SEIHFR Model and the Effects of Transmission and Intervention for Ebola in Liberia 2014-2015

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Summer 2015

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Abstract

In this research, we used mathematical models to study the outbreak of Ebola in Liberia. Using differential equations, numerical analysis, least squared fit and the SEIHFR model, we were able to study the effects on the transmission rates and the effects of intervention. Based upon the research done, our results displayed that the most important parameters to lower the final epidemic size is the time it takes to get to intervention as well as the time it takes to lower transmission rates. Thus, implementing quick and more effective intervention measures and spreading knowledge about the disease will minimize the epidemic.

Background Information

- What is Ebola?
  - Also known as Ebola Hemorrhagic Fever
  - Rare and deadly disease
  - Spreads by direct contact with infected person
    - ie: skin, mucus, bodily fluids, contaminated objects (syringes or needles), or infected fruit bats and primates
  - Symptoms
    - Fever
    - Flu-like symptoms
    - Severe headaches
    - Fatigue
    - Muscle pains
    - Vomiting and diarrhea
    - Bleeding of the stomach

Background Information

- Transmission
  - Initially introduced to humans through close contact from infected animals (primates and fruit bats)
  - Spreads through human to human transmission
    - Healthcare workers are at most risk
  - Remain infectious as long as blood contains virus
- Treatment
  - No proven treatment
    - Blood products, immune therapies and drug therapies are being evaluated
    - 2 potential vaccines are undergoing human safety testing

Background Information

- First appeared in 1976 in two simultaneous outbreaks
  - Nzara, Sudan and Yambuku
  - Democratic Republic of Congo
- Later occurred in a village near the Ebola River- where the disease got its name
- Past Ebola Outbreaks:
  - DRC
  - Gabon
  - South Sudan
  - Ivory Coast
  - Uganda
  - Republic of the Congo (ROC)
  - South Africa
- Current Outbreak- largest since 1976
  - Began in Guinea and spread to Sierra Leone and Liberia

Introduction

- Worked closely on project for approximately 6 ½ weeks
- Studied the transmission rates from each class and how improving the transmission rates can improve the on going of the disease
- Used differential equations to look at the transmission rates
- Model that incorporated the equations was studied and used
- Used Matlab to analyze data and use sensitive analysis

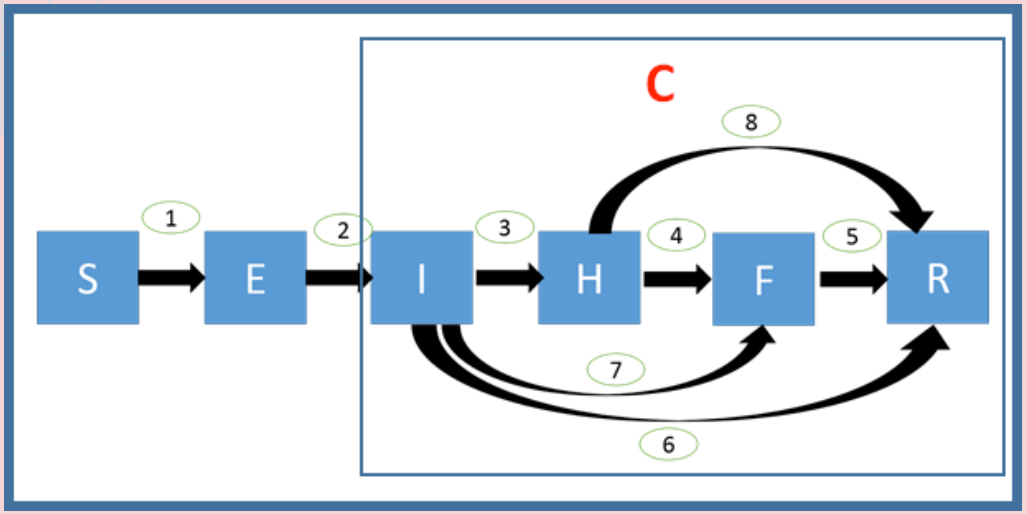
Introduction (cont.)

