KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

DEPARTMENT OF MATHEMATICS

MODELING AND CONTROL OF MEASLES TRANSMISSION IN GHANA

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BY

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CERTIFICATION

I hereby declare that this submission is my own work towards the M.Phil. and that, to the best of my knowledge it contains no material previously published by another person nor material which has been accepted for the award of any other degree of the university or elsewhere, except where due acknowledgement has been made in the text.

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DEDICATION

This work is dedicated to my beloved parents, my mother Hajia Amamatu Ahmed and my father Arimiyao Shuaib for their moral and spiritual support.

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I am highly indebted to Almighty Allah for giving me this wonderful and rare opportunity.

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ABSTRACT

In this study, the Susceptible-Exposed-Infected-Recovered (SEIR) epidemiological model is formulated to determine the transmission of measles in Ghana. The model assumes that individuals are equally likely to be infected by the infectious individuals in a case of contact except those who are immune. The undetected individuals are those contributing to the disease transmission in a population. The numerical and qualitative analyses of the model were performed and different state variables were determined. Qualitative results show that the model has the disease-free equilibrium which is locally asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$. Simulation of different epidemiological classes revealed that most of the individuals undergoing treatment join the recovered class. It is observed that if the proportion of the population that is immune exceeds the herd immunity level for the disease, then the disease can no longer persist in a population. Thus, if this level of immunity can be exceeded by means of mass vaccination, then the disease can be eliminated.

KNUST

TABLE OF CONTENTS

Content Page

CERTIFICATION ii

DEDICATION iii

ACKNOWLEDGEMENTS iv

ABSTRACT v

TABLE OF CONTENTS vi

LIST OF TABLES ix

LIST OF FIGURES x

LIST OF ABBREVIATIONS xi

CHAPTER 1 1

INTRODUCTION 1

1.1 Background 1

1.1.1 Control of measles in Ghana 3

1.2 Problem Statement 3

1.3 Research Objectives 5

1.3.1 General Objective 5

1.3.2 Specific Objectives 6

1.4 Methodology 6

1.5 Significance of the study 6

1.6 Thesis Organization 7

CHAPTER 2 8

LITERATURE REVIEW 8

2.0 Introduction 8

KNUST

2.1 Models for infectious diseases....8

CHAPTER 3....23

METHODOLOGY....23

3.0 Introduction....23

3.1 Definitions....23

3.2 Components of Mathematical Models....24

3.3 Why Epidemiological Models....24

3.4 Purposes of Epidemiological Modeling....25

3.5 Limitations of Epidemiological Modeling....26

3.6 SIR Model....27

3.7 Some SIR Model Assumptions....27

3.8 Equations for SIR Model....28

3.8.1 Differential Equations....29

3.9 Limitations of the SIR Model....30

3.10 The Compartmental Model....31

3.11 Model Assumptions....35

3.12 Properties of the Model Equations....36

3.13 Feasible Solution....36

3.13.1 Positivity of solutions....38

3.13.2 Lemma....38

3.14 Existence of Steady States of the System....40

3.14.1 Global asymptotic stability of the model....41

CHAPTER 4....49

MODEL APPLICATION, STABILITY ANALYSIS AND SIMULATIONS....49

4.0 Introduction....49

KNUST

4.1 Stability Analysis of the Model 50
4.2 Numerical Simulations of the Model 52
4.3 Analysis of the Simulations 54
4.4 Conditions for control of measles 55
4.4.1 Herd immunity 55
4.4.2 When mass vaccination cannot exceed the herd immunity 57
4.5 When mass vaccination exceeds the herd immunity 58
4.6 Discussion 58

CHAPTER 5 60
CONCLUSION AND RECOMMENDATIONS 60
5.0 Introduction 60
5.1 Conclusion 60
5.3 Recommendations 61

APPENDIX A 68
MATLAB CODES FOR OBTAINING THE DYNAMICS OF THE PLOTS 68
APPENDIX B 69
MATLAB CODES FOR PRODUCING DIFFERENT PLOTS 69

KNUST

LIST OF TABLES

Table 3.1: Variables and definitions of sub-populations used as variables.....28

Table3. 2 Parameters and their definitions.....29

Table 3.3 Parameters and their definitions.....34

Table 3.4 Variables and definitions of sub-populations used as variables.....34

Table 4.1: Model parameter values.....49

KNUST

LIST OF FIGURES

Figure 3.1: A diagram showing Susceptible, Infectious and Recovered group 27

Figure 3.2 the diagram showing the compartmental model for SEIR.....33

Figure 4.1: Simulation of Susceptible Population.....52

Figure 4.2: Simulation of Exposed Population. 53

Figure 4.3: Simulation of Infected Population. 53

Figure 4.4: Simulation of Recovered Population. 54

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
GHS	Ghana Health Service
HIV	Human Immune Virus
MATLAB	Matrix Laboratory
WHO	World Health Organisation

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CHAPTER 1

INTRODUCTION

1.1 Background

Measles is one of the most contagious viral diseases through person-to-person transmission mode with > 90% secondary attack rates among susceptible persons. (Tessa,2006). As a result most of the epidemiologists have developed a mathematical model using data pertinent to their country, and this has really helped them determined the prevalence of the disease in their country. In this study, data pertinent to Ghana will be used to formulate SEIR epidemiological model to determine the prevalence of the disease in Ghana.

The measles virus is caused by paramyxovirus, genus morbillivirus. In addition, it is the most dangerous of the children's diseases that result in a red rash and can lead to serious and fatal complications including pneumonia, diarrhaea and encephalitis.

It is fairly easy to catch the disease if you have not been vaccinated and come into contact with someone who has the infection, which is why epidemics often occur among schoolchildren. Many infected children subsequently suffer blindness, deafness or impaired vision. Measles confer lifelong immunity from further attacks.(Tessa, 2006).

In developing countries, 1-5% of children with measles die from complications of the disease. This death rate may be as high as 25% among people who are displaced, malnourished and have poor access to health care. (Hethcote (2000))

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It remains one of the leading causes of death among young children, globally, despite the availability of a safe and effective vaccine. An estimated 16,400 people died from measles in 2008-mostly children under the age of five.(WHO, 2001).

Measles is caused by a virus in the paramyxovirus family. The measles virus normally grows in the cells that line the back of the throat and lungs. Measles is a human disease and is not known to occur in animals. Although global incidence has been significantly reduced through vaccination, measles remains an important public health problem. Targeted vaccination campaigns have had a major impact on reducing measles deaths. From 2000 to 2008 nearly 700million children aged 9 months to 14 years who live in high risk countries were vaccinated against the disease. Global measles deaths decrease by 78% during this period. (Hethcote, 2000).

Severe measles are more likely among poorly nourished young children, especially those with insufficient vitamin A or who immune systems have been weakened by HIV/AIDS or other diseases. Most measles related deaths are caused by complications associated with the disease. Complications are more common in children under the age of five, or adults over the age of twenty. The most serious complications include blindness encephalitis (an infection that cause brain swelling), severe diarrhoea and related dehydration, ear infections or severe respiratory infections such as pneumonia. As 10% of measles cases result in death among populations with high levels of malnutrition and lack of adequate health care.

Measles is still common in many developing countries particularly in parts of Africa and Asia. More than 20million people are affected by measles each year. Overwhelmingly majority (more than 95%) of measles death occur in countries with low per capita incomes and weak health infrastructures.

1.1.1 Control of measles in Ghana

Measles control in Ghana was assessed since vaccinations began in 1978. National measles vaccination coverage increased from 24% in1980 to 84% in 2000.

This achievement is attributed to health sector reforms that included a higher district share of the total recurrent health budget from 20% in 1996 to 42% in 1999. The budget reallocation resulted in improved access to immunization services supply procurement, transport management, staff motivation and information flow.

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Ghana recently developed a strategic plan to reduce measles death to near zero.

In 1977, the Ghana Health Assessment Project ranked measles second to malaria in terms of burden of disease; measles accounted for 7.3% of the health days of life lost through illness, disability and death. Of all pediatric admissions to the korle Bu Teaching Hospital in Accra, 8.8% were attributed to measles over the 10-year period, 1973-1982.

At the Komfo Anokye Teaching Hospital in Kumasi; measles accounted for 9.3% of total pediatric admissions and 15.3% of total deaths between 1974 and 1975. Nearly 1 death in 5 among children aged 1 month to 5 years in the hospital was due to measles.(Ghana Health Service, 2002).

1.2 Problem Statement

Measles is one of the most infectious diseases in Ghana as well as other developing countries.

It has been noted that high transmission rate of the disease is as a result of late detection as well as unsupervised cure or treatment. Most of the measles cases are undetected and this may be one of the accelerating factors to high transmission rate.

Most often, some people also adhere strictly to self-medication at their various home completely unsupervised and this has contributed to the high transmission rate of the disease.

Most people have attributed the main causes of transmission to lack of proper education about the measles disease and low detection rate at early stages, financial constrains is also a major factor as most people prefer the treatment of the disease locally or traditionally than exposing themselves to hospitals for it treatment.

Measles is the childhood disease with the highest rate of mortality especially in developing countries.

Attempts to understand the epidemiology of measles started as far back as 1906. Mathematical models have been applied to infectious diseases since the middle of the 20th century. Infectious diseases like smallpox and measles have been analyzed by both deterministic and stochastic epidemiology models (Hethcote, 2000). Childhood diseases like measles and chicken-pox affect the children and infants much more frequently than the rest of the population. Even though childhood diseases can infect mostly children, in some occasions they can also affect adults that have not been exposed to or inoculated with the pathogen.

The fact that this disease occurs mainly in children is due to various factors.

In the case of infectious diseases, a single attack usually provides immunity for the whole life, so any adult who has had the disease as a child cannot be affected again.

People usually co-exist with the microbes that are present in the environment and there immunity develops with time.

Infectious diseases that target children include measles, chicken pox, whooping cough and scarlet fever (Hethcote, 2000).

Measles is one of the most infectious diseases and has severe complications, including pneumonia encephalitis (inflammation of the brain) and death.

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The objective of this thesis is to analyze some mathematical models, which can help us to understand and analyze the disease better.

The advantage of mathematical models is that the results can be evaluated and compared to the known data, enabling us also to identify a model's strength and weakness (Hethcote, 2000).

