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ABSTRACT

The study showed that chickenpox cases in recent times have increased in Agona West Municipality with $R_0 = 2$. We estimated the reproductive number of chickenpox with vaccination to be $R_0 = 0.3 < 1$. This showed that after vaccination, the disease will die out. We estimated that 46.2% corresponding to 53,241 of the people needs to be vaccinated in order to control the chickenpox. The stability analysis of disease free and endemic equilibrium point of chickenpox transmission with vaccination was estimated to be unstable and asymptotically stable. Sensitivity analysis of the SEIR model with vaccination showed that when vaccination rate coefficient is increased chickenpox will be under control.

Keywords: Chickenpox, equilibrium point, transmission, stability, vaccination, Varicella-Zoster-Virus (VZV)

1. INTRODUCTION

Chickenpox (Varicella) is a highly transmissible infection caused by Varicella-Zoster-Virus (VZV), a DNA virus of the Herpes group transmitted by direct contact with infective individuals. In Europe, 90% of children get infected with VZV before 12 years of age and around 95% of adults are immune to VZV [1]. Chickenpox is characterized by vesicular skin lesions, fever, mild fatigue and general malaise. The primary infection with Varicella - Zoster Virus (VZV) causes Chickenpox. It is associated with pain and body itching [2]. Chickenpox (Varicella) vaccine is a live attenuated viral vaccine derived from the Oka strain of VZV. The vaccine virus was isolated by Takahashi in the early 1970s from vesicular fluid

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35 from a healthy child with varicella disease. Varicella vaccine was licensed for general use in
36 Japan and Korea in 1988 and later licensed in the United States in 1995 for persons who
37 were 12 months of age and older. The virus was attenuated by sequential passage in human
38 embryonic lung cell culture, embryonic guinea pig fibroblasts and in WI-38 human diploid
39 cells. The Oka (Merck) vaccine has undergone further passage through MRC-5 human
40 diploid cell cultures for a total of 31 passages [2].

41 The component of the vaccine contains small amounts of sucrose, processed porcine
42 gelatin, sodium chloride, monosodium L-glutamate, sodium diphosphate, potassium
43 phosphate and potassium chloride and trace quantities of residual components of MRC-5
44 cells, EDTA, neomycin and fetal bovine serum. The vaccine contains no preservative and
45 reconstituted with sterile water [3].

46 Gershon [4] concluded that chickenpox vaccine offers close to 100% protection from severe
47 chickenpox and 90% protection from illness and have a greater impact on the epidemiology
48 of varicella and zoster in countries with high vaccine uptake. Welsby [5] indicated that in the
49 pre licensure era, 95% of adults experienced natural chickenpox which resulted in long-term
50 immunity. Varicella vaccination is less effective than the natural immunity that existed in
51 prevaccine communities.

52 Macartney *et al.* [6] studies on varicella shown that the vaccine is safe and highly effective in
53 reducing varicella-related disease with universal varicella vaccination of children in the USA
54 over the past 10 years. Edmunds and Brisson [7] brought to bear that infant VZV vaccination
55 could lead to an increase in adult disease or a temporary increase in the incidence of
56 shingles. Studies indicate more effective vaccination is at preventing varicella.
57 Understanding the mechanisms for maintaining immunity against varicella is critical for
58 predicting the long-term effects of vaccination.

59 Arvin and Gershon [8] studies reveal that varicella vaccine has clinical efficacy for the
60 prevention of varicella. The vaccine induces persistent immunity to VZV in healthy children
61 and adults. Immunization against VZV lowers the risk of reactivation of herpes zoster virus

which is a serious problem for grownups and immunocompromised individuals. Gershon *et al.*[9] agreed with Arvin and Gershon [8] that live attenuated varicella vaccine is safe and effective in preventing chickenpox. Leukemic children have a 50% incidence of mild-to-moderate adverse effects but have a high degree of protection once immune reactions to varicella-zoster virus (VZV) have developed. Adult vaccinees have a lower degree of protection (70%) compared to children.

