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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 $R_v = 0.3 < 1$. 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

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37 lesions, fever, mild fatigue and general malaise. The primary infection with Varicella - Zoster
38 Virus (VZV) causes Chickenpox. It is associated with pain and body itching [2].

39 Chickenpox (Varicella) vaccine is a live attenuated viral vaccine derived from the Oka strain
40 of VZV. The vaccine virus was isolated by Takahashi in the early 1970s from vesicular fluid
41 from a healthy child with varicella disease. Varicella vaccine was licensed for general use in
42 Japan and Korea in 1988 and later licensed in the United States in 1995 for persons who
43 were 12 months of age and older. The virus was attenuated by sequential passage in human
44 embryonic lung cell culture, embryonic guinea pig fibroblasts and in WI-38 human diploid
45 cells. The Oka (Merck) vaccine has undergone further passage through MRC-5 human
46 diploid cell cultures for a total of 31 passages [2].

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

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

58 Macartney *et al.* [6] studies on varicella shown that the vaccine is safe and highly effective in
59 reducing varicella-related disease with universal varicella vaccination of children in the USA
60 over the past 10 years. Edmunds and Brisson [7] brought to bear that infant VZV vaccination
61 could lead to an increase in adult disease or a temporary increase in the incidence of
62 shingles. Studies indicate more effective vaccination is at preventing varicella.

63 Understanding the mechanisms for maintaining immunity against varicella is critical for
64 predicting the long-term effects of vaccination.

65 Arvin and Gershon [8] studies reveal that varicella vaccine has clinical efficacy for the
66 prevention of varicella. The vaccine induces persistent immunity to VZV in healthy children
67 and adults. Immunization against VZV lowers the risk of reactivation of herpes zoster virus
68 which is a serious problem for grownups and immunocompromised individuals. Gershon *et*
69 *al.*[9] agreed with Arvin and Gershon [8] that live attenuated varicella vaccine is safe and
70 effective in preventing chickenpox. Leukemic children have a 50% incidence of mild-to-
71 moderate adverse effects but have a high degree of protection once immune reactions to
72 varicella-zoster virus (VZV) have developed. Adult vaccinees have a lower degree of
73 protection (70%) compared to children.

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

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81

82 2. METHODOLOGY

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

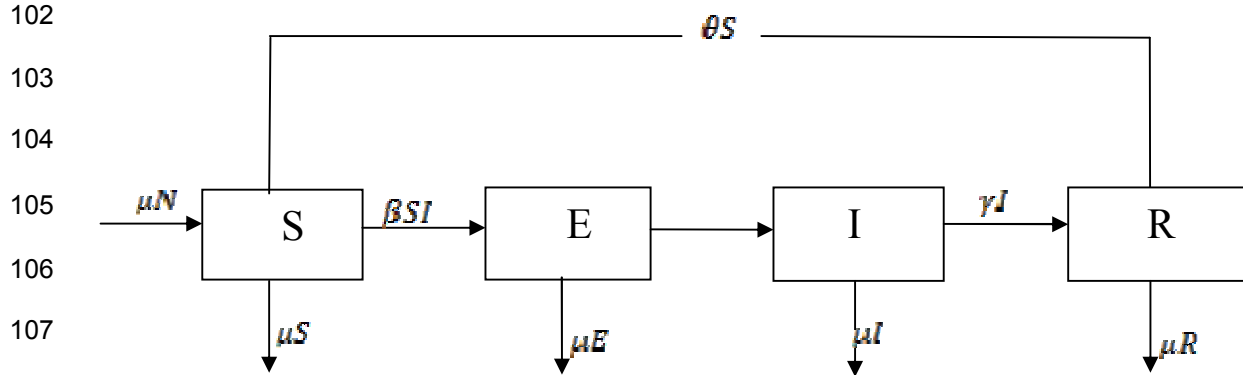
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90 2.1 The Mathematical Model

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92 In the SEIR model, the total population is divided into four separate groups: Susceptible (S),
 93 Exposed (E), Infective (I) and Recovered (R). Susceptible people can contract the disease if
 94 they come into contact with the chickenpox, while those in the exposed group are individuals
 95 infected but not yet infectious with the chickenpox and are not able to pass the chickenpox to
 96 others. Infective are the individuals that are infectious and capable of transmitting the
 97 infection to any susceptible that they come in contact and those in the recovered
 98 compartment are individuals previously infected but now neither infected nor susceptible.
 99 They have an infection-acquired immunity (permanent immunity). The proportion of
 100 individuals in each compartment S , E , I and R at time t is given as $S(t)$, $E(t)$, $I(t)$ and $R(t)$.

