KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

MATHEMATICAL MODEL FOR H1N1 HUMAN TO HUMAN TRANSMISSION IN BRONG AHAFO REGION

By

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Declaration

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

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Dedication

I dedicate this work to God Almighty, my wife Millicent Ofori Atuahene and my son.

Acknowledgements

My humble gratitude goes to God Almighty for his guidance and confidence that has enabled me to complete this work successfully. I would like to express my special appreciation and thanks to my supervisor Rev. Dr. William Obeng Denteh ,you have been tremendous mentor for me . I would like to thanks the this personalities Samuel Okyere, F. T. Oduro, Ebenezer Bonyah and Loius Munkayazi for wonderful publication which guide me through my work. I am also thankful to all the lecturers at the Mathematics Department of Kwame Nkrumah University of Science and Technology, Kumasi who have taught me in diverse ways for the award of this degree.

Abstract

In this work, SEIR model for H1N1 human transmission in Brong Ahafo Region of Ghana is formulated. The method of solution proves that the model possess positive solution. The basic reproduction number and the stability analysis of the disease free equilibrium and endemic states is carried out. The sensitivity analysis and the herd immunity of the model is also established. Numerical simulation of the model is carried out to show the results and represented graphically. The result indicates that by increasing the transmission rate (β) , the disease will spread but when the transmission rate is decreased the disease dies out. The results also indicate that %0.6 of the populate in Brong Ahafo needs to be vaccinated to control the disease in the region.

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Chapter 1

Introduction

1.1 Background of study

Flu, or influenza, is a contagious respiratory infection caused by a variety of flu viruses. Symptoms of flu involve muscle aches and soreness, headache, and fever. Flu viruses enter the body through the mucus membranes of your nose, eyes, or mouth. Every time you touch your hand to one of these areas, you are possibly infecting yourself with a virus. There are three types of flu viruses: A, B, and C. Type A and B cause the annual influenza epidemics that have up to 20% of the population sniffling, aching, coughing, and running high fevers. Type C also causes flu; however, type C flu symptoms are much less severe. There are three types of flu viruses: A, B, and C. Type A and B cause the annual influenza epidemics that have up to 20% of the population sniffling, aching, coughing, and running high fevers. Type C also causes flu; however, type C flu symptoms are much less severe. Type A flu virus is constantly changing and is generally responsible for the large flu epidemics. The influenza A2 virus (and other variants of influenza) is spread by people who are already infected. The most common flu hot spots are those surfaces that an infected person has touched and rooms where he has been recently, especially areas where he has been sneezing. Unlike type A flu viruses, type B flu is found only in humans. Type B flu may cause a less severe reaction than type A flu virus, but occasionally, type B flu can still be extremely harmful. Influenza type B viruses are not classified by subtype and do not cause pandemics. Unlike type A flu viruses, type B flu is found only in humans. Type B flu may cause a less severe reaction than type A flu virus, but occasionally, type B flu can still be extremely harmful. Influenza type B viruses are not classified by subtype and do not cause pandemics. Unlike type A flu viruses, type B flu is found only in humans. Type B flu may cause a less severe reaction than type A flu virus, but occasionally,

type B flu can still be extremely harmful. Influenza type B viruses are not classified by subtype and do not cause pandemics.

Influenza A (H1N1) is transmitted from person to person through large respiratory droplets expelled directly through coughing or sneezing, indirectly through contact with respiratory droplets or secretions, followed by touching the nose or the mouth, and one needs not to be more than one meter to be infected (Racaniello, 2009).Preventing transmission requires removing one or more of the conditions necessary for transmission for example, blocking and or minimizing the ways by which the virus can get to a susceptible host, inhibiting or killing the virus.

The rate at which the disease was spreading made the NADMO to come out with warning of possible outbreak of influenza H1N1(swine flu) in Ghana. The statement further issued that minors and children were the vulnerable groups. the spread of the influenza was also among a number of schools leading to their closed due to the overcrowding. it is against this background that, this research is embarked undertaken to develop a mathematical model to explain and inform the relevant publics about the transmission of H1N1 influenza.

It is against this background that, this research is embarked undertaken to develop a mathematical model to explain and inform the relevant publics about the transmission of H1N1 influenza.

1.2 Statement of the Problem

It has been indicated that the H1N1 virus had infected more than one million people worldwide (World Health Organisation, 2009). In the Ghana, the outbreak of H1N1 predominantly occurs in schools - Eastern, Volta and Brong Ahafo Region. this happens due to the overcrowding situation in most of the schools. All the regions of Ghana reported suspected cases except Upper East Region which did not confirm any suspected H1NI cases. There were 75% of Confirmed cases in Greater Accra Region and 5.5% in Eastern(GHS annual report). Ashanti Region

is no exception to the menace of the influenza virus H1N1. The region was first hit by the influenza A (H1N1) pandemic on August 31, 1918, on a ship arriving from Freetown, Sierra Leone and it spread across Ghana along the main lines of communication, killing at least 100,000 people. This has been followed by so many influenza outbreaks, for instance the 1957 to 1958 Asian Flu (H2N2) and 1968 to 1970 Hong Flu (H3N2). In April, 2005, outbreak of influenza A H5N1 and March, 2010, confirmed first case of pandemic Influenza A (H1N1) (Ghana Health Service, Kumasi, 2009).

The H1N1 poses public health and developmental challenges similar to challenges posed by communicable and chronic diseases. This requires decision makers to act in the face of substantial uncertainties.

Available literature suggests that H1N1 influenza has debilitating effect on any economy of which Ghana is no exception. However, there is no research on H1N1 influenza in the Brong Ahafo Region which has lead to speculations and mysteries regarding the pandemic. Besides, no mathematical model on the transmission of H1N1 influenza has been generated for sensitization .This has created a knowledge gap that needed to be filled.

This research therefore, sought to develop a mathematical model on transmission of H1N1 influenza.

1.3 Objectives

The research sought to achieve the following objectives

- To develop a mathematical model for the spread of H1N1 influenza through human to human transmission in the Brong Ahafo Region.
- To determine the stability of the equilibria and its reproductive number for the spread of the disease in the Brong Ahafo Region.

- Perform sensitivity analysis of the model parameters.

1.4 Justification of the Problem

H1N1 influenza is a pandemic which has created fear and panic in people .H1N1 virus is considered as dangerous due to the way it can spread easily through coughing ,sneezing and touching.The fact that many people lose their life and every individual is vulnerable if effective measures are not instituted to cure the spread of the disease .

Again ,this disease has a potential to reduce productivity since individuals affected will not be healthy engage in productive ventures, thereby reducing the growth of the economy.

It is therefore imperative to design a mathematical model as a means of creating awareness on how the disease is transmitted from one person to another . This will do away with the speculations and mysteries surrounding the disease since individuals will get a better understanding and appreciation of the H1N1 influenza.

1.5 Methodology

Mathematical model was model with compartmental diagrams, their system of ODE's solved at equilibrium, the basic reproductive number determine, diseasefree and endemic equilibrium state determined, stability analysis ,Herd Immunity was carried out.Numerical simulation was carried out using Matlab software and results graph and analyzed .

1.6 Organisation of the Study

This thesis comprises of five chapters. Chapter one reviews the background of the study, statement of the problem, the objectives of the study, the methodology applied in the study, as well as the justification and the organization of the thesis.

Chapter two consists of the review of relevant literature governing the theory. It took us through some of the various method of modeling H1NI diseases and its control.

In chapter three we formulate the SEIR differential equation model of the disease transmission. The equilibrium points or steady states, the stability analysis, as well as herd immunity and the reproductive number were determined.

Chapter four comprise of analysis and results. We determined the parameters of the differential equations and numerical simulation of the model equations by setting initial conditions.

Chapter five, the final chapter contains the conclusions and the recommendations of the thesis.

Chapter 2

Literature Review

2.1 Introduction

This reviewed is an attempt to discussed the historical perspective of the swine flu virus, its epidemiology and route of transmission to better understand the various control measures that may be taken to fight the danger of a global pandemic. Similarly, According to Leedy (1989), the purpose of the review of related literature on a study is to discover facts and findings, concerning the area of study and how they can propel the researcher to explore the unknown.

2.1.1 General Overview

It is interesting to notice the geographic variation in the spread of the H1N1 virus.

From the World Health Organization website, one may obtain daily updates of the number of the laboratory confirmed cases of influenza A (H1N1) for most countries. It indicated that, as of June 17, 2009, there were 39620 confirmed cases in the world, 17855 cases in the United States, and 6241 cases in Mexico. The United States in particular, the H1N1 influenza is linked to between 3,000 and 49,000 deaths and 200,000 hospitalizations each year .

From the Center for Disease Control and Prevention website, one can readily find that as of June 5, 2009, there were 2217 cases in Wisconsin, 858 cases in the New York state, and 247 cases in Florida. One of the goals of my model is to provide a realistic explanation for this geographic variation in the spread of the H1N1 virus. In the mathematical biology literature, several mathematical models have been proposed.

Okyere et al. (2012) presented the epidemiological model of influenza a (H1N1) transmission in Ashanti Region of Ghana. They show that pandemic potential of influenza A (H1N1) required decision makers to act in the face of uncertainties. A deterministic susceptible-exposed-infectious-recovered model was developed to study the spread of H1N1 using population data from the Ashanti region of Ghana.They assumed the population to be constant with birth rate equals death rate and they interact freely (homogeneous mixing).They determined the equilibria and stability of the equilibria with the aim of finding threshold conditions under which the disease spread or die out and illustrate the outcome with numerical solutions. Their results suggest that vaccinating 0.64 %of the susceptible population can significantly control the spread of the disease.

As intimated by Sinha (2009), the novel H1N1 influenza virus that emerged in humans in Mexico in early 2009 and transmitted efficiently in the human population with global spread has been declared a pandemic strain. Here they reviewed influenza infections in swine since 1918 and the introduction of different avian and human influenza virus genes into swine influenza viruses of North America and Eurasia. These introductions often resulted in viruses of

increased fitness for pigs that occasionally transmitted to humans. The novel virus affecting humans is derived from a North American swine influenza virus that has acquired two gene segments [Neuraminidase (NA) and Matrix (M)] from the European swine lineages. This reassortant appears to have increased fitness in humans. The potential for increased virulence in humans and of further reassortment between the novel H1N1 influenza virus and oseltamivir resistant seasonal H1N1 or with highly pathogenic H5N1 influenza stresses the need for urgent pandemic planning

From the point of view ofMalik et al. (2009) the one predictable aspect of influenza is its unpredictability. While attention was focused on the threat of an avian influenza H1N1 pandemic emerging from Asia, a novel influenza virus of swine origin emerged in North America, and is now spreading worldwide. The virus appears to confound us even in its nomenclature and the semantics of what constitutes a pandemic. During April, 2009, a novel H1N1 virus was detected in epidemiologically unrelated cases of influenza-like illness in California and was subsequently recognized to be the cause of a major outbreak of respiratory disease in Mexico that had been ongoing for some weeks previously. The virus was found to be an H1N1 virus that was antigenically and genetically unrelated to human seasonal influenza viruses and genetically related to viruses known to circulate in swine. In the ensuing weeks (as of 1st June 2009) this swine-origin influenza virus (S-OIV) H1N1 virus caused 17,410 virologically confirmed human cases and 115 deaths in 62 countries in the Americas, Europe, Asia and Australasia. The majority of the cases so far have been in Mexico (5029 with 97 deaths), USA (8975 with15 deaths) and Canada (1336 with 2 deaths).

From the standpoint of Racaniello (2009) Influenza A (H1N1) is transmitted from person to person through large respiratory droplets expelled directly through coughing or sneezing, indirectly through contact with respiratory droplets or secretions, followed by touching the nose or the mouth, and one needs not to be

more than one meter to be infected. Indeed, preventing transmission requires removing one or more of the conditions necessary for transmission for example, blocking and or minimizing the ways by which the virus can get to a susceptible host, inhibiting or killing the virus.

Biosei J. At this critical juncture when the world has not yet recovered from the threat of avian influenza, the virus has returned in the disguise of swine influenza, a lesser known illness common in pigs. It has reached pandemic proportions in a short time span with health personnel still devising ways to identify the novel H1N1 virus and develop vaccines against it. The H1N1 virus has caused a considerable number of deaths within the short duration since its emergence.

