Team Control Number

For office use only

T1 _____

T2 _____

T3 _____

T4 _____

38882

Problem Chosen

A

For office use only

F1 _____

F2 _____

F3 _____

F4 _____

2015 Mathematical Contest in Modeling (MCM) Summary Sheet

Models of Ebola and Defensive Strategy

Summary

In this paper, we establish three models to describe and predict the growing trend of Ebola, and optimize the entire process of distributing the medication.

We build a SEIR model to predict the trends of various crowds without medication: susceptible, exposed, infective and removed individuals. The parameters in the epidemic model are determined by the Least Square Method algorithm based on the real data in Kenema, Sierra Leone. We plot the integrate curves of the crowds, which capture and predict the trends well. The sensibility analysis is conducted by changing the value of death rate, which shows that the model is sensible.

Then we improve the SEIR model by involving the implement of medication. It is reasonable since medication is necessary when Ebola outbreaks.

Now we design a practical delivery system. We first design an optimization model to find 6 cities as alternative cities for collecting the medication. Then we choose two factors, such as level of severity and distance, to formulate another optimization model so that we can find the optimal distributing centre. Thereafter, we give three reasonable plans for medicine distribution and choose the best one as the final one. Furthermore, we also conduct sensibility analysis of the optimization models aforementioned.

The model is realistic since it is based on the real data. And during the process of modeling, we attach a great of importance to verifying our model. Finally, we provide a non-technical letter to the World Medical Association, which illustrates our thoughts and suggestions.

Keywords: Ebola SEIR Model Medication Distribution

Contents

I. Introduction

1.1 Problem identification

The outbreak and spread of a fatal disease, Ebola, should be controlled at once, and its pathogens are ought to be eradicated if possible. To achieve these purposes, the medication of Ebola is required to be developed. Meanwhile a mathematical model also needs to be established to analyze the spread of the disease and provide some specific suggestions and methods for dispatching the iatric resources, which is also vital for the treatment of Ebola.

To build a realistic, sensible, and useful model, we are mainly faced with the following problems:

- Build a mathematical model to describe and predict the trend of Ebola;
- Add some necessary factors besides the spread of the disease into our model in order to optimize the eradication or the control of Ebola;
- Simulate the struggle of human society towards Ebola and produce some reasonable conclusions from our model;
- Make sufficient analysis of parameters and testing the generalization and robustness of our model;
- Provide a non-technical letter for world medical association as well as the suggestions.

1.2 Previous Research

Since Ebola virus was discovered in southern Sudan and the catchment of Ebola River in Congo, 1976, many scholars has made ample researches about it. Haario and Ndanguza analyzed the 1995 Ebola outbreak in the Democratic Republic of Congo using statistical data [1]. They built a *SEIR* model to describe the development of Ebola in Congo, and obtained their value of parameters in virtue of the data. Meanwhile, they also introduced a method to get the parameters and define the ranges of them.

Lekone and Finkenstadt provided a method in dealing with the stochastic process of a disease and with Ebola as a case study [2]. Through methods of statistic, they find out the regular behind the random phenomenon of the outbreak of Ebola.

Ousmane, Emmanuel and et al, performed chains of transmission and simulated the control of Ebola virus disease in Guinea, 2014[3].

In the field of modeling disease, Matt Keeling has done abundant work about the mathematics of diseases [4]. With respect to other similar disease such SARS, researchers also did a lot of work in modeling the trend of the disease and the process of containing it.

Gong and Sun et la simulated the analysis of controlling SARS in 2003, using system dynamics model [5].

The previous researchers mostly modeled the spread of disease such as Ebola in virtue of differential equations and the epidemical model. To determine the values of the parameters, some depend on some formulas and others may rely on some statistic ways. To model the disease, Ebola, an obvious character is that it is wreaking now mainly in Africa, and the situation is changeable and with many unknown factors. So, the way we adopt to model the disease and optimize the delivery strategy should be realistic and reasonable, as the same time we need to verify our model by the real data.

1.3 Our Work

In this paper, we establish three models to capture and predict the spread of Ebola and optimize the distribution of the medication. The data we used in our model are collected from official websites and literatures.

We build a SEIR model without medication and we use least square method to obtain the values of the relevant parameters in the differential equations.

Then, we establish a SEIR model with the application of medication. This model is used in optimization for the distribution of medication.

In order to get the minimum value of the loss caused by Ebola, we optimize the process of delivery the medication and decide the amount distributed to the different cities. Finally, we make the sensibility analysis of the parameters in our model. And we provide a non-technical letter to WMA.

II. Assumptions

In order to simplify the course of modeling and draw some reasonable conclusions from our model, we make assumptions as follows:

(1) The exposed individuals are not infectious, during their asymptomatic period. So this part of people will not increase the rate of infection about the susceptible individuals, according to the statement of WMA (World Medical Association)[6], that only if the patient becomes symptomatic, could he inflect the susceptible individuals.

(2) Once the infectious individuals have been cured, they are making no public health risk. Because almost every convalescent would not be allowed to leave hospital until he or she pass the testing of body fluid, which proves that there is on virus in his or her body.

(3). If a patient is cured, he or she would get the immune ability against Ebola. Because the patients will keep the antibody towards Ebola virus for nearly ten years[7].

(4). When we simulate the variation of population, the influence of natural death rate and natural birth rate could be ignored. Because that the impact of population is mainly caused by the disease in a relatively short time.

(5). The vaccine and drug will effect soon, which will cause a transient increase

or decrease of the population of susceptible individuals and infectious individuals, respectively.

(6). The periods of manufactures of the vaccine and drug are the same, while the amounts of vaccine and drug are different produced in a period. This assumption is set to simplify the calculation of our optimization model.

III. Terms and symbols

Symbols	Definition
$s(t)$	The proportion of the susceptible individuals
$e(t)$	The proportion of exposed individuals
$i(t)$	The proportion of infectious individuals
$h(t)$	The proportion of recovered individuals
$g(t)$	The proportion of dead individuals
$1/k$	The average latent period
$1/\beta$	The average infectious period
γ	The death rate
λ	The contact rate between people of S and I
α	The average immune rate
A	The number of decrease of susceptible individuals caused by vaccine
q	The proportion of the infectives whose disease is not advanced
$m(t)$	The proportion of immune individuals
μ	The number of decrease of infectives caused by drug
$F[f(x)]$	Normalize the corresponding function
$i_j(t)$	The number of infectives of the city j at time t
D_{ij}	The sum of distances between the alternative city i and the city j
τ	The period of the production of vaccine and drug
M	The total amount of vaccine transported to Sierra Leone
W	The total amount of drug transported to Sierra Leone

IV. Establishment of the model

4.1 Submodel.1: SEIR model of Ebola without medication

An epidemic model without medication is used to capture the feature of the disease and predict the tendency. The real data reflects the style of disease under some control methods only including general prevention means, isolation of patients and the application of some common medicine. So the effect of controlling Ebola is not so effective, the outbreak of Ebola is difficult to contain.

We build two SEIR models to simulate the development of Ebola. The former one is established without the impact of medication, while the latter takes the effect of

vaccine and drug into consideration.

4.1.1 The main body of the epidemic model

Concentrating on a selected area, we could build an epidemic model to describe the development of a disease based on the theory of differential equation. When Ebola breaks out and spreads naturally, there is no measure carried out by human beings to contain the trend of it. Hence, in our model, we divide the crowd into 4 categories in terms of the course of building an epidemic model. There are susceptible individuals, exposed individuals, infectious individuals and removed individuals, which are depicted as *S, E, I, R*, respectively. And here, *R* includes two parts as recovered and dead individuals, symbolized as *H* and *G*, respectively [1].

There are interactions between the different crowds. Susceptible individuals would get infected by infectious individuals and turned into exposed individuals. And exposed individuals may transform into infectious individuals after the symptom of Ebola is represented. Meanwhile, part of infectious individuals will die in a certain probability thus will turn into dead individuals, or they will recover soon and become healthy people.

Here, we assume that the sum of the population in the selected area keeps as a constant, *N*. So, we build a mathematical model to describe the evolution of the 4 crowds as follows:

$$\frac{ds(t)}{dt} = -\lambda s(t) \cdot i(t) \tag{1}$$

where, $s(t)$----the proportion of susceptible individuals in the total number N;

$i(t)$----the proportion of infectious individuals in the total number N;

λ ----the contact rate between people of S and I;

$$\frac{de(t)}{dt} = \lambda s(t) \cdot i(t) - ke(t) \tag{2}$$

where, $e(t)$----the proportion of exposed individuals in the total number N;

$1/k$----the average latent period [8];

$$\frac{di(t)}{dt} = -\beta i(t) + ke(t) \tag{3}$$

where, $1/\beta$ ----the average infectious period[8];

$$\frac{dh(t)}{dt} = \beta(1-\gamma)i(t) \tag{4}$$

where, $h(t)$----the proportion of recovered individuals in the total number N;

γ ----the death rate[8];

$$\frac{dg(t)}{dt} = \beta \cdot \gamma i(t) \tag{5}$$

where, $g(t)$----the proportion of dead individuals in the total number N;

And the interaction could be demonstrated graphically as follow:

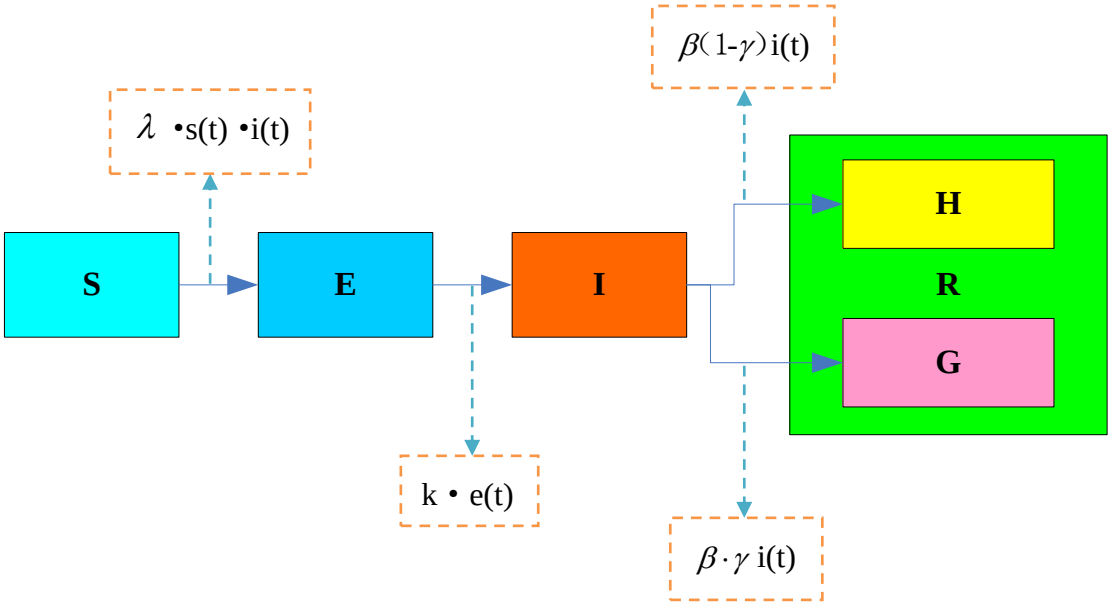


Figure.1 SEIR model

Obviously, the sum of $s(t)$, $i(t)$, $e(t)$, $h(t)$ and $g(t)$ equals 1.Hence, the main body of our model generally established as:

$$\begin{cases} \dfrac{ds(t)}{dt} = -\lambda s(t)\cdot i(t) \\ \dfrac{de(t)}{dt} = \lambda s(t)\cdot i(t) - ke(t) \\ \dfrac{di(t)}{dt} = -\beta i(t) + ke(t) \\ \dfrac{dh(t)}{dt} = \beta(1-\gamma)i(t) \\ \dfrac{dg(t)}{dt} = \beta\cdot\gamma i(t) \end{cases} \tag{6}$$

$$s(t)+e(t)+i(t)+h(t)+g(t)=1$$

To solve the system of differential equations, we need to ensure the value of the parameters, including λ ,k, β , γ . Referring to some literatures and material, we obtained that the average latent period of Ebola is in the interval of 2 to 21 days[9], so the value k belongs to [1/21, 1/2]. Meanwhile, we get the value of the average infectious period is more than 6 days [10], thus the value of β is less than 1/6.

Here we identify the value of contact rate various when the policy of quarantine has been carried out. So, the expressions about the calculation of λ are different. When the infectives are isolated, the frequency of the contact between them and susceptibles

is decreased. We yield the compute method of λ as:

$$\lambda = \begin{cases} \lambda_0 \\ \lambda_0 \cdot p \end{cases} \tag{7}$$

And the differential equation with respect to susceptible individuals is:

$$\frac{ds(t)}{dt} = -\lambda_0 s(t) \cdot [pi(t)] = -[\lambda_0 \cdot ps(t)]i(t) \tag{8}$$

when there is no mean taken to isolate the patients, the contact rate is λ_0, while once the isolation has been carried out, the amount of infectives who may contact with the susceptible individuals becomes $pi(t)$, thus the contact rate change to $\lambda_0 \cdot p$. Here, (1-*p*) stands for the proportion of the isolated patients in the infectives totality.

Although we could define the interval of some parameters, and there are some ways which could be found in literatures [11] to determine the values of the parameters, but the variation is relatively obvious, and the real situation in western Africa is reflected directly in the data published by the local governments. That is, to make our model more realistic and convincing, we may confirm the values of the parameters in virtue of the real data, thus we introduce the ***least square method*** in our model [1].

4.1.2 The selection of the objective region

The epidemic disease situation varies from region to region. Nowadays, the severe outbreaks are mainly taking placing in Liberia, Sierra Leone, and Guinea, all located in the western Africa.

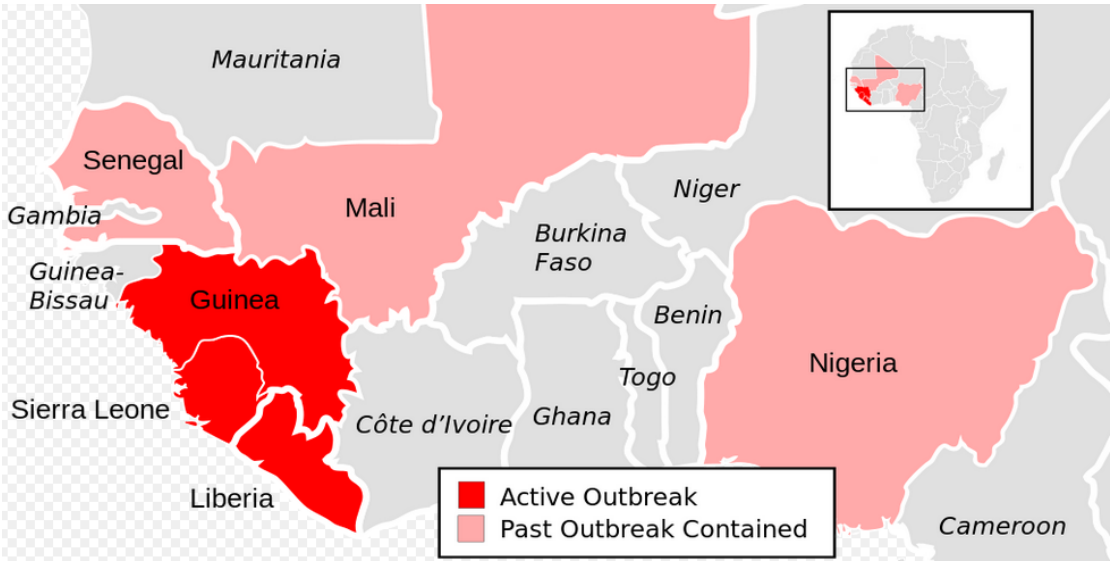


Figure.2 The geographical location of the selected region [12]

And the quantities of cases and deaths in these countries are depicted in figure.3.

The most severe country is Sierra Leone and the situation in this country is characteristic. Hence, we searched for the data about cases and deaths and so on in 6

cities in Sierra Leone as the material for modeling. The data including numbers of cases, deaths, new cures, probable cases, confirmed cases and suspected cases. These data could be used to define the values of the parameters in the SEIR model as well as evaluation of the situations of disease in different cities. Here, we mainly use the data from one city to determine the values in our mentioned SEIR model.

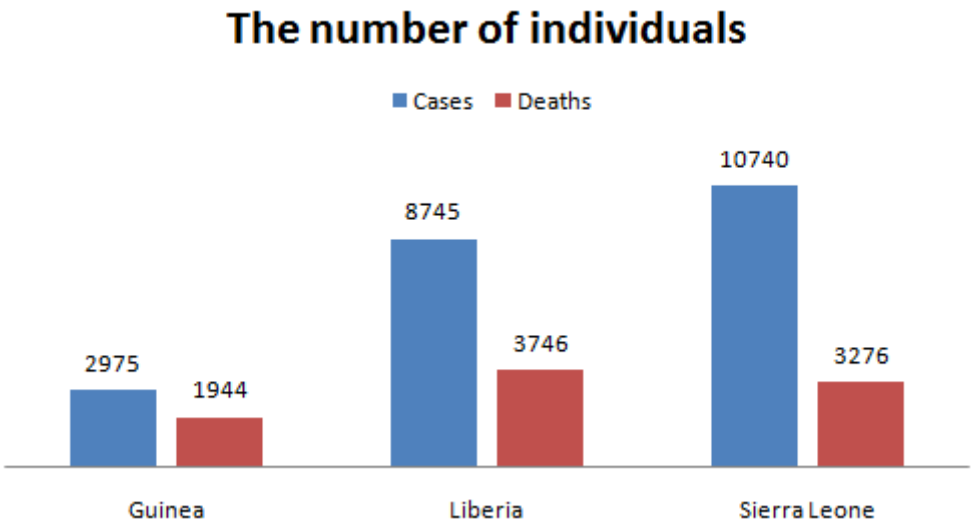


Figure.3 The number of cases and deaths

In Sierra Leone, we choose the city, Kenema. Because, from figure.4 we can see that the cases in this city is in a middle level of epidemic and from figure.5 we can see that the data in Kenema show a average trend obviously. So, we choose Kenema as our study object.