101 Figure 1 is the flow chart of the SEIR model with vaccination.



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

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110 μN = Birth rate of susceptible population, θ = Vaccinated rate coefficient, β = Infection rate,

111 κ = Latency rate, γ = Recovery rate and μ = Natural death rate.

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

113
$$\frac{dS}{dt} = \mu N - \beta SI - \mu S - \theta S \quad (1)$$

114
$$\frac{dE}{dt} = \beta SI - \mu E - \kappa E \quad (2)$$

115
$$\frac{dI}{dt} = \kappa E - \mu I - \gamma I \quad (3)$$

116
$$\frac{dR}{dt} = \gamma I - \mu R + \theta S \quad (4)$$

117 We estimated the reproductive number (R_0) of chickenpox with vaccination using the next
 118 generation matrix (G). The next generation method is given as $(G) = FV^{-1}$, the (i, j) entry of
 119 F is the rate at which infected individuals in compartment j produce new infections in
 120 compartment i , the (j, k) entry of V^{-1} is the average length of time this individual spends in
 121 compartment j during its lifetime, assuming that the population remains near the disease
 122 free equilibrium and barring reinfection. Hence, the (i, k) entry of the product FV^{-1} is the
 123 expected number of new infections in compartment i produced by the infected individual
 124 originally introduced into compartment k . We linearized the infection state of the differential
 125 equation (2) and (3) to obtain $G = F - V$

$$126 \quad F - V = \begin{vmatrix} -(\mu + \kappa) & \beta \\ k & -(\mu + \gamma) \end{vmatrix}$$

$$127 \quad F - V = \begin{vmatrix} 0 & \beta \\ 0 & 0 \end{vmatrix} - \begin{vmatrix} (\mu + \kappa) & 0 \\ -k & (\mu + \gamma) \end{vmatrix}$$

$$128 \quad F = \begin{vmatrix} 0 & \beta \\ 0 & 0 \end{vmatrix} \text{ and } V = \begin{vmatrix} (\mu + \kappa) & 0 \\ -k & (\mu + \gamma) \end{vmatrix}$$

$$129 \quad \text{Det } V = (\mu + \kappa)(\mu + \gamma)$$

$$130 \quad \text{Det } V = (\mu + \kappa)(\mu + \gamma)$$

$$131 \quad V^{-1} = \frac{1}{(\mu + \kappa)(\mu + \gamma)} \begin{vmatrix} (\mu + \gamma) & 0 \\ k & (\mu + \kappa) \end{vmatrix}$$

$$132 \quad V^{-1} = \begin{vmatrix} \frac{1}{(\mu + \kappa)} & 0 \\ \frac{k}{(\mu + \kappa)(\mu + \gamma)} & \frac{1}{(\mu + \gamma)} \end{vmatrix}$$

$$133 \quad FV^{-1} = \begin{vmatrix} 0 & \beta \\ 0 & 0 \end{vmatrix} \begin{vmatrix} \frac{1}{(\mu + \kappa)} & 0 \\ \frac{k}{(\mu + \kappa)(\mu + \gamma)} & \frac{1}{(\mu + \gamma)} \end{vmatrix}$$

$$134 \quad FV^{-1} = \frac{\beta k}{(\mu + \kappa)(\mu + \gamma)}$$

$$135 \quad \text{But } FV^{-1} = R_0$$

$$136 \quad (R_0) = \frac{\beta k}{(\mu + \kappa)(\mu + \gamma)}$$

137 The reproductive number (R_0) is defined as the expected number of secondary infections
 138 arising from a single individual during his or her entire infectious period in a population of
 139 susceptible [11].

140 The reproductive number (R_0) is a threshold that determines whether a disease will spread
 141 in a population or dies out. Whenever R_0 is ≥ 1 , the disease will spread in a population and
 142 each infected individual produces on average more than one new infection and the disease
 143 will invade the population leading to its persistence (endemic). If R_0 is < 1 , the disease will
 144 die out in the population and on average an infected individual produces less than one new
 145 infected individual over the course of its infectious period and the infection [17].