Presently, there are no effective methods to contain this newly emerged virus. Therefore, a proper and clear insight is urgently required to prevent an outbreak in the future and make preparations that may be planned well in advance.

Brockwell-Staats et al. (2009), point out that H1N1 influenza virus that emerged in humans Mexico in early 2009 and transmitted efficiently in the human population with global spread has been declared a pandemic strain. They reviewed that influenza infections in swine since 1918 and the introduction of different avian and human influenza virus genes into swine influenza viruses of North America and Eurasia. These introductions often result in viruses of increased fitness for pigs that occasionally transmit to humans.The novel virus affecting humans is derived from a North American swine influenza virus that has acquired two gene segments [Neuraminidase (NA) and Matrix (M)] from the European swine lineages. This reassortant appears to have increased fitness in humans. The potential for increased virulence in humans and of further reassortment between the novel H1N1 influenza virus and oseltamivir resistant seasonal H1N1 or with highly pathogenic H5N1 influenza stresses the need for urgent pandemic planning.

Shil et al. (2011) studied the transmission dynamics of an outbreak of novel influenza A/H1N1 (2009) in June-July 2009 in a residential school in Maharashtra, India . A mathematical model of the type susceptible-exposed infectiousasymptomatic-recovered was adopted for the purpose. Analyses of epidemiological data revealed that close clustering within population resulted in high transmissibility with basic reproduction number $R_0 = 2.61$ and transmission rate (β) being 0.001566. Model successfully described the dynamics of transmission in a residential school setting and helped in ascertaining the epidemiological parameters for asymptomatic cases and the effectiveness of the control measures. Their study presents a framework for studying similar outbreaks of influenza involving clustered populations. They stated that such models can be used to predict the pattern of disease propagation in the event of introduction of the virus in similar school settings and may also be used to assess the effectiveness of control measures. The transmission dynamics study provided estimates for various parameters for the outbreak such as the partial infectiousness and its duration in the asymptomatic cases, but concluded that such parameters were difficult to determine by clinical observations.

Chong et al. (2013) presented "A mathematical model of avian influenza with halfSaturated incidence".They developed a mathematical model of avian influenza for both bird and human populations. The effect of half-saturated incidence on transmission dynamics of the disease is investigated. The half-saturation constants determine the levels at which birds and humans contract avian influenza. To prevent the spread of avian influenza, the associated half saturation constants must be increased, especially the half saturation constant H_m for humans with mutant strain. The quantity H_m plays an essential role in determining the basic reproduction number of this model. Furthermore, by decreasing the rate b_m at which human-to-human mutant influenza is contracted, an outbreak can be controlled more effectively. To combat the outbreak, they

propose both pharmaceutical (vaccination) and non-pharmaceutical (personal protection and isolation) control methods to reduce the transmission of avian influenza. Vaccination and personal protection will decrease b_m, while isolation will increase H_m. Numerical simulations demonstrate that all proposed control strategies will lead to disease eradication; however, if they only employ vaccination, it will require slightly longer to eradicate the disease than only applying non-pharmaceutical or a combination of pharmaceutical and non-pharmaceutical control methods. In conclusion, it is important to adopt a combination of control methods to fight an avian influenza outbreak.

Hariyanto et al. (2013) stated the Construction of a Model of Pre-Coalition between H1N1-p and H5N1.Influenza Virus in Indonesia Influenza viruses which are often used for a study in Indonesia are H1N1-p, which is able to adapt without both hemaglutine and amino acids, and the H5N1 as a virus with 170 variants, consisting of 3 types whose spread varies widely. They considered the construction of a model of pre-coalition between influenza virus H1N1-p and one of H5N1 strains that attack poultry and humans. The reduction on the model is conducted based on the transition and genetic changes on individual population, via order the analysis of the co-existence of both virus transmissions. Their paper discusses the development of mathematical model of the spread of the virus which has the form of multi strain-multi species by constructing global diffusion only on susceptible and exposed population of both human and poultry hosts. The reduction of model is conducted based on transition and change experiences by every individual population. The approach performed emphasizing more on epidemiological aspect rather than mathematical aspect. Therefore the obtained model construction is more realistic. They concluded from their analysis on the influence of the virus on the system that: '1). On unstable condition of $R_o > 1$, H1N1-p influenza virus does not influence the change of the system if the density magnitude of susceptible population is bigger than the density of infected population and the coefficient of minimum global diffusion, 2) On a stable

condition of $R_0 < 1$, H5N1 influenza virus still influences the change of the system although the influence is little if the density magnitude of susceptible population is the same as the density of infected population , and 3).Co-existence from coinfection on H1N1-p and H5N1 virus can occur almost at the same time with the occurrence of the spread of each of H1N1-p and H5N1 virus.

Modeling the impact of an influenza A/H1N1 pandemic on critical care demand from early pathogenicity data: the case for sentinel reporting was presented by Ercole et al. (2009). Projected critical care demand for pandemic influenza H1N1 in England was estimated in their study. The effect of varying hospital admission rates under statistical uncertainty was examined. Early in a pandemic, uncertainty in epidemiological parameters leads to a wide range of credible scenarios, with projected demand ranging from insignificant to overwhelming. However, even small changes to input assumptions make the major incident scenario increasingly likely. Before any cases are admitted to hospital, 95% confidence limit on admission rates led to a range in predicted peak critical care bed occupancy of between 0% and 37% of total critical care bed capacity, half of these cases requiring ventilation support. For hospital admission rates above 0.25%, critical care bed availability would be exceeded. Further, only 10% of critical care beds in England are in specialist paediatric units, but best estimates suggest that 30% of patients requiring critical care will be children. Paediatric intensive care facilities are likely to be quickly exhausted and suggest that older children should be managed in adult critical care units to allow resource optimization. Their study highlights the need for sentinel reporting and real-time modeling to guide rational decision making. Their results indicate that if none of the first 6162 confirmed cases had been admitted to hospital, 95% confidence intervals for the hospital admission rate are calculated as 0-0.06%. This is significantly different to the United States admission rate of 9%. With these values, the modeled peak required critical care requirements for influenza cases alone ranges between 0% and 37% of capacity, with peak ventilator usage

ranging between 0% and 19% of total capacity. As increasing numbers of patients are hospitalised the lower bound on peak predicted impact rises rapidly. Best case critical care bed capacity is exceeded for hospitalisation rates above 0.25% (approximately 15 out of the current 6162 confirmed cases). Pandemic modeling and forecasting depends critically on epidemiological data. Unfortunately there is considerable statistical uncertainty in these parameters in the early stages of any outbreak, when the case numbers are small. Theyindicate that the available data are inevitably biased due to under-reporting and the lag between disease presentation, diagnostic confirmation and clinical progression making real-time prediction difficult. In the most uncertain scenario, before any patients are reported to have been hospitalised, their model suggests that the predicted effect on critical care resources ranges from no impact to a significant proportion of beds (37%) and ventilators (19%) being utilized. Best case predictions suggest that all critical care beds will be filled with influenza A/H1N1 patients if the hospital admission rate is greater than 0.25%. Disturbingly, even small increases to the observed admission rate make the overwhelming scenario increasingly statistically credible. They used the FLUSURGE model to estimate peak critical care bed occupancy. Whilst their estimates employed contemporary virulence data, the model makes assumptions regarding the detailed kinetics of disease spread which cannot be prospectively verified. This is an unavoidable limitation of their stud. They assumed an arbitrary pandemic duration of 12 weeks. However, their results scale inversely with duration and are thus easily generalizable.

Prosper et al. (2011) presented Modeling control strategies for concurrent epidemics of seasonal and pandemic H1N1 influenza. They state that the lessons learned from the 2009-2010 H1N1 influenza pandemic, as it moves out of the limelight, should not be under-estimated, particularly since the probability of novel influenza epidemics in the near future is not negligible and the potential consequences might be huge. Hence, as the world, particularly the industrialized

world, responded to the potentially devastating effects of this novel A-H1N1 strain with substantial resources, reminders of the recurrent loss of life from a well established foe, seasonal influenza, could not be ignored. The uncertainties associated with the reported and expected levels of morbidity and mortality with this novel A-H1N1 live in a backdrop of 36, 000 deaths, over 200,000 hospitalizations, and millions of infections (20% of the population) attributed to seasonal influenza in the USA alone, each year. So, as the Northern Hemisphere braced for the possibility of a potentially ”lethal” second wave of the novel A-H1N1 without a vaccine ready to mitigate its impact, questions of who should be vaccinated first if a vaccine became available, came to the forefront of the discussion. Uncertainty grew as they learned that the vaccine, once available, would be unevenly distributed around the world. Nations capable of acquiring large vaccine supplies soon became aware that those who could pay would have to compete for a limited vaccine stockpile. The challenges faced by nations dealing jointly with seasonal and novel A-H1N1 co-circulating strains under limited resources, that is, those with no access to novel A-H1N1 vaccine supplies, limited access to the seasonal influenza vaccine, and limited access to antivirals (like Tamiflu) are explored in this study. One and two-strain models are introduced to mimic the influenza dynamics of a single and co-circulating strains, in the context of a single epidemic outbreak. They used Optimal control theory to identify and evaluate the ”best” control policies. The controls account for the cost associated with social distancing and antiviral treatment policies. They also indicate that the optimal policies identified might have, if implemented, a substantial impact on the novel H1N1 and seasonal influenza co-circulating dynamics. Specifically, the implementation of antiviral treatment might reduce the number of influenza cases by up to 60% under a reasonable seasonal vaccination strategy, but only by up to 37% when the seasonal vaccine is not available. Optimal social distancing policies alone can be as effective as the combination of multiple policies, reducing the total number of influenza cases by more than 99% within a single outbreak, an unrealistic but theoretically possible outcome for isolated populations with

limited resources. They concluded that, in addressing the problem by applying optimal control theory to the SAIR model for novel H1N1 allowed them to determine optimal strategies for minimizing the H1N1 outbreak in a cost-effective manner. Using a combination of social distancing and treatment, the optimal strategy reduced the number of H1N1 infections by more than 99% during the 100-day control period; social distancing alone produced similar results. However, the optimal treatment-only strategy only reduced morbidity by 63% when the cost was low. This percentage decreases as the cost of treatment increases. This shows that for them using optimal control theory, they determined that implementing treatment and social distancing control measures optimally has a substantial effect on controlling the number of infections during an outbreak.

Velasco-Hernandez and Leite (2011) stated "A model for the A(H1N1) epidemic in Mexico, including social isolation". They present a model for the 2009 influenza epidemic in Mexico to describe the observed pattern of the epidemic from March through the end of August (before the onset of the expected winter epidemic) in terms of the reproduction number and social isolation measures. The model uses a system of ordinary differential equations. The model is based on a SEIR compartmental scheme and includes compartments for social isolation. They performed computer simulations to optimize trajectories as a function of parameters. They report on the theoretical consequences of social isolation using published estimates of the basic reproduction number. The comparison with actual data provides a reasonable good fit. They indicate that the pattern of the epidemic outbreak in Mexico is characterized by two peaks resulting from the application of very drastic social isolation measures and other prophylactic measures that lasted for about two weeks. Their model is capable of reproducing the observed pattern. They concluded that the epidemic outbreak in Mexico shows two peaks resulting from the application of drastic social isolation and other prophylactic measures that lasted at least two weeks. They reproduced this

pattern, showing that it only occurs within a relatively narrow range of values for crucial parameters, such as the basic reproduction number, the isolation rate and the waning of prevention measures. Significant qualitative changes in this pattern obtained through manipulation of these parameters generated delayed single-peak epidemics appearing many weeks after the end of the isolation period, or two-peaked epidemics but with much greater delay between them. They indicate that Mexico is a large country and the influenza epidemic occurred in geographically distant and different regions. Their model shows that the data reported by the federal Ministry of Health lumps together such geographical complexity, since social isolation and other measures were implemented across the whole country, their effect on local epidemics was likely the same as that observed at the country level. Finally, their model incorporates a minimal amount of information that can reproduce the observed pattern using only known parameters and excluding treatment.

