SEIR Model :
Ebola Outbreak of Sierra Leone for 2014-2015

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Background

Ebola was initially identified in a region within the Democratic Republic of Congo. Since its discovery in 1976, there has been 26 different epidemics confirmed,with the majority of them being located in the West African Region. It wasn't until 2014 that Ebola started to spread due to the citizens of infected regions transporting to different parts of the world causing it to become a global health scare. In this study, we concentrate on the outbreak of 2014-2015 in Sierra Leone.

Introducing Ebola

What is Ebola?

Ebola haemorrhagic fever (EHF) is a fatally infectious disease marked by fever and severe internal bleeding. It is believed to be originated from fruit bats and primates. The Ebola infection can be acquired in many ways, such as the direct contact with an infectious person body fluids, direct contact with patients during a visit at the hospital, and performing traditional burial ceremonies.

When is it Contracted and How Contagious is it?

It is rare to become infected with Ebola during the incubation stage, however, the transmissibility increases with the duration of the disease and with direct contact with infected individuals during the late stage of illness. Which means that the longer a person is infected the more contagious they become.

Surrounding Outbreaks

On March 23, 2014, Guinea proven that an Ebola outbreak was transpiring with the total of 49 cases and 29 deaths, making it the first country confirmed to have an epidemic. On March 30, Liberia confirmed they also had an Ebola outbreak. Sierra Leone was one of the last countries to contract the Ebola virus, even though it was unpreventable. Both of its surrounding borders were far along in their outbreak, and yet they we still actively trading with Guinea and Liberia up until Jun 11.

Sierra Leone Introduction

On May 24, 2014 a tribal healer, who had been treating Ebola patients from towns across the nearby border of Guinea, became the first confirmed case after aiding a woman suffering from a miscarriage. According to tribal tradition, her body was washed for burial, which led to the various infections spreading to other women from neighbouring towns. Intervention methods did not begin until July 30, 2014, which was after a state of emergency was declared, at that time troops were deployed to quarantine hot spots. By that time over 200 Ebola deaths had occurred.

Research Introduction

In this research, we focus solely on the Situation Reports provided by WHO (World Health Organization) for the duration of 36 weeks. In those reports, the amount of confirmed Ebola case per week was provided between dates of Sept 22, 2014 to May 26, 2015. The reports do not start from the beginning of the epidemic, but we decided to use the Situation Reports rather than the Patient Database to guarantee accuracy of the amount of Ebola cases.

Research Plan

- Estimate the reproduction number
- Estimate parameters using the least square method
- Understand the transmission stages using SEIR model differential equations
- Conduct a multivariate analysis of the parameters
- Predict when Sierra Leone will be Ebola free

Reproduction Number

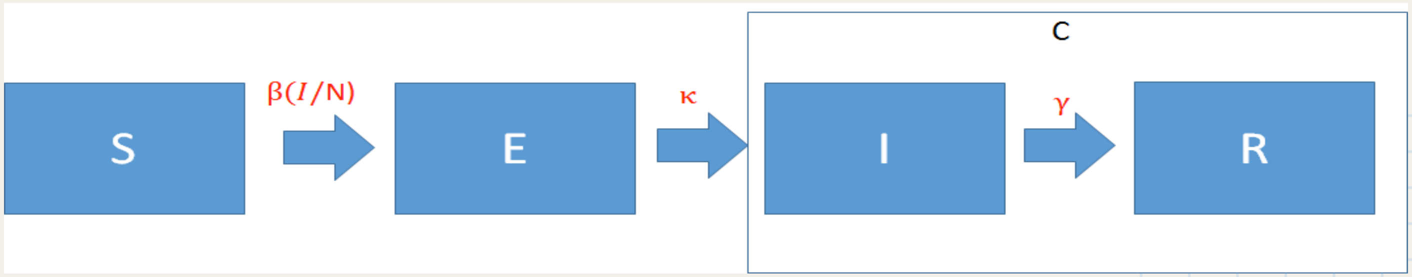
In order to understand how rapidly this epidemic is growing we calculate the reproduction number. The reproduction number (R_0) computes the average number of secondary infections generated by one primary case of Ebola in the entire susceptible population. In order to find those contributions from each stage we have to create a SEIR model to understand the aspects of the transmission.