- Basic Reproduction Number (R_0)
  - The number of secondary infections spread from one primary infection
  - Our estimate: 2.0946
  - Used the SEIHFR model to look deeply into it

Methods

- Data
  - Taken from World Health Organization (WHO) Ebola Case Counts
  - Began the week of June 02 2014 and ended the week of February 23
  - Total Population: 4.294 million
  - 3 initial cases

The Model



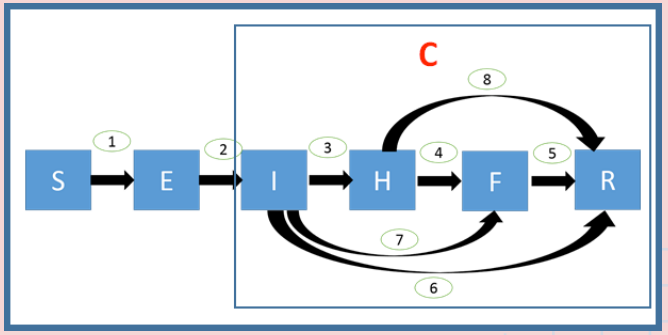
Differential Equations were built to display the transmission from one class to another.

- ★ **S**- Susceptible Individuals
- ★ **E**- Exposed Individuals
- ★ **I**- Infectious individuals within community
- ★ **H**- Infectious individuals in the hospital
- ★ **F**- Dead individuals who are infectious until burial
- ★ **R**- Removed Class (not infectious)

Model Transitions

Over time the populations of each class in our model change from one class to the next. Below is a description of how these changes occur:

- **S**: Entire population is considered initially susceptible, becomes exposed (E) through contact with an infected individual in the community, hospital, during funerals
- **E**: Individuals who become exposed become infectious (I) after an incubation period ($1/\alpha$)
- **I**: Infectious individuals either go to the hospital (H), die (F), or recover (R)
- **H**: Individuals in the hospital either die (F) or recover (R)
- **F**: Deceased individuals become removed (R) from the chain of transmission once buried
- **R**: Individuals who either die or recover from the illness
- **C**: Cumulative number of infectious cases



$$dS/dt = -1/N(\beta_I SI+\beta_H SH+\beta_F SF)$$

The Differential Equation Model

$$\frac{dS}{dt} = -\frac{1}{N}(\beta_I SI + \beta_H SH + \beta_F SF),$$

$$\frac{dE}{dt} = \frac{1}{N}(\beta_I SI + \beta_H SH + \beta_F SF) - \alpha E,$$

$$\frac{dI}{dt} = \alpha E - (\gamma_h \theta_1 + \gamma_i(1-\theta_1)(1-\delta_1) + \gamma_d(1-\theta_1)\delta_1)I,$$

$$\frac{dH}{dt} = \gamma_h \theta_1 I - (\gamma_{dh}\delta_2 + \gamma_{ih}(1-\delta_2))H,$$

$$\frac{dF}{dt} = \gamma_d(1-\theta_1)\delta_1 I + \gamma_{dh}\delta_2 H - \gamma_f F,$$

$$\frac{dR}{dt} = \gamma_i(1-\theta_1)(1-\delta_1)I + \gamma_{ih}(1-\delta_2)H + \gamma_f F.$$

$$\frac{dC}{dt} = \alpha E$$

Parameter Meanings:

- ★ **β_I** - transmission coefficient for community
- ★ **β_H** - transmission coefficient for hospital
- ★ **β_F** - transmission coefficient during funerals
- ★ **θ_1** - % of infectious cases hospitalized
- ★ **δ_1** - community case-fatality ratio
- ★ **δ_2** - hospital case-fatality ratio
- ★ **$1/\gamma_h$** - mean duration in hospital
- ★ **$1/\gamma_{dh}$** - mean duration of hospitalization to death
- ★ **$1/\gamma_i$** - mean duration to end of infectiousness
- ★ **$1/\gamma_f$** - mean duration from death to funeral
- ★ **$1/\alpha$** - incubation period
- ★ **1/q** - time from β0(transmission rates before intervention) to β1(transmission rates after intervention)
- ★ **N** - total population size

Assumptions

In order to conduct our analysis we had to make a few assumptions:

1. Entire population is initially considered susceptible.
2. Individuals are able to contract the disease within the community, hospitals and handling bodies between death and burial.
3. Exposed individuals cannot spread the disease until they become infectious after the incubation period
4. After intervention, transmission rates will progressively decrease rather than immediately plummet.