Coburn et al. (2009) presented "Modeling influenza epidemics and pandemics: insights into the future of swine flu (H1N1)". They presented a review of the literature of influenza modeling studies, and discuss how the models can provide insights into the future of the currently circulating novel strain of influenza A (H1N1), formerly known as swine flu. They discuss how the feasibility of controlling an epidemic critically depends on the value of the Basic Reproduction Number (R_0). They observed that the R_0 for novel influenza A (H1N1) was recently been estimated to be between 1.4 and 1.6. The value was below values of R_0 estimated for the 1918-1919 pandemic strain (mean R_0 2: range 1.4 to 2.8) and is comparable to R_0 values estimated for seasonal strains of influenza (mean R_0 1.3: range 0.9 to 2.1). By reviewing results from previous modeling studies they conclude it is theoretically possible that a pandemic of H1N1 could be contained. However it may not be feasible, even in resource-rich countries, to achieve the necessary levels of vaccination and treatment for control. As a recent

modeling study has shown, a global cooperative strategy will be essential in order to control a pandemic. This strategy will require resource-rich countries to share their vaccines and antivirals with resource-constrained and resource-poor countries. They conclude their review by discussing the necessity of developing new biologically complex models. They suggested that the models should simultaneously track the transmission dynamics of multiple strains of influenza in bird, pig and human populations. Such models could be critical for identifying effective new interventions, and informing pandemic preparedness planning. Finally, they show that by modeling cross-species transmission it may be possible to predict the emergence of pandemic strains of influenza. They also recommend for more biologically complex models to be developed.

Modeling of H1N1 Flu in Iran was stated by Haghdoost et al. (2009). They realized that new H1N1 flu strain has rapidly become a serious threat worldwide. This pandemic calls for urgent preparedness to mitigate its impact as much as possible. Employing this knowledge, they simulated a model of the outbreak of H1N1 in two cities of Iran (middle size: Kerman and metropolitan: Tehran). They developed a compartmental model to predict the expected number of patients who might develop severe (S), very severe (VS) disease or die (D). They assumed that, in winter, the Basic Reproductive Number (R_{0w}) would reach 1.6 in Kerman and 1.8 in Tehran, respectively. Corresponding figures in summer varied from 1.2 (R_{0sMin}) to 1.4 (R_{0sMax}) in Kerman and from 1.3 to 1.5 in Tehran. Also, they checked the effect of the number of imported infectious cases at the beginning of the outbreak based on predictions. The result obtained indicate that a minimum lag of six months was observed between introduction of the virus (June 2009) and beginning of the outbreak (December 2009). The lag was sensitive to the number of infectious cases and the R_0: a lower R_0 postponed the peak. In Kerman, with R_{0sMax} of 1.4, the number of S, VS, and D were 2,728, 546 and 468 respectively. Corresponding numbers in Tehran with R_{0sMax} of 1.5 were 83,363,

16,673, and 14,291. They concluded by stating that, since the number of S and VS cases would be crowded over a short period of time, the health care system most probably would not be able to provide appropriate services unless special measures are taken in advance. By reduction of R_0 and the number of introduced infectious cases the peak of the outbreak might be postponed to the end of 2010. This would provide a golden opportunity to vaccinate a considerable proportion of the population.

A Classical Approach for Estimating the Transmissibility of the 2009 H1N1 Pandemic was showed by Mostaco-Guidolin et al. (2011). Following the emergence of an infectious disease, estimates of parameters pertaining to the nature of infection and its epidemiological characteristics are necessary to inform health policy decision making, and identify the type and intensity of interventions required for the prevention and control of disease spread. Mathematical modeling has proven to be an essential tool for describing disease dynamics in the population, and providing frameworks for estimating such parameters. Here, they apply a classical approach to demonstrate the usefulness of a simple mathematical SEIR model in estimating the reproduction number of a disease, defined as the number of secondary infections generated by a single infected case. Using data for laboratory confirmed cases of the 2009 H1N1 influenza pandemic, they estimate its transmissibility in Winnipeg, an urban center in the province of Manitoba, Canada. While detailing our results, they discuss the importance of integrating modeling, data analysis, simulations, and translating the findings into the context of public health for managing an emerging crisis.

Chao et al. (2011) presented Planning for the control of Pandemic Influenza A (H1N1) in Los Angeles country and the United States Mathematical and computer models can provide guidance to public health officials by projecting the course of an epidemic and evaluating control measures. They built upon an existing collaboration between an academic research group and the Los Angeles County,

California, Department of Public Health to plan for and respond to the first and subsequent years of pandemic influenza A (H1N1) circulation. The use of models allowed the them to,

1) project the timing and magnitude of the epidemic in Los Angeles County and the continental United States; 2) predict the effect of the influenza mass vaccination campaign that began in October 2009 on the spread of pandemic H1N1 in Los Angeles County and the continental United States; and 3) predict that a third wave of pandemic influenza in the winter or spring of 2010 was unlikely to occur. The close collaboration between modelers and public health officials during pandemic H1N1 spread in the fall of 2009 helped Los Angeles County officials develop a measured and appropriate response to the unfolding pandemic and establish reasonable goals for mitigation of pandemic H1N1. The use of epidemic simulation models to influence and direct local health department planning and operational response represents an important collaboration between research and public health practice. As evidenced in the utilization and adaptation of our pandemic influenza simulations by the LA County DPH during the pandemic H1N1 response, realistic and effective models allow local public health planners to use simulations to evaluate various disease control strategies and to better understand and respond to infectious disease events. Based on community demographic data and transportation patterns, the models provide local emergency health planners with a unique tool both to quantify the emerging threat (morbidity, hospitalizations,mortality, etc.) and to predict the effects and benefits of proposed pharmaceutical and non pharmaceutical interventions. They had initially planned for a devastating H5N1 pandemic, and as the FHCRC/UW group quickly adapted the model to pandemic H1N1, they projected a manageable scenario that did not require the disruption of schools or hospitals. The mild pandemic forecasts afforded the LA County DPH the opportunity to allocate scarce public health resources more wisely. Community-based simulation models provide an analytical set of tools, further enabling local health

officials to evaluate proposed strategies and make informed decisions. They also provide a starting point from which other local jurisdictions can evaluate and determine their best intervention and response strategies as well. They believe that their simulation-based approach to influenza pandemic guidance in LA County is general enough to apply to much of the United States. Their simulations of pandemic H1N1 in LA County and the continental United States produced similar results. Simulations for both LA

County and the United States featured unmitigated illness attack rates of approximately 21.5%

Hattaf and Yousfi (2009) presented Mathematical Model of the Influenza A (H1N1) Infection. The aim of their work was to give a mathematical model describing the transmission of influenza A (H1N1) virus and discuss how the model can provide insights into the future of the currently circulating novel strain of influenza A (H1N1). They proved that the disease will die out if the basic reproductive number $R_0 > 1$ while the disease may become endemic if $R_0 < 1$. The stability analysis of both endemic and disease free equilibrium were also discussed. They also gave some numerical simulations to illustrate their results and predict the the evolution of the disease in Morocco. The simulation of the model provides that the number of the infected individuals in Morocco begins to increase from 8 December, 2009. It will reach its maximum on 8 April, 2010 which is about one million and 968 200 cases and it decreases asymptotically to endemic equilibrium state which is 1 937 cases, it will arrive at this state on 22 July, 2010. They concluded that the Ministry of Health of Morocco starts by vaccination people with low immunity from 9 December, 2009, in order to reduce the number of infected cases.

Balbach et al. (2009) showed Mathematical Modeling of H1N1. Mathematical models have been used to understand the dynamics of infectious diseases and to predict the future epidemic or pandemics. In 2009, a new strain of the influenza

A (H1N1) virus spread rapidly throughout the world. This ”swine flu,” as it is commonly known, increased to what is considered an epidemic in a matter of months. In order to understand the spread of this virus, and similar patterns in future outbreaks, they study a simplified SIR mathematical model to answer some epidemiological questions. They solved the model numerically and also study the qualitative properties of the model. It is important to mention that a solution of a mathematical model is not necessarily a solution to the real problem, but a solution to a simplified idealization of the real world problem. By using initial Susceptible, Infected and Recovered values from the CDC website, they were able to model the U.S. H1N1 flu based on a SIR model. A β value of 0.02 and γ value of 0.1 was used based on a report on the SIR Model by Rachel Ragan. They then modeled the flu taking into account seasonal effects. They used different γ corresponding to the periodic nature of the cosine function.

Sato et al. (2010) presented ”When should we intervene to control the 2009 influenza A(H1N1) pandemic”?. They simulated the early phase of the 2009 influenza A(H1N1) pandemic and assessed the effectiveness of public health interventions in Japan. They show that the detection rate of border quarantine was low and the timing of the intervention was the most important factor involved in the control of the pandemic, with the maximum reduction in daily cases obtained after interventions started on day 6 or 11. Early interventions were not always effective. They estimated the number of imported cases of pandemic influenza that passed the border quarantine undetected. The domestic pandemic caused by these cases was simulated using mathematical simulation to assess the optimal public health intervention to the influenza pandemic in the early pandemic phase in Japan. Their estimation of cases undetected in onboard quarantine inspections demonstrated the low detection rate of the technique. On 28 April 2009, the World Health Organization (WHO) advised that no restriction of regular travel or closure of borders be implemented against the pandemic influenza virus. Their results were consistent with these views. To effectively

slow the epidemic curve, the Japanese public health responses to the pandemic influenza virus would have had to shift the emphasis from onboard quarantine inspection to active surveillance and preparation, and such interventions would have been necessary as soon as the first case of the virus was detected by the onboard quarantine inspection. However, their simulation of viral transmission showed that early initiation of an intervention is not always effective in reducing the maximum number of daily cases, as a secondary increase in influenza cases was observed after the implementation of the early intervention. They used the standardised person-day ratio as an indicator of required resources and showed various patterns of effectiveness versus resources. They concluded that the metod adopted by the Japan was ineffective in preventing the spread of the infection.

Yarmand et al. (2010) presented ”A Simulation-Based Analysis of Different Control Policies for H1N1”. They conducted a cost-effectiveness analysis to examine the relative importance of vaccination and self-isolation in case of H1N1 by developing a continuous-time simulation model for the spread of H1N1. The optimization model used consists of two decision variables, vaccination fraction and self-isolation fraction among infectives, and two upperbound constraints for maximum number of individuals under treatment and percentage of infectives. By considering the relative marginal cost for each decision variable, they used a linear objective function representing the relative cost of each control policy. They used grid search to obtain insight into the model and to find ”goo” feasible solutions.

The model they developed in their work is an extension of the SEIR model for H1N1 with three types of interventions (vaccination, antiviral prophylaxis and antiviral treatment, and self-isolation and mandatory quarantine). Their preliminary results show that vaccination is much more effective than self-isolation in controlling the diseases. They concluded based on the following summarized reasons. The direct effect of vaccination is to reduce the number of

susceptibles. But vaccination has an indirect effect as well. Indeed any intervention that reduces the number of susceptibles, would also reduce the number of infectives with a delay. That is because the horizontal incidence, which determines the rate at which susceptibles become infected, depends on the density of both susceptibles and infectives. Therefore fewer susceptibles would result in lower horizontal incidence, which in turn results in fewer infectives, and again lower horizontal incidence. On the other hand, self-isolation only has a direct effect which is to reduce the number of infectives. Due to the two fold impact of vaccination, they stated that health care officials should pay particular attention to vaccination in their attempts to control the spread of an infectious disease and in particular, the current H1N1 outbreak.

The Effect of Risk Perception on the 2009 H1N1 Pandemic Influenza Dynamics was studied by Politti et al. (2011). They observed that the 2009 H1N1 pandemic influenza dynamics in Italy was characterized by a notable pattern: as it emerged from the analysis of influenza-like illness data, after an initial period (September-mid-October 2009) characterized by a slow exponential increase in the weekly incidence, a sudden and sharp increase of the growth rate was observed by mid-October. Their main aim is to understand whether spontaneous behavioral changes in the population could be responsible for such a pattern of epidemic spread. For this issue, they propose a mathematical model of influenza transmission, accounting for spontaneous behavioral changes driven by cost/benefit considerations on the perceived risk of infection, and validated against empirical epidemiological data. The performed investigation revealed that an initial overestimation of the risk of infection in the general population, possibly induced by the high concern for the emergence of a new influenza pandemic, results in a pattern of spread compliant with the observed one. Their finding is also supported by the analysis of antiviral drugs purchase over the epidemic period. Also, by assuming a generation time of 2.5 days, the initially diffuse misperception of the risk of infection led to a relatively low value of the

reproductive number 1:24, which increased to 1:48 in the subsequent phase of the pandemic. Finally, they concluded by indicating that spontaneous behavioral changes in the population, not accounted by the large majority of influenza transmission models, can not be neglected to correctly inform public health decisions. But, individual choices can drastically affect the epidemic spread, by altering timing, dynamics and overall number of cases.