Esson [10] studied the epidemiology of chickenpox in Agona West Municipality and estimated the endemicity of chickenpox with $R_0 = 2$ and Mathematical models for the vaccination dynamics of chickenpox and how the chickenpox can be controlled in the Municipality is not known. This study therefore uses SEIR model with vaccination to model the vaccination dynamics in the Municipality. Differential equations applications are used extensively in many facets [11,12,13,14,15].

2. METHODOLOGY

The population used for this study is Agona West Municipal and the data was obtained from Agona West Municipal Health Directorate. We used SEIR model with vaccination to model the vaccination dynamics of chickenpox. Ordinary differential equations were used to formulate the model equations. Stability and Sensitivity analysis was performed on the model equations and ode45 Matlab software was used for the graph simulation.

2.1 The Mathematical Model

In the SEIR model, the total population is divided into four separate groups: Susceptible (S), Exposed (E), Infective (I) and Recovered (R). Susceptible people can contract the disease if they come into contact with the chickenpox, while those in the exposed group are individuals infected but not yet infectious with the chickenpox and are not able to pass the chickenpox to others. Infective are the individuals that are infectious and capable of transmitting the infection to any susceptible that they come in contact and those in the recovered

compartment are individuals previously infected but now neither infected nor susceptible. They have an infection-acquired immunity (permanent immunity). The proportion of individuals in each compartment S , E , I and R at time t is given as $S(t)$, $E(t)$, $I(t)$ and $R(t)$. The figure below is the flow chart of the SEIR model with vaccination.

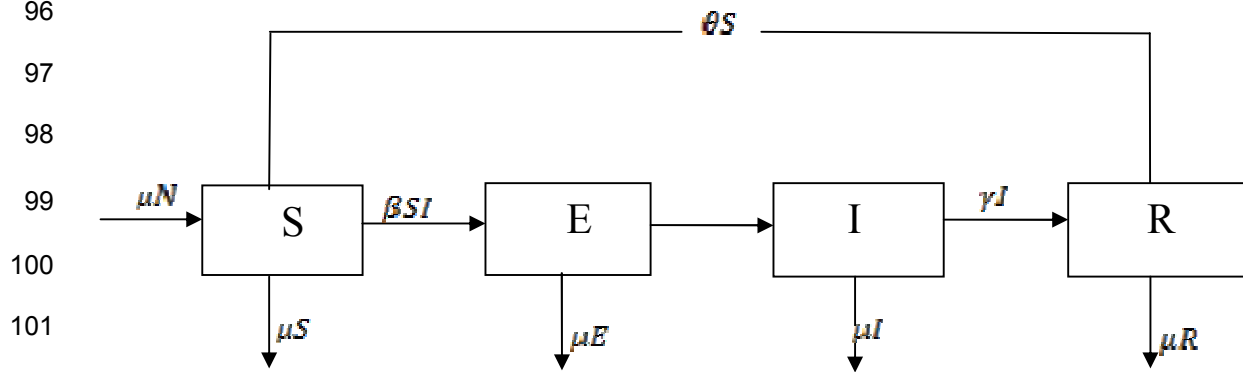


Figure1: Flow chart of SEIR Model of chickenpox transmission with vaccination

μN = Birth rate of susceptible population, θ = Vaccinated rate coefficient, β = Infection rate, κ = Latency rate, γ = Recovery rate and μ = Natural death rate.

