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2015

Mathematical Contest in Modeling (MCM) Summary Sheet

The Optimal Strategy of Drugs Distribution and Transportation In The Case of Ebola

Summary

Aiming at the outbreak of Ebola in West Africa in 2014, the world medical association has announced that medicines which can stop Ebola come out. Therefore, so as to control Ebola even eliminate Ebola fully, we establish the optimal model of drugs distribution and transportation on Ebola.

We begin to establish a tree structure, which describes the traffic network of incidence area. According to their medical conditions, economical conditions and the number of patients, we classify all the incidence cities into different levels.

Then we analyze the influence of drugs distribution on the spread of Ebola.

(1) If the rate of drugs production is large enough to satisfy the demand, then we establish a Auto Regressive Integrated Moving Average Model(ARIMA). The model can predict the number of added patients and total amount of medical demand within a short term by SPSS software.

(2) If the drugs production is so limited that cannot satisfy the demand of all areas, then we should consider the influence of the immigration on the spread of Ebola. In order to define the severity of Ebola η , we introduce the endemic equilibrium $P_1(S_1, E_1, I_1)$. We conclude that if the number of local patients reaches the endemic equilibrium, then the disease will continue to steadily survive. Considering the relationship of η and ξ , which represents the ratio of patients in one city and total amount of patients at that level, we establish a multi-goal model to control the spread of Ebola.

At last, we select three of West African countries where Ebola is most serious, Guinea, Liberia and Sierra Leone, to analyze. We make the model testing and sensitivity analysis. Meanwhile, we figure out the approximate equations of each countries are the same formula, $I(t) = a * \exp(b * t) + c$, besides, the correlation coefficients approaches to 0.95. As for the multi-goal model, we work out the weight of ξ and η are 0.667 and 0.333 by using analytic hierarchy process(AHP).

Keyword: Tree structure, ARIMA model, SEIS model, The endemic equilibrium, Multi-goal model, AHP

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1. Introduction

1.1 Background

Ebola, previously known as Ebola hemorrhagic fever, is a rare and deadly disease caused by infection with one of the Ebola virus strains. Ebola can cause disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees).

Ebola is caused by infection with a virus of the family Filoviridae, genus Ebolavirus. There are five identified Ebola virus species, four of which are known to cause disease in humans: Ebola virus, Sudan virus, Taï Forest virus and Bundibugyo virus. The fifth, Reston virus, has caused disease in nonhuman primates, but not in humans.

Ebola viruses are found in several African countries. Ebola was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo. Since then, outbreaks have appeared sporadically in Africa.

1.2 Question Retelling

In recent years, Ebola has attracted many peoples' eyes. Furthermore, the world medical association has announced that their new medication could stop Ebola and cure patients whose disease is not advanced. Thus, it is necessary that we take measure to optimize the eradication of Ebola.

Since we need consider the spread of the disease, the quantity of the medicine needed, possible feasible delivery systems, locations of delivery, and speed of manufacturing of the vaccine or drug and so on, our task is to design an appropriate mathematical model to work out these problems.

After that, we will prepare a non-technical letter for the world medical association to use in their announcement.

2. Model Assumptions

2.1 Assumptions of Tree Structure

(1) The capitals are large enough to accept a large number of drugs transportation.
(2) The adjacent level in the tree structure can transport medications by railway.
(3) The distance between the two adjacent levels cities are the same.

2.2 Assumptions of ARIMA Model

(1) The short term external factors such as temperature and climate are constant.
(2) There is no infective immigrating.
(3) The Ebola virus did not mutate, and the infection rate or mortality did not change.

2.3 Assumptions of SEIS Model

(1) The natural birth rate and the natural death rate keep unchanged, and the total population is unchanged.
(2) Immigration rate u, has nothing to do with the city variation and keeps constant.
(3) The patients are always moving along the tree structure from bottom to top.
(4) The immigrated people caused by the lack of medicines are only patients.

2.4 Assumptions of Multi-goal Model

(1) Drugs distribution is only related to the severity of Ebola η and the ratio of patients in one city and total amount of patients in that level ξ.

(2) ξ is prior to η.

3. Explanation

3.1 Explanation of Symbols

- $\{I(t)\}$: A non-stationary time series related to Guinea total cases.
- I_t: The time series' present value.
- P: The auto regressive orders.
- q: The moving average orders.
- $\{\varepsilon_t\}$: A zero-mean white noise series.
- μ: The constant term.
- ω: The coefficient of the white noise series.
- ϕ: The autoregressive coefficient.
- S(t): The number of the susceptible at the certain time *t*.
- E(t): The number of the exposed at a certain time *t*.
- I(t): The number of the exposed at a certain time *t*.
- N: The total number of a population.
- β: Mortality due to illness, namely, the radio of deaths due to illness in a unit time and the total infective suffering from Ebola.
- λ: Effective contact rate, namely, the ratio of the susceptible who become the exposed through contacting the infective and the total susceptible.
- θ: The radio of the exposed that become the infective and the total exposed.
- v: Drug production speed, namely, the number of the produced drugs in a unit time.
- m: The average number of drugs needed to cure a patient.
- γ: Recovery rate, namely, the radio of the infective who become the susceptible through drug treatment and the total infective.
- u: The immigration rate.
- R_0: The basic reproduction number.
- P_1: The endemic equilibrium.

