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ABSTRACT

The study shown 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 $R_v = 0.3 < 1$. This shows 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 increase 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 [15]. 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 [14].

35 Chickenpox (Varicella) vaccine is a live attenuated viral vaccine derived from the Oka strain
36 of VZV. The vaccine virus was isolated by Takahashi in the early 1970s from vesicular fluid
37 from a healthy child with varicella disease. Varicella vaccine was licensed for general use in
38 Japan and Korea in 1988 and later licensed in the United States in 1995 for persons who are
39 12 months of age and older. The virus was attenuated by sequential passage in human
40 embryonic lung cell culture, embryonic guinea pig fibroblasts and in WI-38 human diploid
41 cells. The Oka (Merck) vaccine has undergone further passage through MRC-5 human
42 diploid cell cultures for a total of 31 passages [14].

43 The component of the vaccine contains small amounts of sucrose, processed porcine
44 gelatin, sodium chloride, monosodium L-glutamate, sodium diphosphate, potassium
45 phosphate and potassium chloride and trace quantities of residual components of MRC-5
46 cells, EDTA, neomycin and fetal bovine serum. The vaccine contains no preservative and
47 reconstituted with sterile water [11].

48 Gershon [8] concluded that chickenpox vaccine offers close to 100% protection from severe
49 chickenpox and 90% protection from illness and have a greater impact on the epidemiology
50 of varicella and zoster in countries with high vaccine uptake. Welsby [19] indicated that in the
51 pre licensure era, 95% of adults experienced natural chickenpox children which resulted in
52 long-term immunity. Varicella vaccination is less effective than the natural immunity that
53 existed in prevaccine communities.

54 Macartney et al [12] studies on varicella shown that the vaccine is safe and highly effective
55 in reducing varicella-related disease with universal varicella vaccination of children in the
56 USA over the past 10 years. Edmunds and Brisson [6] brought to bear that infant VZV
57 vaccination could lead to an increase in adult disease or a temporary increase in the
58 incidence of shingles. Studies indicate more effective vaccination is at preventing varicella.
59 Understanding the mechanisms for maintaining immunity against varicella is critical for
60 predicting the long-term effects of vaccination.

Arvin and Gershon [2] studies reveal that varicella vaccine has clinical efficacy for the prevention of varicella. The vaccine induces persistent immunity to VZV in healthy children 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 [3] 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 studied the epidemiology of chickenpox in Agona West Municipality and estimated the endemicity of chickenpox with $R_0 = 2$ [7] 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 [3,4,5,16,17].

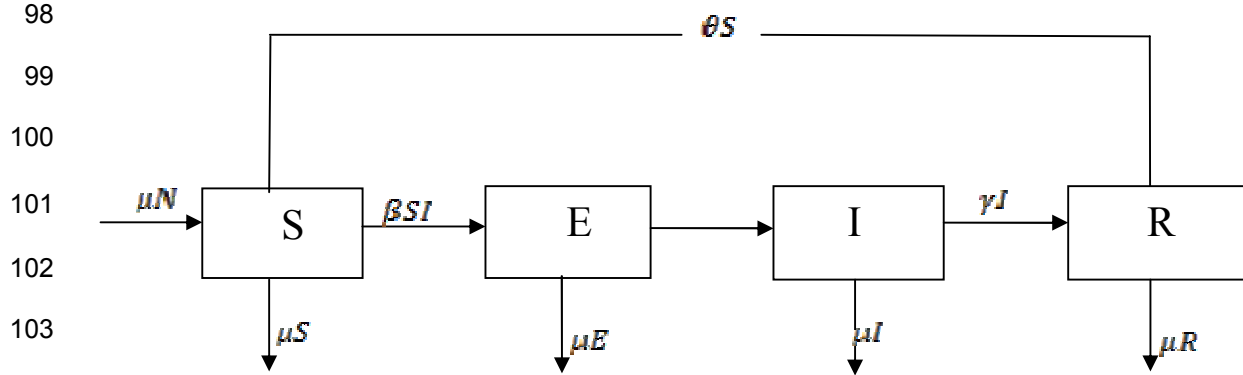
2. METHODOLOGY

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 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

91 infected but not yet infectious with the chickenpox and are not able to pass the chickenpox to
 92 others. Infective are the individuals that are infectious and capable of transmitting the
 93 infection to any susceptible that they come in contact and those in the recovered
 94 compartment are individuals previously infected but now neither infected nor susceptible.
 95 They have an infection-acquired immunity (permanent immunity). The proportion of
 96 individuals in each compartment S , E , I and R at time t is given as $S(t)$, $E(t)$, $I(t)$ and
 97 $R(t)$. The figure below is the flow chart of the SEIR model with vaccination.