Methods

The Model

- Model used for:
- ❑ Estimate the basic reproductive number **(R_0)**
- ❑ We used the least-square fit of the model to provide estimates for the epidemic parameters.
- SEIR epidemic model

Represents the flow of individuals between the epidemic classes.



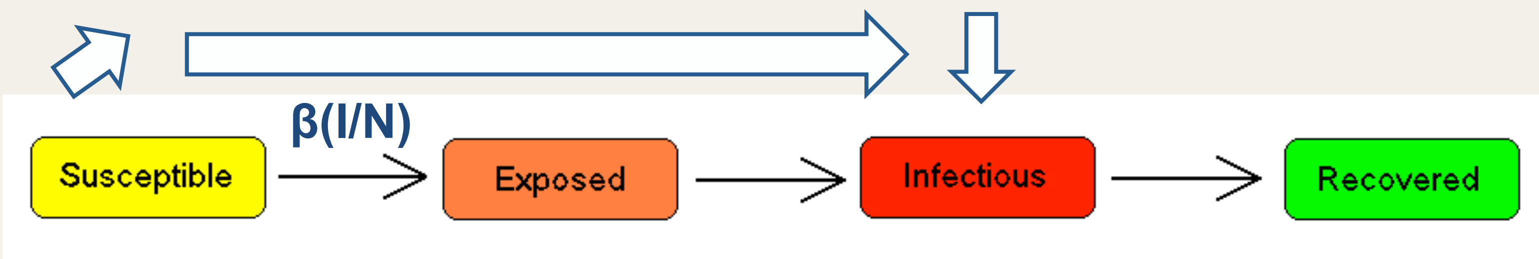
Differential Equations Model

1. $S'(t) = -\beta S(t)I(t)/N$
2. $E'(t) = \beta S(t)I(t)/N - \boldsymbol{\kappa} E(t)$
3. $I'(t) = \boldsymbol{\kappa} E(t) - \gamma I(t)$
4. $R'(t) = \gamma I(t)$
5. $C'(t) = \boldsymbol{\kappa} E(t)$

Model Breakdown

$$S'(t) = -\beta S(t)I(t)/N$$

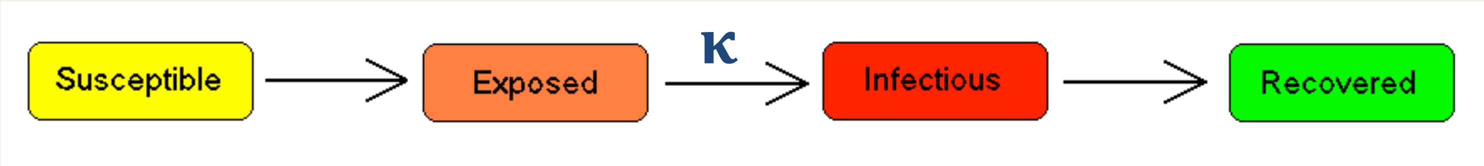
The rate of change at which the susceptible class is proportional to the interaction between the number of susceptible and infected individuals.



Model Breakdown (cont.)

$$E'(t) = \beta S(t)I(t)/N - \kappa E(t)$$

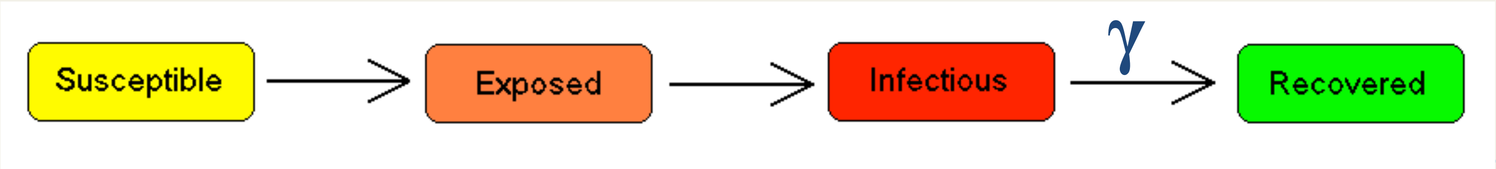
The rate of change at which the exposed class become infectious.