Hence, this study is been motivated by the fact that though measles is one of the most contagious diseases in Ghana, not much research has been done in the area of its epidemiological modeling.

1.3 Research Objectives

The research objective is group into general and specific objectives respectively

1.3.1 General Objective

The main objective of this study is to model the measles transmission in Ghana and also come up with the control measures to enable the reduction of the transmission of the disease in the country.

1.3.2 Specific Objectives

The specific objectives of this study are:

(i) to formulate SEIR epidemiological model for measles transmission in Ghana using compartmental model approach to derive a system of differential equations

(ii) to find the basic reproductive number, the disease free equilibrium and the endemic equilibrium states of the model for Ghana

(iii) to discuss the implications of the model for the management of the disease.

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1.4 Methodology

The methods to be used in this study are to divide the population into four compartments (S, E, I, R), consisting of Susceptible, Exposed, Infectious and Recovered class and then to identify system model by differential equations. The parameters of the model are incorporated using mortality, birth rate, infection rate etc pertinent to Ghana. Determination of equilibrium points and their stability is then performed as well as basic reproductive number found. Numerical simulation using MATLAB is then performed in the neighbourhood of the endemic equilibrium point.

1.5 Significance of the study

The study will be significant to the society in the following ways

(i) It will help the public health managers to plan and improve the detection which will help in bringing down the incidence and prevalence of measles in the country.

(ii) It will assist the society to be more aware of the disease dynamics so as to reduce the measles related morbidity and mortality.

(iii) It will help the government, public health agencies and health care providers to determine how best to allocate scarce resources for measles prevention and treatment.

1.6 Thesis Organization

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The thesis consists of five (5) main chapters, Chapter 1 talks about introduction, problem statement, objectives as well as significance of the study. In Chapter two 2 we reviewed some literatures relevant to our study. Chapter 3 consists of methodology used in carrying out this study. In Chapter 4 we will come up with the numerical simulation of the model using MATLAB. In Chapter 5, we will discuss the research findings and then make the necessary conclusions and recommendations.

CHAPTER 2

LITERATURE REVIEW

2.0 Introduction

For the last few decades, different people have developed many mathematical models for measles. In this chapter, some of these models are reviewed particularly those having the close relation to the objectives of this study.

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2.1 Models for infectious diseases

The diseases that motivated the development of modern epidemiological theory are arguably those due to childhood infections, most notably measles. This arose predominantly from their large public health importance in the late 19th and early 20th century.

The most striking aspect of measles epidemics, i.e. their regular cyclic behavior, was noticed first by Arthur Ransome around 1880. Speculation about the underlying cause centered on the availability of sufficiently many susceptible individuals of the right age-class in close enough proximity to each contact other; hence precursory ideas of critical community sizes for sustaining endemic measles were present.

Two factors that commonly occur in many current models to investigate epidemic spread of measles and other infections are the age-structure of the population and the periodicity.

The age and school season were recognized as important as early as 1896. William Hamer published a discrete time epidemic "model" for the transmission of measles in 1906.

His observation can be reformulated as stating that the incidence of new cases in a time interval is proportional to the product *SI* of the (spatial) density *S* of susceptible and the (spatial) density *I* of infectives in the population. This assumption of mass action - in analogy to its origin in chemical reaction kinetics – is fundamental to the modern theory of deterministic epidemic modeling. The popularity of mass action is explained by its mathematical convenient and the fact that at low population densities it is a reasonable approximation of a much more complex contact process.

Trottier and Philippe (2003) presented a model which investigated measles cycles and the Role of Births and vaccination. Their work had a target on providing a more realistic portrait of the infection by introducing births and deaths in the SEIR model, vaccination, and finally time vaccination in the contact rate.

Their work also shows how the recruitment of susceptible by births yields the well known cycling of epidemics. They also indicated how vaccination could alter population pattern of infectious in the same way that the birth rate does it.

Varying the birth or vaccination rates is however insufficient to avoid tapering off of epidemics with time. Since the tapering off is at variance with real data, seasonality in the contact/transmission rate was added to the equations. Including seasonal variations introduced chaos in the pattern of population infection.

The resulting sensitivity to demographic data is sufficient to explain most epidemic patterns at least from a quality standpoint. They concluded their work on population

patterns of infections by urging for efforts to understand how complex work evolves since this provides a key to appropriate public-health interventions. The population dynamic approach can help control many types of population disease patterns.

Franceschetti and Pugliese (2008), considered an age-structured SIR model with immigration of infectives in all compartments with the population size assumed to be in demographic equilibrium between below replacement fertility and immigration.

In Inaba (2007), he divided the population into n subpopulations (compartments) corresponding to different epidemic states, e.g. susceptible etc. The state of such a population is described by the introduction of age density functions Uj (t, a) where t denotes time, a is for age and j denotes the jth epidemic state. He used a system of PDEs as models and applies them to a MSEIR type one.

Hilary (2007) proposed stochastic models for epidemics. He analyzed two epidemic models the Susceptible-Infective-Recovered (SIR) model and the Reed-Frost Epidemic Model. He tried to estimate the infection rate for the Reed-Frost Epidemic model using both classical maximum likelihood methods and Gibbs Sampling. He also used Approximate Bayesian Computation to estimate the rate of infection and recovery for the SIR model. He could not apply maximum likelihood and Gibbs Sampling methods to the SIR model as its likelihood is not readily computed. The results for the maximum likelihood and Gibbs Sampling methods for the Reed-Frost model agree, but the model does not appear to fit the data well. When considering the SIR model Approximate Bayesian Computation accurately returns parameter values when he has complete data. It performs less well when he has incomplete data. Further work needs to be carried out before he can say whether Approximate Bayesian Computation is useful when considering real-life data sets, which often have incomplete data.

In Gao, Teng and Xie (2008), the dynamics of a SEIR model with two delays and pulse vaccination were analyzed.

Olinky, Huppert and Stone (2008) considered a seasonally forced SIR epidemic model and provided insights into the dynamics of recurrent diseases with specific predictions about individual outbreaks. they develop a 'language of skips' that makes it possible to predict how many 'skips' might be expected after any given outbreak. They show that in the presence of seasonality, forecasts based on the susceptibility are more reliable than those based on the reproduction number R_0.

In Zhao, Chen and Song (2008) considered an SEIR model with delay and nonlinear incidence rate of the form βIS and they studied the dynamical behavior of the system under pulse vaccination.

In Conlan and Grenfell (2007) examined how the critical community site (CCS) scales with birth rates for measles.

In Jodar and Villanueva (2008) established the existence and uniqueness of periodic solutions of seasonal epidemiological diseases of SIRS type using a continuation theorem based on the so called coincidence degree theory. Global asymptotic stability of the periodic solution of the system is considered too.

In Huang (2008), a new SEIR epidemic model in the form of an integrodifferential system is introduced which uses two distribution functions W (t) and A (t, s) such that W (t) is the probability that an exposed individual will remain in the exposed state (E) for t units of time and A (t, s) is the probability such that an infective individual that emerges at time t will be recovered at time t + s. The classical SEIR model is produced as a special case.

In Moneim (2007) considered an SEIR epidemic model with three types of seasonally varying contact rates β (t) (sinusoidal, a step function and a linear combination of the two) and perform simulations studies together with proofs of some theoretical results.

Mann (2009) presented a mathematical model for the dynamics of vaccine preventable diseases through the use of integral and differential equations, he was able to come up with a model and compare the results of the model to known data. Using game theory analysis, he was able to determine and compared the proportion of the population that needs to be vaccinated in order to minimize the expected costs to the individuals in the population and to the community.

Two different scenarios and methods were considered, where the effect of vaccination last only one epidemic cycle (using the integral equation method) and where vaccination is effective over an entire lifetime (using a differential equation method). For both scenarios, he find out that the minimum cost for the individuals is reached when a lower proportion of the population is vaccinated than needed for the minimum cost to the community.

He then elaborated on the integral equation method to produce a model for repeated epidemics of measles in a population where a discrete mapping is used to include the year-to-year demographics of the population. The result of this model indicated a different epidemic pattern than that produced from a differential equation model with numerical problems encountered.

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He then used a differential equation model in his analysis. The effect of vaccination was included in his model so that he can explore the future of the infection in the population and how best to tackle any future epidemics.

In the paper of (Chinviriyasit, 2007) an SIQ epidemic model is studied and analyzed. In the model the susceptible and the infectious have constant immigration. The model exhibits a unique endemic state if $p > 0$, a disease-free state and an endemic state if $p = 0$. A basic reproduction number R_0 is derived.

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If $R_0 > 1$, the global stability of the endemic equilibrium is proved when $p \geq 0$.

The aim of this paper was to study global stability of a model for the transmission dynamics of infectious diseases that include a new class Q of quarantined individuals, who have been removed and isolated either voluntarily or coercively from the infectious class. The resulting model is of SIQ type. This paper was organized as follows: First, he formulated the model and discussed the existence of equilibrium; then, he considered the global stability of the endemic equilibrium when $p \geq 0$

Andreasen and Frommelt (2005) presented a model that divided the population into m cohorts and they considered a discrete dynamical system for which they present theoretical results for the cases when the disease transmission is age-independent.

In Zhao, Chen and Song (2008) considered an SEIR model with delay and nonlinear incidence rate of the form βISq and they studied the dynamical behavior of the system under pulse vaccination.

Ouncharoen (2010) studied the SIR epidemic model with varying total population size and constant immigration rate. He derived the sufficient conditions on parameters of

the system to guarantee that the equilibrium points of the system are locally asymptotically stable or globally asymptotically stable.

If the disease-free equilibrium point is stable, then the disease will not affect the population in the system. On the contrary, if the endemic equilibrium point is stable, the number of infectives will not change which means the infected rate equals to the recovery rate. Consequently, they stated that, the disease behavior and the prevention program can be efficiently instituted.

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Moneim (2005) studied two classes of epidemic models. These models are the standard SIR and SEIR models with time-varying periodic contact rate. The importance of the latent period was his target. When the latent period can be ignored and when it must be taken into account are the main points of his simulation. The comparison of the simulation results of his two models shows that the latent period is affecting the pattern of the dynamics of the disease. His paper addressed how model predictions are affected by the assumed form of the seasonally varying transmission rate and whether or not a latent class is included.