Pongsumpun (2013) presented Model for the Transmission of Influenza Pandemic

Due to a New-Strain of the H1N1 Influenza a Virus with the Risk of Infection in Human. A New-strain of the H1N1 Influenza A Virus is transmitted between the people through coughing and sneezing. The virus spreads when droplets from a cough or sneeze of an infected person are propelled through the air and deposited on the mouth or nose of people nearby. This virus can also be contacted by touching something, contaminated with flu viruses and then touching their eyes. He study the transmission of this disease by constructing the mathematical model. The model is formulated by dividing the human into 5 groups such that Susceptible, Exposed, Infectious, Quarantine and Recovered classes. The contact between risk and non-risk groups is considered. Analysis of the dynamical model is done by using standard dynamical modeling method. He showed analytical and numerical results of the model. The output of the model were simulated for 2 cases. The case 1 was for the local stability when $V_0 > 1$, and observed that the fractions of populations oscillate to the endemic state. For case 2, when $V_0 < 1$, the fractions of populations converge to the disease free state. He also compare the solution behaviors when there is the different basic reproductive numbers. It was observed that the length of epidemic outburst is shorter and the fraction of populations is higher when the basic reproductive number is bigger. The period of oscillations as they oscillate to the endemic state by means of solutions of the linearized system are calculated, he get 9 days, 5 days for $V_0 = 20$ and $V_0 = 30$, respectively. This means that if the number of secondary infectious cases

reproduced from primary cases is higher, then the time for controlling the epidemic outbreak is shorter.

2.1.2 Types of H1N1

According to World Health Organization (WHO), There are three types of influenza viruses: A, B and C. Human influenza A and B viruses cause seasonal epidemics of disease almost every winter in the United States. The emergence of a new and very different influenza virus to infect people can cause an influenza pandemic. Influenza type C infections cause a mild respiratory illness and are not thought to cause epidemics.

Influenza A viruses are divided into subtypes based on two proteins on the surface of the virus: the hemagglutinin (H) and the neuraminidase (N). There are 18 different hemagglutinin subtypes and 11 different neuraminidase subtypes. Influenza A viruses can be further broken down into different strains. Current subtypes of influenza A viruses found in people are influenza A (H1N1) and influenza A (H3N2) viruses. In the spring of 2009, a new influenza A (H1N1) virus (CDC, 2009) emerged to cause illness in people. This virus was very different from regular human influenza A (H1N1) viruses and the new virus caused the first influenza pandemic in more than 40 years. That virus (often called "2009 H1N1") has now mostly replaced the H1N1 virus that was previously circulating in humans.

Influenza B viruses are not divided into subtypes, but can be further broken down into different strains.CDC follows an internationally accepted naming convention for influenza viruses. This convention was accepted by WHO in 1979 and published in February 1980 in the Bulletin of the World Health Organization. Influenza A (H1N1), A (H3N2), and influenza B viruses are included in each year's influenza vaccine. Getting a flu vaccine can protect against flu viruses that are the same or related to the viruses in the vaccine. Information about this season's vaccine can be found at preventing seasonal flu with vaccination. The seasonal flu

vaccine not protect against influenza C viruses. In addition, flu vaccines will not protect against infection and illness caused by other viruses that can also cause influenza-like symptoms. There are many other non flu viruses that can result in influenza-like illness (ILI) that spread during the flu season.

2.1.3 Causes and Prevention

Flu, or influenza, is a contagious respiratory infection caused by a variety of flu viruses. Symptoms of flu involve muscle aches and soreness, headache, and fever. Flu viruses enter the body through the mucus membranes of your nose, eyes, or mouth. Every time you touch your hand to one of these areas, you are possibly infecting yourself with a virus. This makes it very important to keep your hands germ-free with frequent and thorough hand washing. Encourage family members to do the same to stay well and prevent flu.

In Ghana,World Health Organisation(WHO) was assisting Ghana to receive additional vaccines for the general public of which the country would have had to take care of the shipping cost and also the cost of distribution. The Director of Public Health in Ghana said his outfit was beginning an orientation programme for health professionals who would administer the vaccines at the national level and said all the ten regions would have their training within the regions, to be followed with the administration of the vaccines to the identified group. The vaccines had already been sent to the various regions ready to be administered.They also indicated that the rate at which people were catching the influenza had slowed down as compared to March this year and added that Ghana was recording more cases because health workers had been vigilant in looking up for the cases. He indicated that in some countries the case was different, as health professionals were rather playing down on the spread of the disease, a situation he pointed out was not the best and reiterated the need for the observance of personal hygiene to prevent the spread of the disease, since it was not yet over.

Posted by Lucy Adoma Yeboah

Stories at 2 : 59 AM http://lucyadoma.blogspot.com/2010/0...1n1-death.html

July 28th, 2010

2.1.4 Mathematical Model

The SIR Model is the relatively good predictor for infectious diseases such as measles, mumps, and rubella. Under this model, when an individual becomes infected, he/she becomes immediately infectious and is able to infect other individuals.

However, the infected individuals may recover from the disease and therefore move to a recovered class, where they will be no longer infectious while acquiring immunity to the disease.

Chapter 3

Methodology

The model we decided to use in studying the H1N1 virus is the susceptibleexposed-infectious-recovered compartmental model, or more commonly the SEIR model (Anderson and May, 1991). This model is the same as the SIR model, except that before the individual becomes infectious, of course he/she will be exposed to the environment. For the model, we consider four basic classes: 1. Susceptible (S); 2. Exposed (E); 3. Infectious (I); 4. Recovered (R). Susceptible class are individuals in the population who are at risk of becoming infected with

H1N1 virus. The exposed class are individuals who have been infected with the H1N1 virus but not infectious (show no symptoms and cannot pass on the disease). Infectious class are Individuals who have been infected with the H1N1 and can pass it on to susceptible persons. Lastly, the recovered class are individuals who have recovered or been removed from H1N1 infection (Uhavax, 2001). For the model, we assume births and deaths occur at equal rate and that all newborns are susceptible (no inherited immunity). We denote the average birth and death rate by μ . The rate at which individuals are born into the susceptible class with no passive is μS . We also assume the population mix homogeneously, with no restriction of age, mobility or other social factors. Once infected, you become exposed to the environment before becoming infectious. The rate at which susceptible enters the exposed class without been infectious is βSI and the rate at which an exposed person becomes infectious is αE . The rate at which an infected individual may recover and will remain until death is γ . The transmission coefficient is $\beta > 0$, the latency coefficient $\alpha > 0$, the recovery coefficient $\gamma > 0$ and the capital death rate $\mu > 0$. The flow diagram for the SEIR model is given in Figure 3.1

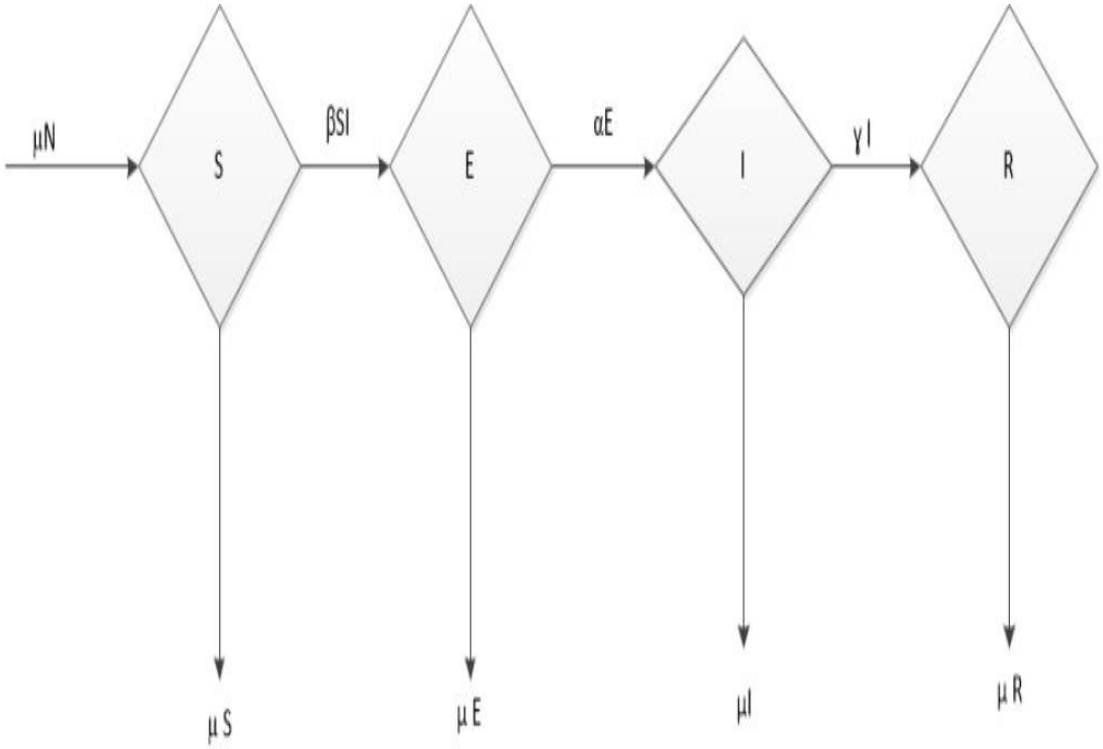


Figure 3.1:

The following system of ordinary differential equations (ODEs) is used to represent this model:

$$S^1 = \mu N - \mu S - \beta SI$$

$$E^1 = \beta SI - (\mu + \alpha)E$$

$$I^1 = \alpha E - (\gamma + \mu)I \qquad (3.1)$$

$$R^1 = \gamma I - \mu R$$

From equation (3.1) the ODE's shows that $S^1 + E^1 + I^1 + R^1 = 0$

Hence the total population

$N = S + E + I + R$

That is $N = \mu N - \mu S - \beta SI + \beta SI - (\mu + \alpha)E + \alpha E - (\gamma + \mu)I + \mu I - \mu R$

$N = \mu N - \mu S - \mu E - \mu I - \mu R$

$N = \mu N - \mu(S + E + I + R)$

$N = \mu N - \mu N = 0$

This shows that the total population is constant;

Normalising the system we have
$s(t) = \frac{S(t)}{N}, e(t) = \frac{E(t)}{N}, i(t) = \frac{I(t)}{N}, r = \frac{R(t)}{N}$

Now since the total population N=1, then $s(t) + e(t) + i(t) + r(t) = 1$ $r(t)$

$= 1 - s(t) - e(t) - i(t)$ We now have the ODE's as $s^1 = \mu - (\mu + \beta)si$ $e^1 = \beta si$

$- (\mu + \alpha)e$

$i^1 = \alpha e - (\gamma + \mu)i$ (3.2)

3.1 Method of Solution

For this section we show that equation (3.1) has positive solution.