The model equations [16] for chickenpox with vaccination are as follows:

$$\frac{dS}{dt} = \mu N - \beta SI - \mu S - \theta S \quad (1)$$

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

$$\frac{dI}{dt} = \kappa E - \mu I - \gamma I \quad (3)$$

$$\frac{dR}{dt} = \gamma I - \mu R + \theta S \quad (4)$$

We estimated the reproductive number (R_0) of chickenpox with vaccination using the next generation matrix (G). The next generation method is given as $G = FV^{-1}$. the (i, j) entry of F is the rate at which infected individuals in compartment j produce new infections in compartment i , the (j, k) entry of V^{-1} is the average length of time this individual spends in compartment j during it's lifetime, assuming that the population remains near the disease free equilibrium and barring reinfection. Hence, the (i, k) entry of the product FV^{-1} is the expected number of

118 new infections in compartment i produced by the infected individual originally introduced into
 119 compartment

120 ~~k~~. We linearized the infection state of the differential equation (2) and (3) to obtain

121 $G = F - V$

122 $F - V = \begin{vmatrix} -(\mu + \kappa) & \beta \\ k & -(\mu + \gamma) \end{vmatrix}$

123 $F - V = \begin{vmatrix} 0 & \beta \\ 0 & 0 \end{vmatrix} - \begin{vmatrix} (\mu + \kappa) & 0 \\ -k & (\mu + \gamma) \end{vmatrix}$

124 $F = \begin{vmatrix} 0 & \beta \\ 0 & 0 \end{vmatrix}$ and $V = \begin{vmatrix} (\mu + \kappa) & 0 \\ -\kappa & (\mu + \gamma) \end{vmatrix}$

125 $\text{Det } V = (\mu + \kappa)(\mu + \gamma)$

126 $\text{Det } V = (\mu + \kappa)(\mu + \gamma)$

127 $V^{-1} = \frac{1}{(\mu + \kappa)(\mu + \gamma)} \begin{vmatrix} (\mu + \gamma) & 0 \\ \kappa & (\mu + \kappa) \end{vmatrix}$

128 $V^{-1} = \begin{vmatrix} \frac{1}{(\mu + \kappa)} & 0 \\ \frac{k}{(\mu + \kappa)(\mu + \gamma)} & \frac{1}{(\mu + \gamma)} \end{vmatrix}$

129 $FV^{-1} = \begin{vmatrix} 0 & \beta \\ 0 & 0 \end{vmatrix} \begin{vmatrix} \frac{1}{(\mu + \kappa)} & 0 \\ \frac{k}{(\mu + \kappa)(\mu + \gamma)} & \frac{1}{(\mu + \gamma)} \end{vmatrix}$

130 $FV^{-1} = \frac{\beta \kappa}{(\mu + \kappa)(\mu + \gamma)}$

131 But $FV^{-1} = R_0$

132 $(R_0) = \frac{\beta \kappa}{(\mu + \kappa)(\mu + \gamma)}$

133 The reproductive number (R_0) is defined as the expected number of secondary infections
 134 arising from a single individual during his or her entire infectious period in a population of
 135 susceptible [1].

136 The reproductive number (R_0) is a threshold that determines whether a disease will spread
 137 in a population or dies out. Whenever R_0 is ≥ 1 , the disease will spread in a population and
 138 each infected individual produces on average more than one new infection and the disease

will invade the population leading to its persistence (endemic). If R_0 is < 1 , the disease will die out in the population and on average an infected individual produces less than one new infected individual over the course of its infectious period and the infection [17].

The equilibrium point of chickenpox with vaccination is $(S^*, E^*, I^*, R^*) =$

$$\left(\frac{(\mu + \gamma)(\mu + k)}{\beta k}, \frac{\mu \beta k N - (\mu + \theta)(\mu + \gamma)(\mu + k)}{\beta k(\mu + k)}, \frac{\mu \beta k N - (\mu + \theta)(\mu + \gamma)(\mu + k)}{\beta k(\mu + \gamma)(\mu + k)}, \frac{\mu \gamma \beta k N - \gamma k(\mu + \theta)(\mu + k) + \theta((\mu + k)(\mu + \gamma))^2}{\mu \beta k(\mu + \gamma)(\mu + k)} \right)$$