Moreover, for some infectious diseases, using latent period leads to appearance or disappearance of some periodic solutions for the same parameter set. A key parameter for his models was the basic reproductive number R_0. He simulated his models for a set of values of parameters insuring that $R_0 > 1$, which represent the endemic case.

Hethcote, Ma (2002) and Takeuchi (2000), studied the SIR infectious disease model in which an infectious disease is transmitted by a vector after an incubation time. Their model assumes that the birth rate and the death rate are all constant, so the dynamics of the total population is very simple. In order to investigate disease dynamics for the

model with more demographic effects, it would be necessary to isolate the fraction of arriving infectives.

Beretta and Takeuchi (1995) investigated SIR models with constant and varying population size, respectively.

Greenhalgh (2005) obtained different patterns for each of the SIR and SEIR; these patterns representing the filtered results of the long-term behavior of the endemic periodic solution for a range of amplitude parameter values of the periodic contact rate. So it is too important to determine which type of model SIR or SEIR is more likely to describe the actual nature of the dynamics of each disease.

Lima (2009) stated in his ecology letter the role played by interannual climatic variability on the temporal dynamics of infectious diseases. In his report, he presented evidence from data on measles cases in England and Wales showing that during the post-vaccination period, the interannual variability of winter weather (represented by the North Atlantic Oscillation, (NAO) influences the annual dynamics of the disease. Using annual measles data from seven cities and simple logistic models, this study reveals how, after vaccination, NAO increases its effects on measles fluctuations. In addition, his study shows that vaccination may be represented as a simple vertical and lateral perturbation effect (Royama's classification), by reducing the maximum per capita growth rate and the equilibrium number of infected individuals. The results suggest that vaccination will not lead to outbreaks of measles from regular cyclic to irregular chaotic dynamics. In contrast, because of the reduction in per capita growth rates, the disease dynamics appear to be more stable than during the pre-vaccination period.

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The analysis of annual data on infectious diseases may be useful for detecting long-term effects of climate and complements the classical analyses and modeling based on monthly or seasonal time-step data.

Keeling & Grenfell (2002) stated that, ever since the pattern of localized extinction associated with measles was discovered by Bartlett in 1957, many models have been developed in an attempt to reproduce this phenomenon. Recently, the use of constant infectious and incubation periods, rather than the more convenient exponential forms, has been presented as a simple means of obtaining realistic persistence levels. However, this result appears at odds with rigorous mathematical theory; they then reconcile these differences using a deterministic approach, they parameterize a variety of models to fit the observed biennial attractor, thus determining the level of seasonality by the choice of model. They compare fairly the persistence of the stochastic versions of these models, using the 'best-fit' parameters. Finally, they considered the differences between the observed fade-out pattern and the more theoretically appealing 'first passage time'.

Bartlett (1957) made the seminal observation that the number of localized extinctions, or fade-outs, of measles was related to the population size of the community. Small populations demonstrated much extinction, whereas large populations showed very few; similar results have also been observed for other diseases and also larger organisms. This led to the notion of the critical community size (CCS), which is defined as the smallest population size that does not exhibit disease extinctions. The CCS has been estimated for a variety of communities, including cities in England and Wales (Bartlett, 1957), cities in the United States (Bartlett 1960) and isolated islands

(Black 1966). Surprisingly, its value is remarkably consistent between datasets, lying between three and five hundred thousand.

Keeling and Grenfell (1997) proposed a simple modification to the standard models that vastly increased persistence by forcing the incubation and infectious periods to be closer to fixed intervals, rather than the standard exponential distribution that is commonly implemented. These more constant periods agree well with observations of disease transmission within household and demonstrate the high frequency 'pulsing' detectable at the start of many epidemics with such constant periods, however, there appears to be a discrepancy between theory and simulation. Work on SIR-type (susceptible, infectious, recovered) models has shown theoretically that constant periods destabilized disease dynamics (Grossman, 1980).

Britton (2000) and Lloyd (2001) observed that numerical simulations of Keeling & Grenfell (1997) showed far greater persistence for constant periods. This difference between theory and simulation can be resolved by realizing that all models should be able to accurately reproduce the general biennial pattern of measles epidemics observed before vaccination. That is, by forcing a model to be an accurate description of the observed measles dynamics, the parameter values are governed by our choice of model. The previous theoretical work kept the parameters fixed while varying the model and therefore has not necessarily been comparing reliable models of measles.

Korobeinikove & Maini (2004) considered the impact of the form of the non-linearity of the infectious disease incidence rate on the dynamics of epidemiological models.

They considered a very general form of the non-linear incidence rate (in fact, they assumed that the incidence rate is given by an arbitrary function $f(S, I, N)$ constrained by a few biologically feasible conditions) and a variety of epidemiological models.

They show that under the constant population size assumption, these models exhibit asymptotically stable steady states. Precisely, they demonstrated that the concavity of the incidence rate with respect to the number of infective individuals is a sufficient condition for stability. If the incidence rate is concave in the number of the infectives, the models they consider have either a unique and stable endemic equilibrium state or no endemic equilibrium state at all; in the latter case the infection-free equilibrium state is stable. For the incidence rate of the form $g(I)\,h(S)$, they proved global stability, constructing a Lyapunov function and using the direct Lyapunov method. It is remarkable that the system dynamics is independent of how the incidence rate depends on the number of susceptible individuals. They demonstrated this result using a *SIRS* model and a *SEIRS* model as case studies. For other compartment epidemic models, the analysis is quite similar, and the same conclusion, namely stability of the equilibrium states, holds.

De la Sen & Ibeas (2011) presented a paper that is devoted to the design of a vaccination strategy for a SEIR model with incomplete knowledge about the populations. The design is oriented towards the measurement and use of the infectious population in the design of the vaccination rule with the eventual incorporation of an observer to deal with uncertain model state knowledge.

The observer is not necessarily parameterized with the exact known parameters of the epidemic model.

Guihua & Zhen (2005) formulated an SEIR epidemic model in which the infectious force in the latent (exposed), infected and recovered period is studied. It is assumed that susceptible and exposed individuals have constant immigration rates. The model exhibits a unique endemic state if the fraction p of infectious immigrants is positive.

If the basic reproduction number R_0 is greater than 1, sufficient conditions for the global stability of the endemic equilibrium are obtained by the compound matrix theory.

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In (Chengjun & Ying-Hen, 2009), an SEIR model with varying population size and vaccination strategy is investigated. Three different threshold parameters were obtained to govern the disease eradication, which involve the total number of infectives and their proportion in the population. Parameter conditions on the uniform persistence, the global stability of the disease – ‘‘free” equilibrium and the ‘‘endemic” equilibrium were derived. The global dynamics of model in population size are studied. The correlations of the two systems in terms of disease eradication, endemicity and disease explosion were summarized and compared. They conjecture that substantially low product of vaccination rate and low vaccine efficacy may lead to complicated dynamics for the system in question.

Demirci and Unal (2010), introduced a fractional order SEIR epidemic model with vertical transmission, where the death rate of the population is density dependent, i.e., dependent on the population size. It is also assumed that there exists an infection related death rate. They also show the existence of nonnegative solutions of the model, and also give a detailed stability analysis of disease free and positive fixed points. A numerical example is also presented.

Izewski, Sokal and Verbus (2010) studied the spread of an infectious disease, and realized that it is important to consider the existence of infected individuals who do not exhibit symptoms. These "carriers" are still capable of spreading the disease, but are asymptomatic, meaning they do not visibly display any symptoms, and are thus difficult to identify as infected. They will affect the spread of the infectious disease and must be taken into account as a third class of people who do not fall into the usual categories of those who are noticeably infected and those who are susceptible to the

disease. They noted that this is different from an asymptomatic disease, one in which all infected individuals are asymptomatic, and display no perceptible symptoms. The purpose of their paper was to use differential equations to model the change that arises in a closed population within which an infectious disease is present. By comparing the spread of both a disease that produces only symptomatic infected persons and a disease that allows for a certain fraction of the infected to be asymptomatic, they observed the extended effects of this added class.

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Rost (2008) came up with a new SEIR model with distributed infinite delay. The author stated that the infectivity depends on the age of infection. The basic reproduction number R_0, which is a threshold quantity for the stability of equilibria, is calculated. If $R_0 < 1$, then the disease-free equilibrium is globally asymptotically stable and this is the only equilibrium. On the contrary, if $R_0 > 1$, then an endemic equilibrium appears which is locally asymptotically stable. Applying a permanence theorem for infinite dimensional systems, he obtain that the disease is always present when $R_0 > 1$.

Glass, Xia and Grenfell (2003) stated that an increasing number of recent studies involve the fitting of mechanistic models to ecological time-series. In some cases, it is necessary for these models to be discrete-time approximations of continuous-time processes. They tested the validity of discretization in the case of measles, where time-series models have recently been developed to estimate ecological parameters directly ssfrom data. They find out that a non-homogeneous contact function is necessary to capture the host–parasite interaction in a discrete-time model, even in the absence of heterogeneities due to spatial or age structure. They then derive a mathematical relationship describing the expected departure from mass-action transmission in terms of

the epidemiological parameters in the model, and identify conditions under which the discretization process may fail.

d'Onofrio, Manfredi & Salinelli (2007) presented simple epidemiological models with information dependent vaccination functions which can generate sustained oscillations via Hopf bifurcation of the endemic state. The onset of these oscillations depends on the shape of the vaccination function. They used "global" approach to characterize the instability condition and identify classes of functions that always lead to stability/instability. The analysis allows the identification of an analytically determined "threshold vaccination function" having a simple interpretation: coverage functions lying always above the threshold always lead to oscillations, whereas coverage functions always below never lead to instability.

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CHAPTER 3

METHODOLOGY

3.0 Introduction

In this chapter, a model for measles transmission is formulated in respect of the dynamics of the disease in Ghana to determine effective ways of controlling it. Some key terms necessary for this mode are first presented.

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3.1 Definitions

A differential equation is an equation that contains a derivative (or derivatives) of an unknown function. A differential equation is ordinary if all derivatives are with respect to a single independent variable and is partial if there are derivatives with respect to two or more independent variables.

The order of a differential equation is the order of the highest derivatives in the equation.