(1). For, $S^0 = \mu N - \mu S - \beta SI$

That is, $\frac{dS}{dt} = \mu N - \mu S - \beta SI$

$$\frac{dS}{dt} = \mu N - S(\mu + \beta I) \Rightarrow \frac{dS}{dt} + (\mu + \beta I)S = \mu N$$

This is an equation of the form $\frac{dS}{dt} + P(t)S = Q(t)$

By using integration factor , we can solve the equation by multiplying by $\epsilon(t) = e^{\int P(t)dt}$

$\epsilon(t) = e^{\int(\mu+\beta I)dt} = e^{(\mu+\beta I)t+c}$ if c= 0 then $\epsilon(t) = e^{(\mu+\beta I)t}$

We have, $e^{(\mu+\beta I)t}\frac{dS}{dt} + e^{(\mu+\beta I)t}(\mu + \beta I)S = \mu N e^{(\mu+\beta I)t}$

This implies that, $\frac{d}{dt}(e^{(\mu+\beta I)t}S) = \mu N e^{(\mu+\beta I)t}$

$$e^{(\mu+\beta I)t}S = \int \mu N e^{(\mu+\beta I)t}dt = \frac{\mu N}{(\mu + \beta I)}e^{(\mu+\beta I)t} + c$$

Thus, we have, $S(t) = \frac{\mu N}{(\mu + \beta I)} + ce^{-(\mu+\beta I)t}$

Now if t = 0, then, $S(0) = \frac{\mu N}{(\mu + \beta I)} + c \geq 0$

(2). For, $E^0 = \beta SI - (\mu + \alpha)E$

That is, $\frac{dE}{dt} = \beta SI - (\mu + \alpha)E$

$\frac{dE}{dt} + (\mu + \alpha)E = \beta SI$. By using integration factor, that is

$\epsilon(t) = e^{\int(\mu+\alpha)dt} = e^{(\mu+\alpha)t}$. Then we have

$$e^{(\mu+\alpha)t}\frac{dE}{dt} + e^{(\mu+\alpha)t}(\mu + \alpha)E = \beta ISe^{(\mu+\alpha)t}$$

This implies that, $\frac{d}{dt}(e^{(\mu+\alpha)t}E) = \beta ISe^{(\mu+\alpha)t}$

$$e^{(\mu+\alpha)t}E = \int \beta ISe^{(\mu+\alpha)t}dt = \frac{\beta IS}{(\mu + \alpha)}e^{(\mu+\alpha)t} + c$$

Thus, we have, $E(t) = \frac{\beta IS}{(\mu + \alpha)} + ce^{-(\mu+\alpha)t}$

Now if $t = 0$, then, $E(0) = \frac{\beta IS}{(\mu + \alpha)} + c \geq 0$

(3).For, $I^0 = \alpha E - (\gamma + \mu)I$

That is, $\frac{dI}{dt} = \alpha E - (\gamma + \mu)I$

$\frac{dI}{dt} + (\gamma + \mu)I = \alpha E$, multiplying by the factor
$\epsilon(t) = e^{\int(\gamma+\mu)dt} = e^{(\gamma+\mu)t}$. Then we have

$$e^{(\gamma+\mu)t}\frac{dI}{dt} + e^{(\gamma+\mu)t}(\gamma + \mu)I = \alpha Ee^{(\gamma+\mu)t}$$

This implies that, $\frac{d}{dt}(e^{(\gamma+\mu)t}I) = \alpha Ee^{(\gamma+\mu)t}$

$$e^{(\gamma+\mu)t}I = \int \alpha Ee^{(\gamma+\mu)t}dt = \frac{\alpha E}{(\gamma + \mu)}e^{(\gamma+\mu)t} + c$$

Thus, we have, $$I(t) = \frac{\alpha E}{(\gamma + \mu)} + ce^{-(\gamma+\mu)t}$$

Now if $t = 0$, then, $$I(0) = \frac{\alpha E}{(\gamma + \mu)} + c \geq 0$$

(4). For, $R^0 = \gamma I - \mu R$

That is, $$\frac{dR}{dt} = \gamma I - \mu R$$

$$\frac{dR}{dt} + \mu R = \gamma I$$, multiplying by the factor

$\epsilon(t) = e^{\int \mu dt} = e^{\mu t}$. Then we have

$$e^{\mu t}\frac{dR}{dt} + e^{\mu t}\mu R = \gamma I e^{\mu t}$$

This implies that, $$\frac{d}{dt}(e^{\mu t}R) = \gamma I e^{\mu t}$$

$$e^{\gamma t}R = \int \gamma I e^{\mu t} dt = \frac{\gamma I}{\mu}e^{\mu t} + c$$

Thus, we have, $$R(t) = \frac{\gamma I}{\mu} + ce^{-\mu t}$$

Now if $t = 0$, then, $$R(0) = \frac{\gamma I}{\mu} + c \geq 0$$

This shows that equation (3.1) has positive solutions.

3.2 Equilibrium Point

To evaluate the equilibrium point of the system we equate

$s^1 = 0$ e^1
$= 0$ $i^1 =$
0
$\mu - (\mu + \beta i)s = 0$ (3.3)

$\beta si - (\mu + \alpha)e = 0$ (3.4)

$\alpha e - (\gamma + \mu)i = 0$ (3.5)

For disease free equilibrium $i = 0$

From equation (3.5) $\alpha e - (\gamma + \mu)0 = 0$

$\alpha e = 0$ $e = 0$

substitute $i = 0$ into equation (3), we have $\mu - \mu s = 0$ where $s = \frac{\mu}{\mu} = 1$

At disease free $(s^*, e^*, i^*) = (1,0,0)$

3.3 Basic Reproductive Number

Definition: The basic reproduction number (R_o) is defined as the average number of secondary infections produced by a single infectious host introduced into a totally susceptible population. In most cases, if $R_0 > 1$, then the outbreak generates an epidemic; whereas, if $R_0 < 1$, then the infection will disappear from the population. Since R_0 synthesizes important elements of the infection transmission process, it identifies the most important factors in the infection transmission cycle. A method often used to derive R_0 expression is the next generation matrix (NGM) approach. When the interactions within and between disease compartments are interpreted differently, the NGM approach may lead to different R_0

expressions.

By using the next generation matrix approach $NGM(K) = FV^{-1}$ we reorder the above equation to get

$i^1 = \alpha e - (\gamma + \mu)i - f_1(i,s,e)$

$s^1 = \mu - (\mu + \beta i)s - f_2(i,s,e)$

$e^1 = \beta si - (\mu + \alpha)e - f_3(i,s,e)$

Linearization of the above model gives the Generation matrix (G)

$$G = \begin{matrix} f_1 i & f_1 e \\ f_1 s & \\ f_2 s & \\ f_3 s & f_2 e \\ f_3 i & f_3 e \end{matrix}$$

$$J = \begin{matrix} -(\gamma + \mu) & 0 & 0 & \alpha \\ & & & 0 \\ -(\mu + \beta)s & -(\mu + \beta i) & & \\ \beta s & \beta i & -(\mu + \alpha) & \end{matrix}$$

But at the disease free equilibrium ($s^* = 1, e^* = 0, i^* = 0$) this implies

$$J_{DFE} = \begin{matrix} -(\gamma + \mu) & 0 & \alpha \\ & & 0 \\ -(\mu + \beta) & -\mu & \\ \beta & 0 & -(\mu + \alpha) \end{matrix}$$

since

$$J_{DFE} = \begin{pmatrix} \beta & -(\mu+\alpha) \\ -(\gamma+\mu) & \alpha \end{pmatrix}$$

$$J_{DFE} = \begin{pmatrix} \beta & 0 \\ 0 & 0 \end{pmatrix} - \begin{pmatrix} 0 & (\mu+\alpha) \\ (\gamma+\mu) & -\alpha \end{pmatrix}$$

$$F = \begin{pmatrix} \beta & 0 \\ 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} 0 & (\mu+\alpha) \\ (\gamma+\mu) & -\alpha \end{pmatrix} \quad V^{-1} = \frac{-1}{} \begin{pmatrix} -\alpha & -(\mu+\alpha) \\ -(\gamma+\mu) & 0 \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \beta & 0 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{\alpha}{(\mu+\alpha)(\gamma+\mu)} & \frac{(\mu+\alpha)}{(\mu+\alpha)(\gamma+\mu)} \\ \frac{\gamma+\mu}{(\mu+\alpha)(\gamma+\mu)} & -\frac{0}{(\mu+\alpha)(\gamma+\mu)} \end{pmatrix}$$

$$FV^{-1} = \begin{pmatrix} \frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)} & \frac{\beta}{(\gamma+\mu)} \\ 0 & 0 \end{pmatrix}$$

Thus [illegible] = [illegible] = $\frac{}{(\mu+\alpha)(\gamma+\mu)}$ [illegible]

Since R_0 is the most dominant eigenvalues of the NEM, then

$$R_0 = \frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)}$$

3.4 An Endemic Equilibrium Point

This is where there is no infection, thus $I \neq 0$, From equation (3.5)

Thus, $\alpha e - (\gamma + \mu)i = 0$

$e = \frac{(\gamma+\mu)i}{\alpha}$, (3.6)

substitute e into equation (3.4) to get s, thus

$\beta si - (\mu + \alpha)\frac{(\gamma+\mu)i}{\alpha} = 0$

$\beta si = \frac{(\mu+\alpha)(\gamma+\mu)i}{\alpha}$

$s = \frac{(\mu+\alpha)(\gamma+\mu)i}{\beta\alpha i}$

$s = \frac{1}{\beta\alpha}(\mu + \alpha)(\gamma + \mu) = \frac{1}{R_0}$

since $R_0 = \frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)}$

Now putting s into equation (3.3) to get i, we have

$\mu - (\mu + \beta i)\frac{1}{\beta\alpha}(\mu + \alpha)(\gamma + \mu) = 0$

$\frac{\mu\beta\alpha}{(\mu+\alpha)(\gamma+\mu)} = \mu + \beta i$

$i = \frac{\mu\alpha}{(\mu+\alpha)(\gamma+\mu)} - \frac{-\mu}{\beta}$

$i = \frac{\beta\mu\alpha - \mu(\mu+\alpha(\gamma+\mu))}{\beta(\mu+\alpha)(\gamma+\mu)}$

$i = \beta\_\mu(R_0 - 1)$

substitute i into equation (3.6) to get e we have

$e = \frac{(\gamma+\mu)}{\alpha}\frac{\mu}{\beta}(\frac{\alpha\beta}{(\mu+\alpha)(\gamma+\mu)} - 1)$

$\frac{\gamma+\mu}{\alpha}\frac{\mu}{\beta}(R_0 - 1)$

$e = \frac{\mu}{\beta\alpha}(\gamma + \mu)(R_0 - 1) = \frac{\mu(R_0-1)}{R_0(\mu+\alpha)}$

The endemic equilibrium point are

$$(s^*, e^*, i^*) = (\frac{1}{R_0}, \frac{\mu(R_0-1)}{R_0(\mu+\alpha)}, \frac{\mu(R_0-1)}{\beta})$$

3.4.1 Stability Analysis of Disease-free Equilibrium Point

Theorem 1: At disease-free equilibrium the system is locally asymptotically stable if $R_0 < 1$

Proof: To prove this, we consider the equations below about the equilibrium point.