- k: The number of total children cites of their parent city.
- b_i : The number of the total infective in the i-th children city.
- a_i : The number of the infective that drugs in the i-th children city can meet.
- α : The number of the infective who immigrate from children cities to their parent city, we can easily find $\alpha = u \cdot \sum_{i=1}^{k} (b_i - a_i)$.
- η : The severity of Ebola.
- ξ : The ratio of the number of the infective in the city and the number of the total infective in the same level city.
- A: The comparison matrix.
- M: The weight vector of the matrix A.
- $\lambda_{\max}$: The maximum eigenvalue.
- CI: The consistency index.
- RI: The random consistency index.
- CR: The consistency ratio index.
- d: The difference frequency.

3.2 Extra Explanation

• **Susceptible** The susceptible are those who are potentially infected individuals and have no immunity to this disease.

• **Exposed** The exposed are those who are infected and become infectious but do not show symptoms.

• **Infective** The infective are those who show the corresponding symptoms and are infectious.

• **Recovered** The recovered are those who recovered from the disease.

4. The Models

Our goal is devising a most reasonable mode of drug transport to control Ebola. Referring to the data, we begin to select three of West African countries where Ebola

is most serious to analyze. Moreover, we classify all the infected cities in the three countries into four levels, according to their medical conditions, economical conditions and the number of the infective. We establish a tree structure chart. (see 4.1 The Tree Structure Chart)

If the drug production speed is large enough to satisfy the demand, then we will predict the possible number of new patients within a short time and calculate the needed drugs. Then we can distribute the drugs in advance. Doing these, we can stop Ebola within a short time. In order to calculate the possible number of new patients within a short time, we establish a time-series analysis model and using Auto Regressive Integrated Moving Average Model (ARIMA for short) and SPASS to simulate the number.(see 4.2 The Time Series Analysis)

If the drug production is limited, the speed cannot satisfy the current demand, and then we establish a multi-goal programming model to work out the optimal allocation. We select two factors, the portion of the number of the patients in the city ξ and the severity of Ebola η, and calculate their respective weight. When calculating the value of η, we establish a SEIS model. We work out the endemic equilibrium and get the number of patients I_1 at the endemic equilibrium. Through comparing the ratio of the number of existing patients $I(t)$ and I_1, $I(t)/I_1$, we definite the value of η. The larger $I(t)/I_1$ is, the larger η is, namely, the more serious Ebola is.(see 4.3 Establishing SEIS Models) Last, we use the multi-goal formulas to calculate the number of needed drugs in each level cities.(see 4.4 The Multi-goal Programming Model)

4.1The Tree Structure Chart

According to the statistics of Ebola incidence (see fig.4-1-1), we select three of West African countries where Ebola is most serious to analyze. They are Guinea, Liberia and Sierra Leone. **We collect all the infected cities in the three countries into four levels, according to their medical conditions, economical conditions and the number of the infective.** The capitals are the first-level cities; the cities slightly smaller than their respective capital are the second-level cities. And like that, the cities slightly smaller than their respective second-level cities are the third-level cities and the cities slightly smaller than their respective third-level cities are the forth-level cities.

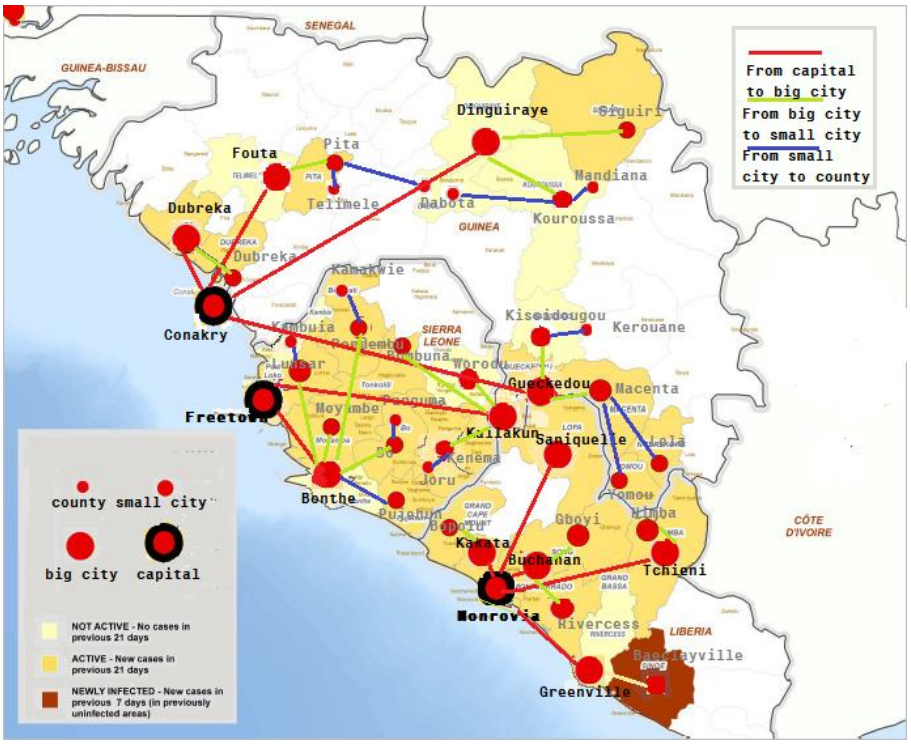


FIGURE 4-1-1. The distribution of the infected cities in Guinea, Liberia and Sierra Leone

