For office use only		Team Control Number		For office use only	
T1		**38240**		F1	
T2				F2	
T3		Problem Chosen		F3	
T4		**A**		F4	

2015 Mathematical Contest in Modeling (MCM) Summary Sheet

Summary

Last year, the strong-contagious virus of high fatality rate known as **Ebola** has gone from localized spread in many countries in West Africa.

Vaccination and drug therapy for people in epidemic areas have become a quite urgent task. In order to achieve this goal, the transportation system of vaccine and drug is one of the most important aspects. So, considering the production speed, spreading velocity of virus, the transportation location and population composition in epidemic areas, we choose to develop the best transportation system and distribution system for vaccine and drug to provide assistance to epidemic areas in the highest speed.

By investigating the characteristics of Ebola and the number of infected cases per day, on the basis of the FIR epidemic model, we establish a virus diffusion model without the consideration of latency and predict the time of epidemic outbreak in the future. Then, considering that Ebola virus has latency period of *2-21* days, we build a regeneration rate estimation model with family as the basic unit to study the spread of virus. On this basis, we build a vaccine allocation model to design the best vaccination program with known number of family and total amount of vaccine. Finally, considering that some flights have been cancelled because of the outbreak, we choose transit point beside epidemic areas. By comparing traditional point-to-point transportation and transshipment mode, we build a vaccine and drug transportation model which regards the delivery time as the transportation optimization goal by empowerment. By analysing the characteristics of the model, we design a simulated annealing algorithm embedded by linear iterative algorithm and calculate the model to certify it.

By testing and analysing each model, we conclude that vaccination success rate determines the allocation of vaccine and transit mode relatively has high stability and little uncertainty. Thus, we believe that our model will be useful and effective in the prevention and control of epidemic. In view of the difference between the transportation location of vaccine and drug, we investigate the increasing number of cases in main provinces of Guinea and Sierra Leone per day. We draw the preliminary conclusion that drugs should be transported to serious epidemic areas while vaccine should be transported to those areas which are around epidemic areas in order to prevent the outward diffusion of the epidemic.

We perform sensitivity analysis on some parameters and discuss the strengths and weaknesses of our model. We recommend our model because of its reasonable assumptions and certified accurate results.

Contents

1 Introduction **4**

1.1 Research goals and plans 4

1.2 Research background 4

2 Nomenclatures **5**

3 Model One: Virus Diffusion Model without latency **5**

3.1 Introduction 5

3.2 Assumption 5

3.3 Model analysis 6

3.4 Model testing 7

3.5 Conclusion 10

4 Model Two:Regeneration Rate Estimation Model(including latency) **10**

4.1 Introduction 10

4.2 Assumptions 10

4.3 Model analysis 10

4.4 Model testing 13

4.5 Conclusion 13

5 Model Three: Optimization Vaccination Model **14**

5.1 Introduction 14

5.2 Assumptions 14

5.3 Model analysis 14

5.4 Model testing 16

5.5 Conclusion 17

6 Model Four: Vaccine and Drug Transportation Model **17**

6.1 Introduction 17

6.2 Assumption 17

6.3 Model analysis 18

6.3.1 Simulated annealing algorithm 19

6.4 Model testing 20

6.5 Conclusion 21

7 Strengths and Weaknesses **21**

7.1 Strengths 21

7.2 Weaknesses 21

8 Future Research **22**

9 Proclamation for the World Medical association **23**

A Design of Epidemic Prevention and Control System

1 Introduction

Since the Ebola virus was discovered in 1976, 38 years later, the virus outbreak bounce back in West Africa with an irresistible tendency to spread. The fast diffusion rate of Ebola virus in West Africa and the harm of this virus make it a global critical mission to develop and product anti-viral vaccine and drugs. Nowadays, the world medical association has developed a treatment system which can fight Ebola virus. The vaccine and drug will soon be in mass production and be delivered to serious epidemic areas to prevent or control Ebola virus as soon as possible.

1.1 Research goals and plans

By researching the characteristics, development history, transmission route of Ebola virus and the environment, regional distribution, living custom in West Africa, we are searching for the most effective way to prevent and control the spread of Ebola virus and analyse the feasibility of it. Thus, we decide to build models which can achieve the following functions:

- The virus transmission characteristic can be reflected according to virus with different features.
- The transmission time of vaccine and drug is shortest and most efficient and there are few uncertainties in this process.
- The delivery method in epidemic areas can maximum the use of vaccine and that will made more people be immune.

1.2 Research background

Ebola virus is a kind of fulminating infectious virus which can make humans and primates with symptoms of Ebola hemorrhagic fever. Ebola virus is mainly spread through the following aspects such as blood, saliva, sweat and secretions of patients. Infected people have a high mortality rate of about *50-90%*. Ebola hemorrhagic fever first appeared in the Congo and southern Sudan in 1976, and often cause intermittent epidemic in sub-Saharan Africa. On December 2013, Ebola virus epidemic broke out in Guinea and then spread to Liberia and Sierra Leone. On 6 October 2014, it was reported that the first human infected Ebola virus outside Africa.

Countries have started to develop drugs and vaccines to control and prevent Ebola. A drug called ZMapp has been developed by Mapp Biopharmaceutical which is still under development as a treatment for Ebola virus disease. The effectiveness of this drug has been certified in infected macaques and for sick people it is still in the experimental stage.On August 12, 2014, World Health Organization announced that, on the Premise of obtaining consent, medical institutions from patients are allowed to use therapeutic drugs which are still in the experimental stage.

According to the latest figures released by the World Health Organization, as of February 1, 2015, *22495* Ebola cases have been found in nine countries, including *8981* deaths. Besides *15*

dead cases, the rest of deaths are all from Guinea, Liberia and Sierra Leone. The probability of becoming infected is shown in Fig.1.

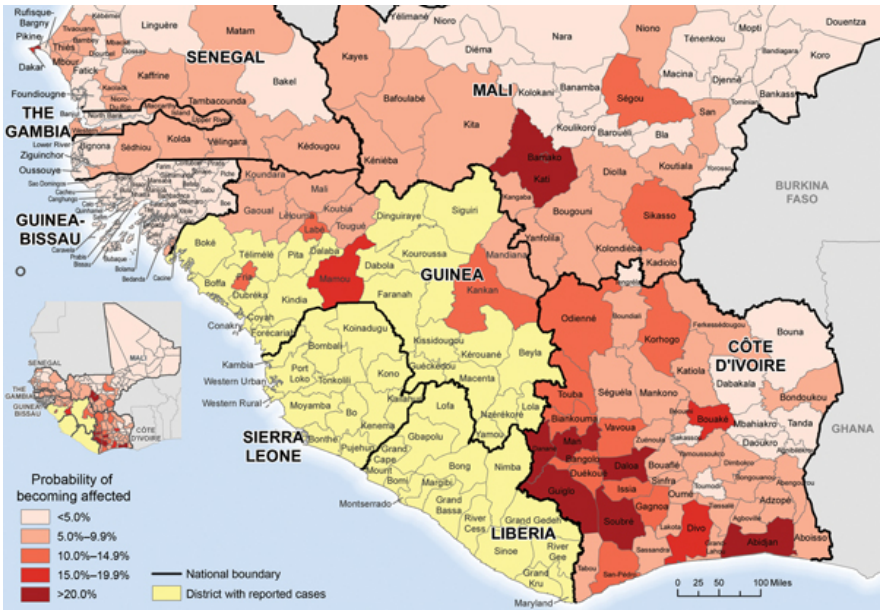

Figure 1: The probability of becoming infected

And the Ebola case number in three countries with severe situation suddenly increased with 124 cases in the week before 1st February. Therefore, based on the investigation and research, we need to apply the scientific analytical method to reveal spreading trends and predict the development of epidemic in order to prevent and control the epidemic.