Model Breakdown (cont.)

$$I'(t) = \kappa E(t) - \gamma I(t)$$

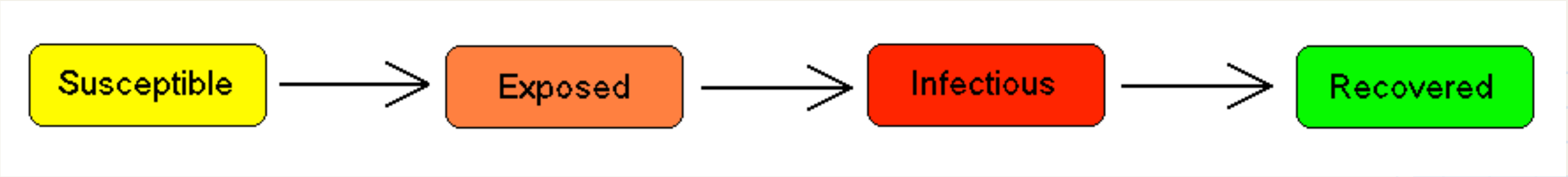
The rate of change at which the infected class is removed from the chain of transmission.



Model Breakdown (cont.)

$$R'(t) = \gamma I(t)$$

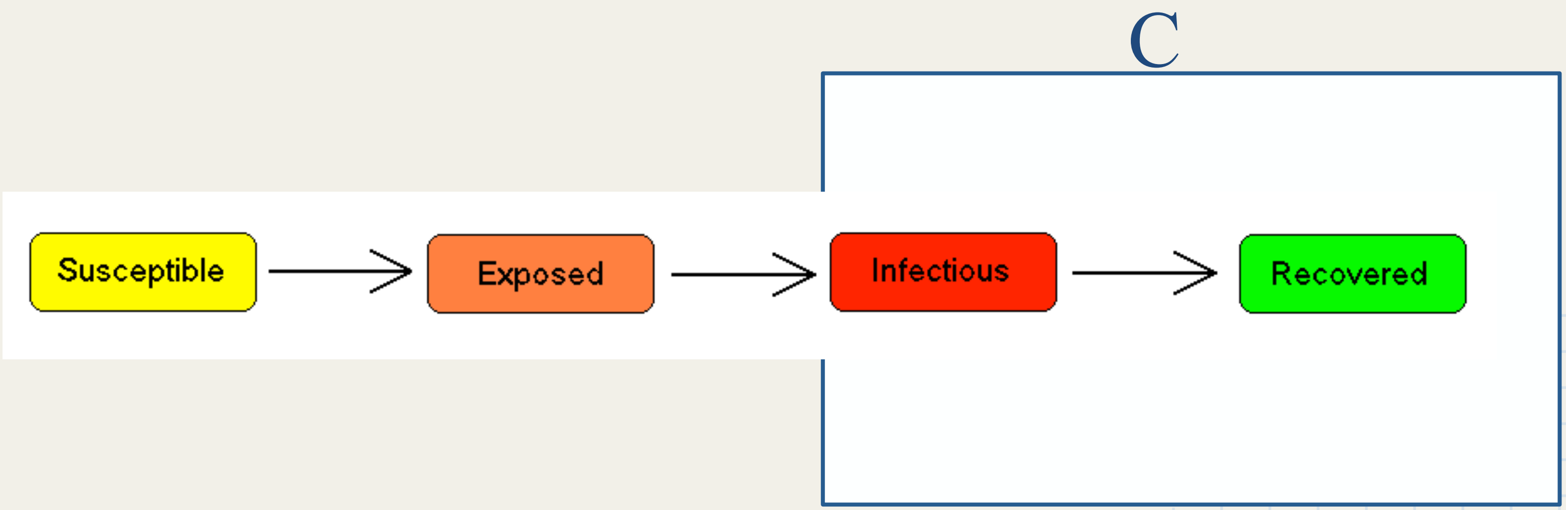
The rate of change at which the removed class recovered from the disease or die.