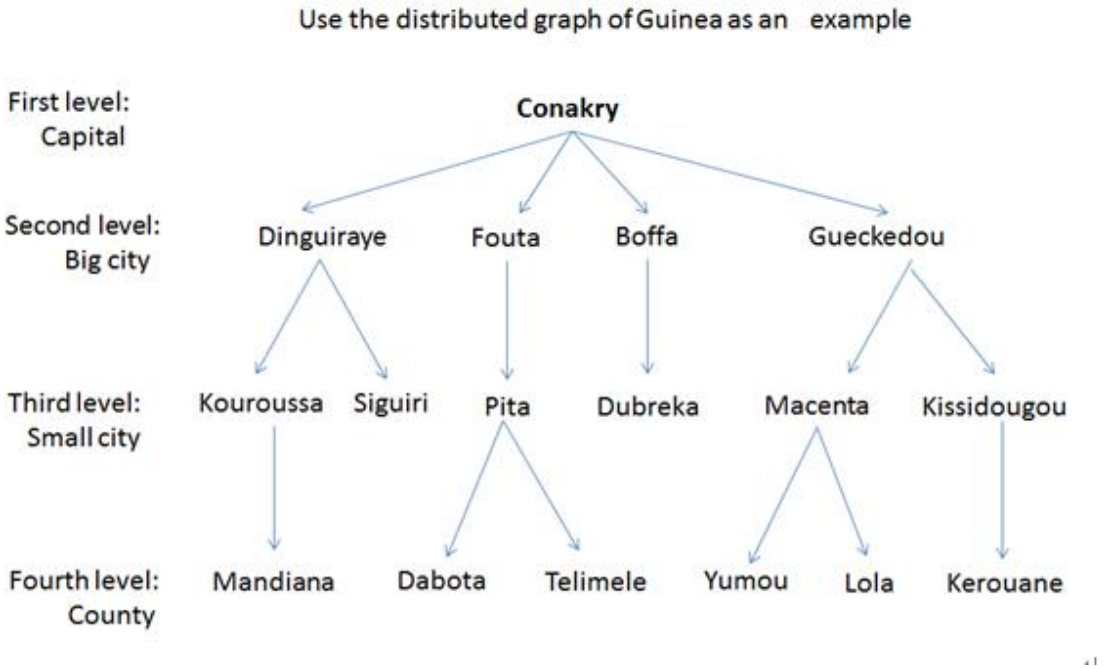


FIGURE 4-1-2. A tree structure chart of four level cities in Guinea

In order to count the ratio of the distributed drugs more conveniently, we construct a tree structure chart (see fig.4-1-2). In order to achieve the goal of transporting the drugs most fast, we distribute the drugs to the first-level cities, then the first-level cities distribute the drugs to their second-level cities, then the second-level cities

distribute the drugs to their third-level cities, and last the third-level cities distribute the drugs to their forth-level cities. Notably, across-level distribution is not allowed. The mode of drugs transportation of the first-level cities is air transportation, the others are railway transportation. The number of distributed drugs of each city is proportional to the ratio of the number of the infective in the city and the number of the total infective in the same level city. Notably, the distributed drugs in each city equal to the sum of the native needed drugs in the city and the total needed drugs in its children cities.

4.2 The Time Series Analysis

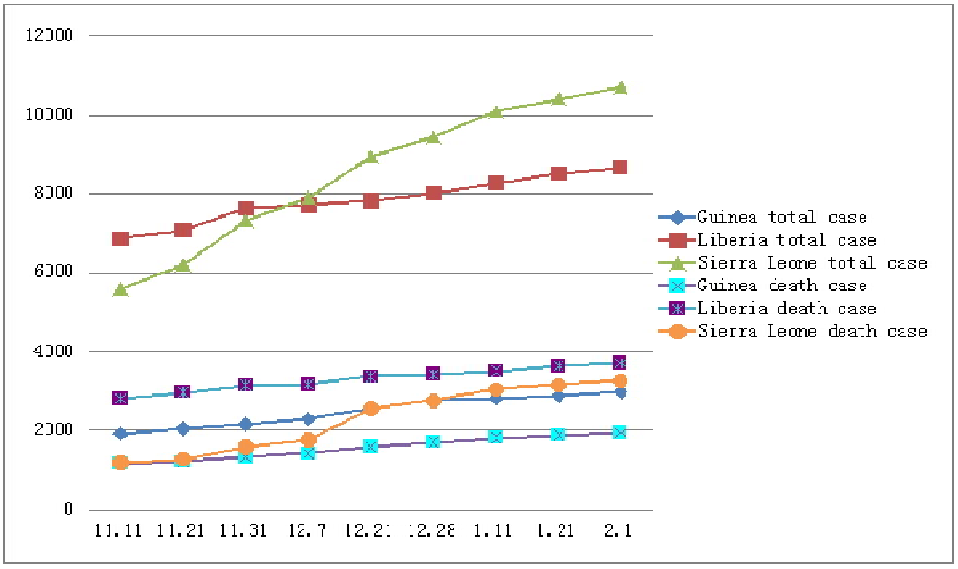


FIGURE 4-2-1. A line chart of total cases and death cases weekly in Ebola main outbreak area from November, 2014 to February, 2015

Combined with the above development relationship between Ebola cases and time (see fig.4-2-1), we establish a time-series analysis model. Studying the model, we can forecast the future Ebola cases at a certain time t. We can analyze how to carry out the optimal strategy to transport the drugs so as to control Ebola.