2 Model One: Virus Diffusion Model without latency

2.1 Introduction

According to the characteristics and transmission of Ebola virus, we establish a virus diffusion model. In this model, we consider two cases of virus spreading, one neglects the latency of virus, while another involves it. We use this model to simulate the epidemic broke out in some countries of West Africa and predict the development of epidemic in the future. This model can to some extent prevent the outbreak of epidemic.

2.2 Assumption

In the model we made some assumptions as follows:

- The research object is ideal people.
- The total number of people is constant and equals to **N**.
- There is no mortality caused by other reasons.
- After infected people are fully recovered, they will have long-term immunity.

Under the basic assumptions above, we can show our approach in detail.

2.3 Model analysis

Under the assumptions, we divide all the citizens in infected area into three catelories: susceptible(**S**), infected(**I**) and removed people(**R**) which refer to s(t),i(t) and r(t). The sum of the three is N.

$$s(t) + i(t) + r(t) = N \tag{1}$$

The equations of the model is

$$\begin{cases} \frac{ds}{dt} = -\lambda si, s(0) = s_0 \\ \frac{di}{dt} = \lambda si - i\mu, i(0) = i_0 \\ \frac{dr}{dt} = i\mu \end{cases} \tag{2}$$

where
λ is daily contact rate of patients
μ is daily cure rate.
$\sigma = \frac{\mu}{\lambda}$ is the number of contact in infectious period

By solving Eqs.(1) and (2),

$$s(t) = s_0 e^{-\frac{r}{\sigma}} \tag{3}$$

We take the first three terms of Taylor expansion of $e^{-\frac{r}{\sigma}}$ and calculate that the change rate of removed population approximately equals to

$$\frac{di}{dt} = \mu \left[N - r - s_0 \left(1 - \frac{r}{\sigma} + \frac{1}{2} \Big(\frac{r}{\sigma} \Big)^2 \right) \right] \tag{4}$$

When initial value $r_0 = 0$,we can get that the accumulative removed population is

$$r(t) = \frac{\sigma^2}{s_0} \left[\frac{s_0}{\sigma} - 1 + \alpha \tanh \left(\frac{1}{2} \alpha \mu t - \varphi \right) \right]$$

where $\alpha = [(\frac{s_0}{\sigma} - 1)^2 + \frac{2 s_0 i_0}{\sigma^2}]^{\frac{1}{2}}, \tanh \varphi = \frac{s_0 - \sigma}{\alpha \sigma}$.

So we can simplify Eq.(4) to be

$$\frac{dr}{dt} = \frac{\mu \alpha^2 \sigma^2}{2 s_0} \frac{1}{ch^2 \left(\frac{\mu \alpha t}{2} - \varphi \right)} \tag{5}$$

Because $ch^2 \left(\frac{\mu \alpha t}{2} - \varphi \right) \geq 1$, $\frac{1}{ch^2 \left(\frac{\mu \alpha t}{2} - \varphi \right)} \leq 1$. If and only if $\frac{\mu \alpha t}{2} - \varphi = 0$, $\frac{dr}{dt}$ can get maximum. That means in this case the number of removed people is largest.

Then, we analyse the change on $s(t)$, $i(t)$ and $r(t)$. The first two equations of our model is unrelated to $r(t)$, so we can obtain the relationship between $s(t)$ and $i(t)$ from the first two equations.

$$\begin{cases} \frac{ds}{dt} = -\lambda si, s(0) = s_0 \\ \frac{di}{dt} = \lambda si - i\mu, i(0) = i_0 \end{cases} \tag{6}$$

Solving for $i(s)$,

$$i(s) = i_0 + s_0 - s + \sigma \ln \frac{s}{s_0} \tag{7}$$

Let $\lim\limits_{t \to \infty} s(t) = s_\infty$, $\lim\limits_{t \to \infty} i(t) = i_\infty$, $\lim\limits_{t \to \infty} r(t) = r_\infty$, we can get the conclusion as follow:

- No matter what $s(t)$ and $i(t)$ is, $i_\infty = 0$. Patients will finally been cured or dead.
- Finally, the rate of healthy people who are uninfected is s_∞. In Eq.(7), we make $i(s)$ equals to 0 and then we can conclude that s_∞ is the root of the equation $i_0 + s_0 - s + \sigma \ln \frac{s}{s_0} = 0$ when s belongs to $(0, \sigma)$.
- If $s_0 > \sigma$, then $i(t)$ will increase first. When $s = \sigma$, $i(t)$ achieve the maximum $i_m = s_0 + i_0 - \sigma(1 + \ln \frac{s}{s_0})$. After that, $i(t)$ decreases and approaches to 0 while $s(t)$ monotonously decreases to s_∞. That means only if the rate of infected people $i(t)$ grows during a period of time, it can be considered that the infectious disease is spreading. Thus, the parameter σ is a threshold value that when $s_0 > \sigma$, the virus will spread.
- If $s_0 \leq \sigma$, then $i(t)$ will monotonously decrease to 0 and $s(t)$ will reduce to s_∞. In this case, reducing the contact number in infectious period σ can make s_0 less than or equal to σ and prevent the spread of virus. Thus, reducing the rate of contact is an effective way to control the spread of virus.

2.4 Model testing

According to the existing research findings, we know that Ebola virus mainly spread through blood, saliva, sweat and secretions of patients and this infection has an incubation period of 2-21 days. Based on the property of Ebola, we test the performance of this model in its application scope. Table 1 shows the data announced by World Health Organization which reflects the evolution of Ebola virus outbreak in Guinea from March 26 to July 20. Then we draw the scatter plot of the daily number of infections and death toll shown in Fig.1

Table 1 2014 Guinea Ebola cumulative cases and death numbers
From March 26th to July 20

Date	3.26	3.27	3.28	3.31	4.1	4.4	4.7	4.9	4.14	4.16
Number of cases	86	103	112	122	127	143	151	158	168	197
Number of deaths	62	66	70	80	83	86	95	101	108	122
Date	4.20	4.23	4.26	5.1	5.3	5.5	5.7	5.10	5.12	5.23
Number of cases	208	218	224	226	231	235	236	233	248	258
Number of deaths	136	141	143	149	155	157	158	157	171	174
Date	5.27	5.28	6.1	6.3	6.5	6.16	6.18	6.20	6.25	6.30
Number of cases	281	291	328	344	351	398	390	390	393	413
Number of deaths	186	193	208	215	226	264	267	270	275	303
Date	7.2	7.6	7.8	7.12	7.14	7.17	7.20			
Number of cases	412	408	409	406	411	410	415			
Number of deaths	305	307	309	304	310	310	314			

Data Source: World Health Organization

According to Eq.(3), we select $\lambda = 3.72$ and $\mu = 0.863$, and then we can estimate daily infecting number $s = \frac{1882}{ch^2(0.195t - 6.02)}$ which is shown in Fig.2 In Fig.2 we found that in the 32^{nd} or 33^{rd} week, the infection number will obtain maximum which means if we make March 26th as the basic point, then the increasing infection number will get the maximum in late November or early December.