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

147
$$\left(\frac{(\mu - \gamma)(\mu - k)}{\beta k}, \frac{\mu \beta k N - (\mu - \theta)(\mu - \gamma)(\mu + k)}{\beta k(\mu + k)}, \frac{\mu \beta k N - (\mu - \theta)(\mu + \gamma)(\mu + k)}{\beta k(\mu + \gamma)(\mu + k)}, \frac{\mu \gamma \beta k N - \gamma k(\mu - \theta)(\mu + k) + \theta(\mu + k)(\mu + \gamma)^2}{\mu \beta k(\mu + \gamma)(\mu + k)} \right)$$

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

149 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

150
$$|J - \lambda I| = \begin{vmatrix} -\beta I - (\mu + \theta) - \lambda & 0 & -\beta S & 0 \\ \beta I & -(\mu + k) - \lambda & \beta S & 0 \\ 0 & k & -(\mu + \gamma) - \lambda & 0 \\ 0 & 0 & \gamma & -\mu - \lambda \end{vmatrix}$$

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

153

154 3.0 RESULTS AND DISCUSSION

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

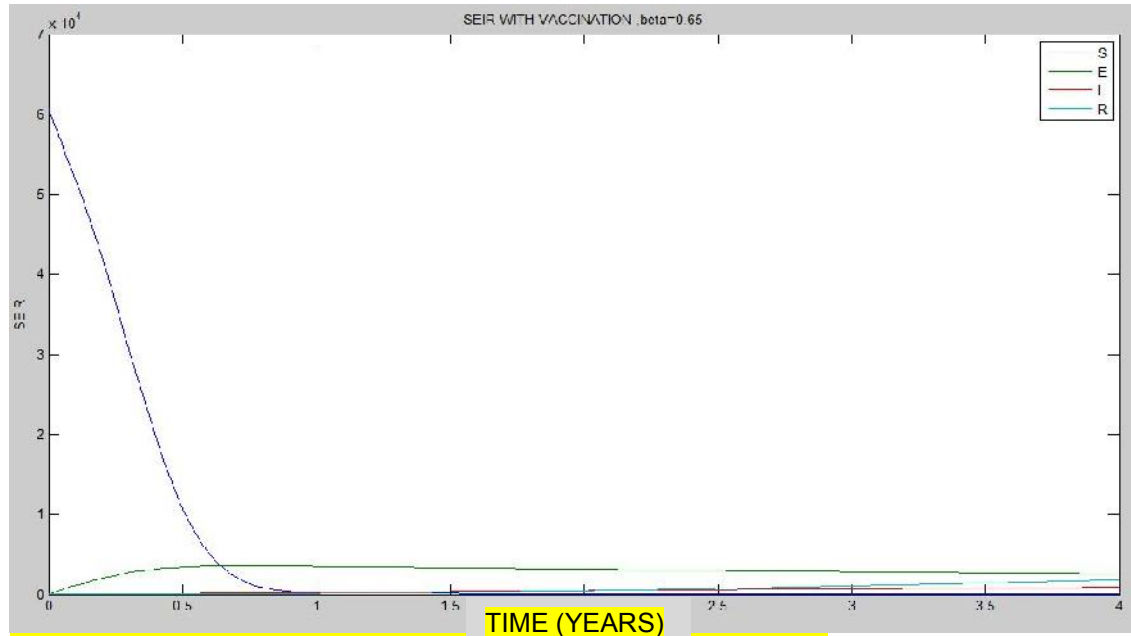
159 Municipal Health Directorate can be found at the Appendix (Table 1). Figures 2, 3, 4 and 5
160 show various analyses.

161 From the studies, we estimated the reproductive number of chickenpox with vaccination to
162 be $R_0=0.03 < 1$ 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.