$s^1 = \mu - (\mu + \beta i)s$

$e^1 = \beta si - (\mu + \alpha)e$

$i^1 = \alpha e - (\gamma + \mu)i$

The Jacobian matrix J of the system is

$$J = \begin{bmatrix} -(\mu + \beta i) & 0 & -\beta S \\ \beta i & -(\mu + \alpha) & \beta S \\ 0 & \alpha & -(\gamma + \mu) \end{bmatrix}$$

At disease free equilibrium, $s = 1$, $e = 0$ and $i = 0$

By inserting the Jacobian matrix becomes

$$J_{DFE} = \begin{bmatrix} -\mu & 0 & -\beta\beta \\ 0 & -(\mu + \alpha) & \\ 0 & \alpha & -(\gamma + \mu) \end{bmatrix}$$

Finding the characteristics equation, then it becomes

$$J_{DFE} - \lambda I = \begin{bmatrix} -\mu - \lambda & 0 & -\beta \\ 0 & -(\mu + \alpha) - \lambda & \beta \\ 0 & \alpha & -(\gamma + \mu) - \lambda \end{bmatrix}$$

Now dividing the matrix into three 2 × 2 matrix, thus

$$d_1 = \begin{bmatrix} -(\mu + \alpha) - \lambda & \beta \\ \alpha & -(\gamma + \mu) - \lambda \end{bmatrix}$$

$$d_2 = \begin{bmatrix} 0 & \beta \\ 0 & -(\gamma + \mu) - \lambda \end{bmatrix}$$

$$d_3 = \begin{bmatrix} 0 & -(\mu + \alpha) - \lambda \\ 0 & \alpha \end{bmatrix}$$

After finding d_1,d_2 and d_3, then substitute into the formula below

$$det(J - \lambda I) = (-\mu - \lambda) \times d_1 - 0 \times d_2 + (-\beta) \times d_3 = 0$$

$$d_1 = (-(\mu + \alpha) - \lambda)(-(\gamma + \mu) - \lambda) - \beta\alpha$$

$$d_1 = ((\mu + \alpha) + \lambda)((\gamma + \mu) + \lambda) - \beta\alpha$$
$$d_1 = (\mu + \alpha + \lambda)(\gamma + \mu + \lambda) - \beta\alpha$$

$$d_1 = \mu\gamma + \mu^2 + \lambda\mu + \alpha\gamma + \alpha\mu + \alpha\lambda + \lambda\gamma + \lambda\mu + \lambda^2 - \beta\alpha$$

$$d_2 = 0$$

$$d_3 = 0$$

By substituting into the formula, that is

$$det(J - \lambda I) = (-\mu - \lambda)((\mu + \alpha + \lambda)(\gamma + \mu + \lambda) - \beta\alpha) = 0$$

$$\Rightarrow (-\mu - \lambda)(\mu\gamma + \mu^2 + \lambda\mu + \alpha\gamma + \alpha\mu + \alpha\lambda + \lambda\gamma + \lambda\mu + \lambda^2 - \beta\alpha) = 0$$

$$-\mu^2\gamma - \mu^3 - \lambda\mu^2 - \alpha\gamma\mu - \alpha\mu^2 - \alpha\lambda\mu - \lambda\mu\gamma - \lambda\mu^2 + \mu\alpha\beta - \mu\gamma\lambda - \mu^2\lambda - \lambda^2\mu - \alpha\gamma\lambda - \alpha\mu\lambda - \alpha\lambda^2 - \lambda^2\gamma - \lambda^2\mu - \lambda^3 + \alpha\beta\lambda = 0$$

$$\lambda^3 + \lambda^2(\mu+\alpha+\gamma+\mu) + \lambda(\mu^2 + \alpha\mu + \mu\gamma + \mu^2 + \alpha\beta + \mu\gamma + \mu^2 + \alpha\gamma + \alpha\mu) + \mu^2\gamma + \mu^3 + \alpha\gamma\mu + \alpha\mu^2 - \mu\alpha\beta = 0$$

$$\lambda^3 + \lambda^2(2\mu + \alpha + \gamma) + \lambda(3\mu^2 + 2\mu\gamma + 2\alpha\mu + \alpha\gamma + \alpha\beta) + \mu[(\mu + \alpha)(\mu + \gamma) - \beta\alpha]$$

Let

$a_1 = (2\mu + \alpha + \gamma)$

$a_2 = (3\mu^2 + 2\mu\gamma + 2\alpha\mu + \alpha\gamma + \alpha\beta)$

$a_3 = \mu[(\mu + \alpha)(\mu + \gamma) - \beta\alpha]$
$\Rightarrow \lambda^3 + a_1\lambda^2 + a_2\lambda + a_3$ (3.7)

Using the Routh-Hurwitz Criteria on (3.7) , we can prove that all roots of the polynomial(3.7) have negative real parts. The Routh-Hurwitz Criteria is stated as follows: Important criteria that give necessary and sufficient conditions for all of the roots of the characteristic polynomial (with real coefficients) to lie in the left half of the complex plane are known as Routh-Hurwitz criteria (Flores, 2013).

Theorem 2: Routh-Hurwitz Criteria

Given the polynomial

$P(\lambda) = \lambda^n + a_1\lambda^{n-1} + ... + a_{n-1}\lambda + a_n.$

Where the coefficient a_i are real constants, $i = 1,...,n$ define the n Hurwitz matrices using the coefficients a_i of the characteristic polynomial:

$H_1 = (a_1)$, $H_2 = \begin{bmatrix} a_1 & 1 \\ a_3 & a_2 \end{bmatrix}$, $H_3 = \begin{bmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & a_4 & a_3 \end{bmatrix}$, $H_4 = \begin{bmatrix} a_1 & 1 & 0 & 0 \\ a_3 & a_2 & a_1 & 1 \\ 0 & a_4 & a_3 & a_2 \\ 0 & 0 & 0 & a_4 \end{bmatrix}$, ..., $H_n = \begin{bmatrix} a_1 & 1 & 0 & 0 & \cdots & 0 \\ a_3 & a_2 & a_1 & 1 & \cdots & 0 \\ a_5 & a_4 & a_3 & a_2 & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & 0 & 0 & \cdots & a_n \end{bmatrix}$

$$H_n = \begin{bmatrix} a_1 & 1 & 0 & 0 & \cdots & 0 \\ a_3 & a_2 & a_1 & 1 & \cdots & 0 \\ a_5 & a_4 & a_3 & a_2 & \cdots & 0 \\ \cdots & \cdots & \cdots & \cdots & \cdots & \cdots \\ 0 & 0 & 0 & 0 & \cdots & a_n \end{bmatrix}$$

where $a_J = 0$ if $j > n$. All of the roots of the polynomial $P(\lambda)$ are negatives or have negative real parts if and only if the determinants of all Hurwitz matrices are positive:

$$det(H_j) > 0, j = 1,2,...,n.$$

For the characteristic polynomial in (3.7), when $n = 3$, the Routh-Hurwitz criteria are

$a_1 > 0, a_2 > 0, a_3 > 0$, and $det(H_1) = a_1 > 0$,

$$det(H_2) = \begin{vmatrix} a_1 & 1 \\ 1 & a_2 \end{vmatrix} = a_1 a_2 > 0, \text{and}$$

$$det(H_3) = \begin{vmatrix} a_1 & 1 & 0 \\ a_3 & a_2 & a_1 \\ 0 & 0 & a_3 \end{vmatrix} = a_1 a_2 a_3 - a_3^2 > 0 \Rightarrow a_1 a_2 - a_3 > 0, a_2$$

Since all the determinants of the Hurwitz matrices are positive, then it means all the eigenvalues of the Jacobian matrix have negative real part and $R_0 < 1$. Therefore, disease-free equilibrium point is stable.

Conversely, if $R_0 > 1$ it implies that $a_3 < 0$, and since the remaining coefficients (a_2, and a_3) of the polynomial (3.7) are positive then all the roots of this polynomial cannot have negative real parts. Therefore, the disease-free equilibrium point is unstable.

3.4.2 Stability Analysis of Endemic Equilibrium Point

Theorem 3: At endemic equilibrium the system is locally asymptotically stable if $R_0 > 1$

Proof: To prove this, we consider the equations below about the equilibrium point.

$s^1 = \mu - (\mu + \beta i)s$

$e^1 = \beta si - (\mu + \alpha)e$
$i^1 = \alpha e - (\gamma + \mu)i$

The Jacobian matrix J of the system is

$$J = \begin{bmatrix} -\mu - \beta i) & 0 & -\beta S \\ \beta i & -(\mu + \alpha) & \beta S \\ 0 & \alpha & -(\gamma + \mu) \end{bmatrix}$$

but, for endemic equilibrium, $s^* = \frac{1}{R_0}, e^* = \frac{\mu(R_0-1)}{R_0(\mu+\alpha)}, i^* = \frac{\mu(R_0-1)}{\beta}$

$$J_{EE} = \begin{pmatrix} -\mu - \frac{\beta\mu(R_0-1)}{\beta} & 0 & -\frac{\beta}{R_0} \\ \frac{\beta\mu(R_0-1)}{\beta} & -(\mu+\gamma) & \frac{\beta}{R_0} \\ 0 & & -(\gamma+\mu) \end{pmatrix}$$

α

Finding the characteristics equation we have

$$J_{EE} - \lambda I = \begin{pmatrix} -\mu R_0 - \lambda & 0 & -\frac{\beta}{R_0} \\ \mu(R_0-1)i & -(\mu+\gamma)-\lambda & \frac{\beta}{R_0} \\ 0 & \alpha & -(\gamma+\alpha)-\lambda \end{pmatrix}$$

Now dividing the matrix into three 2 × 2 matrix, thus

$$d_1 = \begin{pmatrix} -(\mu+\gamma)-\lambda & \frac{\beta}{R_0} \\ \alpha & -(\gamma+\alpha)-\lambda \end{pmatrix}$$

$$d_2 = \begin{pmatrix} \mu(R_0-1) & \frac{\beta}{R_0} \\ 0 & -(\gamma+\alpha)-\lambda \end{pmatrix}$$

$\mu(R_0 - 1)$ $-(\mu + \gamma) - \lambda$ $d_3 =$

0 α

After getting d_1, d_2, d_3 we substitute into the formula

$$det(J - \lambda I) = -(\mu R_0 + \lambda) \times d_1 - 0 \times d_2 + (-\frac{\beta}{R_0}) \times d_3 = 0$$

$$d_1 = (-(\mu+\gamma)-\lambda)(-(\gamma+\alpha)-\lambda) - \frac{\beta}{R_0}(\alpha)$$

$$d_1 = (\mu+\gamma+\lambda)(\gamma+\alpha+\lambda) - \frac{\alpha}{R_0}$$

$$d_1 = \mu\gamma + \alpha\mu + \lambda\mu + \gamma^2 + \alpha\gamma + \lambda\gamma + \lambda\gamma + \alpha\lambda + \lambda^2 - \frac{\alpha\beta}{R_0}$$

$d_2 = \mu(R_0 - 1)(-(\gamma + \alpha + \lambda))$

$d_3 = \alpha\mu(R_0 - 1)$

By substituting into the formula, we have

$$-(\mu R_0+\lambda)(\mu\gamma+\alpha\mu+\lambda\mu+\gamma^2+\alpha\gamma+2\lambda\gamma+\alpha\lambda+\lambda^2-\frac{\alpha\beta}{R_0})+(-\frac{\beta}{R_0})(\alpha\mu)(R_0-1)=0$$

$$-(\mu^2\gamma R_0 + \alpha\mu^2 R_0 + \lambda\mu^2 R_0 + \mu R_0\gamma^2 + \alpha\gamma\mu R_0 + 2\lambda\mu\gamma R_0 + \lambda\alpha\mu R_0 + \lambda^2\mu R_0 -$$
$$\alpha\beta\mu + \lambda\mu\gamma + \lambda\alpha\mu + \lambda^2\mu + \lambda\gamma^2 + \lambda\alpha\gamma + 2\lambda^2\gamma + \lambda^2\alpha + \lambda^3 - \frac{\lambda\alpha\beta}{R_0}) - \alpha\mu\beta + \frac{\alpha\mu\beta}{R_0} = 0$$

$$\mu^2\gamma R_0 + \mu^2\alpha R_0 + \lambda\mu^2 R_0 + \mu R_0\gamma^2 + \alpha\gamma\mu R_0 + 2\lambda\mu\gamma R_0 + \alpha\lambda\mu R_0 + \lambda^2\mu R_0 - \alpha\beta\mu +$$
$$\lambda\mu\gamma + \lambda\alpha\mu + \lambda^2\mu + \lambda\gamma^2 + \lambda\alpha\gamma + 2\lambda^2\gamma + \lambda^2\alpha + \lambda^3 - \frac{\lambda\alpha\beta}{R_0} + \alpha\mu\beta + \frac{\alpha\mu\beta}{R_0} = 0$$

$\Rightarrow \lambda^3 + \lambda^2(\mu R_0 + \mu + 2\gamma + \alpha) + \lambda(\mu^2 R_0 + 2\mu\gamma R_0 + \mu\gamma R_0 + \mu\gamma + \alpha\mu + \gamma^2 +$
$\alpha\gamma - \frac{\alpha\beta}{R_0} + \alpha\mu R_0) + \mu^2\gamma R_0 + \mu^2\alpha R_0 + \mu R_0\gamma^2 + \alpha\gamma\mu R_0 + \frac{\alpha\mu\beta}{R_0} = 0$

Now we let,

$\lambda^3 + \lambda b_1 + \lambda b_2 + b_3 = 0$

Where,

$b_1 = \mu R_0 + \mu + 2\gamma + \alpha$

$$b_2 = \mu^2 R_0 + 2\mu\gamma R_0 + \mu\gamma R_0 + \mu\gamma + \alpha\mu + \gamma^2 + \alpha\gamma - \frac{\alpha\beta}{R_0} + \alpha\mu R_0$$

$$b_3 = \mu^2\gamma R_0 + \mu^2\alpha R_0 + \mu R_0\gamma^2 + \alpha\gamma\mu R_0 + \frac{\alpha\mu\beta}{R_0}$$

Similarly,from Routh-Hurwitz stability criteria, if the coefficient of the characteristic equation $b_1 > 0, b_3 > 0$ and $b_1b_2 - b_3 > 0$ are true then all the roots of the characteristic equation have negative real parts which means a stable equilibrium (Flores, 2013). The first two conditions are true for $R_0 > 1$ as b_1 and b_3 are both positive quantities. The third condition

$b_1b_2 - b_3 > 0$ given by $\mu[R_0(3\mu + \alpha + \mu R_0)(\alpha + \gamma) + \mu^2(3 + 2R_0) + \mu^2 + \mu(\alpha + \gamma) + \alpha\gamma]$ is greater than zero (for all parameter values and $R_0 > 1$), hence it is also true.