According to the data of the number of cases and deaths as of February 5th 2015 shown in Table 2, we draw a line chart (Fig.3) which reflects casualties per day in Guinea and observe the trend

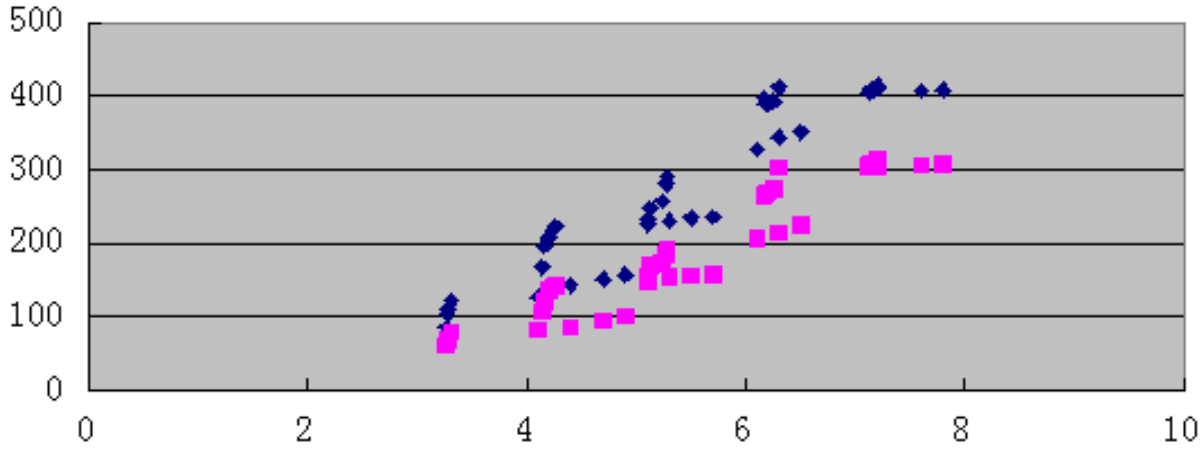

Figure 2: Scatter plot of number of cases and deaths per day

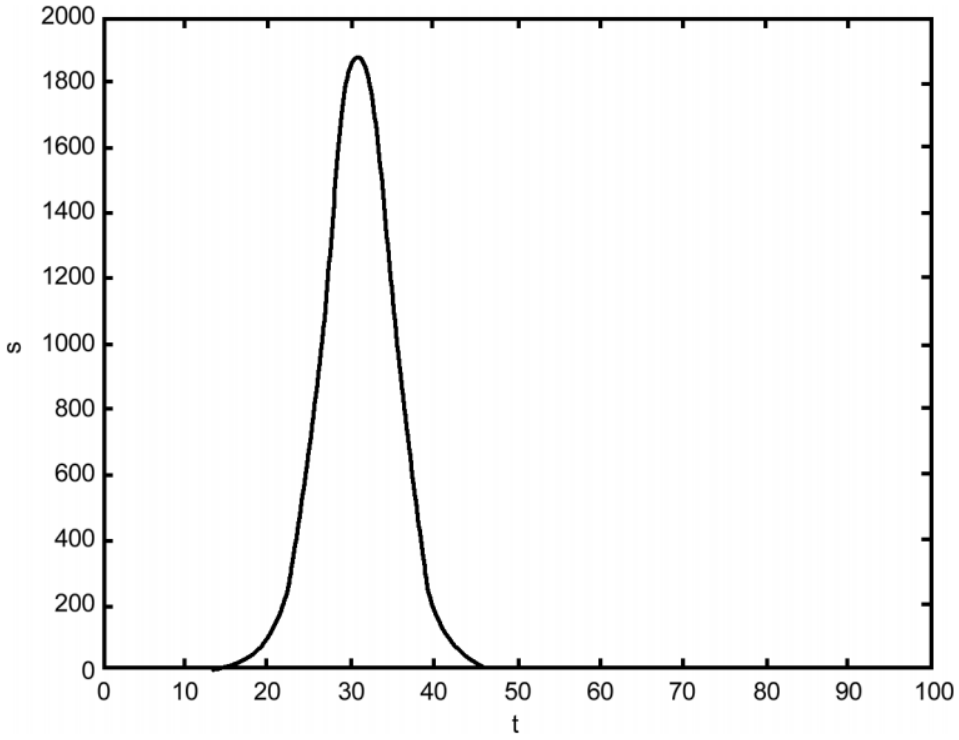

Figure 3: Relationship between daily infecting numbers and weeks

of it.

Table 2 Guinea Ebola increasing infection number and rate per day from July 20 2014 to February 5 2015

Date	7.20	7.23	7.27	7.30	8.1	8.4	8.6	8.9	8.11	8.13
Increasing number	5	12	33	12	13	10	0	11	4	9
Increasing rate	3	4	8	4	7	3	0	4	2	5
Date	8.16	8.18	8.20	8.26	8.31	9.3	9.7	9.10	9.14	9.17
Increasing number	24	36	28	41	123	52	38	38	43	23
Increasing rate	8	18	14	7	25	17	10	13	11	8
Date	9.21	9.23	9.25	9.28	10.1	10.5	10.7	10.12	10.17	10.19
Increasing number	57	52	29	54	42	99	52	122	29	39
Increasing rate	14	26	15	18	14	25	26	24	6	20
Date	10.24	10.30	11.2	11.4	11.9	11.11	11.16	11.18	11.23	11.30
Increasing number	58	77	56	29	118	41	52	76	87	30
Increasing rate	12	13	19	15	24	21	10	38	17	4

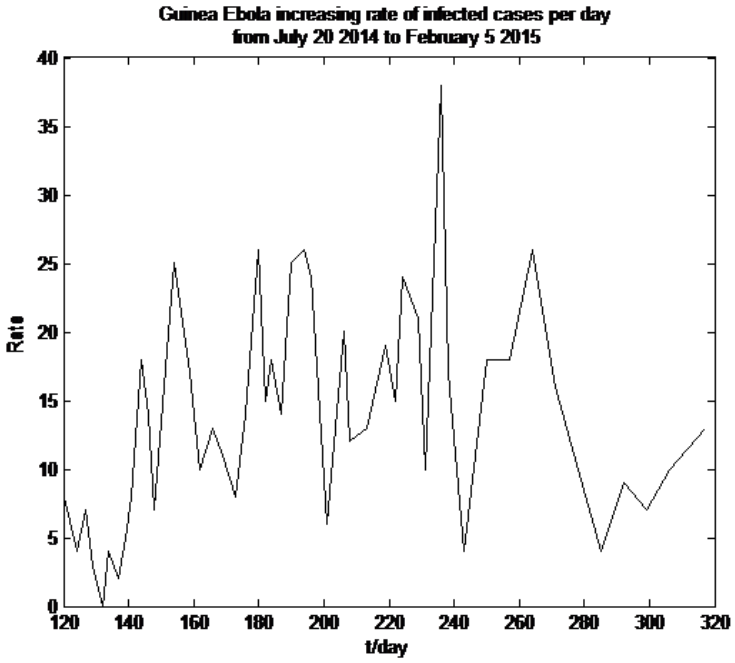

Figure 4: Guinea virus increasing rate per day

It can be found that in November, the number of infection per day is fluctuating with upward trend and achieve the maximum in mid-December.In late December, the growth rate of infectious cases reached the maximum. Compared the theoretical and actual data, we could find that the actual condition is very close to what we predicted before.