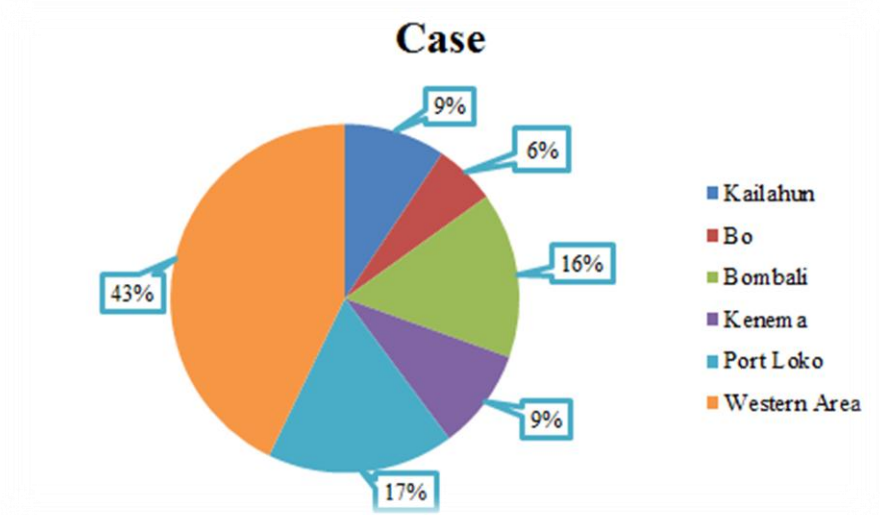


Figure.4 The pie chart of the cities

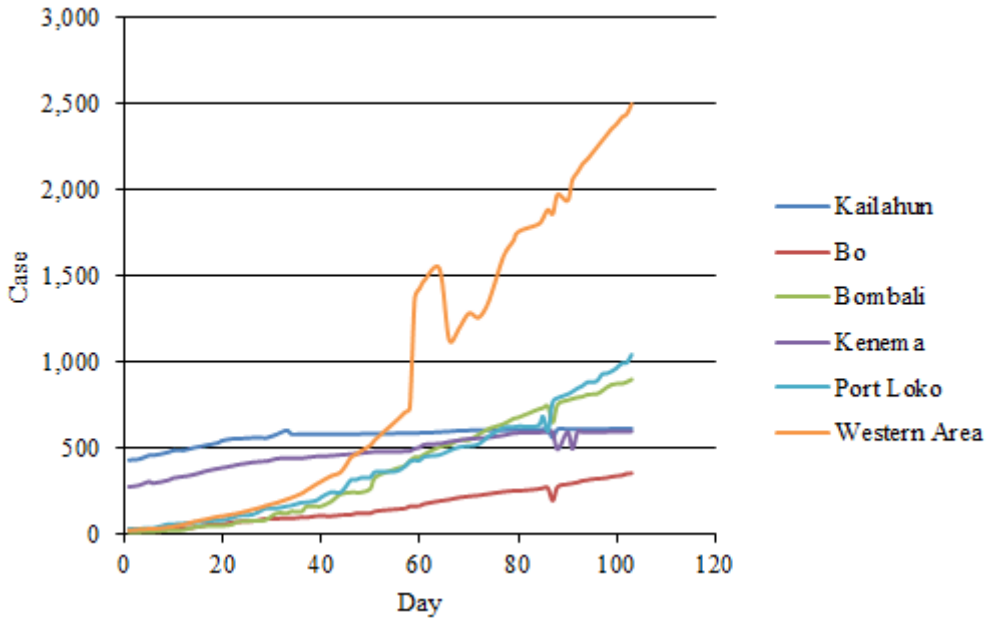


Figure.5 Tendencies in cities

4.1.3 Ascertain the parameters: the least square method

We searched the data from May.25 to Dec.25, 2014, in Kenema, Sierra Leone. In the paper, we use the data of cases, deaths, suspected cases in Kenema to fit the curve of $s(t)$, $i(t)$ and $g(t)$, and determine the values of λ, β, γ and k. Then, we form the differential equations and obtain the integrate curves of $s(t)$, $e(t)$, $i(t)$, $g(t)$, and $h(t)$.

The reference data to measure out precision of fitting are from the materials published by the government of Sierra Leone [13].

To illustrate our method of fitting, we set the function of the number of dead people, $f = g(t)$ as an example:

The real number of dead people is symbolized as $g_0(t)$, and the function yield by out differential equation model is $g(t)$, so we requires the minimization of

$$\sum_{i=1}^{n}[g_0(t) - g(t)]^2 \tag{9}$$

Then, the value in the appropriate interval minimize the sum of square will be chosen.

Similarly, we could get the values of other parameters.

Calculated by MATLAB, we obtain the numerical solution with respect to the differential equations about diverse crowds. The values of the parameters are showed in Table.1.

Table.1 The values of the parameters in Kenema

Parameters	λ	k	β	γ
Values	0.01486	0.09677	0.00508	0.23517

4.1.4 Verification of the model

Compared with the real data, we could find out the deviation between our resultant curves and the tendencies in reality.

The data we choose for us to contrast with our result is the number of death in Kenema. Here, we found the specific number of dead individuals during a period of 200 days. We plot the predicted result by our model and the real data together to see the accuracy of out SEIR model, which is showed in figure.5.

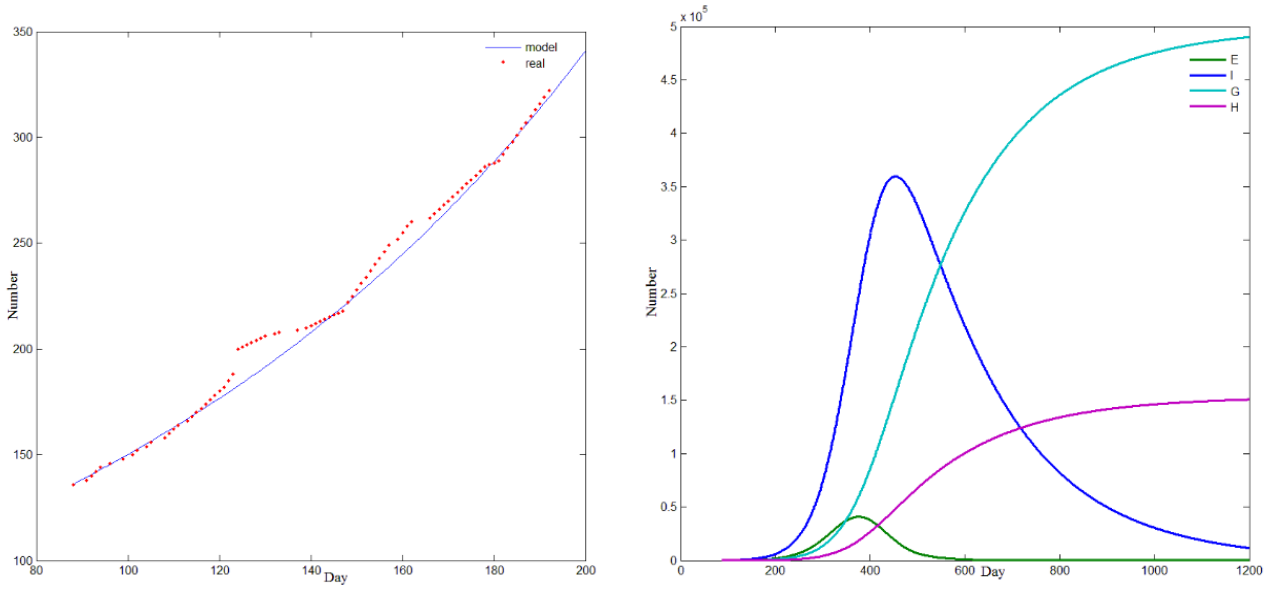


Figure.6 The comparison of result

We obtain the data of death from May.25 to Dec.25. The figure.5 illustrate that the prediction performed by our model is precise during the time between 88th to 200th days. So in a way, we could consider that the model is accurate to the real world and the result given by submodel.1 is reasonable.

4.1.5 The results of submodel.1 and its analysis

The differential equations would not be solved analytically. We yield the numerical solution for submodel.1. The integrate curves are plotted as follows:

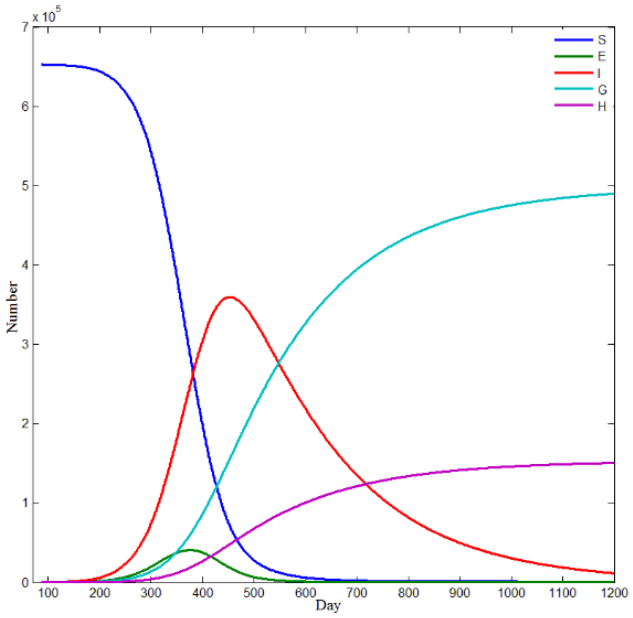


Figure.7 The curves of the functions about S, E, I, R (G, H) in Kenema

From figure.6, we could see that the number of infectives is raise sharply at a certain period of time, and then decreases with a maximum at almost half of the citizens. Nowadays, the number of people died every day is almost under controlled by the government, and the explosion of the infective individuals has not launched yet. If, there is no efficient measurement carried out timely, the amount of infectives and death would skyrocket in a short time. Finally, nearly all the susceptible individuals will turns to be healthy people or die. That's the worst situation resulting from Ebola.

With time going by, the amounts of various crowds all turn to be stable, but it costs a quite long time for them to reach this kind of situation. Before the number of infectives reaches the state of stabilization, it will go through a period of outbreak. After that, the number of death would rise faster and there would be a disaster to a city containing a population of nearly 653013.

The top value of infectives appears on the 453^{th} day after its outbreak. And the stabilization will finally achieved on the nearly 600^{th} day, where the number of the different sorts of crowds.

So, in order to avoid the period of outbreak of Ebola, we need to take some efficient measures and restrain the disease in a stage where it is controllable. If Ebola is indulged to spread unlimited, we would pay for it. Now, the city is in a stage where the number of infectives is increasing slowly and the number of the susceptible individuals is relatively high, at a time before 300^{th} day. So, we should pay attention to avoid the sharp rise of the infectives.