A set of n first-order ordinary differential equations with n unknown functions is a system of first order ordinary differential equations; the number n is the dimension of the system. An ordinary differential equation or system of ordinary differential equations is autonomous if the independent variable does not appear explicitly in the equation.

Degree: The degree of a differential equation is the power of the highest derivative term.

Linear: A differential equation is called linear if there are no multiplications among dependent variables and their derivatives. In other words, all coefficients are functions of independent variables, and Non-linear otherwise.

Homogeneous: A differential equation is homogeneous if every single term contains the dependent variables or their derivatives, and Non-homogeneous otherwise

3.2 Components of Mathematical Models

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Mathematical model: is a set of formulas and/or equations based on a quantitative description of real phenomena and created in the hope that the behavior it predicts will resemble the real behavior on which it is based.

Mathematical quantities in models can be classified as variables, constants, parameters and input functions. An independent variable is a quantity that takes on a range of values. Usually, independent variables are measures of time or position. The set of all possible values of the independent variable is the domain of the problem. A dependent variable is a quantity that changes during a given problem, depending on the value(s) of the independent variable(s).

A constant is a quantity that has a single fixed value. And a parameter is a quantity whose value is fixed throughout the domain of the model but can be varied to a family of related problems.

3.3 Why Epidemiological Models

Epidemiology is the study of the distribution and determinants of disease prevalence in humans. One function of epidemiology is to describe the distribution of the disease, i.e. find out who has how much of what, where and when. Another function is to identify

the causes or risk factors for diseases in order to find out why everyone does not have the same thing uniformly. A third function of epidemiology is to build and test theories.

A fourth function is to plan, implement and evaluate detection, control and prevention programs.

Epidemiology modeling can play an important role in these last two functions.

Mathematical models have become important tools in analyzing the spread and control of infectious diseases. The model formulation process clarifies assumptions, variable, and parameters; moreover, models provide conceptual results such as thresholds, basic reproduction numbers and contact numbers.

Mathematical models and computer simulations are useful experimental tools for building and testing theories assessing quantitative conjectures, answering specific questions, determining sensitivities to changes in parameter values, and estimating key parameters from data. Understanding the transmission characteristics of infectious diseases in community, regions and countries can lead to better approaches to decreasing the transmission of diseases. Mathematical models are used in comparing, planning, implementing, evaluating, and optimizing various detection, prevention, therapy and control programs.

Epidemiological modeling can attribute to the design and analysis of epidemiology surveys, suggest crucial data that should be collected, identify trends, make general forecasts, and estimate the uncertainty in forecast.

3.4 Purposes of Epidemiological Modeling

The following are some purposes of epidemiological modeling

(i) The model formulation process clarifies assumptions, variables and parameters.

(ii) The behavior of precise mathematical models can be analyzed using mathematical methods and computer simulations.

(iii) Modeling provides concepts such as a threshold, reproduction number, etc.

(iv) Modeling is an experimental tool for testing theories and assessing quantitative conjectures.

(v) Modeling can be used to estimate key parameters by fitting data.

(vi) Models can be used in comparing diseases of different types or at different times or in different populations.

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(vii) Models can be used to theoretically evaluate, compare or optimize various detection, prevention, therapy and control programs.

(viii) Model can suggest crucial data which needs to be collected.

3.5 Limitations of Epidemiological Modeling

The following are some of the limitations of epidemiological modeling.

(i) An epidemiological modeling is not reality; it is an extreme simplification of reality.

(ii) Deterministic models do not reflect the role of chance in disease spread and do not provide confidence interval on results.

Before we start with our SEIR model, let us analyze some of the shortcomings of SIR model as we are aware that a model should simulate the spread of the disease as accurate as possible, which means that the resulting graph of the model should fit the empirical data. Above all, an accurate prediction of the disease dynamics will allow us to evaluate the effectiveness of the control measures.

3.6 SIR Model

Almost all epidemiological models start from this same basic model. The SIR model is used for modeling general epidemics and to know how the spread of a disease is in a particular population and some possible ways of controlling such a disease.

3.7 Some SIR Model Assumptions

Here the population is divided into three compartments, namely Susceptible, Infectious and Recovered population as represented below

Figure 3.1: A diagram showing Susceptible, Infectious and Recovered group

The above model has some few assumptions:

1) It is assumed that if the infected person did not die from the disease, then he/she becomes immune upon recovery.
2) In addition, the model assumes that the population is mixing homogenously. ie there is an interaction within the population.
3) The total population at any time is assumed to be constant.
4) It is also assumed that, at any given day a fixed fraction of the infected group will recover. For example, if the average duration of infection (infectious period) is four days, then, on average, one-fourth of the currently infected population recovers each day.

3.8 Equations for SIR Model

In this model the total population is divided into three distinct groups. We first have the Susceptible(S), Infected (I) and the Recovered (R). The total population is assumed to be constant. ie S+I+R=N

Assuming the disease spreads into a population that is totally susceptible, the susceptible individuals have never come into contact with the disease and are able to catch the disease, after which they move into the infectious class. Infectious individuals spread the disease to the susceptible, and remain in the infectious class for a given period of time (the infectious period) before moving into the recovered/removed class.

This description of the SIR model was made more mathematical by a formulated differential equation for the proportion of individuals in each class.

Table 3.1: Variables and definitions of sub-populations used as variables

Variables	Definitions
S(t)	The number of susceptible individuals at time, t
I(t)	The number of infected individuals at time, t
R(t)	The number of recovered individuals at time, t

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Table3. 2 Parameters and their definitions

Parameter	Parameter definition
Λ	Rate of infection per unit time
A	The rate at which an infectious individual recovered per unit time

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3.8.1 Differential Equations

The differential equations for the SIR model are given by the following

$$\frac{dS}{dt} = -\lambda S(t) I(t)$$

$$\frac{dI}{dt} = \lambda S(t) I(t) - \alpha I(t)$$

$$\frac{dR}{dt} = \alpha I(t)$$

Where, S stands for Susceptible (those who can contract the disease), I stands for Infectious (those who have the disease and can infect others) and R represents Recovered or Removed.

The parameters λ and α characterize the propagation of the disease and can also be used as control parameters in order to stop the epidemic.

3.9 Limitations of the SIR Model

Even though the SIR model provides a general framework to understand the spread of a disease, it may be too simple to accurately model a real epidemic like the outbreak of measles in Ghana.

There are various limitations or shortcomings in this model, which are explained as follows:

1) There should be an Exposed (but not yet infected) class; people have to be exposed to the disease before they can be infected and consequently become infectious. In fact, this is the case for the measles. A measles patient becomes infectious only after the infected person develops the symptoms.

Therefore, the limitations and flaws in the SIR model can be modified and extended to the SEIR model.

The model equation is kept simple: a deterministic, compartmental, mathematical model is formulated to describe the transmission dynamics of measles.

The progression of measles within the total population can be simplified to four differential equations.

These four equations represent four different groups of people:

the susceptibles, the exposed, the infectives, and the recovered. The susceptibles (represented by "S") are people that have never come into contact with measles, the exposed (represented by"E") are people who have come into contact with the disease but are not yet infectives, the infectives (represented by "I") are people who have

become infected with measles and are able to transmit the disease, and the recovered (represented by "R") are people that have recovered from measles.

Note that S+E+I+R=N, where N being the total population is constant.

In all, the assumption is that the population is a value somewhere between zero and N, with N meaning the population is at full capacity.

It is further assumed that all individuals are equally likely to be infected by the infectious individuals in a case of contact except those who are immune. The undetected or late detected infectious individuals are ones contributing to disease transmission and spread. Those detected are isolated to the hospital for immediate treatment and education.

It is further assumed that those recovered become immune and they get some form of education about the transmission of the disease. The transmission of the disease within the sanatorium is negligible. I further assume that there is no treatment failure in the sanatorium, therefore a patient will either recover or die.

Let **Λ** be the Recruitment rate (new-born or immigrants), **μ** be the natural death rate or emigrants, **β** be the rate (force) of infection per unit time , **λ** is rate at which an infected individual becomes infectious per unit time, **α** is the rate at which an infectious individual recovered per unit time.

3.10 The Compartmental Model

The rate at which people become susceptible starts with the birth rate, Λ. From that rate is subtracted the normal death rate of people that have not yet been exposed to measles, μS.

with infectives and become exposed, βSI. To determine the rate at which people become exposed in the population, the last term is considered in the susceptible equation which is the rate at which susceptibles, by meeting infectives, become exposed, βSI. From this amount, is subtracted the exposed people that die (not necessarily from the measles disease) denoted by μE, and those people who, after being exposed, become infected, λE. The rate of influx in the population of infectives is given by the last term in the exposure equation, which is the rate of exposed people becoming infected, denoted by λE. From that amount, is subtracted the percentage of death among infectives, μI, and the percentage of recovery from the measles infection, αI.

The last equation describe the rate at which people in the population recover from a disease. The recovered population is given by the last term in the infective equation, αI, which is the rate at which infectives recover. From that amount is subtracted the normal death rate of already-recovered people, μR. Since there is no other way to eliminate people from the recovered group (since measles can only be contracted once).