4.2.1 Auto Regressive Integrated Moving Average Model

Referring to the statistics (see table 4-2-1), we build up a time series $\{\mathrm{I}(t)\}$related to Guinea total cases. Time series is classified into the stationary time series and the non-stationary time series. The mean and the variance is constant in stationary time

series, but having an obvious trend or periodicity in non-stationary time series.[1] Since Guinea's Ebola total cases show a rising trend, **we can conclude that our time series $\{I(t)\}$ is a non-stationary time series.**

Date	Guinea total case (total deaths)	Liberia total case (total deaths)	Sierra Leone total case (total deaths)
2014.11.11	1919(1166)	6878(2812)	5586(1187)
2014.11.21	2047(1214)	7082(2963)	6190(1267)
2014.11.30	2164(1327)	7635(3145)	7312(1583)
2014.12.7	2292(1428)	7719(3177)	7897(1768)
2014.12.20	2571(1586)	7830(3376)	8939(2256)
2014.12.28	2767(1790)	8018(3423)	9446(2758)
2014.1.10	2799(1807)	8278(3515)	10094(3049)
2014.1.20	2873(1880)	8524(3636)	10400(3159)
2015.2.1	2975(1944)	8668(3710)	10707(3274)
Total	**22407(14142)**	**70632(29757)**	**76571(20301)**

TABLE 4-2-1. Total cases and death cases statistics weekly in West African Ebola main outbreak area from November, 2014 to February, 2015

Auto Regressive Integrated Moving Average Model (ARIMA for short) is an important prediction tool suitable for non-stationary time series.[2] **So we collect *ARIMA(p,d,q)* to predict and modify our non-stationary time series $\{I(t)\}$.**

The time series' present value is denoted as I_t. Not only does I_t relate to the time series' past value, but a certain dependency also exists between I_t and the disturbance which the time series generated in the past time when entering the system. So we use the linear combination of the series' past value and the linear combination of white noise perturbation term to express I_t. I_t is as follows:

$$I_t = \mu + \phi_1 I_{t-1} + \cdots + \phi_p I_{t-p} + \varepsilon_t - \omega_1 \varepsilon_{t-1} - \cdots - \omega_q \varepsilon_{t-q} \quad (1)$$

Where the auto regressive orders is denoted as p, the moving average orders is denoted as q, the zero-mean white noise series is denoted as $\{\varepsilon_t\}$, the constant term is denoted as μ, the autoregressive coefficient is denoted as ϕ, the coefficient of the white noise series is denoted as ω.

Because $\{I_t, t = 1,2,3,\cdots,n\}$ of *d-th* order difference is stationary and I_t meets the eq.2, the time series' present value I_t belongs to ARIMA. *A*fter centralizing I_t, the operator form is as follows:

$$\begin{cases} \varphi(B)\nabla^d I_t = \omega(B)\varepsilon_t \\ E(\varepsilon_t) = 0, Var(\varepsilon_t) = \sigma_E^2, E(\varepsilon_t\varepsilon_s) = 0, s \neq t \\ E(I_s\varepsilon_t) = 0, \forall s < t \end{cases} \quad (2)$$

Where $|B| \leq 1$, $\varphi(B)$ and $\theta(B)$ are relatively prime, $\varphi_p\theta_q \neq 0$.

4.2.2 The Judgment of Models

First, we introduce AIC(An Information Criterion). The definition of AIC principle is as follows: The minimum information principle. It is applicable to the problem whose sample data is pretty little. We usually use AIC to judge the development process of forecasting target is closest to which model.

$$AIC = (n-d)\log\sigma^2 + 2(p+q+2)$$

Where the sample number is denoted as *n*, the fitting residual square is denoted as σ.

We collect the model whose parameters are least and AIC is minimum as the optimal model. We collect the model's order which can make AIC minimum as the optimal order. The fitting model is closer to theoretical distribution when the value of *AIC* is smaller.

4.3 Establishing SEIS Models

4.3.1 The Feature of Ebola

In natural state, the number of a population is constant, natural birth rate and natural death rate keep a balance. Ebola is characterized by quick onset. Its incubation period is usually 2~21 days. Besides, the infective will die in 3~5 days since becoming ill and they do not have immunity after cured. So when Ebola outbreaks, it will have no impact on the natural birth rate and natural death rate of the population in

a short time. So we neglect the natural birth rate and the natural death rate, we only consider mortality due to illness. Moreover, Ebola is basically transmitted through body fluids, so we conclude that the transmission mode of Ebola is horizontal transmission. Referring the data, we sort out a table (see table 4-3-1).[3]

Age	Gender	Data Package	Cases
All ages(total)	Female	2015-02-04	9458
All ages(total)	Male	2015-02-04	9150
0~14	Both sexes	2015-02-04	3618
15~44	Both sexes	2015-02-04	10095
45+	Both sexes	2015-02-04	4226

TABLE 4-3-1. West African Ebola epidemic cases statistics in a year about age and gender

We conclude that Ebola infection rate is irrelevant with gender or age.