2.5 Conclusion

By testing and verifying virus diffusion model, we preliminarily conclude that this model can to some extent predict when the Ebola virus outbreak will happen next time and then we can activate contingency plans in advance and prepare greatly to control and prevent the outbreak. Meanwhile, although the result we calculate is very close, there are still some errors. By analyzing the existing error, we consider that this model need further optimization to improve the predicting accuracy and expand the range of predicting time.

3 Model Two:Regeneration Rate Estimation Model(including latency)

3.1 Introduction

To some extent, the outbreak of Ebola virus happened in West Africa have a great relationship with habits and customs of local people. In some areas, residents have customs that they will embrace and kiss bodies of their dead relatives. These deep-rooted customs are quite not conducive to control and prevent the spread of Ebola. Thus, the infection in each family unit accounts for a sizeable proportion. For this phenomenon, we established another virus diffusion model which treats family as the basic unit of society. This model is mainly used to research the impact of basic reproductive number**(R)** on family size.

3.2 Assumptions

In the this we made some assumptions. They are as follows:

- Individuals are located in each family, and their distribution outside the home is random and uniform.
- In a very small period of timeδ, the probability of a vulnerable person being infected by someone outside family is $R_G w(\tau)\delta$.
- In a very small period of timeδ, in a family with n members, the probability of other family members being infected by the member who has been infected is $r_n w(\tau)\delta$.
- The population is large enough and the probability of repeated infection in a family is almost 0.
- In this model, the population of each family is less than or equal to 6.
- There is only one person in a family unit can be infected from outside.
  where
  w(t) is time distribution of infectious period on one generation.
  R_G is the average number of family members who are infected by the member who have already been infected.
  r_n is a parameter of infection happened in a family with n family members.

3.3 Model analysis

We assume that in a family with two members, one has been infected from outside and the other one has been infected by the one infected outside so that 1->1. We can get a likelihood equation

$$(p_1)^{y_1}(q_1p_2)^{y_2} \times \cdots \times (q_1 \cdots q_{s-1}p_s)^{y_s}$$

where

$$q_i = 1 - p_i, q_i = \exp\{-r_2 \int_{-1}^{i} w(s)ds\}$$

y_t is the number of family member who is infected t days later since the day one member brought the virus back home. t=1,2,âĂę..
p_t is the probability of the second member infected t days after the first one infected. T=1,2,...
The probability that the second person will never be infected is

$$Q_2 = \lim_{n\to\infty} q_1q_2 \cdots q_n = \exp\{-r_2 \int_0^{\infty} w(s)ds\} = \exp\{-r_2\}$$

Then, we can estimate$\exp\{-r_2\}$.
For a family unit with three members, we consider that only one person is infected from outside. We assume that there is ${y_{t,d}}^3$ families and the second person is infected *t* days later. The last person is infected *(t+d)* days later since the day the first one being infected. So the probability that the second one is infected *t* days later is $q_1...q_{t-1}p_t$. Obviously the last one might be infected by the first or the second one. Thus, the probability of the last one being infected is

$$q_1 \cdots q_{i+d-1}q_1 \cdots q_{d-1}(1 - q_{t+d}q_d)$$

where

$$q_i = 1 - p_i, q_i = \exp\{-r_3 \int_{-1}^{i} w(s)ds\}$$

Therefore, the probability of the whole family being infected is

$$(q_1 \cdots q_{t-1} p_t)(q_1 \cdots q_{i+d-1} q_1 \cdots q_{d-1}(1 - q_{t+d} q_d))$$

Substituting the likelihood equation,

$$[(q_1 \cdots q_{t-1} p_t)(q_1 \cdots q_{i+d-1} q_1 \cdots q_{d-1}(1 - q_{t+d} q_d))]^{y^3_{t,d}}$$

We can also assume that there are families that the second one is infected by the first one t days later. The probability of the second person being infected is

$$q_1 \cdots q_{t-1} p_t$$

where

$$q_i = 1 - p_i, q_i = \exp\{-r_3 \int_{-1}^{i} w(s)ds\}$$

Substituting in the likelihood equation,

$$[q_1 \cdots q_{t-1} p_t]^{y^3_t}$$

Analogizing with families of 2 members,

$${Q_3}^2 = (\exp\{-r_3\})^2 = \frac{y^3 - \sum_t y^3_t - \sum_{t,d} y^3_{t,d}}{y^3}$$

where

$$Q_3 = \exp\{-r_3\}$$

y^3 is the family number with only one infected person
Solving for q_t, $q_t = \exp\{-r_3 \int_{-1}^{t} w(s)ds\}$. Then we can estimate *w(t)*. We have known that for a family with two members, the infectious ability to the other family is

$$\beta_2^*(\tau^*) = R_G[w(\tau^*) + (1 - Q_2) \int_0^{\tau^*} w_2(s) w(\tau^* - s)ds]$$

where

$$q_2(\tau^*) = \exp\{-r_2 \int_0^{\tau^*} w(s)ds\}, w_2(t) = -\frac{1}{1 - Q_2} \frac{dq_2(t)}{dt} = \frac{r_2 w(t) \exp(-r_2 \int_0^t w(s)ds)}{1 - Q_2}$$

Considering a family with 3 members, one person is infected from outside when $\tau^* = 0$. If the first one infect the second one, then both the two may infect the third one. The infectious ability is

$$r_3[w(t) + 2Q_3(1 - Q_3)] \int_0^t w_2^3(s) w(t - s)ds)$$

Thus, until *t*, the probability that the third one is still not infected is

$$q_2^3(t) = \exp\{-r_3 \int_0^t [w[w(s) + 2Q_3(1-Q_3)] \int_0^x w_2^3(s)w(x-s)dsdx]\}$$

where

$$w_2^3(t) = -\frac{1}{1-Q_3}\frac{dq_1^3(t)}{dt}$$

The probability that the third one is uninfected is

$$Q_1^3 = \exp\{-r_3[1 + 2Q_3(1-Q_3)\} = Q_3^{1+2Q_3(1-Q_3)}$$

So, for a family with 3 members, the infectious ability to the other family is

$$\beta_3^*(t) = R_G[w(t) + 2Q_3(1-Q_3)\int_0^t w_2^3(s)w(t-s)ds + (1-Q_1^3)\int_0^t w_3^3(s)w(t-s)ds]$$

where

$$w_3^3(t) = -\frac{1}{1-Q_3}\frac{dq_3^3(t)}{dt}$$

Similarly, we can get $\beta_4^*(t)$,$\beta_5^*(t)$,$\beta_6^*(t)$. Assuming that *i* family number proportion in all families is k_i, the family average infection rate is