And then we substitute the data of deaths and cases about other cities into our model and obtain the resultant curves and parameters of other cities. We yield the 4 of

them:

Table.2 The values of the parameters in Bo

Parameters	λ	k	β	γ
Values	0.03385	0.12417	0.01113	0.37905

Table.3 The values of the parameters in Kailahun

Parameters	λ	k	β	γ
Values	0.00259	0.14015	0.00098	0.13953

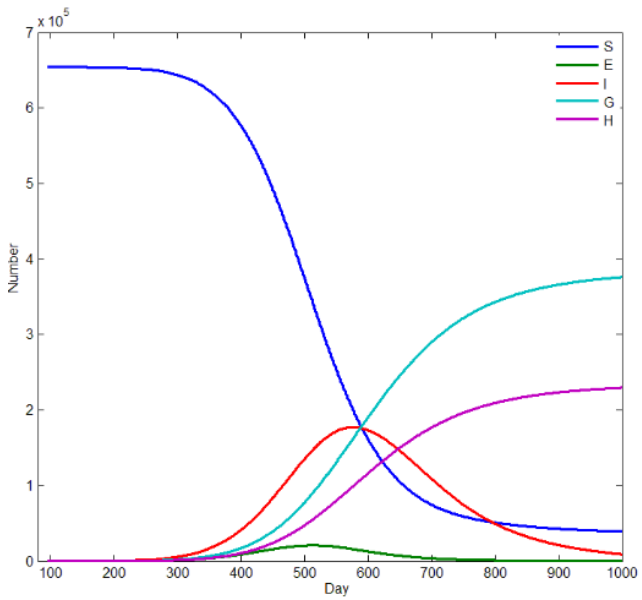
Table.4 The values of the parameters in Port Loko

Parameters	λ	k	β	γ
Values	0.04664	0.44795	0.01139	0.29660

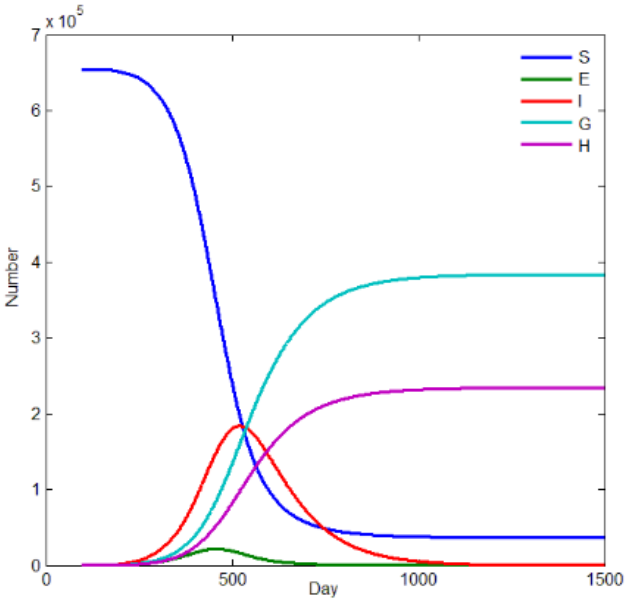
Table.5 The values of the parameters in West Area

Parameters	λ	k	β	γ
Values	0.04535	0.43050	0.01475	0.49302

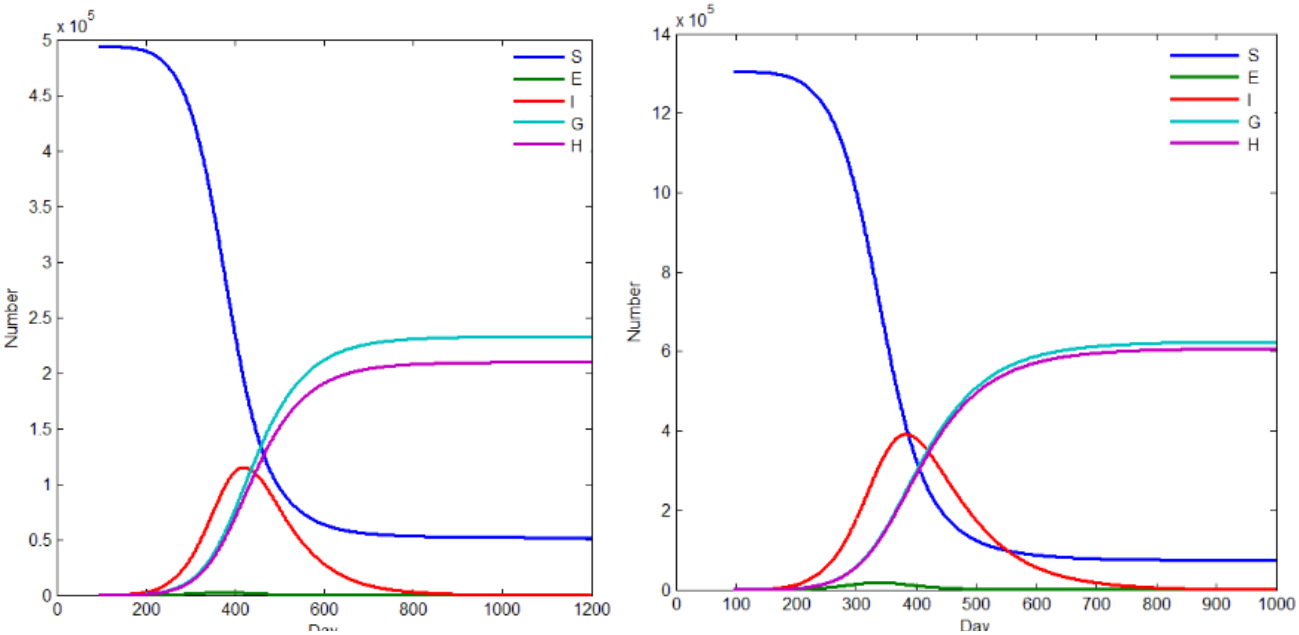
And the curves are plotted as:



A. Bo



B. Kailahun



C. Port Loko D. Western Area

Figure.8 The other 4 cities

From the curves of different cities in Sierra Leone, we can draw a conclusion that the functions describing the change of population will finally reach the stable state. But the time they get to this situation is various, for the reason that the initial values and the local conditions are distinguishing. The top values of the infectives are all reached around approximately 400^{th} to 500^{th} day.

4.2 Submodel.2: SEIR model of Ebola with medication

Now, we introduce the premise that the medication with respect to Ebola has been developed into our model. The medication could curb Ebola and curve the patients whose disease does not deteriorate. To modify our former model so as to conform to this new situation, we need to add a term to depict the number of individuals removed with immunity, M. And the amount of people recovered after infection, H, would be increase under the treatment of medication.

According to the assumption.4, the effect of medication should be described in a difference equations model. So, the submodel.2 is built as:

$$N[s(t)-s(t-1)]=N[-\lambda s(t)\cdot i(t)]-A \tag{10}$$

where, α ----the average immune rate;

A----the number of decrease of susceptible individuals caused by vaccine;

Correspondingly, the differential equation of the amount of individuals removed with immunity, symbolized by M, could be yield as:

$$N[m(t)-m(t-1)]=A \tag{11}$$

where, $m(t)$----the proportion of immune individuals in the total number N;

And the modifications of other terms are as:

$$N[i(t)-i(t-1)]=N[ke(t)-(1-q)\cdot\beta i(t)]-\mu \tag{12}$$

where, q----the proportion of the infectives whose disease is not advanced, here we assign q with 0.5[7];

μ ----the number of decrease of infectives caused by drug;

Add other conditions here, the submodel.2 will be:

$$\begin{cases} N[s(t)-s(t-1)]=N[-\lambda s(t)\cdot i(t)]-A \\ N[e(t)-e(t-1)]=N[\lambda s(t)i(t)-ke(t)] \\ N[i(t)-i(t-1)]=N[ke(t)-(1-q)\cdot\beta i(t)]-\mu \\ N[h(t)-h(t-1)]=N[q\cdot\beta(1-\gamma)i(t)]+\mu \\ N[g(t)-g(t-1)]=Nq\cdot\beta\gamma i(t) \\ N[m(t)-m(t-1)]=A \end{cases} \tag{13}$$

The submodel.2 could be illustrated as:

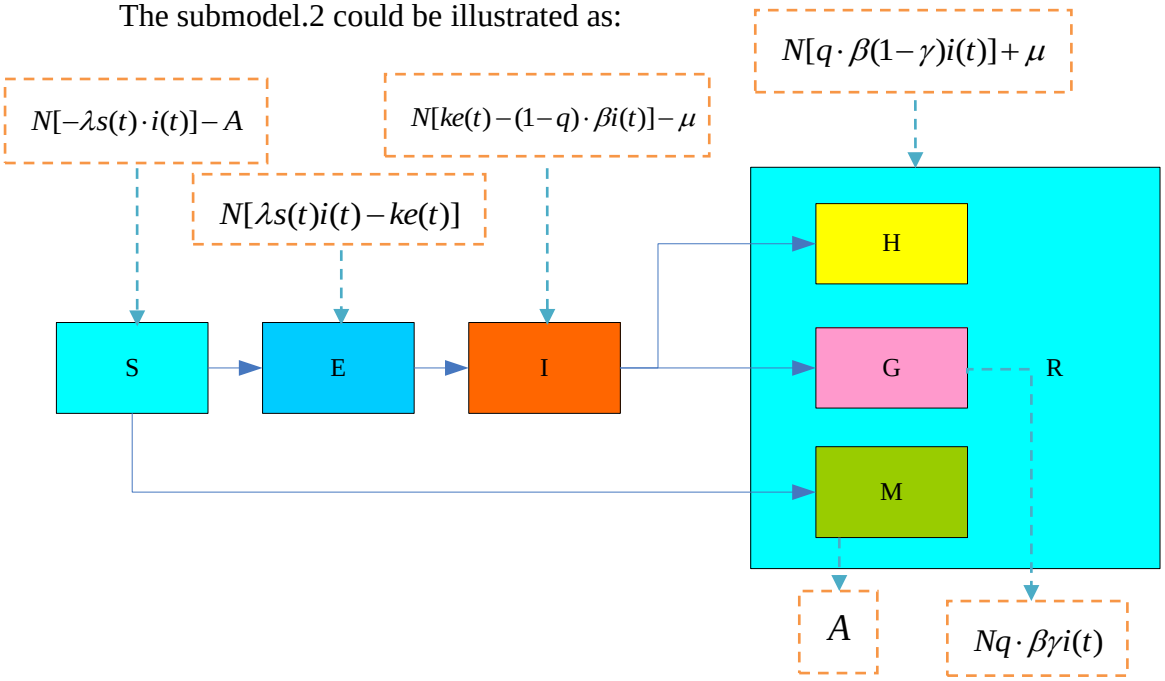


Figure.9 The SEIR model with M

When it comes to the submodel.3, the SEIR model of Ebola with medication will be solved to simulate the effect of medication, including vaccine and drug.