We know the world medical association has announced that their new medication could stop Ebola and cure patients whose disease is not advanced, therefore, we need deliver the drugs to each Ebola outbreak city.

4.3.2 The SEIS Model

When the delivered drugs cannot meet the city node's patients, the infective in the secondary city will immigrate higher level city because of its better medical condition and economical strength. The immigration rate is denoted as *u, u* is a fixed constant. The corresponding SEIS model is

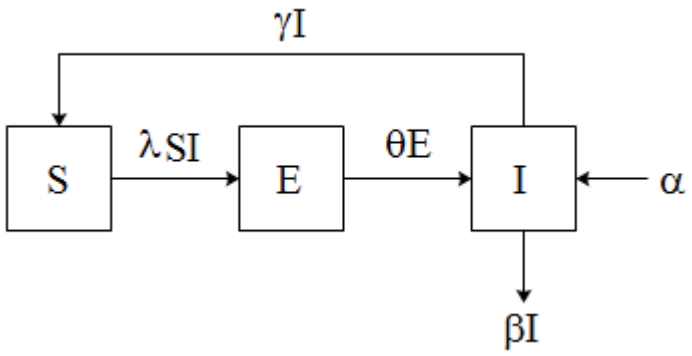


FIGURE 4-3-1. A SEIS model of one mode describes the quantitative change relations among the susceptible *S(t)*, the exposed *E(t)* and the infective *I(t)*.

The flow chart describes the quantitative changing relationships among the susceptible *S(t)*, the exposed *E(t)* and the infective *I(t)*. For the susceptible compartment *S(t)*, we can see only one arrow inflows, which shows the number of people in the compartment increases. Since the recovery rate is denoted as γ and the infective is denoted as *I(t),* $\gamma \mathrm{I}$ represents the number of the recovered. Effective contact rate is denoted as λ, so $\lambda \mathrm{SI}$ represents the number of the susceptible *S(t)* who become the exposed *E(t)* through effective contacting the infective *I(t)*. Consequently, we can obtain the equation $\frac{ds}{dt} = \gamma \mathrm{I} - \lambda S \mathrm{I}$.

Similarly, analyzing the remaining compartments, the exposed *E(t)* and the infective *I(t),* we can get the following equations.

$$\begin{cases} \frac{dS}{dt} = \gamma \mathrm{I} - \lambda SI \\ \frac{dE}{dt} = \lambda S \mathrm{I} - \theta \mathrm{E} \\ \frac{d\mathrm{I}}{dt} = \alpha + \theta \mathrm{E} - \gamma \mathrm{I} - \beta \mathrm{I} \end{cases} \tag{3}$$

In eq.3, the radio of the exposed who become the infective and the total exposed is denoted as θ, $\theta \mathrm{E}$ represents the number of the exposed who become the infective. And since mortality due to illness is denoted as β, $\beta \mathrm{I}$ represents the number of deaths due to illness in the infective compartment *I(t)*.[4]

4.3.3 Analyzing the Severity of Ebola

In order to analyze the severity of Ebola, we introduce the basic reproduction number R_0. R_0 represent the number of the second generation of infected cases which a patient generated when he mixed himself inside the susceptible population in his effective infectious period.

If $R_0 > 1$, then the disease is contagious and endemic equilibrium exists. When the disease isn't controlled before $P_1(S_1,E_1,I_1)$, then the disease will continue to steadily survive. Whereas if $R_0 < 1$, the disease will gradually disappear.

It is obvious that the number of Ebola patients is increasing, so we only consider the situation of $R_0 > 1$. Now we will calculate our endemic equilibrium $P_1(S_1,E_1,I_1)$.

According to the equation(3), we devise the equations (4).

$$\begin{cases} \dfrac{dS}{dt} = \gamma \mathrm{I} - \lambda S \mathrm{I} \underline{\underline{\Delta}} Q(S, E, I) \\ \dfrac{dE}{dt} = \lambda S \mathrm{I} - \theta \mathrm{E} \underline{\underline{\Delta}} W(S, E, I) \\ \dfrac{dI}{dt} = \theta \mathrm{E} + \alpha - \beta \mathrm{I} - \gamma \mathrm{I} \underline{\underline{\Delta}} T(S, E, I) \end{cases} \tag{4}$$

The equations (4) are the functions of *Q(S,E,I), W(S,E,I), T(S,E,I)* related to *S,E,I.*

Calculating the equations $\begin{cases} Q(S_1, E_1, I_1) = 0 \\ W(S_1, E_1, I_1) = 0 \\ T(S_1, E_1, I_1) = 0 \end{cases}$ (5)

equals to calculating $\begin{cases} \gamma \mathrm{I}_1 - \lambda S_1 \mathrm{I}_1 = 0 \\ \lambda S_1 \mathrm{I}_1 - \theta \mathrm{E}_1 = 0 \\ \theta \mathrm{E}_1 + \alpha - \beta \mathrm{I}_1 - \gamma \mathrm{I}_1 = 0 \end{cases}$ (6)

We can work out $S_1 = \dfrac{\gamma}{\lambda}$, $\mathrm{E}_1 = \dfrac{\gamma \mathrm{I}}{\theta}$, $\mathrm{I}_1 = \dfrac{\alpha}{\beta}$.