Thus the endemic steady state is stable when $R_0 > 1$ by Routh-Hurwitz criteria.

3.4.3 Herd Immunity

Definition: Herd immunity has to do with the protection of populations from infection which is brought about by the presence of immune individuals. The concept has a special aura,,in its implication of an extension of the protection imparted by an immunization program beyond vaccinated to unvaccinated individuals and in its apparent provision of a means to eliminate totally some infectious diseases. It is a recurrent theme in the medical literature and has been discussed frequently during the past decade. This new popularity comes as a consequence of several recent major achievements of vaccination programs.

According to the equation given by Diekmann and Heesterbeek (2000), the herd immunity can be estimated by the formula, $H = 1 - \frac{1}{R_0}$

By this procedure we estimate the herd immunity and is given as

$$H_1 = 1 - \frac{(\mu+\alpha)(\gamma+\mu)}{\beta\alpha}$$

3.4.4 Sensitivity Analyis

Sensitivity Analysis is the study of how the uncertainty in the output of a mathematical model or system can be apportioned to different sources of uncertainty in its inputs.

$R_0^s \longrightarrow$ reproductive number based on the disease-free equilibrium.

Thus, $R_0^s = \frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)}$ (7)

This indicate that the analysis depends on β,α,μ and γ.

(a) By doubling β and inserting in equation (7), that is if $\beta = 2\beta$

Then, $R_{01}^s = \frac{2\beta\alpha}{(\mu+\alpha)(\gamma+\mu)} = 2(\frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)})$

$\Rightarrow R_{01}^s = 2R_0^s$

(b) By doubling α and inserting into equation (7), that is , $\alpha = 2\alpha$

Then, $R_{02}^s = \frac{2\beta\alpha}{(\mu+2\alpha)(\gamma+\mu)}$ (8)

Now dividing equation (8) by equation (7), we have

$$R_{02}^s : R_0^s = \frac{2\beta\alpha}{(\mu+2\alpha)(\gamma+\mu)} : \frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)}$$

$$\frac{R_{02}^s}{R_0^s} = 2\frac{(\mu+\alpha)}{(\mu+2\alpha)}$$

Since the numerator is greater than the denominator, then

$$\frac{R_{02}^s}{R_0^s} > 1$$

$\Rightarrow R_{02}^s > R_0^s$, thus doubling α increases R_0^s.

(c). Doubling μ and inserting into (7) then

$$R_{03}^s = \frac{\beta\alpha}{(2\mu+\alpha)(\gamma+2\mu)} \qquad (9)$$

Dividing (9) by (7) , we have

$$R_{03}^s : R_0^s = \frac{\beta\alpha}{(2\mu+\alpha)(\gamma+2\mu)} : \frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)}$$
$$\frac{R_{03}^s}{R_0^s} = \frac{(\mu+\alpha)(\gamma+\mu)}{(2\mu+\alpha)(\gamma+2\mu)}$$

Since the denominator is greater than the numerator then

$$\frac{R_{03}^s}{R_0^s} < 1$$

$\Rightarrow R_{03}^s < R_0^s$

This implies that doubling μ decreases R_0^s

(d). Doubling γ and putting into (7), we have

$$R_{04}^s = \frac{\beta\alpha}{(\mu+\alpha)(2\gamma+\mu)} \qquad (10)$$

Now dividing (10) by (7) , we have

$$R_{04}^s : R_0^s = \frac{\beta\alpha}{(\mu+\alpha)(2\gamma+\mu)} : \frac{\beta\alpha}{(\mu+\alpha)(\gamma+\mu)}$$

$$\frac{R_{04}^s}{R_0^s} = \frac{(\mu+\alpha)(\gamma+\mu)}{(\mu+\alpha)(2\gamma+\mu)}$$

Since the denominator is greater than the numerator then

$$\frac{R_{04}^s}{R_0^s} < 1$$

Thus $R_{04}^s < R_0^s$. This implies that doubling γ decreases R_0^s.

Chapter 4

Analysis

4.1 Introduction

This chapter deals with the analysis and numerical simulation of the Brong Ahafo regional data collected from Ghana Statistical Service on H1N1 from 2010. The simulation analysis to illustrate our results on stability as well as numerical simulation and graphical representation of the data is also done using MATLAB to see how the model works practically.

4.2 Parameter Determination

We used Brong Ahafo regional data and the population N = 2282128, β = 0.1508,α = 0.25,γ = 0.14285 and μ = 0.0044

4.3 Numerical Simulation

From the parameter values given , we estimate that $R_0 = \frac{0.1508 \times 0.25}{(0.0044 + 0.25)(0.14285 + 0.0044)}$

$\Rightarrow R_0 = 1.006396$. Thus the basic reproductive number $R_0 = 1.006396 > 1$ From Theorem 1 the disease-free equilibrium $(s^*,e^*,i^*) = (1,0,0)$ is unstable since $R_0 > 1$ and from theorem 3 ($s^*, e^*, i^*) = (\frac{1}{R_0}, \frac{\mu(R_0 - 1)}{R_0(\mu + \alpha)}, \frac{\mu(R_0 - 1)}{\beta})$

Thus ($s^*, e^*, i^*) = (\frac{1}{1.006396}, \frac{0.0044(1.006396 - 1)}{1.006396(0.0044 + 0.25)}, \frac{0.0044(1.006396 - 1)}{0.1508})$

$\Rightarrow (s^*,e^*,i^*) = (0.9936,0.0001099,0.0001866)$. Showing that the endemic equilibrium is stable for $R_0 > 1$

Now estimating the herd immunity from the data , we have

$H_1 = 1 - \frac{1}{R_0}$ $H_1 = 1 - \frac{1}{1.006396} \Rightarrow H_1 = 0.006355$

Thus the herd immunity is 0.6355%.

Sensitivity Analysis of the data

1. For $\beta = 2\beta = 2(0.1508) = 0.3014, \alpha = 0.25, \gamma = 0.14285, \mu = 0.0044$ then $R_0 = 2.0128$

2. For $\alpha = 2\alpha = 2(0.25) = 0.50, \beta = 0.1508, \gamma = 0.14285, \mu = 0.0044$ then $R_0 = 1.0152$

3. For $\gamma = 2\gamma = 2(0.14285) = 0.2857, \beta = 0.1508, \alpha = 0.25, \mu = 0.0044$ then $R_0 = 0.5108$

4. For $\mu = 2\mu = 2(0.0044) = 0.0088, \beta = 0.1508, \alpha = 0.25, \gamma = 0.14285$ then $R_0 = 0.96$

Table 4.1: Sensitivity analysis of the disease-free equilibrium state

Nature of steady state	β	α	γ	μ	R_0
Unstable	0.3014	0.25	0.14285	0.0044	2.0128
Unstable	0.1508	0.50	0.14285	0.0044	1.0152
Stable	0.1508	0.25	0.2857	0.0044	0.5108
Stable	0.1508	0.25	0.14285	0.0088	0.96

Table 4.1 and 4.2 indicates the sensitivity analysis for both the diseasefree and endemic equilibrium point respectively.

Table 4.2: Sensitivity analysis of the endemic equilibrium state

Nature of steady state	β	α	γ	μ	R_0
Stable	0.3014	0.25	0.14285	0.0044	2.0128
Stable	0.1508	0.50	0.14285	0.0044	1.0152
Unstable	0.1508	0.25	0.2857	0.0044	0.5108
Unstable	0.1508	0.25	0.14285	0.0088	0.96

From Table 4.1, increasing the rate of transmission and the rate of latency , the $R_0 > 1$ and the disease-free equilibrium state is found to be unstable. This shows that the cause of an outbreak, that is, the disease will spread. On the other hand, as the recovery rate and death rate increases , the $R_0 < 1$ and the disease-free equilibrium is found to be stable, meaning the disease can die out.

From Table 4.2, increasing the rate of transmission and the rate of latency , the $R_0 > 1$ and the endemic equilibrium point is stable.On the other hand , as the recovery rate and death rate increases , the $R_0 < 1$ and the endemic equilibrium is found to be unstable.

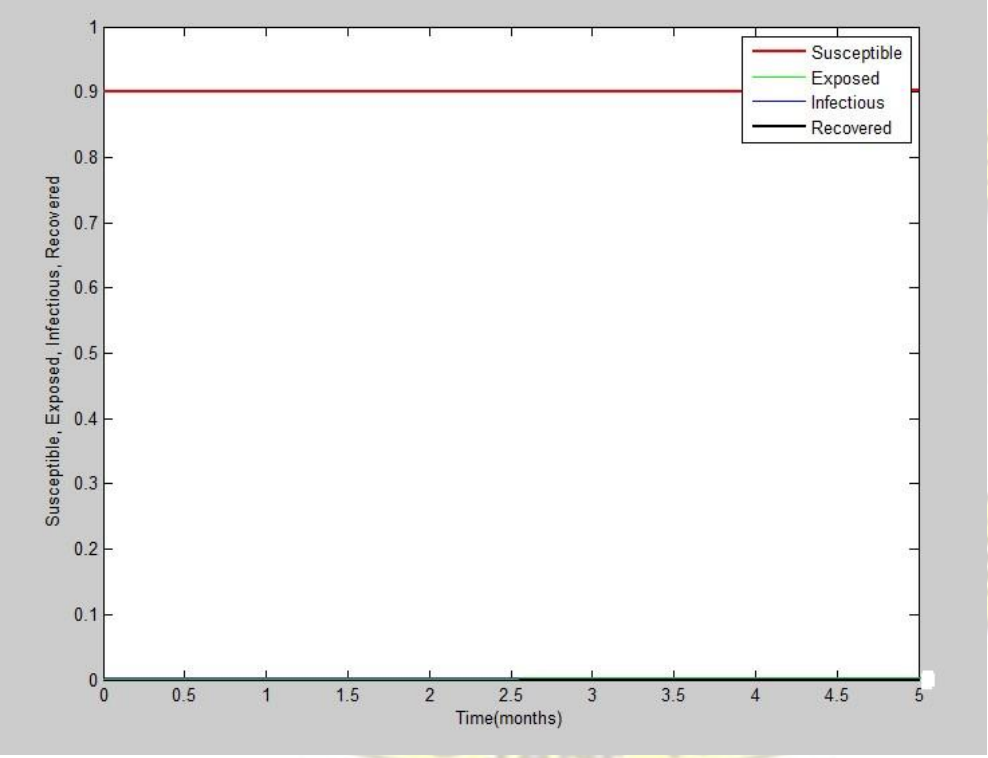
Using the parameter values given, we ran simulate for a period of 5 months for interaction between susceptible, exposed, infectious and recovered.

The Brong Ahafo regional data obtained indicate that $S(0) = 2282126, E(0) = 2, I(0) = 2$ and $R(0) = 0$.

Dividing through by the total population of Brong Ahafo region which is 2282128 (Ghana statistical service, 2010), we have; $s(0) = 0.999999123$, $e(0) = 8.763750 \times 10^{-7}$, $i(0) = 8.763750 \times 10^{-7}$, and $r(0) = 0.0$, from this simulation we obtain Figure 4.1

From Figure 4.2, we varied the proportion of infective, that is $i(0) = 0.4$ around the neighborhood of the endemic equilibrium point for a period of 5

Figure 4.1: Dynamics of the various compartments at the initial outbreak of H1N1 in Brong Ahafo



months.It can be observed that the proportion of exposed individuals initially increased from 0.00 to 0.03 in the second month and then reduce to a minimum of 0.02 in the fifth month. The proportion of the susceptible declines from a value

of 0.6 during the first month to a minimum value of 0.5 by the fifth month. The proportion of the recovered on the other hand increases exponentially with time.