$$\beta^*(t) = \sum\nolimits_{k=1}^{6} k_i\beta_i^*(t)$$

.
Thus, the family basic reproduction rate is

$$R^* = \int_0^\infty \beta^*(t)dt$$

3.4 Model testing

From the assumption above, we have known that in our model one family has less than or equal to 6 members and if a family has more than 6 persons, we assume that the number of family members is *6*. To simplified the model testing, I simulate a region with M families. Family distribution in this area is k_n, $n = 1, ..., 6$. We use n_α to represent Family *1* to Family *M*, $\alpha = 1, ..., M$ and mark each person in a family (i, α), $i = \{1, ..., n_\alpha\}$. The condition of (i, α) is $I_{i,\alpha}$. The time from (i, α) being infected to now is $\tau_{i,\alpha}$. The equation $I_{i,\alpha} = 0$ means (i, α) is still uninfected while $I_{i,\alpha} = 1$ means (i, α) has been infected. The value $N = \sum\limits_{\alpha=1}^{M} n_\varepsilon$ represents the total population in this region. When $\tau^* = 0$, we assumed that $I_{1,1}$ is infected by someone outside the region. In a very small period of time δ, the probability of α being infected by whatever inside or outside family is

$$p_\alpha = \delta(\sum_{i=1}^{n_\alpha} I_{i,\alpha} r_{n_\alpha} w(\tau_{i,\alpha}) + (1/N)\sum_{\beta=1}^{M}\sum_{i=1}^{n_\beta} I_{i,\beta} R_G w(\tau_{i,\alpha}))$$

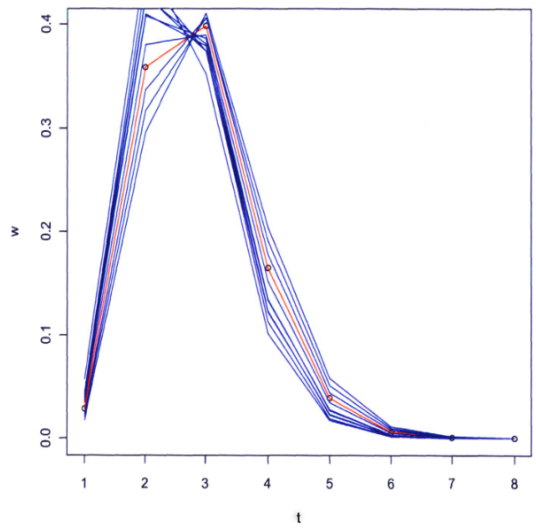

Figure 5: Comparison between estimated parameter and original parameter of $w(t)$

After a time δ, for every (i, α) with $I_{i,\alpha} = 1$, $\tau_{i,\alpha}$ becomes $\tau_{i,\alpha} + \alpha$. Then We assume *M=2000* and simulate this kind of region *10* times. After simulation, we draw the function of probability density shown in Fig.2 to reflect the difference between original parameter and estimated parameters. We obtain the parameter estimation average of $w(t)$ is

$$(9.44, 3.41)$$

while the assumed value is

$$(9.4, 3.3)$$

Compared these two values, it can be seen that the value of parameter estimation average and assumed value are very close.

3.5 Conclusion

With this virus diffusion model based on family basic regeneration rate, we can estimate the distribution parameters in infectious periods by using the time when patients being infected. In this model, we need about 100 data to test whether this model is still effective in practice. After we get the distribution of infectious period, we can set the isolation time for infected people more scientifically. In addition, the isolation time of people who have contacted with infected people is also a important factor that we need to consider during the prevention process.

4 Model Three: Optimization Vaccination Model

4.1 Introduction

In order to control and prevent the proliferation of Ebola virus to a large extent, we decide to research for the optimization of vaccination. Considering the application of personal basic reproductive rate has been greatly and widely used in this aspect. On the basis of family basic reproductive rate, we build an optimization vaccination model and test the actual applying effect of the model.

4.2 Assumptions

Based on the assumptions of model two, we also made the following hypotheses.

- The probability of vaccination successfully is only ε.
- Vaccine is only effective to uninfected people and cannot improve the state of infected people which means vaccine do not change R_G, r_n and $w(t)$.

4.3 Model analysis

From model two, we can see that family basic reproductive rate is $R^* = \int_0^\infty \beta^*(\tau^*)\mathrm{d}\tau^*$. When $n = 1, 2, ...,$ and $v = 0, 1, ..., n$, we define that x_{nv} represents the proportion of family with n members and v vaccinated members. If *(n-k)* people are vaccinated successfully, $k = n - v, n - v + 1, ..., n$, then there will be k vulnerable people in this family. The probability of this is

$$\begin{pmatrix} v \\ n-k \end{pmatrix} \varepsilon^{n-k}(1-\varepsilon)^{v-n+k}$$

where
$h_{n,v,k}$ is the proportion when the number of family members is n, the number of vaccinated people is v and the number of family vaccinated successfully is k.

$$h_{n,v,k} = k_n x_{nv} \sum_{k=n-v}^{n} k \begin{pmatrix} v \\ n-k \end{pmatrix} \varepsilon^{n-k}(1-\varepsilon)^{v-n+k}$$

After vaccination, family distribution changes in the case of only considering vulnerable persons. We do not consider people who have successfully vaccinated because those people are immune to infectious disease. The new family distribution ${k_n}'$ is as follows:

$$\begin{gathered} K = 0, \sum_{n=1}^{\infty}\sum_{v=0}^{n} h_{n,v,0} \\ K = 1, \sum_{n=1}^{\infty}\sum_{v=0}^{n} h_{n,v,1} \\ K = 2, \sum_{n=1}^{\infty}\sum_{v=0}^{n} h_{n,v,2} \\ ..... \end{gathered}$$

The total number of vulnerable people in this region is

$$M' = \sum_{n=0}^{\infty} nM{k_n}'$$

From the assumption, we know that the infection function can be divided into $\beta_G(\tau) = \frac{M'}{M} R_G w(\tau)$ and $\beta_n(n, \tau) = r_n w(\tau)$. Where
$\frac{M'}{M}$ is the probability of contacting vulnerable people outside family.
R_G is the probability of vulnerable people who are infected by a infected person outside family.
$w(\tau)$ is the distribution of infectious period of epidemics. r_n is a parameter of infection happened inside a family. Considering family with two members, one is infected from outside when $\tau^* = 0$. The probability of the second person who is still uninfected when τ^* is

$$q_2(\tau^*) = \exp\left(-r_2 \int_0^{\tau^*} w(s)ds\right)$$

The probability that the second person will never be infected is

$$Q_2 = q_2(\infty) = \exp(-r_2)$$

If the second person is infected, the time when he is infected is

$$w_2(\tau^*) = -\frac{1}{1-Q_2}\frac{dq_2(\tau^*)}{d\tau^*} = \frac{r_2 w(\tau^*)\exp(-r_2\int_0^{\tau^*} w(s)ds)}{1-Q_2}$$

where $\frac{dq_2(\tau^*)}{d\tau^*}$ is the changing rate of the total probability that the second person is uninfected.
$1-Q_2$ is the total probability of being infected.
Therefore, after vaccination,

$${\beta_2}^*(\tau^*) = \frac{M'}{M}R_G[w(\tau^*) + (1-Q_2)\int_0^{\tau^*} w_2(s)w(\tau^*-s)ds]$$