Now that we have worked out our endemic equilibrium $P_1(S_1,E_1,I_1)$, we begin to analyze the severity of Ebola in a certain area. The severity is denoted as η. **The larger the value of η is, the more serious Ebola is.** We design a table (see table 4-3-2) to distinguish the severity.

$I(t)/I_1$	0~30%	30%~70%	70%~100%
η	1	3	5

Table 4-3-2. Our division of the severity according to the ratio of I(t) and I_1

4.4 The Multi-goal Programming Model

We should consider the drug production speed and economical factors when we distribute the drugs.

If the medical supply is adequate enough to satisfy the current demand, then we establish the time series model for **short-term forecast of the infected area**. We predict the possible number of the new infective within a short time and calculate the needed drugs within a short time. Then we can distribute the drugs in advance. Our thought is to nip in the bud. The measure necessarily decreases the number of the new

infective in the future, and succeed in stopping Ebola.

Whereas if the medical supply is limited, the speed cannot satisfy the current demand, then we establish the multi-goal programming model to **work out the optimal allocation**. We draw up the principles of drug allocation. One is the ratio of the number of the infective in the city and the number of the total infective in the same level city, the ratio is denoted as ξ. Notably, the number of the infective in the city equals to the sum of the number of the native patients in the city and the number of the total patients in its children cities. The other is the severity of Ebola, the severity is denoted as η.

4.4.1 The Analytic Hierarchy Process (AHP)

First, we use the Analytic Hierarchy Process (AHP for short) to calculate the weights of the two principles.[5] The hierarchical structure diagram is

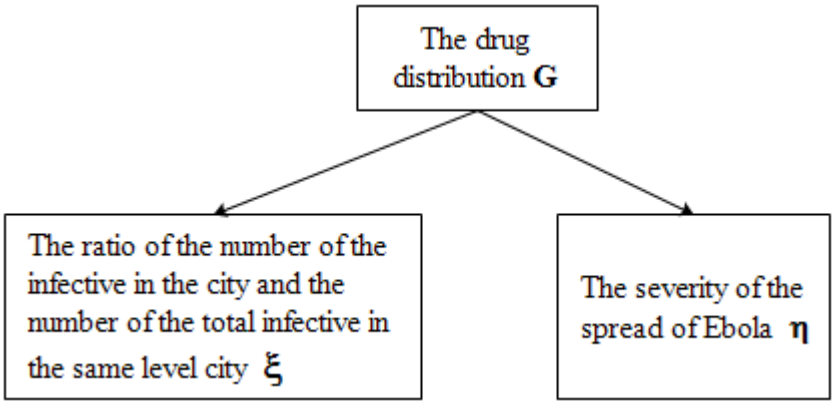


FIGURE 4-4-1. The hierarchical structure diagram about the drug distribution

In the hierarchical structure diagram, the first level is the target, the second is the factors determining the target.[6]

We compare the influence degree of the two factors ξ and η on the target factor, the drug distribution. We use $a_{i,j}$ to represent the ratio of the influence degree of ξ and η on the target factor. Meanwhile, we measure $a_{i,j}$ according to the 1~9 scale. The matrix is

$$A = (a_{i,j})_{2\times 2},\ a_{i,j} > 0,\ a_{j,i} = \frac{1}{a_{i,j}},\ a_{i,i} = 1(i = j = 1,2) \tag{7}$$

The scale value is

Scale $a_{i,j}$	Meaning
1	The effects of ξ and η are the same.
3	The effect of ξ is slightly stronger than the effect of η.
5	The effect of ξ is stronger than the effect of η.
7	The effect of ξ is obviously stronger than the effect of η .
9	The effect of ξ is absolutely stronger than the effect of η.
2, 4, 6, 8	The ratio of the effects of ξ and η is between the two above-mentioned adjacent levels
1/2, ⋯, 1/9	The ratio of the effects of ξ and η is the reciprocal number of the above $a_{i,j}$

TABLE 4-4-1. Scale value

According to the scale value (see table 4-4-1), we establish our comparison matrix *A*. It is as follows

$$\begin{array}{ccc} \mathrm{G} & \xi & \eta \\ \xi & 1 & 2 \\ \eta & \frac{1}{2} & 1 \end{array} \tag{8}$$

Through normalizing the matrix's column vector, we can obtain the weight vector. The weight vector is denoted as *M*.

$$A=\begin{pmatrix} 1 & 2 \\ \frac{1}{2} & 1 \end{pmatrix} \xrightarrow{\textit{normalizing the volumn vector}} \begin{pmatrix} 0.667 & 0.667 \\ 0.333 & 0.333 \end{pmatrix} \xrightarrow{\textit{calculating sum of each row}} \begin{pmatrix} 1.334 \\ 0.666 \end{pmatrix}$$

$$\xrightarrow{\textit{normalizing the volumn vector}} \begin{pmatrix} 0.667 \\ 0.333 \end{pmatrix} = \mathrm{M}$$

$$AM=\begin{pmatrix} 1 & 2 \\ \frac{1}{2} & 1 \end{pmatrix}\begin{pmatrix} 0.667 \\ 0.333 \end{pmatrix}=\begin{pmatrix} 1.333 \\ 0.665 \end{pmatrix} \tag{9}$$