104 Figure 1: Flow chart of SEIR Model of chickenpox transmission with vaccination

105 Where

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

108 The model equations [1] for chickenpox with vaccination are as follows

109
$$\frac{dS}{dt} = \mu N - \beta SI - \mu S - \theta S \quad (1)$$

110
$$\frac{dE}{dt} = \beta SI - \mu E - \kappa E \quad (2)$$

111
$$\frac{dI}{dt} = \kappa E - \mu I - \gamma I \quad (3)$$

112
$$\frac{dR}{dt} = \gamma I - \mu R + \theta S \quad (4)$$

113 We estimated the reproductive number (R_0) of chickenpox with vaccination using the next
 114 generation matrix (G). The next generation method is given as $(G) = FV^{-1}$, the (i, j) entry of
 115 F is the rate at which infected individuals in compartment j produce new infections in
 116 compartment i ,

the (j, k) entry of V^{-1} is the average length of time this individual spends in compartment j during its 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 new infections in compartment i produced by the infected individual originally introduced into compartment

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

$$G = F - V$$

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

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

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

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

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

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

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

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

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

$$\text{But } FV^{-1} = R_0$$

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

The reproductive number (R_0) is defined as the expected number of secondary infections arising from a single individual during his or her entire infectious period in a population of susceptible [15].

138 The reproductive number (R_0) is a threshold that determines whether a disease will spread
 139 in a population or dies out. Whenever R_0 is ≥ 1 , the disease will spread in a population and
 140 each infected individual produces on average more than one new infection and the disease
 141 will invade the Population leading it persistence (endemic). If R_0 is < 1 , the disease will die
 142 out in the population and on average an infected individual produces less than one new
 143 infected individual over the course of its infectious period and the infection [18].

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

145
$$\left(\frac{(\mu + \gamma)(\mu + k)}{\beta k}, \frac{\mu \beta k N - (\mu + \theta)(\mu + \gamma)(\mu + k)}{\beta k(\mu + k)}, \frac{\mu \beta k N - (\mu + \theta)(\mu + \gamma)(\mu + k)}{\beta k(\mu + \gamma)(\mu + k)}, \frac{\mu \gamma \beta k N - \gamma k(\mu + \theta)(\mu + \gamma)(\mu + k) + \theta[(\mu + k)(\mu + \gamma)]^2}{\mu \beta k(\mu + \gamma)(\mu + k)} \right)$$

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

147 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

148
$$|J - \lambda I| = \begin{vmatrix} -\beta I - (\mu + \theta) - \lambda & 0 & -\beta S & 0 \\ \beta I & -(\mu + k) - \lambda & \beta S & 0 \\ 0 & k & -(\mu + \gamma) - \lambda & 0 \\ 0 & 0 & \gamma & -\mu - \lambda \end{vmatrix}$$

149 The eigenvalues of the matrix for the disease free and the endemic equilibrium point of
 150 chickenpox with vaccination are $\lambda = -\beta I - (\mu + \theta)$, $\lambda = -(\mu + k)$ and $\lambda = -(\mu + \gamma)$ and
 151 $\lambda = -\mu$

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153 3.0 RESULTS AND DISCUSSION