Methods

Some parameters we found from the 2014 Liberia epidemic were:

- θ_1 (hospitalization rate) = 19.7%
- δ_1 (death rate in community) = 45%
- δ_2 (death rate in hospital) = 45%
- $1/\alpha$ (duration of incubation period) = 1.71 weeks
- $1/\gamma_h$ (duration of hospitalization) = .463 weeks
- $1/\gamma_i$ (duration of infection) = 2.14 weeks
- $1/\gamma_d$ (duration from infection to death) = 1.9 weeks
- $1/\gamma_f$ (duration from death to burial) = .287 weeks
- $1/\gamma_{dh}$ (duration from hospitalization to death) = 1.44 weeks
- $1/\gamma_{ih}$ (duration from hospitalization to recovery) = 2.27 weeks

Methods

By utilizing the epidemic data as well as the SEIHFR model we were able to estimate the starting values of each class at:

- S = 4293974 (total population minus initial infected and exposed)
- E = 23 (estimated by trial and error for best fit)
- I = 2 (3 initial infected with 1 hospitalized)
- H = 1 (estimated by trial and error for best fit)
- F = 0 (none dead at start of epidemic)
- R = 0 (none removed at start of epidemic)

Methods

Using the known parameters as well as the starting values for each class we were able to generate a MatLab program that estimates the transmission rates (before and after intervention), intervention time, as well as time for $\beta_0 \Rightarrow \beta_1$ that best fits the epidemic data using the lsqnonlin package (red) to minimize the error between our curve and the actual data as well as the ODE45 package (blue) to solve our differential equations

```
case 1 %Estimate the trasmission rate beta by fixed alpha and gamma
    p0=[1.5796    0.1347    0.2017    0.0041    0.0714    0.0000   11.7304    0.2192]; %[betaI0, betaI1, betaH0, betaH1, betaF0, betaF1, t-intervention time,
    lb=[0 0 0 0 0 0 0 0]; %lower bound;
    ub=[4 4 4 4 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=[1.4111    0.4008    0.9198    0.0002    1.3805    0.4339   11.9636    0.4595]; %ndata=18
    %p0=[1.4113    0.3758    0.9612    0.0001    1.5123    0.4210   13.1697    0.8582]; %ndata=28
    p0=[1.5796    0.1347    0.2017    0.0041    0.0714    0.0000   11.7304    0.2192]; %ndata=38

options = odeset('RelTol',1e-4,'AbsTol',[1e-4 1e-4 1e-5 1e-5 1e-5 1e-5 1e-5]);
T0=0:1:38;

[T,Y] = ode45(@(t,y)SEIHFR(t,y,p0),T0,[4294000-26 23 2 1 0 0 3],options);

pI=[3 15 26 25 20 27 23 66 59 79 140 265 255 248 321 352 442 358 389 316 258 132 129 87 70 64 53 37 23 31 9 8 8 4 5 4 5 1 0];
C1=[3 18 44 69 89 116 139 205 264 343 483 748 1003 1251 1572 1924 2366 2724 3113 3429 3687 3819 3948 4035 4105 4169 4222 4259 4282 4313 4322 4330 4338 4342 43
```

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

Methods

Estimated parameters:

- t_0 (time to intervention) = 11.7304 weeks
- 1/q (time for $\beta_0 \Rightarrow \beta_1$) = 4.56 weeks

Estimated transmission rates (before intervention):