Model Breakdown (cont.)

$$C'(t) = \kappa E(t)$$

The cumulative number of infected individuals



Differential Equations Model and Variables

Differential Eq. Model

1. $S'(t) = -\beta S(t)I(t)/N$
2. $E'(t) = \beta S(t)I(t)/N - \boldsymbol{\kappa} E(t)$
3. $I'(t) = \boldsymbol{\kappa} E(t) - \gamma I(t)$
4. $R'(t) = \gamma I(t)$
5. $C'(t) = \boldsymbol{\kappa} E(t)$

- **β = transmission rate per person per day**
- **N = total population size**
- **(I/N) = probability of contact made with infectious individual**
- **($1/\kappa$) = average incubation period**
- **($1/\gamma$) = infectious period**
- **C(t) = total number of cases after onset of symptoms**

Assumptions

- The entire population is believed to be susceptibles
- The transmission rate will gradually decrease from β_0 to β_1 between the time of onset of the intervention to the time of full compliance.

Parameters

Least square method using MatLab

**The parameters we estimated were β0, β1, t-intervention time, and q.

Parameters	Definitions	Estimation
$\beta 0$	Transmission rate before intervention	?
$\beta 1$	Transmission rate after intervention	?
q	Controls the rate of the transmission from $\beta 0$ to $\beta 1$	?
t	T-intervention time	?
R0	Basic Reproduction Number	?
$1/k$	Average incubation period	5.3
$1/\gamma$	Average infectious period	5.61
N	Total Population	6092000

Least Square Data Fitting

- We selected initial points based on actual data from the situation reports. (initial value for ODE45)

  S = 6092000 E = 90 I = 254 R = 175 C = 429
- Least square method:

$$\text{Min} \sum_{i=1}^{n} [(Ci - Ci^*)^2 + (Ii - Ii^*)^2]$$

used to minimize the square of the difference between the cumulative data and infected data.

- The average of the difference of data and the best fit is about 1.7%.

Program

```
function [p,resnorm]=Ex_LSQ3
%This program use the data from WHO situation report; Sierra Leone Patient database starting
%from Sept 22, 2014 to May 27, 2015 (36 weeks);
casenumber=3;
switch casenumber
    case 1 %Estimate the trasmission rate beta by fixed k and gamma
p0=[0.12 0.01 7.5 1.5];%[beta0,beta1,t-intervention time, q]
lb=[0 0 0 0];% lower bound;
ub=[4 4 20 20];% upper bound;
[p,resnorm] = lsqnonlin(@myfun,p0,lb,ub);  % Invoke optimizer
    case 3 %use the estimated paramter to system by copying the resulting p
p0=[    1.4988    0.8795    5.3109    0.2367];%ndata=30;
beta=p0(1);
gamma= 7/5.61;
R0=beta/gamma
        options = odeset('RelTol',1e-4,'AbsTol',[1e-4 1e-4 1e-5 1e-5 1e-5]);
T0=0:1:35;
        [T,Y] = ode45(@(t,y)SEIR(t,y,p0),T0,[6092000 90 254  175 429],options);
pI=[254 350 315 371 386 399 435 421 533 385 537 397 327 315 337 248 184 117 65 80 76 96 63 81 58 55 33 25 9 9 12 11 9 2 8 3];
SC=[254 604 919 1290 1676 2075 2510 2931 3464 3849 4386 4783 5110 5425 5762 6010 6194 6311 6376 6456 6532 6628 6691 6772 6830 6885 6918

figure(1)
```