154 Table1 below shows the summary of the data obtained from the Agona West Municipal
 155 Health Directorate

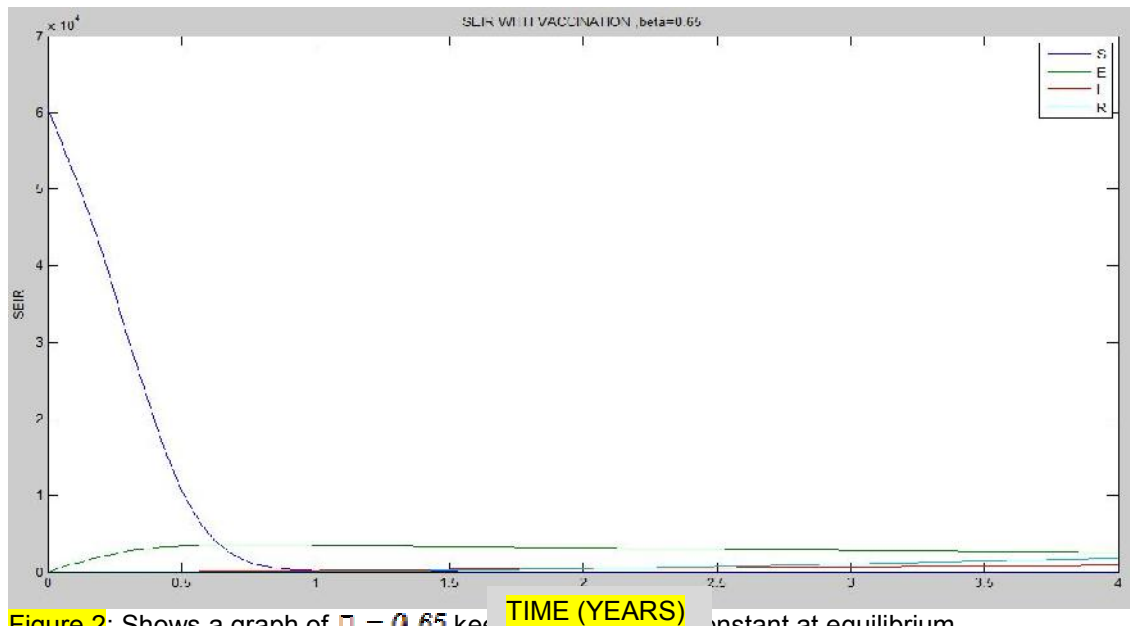
Time(years)	Susceptible	Exposed	Infective	Recovered
$t = 0$	60684	9	23	0
$t = 1$	55950	5	13	15

$\beta = 2$	58265	7	18	20
$\beta = 3$	48463	11	28	41
$t = 4$	31527	16	41	43

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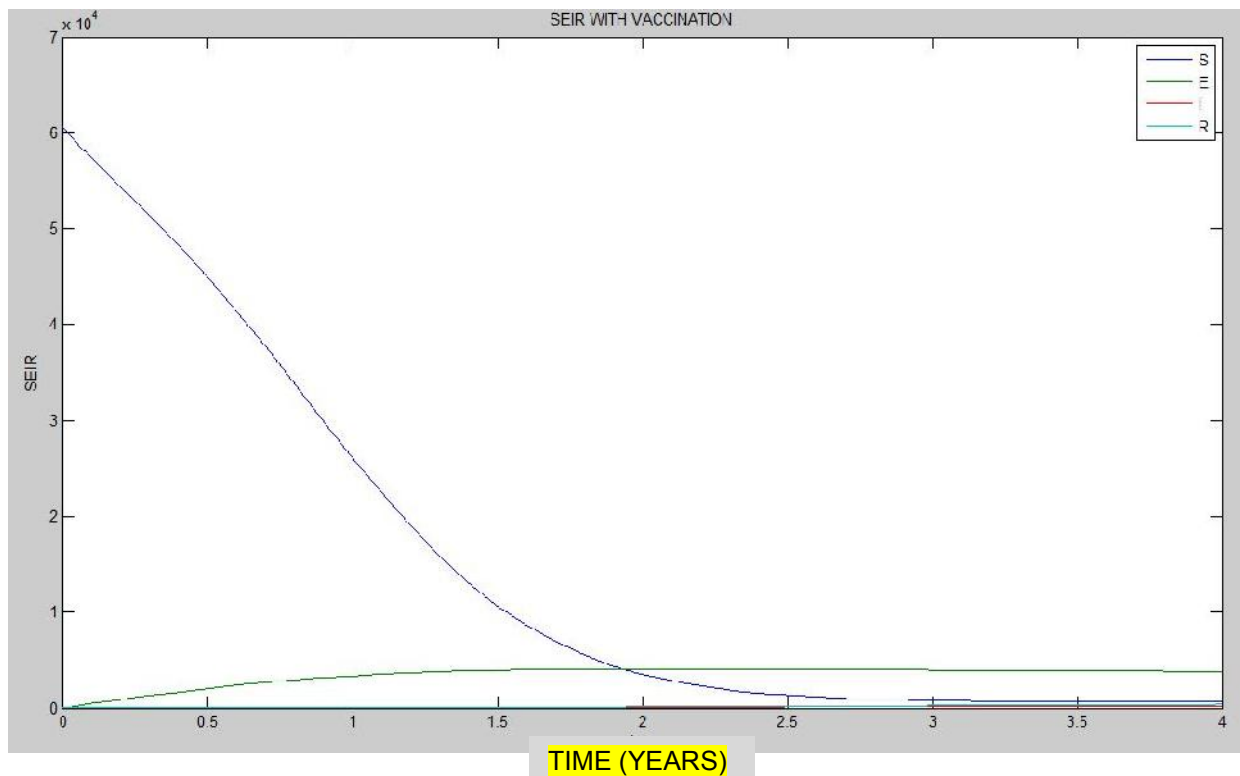
157 We estimated the parameter values from the data obtained from the Agona West Municipal
158 Health Directorate as follows: Transmission rate (β) = 0.026, Latency rate (σ) = 0.036,
159 Recovery rate (γ) = 0.014, Death rate (δ) = 0.02, Vaccinated rate coefficient
160 (η) = 0.00019 and Population (N) = 115,358