From Figure 4.3, we varied the proportion of infective, that is $i(0)$ = 0.4 around the neighborhood of the endemic equilibrium point for a period of 20 months.From the Figure the proportion of the exposed individuals initially increased from 0 to 0.05 in the second month then decrease gradually to 0.01 by the twentieth month. The proportion of the susceptible declines from a value of 0.6 during the first month to a minimum value of 0.41 by the twentieth month. The proportion of the recovered on the other hand increases exponentially with time and reaches a maximum value of 0.52 by the twentieth month.

Figure 4.2: Graph of an increased in the proportion of infectious (5 months period) on various compartments.

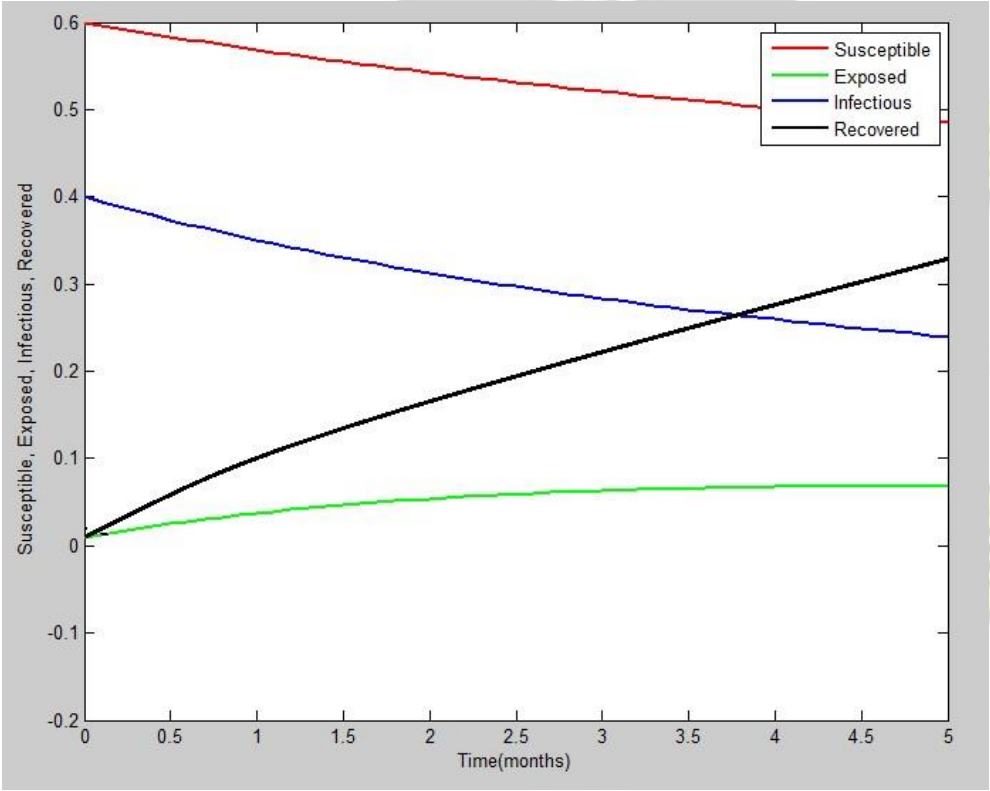
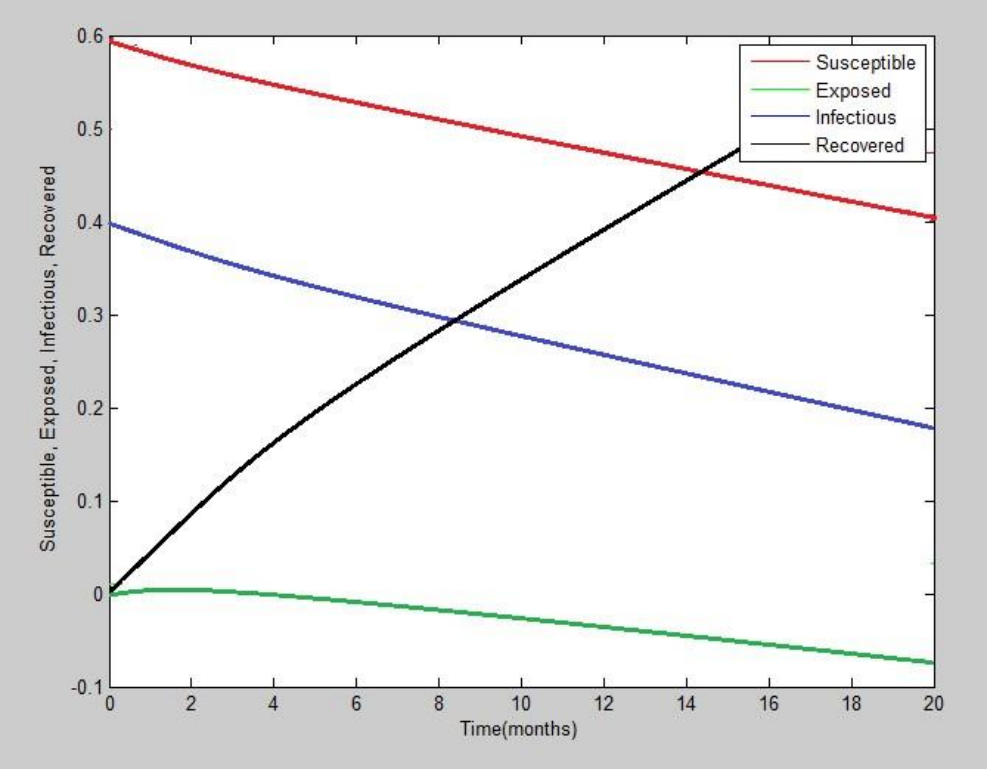


Figure 4.3: Graph of an increased in the proportion of infectious (20 months period) on various compartments.



Chapter 5

Conclusion

In analyzing the mathematical behavior of the SEIR model we obtained the nonnegative solutions of the model by integration factor.The reproductive number of the SEIR epidemiological model was estimated by the next generation method approach and the results indicated that $R_0 > 1$.

We obtained the stability analysis of the model by Routh-Hurwitz stability criteria. The mathematical behavior indicate that the disease-free equilibrium point was asymptotically stable since $R_0 < 1$ and the endemic equilibrium point was also asymptotically stable since $R_0 > 1$.

The sensitivity analysis carry out indicate that doubling or increasing the transmission rate (β),the disease spread but when the transmission rate is decreased the disease dies out.

The simulated results indicate that the initial proportion of the infectives has no effect on the model, but as the infectives increases, the proportion of the susceptible decreases. This shows that as more people are infected with the H1N1

virus, the disease will spread in the Brong Ahafo region. The herd immunity was estimated and the data obtained shows that about 0.6% of the populate needs to be vaccinated to control the diseases in the region.

We obtained the numerical solution of the model by using generalized Euler's method.

Findings: The major contribution to this work is our ability to provide numerical simulation of the model using Euler's method and also providing solution to the model using integration factor.

5.1 Recommendations

Since H1N1 is a public health issue we recommend that the health sectors in the region can adopt the model to help control the disease.

In addition, we recommend researchers and academicians to further discuss the global asymptotic behavior of the model.

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Appendix A

CODES FOR FIGURE 4.1

Title: Dynamics of the various compartments at the initial outbreak of H1N1 in Brong Ahafo

clear, clc, $beta = 0.1508$; $alpha = 0.25$;

$gamma = 0.14285$ $mu = 0.0044$; $h = 0.1$ t

$= 0 : 0.5 : 5$; $n = length(t)$; $solS = []$; $solE =$

$[]$; $solI = []$; $solR = []$;

$S = zeros(n,1)$; $E = S$; $I = S$; $R = S$;

$S(1) = 0.9$;$E(1) = 8.763750 \times 10^{-7}$;$I(1) = 8.763750 \times 10^{-7}$;$R(1) = 0.0$;

for $i = 1 : n - 1$

$S(i + 1) = S(i) + h * (mu - mu * S(i) - beta * I(i) * S(i))$;

$E(i + 1) = E(i) + h * (beta * I(i) * S(i) - (mu + alpha) * E(i))$;

$I(i + 1) = I(i) + h * (alpha * E(i) - (gamma + mu) * I(i))$; $R(i + 1) = R(i)$

$+ h * (alpha * E(i) - (gamma + mu) * I(i))$; end $solS(:,2) = S(:)$; $solE(:,2)$

$= E(:)$; $solI(:,2) = I(:)$; $solR(:,2) = R(:)$;

figure(1); plot(t,sol S(:,2),'r',t,sol E(:,2),'g',t,sol I(:,2),'b' ,t,sol R(:,2),'k');

xlabel('Time(months)'), ylabel('Susceptible, Exposed, Infectious, Recovered');

legend('Susceptible','Exposed', 'Infectious', 'Recovered')

CODES FOR FIGURE 4.2

Title: Graph of an increased in the proportion of infectious (5 months period) on various compartments.

clear, clc, $beta = 0.1508$; $alpha = 0.25$;

$gamma = 0.14285$ $mu = 0.0044$; $h = 0.1$ t

$= 0 : 0.5 : 5$; $n = length(t)$; $solS = []$; $solE =$

$[]$; $solI = []$; $solR = []$;

$S = zeros(n,1)$; $E = S$; $I = S$; $R = S$;

$S(1) = 0.6; E(1) = 0.001; I(1) = 0.4; R(1) = 0.001;$

for $i = 1 : n - 1$

$S(i + 1) = S(i) + h * (mu - mu * S(i) - beta * I(i) * S(i));$

$E(i + 1) = E(i) + h * (beta * I(i) * S(i) - (mu + alpha) * E(i))$;

$I(i + 1) = I(i) + h * (alpha * E(i) - (gamma + mu) * I(i)); R(i + 1) = R(i)$

$+ h * (alpha * E(i) - (gamma + mu) * I(i))$; end $solS(:,2) = S(:); solE(:,2)$

$= E(:); solI(:,2) = I(:); solR(:,2) = R(:);$

figure(1); plot(t,sol S(:,2),'r',t,sol E(:,2),'g',t,sol I(:,2),'b' ,t,sol R(:,2),'k');

xlabel('Time(months)'), ylabel('Susceptible, Exposed, Infectious, Recovered');

legend('Susceptible','Exposed', 'Infectious', 'Recovered')

Appendix B

CODES FOR FIGURE 4.3

Title:Graph of an increased in the proportion of infectious (20 months period) on various compartments.

clear, clc, $beta = 0.1508$; $alpha = 0.25$;

$gamma = 0.14285$ $mu = 0.0044$; $h = 0.1$ t

$= 0 : 2 : 20$; $n = length(t)$; $solS = []$; $solE =$

[]; $solI = []$; $solR = []$;

$S = zeros(n,1)$; $E = S$; $I = S$; $R = S$;

$S(1) = 0.5; E(1) = 0.01; I(1) = 0.4; R(1) = 0.02;$

for $i = 1 : n - 1$

$S(i + 1) = S(i) + h * (mu - mu * S(i) - beta * I(i) * S(i));$

$E(i + 1) = E(i) + h * (beta * I(i) * S(i) - (mu + alpha) * E(i))$;

$I(i + 1) = I(i) + h * (alpha * E(i) - (gamma + mu) * I(i)); R(i + 1) = R(i)$

$+ h * (alpha * E(i) - (gamma + mu) * I(i))$; end $solS(:,2) = S(:); solE(:,2)$

$= E(:); solI(:,2) = I(:); solR(:,2) = R(:);$

figure(1); plot(t,sol S(:,2),'r',t,sol E(:,2),'g',t,sol I(:,2),'b' ,t,sol R(:,2),'k');
xlabel('Time(months)'), ylabel('Susceptible, Exposed, Infectious, Recovered');
legend('Susceptible','Exposed', 'Infectious', 'Recovered')