The compartmental model becomes

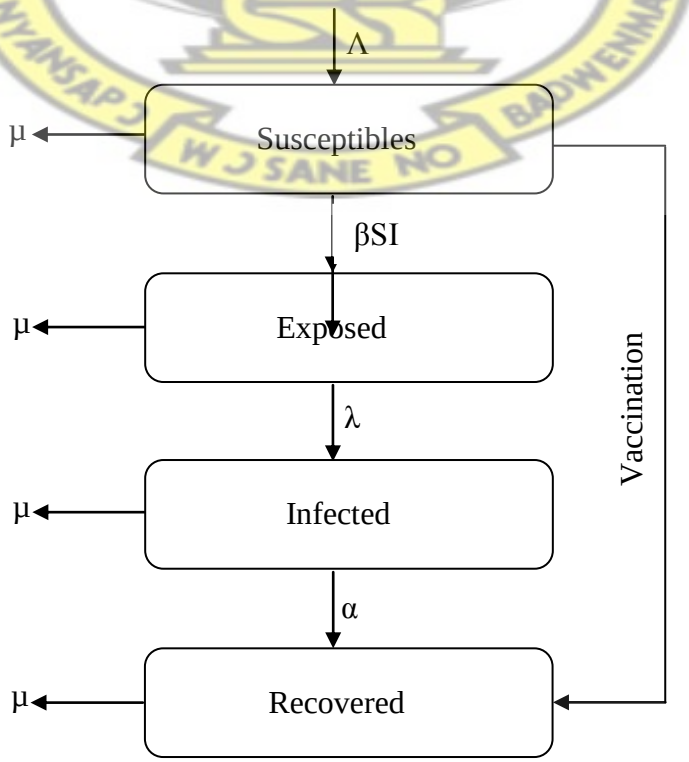

Figure 3.2 the diagram showing the compartmental model for SEIR

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Table 3.3 Parameters and their definitions

Parameter	Parameter definition
Λ	Recruitment rate(New born or immigrants)
μ	Natural death rate
β	The contact rate, defined to be the average number of effective contacts with other(susceptible) individuals per infective per unit time
λ	Rate at which exposed become infective
α	The rate at which an infectious individual recovered per unit time

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Table 3.4 Variables and definitions of sub-populations used as variables

Variable	Definition
S(t)	The number of susceptible individuals at time, t
E(t)	The number of exposed individuals at time, t
I(t)	The number of infected individuals at time, t
R(t)	The number of recovered individuals at time, t

3.11 Model Assumptions

The model assumptions for the SEIR model are as follows:

i. Individuals are equally likely to be infected by the infectious individuals in a case of contact except those who are immune
ii. There is no treatment failure, a patient will either recover or die
iii. Recovered individuals are permanently immune
iv. Infectious individuals are detected early and isolated for immediate treatment and education
v. There is equal birth and death rates and all Newborns are assume to be susceptible
vi. That every person in our population is susceptible to the measles disease
vii. The population is homogeneously mixed, i.e. A population that interacts in such uniformly random and independent way between time steps

The SEIR model

The classic model for microparasite dynamics is the flow of hosts between Susceptible, Exposed (but not infectious) Infectious and Recovered compartments. This leads to the following formulation of the SEIR model from the description, assumptions and compartmental diagram above.

$$\frac{ds}{dt} = \Lambda - \mu S - \beta SI \quad (1)$$

$$\frac{dE}{dt} = \beta SI - (\mu + \lambda)E \quad (2)$$

$$\frac{dI}{dt} = \lambda E - (\mu + \alpha) I \quad (3)$$

$$\frac{dR}{dt} = \alpha I - \mu R \quad (4)$$

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$\frac{dN}{dt}$ = 0, and N = S+E+I+R is thus constant.

3.12 Properties of the Model Equations

In this section, we show a description of some basic properties of the model equations (1) – (4), such as feasible solution and the positivity of solutions.

The feasible solution shows the region in which the solutions of the equations (1) – (4) are biologically meaningful and the positivity of the solutions describes the non-negativity of the solutions of the equations (1) – (4).

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3.13 Feasible Solution

The feasible solution set which is positively invariant set of the model is given by,

$\Phi = \{(S, E, I, R) \in R_+^4 : S+E+I+R = N \leq \frac{\Lambda}{\mu}\}$

From the model equations (1) – (4) It will be shown that the region is positively invariant.

Consider the steps below

From the model equations, the total population of individuals is given by

$$N = S+E+I+R$$

Therefore adding the differential equations (1) – (4), the results becomes

$\frac{dN}{dt} = \Lambda - \mu N$

METHOD OF SOLUTION

A first-order linear differential equation of the form

$$\frac{dN}{dt} = \Lambda - \mu N$$

Has an integrating factor $I(t) = e^{\mu t}$

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Therefore

$$\frac{dN}{dt} e^{\mu t} = \Lambda e^{\mu t} - \mu N e^{\mu t}$$

Or $$\frac{dN}{dt} e^{\mu t} + \mu N e^{\mu t} = \Lambda e^{\mu t}$$

On integrating inequalities the result becomes as follows,

$N(t) = \frac{\Lambda}{\mu} + Ce^{-\mu t}$, at $t = 0$ we obtain

$N(0) = \frac{\Lambda}{\mu} + C$

The solution of the linear differential equation then becomes

$N(t) = N(0)e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t})$, So that as $t \to \infty$, $N(t) \leq \frac{\Lambda}{\mu}$.

Therefore, Φ is positively invariant.

3.13.1 Positivity of solutions

It is now proved that all the variables in the model equations (1) – (4) are non-negative.

3.13.2 Lemma

Let the initial data set be $(S,E,I,R)(0) \geq 0 \in \Phi$, then the solution set (S, E, I, R) (t) of the equations (1) – (4) is positive for all $t > 0$.

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Proof: from equation (1) if it is assumed that,

$$\frac{dS}{dt} = \Lambda - \mu S - \beta SI \geq -(\mu + \beta I) S$$

then

$$\frac{dS}{dt} \geq -(\mu+\beta I)S \text{ or } \frac{dS}{S} \geq -(\mu+\beta I)dt$$

Integrating both sides of the inequalities, gives

$$\ln S(t) \geq -(\mu+\beta I)t + C$$

$$S(t) \geq Ce^{-(\mu+\beta)t} \text{ but at } t = 0, \text{ we have}$$

$$S(t) \geq S(0)e^{-(\mu+\beta)t} \geq 0, \text{ since } (\mu+\beta) > 0.$$

From equation (2),

$$\frac{dE}{dt} = \beta SI - (\mu+\lambda)E \geq -(\mu+\lambda)E$$

Therefore

$$\frac{dE}{dt} \geq -(\mu+\lambda)E$$

Integrating both sides of the inequalities, gives

$$\ln E(t) \geq -(\mu+\lambda)t + C \text{ , at } t=0 \text{ we have}$$

$$E(t) \geq E(0)e^{-(\mu+\lambda)t} \geq 0, \text{ since } (\mu+\lambda) > 0.$$

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From equation (3)

$$\frac{dI}{dt} = \lambda E - (\mu+\alpha)I \geq -(\mu+\alpha)I$$

Therefore

$$\frac{dI}{dt} \geq -(\alpha+\mu)I$$

Integrating both sides of the inequalities

$$\ln I(t) \geq -(\mu+\alpha)t + C \text{ , at } t=0 \text{ we have}$$

$$I(t) \geq I(0)e^{-(\mu+\alpha)t} \geq 0, \text{ since } (\mu+\alpha) > 0.$$

From equation (4), is obtained

$$\frac{dR}{dt} = \alpha I - \mu R$$

Which has an integrating factor $I(t) = e^{\mu t}$

Therefore

$$\frac{dR}{dt}e^{\mu t} = \alpha I e^{\mu t} - \mu R(t)e^{\mu t}$$

integrating inequalities above, the results then become

$$R(t) = \frac{\alpha I}{\mu} + Ce^{-\mu t}, \text{ at } t = 0 \text{ we obtain}$$

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$$R(0) = \frac{\alpha I}{\mu} + C,$$

The solution of the linear differential equation then becomes

$$R(t) = R(0)e^{-\mu t} + \frac{\alpha I}{\mu}(1 - e^{-\mu t})$$

Therefore $R(t) = R(0)e^{-\mu t} + \frac{\alpha I}{\mu}(1 - e^{-\mu t}) \geq 0$, since $\mu > 0$

Hence, all variables are positive for all time $t > 0$.

3.14 Existence of Steady States of the System

The equilibrium points of the system can be obtained by equating the rate of changes to zero.

$$\frac{dS}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$$

3.14.1 Global asymptotic stability of the model

Before proving the global stability of the SEIR model above, there is the need to find the equilibrium points of the system (1) – (4).

If the system (1) – (4) is set to zero, this will give

$$\Lambda-\mu S-\beta SI= 0 \tag{3.61}$$

$$\beta SI - (\mu+\lambda)E = 0 \tag{3.62}$$

$$\lambda E – (\mu+\alpha)I = 0 \tag{3.63}$$

$$\alpha I - \mu R = 0 \tag{3.64}$$

adding (3.61) and (3.62)

$$\Lambda - \mu S - (\mu + \lambda)E = 0$$

Assuming that birth rate is equal to death rate, ie. $\Lambda= \mu$

$$\Rightarrow S = \frac{-(\lambda+\mu)E+\mu}{\mu} \tag{3.65}$$

From (3.63)

$$\lambda E = (\mu+\alpha)I \tag{3.66}$$

$$\Rightarrow I= \frac{\lambda E}{(\mu+\alpha)} \tag{3.66}$$

From (3.62)

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$$(\lambda+\mu)E = \beta SI = \beta\frac{[(-(\lambda+\mu)E+\Lambda)(\lambda E)]}{\mu(\mu+\alpha)}$$

$$(\lambda+\mu)E = \frac{-\beta(\lambda+\mu)\lambda E^2+\lambda\beta\Lambda E}{\mu(\mu+\alpha)} \qquad (3.67)$$

$$\frac{-\beta(\lambda\mu)\lambda E^2+\lambda\beta\Lambda E}{\mu(\mu+\alpha)} - (\lambda+\mu)E = 0$$

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$$\frac{-\beta(\lambda+\mu)\lambda E^2}{\mu(\mu+\alpha)} + \frac{\lambda\beta\Lambda E}{\mu(\alpha+\mu)} - (\lambda+\mu)E = 0$$

$$E[\frac{E(-\beta(\lambda+\mu)\lambda)}{\mu(\mu+\alpha)} + \frac{\lambda\beta\Lambda}{\mu(\mu+\alpha)}] - (\lambda+\mu)] = 0$$

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Either E = 0, OR

$$\frac{E(-\beta(\lambda+\mu)\lambda)}{\mu(\mu+\alpha)} + \frac{\lambda\beta\Lambda}{\mu(\mu+\alpha)} - (\lambda+\mu) = 0 \qquad (3.68)$$

$$E\left(\frac{-\beta(\lambda+\mu)\lambda}{\mu(\mu+\alpha)}\right) = (\lambda+\mu) - \frac{\lambda\beta\Lambda}{\mu(\mu+\alpha)}$$

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$$E\,(-\beta(\lambda+\mu)\lambda) = \mu\,(\mu+\alpha)(\lambda+\mu) - \frac{\mu\Lambda\lambda\beta\,(\alpha+\mu)}{\mu(\mu+\alpha)}$$

$$= \mu\,(\alpha+\mu)(\lambda+\mu) - \lambda\beta\Lambda$$

$$E = \frac{-\mu(\alpha+\mu)(\lambda+\mu)}{\beta(\lambda+\mu)\lambda} + \frac{\lambda\beta\Lambda}{\beta(\lambda+\mu)\lambda}$$

$$= \frac{-\mu(\alpha+\mu)}{\beta\lambda} + \frac{\Lambda}{(\lambda+\mu)}$$

$$E = \frac{\Lambda}{(\lambda+\mu)} - \frac{-\mu(\alpha+\mu)}{\beta\lambda}$$

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$$E = \frac{\Lambda}{(\lambda+\mu)}\left[1 - \frac{\mu(\alpha+\mu)(\mu+\lambda)}{\lambda\beta\Lambda}\right]$$

Since birth rate is equal to death rate, ie. $\Lambda=\mu$

Thus

$$E = E^* = \frac{\mu}{(\lambda+\mu)}\left[1 - \frac{(\alpha+\mu)(\lambda+\mu)}{\beta\lambda}\right] \qquad (3.68)$$

Realizing that given E = 0, from (3.65) S = 1 and from (3.66) and (3.64),

I = 0 and R = 0.