The stability analysis of the disease free and the endemic equilibrium point of the model with

vaccination are given by $|J - \lambda I| = \begin{vmatrix} -(\mu + \theta) - \lambda & 0 & -\beta & 0 \\ 0 & -(\mu + k) - \lambda & \beta & 0 \\ 0 & k & -(\mu + \gamma) - \lambda & 0 \\ \theta & 0 & \gamma & -\mu - \lambda \end{vmatrix}$ and

$$|J - \lambda I| = \begin{vmatrix} -\beta I - (\mu + \theta) - \lambda & 0 & -\beta S & 0 \\ \beta I & -(\mu + k) - \lambda & \beta S & 0 \\ 0 & k & -(\mu + \gamma) - \lambda & 0 \\ 0 & 0 & \gamma & -\mu - \lambda \end{vmatrix}$$

The eigenvalues of the matrix for the disease free and the endemic equilibrium point of chickenpox with vaccination are $\lambda = -\beta I - (\mu + \theta)$, $\lambda = -(\mu + k)$, $\lambda = -(\mu + \gamma)$ and $\lambda = -\mu$

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3.0 RESULTS AND DISCUSSION

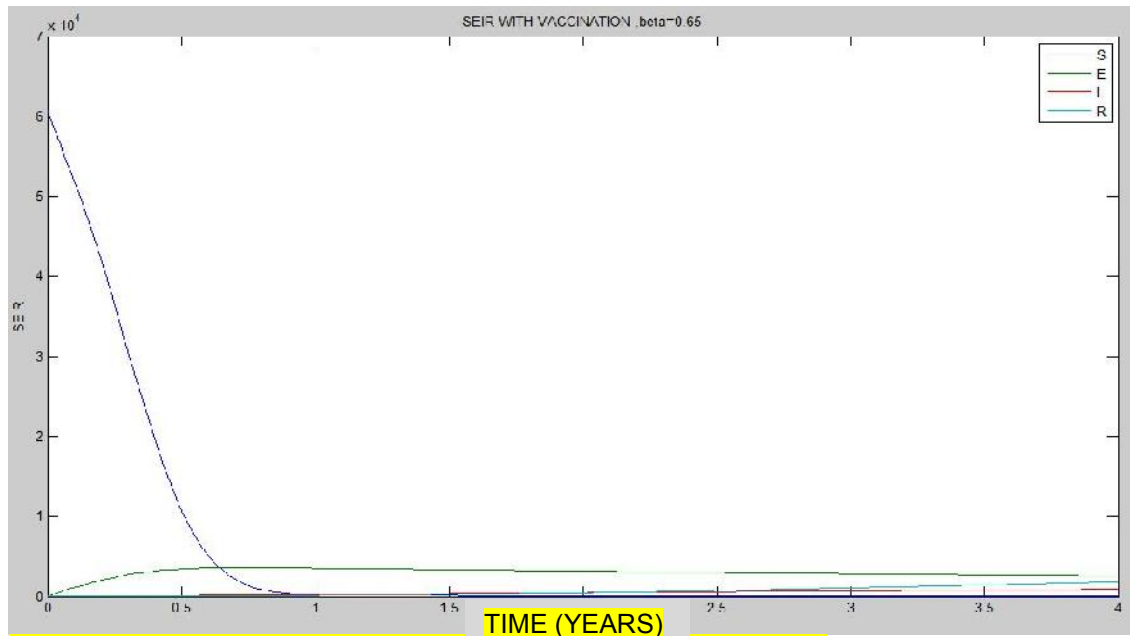
We estimated the parameter values from the data obtained from the Agona West Municipal Health Directorate as follows: Transmission rate (β) = 0.026, Latency rate (κ) = 0.036, Recovery rate (γ) = 0.014, Death rate (μ) = 0.02 Vaccinated rate coefficient (θ) = 0.00019 and Population (N) = 115,358. The summary of the data obtained from the Agona West Municipal Health Directorate can be found at the Appendix (Table 1).