4.3 Submodel.3: optimization model of deploying the medication

What we should recognize is that until now, the medication against Ebola has not been developed perfectly and put into production, so what we need to analyze is the distribution strategy of the new medication if the medication has been developed completely and put into manufacture in assembly lines.

Thus, we should take the spread of Ebola into consideration in order to measure the seriousness of the disease in a selected area. Furthermore, we need to calculate the amount of the medication necessary to an area according to the prediction of the number of the infectious individuals and susceptible individuals.

The delivery system will also influence the effect of controlling or eradicating Ebola in a certain region, as well as the locations of delivery. Meanwhile, the speed of manufacturing of the vaccine and the drug would also limit the immunity rate of the susceptibles and the cure rate of the patients.

Here, we also take the factors into consideration such as:

1. The different effect caused by vaccine and drug;
2. The convenience of distributing the medication.

Then we start to establish the optimization model. The process of modeling could be depicted in the following flow diagram:

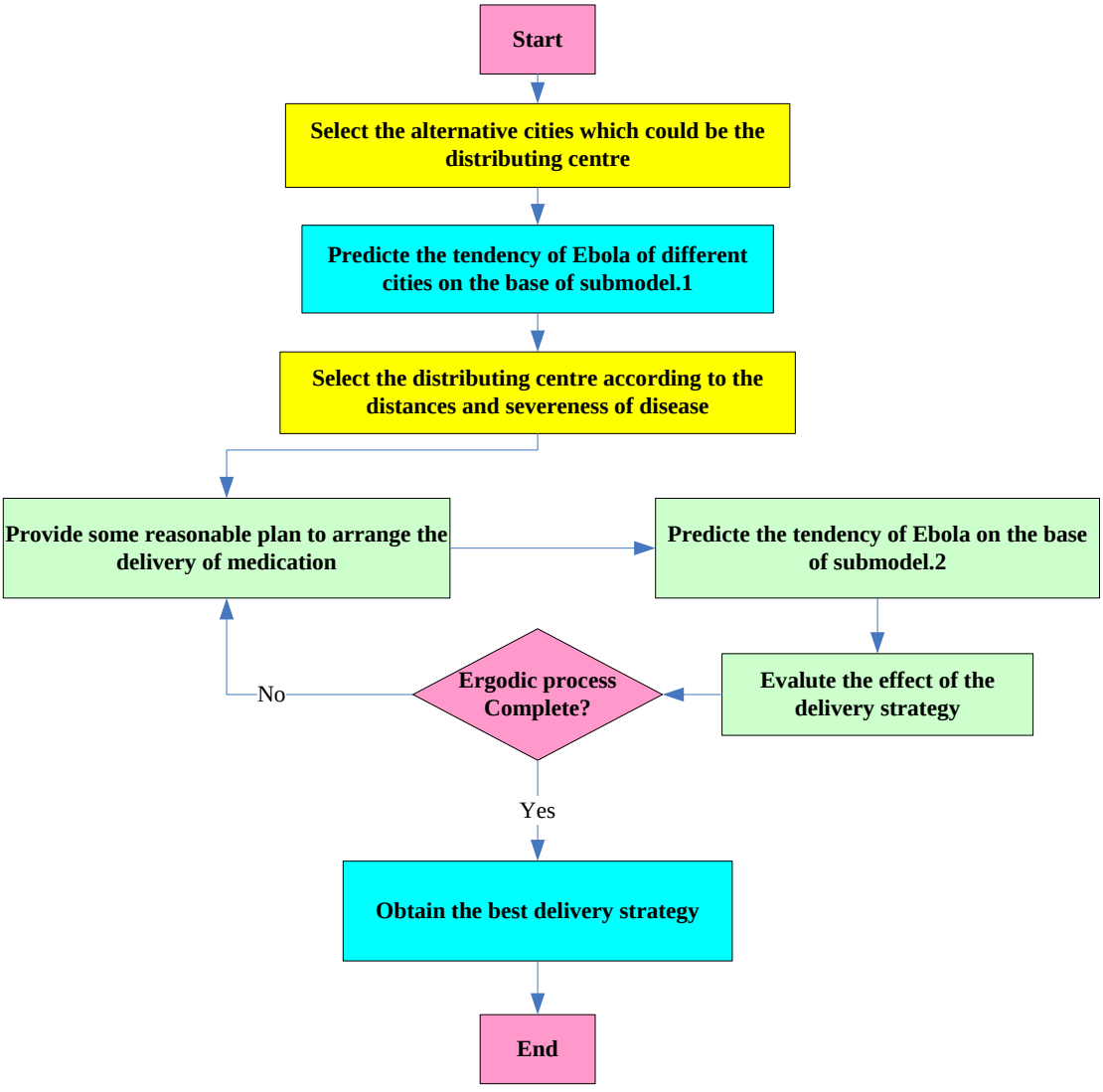


Figure.10 The process of modeling

4.3.1 Select the alternative distributing centres

To optimize the process of the eradication or control of Ebola, we need to choose the areas as our targets where we delivery the medication. These areas should be suffering from Ebola and require for treatment towards the citizens. In this paper, we choose 6 cities in Sierra Leone, including Kailahun, Bo, Bombali, Kenema, Port Loko and Western Area, where the situations of disease of Ebola are relatively critical.

If we want to deliver the medication to the target cities in Sierra Leone, the general way is: 1. Convey the medication to a selected spot by helicopters or airplanes; 2. Transport the medication to the worst-hit areas by goods vans or even helicopters. Because the medication is manufactured in other countries out of the mainland of Sierra Leone, the selected spot shall be only one specifically in terms of the convenience and effectiveness of delivery. And, once the goods have been transported in the country, then they should be distributed to the worst-hit areas.

Furthermore, when we distribute the medication, we need not only the medication itself, but also corresponding facilities to support the transportation of our delivery strategy. So, what we need to select are some existing cities instead of random spots. These cities are likely to become the distributing centre of medication. So, before we choose the location of delivery, we need to find out the cities in the region enclosed by the worst-hit areas, i.e. the mentioned 6 cities. The procedure is as follows:

- Step.1 Measure the distances between cities which are suffering from the disease, Ebola, geographically;
- Step.2 Transform the real map into a geometric graph;
- Step.3 Locate some spots symbolized with a white cross in the region enclosed by the 6 cities;
- Step.4 Calculate the distance and select some reasonable spots.

The distance matrix of the 6 cities is showed in table.2. The distance is the length of a straight line connected any 2 cities.

Table.6 Distance Matrix

Distance (km)	Kailahun	Port Loko	Bombali	Western Area	Bo	Kenema
Kailahun	0	401	367	425	180	112
Port Loko	401	0	118	127	210	276
Bombali	367	118	0	254	195	253
Western Area	425	127	254	0	247	313
Bo	180	210	195	247	0	685
Kenema	112	276	253	313	685	0

Then, we transform the matrix into a 2D geometrical model in virtue of the

designing software, CATIA. The result is showed in figure.10. The 35 small white crosses are the possible positions we might choose. From the geometric model, we could get the distances between the alternative spots and the target cities conveniently.

The selection standard is the total distances from a spot to the 6 cities:

$$D_i = d_{i1} + d_{i2} + d_{i3} + d_{i4} + d_{i5} + d_{i6} \tag{14}$$

where, the subscript *i* is the mark of the spots.

After calculating the total distances and compared each of them, we choose 6 spots with the top. 6 minimum of *D*, and find out the cities near these spots as our alternative existing cities in the process of optimizing the delivery system.

The selected cities for us to collect and distribute the medication against Ebola are showed in figure.9.

