have not been reliable mathematical model for childhood pneumonia in Kenya. This research study developed a deterministic model based on the Susceptible-Vaccinated-Infected-Treated-Recovered-Susceptible compartment classes. The study used the partial differentiation of control reproduction number (R_C) toinvestigate effects of; environment, efficacy of vaccination drug and treatment. Model analysis indicates the system lie in feasible region, it is bounded, has no backward bifurcation and there exists unique endemic equilibrium point when control reproduction number is greater than unity. Local and global stability of the equilibrium points indicated that control reproduction has to be maintained at less than unity to eradicate the disease. Sensitivity analysis of the control reproduction number indicates that improved vaccination drug's efficacy, attaining herd immunity, higher treatment rates and lower effects of environment are the best intervention strategies to lower impact of the pneumonia of the children under the age of five years in Kenya.

Keywords: Control reproduction number; herd immunity; sensitivity analysis; disease free equilibrium point (DFE); endemic equilibrium point (EEP); local and global stability.

ii Snapshot of the first page of the second published paper

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ESTIMATED NUMERICAL RESULTS FOR THE DETERMINISTIC MODEL OF THE UNDER FIVE YEARS PNEUMONIA IN KENYA

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AUTHORS' CONTRIBUTIONS
This work was carried out in collaboration between authors CGN, GPP and JKK. Author CGN designed the study, gathered the initial data, wrote the algorithm, methodology programming and interpreted the results. Author GPP guided in writing academic paper and helped to interpret the results. Author JKK approved the final manuscript.

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Original Research Article

ABSTRACT

In this paper the numerical results are estimated for childhood pneumonia deterministic model, using Kenyan data. The estimates of data and parameters from Kenya Health information system, ministry of Health of Kenya and UNICEF for the years 2012 and 2013 were fitted in the developed model using Matlab software. The estimated numerical value for control reproduction number (R_C) and basic reproduction number (R_0) were obtained as 9.31808 and 22.5914 respectively, by substituting estimated parameters in the expression for the determined analytical results. The herd immunity was estimated as 95.57% using the basic reproduction number. Impact of treatment value was found to be found to be positive. Sensitivity analysis of the control reproduction number indicates that improved vaccination drug's efficacy, attaining herd immunity, higher treatment rates and lower effects of environment are the best intervention strategies to lower impact of the pneumonia of the children under the age of five years in Kenya.

Keywords: Control reproduction number; basic reproduction number; herd immunity and sensitivity analysis.

iii Snapshot of the first page of the third published paper

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NUMERICAL SIMULATION OF THE DETERMINISTIC MODEL OF THE UNDER-FIVE YEAR'S PNEUMONIA IN KENYA

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AUTHORS' CONTRIBUTIONS
This work was carried out in collaboration between authors CGN, GPP and JKK. Author CGN designed the study, gathered the initial data, wrote the algorithm, methodology programming and interpreted the results. Author GPP guided in writing academic paper and helped to interpret the results. Author JKK approved the final manuscript.

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ABSTRACT

In this paper the numerical simulation of the childhood pneumonia deterministic model are determined. The estimated parameters and the under-five year's population data for year 2013 was used to simulate the developed deterministic model, using Matlab inbuilt ordinary differential equation (ode) solver. Graphical results predicting the dynamics of the under-five year's pneumonia were obtained for a period of twenty years. Simulations indicated that sustained vaccination and treatment are likely to reduce the burden of the under-five year's pneumonia over a period twenty years.

Keywords: Ode solver and simulation.