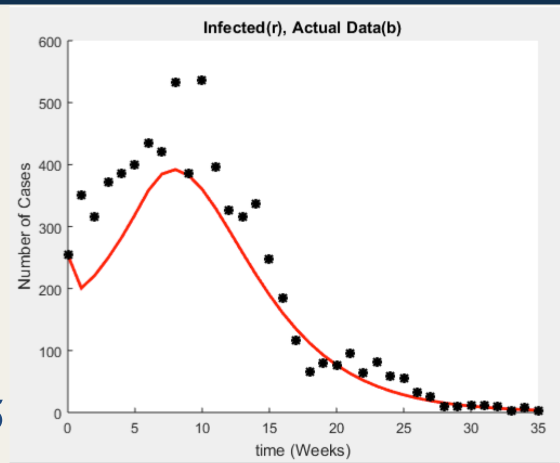
Estimated Parameters

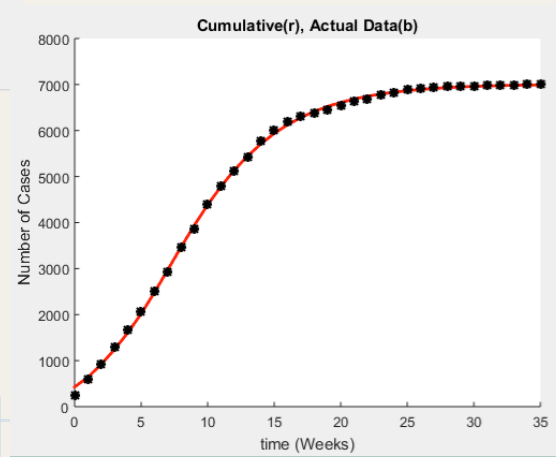
Parameters	Definitions	Estimation
β0	Transmission rate before intervention	1.4988 (weeks)
β1	Transmission rate after intervention	0.8795 (weeks)
q	Controls the rate of the transmission from β0 to β1	0.2367 (weeks)
t	T-intervention time	5.3109 (weeks)
R0	Basic Reproduction Number	1.2127
1/k	Average incubation period	5.3
1/γ	Average infectious period	5.61
N	Total Population	6092000

Results

Initial Results

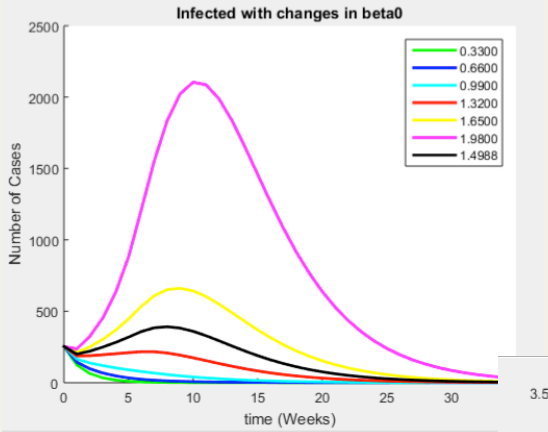
The Sierra Leone epidemic reached approximately 7,000 cases. Our results showed that the infected individuals only reached a high of ~375 cases, but the actual data says otherwise, this is due to the error in the data fitting.

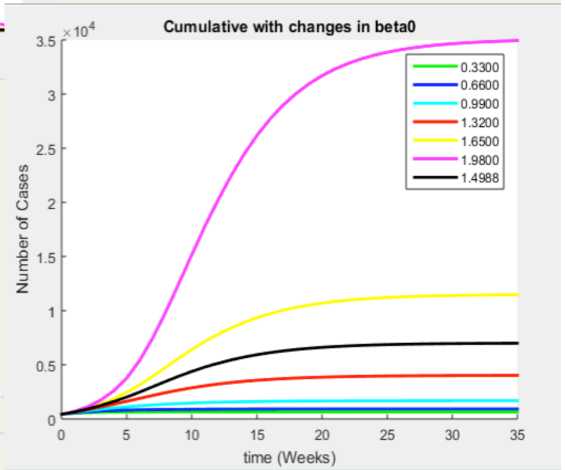




Transmission Rate, β_0

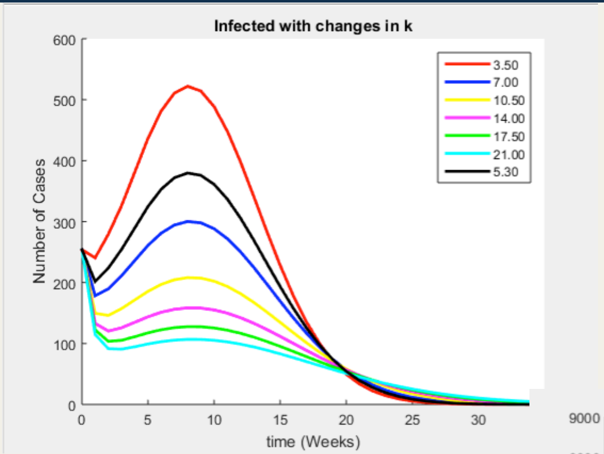
In manipulating the transmission rate, we gradually increased β_0 from 0 to 2. In doing so, we discovered just how important this parameter is in epidemics. When β_0 is closer to 0 the infected cases declines and becomes constant. When β_0 is closer to 2 the epidemic skyrocket. The cumulative cases reached 35,000 at 1.98 but when dropped to 10,000 at 1.65. This was 250% increase. This means the higher the transmission rate the bigger the outbreak.