161 From the studies, we estimated the reproductive number of chickenpox with vaccination to
162 be $R_0 = 0.3 < 1$ which shows that after vaccination, the chickenpox will die out and will not
163 populate. We estimated that 53,241 out of 115,358 people needs to be vaccinated against
164 chickenpox and this corresponds to 46.2% of the Agona West Municipality needs to be
165 vaccinated in order to control the chickenpox. We estimated the stability analysis of disease
166 free and endemic equilibrium point with vaccination to be unstable and asymptotically stable.
167 Sensitivity analysis of SEIR model with vaccination showed that the susceptible population
168 decreases sharply with time while the infective and recovered population also decreases
169 asymptotically when the value of transmission rate (β) was varied from 0.08 to 0.65 as time
170 increases.



171
 172 **Figure 2:** Shows a graph of $\beta = 0.65$ kept constant at equilibrium
 173
 174 We observed that as the recovery rate (γ) varies from 0.07 to 0.99 , the susceptible
 175 population decreases with no significant increase or decrease in the exposed population.
 176 While the infective and the recovered population decreases asymptotically to the time axis

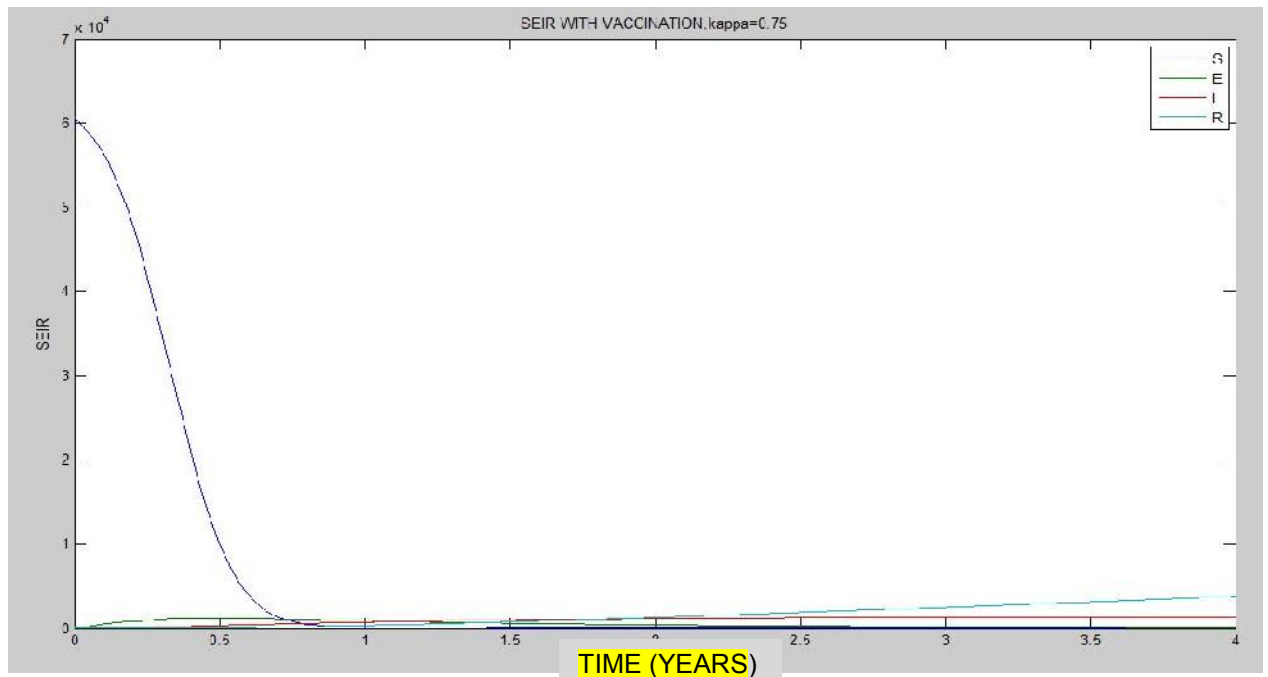
177 as time increases.