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

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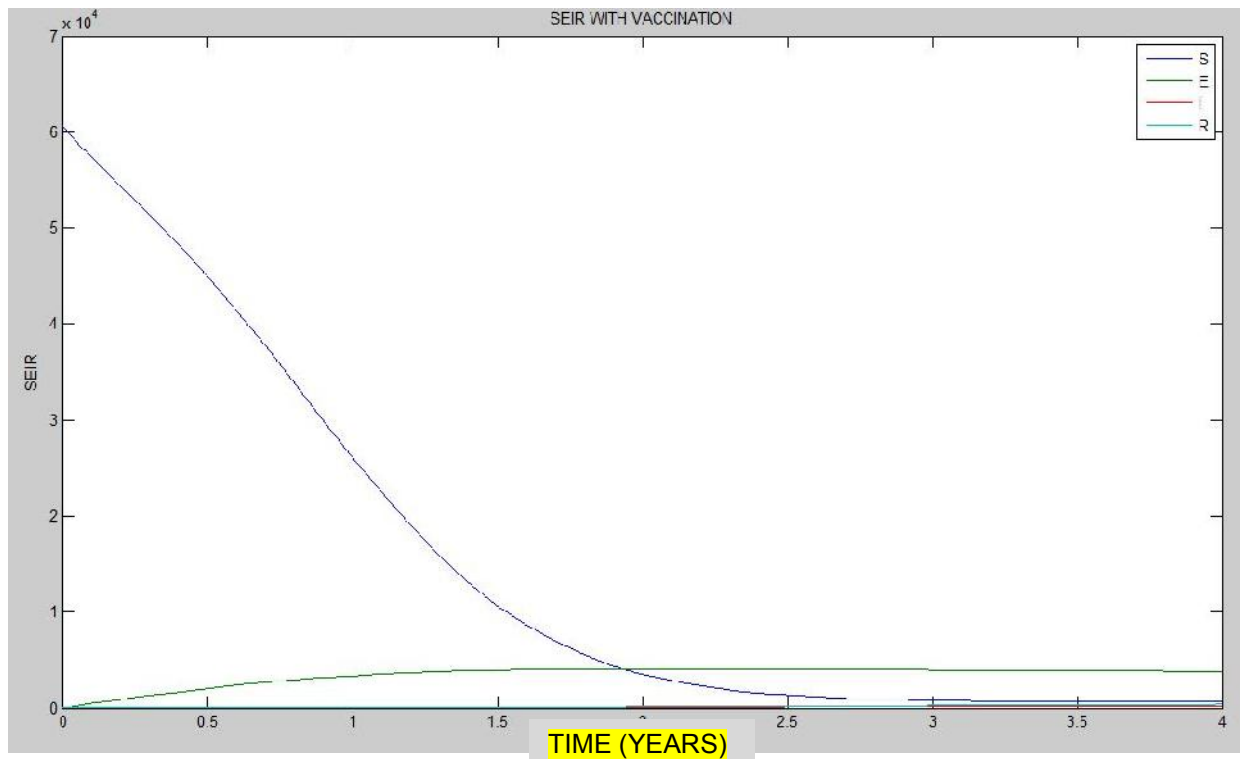
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175 Figure 2: Shows a graph of $\beta=0.65$ keeping κ , γ and θ constant at equilibrium