Thus the disease free equilibrium Z_o is $Z_o = (1, 0, 0, 0)$

Consider S from (3.65) and E from (3.68).

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ie

$$S = \frac{-(\lambda+\mu)E+\mu}{\mu} \quad \text{and} \quad E = \frac{\mu}{(\lambda+\mu)}\left[1 - \frac{(\alpha+\mu)(\lambda+\mu)}{\lambda\beta}\right]$$

It is realised that, $$S = \frac{-(\lambda+\mu)\mu}{(\lambda+\mu)}\left[1 - \frac{(\alpha+\mu)(\lambda+\mu)}{\beta\lambda}\right] + 1$$

$$S = \frac{-(\lambda+\mu)\mu}{(\lambda+\mu)\mu} + \frac{\mu(\lambda+\mu)(\alpha+\mu)(\lambda+\mu)}{\mu\beta\lambda(\lambda+\mu)} + 1$$

$$S = 1 + \frac{(\alpha+\mu)(\lambda+\mu)}{\beta\lambda} - 1$$

Clearly

$$S = \frac{(\alpha+\mu)(\lambda+\mu)}{\beta\lambda} \quad \text{thus}$$

$$S = S^* = \frac{(\alpha+\mu)(\lambda+\mu)}{\beta\lambda}$$

Also considering I from (3.66) and E from (3.68).

ie

$$I = \frac{\lambda E}{(\lambda+\mu)} \quad \text{and } E = \frac{\mu}{(\lambda+\mu)}\left[1 - \frac{(\alpha+\mu)(\lambda+\mu)}{\beta\lambda}\right]$$

It is clear that,

$$I = \frac{\lambda\mu}{(\lambda+\mu)(\alpha+\mu)}\left[1 - \frac{(\alpha+\mu)(\lambda+\mu)}{\beta\lambda}\right]$$

$$I = \frac{\lambda\mu}{(\alpha+\mu)(\lambda+\mu)} - \frac{\lambda\mu(\alpha+\mu)(\lambda+\mu)}{\beta\lambda(\alpha+\mu)(\lambda+\mu)}$$

$$I = \frac{\lambda\mu}{(\alpha+\mu)(\lambda+\mu)} - \frac{\mu}{\beta}$$

$$I = I^* = \frac{\lambda\mu}{(\alpha+\mu)(\lambda+\mu)}\left[1 - \frac{(\alpha+\mu)(\lambda+\mu)}{\lambda\beta}\right]$$

Using $R_0 \times S^* = 1$

$$R_O = \frac{\beta\lambda}{(\alpha+\mu)(\lambda+\mu)}$$

Therefore $S^* = \frac{1}{R_0}$, and $R^* = \frac{\lambda\alpha}{(\alpha+\mu)(\lambda+\mu)}\left[1 - \frac{1}{R_0}\right]$

$$E^* = \frac{\mu}{(\lambda+\mu)}\left[1 - \frac{1}{R_0}\right] \text{ and } I^* = \frac{\lambda\mu}{(\lambda+\mu)(\alpha+\mu)}\left[1 - \frac{1}{R_0}\right]$$

Which corresponds to an endemic steady state with constant number of people in the population being infected with the disease.

This is biologically reasonable when S* < N, that is when $R_o = \frac{\lambda\beta}{(\alpha+\mu)(\lambda+\mu)} > 1$

Where R_o is the basic reproduction ratio of the infection.

The local stability may be determined from the eigenvalues of the Jacobian matrix of the model equations (1) - (4). The Jacobian derivative is given as

$$J(S, E, I, R) = \begin{bmatrix} -(\mu+\beta I) & 0 & -\beta S & 0 \\ \beta I & -(\mu+\lambda) & \beta S & 0 \\ 0 & \lambda & -(\mu+\alpha) & 0 \\ 0 & 0 & \alpha & -\mu \end{bmatrix}$$

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Disease-free equilibrium

$$J(1,0,0,0) = \begin{bmatrix} -\mu & 0 & -\beta & 0 \\ 0 & -(\mu+\lambda) & 0 & 0 \\ 0 & \lambda & -(\mu+\alpha) & 0 \\ 0 & 0 & \alpha & -\mu \end{bmatrix}$$

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The eigenvalues at the disease 'free equilibrium' are given by {- μ, - (μ + λ),-(μ + α), -μ}. All the eigenvalues being negative means that the disease-free equilibrium is asymptotically stable. The basic reproductive number R_0 can be computed by

$R_0 \times S^* = 1$, Therefore, $Ro = \frac{\lambda\beta}{(\lambda+\mu)(\alpha+\mu)}$, where $(\mu + \alpha)(\mu + \lambda) \neq 0$

This means the transmission rate, i.e, the rate at which exposed become infected and the contact rate, that is the average number of effective contacts with other (susceptible) individuals per infective per unit time relative to the rate at which an infectious individuals recovered per unit time play an important role in determining whether or not an epidemic will occur. Hence the disease free equilibrium (1, 0, 0, 0) is locally asymptotically stable provided that $R_o < 1$, that is, $\lambda\beta < (\mu+\alpha)(\mu+\lambda)$.Where as if $R_o > 1$, then the disease free equilibrium is unstable, that is the system is said to be uniformly persistent, in other words the disease is endemic. Thus, R_o is a threshold parameter for the model.

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CHAPTER 4

MODEL APPLICATION, STABILITY ANALYSIS AND SIMULATIONS

4.0 Introduction

This chapter gives an illustration of the analytical results of the model by carrying out stability analysis and numerical simulations of the model using the parameter values pertinent to Ghana given in Table 4.1 below. These parameters were obtained from different sources in the literature (Index Mundi, 2011; Immunization Action Coalition, 2004; Trottier and Philippe, 2003).

Table 4.1: Model parameter values

Parameter symbol	Parameter value	Source
Λ	0.02755 per year	Index Mundi,2011
μ	0.00875 per year	Index Mundi,2011
β	0.09091 per day	Immunization Action Coalition
λ	0.125 per day	Trottier & Philippe,2003
α	0.14286 per day	Trottier & Philippe,2003

4.1 Stability Analysis of the Model

Endemic Model

$$\frac{ds}{dt} = \mu - (\mu + \beta i)s$$

$$\frac{de}{dt} = \beta si - (\mu+\lambda)e$$

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$$\frac{di}{dt} = \lambda e - (\mu + \alpha)i$$

$$\frac{dr}{dt} = \alpha i - \mu r$$

Linearising the system of the differential equations, the Jacobian matrix is given a

$$J(s, e, i, r) = \begin{bmatrix} -(\mu+\beta i) & 0 & -\beta s & 0 \\ \beta i & -(\mu+\lambda) & \beta s & 0 \\ 0 & \lambda & -(\mu+\alpha) & 0 \\ 0 & 0 & \alpha & -\mu \end{bmatrix}$$

For the infection free equilibrium (s, e, i) = (1,0,0), the Jacobian Matrix then becomes

$$J(1, 0, 0) = \begin{bmatrix} -\mu & 0 & -\beta \\ 0 & -(\mu+\lambda) & \beta \\ 0 & \lambda & -(\mu+\alpha) \end{bmatrix} = \begin{bmatrix} -0.0875 & 0 & -0.09091 \\ 0 & -0.2125 & 0.09091 \\ 0 & 0.125 & -0.23036 \end{bmatrix}$$

The important sub-matrix is the second 2×2 matrix. From this, the trace (T) < 0, but if $R_0 < 1$, then the determinant (D) > 0 and if $R_0 > 1$ then D < 0 for all parameters.

Routh-Hurwitz stability condition for T and D is given as follows:

$$T = -(2\mu+\lambda+\alpha) = -0.44286$$

$$D = (\mu+\alpha)(\mu+\lambda)(1-R_0) = 0.02488$$

Hence disease free study state is stable when $R_0 < 0$, and unstable when $R_0 > 0$. The eigenvalues at the disease 'free equilibrium' are given by

{- μ, - (μ + λ), - (μ + α),}. All the eigenvalues are negative meaning the disease-free equilibrium(1,0,0,0) is locally asymptotically stable.