If k_n represents family distribution, then $K_n = \frac{nk_n}{\sum_{u=0}^{\infty} uk_n}$ means new family distribution function based on the number of family members. If someone in a family with n' persons is infected, we can use Reed-Frost Model to calculate the probability of chain infection process:

$$pr(\{n', {m_1}', ..., {m_n}'\})$$

where ${m_1}'$ means ${m_1}'$ in the first generation are infected.
Thus, the distribution of Random variable $X = \{n', {m_1}', ..., {m_n}'\}$ is $f(X) = K_n pr(\{n', {m_1}', ..., {m_n}'\})$.
The average infection ability of a family is

$$\tilde{\beta}^*(\tau^*) = \int dX f(X)\beta^*(X,\tau^*) = \frac{M'}{M}R_G\sum_{i=1}^{\infty} R_G u$$

where
u_i is the mathematical expectation of m_i with the probability distribution $f(X)$. The family basic reproductive rate after vaccination is Where $u = \sum_i u_i$ Simplifying R^*, We find that R^* is the linear equation of $x_{n,v}$ and the coverage of vaccines is

$$C_v = \frac{1}{u_N}\sum_n\sum_{v=0}^{n} vk_n x_{n,v} = \frac{u_V}{u_N}$$

where
u_V is the average of V, u_N is the average of N.

4.4 Model testing

Now what we need to do is to solve the problem that how to minimize R^* when vaccine coverage is constant. According to the known theoretical algorithm of this optimization vaccination model, we analyse some specific situation in order to find the difference on vaccination allocation methods when the vaccination rates of success are not the same. We assume that the distribution of family structure is $k_2 = k_4 = 0.5$. The probability of not being infected in a family is $Q_2 = 50\%$ and $Q_4 = 72\%$. We can obtain that $u_N = 3$ and

$$u_2 = 0.64, u_4 = 0.036$$

Thus, an infected family has $u = \sum_{i=1}^{6} u_i = 0.696$ in average.

First of all, we assume that all the people vaccinated will never be infected any more, $\varepsilon = 1$. Optimizing the model,

$$R^* = R_G u \sum_{d=1}^{6} \sum_{v=0}^{d} k_d x_{dv}(d-v)$$

$$= \frac{R_G u}{2}(2x_{20} + x_{21} + 4x_{40} + 3x_{41} + 2x_{42} + x_{43})$$

$$\sum_{n=1}^{6} \sum_{v=0}^{n} v k_n x_{n.v} = 3 * C_{\max}$$

$$\sum_{v=0}^{n} x_{n.v} = 1, n = 1, 2, ...6.$$

$$x_{n.v} \geq 0, v = 0, 1, 2, ..., n; n = 1, 2, ...6.$$

- Assuming the maximum coverage $C_{\max} = 2/3$,

  $$x_{22} = 1, x_{40} = x_{44} = 0.5, x_{20} = x_{21} = x_{41} = x_{42} = x_{43} = 0$$

  It reflects that we should vaccinate family with less people first and then vaccinate everyone in those families with more people.

- Assuming the maximum coverage $C_{\max} = 1/3$,

  $$x_{22} = x_{40} = 1, x_{20} = x_{21} = x_{41} = x_{42} = x_{43} = x_{44} = 0$$

  This also means people in families with fewer members should be vaccinated first. At this moment, the coverage is too low to vaccinate families with more members.

If $\varepsilon = 0.5$ and other assumptions are constant,

$$R^* = R_G u \sum_{d=1}^{6} \sum_{v=0}^{d} k_d x_{dv} \sum_{k=d-v}^{d} k \begin{pmatrix} v \\ d-k \end{pmatrix} \varepsilon^{d-k}(1-\varepsilon)^{v-d+k}$$

$$= \frac{R_G u}{2}(2x_{20} + 1.5x_{21} + x_{22} + 4x_{40} + 3.5x_{41} + 3x_{42} + 2.5x_{43} + 2x_{44}).$$

- Assuming the maximum coverage $C_{\max} = 1/3$,

  $$x_{20} = x_{42} = 1, x_{20} = x_{21} = x_{41} = x_{40} = x_{43} = x_{44} = 0$$

  It shows that when $\varepsilon = 0.5$, we should vaccinate people with more people first to reduce vulnerable people in those families.

- Assuming the maximum coverage $C_{\max} = 2/3$,

  $$x_{22} = x_{42} = 1, x_{20} = x_{21} = x_{41} = x_{40} = x_{43} = x_{44} = 0$$

  It means when $\varepsilon = 0.5$, with high coverage, we should vaccinate people with more people first to reduce vulnerable people in those families and then vaccinate families with two members.

4.5 Conclusion

By testing and simulating this model, we conclude that when the success rate of vaccination is high, families with less people should be vaccinated first while on the condition of lower success rate, families with more people should be vaccinated first in order to reduce vulnerable people. In addition, if this model is used to control Ebola virus, we think that we need to consider all the uncertainties and the efficiency of the model.

5 Model Four: Vaccine and Drug Transportation Model

5.1 Introduction

Ebola outbreak in West Africa come back unstoppably. The situation of virus spreading in Guinea, Liberia and Sierra Leone is so serious that the produce and transportation of vaccine and drug become a crucial factor to control and prevent Ebola epidemic. Thus, we build a vaccine and drug transportation model to solve the problem on how to schedule produced vaccine and drug quickly and efficiently. Because some flights to serious epidemic areas have been canceled for reducing the spread of the epidemic, we choose some transit points beside epidemic areas in order to deliver vaccine and drug with the highest speed and the least time.

5.2 Assumption

We assume that there are cm supply points, n demand points and l candidate transit points for vaccine and drug. Other assumptions are as follows:

- The transportation time between each supply point, demand point and candidate transit point is known.
- Both the demands of vaccine and drug on supply points and demand points are known.
- The urgency on needs for vaccine and drug for each demand point is known.
- The supply quantity is greater than requirement.
- All the vaccine and drug transported by transship model will be centralized on transit points and transported to demand points.
- Each demand point has at most one transit point for vaccine and drug transshipment.

5.3 Model analysis

We assume that the function of time satisfaction is

$$g_t(t) = e^{-t^2\theta_j} \tag{1}$$

where point j is a demand point.
The variable t is transportation time.
The value of means the urgency of point j on transportation time.
The smaller θ_j is, the greater the urgency will be.

The total requirement quantity of demand point *j* can be regarded to be transported in batches at different times. We assume that each vaccine or drug can make one person on point *j* cured. The quantity of vaccine and drug arrived each batch can be seen as the empowerment of delivery time satisfaction. Thus the total time satisfaction of demand point *j* can represents the empowerment of delivery time satisfaction in all patches:

$$z_j = \sum_i m_{ij} g_j(t_{ij})$$

where
the value of m_{ij} means the quantity of vaccine and drug transported from supply point *i* to demand point *j* the value of t_{ij} is the corresponding delivery time.