From the studies, we estimated the reproductive number of chickenpox with vaccination to be $R_0 = 0.03 < 1$ which shows that after vaccination, the chickenpox will die out and will not populate. We estimated that 53.241 out of 115,358 people needs to be vaccinated against chickenpox and this corresponds to 46.2% of the Agona West Municipality needs to be vaccinated in order to control the chickenpox. We estimated the stability analysis of disease free and endemic equilibrium point with vaccination to be unstable and asymptotically stable.

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163 Sensitivity analysis of SEIR model with vaccination showed that the susceptible population
164 decreases sharply with time while the infective and recovered population also decreases
165 asymptotically when the value of transmission rate (β) was varied from 0.08 to 0.65 as time
166 increases.

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170 Figure 2: Shows a graph of $\beta = 0.65$ keeping κ , γ and θ constant at equilibrium

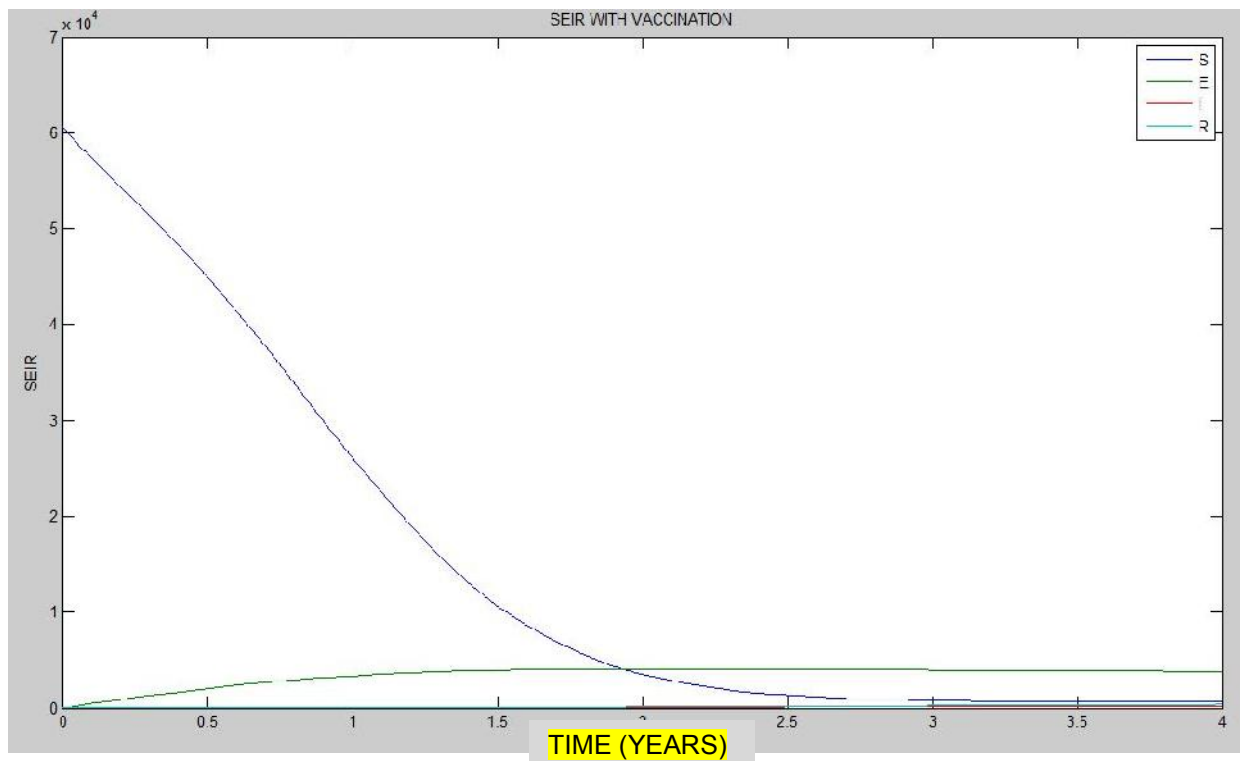
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173 We observed that as the recovery rate (γ) varies from 0.07 to 0.99, the susceptible
174 population decreases with no significant increase or decrease in the exposed population.