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The endemic equilibrium (s*, e*, i*) = $\left(\frac{1}{R_0}, \frac{\mu(R_0-1)}{R_0(\mu+\lambda)}, \frac{\mu(R_0-1)}{\beta}\right)$

Jacobian Matrix for the endemic equilibrium is given as

$$J_{endemic} = \begin{bmatrix} -\mu R_0 & 0 & \frac{-(\mu+\alpha)(\mu+\lambda)}{\lambda} \\ \mu(R_0-1) & -(\mu+\lambda) & \frac{(\mu+\alpha)(\mu+\lambda)}{\lambda} \\ 0 & \lambda & -(\mu+\alpha) \end{bmatrix}$$

Characteristic equation is given as $Z^3+a_1Z^2+a_2Z+a_3= 0$, where

$a_1 = \lambda + \alpha + (2+R_0)\mu$,

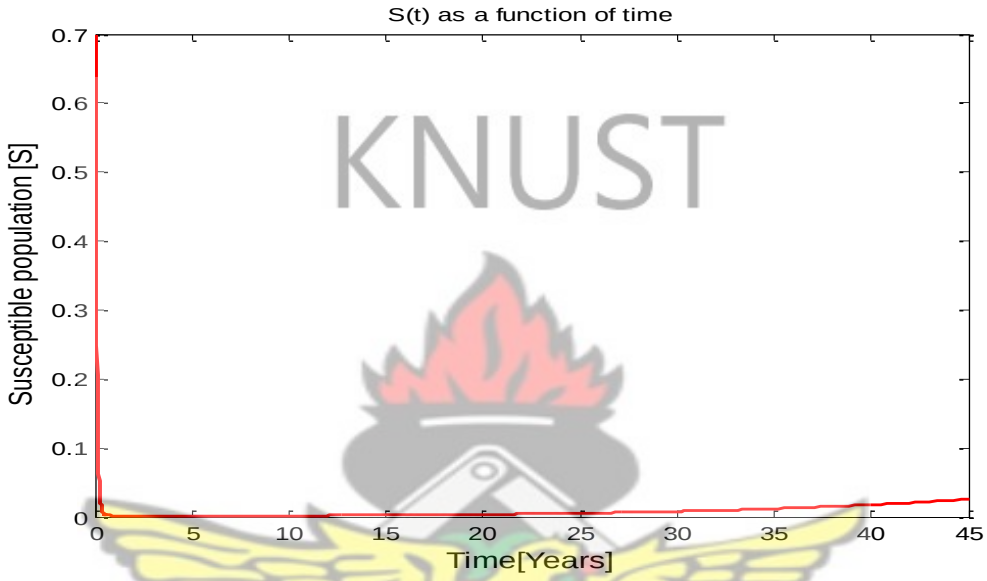
$a_2 = \mu R_0(2\mu + \lambda + \alpha)$,

$a_3 = \mu(R_0-1)[\mu^2 +\mu(\lambda + \alpha)+\lambda\alpha]$

If $a_1 > 0$, $a_2 > 0$ and $a_1a_2 - a_3 > 0$ are true then from the Routh-Hurwitz criteria for stability, all the roots of the characteristic equation have negative real part which means stable equilibrium.

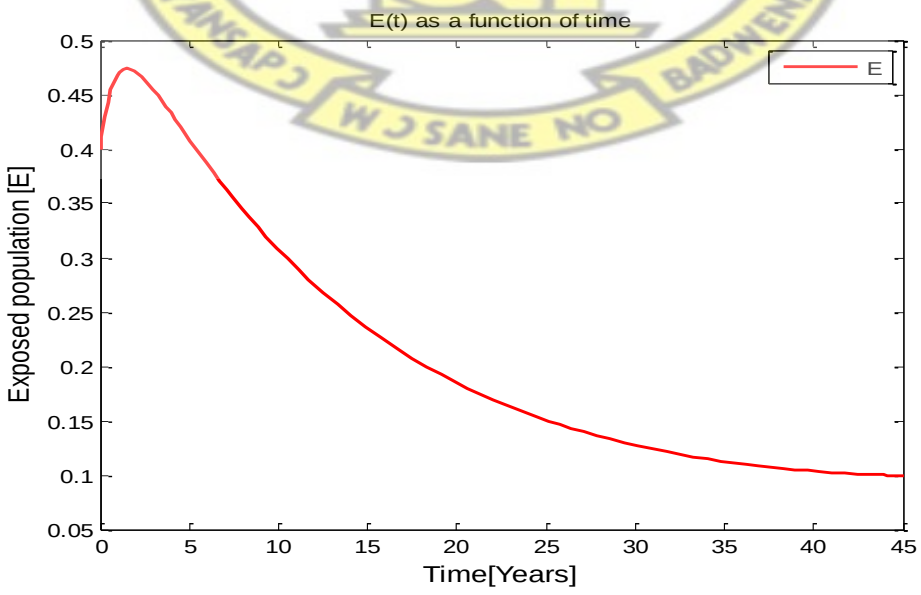
4.2 Numerical Simulations of the Model

For IVP (3.61) – (3.64), the approximate solutions S (t), E (t), I (t) and R (t) are displaced in Figures (4.1) - (4.4).



(4.1)

Figure 4.1: Simulation of Susceptible Population



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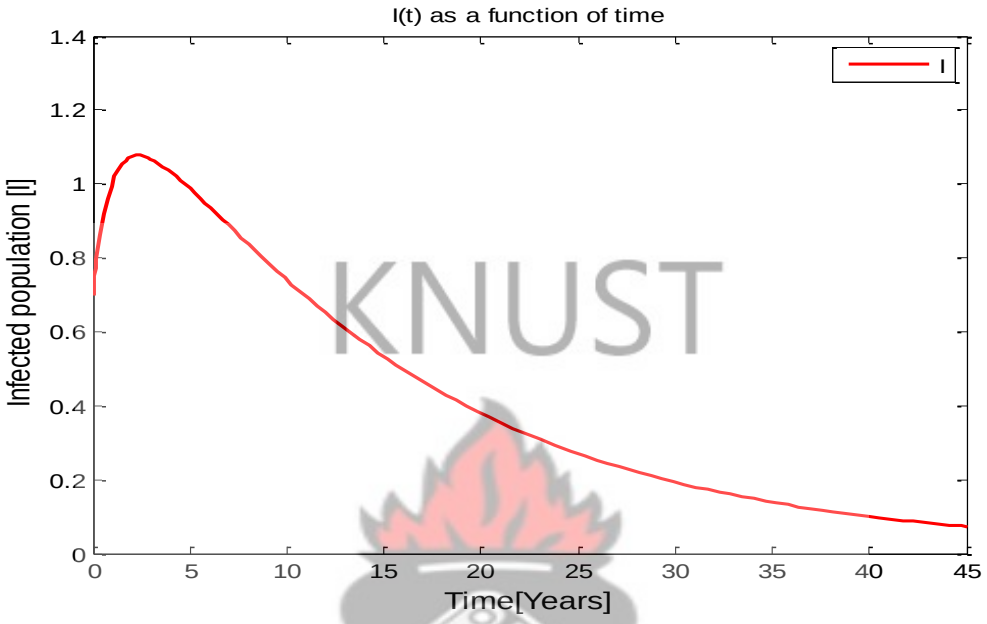
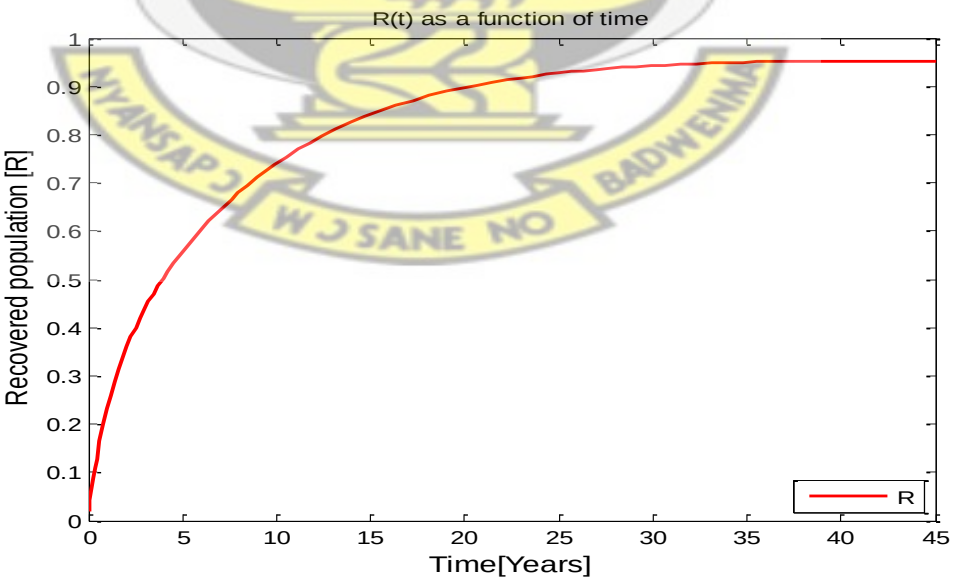
(4.2)

Figure 4.2: Simulation of Exposed Population.



(4.3)

Figure 4.3: Simulation of Infected Population.



(4.4)

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Figure 4.4: Simulation of Recovered Population.

4.3 Analysis of the Simulations

Figure 4.1 is the diagram showing the dynamics of the susceptible population.

The Susceptible population decreases as time increases. This decrease may be possibly because of the high rate of recovery due to mass vaccination, since individual become permanently immune upon recovery. The contact rate also has large impact on the spread of a disease through a population. The higher the rates of contact, the more rapid the spread of the disease, it is also observed that as the contact rate decreases, the fraction of individuals infected decreases at a faster rate as would be expected logically.

In Figure 4.2 it can be observed that as the rate increases, the population of exposed individuals shows some rapid decrease after the earlier intervals of rise. The decrease in the exposed population could be due to early detection and also possibly due to those who enter the infective class. This decrease could also be due to the education about the measles transmission, very few individuals are coming out as infected individuals. Also the dynamics of the exposed population depend on the contact number.

Observing Figure 4.3 carefully, it is realized that the population of infected individuals at the very beginning rise sharply as the rate increases and then fall uniformly as time increases. This rapid decline of the infected individuals may be due to early detection of the measles and partly due to those who revert to the Exposed class. This graph also demonstrates that the contact rate has large impact on the spread of the disease through population. If the contact rate is observed to be high then the rate of infection of the disease will also be high as would be expected logically. However, there exists another

parameter to consider, as more individuals are infected with the disease and I (t) grows, some individuals are also leaving the infected class by being cured and then join the Recovered class.

In figure 4.4 it is realized that the number of individuals Recovered rise steadily as rate increases.

This may be due to early detection of the disease as well as education about the measles transmission. It can also be observed that the population of the recovered individuals rise up steadily for some number of years and then drops and remains nearly a constant. This could be due to the greater number of infectious individuals who have been treated and also acquired education about the measles transmission.

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4.4 Conditions for control of measles

4.4.1 Herd immunity

Herd immunity is defined as the level of immunity in a population which can prevents epidemics of a disease, even if some transmission of that particular disease may still occur in a population.