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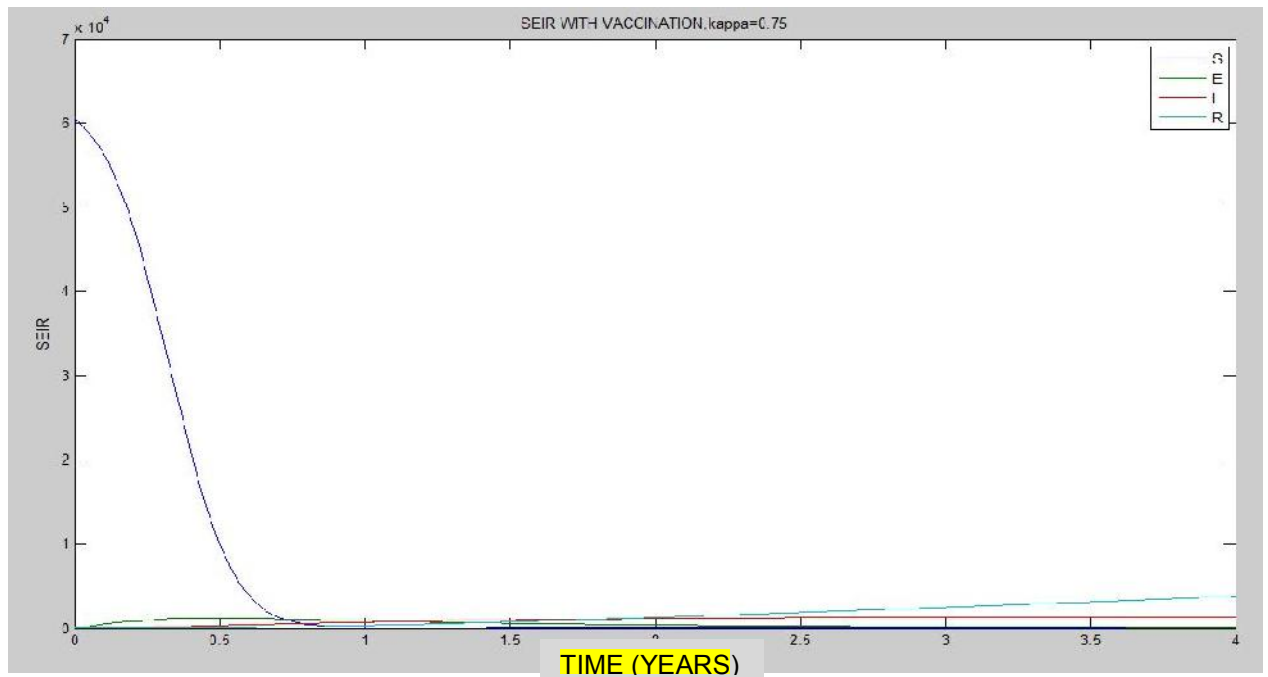
178 We observed that as the recovery rate (γ) varies from 0.07 to 0.99, the susceptible
 179 population decreases with no significant increase or decrease in the exposed population.
 180 While the infective and the recovered population decreases asymptotically to the time axis
 181 as time increases.



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

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



191

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

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

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

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

198 in the infective as time increases.

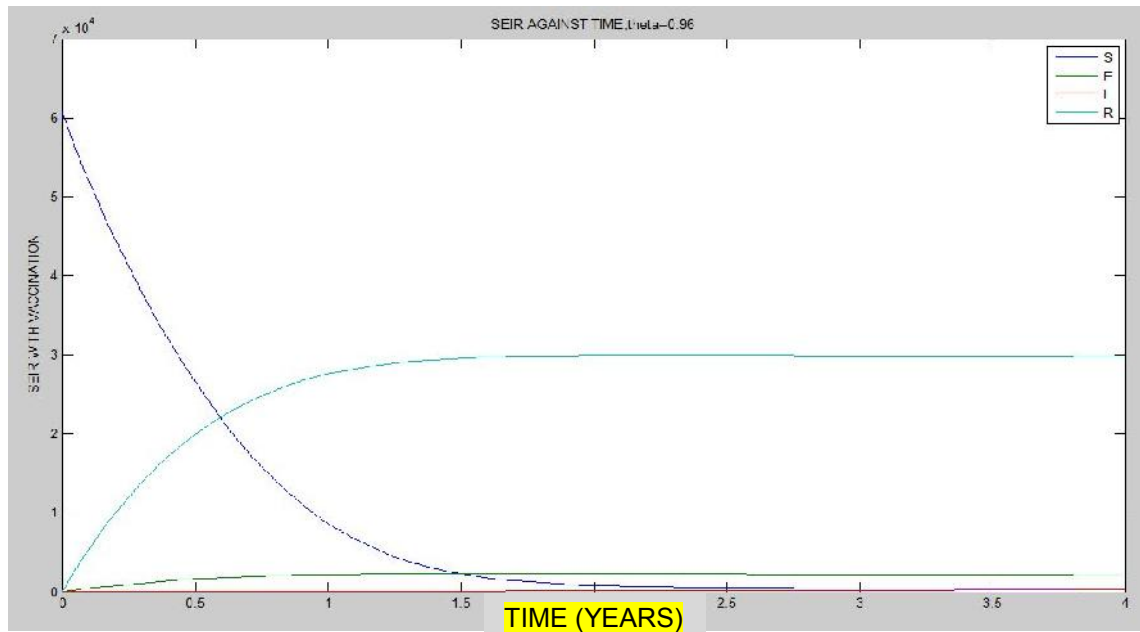


Figure 5: Shows a graph of $\theta=0.96$ keeping β, γ and κ constant at equilibrium