178
179 **Figure 3:** Shows a graph of $\beta = 0.99$ keeping μ , δ and σ constant at equilibrium

180
181 We observed that as the latency rate (δ) 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.



186

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

188

189 As the vaccination rate coefficient (κ) varies from 0.02 to 0.96, we observed that more
190 chickenpox patients recovered from approximately 200 to 30,000 with a decrease in the
191 exposed population from approximately 300 to 250 with no significant increase or decrease
192 in the infective as time increases.

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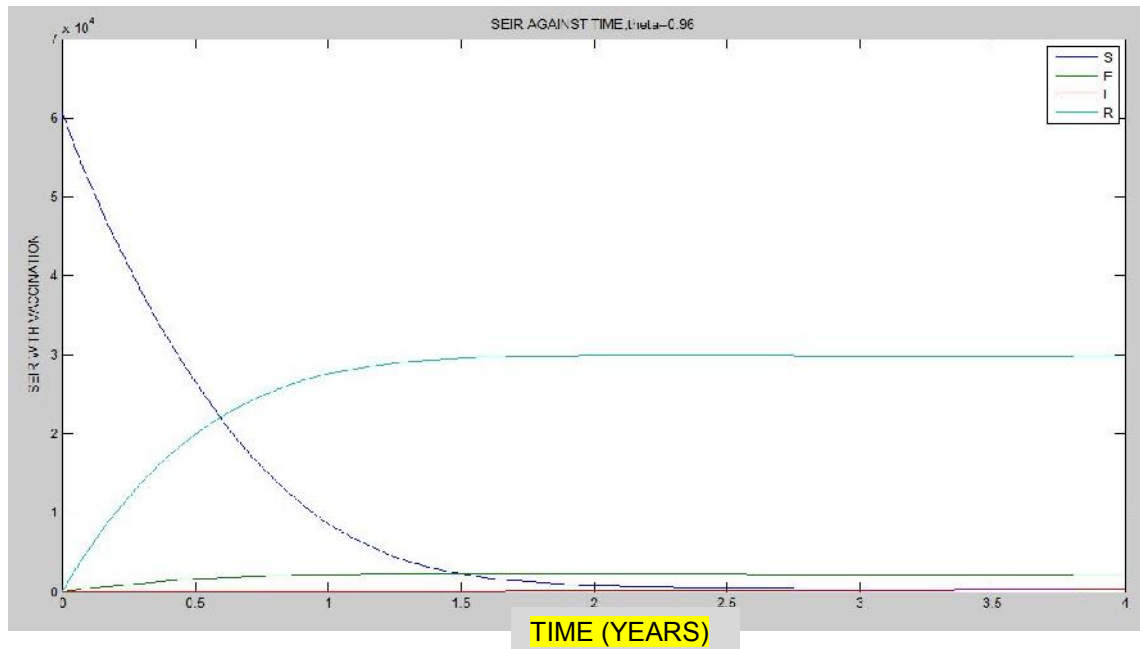


Figure 5: Shows a graph of $\theta = 0.96$ keeping β , σ and γ constant at equilibrium

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

4. CONCLUSION

From the studies, we observed that if vaccination rate coefficient (θ) is increase (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 to unequal birth/death rate

225

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227

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233 writing of the manuscript. If the study sponsors had no such involvement, the authors should
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250

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252 performed the statistical analysis, wrote the protocol, and wrote the first draft of the
253 manuscript. 'Author B' and 'Author C' managed the analyses of the study. 'Author C'
254 managed the literature searches..... All authors read and approved the final manuscript."

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257

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APPENDIX

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