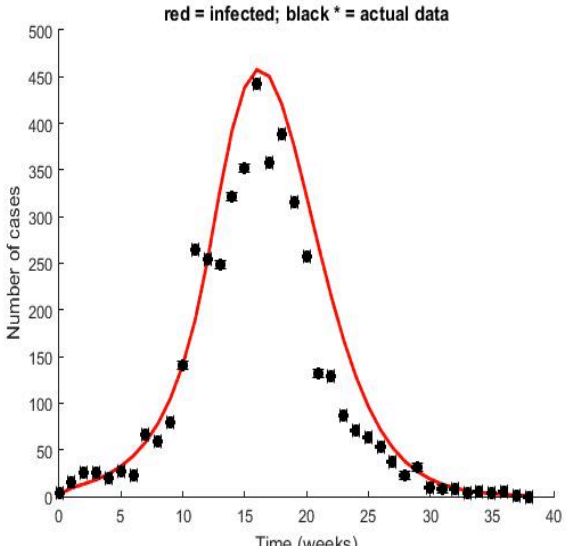
- β_I (community transmission rate) = 1.5796
- β_H (hospital transmission rate) = 0.2017
- β_F (funeral transmission rate) = 0.0714

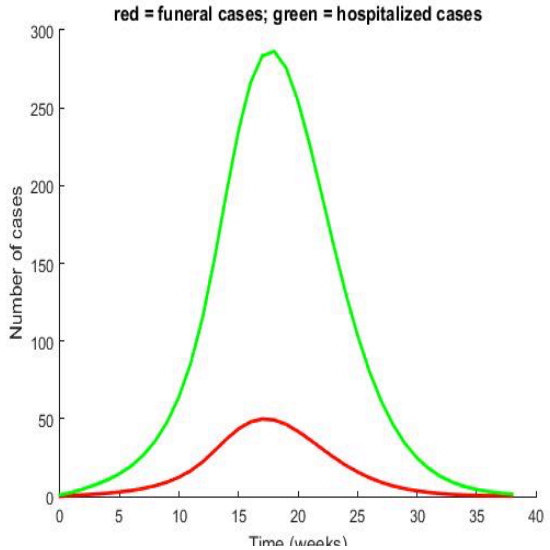
Estimated transmission rates (after intervention):

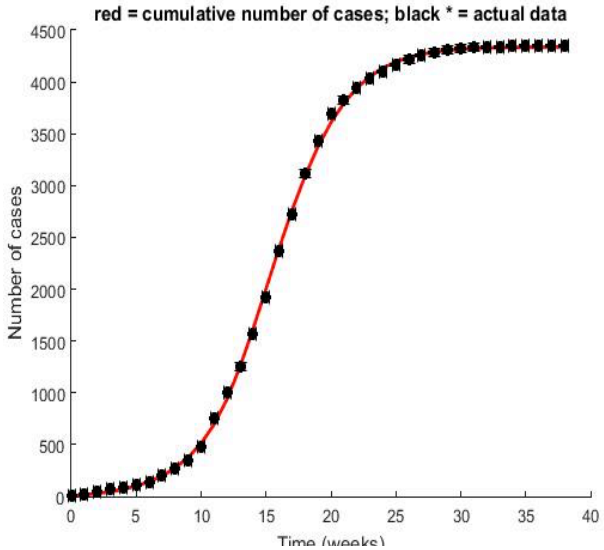
- β_I (community transmission rate) = 0.1347
- β_H (hospital transmission rate) = 0.0041
- β_F (funeral transmission rate) = 0.0000

Methods

Using these parameters we graphed our curves with the actual data points (black dots) to see how well our estimations fit with the actual epidemic. The percentage of error between our curve and the cumulative number of cases is 2.12%
These graphs are shown below:







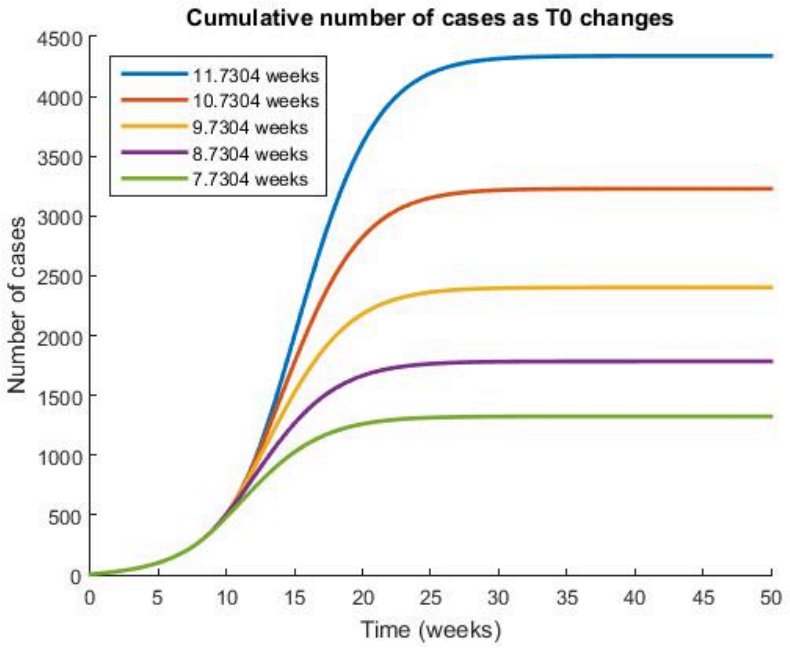
Methods

Using the estimated parameters we were able to calculate the basic reproductive number (R_0) at 2.0946 before intervention and 0.1677 after intervention.
In order to study how each of the parameters affects the final epidemic size we conducted a multivariate sensitivity analysis on the following parameters (after intervention):

- Time to intervention(t_0)
- Transmission rate in the community(β_I)
- Transmission rate in the hospital(β_H)
- Transmission rate between death and burial(β_F)
- Time it takes for $\beta 0 \Rightarrow \beta 1$ (1/q)
- Duration from death to burial($1/\gamma_f$)
- Hospitalization rate(θ_1)

Results

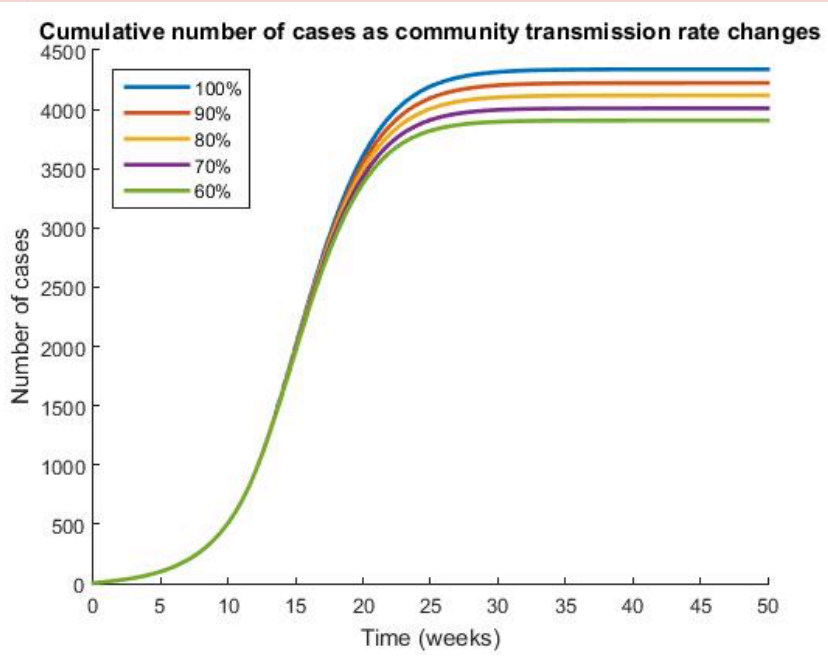
Below is a graph of the total number of cases as time to intervention decreases in one week intervals:



- As the time to intervention gets shorter, the total number of cases decreases dramatically
- For each 1 week decrease in t_0, the total number of cases decreases ~25%
- The change in t_0 has no effect on the final basic reproduction number; however, it does lower R_0 sooner