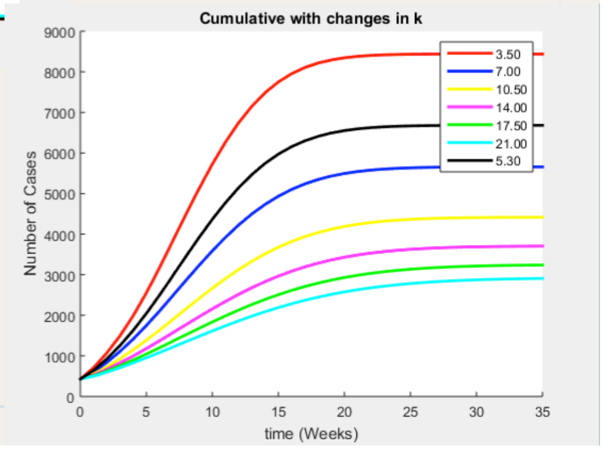




Incubation Period, κ^{-1}

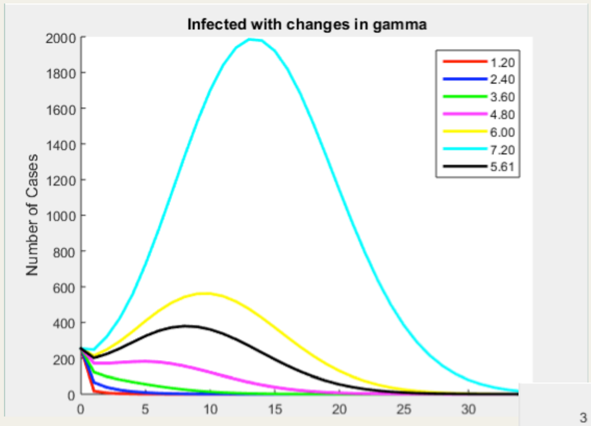
In manipulating the parameter k, we converted the incubation days in to weeks by dividing κ^{-1} by 7 days ($\kappa^{-1}/7$). The increase in $7/\kappa$ was 3.5 days. As the number increase to 21, which is the maximum days of the incubation period, the changes became more and more insignificant. When the incubation period is at 3.5 there were over 8000 cases, when changed to 7 days the cases nearly dropped to approximately 5500 cases which was a 45% drop. This indicates that the longer the incubation period the less likely a person is going to affect someone else.

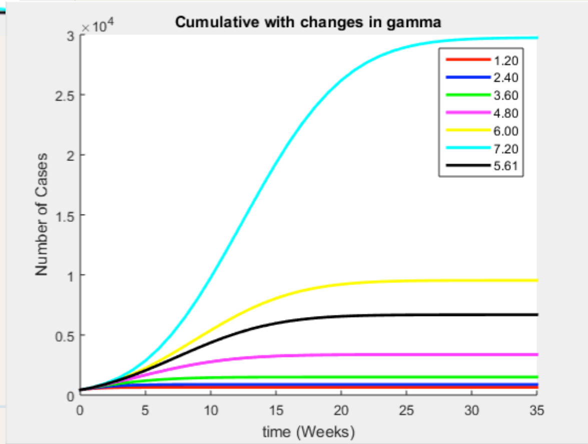




Infectious Period, γ^{-1}

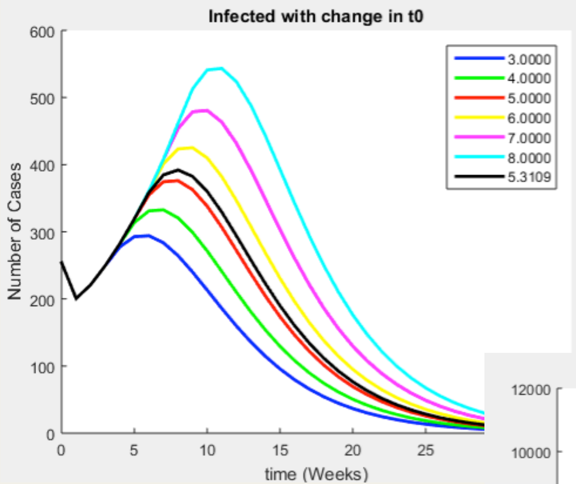
In manipulating the parameter γ, we also converted the infectious days into weeks($\gamma^{-1}/7$). The infectious period is estimated to be in between 3.5 and 10.7 days. Each data point was increased by 1.2 days until it reached its maximum of 7.2 days. In the beginning there were slight changes, but as the duration of the infectious time increased the changes became drastic. For example, at 6 days there was only ~7500 cases but when increased to 7.2 days it jumped 300% totaling in over 30,000 cases . Which confirms that the disease is more infectious with time as the illness further develops.