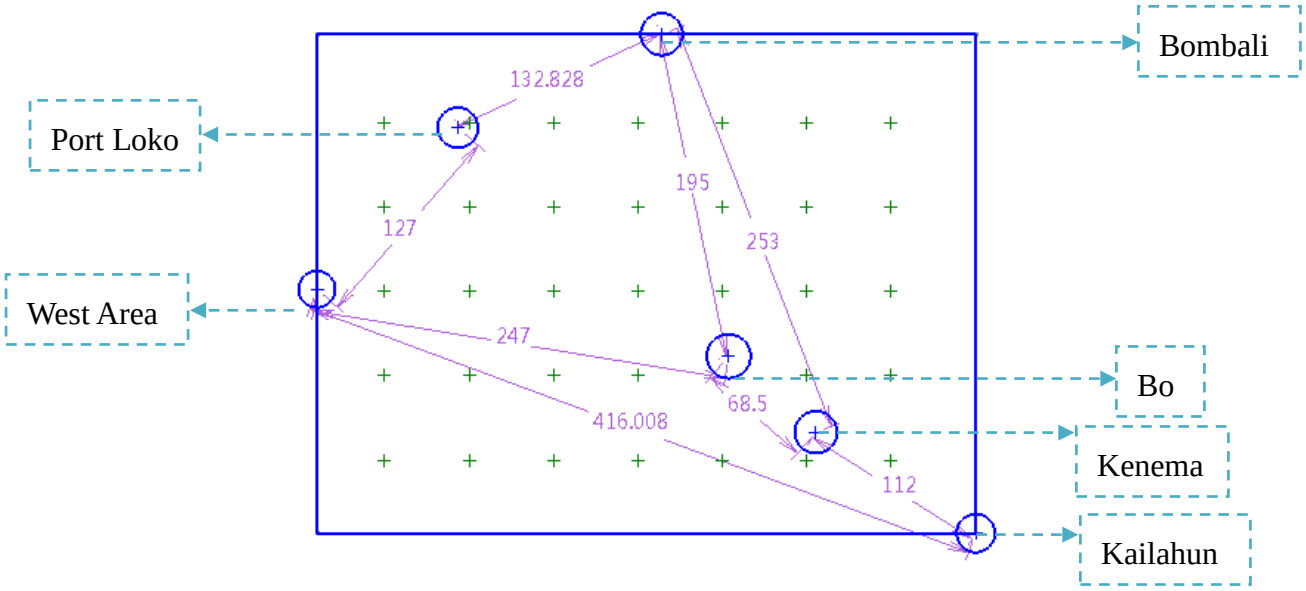


Figure.11 The 2D geometric model of cities

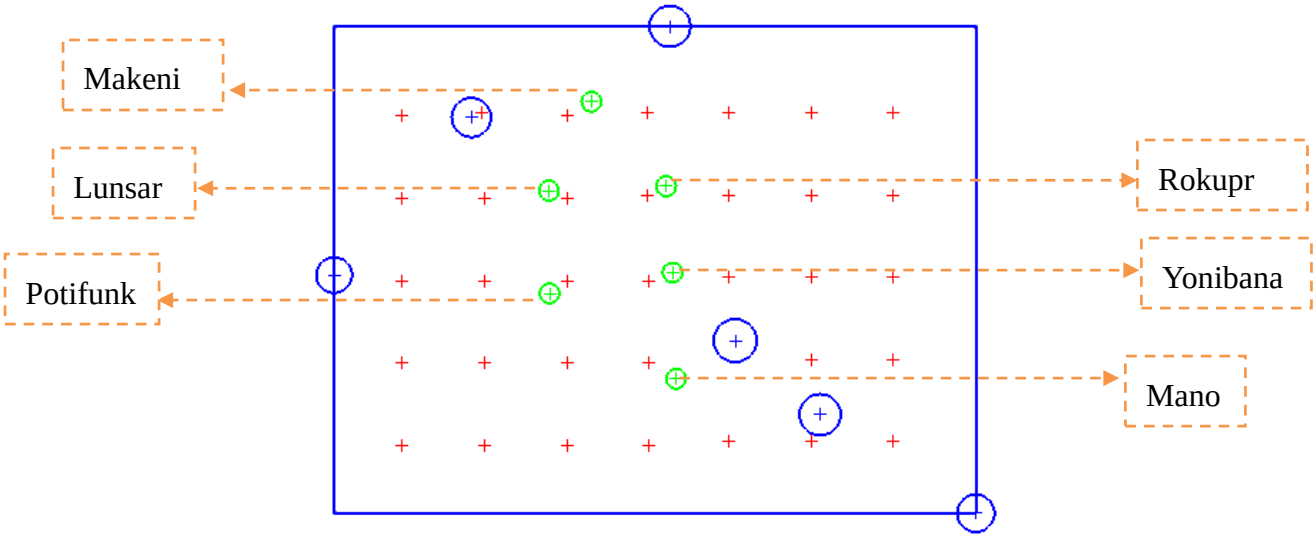


Figure.12 The selected distributing centre

Cities which may be selected as our distributing centre are: Makeni, Lunsar, Potifunk, Rokupr, Yonibana and Mano.

Then we select the city to collect and distributing the medication in the 6 cities yield in figure.11 through our optimization model.

4.3.2 Optimization model for the selection of the distributing centre

Then, we choose the city we deliver the medication to. When Ebola breaks out, the situation of cities are different. Now, there are 6 cities in danger where people died from Ebola every day, including Kailahun, Bo, Bombali, Kenema, Port Loko and Western Area.

And the alternative cities are: Makeni, Lunsar, Potifunk, Rokupr, Yonibana and Mano.

To select the distributing centre, we build an optimization model with the objective function as:

$$\begin{cases} \min \quad f = \sum_{j=1}^{6} (d_{ij} \cdot s_j) \\ s_j = F_1[i_j(t)] + F_2[\dfrac{di_j(t)}{dt}] \\ d_{ij} = F_3[D_{ij}] \end{cases} \tag{15}$$

where, $F[f(x)]$ means normalize the corresponding function;

$i_j(t)$ ----the number of infectives of the city j at time t;

D_{ij} ----the sum of distances between the alternative city i and the city j which

is in danger.

Meanwhile, s_j and d_{ij} indicate the seriousness of disease in a city and the relative amount of distance between the two cities.

Substitute the real data about the mentioned cities into our model and computed by MATLAB, we get the values of *f* and obtain the best city in the current situation, which is showed in table.7.

Table.7 The values of *f*

Makeni	Lunsar	Rokupr	Rotifunk	Yonibana	Mano
1.996	2.063	2.535	2.072	2.707	3.230

Thus, we choose the city, **Makeni**, as the collecting and distributing centre in this situation. And then, we start to distribute the amount of medication and take some factors into consideration.

4.3.3 Optimization model for the delivery strategy

We need to yield the delivery location and the amount of vaccine as well as the quantity of drug.

To determine the collecting and distributing centre corresponding to the current situation, we use submodel.1 to predict the tendency of the spread of Ebola in a city. After that, we describe the change caused by the drug and the vaccine relying on the submodel.2. Then, we could obtain the evaluation of the seriousness of Ebola in different cities.

Our optimization model effects between the 6 selected cities, and the objective function is given as:

$$\max \quad z=\sum_{m=1}^{6}[N(i_{m1}(t+n\cdot\tau)-i_{m2}(t+n\cdot\tau))+N(g_{m1}(t+n\cdot\tau)-g_{m2}(t+n\cdot\tau))] \quad (16)$$

where, z----the decrease of infectives and deaths after application of medication;

$i_{m1}(t)$ ----the function of infectives without medication;

$i_{m2}(t)$ ----the function of infectives with medication;

$g_{m1}(t)$ ----the function of death without medication;

$g_{m2}(t)$ ----the function of death with medication;

τ ----the period of the production of vaccine and drug;

n----the number of periods.

The constraints are:

$$\begin{cases} \sum_{j=1}^{6} A_j \le \dfrac{M}{\tau} \\ \sum_{j=1}^{6} \mu_j \le \dfrac{W}{\tau} \end{cases} \tag{17}$$

where, *M*----the total amount of vaccine transported to Sierra Leone;

W----the total amount of drug transported to Sierra Leone;

the subscript *j*----the mark of city.

Then we use COMSOL Multiphysics and MATLAB to compute the model.

4.3.4 The results of optimization and its analysis

Now, we transport the total medication to **Makeni** and distribute the vaccine and drug to the 6 cities.

Here, we select the best project from some reasonable plans. The amount of medication is measured in dosages, that is to say, 1 dosage of medication will be used to 1 person. The plans of delivering medication are given as:

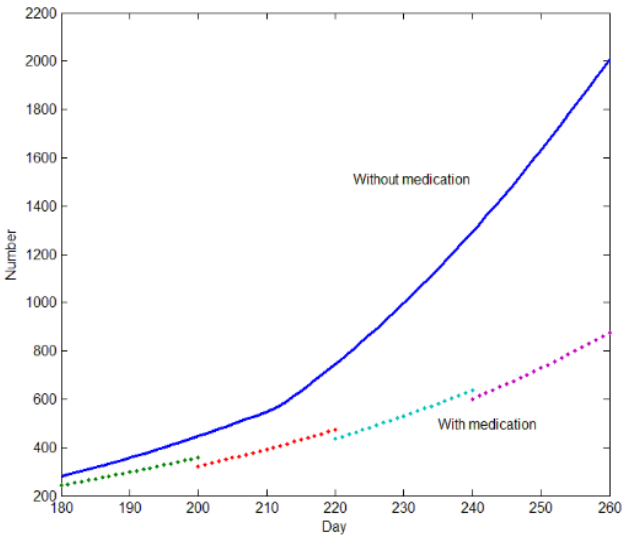
Table.8 The plans

Amount(dosage)		Bo	Kailahun	Bombali	Port Loko	Western Area	Kenema
Plan.1	**Drug**	612	1063	1559	1729	3987	1049
	Vaccine	37	64	94	104	239	63
Plan.2	**Drug**	852	1834	1587	1504	2397	1827
	Vaccine	51	110	95	90	144	110
Plan.3	**Drug**	661	1219	1564	1684	3666	1206
	Vaccine	40	73	94	101	220	72

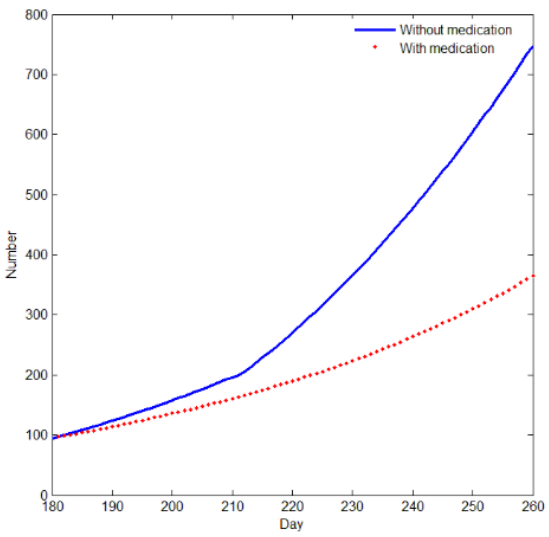
After calculating the values of the objective function, the best project of the delivery of medication is **plan.1**, the results of optimizing are:

- The sum of death and infectives before the application of medication is: 33767;
- The sum of death and infectives after the application of medication is: 16180;
- The decrease (objective function): 17587.