If the percentage or proportion of the population that is immune exceeds the herd immunity level for the disease, then the disease can no longer persist in that particular population. Thus, if this level of immunity can be exceeded by means of mass vaccination, then the disease can indeed be eliminated.

Assuming that, the herd immunity level is denoted by *v*. Recall that, for a stable state:

$R_0 \times S = 1$.

So that, S will be $(1 - v)$, since v is the proportion of the population that are immune and $v + S$ must equal one (since in this simplified model, everyone is either susceptible or immune). Then:

$R_0 \times (1- v) = 1$, $1- v = \frac{1}{R_0}$, $v = 1- \frac{1}{R_0}$

Therefore, $V = (1- 0.0625) \times 100 = 93.75\%$

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Remember that this is the threshold level. If the proportion of immune individuals exceeds this level due to a mass vaccination programme, the disease will die out.

For instance, when a cohort of 400,000 newborns benefits 90% vaccine coverage, it yields 360,000 vaccinated and 40,000 unvaccinated. If vaccine efficacy is only 95%, it results 342,000 immune and 18,000 vaccinated but non-immune. Thus, it sums up to 342,000 immune and 58,000 susceptible, and the corresponding herd immunity is 85.5%. It is well known that, the higher R_0 is for a disease, the higher the proportion of the population that need to be vaccinated to achieve herd immunity.

Now let me assume that, in a given population if the average age at which a disease is contracted is A and the average life expectancy in that same population is given as L.

And it is assumed that everyone in the population lives to age L and then dies. If the average age of infection is A, then on average, individuals younger than A are susceptible and those older than A are immune. Thus the proportion of the population that is susceptible is given by

$S = \frac{A}{L}$

But the mathematical definition of the endemic steady state can be rearranged to give:

S = $\frac{1}{R_0}$, therefore, $\frac{1}{R_0} = \frac{A}{L}$ and this implies that, $R_0 = \frac{L}{A}$

By using the available data, we can estimate R_0

4.4.2 When mass vaccination cannot exceed the herd immunity

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If the mass vaccination due to the outbreak of a disease is insufficiently effective or the required coverage cannot be reached due to some reasons, for example in some community where the people have agree not to permit their children to be vaccinated due to some personal reasons, the programme may not be able to exceed q_c.

Suppose that a proportion of the population v (where $v < q_c$) is immunised at birth against an infection with $R_0 > 1$. The vaccination programme changes R_0 to R_q where

$R_q = R_0 (1- v)$, this change is as a result of now fewer susceptible will be in the population who can be infected. R_q is simply R_0 minus those that would normally be infected but that cannot be now since they are immune.

As a consequence of this lower basic reproduction number, the average age of infection A will also change to some new value A_q in those who have been left unvaccinated.

Assuming that life expectancy has not changed, now

$$R_q = \frac{L}{A_q}, \quad A_q = \frac{L}{R_q}, \quad A_q = \frac{L}{R_0(1-V)}$$

But $R_0 = L/A$ so

$$A_q = \frac{L}{L/A(1-V)},\ A_q = \frac{AL}{L(1-V)},\ A_q = \frac{A}{(1-V)},\ A_q = \frac{A}{S}$$

The vaccination programme caused the lowering of basic reproductive number, and this will also produce an increase in the average age of infection. Unvaccinated individuals now experience a reduced force of infection due to the presence of the vaccinated group.

4.5 When mass vaccination exceeds the herd immunity

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If a vaccination programme causes the proportion of immune individuals in a population to exceed the critical threshold for a significant length of time, transmission of the infectious disease in that population will gradually come to a halt.

4.6 Discussion

The main objective of this study is to model the transmission of measles in Ghana and also establish a possible way of reducing the disease transmission. In this thesis, a measles model is presented and analyzed to that effect. The basic reproductive number has been computed to determine the stability of the disease because theoretical determination of threshold conditions for R_0 is of important public heath interest. It was established qualitatively that the model has the disease- free equilibrium and endemic equilibrium points. It was realized that whenever $R_0 < 1$, the disease- free equilibrium point is locally asymptotically stable and unstable whenever $R_0 > 1$.

It was also realized that, in the absence of mass vaccination programme as well as early detection and supervised treatment, the transmission of the disease cannot be eradicated from the population. The introduction of proper treatment and education about the

disease transmission as well as early detection of the disease can help reduce the disease in a population.

The results has also shown that effective contact with the infectious individuals cause a major increase of the disease transmission, hence individuals with active measles must be detected as early as possible in order to reduce high transmission in a population. Education about measles can help many appear for diagnosis and get detected early.

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CHAPTER 5

CONCLUSION AND RECOMMENDATIONS

5.0 Introduction

In this chapter, a conclusion and recommendations are offered to stakeholders, the government, public health agencies and health care providers to enable them determine how best to allocate scarce resources for measles prevention and treatment in the country.

5.1 Conclusion

The model has shown success in attempting to predict the causes of measles transmission within a population. The model strongly indicated that the spread of a disease largely depend on the contact rates with infected individuals within a population.

From the model the herd immunity level for measles in Ghana was found to be 93.75%. It is also realized that if the proportion of the population that is immune exceeds the herd immunity level for the disease, then the disease can no longer persist in the population. Thus if this level can be exceeded by mass vaccination, then the disease can be eliminated.

The model also pointed out that early detection has a positive impact on the reduction of measles transmission; that is there is a need to detect new cases as early as possible so as to provide early treatment for the disease. More people should be educated in

order to create awareness to the disease transmission so that society will be aware of this deadly disease.

5.3 Recommendations

Eradication of contagious diseases such as measles has remained one of the biggest challenge facing developing countries like Ghana. It is realized that the herd immunity level for the disease which is 93.75% is high, and mostly when there is an outbreak of the disease, and there is an introduction of a mass vaccination programme which can cover about 97% of the population, not everybody will be immune because vaccine efficacy is usually not 100%. It therefore means that part of the population will be immune and others will be vaccinated but not immune. Therefore there is an urgent need for Ghana Health Service to come up with some new control strategies and more efficient ones to fight the spread of the disease in the country.

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Therefore; from the outcome of the results,

1) The model shows that the spread of a disease largely depend on the contact rate, therefore, the National Measles Control Programme should emphasize on the improvement in early detection of measles cases so that the disease transmission can be minimized.
2) To attain herd immunity level of 93.75% for the disease, mass vaccination exercise should be encouraged to cover the majority of the population whenever there is an outbreak of the disease in Ghana.

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APPENDIX A

MATLAB CODES FOR OBTAINING THE DYNAMICS OF THE PLOTS

```
%The function M-file used to obtain different plots

%function dy=s(t,y)

function dy=an(t,y)

dy=zeros(4,1);

Rec=0.02755;

%Rec=661200

%1beta=1.9466;mu=0.00875; alpha=0.14286;lamda=0.125;

%beta=0.001333;mu=0.02755; alpha=0.14286;lamda=0.125

1beta=0.00833;mu=0.00875; alpha=0.14286;lamda=0.125;

Ro=(alpha*beta)/((mu+alpha)*(mu+lamda));

S=y1(1); E=y2(2); I=y3(3);

R=y4(4); N=S+E+I+R;

dy(1)=Rec-mu*y1(1)-beta*y1(1)*y3(3);

dy(2)=beta*y(1)*y(3)-mu*y(2)-lamda*y(2);

dy(3)=lamda*y(2)-mu*y(3)-alpha*y(3);

dy(4)=alpha*y(3)-mu*y(4)
```

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APPENDIX B

MATLAB CODES FOR PRODUCING DIFFERENT PLOTS

```
%The function M-file used to obtain different plots

h0=[750 380 125 105];

h1=[80 15 10 65];

tspan=[0 45];

%Respan=[0.515 4.25]

%[t,y]=ode45(@anas,tspan,h0,h1);

%[t,y]=ode45(@an,tspan,h1);

[t11 y11]=ode45(@an,tspan,h0);

[t22 y22]=ode45(@an,tspan,h0);

[t33 y33]=ode45(@an,tspan,h0);

[t42 y42]=ode45(@an,tspan,h0);

%[Ro y]=ode45(@anas,Respan,h0)

%plot(t,y,'LineWidth',2)

%plot(t1,y1(:,1),'r',t1,y2(:,2),'g',t3,y3(:,3),'b',t2,y4(:,4),'k','LineWidth',2)

%plot(t1,y1(:,1),'r',t2,y2(:,2),'g','LineWidth',2)

%hold on plot(t,y(:,1),'-')
```

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```
%plot(t1,y1(:,1),'r','LineWidth',2)S

%plot(t2,y2(:,2),'r','LineWidth',2)E

%plot(t4,y4(:,4),'r','LineWidth',2)R

%plot(t,y1(:,1),'r',t4,y4(:,4),'g','Linewidth',2)

%plot(t1,y1(:,1),t2,y2(:,2),t3,y3(:,3),t4,y4(:,4),'LineWidth',2)

%%hold on plot(y(:,1),y(:,3),'b','LineWidth',2)

%plot(t2,y2(:,1),'r','LineWidth',2)

%hold on plot(t,y(:,4),'k')

%plot(t,y(:,1),'r',t,y(:,3),'b','LineWidth',2)

%hold on plot(t,y(:,2),'g')

%legend('\omega = 0.22','\omega = 0.51','\omega = 0.65','\omega = 0.85')

%legend('S','E')

%legend('R','Location','SouthEast')

%legend('I')

%legend('I','R','Location','SouthEast')

%legend('S','E','I','R','Location','NorthEast')

%legend('S','R')

%plot(t,y(:,4),'r','LineWidth',2) T
```

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```
%plot(t4,y4(:,4),'r','LineWidth',2)

%plot(t,(y(:,2)+y(:,3)+y(:,4)),'r','LineWidth',2)

%plot(Re,y(:,1),'r')

%plot(t1,y1(:,1),'r',t3,y3(:,3),'b')

%xlabel('Time[Years]','FontSize',12);

%ylabel('Exposed population','FontSize',12);

%ylabel( 'Infected population','FontSize',12);

%ylabel( 'Recovered population','FontSize',12);

%ylabel( 'Various Epidemiological Classes','FontSize',12);

%title('Epidemiological classes as a function of time');

%xlabel('Time[Years]','FontSize',12);

%ylabel('Various Epidemiological classes','FontSize',12)
```

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