The equation of model *(P)* is

$$\max z = \sum_{j\in N}\sum_{i\in M} {x_{ij}}^d g_j({t_{ij}}^d) + \sum_{j\in N}\sum_{i\in M} {x_{kj}}^h g_j(\max_{i\in M}\{{t_{ik}}^h \delta({x_{ik}}^h)\}{t_{kj}}^h)$$

$$\sum_{j\in N} {x_{ij}}^d + \sum_{k\in l} {x_{ik}}^h \le a_i, i \in M \tag{2}$$

$$\sum_{i\in M} {x_{ij}}^d + \sum_{k\in L} {x_{kj}}^h \le a_i, j \in N \tag{3}$$

$$\sum_{i\in M} {x_{ik}}^h + \sum_{j\in N} {x_{kj}}^h \le a_i, k \in L \tag{4}$$

$$\sum_{j\in N} {x_{kj}}^h \le c_k \delta(\sum_{j\in N} {y_{kj}}^h), k \in L \tag{5}$$

$${x_{kj}}^h \le y_{kj} c_k, k \in L, j \in N \tag{6}$$

$$\sum_{k\in L} y_{kj} \le 1, j \in N \tag{7}$$

$${x_{ij}}^d, {x_{ik}}^h, {x_{kj}}^h \ge 0 \tag{8}$$

$$y_{kj} \in \{0,1\}, i \in M, k \in L, j \in N$$

where $\delta(x)$ is indicator function that when $x > 0$, $\delta(x)$ equals to 1, otherwise $\delta(x) = 0$
The first term of objective function in Model *(P)* is the satisfaction that supply point deliver vaccine and drug to demand point by *PTP*. It represents the product of the arrived number of vaccine and drug and satisfaction of time.The second term is the satisfaction of transportation through transit points. The constraint condition equation (2) represents that the total amount of vaccine and drug is limited by the supply quantity in every supply point. Eq.(3) means the demand quantity of each point is satisfied by two transportation methods. Eq.(4) shows the balance requirements of vaccine and drug which is satisfied by the transit quantity. Eq.(5) represents the condition that the transport volume delivered without transit point is 0 and the transportation volume delivered from the transit point to the demand point is smaller than or equal to the capacity of this transit point. Eq.(6) shows that transport volume is restrained by the 0-1 variable ykj. Eq.(7) means that for any requirement point, there is at most one transit point to provide services. Eq.(8) means that all the transportation volume satisfy non-negative conditions and the service pairing relationship between transit point and demand point is called 0-1 variable.

*

5.3.1 Simulated annealing algorithm

(1)To solve the initial solution y_{ik}^0 for each $j \in N$, assuming

$$S(j) = \{k \in L \left| \min_{i \in M} \{t_{ik}^h + t_{kj}^h < t_{ij}^d\} \right.\}$$

If $S(j)$ is empty set, $y_{kj}^0 := 0, k \in L$, or, k is $t_{ik}^h + t_{kj}^h = \min_{k \in S(j)} \{t_{ik}^h + t_{kj}^h\}$

$$y_{kj}^0 := 1$$

(2)With the initial value of y_{kj}^0, we have calculate that the optimal value of objective function is $z(y_{kj}^0)$,

$$z^{opt} := z(y_{kj}^0)$$

The optimal value is $x(y_{kj}^0)$. Save $x^{opt} := [y_{kj}^0; x(y_{kj}^0)]$ as the best value.

(3)We assume that the initial temperature is T_0 and the terminal temperature is T_f. When $k = 0$, $T_k = T_0$.

(4)Random solution y_{kj}^1: we select $j_1 \in N$ randomly, $D(:, j_1)$ is column j_1 in D and column j_1 in matrix $[y_{kj}^0]$ is $y^0(:, j_1)$. We assume that $fd(:, j_1) = D(:, j_1) - y^0(:, j_1)$. If $\sum_{k \in L} fd(:, j_1) > 0$, then we select $k \in \{k \,|\, fd(k, j_1) = 1\}$ randomly. If all the other elements in $y^1(k, j_1) = 1, y^1(:, j_1)$ are 0 and $\sum_{k \in L} fd(k, j_1) = 0$, then we choose $j_1 \in N$ again and repeat step (4).

(5)If $\Delta z < 0$,

$$y_{kj}^0 := y_{kj}^1, x(y_{kj}^0) := x(y_{kj}^1)$$
$$x^{opt} := [y_{kj}^0; x(y_{kj}^0)], z^{opt} := z(x^{opt})$$

then perform step (7). If not, perform step (6).

(6)Generate a random number $\xi \in U(0, 1)$, if $\exp(\frac{\Delta z}{T_k}) > \xi$,

$$y_{kj}^0 := y_{kj}^1, z(y_{kj}^0) := z(y_{kj}^1)$$

(7)If $T_k := rT_k$, when $T_k \leq T_f$, stop and output the current optimal solution x^{opt} and the optimal value z^{opt} ,or turn to step (4).

5.4 Model testing

Now we assume that we need to transport vaccine and drug from *6* supply points to *8* demand points. There are *4* transit points around the epidemic areas. We generate *10* groups of random numbers for calculation. The supply of vaccine and drug in supply points are random integers from $[100, 300]$. The supply in demand points is random integers from $[80, 100]$. The

capacity of transit point is random integers from $[30, 80]$. The transportation time from supply point to demand point is random integers from $[30, 150]$. The transportation time from supply point to transit point is random integers from $[10, 80]$. The transportation time from transit point to demand point is random integers from $[10, 40]$. The parameter θ_j in the function of time satisfaction Eq.(1) is random integers from $[1000, 3000]$. We program the algorithm of the model with MATLAB 2014a. The parameter of simulated annealing algorithm is: $T_0 = 100, T_f = 1, r = 0.95$. The calculation result is shown in Table 3.

Table 3 Calculation Results with 10 groups of random numbers

	Optimal	Worst	Mean	Standard deviation	Average time	PTP optimal value
1	261.773	251.600	257.127	3.977	5.676	234.226
2	295.248	286.588	292.176	3.717	6.878	281.153
3	240.270	227.979	233.418	4.962	6.554	219.819
4	285.194	276.048	280.912	3.101	6.021	251.612
5	235.354	226.659	230.515	3.448	5.212	203.350
6	312.072	298.558	304.686	4.258	7.146	278.714
7	270.260	257.505	261.751	4.591	7.414	241.309
8	327.577	315.544	323.113	3.817	5.870	315.544
9	260.374	249.956	255.161	4.210	6.306	242.481
10	264.643	256.091	259.029	2.313	6.257	221.411

From Table 3, we find that the average value of the objective function in transshipment model which mixed two transport modes has greater growth than that in PTP model. In numerous calculations, average time is relatively short and standard deviation is small which means the stability is good. Then we use the last group of data to describe it in details.

$$\theta = [1735, 1677, 2046, 1901, 1852, 2153, 1303, 2161]$$
$$a = [252, 242, 191, 169, 194, 201]$$
$$b = [85, 82, 83, 90, 99, 94, 82, 93]$$
$$c = [73, 63, 54, 75]$$

If this group of data transport by PTP model, we can calculate that the optimal value of objective function is 221.411. If it uses mixed transshipment model, the optimal value of objective function is 264.643. The time satisfaction grows 19.53% than PTP model which reflects good effect. The optimal values are shown in Table 4.