The results of different cities including the tendency of deaths and infectives after the application of medication are as follows:



A. Infectives in Bo

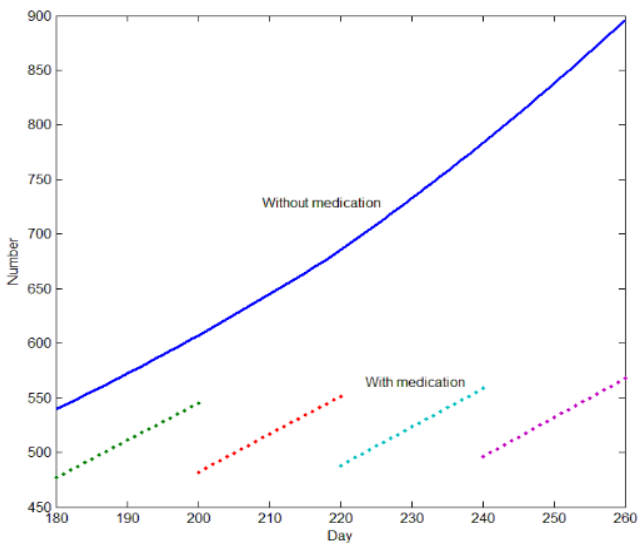


B. Deaths in Bo

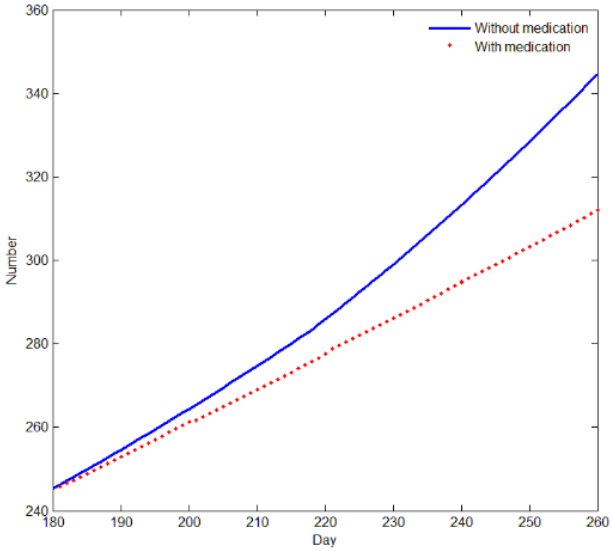
Figure.13 Medication used in Bo

The number of deaths is decrease and the slope of curve is also decrease. The tendency showed that the number of infectives decrease at the time point when we apply the medication, including vaccine and drug. After that the number reverts to rise in the similar trend. That indicates that the amount of medication delivered to Bo might be too low.

Take a deep research into this figure, we can see the trends of different period show a dynamic variation because the decrease of susceptible individuals and infectives would cause the change in the tendency captured by the equations.



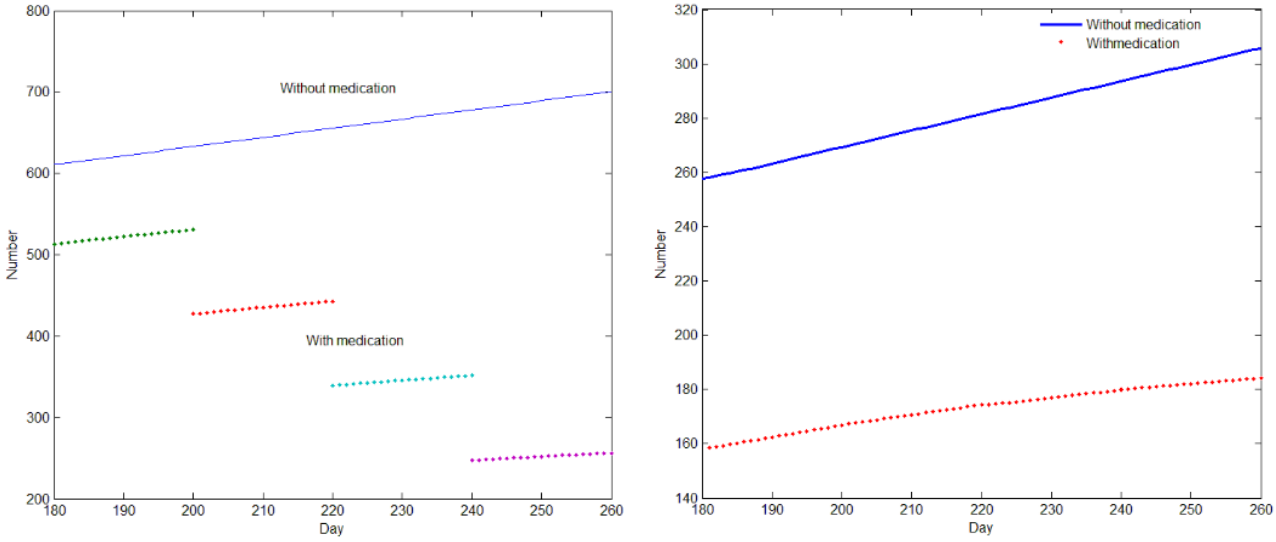
A. Infectives in Kenema



B. Deaths in Kenema

Figure.14 Medication used in Kenema

The tendency in figure.13 shows that the spread of disease is nearly controlled, because the trend of rise is contained by the application of medication. And the number of death is relatively low.



A. Infectives in Bombali B. Deaths in Bombali

Figure.15 Medication used in Bombali

The tendency of infectives in Bombali is different from the former two cities. The number is getting smaller and smaller after the application of medication. So, the outbreak of Ebola is eradicated finally under this delivery strategy.

The tendency of Ebola is nearly be controlled by the delivery strategy.

4.3.5 The amount of medication required and its production speed

The total amount of drug required by our plan in 6 cities in Sierra Leone is calculated as:

$$N_1 = \sum_{j=1}^{6} \delta_1 i(t) \tag{18}$$

where, N_1----the total amount of drug in Sierra Leone;

δ_1----the proportion of patients whose disease is not advanced;

$$N_2 = \sum_{j=1}^{6} \delta_2 s(t) \tag{19}$$

Where, N_2 ----the total amount of vaccine in Sierra Leone;

δ_2----the proportion of susceptible individuals;

The sum of the amount of drug over the world is:

$$N_{1t} = \sum_k N_{1k}$$
$$N_{2t} = \sum_k N_{2k} \tag{20}$$

where, N_{1t} ----the sum of drug over the world;

N_{2t} ---- the sum of vaccine over the world;

So, the speed of the manufacture of vaccine or drug is given by:

$$v = \begin{cases} v_{\max} & , P \le N_t \\ \dfrac{N_k}{\tau} & , P > N_t \end{cases} \tag{21}$$

where, $v_{\max}$ ----the maximum speed of manufacture of the vaccine or drug;

P ----the output of the vaccine or drug;

v ----the speed of manufacture of the vaccine or drug.

V. Sensitivity Analysis

5.1 The sensibility with respect to the death rate

We change the death rate, γ, and test the sensibility of the amount of dead people to it. The result is given as follows:

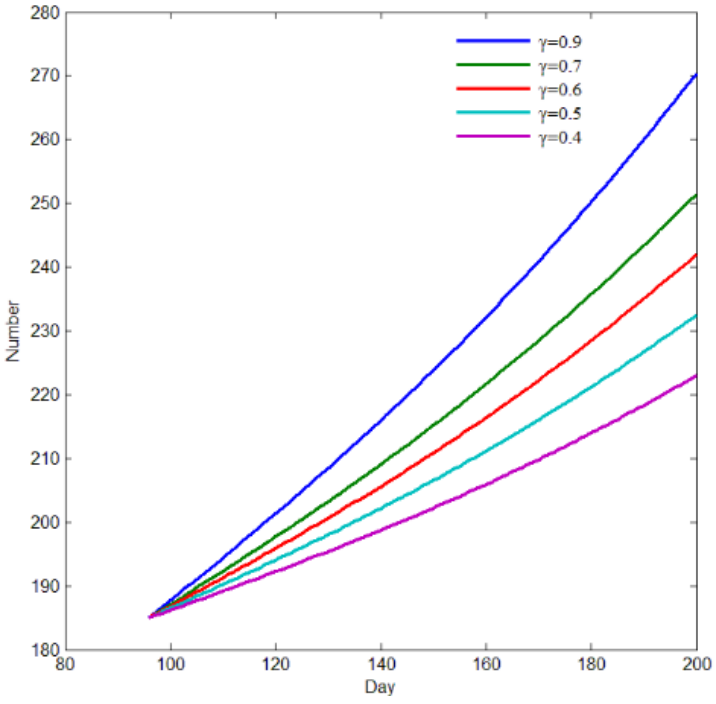


Figure.16 The sensibility of G to the death rate

We can see that the amount of deaths is rising with the value of death rate increasing, which is consistent to the fact.

5.2 The sensibility with respect to the amount of drug and vaccine

We now change the amount of the amount of drug and vaccine we used to the patients, and calculate the tendency of the infectives in different situations.