Results

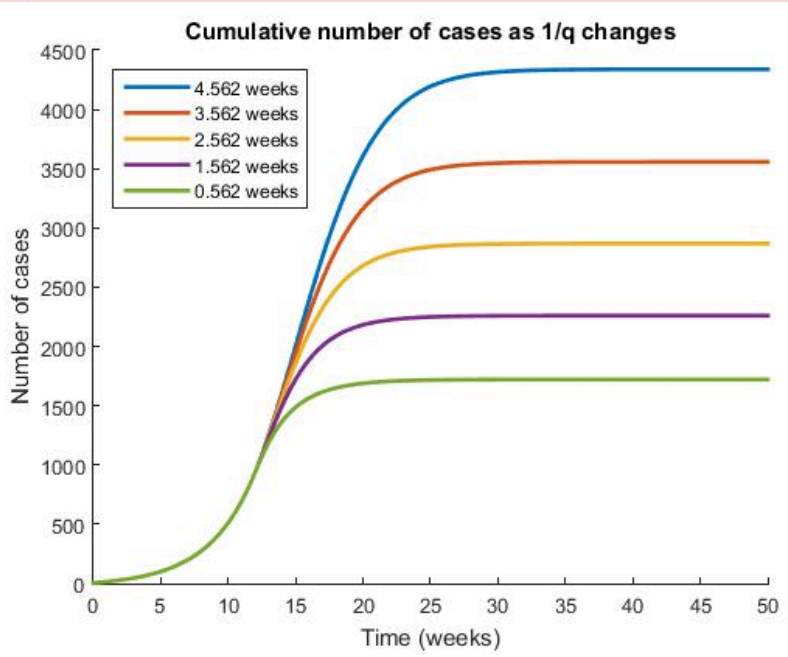
Below is a graph of the total number of cases as the transmission rate in the community decreases in ten percent intervals:



- As the transmission rate in the community is decreased the total number of cases as well
- For each 10% decrease in β_I, the total number of cases decreases ~4%
- For each 10% decrease in β_I, the basic reproductive number decreases ~12%

Results

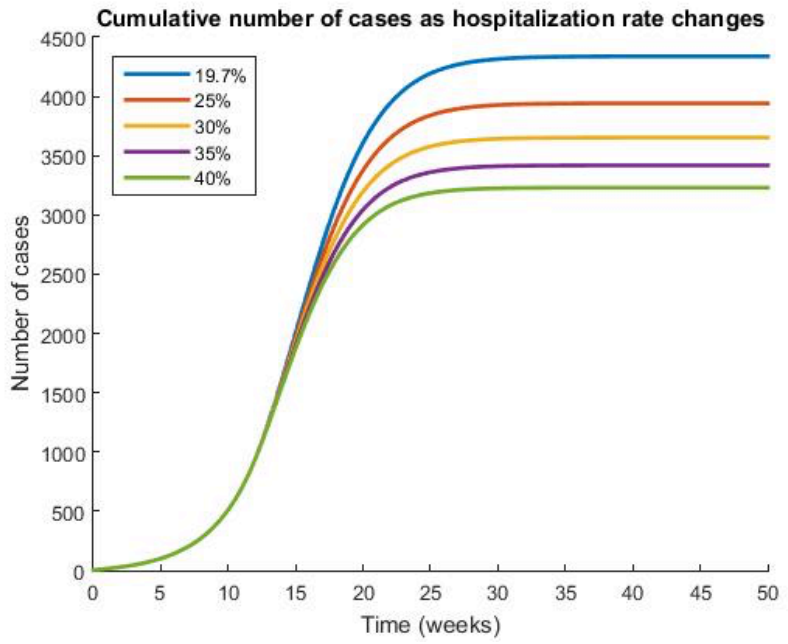
Below is a graph of the total number of cases as the time it takes for $\beta_0 \rightarrow \beta_1$ decreases in one week intervals:



- As the time to intervention gets shorter, the total number of cases decreases dramatically
- For each 1 week decrease in q, the total number of cases decreases ~21%
- The change in t_0 has no effect on the final basic reproduction number; however, it does lower R_0 at a faster rate

Results

Below is a graph of the total number of cases as the hospitalization rate increases in 5% intervals:



- As the hospitalization rate increases, the total number of cases decreases as well
- For each 5% increase in θ_1, the total number of cases decreases ~7%
- For each 5% increase in θ_1, the total basic reproductive number decreases ~8%

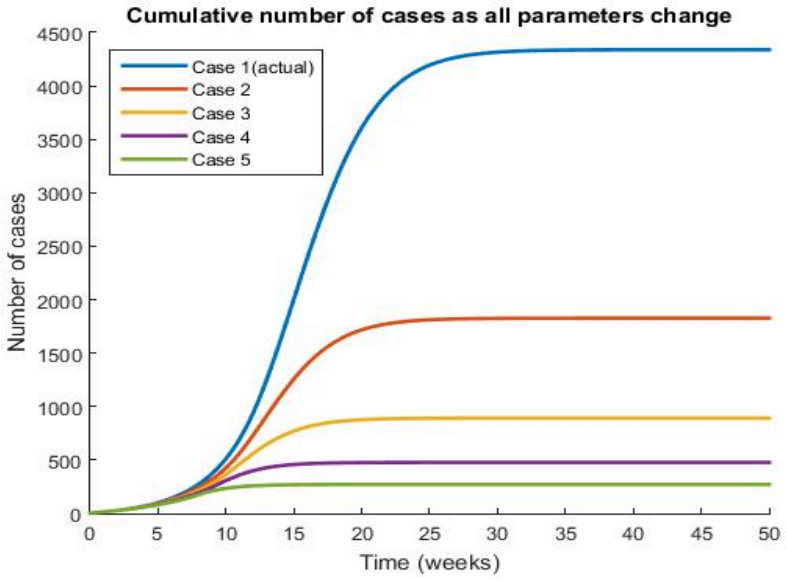
Results

In the case of the 2014-2015 Liberia epidemic changes in the transmission rate in the hospital(β_H), transmission rate between death and burial(β_F), and duration between death and burial($1/\gamma_f$) would cause only an insignificant change in both the total number of cases and the basic reproduction number.

- After intervention, the transmission rate in the hospital was estimated at 0.0041. This number is so close to 0 already so any change to the final epidemic size would be miniscule
- After intervention, the transmission rate between death and burial is estimated to be 0 so there is no room for improvement
- The duration between death and burial is estimated to be 2.01 days. However, since the transmission rate at funerals after intervention is 0 any change to $1/\gamma_f$ would be insignificant

Results

Each of the parameters have an effect on the final size of the epidemic on their own. But in order to minimize the number of total cases and control the epidemic as quickly as possible all of the parameters must be lowered simultaneously. Below is a graph showing the total number of cases as all of the parameters are changed by the amounts they were previously for each case



- After each case of all parameters changing the total number of cases lowers drastically
- After each case the total number of cases decreases by ~50%
- After each case the basic reproductive number decreases by ~20%

Conclusion

- By analyzing the parameters from the 2014-2015 Liberia epidemic we were able to conclude that the two most important parameters when it comes to lowering the final epidemic size is the time to intervention as well as the time it takes for $\beta_0 \Longrightarrow \beta_1$
- However, in order to control the epidemic as quickly as possible all of the parameters have to change simultaneously
- Through quick intervention, more effective intervention measures, as well as spreading awareness it is possible to minimize the total number of cases and control the epidemic as quickly as possible
- While these conclusions are true for the 2014-2015 Liberia epidemic they may not be true for others

Acknowledgements

This research is supported by the National Science Foundation (NSF) through the HBCU-UP Program. We would like to extend our thanks to Dr. Dawit Haile and Dr. Zhifu Xie for their support and guidance throughout this research experience. We also would like to thank Virginia State University for allowing us to use their facilities to conduct our research.