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

218 to unequal birth/death rate

219

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228 COMPETING INTERESTS

229

230 Authors have declared that no competing interests exist.

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234 REFERENCES

235 [1] Nardone A, De Orby F, Carton M, Cohen D, Van Damme P, Davidkin I et al (2007). The
236 comparative seroepidemiology of varicella zoster virus in 11 countries in the European
237 region. *Vaccine* 25(45): 7866–7872. [PubMed]

238

239 [2] National Centre for Immunization Research and Surveillance (NCIRS) Fact Sheet (2009):
240 Varicella-Zoster (Chickenpox) Vaccines for Australian children. Available on [http:](http://www.ncirs.edu.au)
241 www.ncirs.edu.au (accessed on 12th December, 2012)

242

243 [3] Young, L. (2009). Components of Chickenpox Vaccine. (available on [http:](http://www.netplaces.com)
244 www.netplaces.com Accessed on 1st October, 2012)

245

246

247 [4] Gershon AA (2001). The Current Status of Live attenuated varicella vaccine. *Arch Virol*
248 *suppl*;17:1 – 6

249

250 [5] Welsby PD (2006). Chickenpox, chickenpox vaccination and shingles. *postgrad med*
251 *J*;82(967):351 - 2

252

253 [6] Macartney KK, Beutels F, Burgess MA, McIntyre F (2005). Varicella vaccination in
254 Australia. *J paediatr child Health*;41(11) :544 - 52

255

256 [7] Edmunds WJ, Brisson M (2002). The effect of vaccination on the epidemiology of
257 varicella zoster virus. *J.Infect*;44(4):211 - 9

258

259 [8] Arvin AM, Gershon AA(1992). Live attenuated vaccine. *Annu Rev microbial*; 50: 59 - 100

260

261 [9] Gershon AA, La Russa P, Hardy I, Steinberg S, Silverstein S (1992). Varicella vaccine;
262 the American experience; *J. Infect Dis*;166 suppl 1: S63 – S68

263

264 [10] Esson AB (2013). Epidemiology of Chickenpox in Agona West Municipality, Ghana.
265 MPhil Thesis, Department of Mathematics, Kwame Nkrumah University of Science and
266 Technology, Kumasi, Ghana.

- 267 [11] Dontwi IK, Obeng-Denteh, W, Bilson DF, Tackie OF, Batsa TF, Ewoenam K et al
 268 (2013). Modeling Memorization and Forgetfulness Using Differential Equations, Progress in
 269 Applied Mathematics, 5 (2): 1-12
 270
 271 [12] Dontwi IK, Obeng-Denteh, W, Andam EA, Obiri AL (2014). A Mathematical Model to
 272 Predict the Prevalence and Transmission Dynamics of Tuberculosis in Amansie West
 273 District, Ghana, British Journal of Mathematics and Computer Science, 4(7): 969-988
 274
 275 [13] Dontwi K., Obeng-Denteh, W. (2011). Using Differential Equations to Model the Number
 276 of Bats in a Habitat, Continental J. Applied Sciences 6 (2): 29 – 33
 277
 278 [14] Obeng-Denteh, W. (2011). Modelling students' affinity for pure mathematics using
 279 differential equations: The case of students of Kwame Nkrumah University of Science and
 280 Technology, Continental J. Applied Sciences 6 (2): 34 – 40
 281
 282 [15] Obeng-Denteh,W, Kodua NO, Owusu AS, Kwame Ansah R, Quashie Nyamadu A
 283 (2012). Modelling students' affinity for lecture attendance using differential equations: The
 284 case of students of Kwame Nkrumah University of Science and Technology, British Journal
 285 of Education, Society and Behavioural Science, 2 (4): 389 – 401
 286
 287 [16] Anderson RM, May RM. (1991). Infectious Diseases in Human: Dynamics and control,
 288 Oxford University Press. Oxford
 289
 290 [17] Van Den Driessche P and Watmough J. (2002). Reproduction number and sub-
 291 threshold endemic equilibria for compartmental models. Math Biosci, 180, 29 - 48
 292

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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