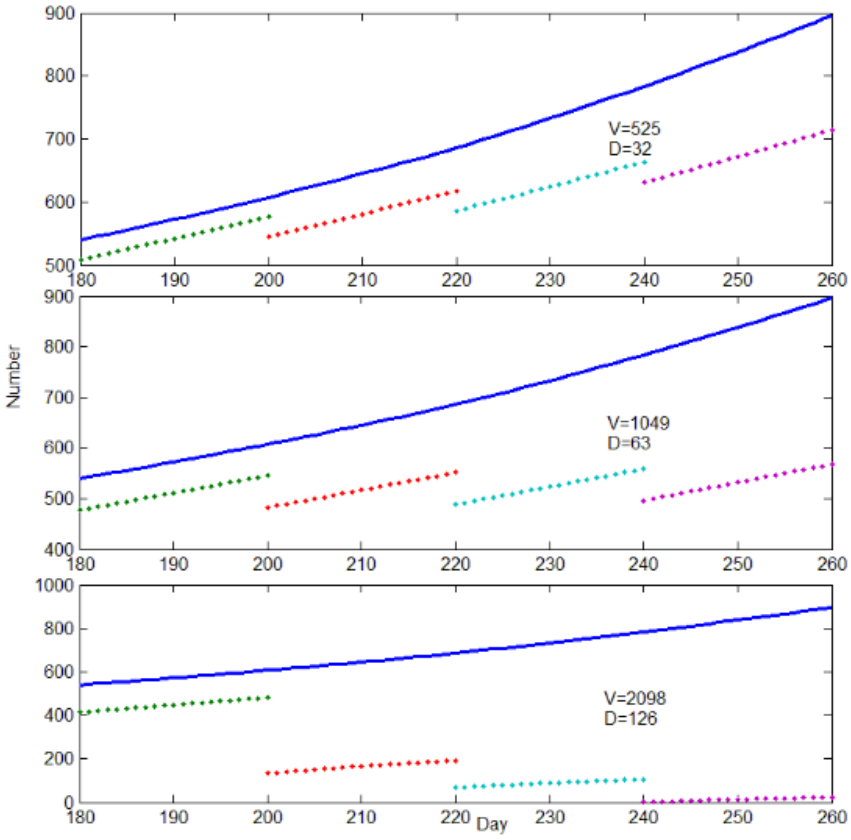


Figure.17 The sensibility of I to W and M

During the time of changing the amount of drug and vaccine, the tendency of the amount of infectives is showed in 3 different situations. When the dosage of vaccine is 525 and the dosage of drug is 63, the disease has not been controlled. When the values changed to 1049 and 63, Ebola has been controlled which is illustrated by the steady tend of the partitioned curves in the picture. Then the values change to 2098 and 126, the disease has been eradicated by the medication.

5.3 The sensibility with respect to the production period

Then, we change the length of the period of manufacturing the medication. Here we yield 3 different values: 10 days, 20 days, and 30 days. And the results are shown as follows:

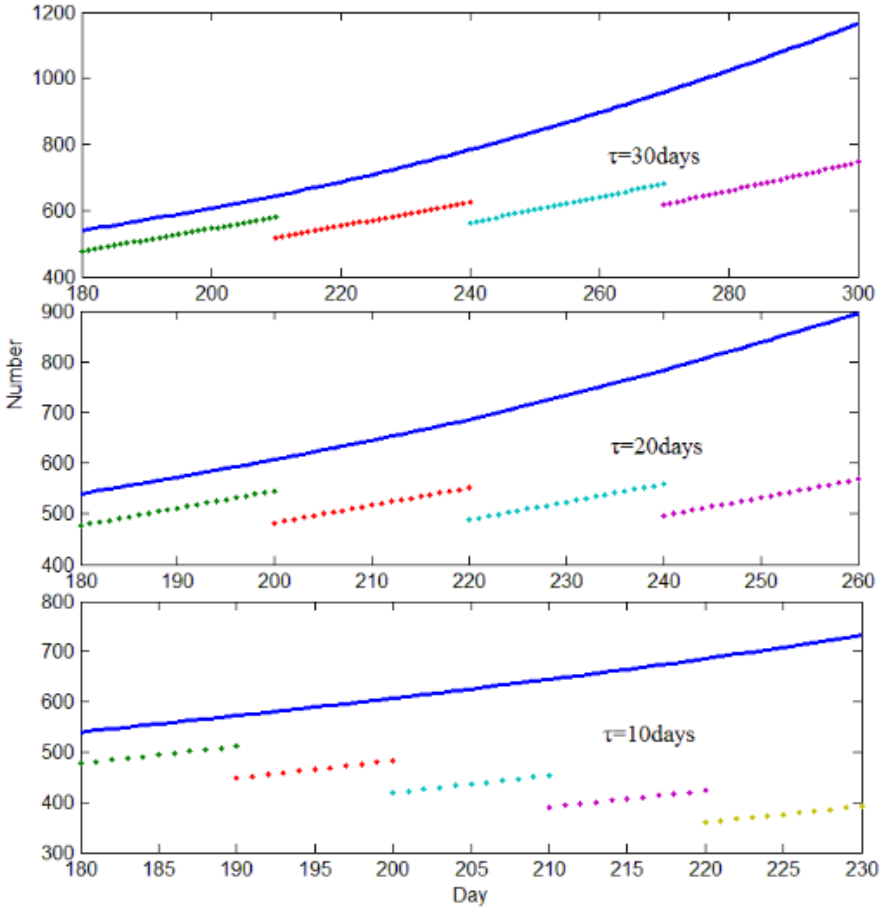


Figure.18 The sensibility of I to τ

From the picture, we see the obvious phenomenon that the amount of infectives is rising slower and slower with the period of manufacture. We can infer that there is a critical point of period where the disease is controlled exactly. This kind of tendency confirms to the reality well.

VI. Strength and Weakness

Strength:

(1). We established a submodel first to describe the tendency of Ebola without medication, which we used to predict the development of Ebola under the current condition. Then we built a submodel to simulate the trend of Ebola with the application of medication. Hence, we could model the disease pretty well, and it is convenient for us to capture the tendencies of Ebola in different situations;

(2). The least square method is introduced in our model to determine the values of the parameters. This kind of method utilizes the real data so our model is relatively realistic;

(3). The optimization model we build performed the situation in existing cities, so the optimized delivery location is a spot which can be found in real world.

Meanwhile, in this way, we could obtain a reasonable result from our optimization model;

(4). Take the different situation in prime and telephase of Ebola into consideration, which makes our model more close to the reality.

Weakness:

(1). Our parameters are static in submodel.1 and submodel.2, but the real situation may requires some dynamic parameters. So, the precision of the model will decrease in a way;

(2). We haven't divided the crowds into groups according to the age. People in different period of life will have a distinguishing reaction towards Ebola. Thus, it will also influence the accuracy of our model.

VII. Further Work

● In terms of modeling the disease as Ebola, we may transform the parameters in our epidemic model to certain functions. Because the dynamic variation of the development shall be captured by functions, and the precision of a dynamic model is higher than a static one;

● To take the characteristic of people in different ages, we may modify our submodel.1 and submodel.2 by adding the factor of age into our model. We might divide the sensible individuals into 3 or 4 sections and then model the disease.

● The model could be generalized to a country or the world by adding some conditions to the model itself.

Reference

[1].D. Nadnguza, J.M. Tchuenche, H. Haario, *Statistical Data Analysis of the 1995 Ebola Outbreak in the Democratic Republic of Congo*, Springer-Verlag, July 2011.

[2].Phenyo E. Lekone, Barbel F. Finkenstadt, *Statistical Interference in a Stochastic Epidemic SEIR Model with Control Intervention*: Ebola as a Case Study, University of Warwick, Biometrics 62,Dec. 2006 :1170-1177.

[3].Ousmane Faye, Pierre-Yves Boelle, Emmanuel Heleze, et la, *Chains of Transmission and control of Ebola Virus Disease in Conakry, Guinea, in 2014: an Observational Study*, The Lancet Infectious Diseases, Jan.23,2015.

[4].Matt Keeling, *The Mathematics of Diseases*, University of Cambridge, Mar. 2001.

[5].Gong Jianhua, Sun Zhanli and Li Xiaowen, et la, Simulation and Analysis of the control of SARS, Journal of Remote Sensing, vol.7, No.4, July, 2003: 260-265.

[6]. http://www.wma.net/en/30publications

[7]. http://zh.wikipedia.org/zh-cn

[8]. http://en.wikipedia.org/wiki/Epidemic_model

[9].Goeijenbier M, van Kampen JJ, Reusken CB, Koopmans MP, van Gorp EC. *Ebola*

virus disease: a review on epidemiology, symptoms, treatment and pathogenesis, Neth J Med, Nov.2014, 72 (9): 442–8.
[10].Ruzek and Daniel, Viral hemorrhagic fevers, CRC Press, Taylor & Francis Group, 2014: 444.
[11].Jaime Astacio, Delmar Briere, Milton Guillen, Josue Martinez, Francisco Rodriguez, Noe Valenzuela-Campos, *Mathematical Models to Study the Outbreaks of Ebola*.
[12]. http://en.wikipedia.org/wiki/Ebola_virus_epidemic_in_West_Africa
[13]. http://www.healthmap.org/ebola/#timeline

A Non-technical letter

Dear president of World Medical Association,

The situation of defending the disease, Ebola, is austere nowadays, especially in Africa. The people died every day in some worst-hit areas and the spread of disease requires treatment from WMA, and other associations around the world. The governments are preparing for the defense of Ebola. These days, we have modeled the tendency of Ebola in a mathematical way and obtained some conclusions from our analysis.

We must pay attention to the outbreak point of Ebola, which will appear after nearly 200 days since the first patient of Ebola is found. If we don't take any efficient methods to fight against Ebola, the amount of people infected by Ebola will rise rapidly in a short time. If there are people found infected continuously, we must pay highly attention to the situation.

When the medication of Ebola including the vaccine and drug is produced by the factories, we also need to make a plan to guide the distribution of medication, if the amount of medicine is limited by the current condition. The amount of medication is related to the situation of the region suffering from Ebola.

Meanwhile, we should also take a global aspect when we distribute the medication to different cities or countries. We also need to set some storage of vaccine and drug in some places of a country in case of the accident outbreak of Ebola, because there may be other sources of Ebola virus in the forest or cities.

Some preventive actions should be carried out by the health departments. These kind of actions would prevent the outbreak of Ebola in a reasonable way, especially in the cities where a lot of citizens live in. the big cities should be monitored because if Ebola outbreaks in these cities, we shall get a severe result. Because the epidemic spreads very fast in some places with a large amount of population and finally the situation would exceed the range of control, according to the current condition.

The speed of producing the medication is also an important factor in controlling

the disease or even eradicating it. So, the distribution of medication to different areas should also be determined according to the period of manufacture. There are different situations in different places, so the delivery of medication should also depend on the local condition, which will make the action more efficient.

Finally, we wish the Ebola will be controlled or eradicated soon.

Best wishes!