We can work out the maximum eigenvalue. It is denoted as $\lambda_{\max}$.

$$\lambda_{\max}=\frac{1}{2}\left(\frac{1.333}{0.667}+\frac{0.665}{0.333}\right)=1.998 \tag{10}$$

4.4.2 Testing Consistency

Typically, the actual judgment matrix obtained is not necessarily consistent, that is, it is not necessarily meet the transitivity and the consistency. Actually, we should

promise our matrix is roughly consistent, that is, the degree of inconsistency should be in the allowable range.

Consistency index: $CI = \frac{\lambda_{\max} - n}{n-1}$. In our model , n=2.

Random consistency index: *RI*. *RI* is usually defined by the actual experience. It is as follows:

n	1	2	3	4	5	6	7	8	9	10	11
RI	0	0	0.58	0.90	1.12	1.24	1.32	1.41	1.45	1.49	1.51

TABLE 4-4-2. Random consistency index

Consistency ratio index: $CR = \frac{CI}{RI}$. When $CR < 0.1$, we can regard the judgment matrix is consistent.

For judging the matrix *A*,

We have worked out the maximum eigenvalue of the matrix *A,* $\lambda_{\max}$ (see eq.10).

$$\lambda_{\max} = 1.998$$

Because the matrix A is a second order matrix (n=2), the consistency index

$$CI = 0$$

Consequently, the consistency ratio index *CR* meets $CR < 0.1$. We can conclude the matrix A is consistent, so we can use its feature vector to substitute its weight. So the weight of ξ is 0.667, the weight of η is 0.333.

4.4.3 The Multi-goal Programming Model Equation

Then we discuss the multi-goal programming model of different level cities respectively.

We set the forth-level cities as an example.

We can get

$$\mathrm{F}_i^4 = 0.667\xi_i^4 + 0.333\eta_i^4$$

The meaning of the equation is as follows:

The total number of drugs equals to the product of the number of the infective in the city and the proportional coefficient of the infective that can get drugs.

Where F_i^4 represents the multi-goal coefficient of the i-th forth level city. ξ_i^4 represents the ratio of the number of the infective in the i-th forth-level city and the

number of the total infective in the total forth-lever city. η_i^4 represents the severity of Ebola in the i-th forth level city.

We also get

$$H_i^4 = I(t)_i^4 \cdot m \cdot \frac{F_i^4}{\sum_{i=1}^{n} F_i^4}$$

The meaning of the equation is as follows:

The total number of drugs equals to the sum of the product of the total number of the city, the proportional coefficient of the infective who can get drugs and the number of needed drugs of each patient.

Where n represents the number of a certain level cities. $I(t)_i^4$ represents the number of the infective in the i-th forth-level city. H_i^4 represents the number of the distributed drugs in the i-th forth-level city. m represents the number of needed drugs of each patient.

To sum up, the forth-level cities is

$$\mathrm{F}_i^4 = 0.667\xi_i^4 + 0.333\eta_i^4 \tag{11}$$

$$H_i^4 = I(t)_i^4 \cdot m \cdot \frac{F_i^4}{\sum_{i=1}^{n} F_i^4} \tag{12}$$

Because drugs are only transported from the father city to its children cities, so when we calculate each level's multi-goal factors, we must add up all the multi-goal factors of its total children cities, which is denoted as $\sum_{i=1}^{n} F_i^4$. Similarly, when we calculate $I(t)_i^3$, we must add up the number of the infective in its children cites.

According to the forth-level cities, we can work out the equations of the third-level and the second-level cities.

The third-level cities is

$$\mathrm{F}_i^3 = 0.667\xi_i^3 + 0.333\eta_i^3 + \sum_{i=1}^{n} F_i^4 \tag{13}$$

$$H_i^3 = I(t)_i^3 \cdot m \cdot \frac{F_i^3}{\sum_{i=1}^{n} F_i^3} \tag{14}$$

The second-level cities is

$$\mathrm{F}_i^2 = 0.667\xi_i^2 + 0.333\eta_i^2 + \sum_{i=1}^{n} F_i^3 \tag{15}$$

$$H_i^2 = I(t)_i^2 \cdot m \cdot \frac{F_i^2}{\sum_{i=1}^{n} F_i^2} \tag{16}$$

We set the total number of existing drugs as *Y*. It is easy to know that

$$H_i^1 = Y \tag{17}$$

Besides, the total number of drugs in the i-th c-th-level city is

$$K_i^c = H_i^c \cdot \frac{Y}{H_i^1} \tag{18}$$

5. Conclusion and Sensitivity Analysis

5.1 The Predicted Result of ARIMA Model.

(1) In the time series model, we have found Ebola cases always keep a rising trend in a year, so we can conclude that Ebola cases are independent of the season. That is, the changing relationship between the number of patients and time does not exist seasonal difference. In ARIMA, we take $sp = 0, sd = 0, sq = 0$.