Table 4 The optimal values

		Demand point j								Transit point k			
		1	2	3	4	5	6	7	8	1	2	3	4
Supply point i	1	4			90				93				
	2	81											
	3		82										
	4							28					
	5			10						65		54	
	6					99	94			8			
Transit point k	1			73									
	2												
	3							54					
	4												

5.5 Conclusion

We build the vaccine and drug transportation model to compare point-to-point transportation and transship delivery. After testing by random number, we conclude that when the amount of supply points and demand points is less than 100 and the number of transit point is less than 20, the approximate optimal solution can be solved quickly. It means that this model has the ability to adapt the transportation problem of vaccine and drug in West Africa. This model has not been actually used in epidemic areas because of the lack of data. If we have sufficient time and data resource, we could solve the problem and apply this model in reality.

6 Strengths and Weaknesses

6.1 Strengths

- We can predict when the epidemic outbreak will happen in the future according to the number of daily infected cases that we have known. With the range of time, we can prevent and control the epidemic more efficiently and deploy the transportation of vaccine and drug more rationally to deliver them to serious epidemic areas as soon as possible.
- We can predict when the epidemic outbreak will happen in the future according to the number of daily infected cases that we have known. With the range of time, we can prevent and control the epidemic more efficiently and deploy the transportation of vaccine and drug more rationally to deliver them to serious epidemic areas as soon as possible.
- By setting transit points beside epidemic areas, we optimize the vaccines and drug transport system to make the delivery time shortest. This manner can reduce the mortality of infected patients and improve the immunity of uninfected people.

6.2 Weaknesses

- The prediction in virus diffusion model is not precise enough and the predicted range of outbreak time is large. These factors will to some extent impact on prevention work. If we warn the epidemic outbreak too early, the attention of people on the virus will gradually reduce. This phenomenon is not conducive to the prevention of work.
- When the model with family as a unit is applied to practice, it is difficult to collect specific data in West Africa. The change in family size is also a factor that we need to consider. So, when we use this model, the preparatory work will take a long time.
- When we choose the location of transit point, we do not consider specific geographical environment and construction cost. In reality, we also need to consider the traffic convenience of transit points and specific distribution location inside demand point.

Due to the limit on time and data resources, we just make a certain idea on the difference between the delivery positions of vaccine and drug. If we achieve sufficient time and data, we are able to solve this problem.

7 Future Research

Based on the four models we have made, we imagine our future research as follows:

- According to the data of Ebola epidemic on main provinces of Guinea and Sierra Leone shown in Table 7 and Table 8, we can predict when Ebola will break out in each province based on virus diffusion model we built in Model One. With these predictions, we could know somewhere that the epidemic will break out in a period of time in advance. So, we could schedule the location of delivery and transport vaccine and drug before the outbreak. The ultimate goal is to prevent the outbreak as much as possible.

Table 5 The number of cases in main provinces of Sierra Leone

Date	Total number	Kailahun	Kenema	Port loko	Western Area	Bombali	Pujehun
2-5	8111	2949	565	502	1348	3173	992	31
1-26	7982	2834	565	498	1298	3133	985	31
1-20	7924	2788	565	498	1294	3099	979	31
1-14	7839	2718	565	498	1267	3068	974	31
1-8	7696	2630	565	497	1239	2998	969	31
1-2	7505	2501	565	496	1202	2901	965	31
12-27	7275	2345	565	496	1164	2766	960	31
12-20	6932	2163	565	496	1094	2604	927	31
12-13	6592	1952	565	494	998	2430	907	31
12-7	6317	1708	562	494	956	2288	880	31
11-30	5906	1522	562	494	860	2103	819	31
11-23	5402	1333	561	494	779	1840	763	30
11-17	5056	1223	559	493	720	1686	709	28
11-10	4523	1142	558	493	625	1416	657	28
10-29	3762	1057	551	485	518	1079	540	28
10-23	3391	1008	550	474	480	905	470	26
10-11	2700	904	533	433	372	629	347	24
9-29	2095	544	529	426	270	366	227	19
9-21	1696	501	529	414	177	233	148	10
9-9	1305	433	508	387	101	118	67	10

Data source:World Health Organization

Table 6 The number of cases in main provinces of Guinea

	Total	Macenta	Gueckedue	Conakry	Le Enze Kohler	Kerouane	Coyah
2-4	2993	743	381	433	256	161	175
2-1	2975	744	381	434	256	161	178
1-28	2926	743	381	425	255	161	176
1-22	2893	742	381	413	256	161	175
1-16	2868	742	381	414	254	161	176
1-12	2817	742	381	404	250	161	173
1-9	2798	743	381	402	250	161	169
1-5	2776	744	382	396	252	161	164
12-30	2739	747	383	373	249	161	162
12-25	2659	745	382	362	245	161	156
12-17	2486	729	379	338	244	155	140
12-9	2339	726	378	307	233	147	121
12-2	2187	689	373	292	223	141	100
11-27	2145	688	374	278	223	141	91
11-21	2094	679	373	269	226	146	70
11-14	1936	652	371	265	192	132	66
11-6	1818	621	370	266	167	120	62
10-25	1612	551	366	242	131	80	53

Data source:World Health Organization

- According to the vaccine and drug transportation model, we further consider that vaccine and drug need to be transported separately. Drug is delivered to areas with serious epidemic, while vaccine are focused on delivering to the surrounding areas of serious epidemic provinces. Because if all the vaccine are still delivered to areas with serious epidemic, the virus will soon spread to the surroundings and the epidemic will be more difficult to control and prevent.

8 Proclamation for the World Medical association

Dear Sir or Madam:

I am very happy to hear that you have developed a new therapy to cure infected people and stop Ebola epidemic. I believe the appearance of vaccines and drug can be greatly help the prevention and control of epidemic.

Since Ebola virus outbreak happened in 1976 first, the virus kept spreading but was not concerned by government. This phenomenon causes the outbreak happened last year in West Africa. Because the virus has high spreading speed and high mortality, vaccine and drug are quite important in epidemic areas. In order to transport the vaccine and drug more efficiently and smoothly, I suggest that we could set some transit points around epidemic areas because some flights have been cancelled because of the spreading Ebola virus. According to our research, vaccinate for people living around epidemic areas plays a more prominent role on the prevention to the spreading of virus. If we mainly vaccinate for people in serious epidemic areas, the epidemic will soon spread out and we might be in a mess.

Furthermore, vaccine and drug are not the only way to prevent and control epidemic. When we tell the public that a new efficient medication has been developed, we also need to remind them not let their guard down. For an individual, to prevent Ebola epidemic, we also need to avoid direct contact with patients and infected corpse. We also need to notice the physical condition of people around. For the government of epidemic areas, I think they need an optimal vaccine distribution plan which can vaccinate with high efficiency. The other important work that the government need to do is to emphasize the seriousness to the public and persuade them to assist the government on the process of prevention and control.

No matter how strong Ebola is, there is always a way to deal with it. We should unite to face the epidemic and prevent it.

Thank you very much for reading my letter.

Yours truly

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