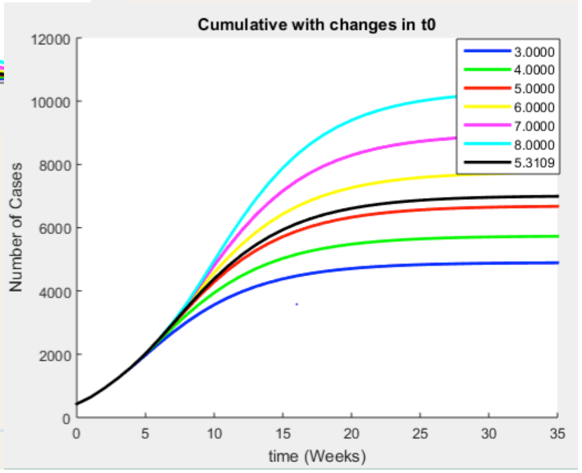




Time before Intervention, t_0

In manipulating the parameter t_0, which is the time before the intervention method are put in place, we increase the time by a week. We started a 3 week and ended at 8 weeks. As we gradually increased the weeks the epidemic cases gradually increased. At 8 weeks the epidemic reached 10,000 cases, when our initial data only reached about 6,000 cases. Meaning, if intervention method are put in place quickly the epidemic will be much smaller and easier to control.