175 While the infective and the recovered population decreases asymptotically to the time axis

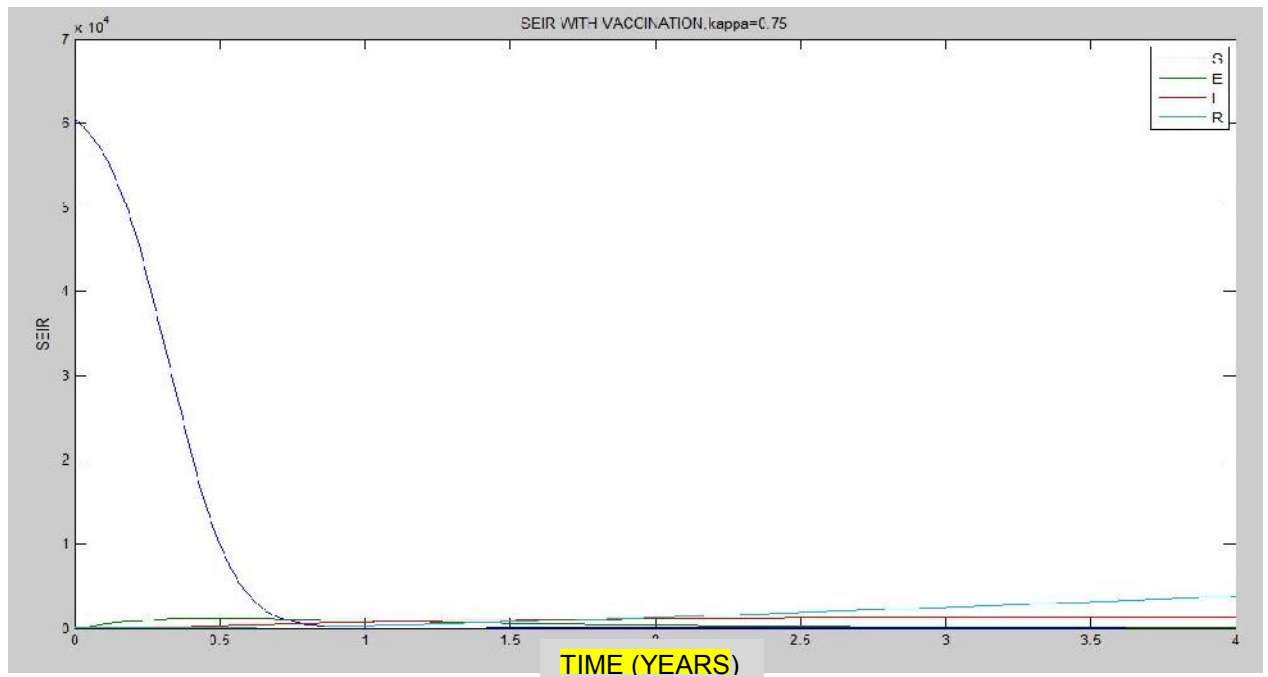
176 as time increases.



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178 **Figure 3:** Shows a graph of $\kappa = 0.99$ of keeping β , γ and θ constant at equilibrium
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181 We observed that as the latency rate (κ) increases from 0.05 to 0.75 there is a sharp
182 decrease in the susceptible population from approximately 60,000 to 100 within the 4 years
183 with more chickenpox patients recovering from approximately 2 to 400 and a small increase
184 in the infective population from approximately 2 to 150 with a decline in the exposed

185 population from approximately 300 and asymptotically to the time axis as time increases.



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187 **Figure 4:** Shows a graph of $\kappa=0.75$ keeping β , γ and θ constant at equilibrium

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190 As the vaccination rate coefficient (θ) varies from 0.02 to 0.96, we observed that more

191 chickenpox patients recovered from approximately 200 to 30,000 with a decrease in the

192 exposed population from approximately 300 to 250 with no significant increase or decrease

193 in the infective as time increases.