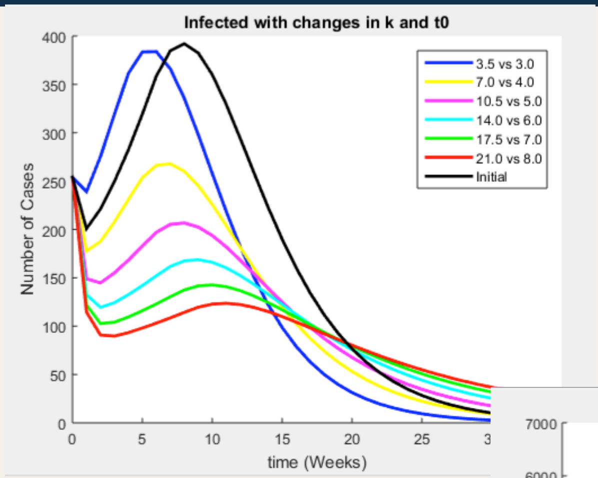


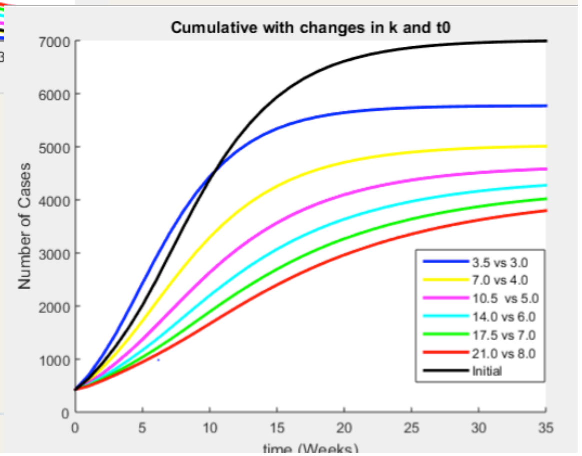


Multivariate Sensitivity Analysis

κ^{-1} vs t_0

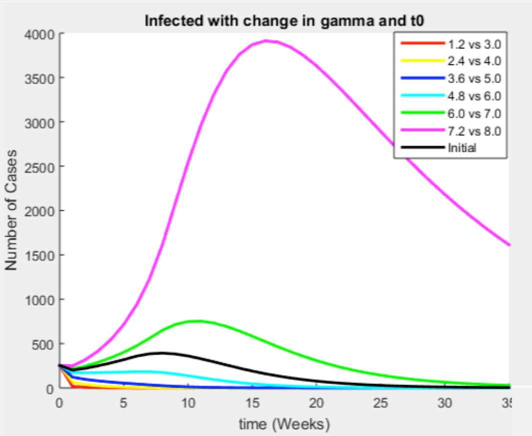
To farther understand the epidemic we perform a multivariate analysis of the incubation period and the time before intervention using the prior data points that were previously discussed. We discovered that the time before intervention had a bigger effect on the outbreak. When 1/**κ** was 3.5 and the t0 was 3 weeks the epidemic was very high but it ended quickly, compared to the 21 days of incubation with t0 being 8 weeks. This further verifies how important intervention methods are in controlling outbreaks.

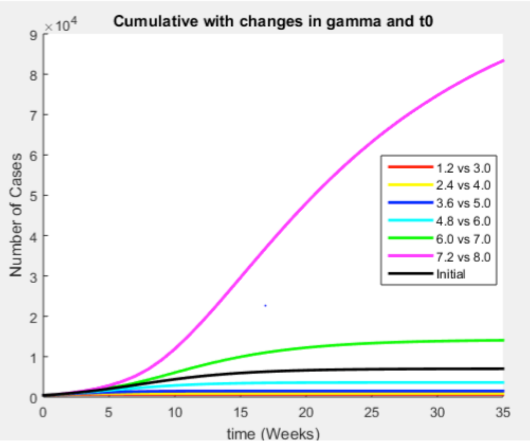




γ^{-1} vs t_0

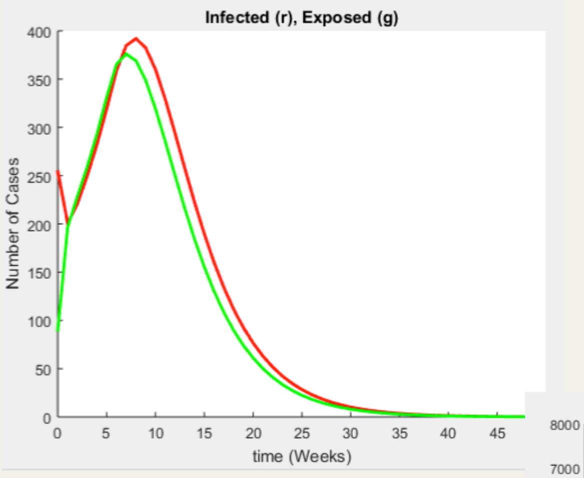
We also perform a multivariate analysis of the infectious period compared to the time before intervention with the priorly discussed information. When the infectious period is short with a quick intervention it is barely an epidemic. But when both began to reach the maximum time the epidemic quickly spirals out of control. When t_0 is at 8weeks and the infectious period is 7.2 days it reaches over 80,000 cases. This means both are equally important and both have a large impact on outbreaks.

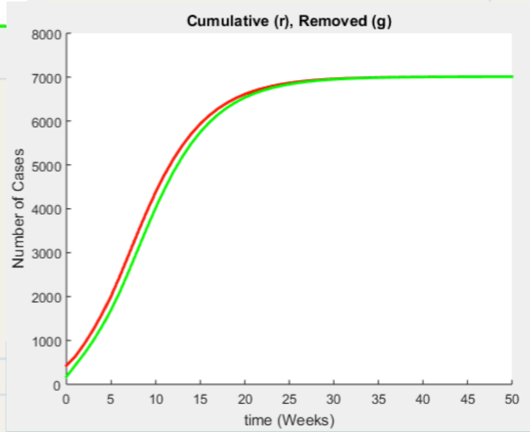




Future of Epidemic

When the outbreak was increased from the initial 36 weeks to 51 weeks. As you can see the epidemic died out. This means that the Sierra Leone outbreak is coming to a conclusion. This is a result of the successful intervention methods. We predicted that they will be Ebola free between dates of June 14 and July 5, 2015.





Conclusion

By analyzing the parameters from the Sierra Leone 2014-2015 outbreak, we were able to conclude the following:

- The longer the incubation period (*k*), the total number of cases will decrease.
- A lower average infectious period (γ^{-1}) effectively lowers the total number of cases.
- Time to intervention is the most important parameter when controlling an epidemic.

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