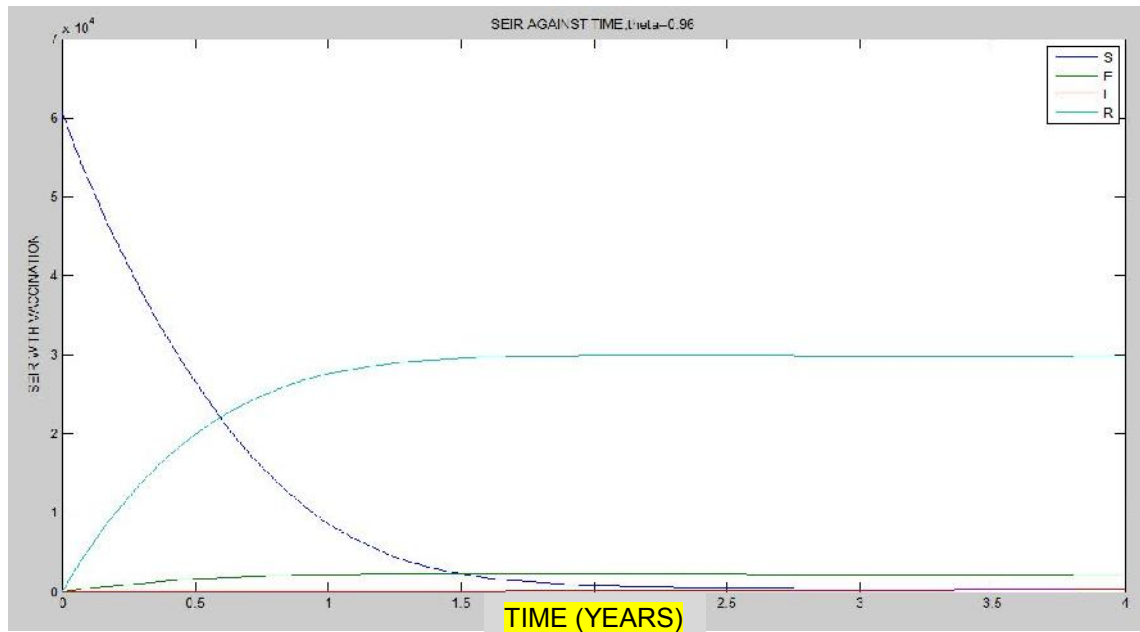


Figure 5: Shows a graph of $\theta=0.96$ keeping β, γ and κ constant at equilibrium

From the sensitivity analysis of the studies, It was observed that vaccination rate coefficient (θ) was more sensitive to the model than the transmission rate (β), latency rate (κ) and the recovering rate (γ).

4. CONCLUSION

From the studies, it was observed that if vaccination rate coefficient (θ) is increased (more people are vaccinated against chickenpox), chickenpox will be under control in the Municipality. We estimated that 53.241 out of 115.358 people needs to be vaccinated against the chickenpox and this corresponds to 46.2% of the people in the Municipality.

We call on all stakeholders in the health sector to come together to ensure that there is a law that enforces all the health sector to keep up to date on all the diseases reported at the various hospitals, clinics and the health centers due to the difficulties in obtaining data for research. We recommend further studies on

(1) SEIR model using non constant population and incorporation of age.

(2) Researchers and students can extend the model to non constant population size and

213 to unequal birth/death rate

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216

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223 **COMPETING INTERESTS**

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225 Authors have declared that no competing interests exist.

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APPENDIX

The Table below shows the summary of the data obtained from the Agona West Municipal Health Directorate

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Time(years)	Susceptible	Exposed	Infective	Recovered
t=0	60684	9	23	0
t=1	55950	5	13	15
t=2	58265	7	18	20
t=3	48463	11	28	41
t=4	31527	16	41	43

Table1: Summary of the data obtained from the Agona West Municipal Health Directorate