(2) We calculate the difference of a non-stationary time series until the series becomes a stationary series, the difference frequency is denoted as *d*.

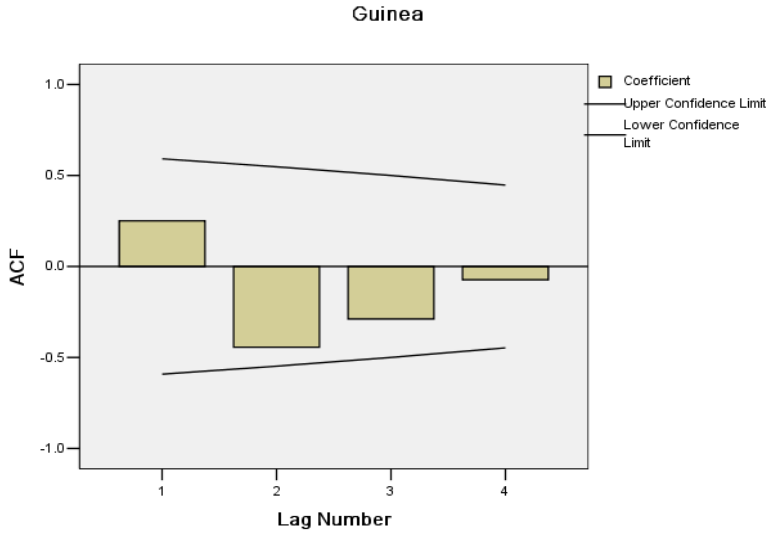


FIGURE 5-1-1. The difference situation of the prepared time series of Guinea

We take the prepared data of Guinea as an example. In the fig.5-1-1, we find out after the first difference, the non-stationary series has become a stationary series. So we take $d=1$.

(3) We know $d=1$, according to the different value of p and q, we produce four kinds of combination, then calculate the value of AIC and determine the best value of *(p,d,q)*.

ARIMA(p,d,q)	σ^2	**AIC**
(1,1,0)	37665.82	15.1519
(0,1,0)	40226	13.209
(1,1,1)	26886.69	25.7181
(0,1,1)	27251.66	23.7416

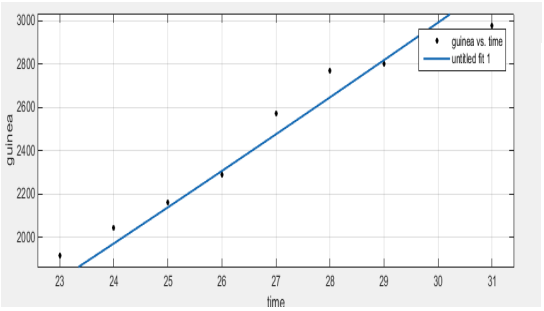
TABLE 5-1-1. The value of AIC of four kinds of (p,d,q) combination

We take the AIC analysis of Guinea as an example, we can conclude that the most suitable combination of (p,d,q) is (0,1,0). Similarly, the other two analysis of Liberia and Sierra Leone are (0,1,0) as well.

Therefore, we have the formula of our equation. It is

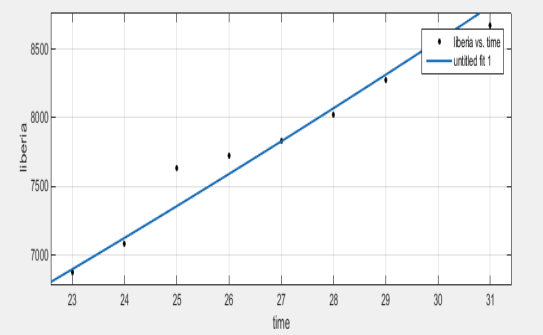
$$I(t) = a * \exp(b * x) + c \tag{19}$$

(4) According to the solved formula (eq.19), we can give the fitting curve and accurate expression as follows:



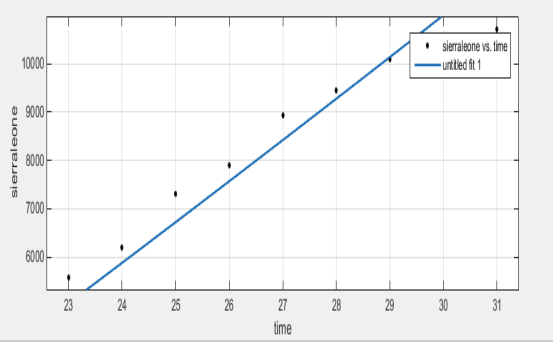
General model:
f(x) = a*exp(b*x)+c
Coefficients (with 95% confidence bounds):
a = 1.839e+04 (-5.825e+05, 6.193e+05)
b = 0.00753 (-0.1969, 0.2119)
c = -2.006e+04 (-6.319e+05, 5.918e+05)

Figure 5-1-2. The fitting curve and accurate expression of Guinea




```
General model:
     f(x) = a*exp(b*x)+c
Coefficients (with 95% confidence bounds):
       a =   1.212e+04  (-1.902e+05, 2.144e+05)
       b =    0.01365  (-0.1527, 0.18)
       c =      -9693  (-2.233e+05, 2.039e+05)
```

Figure 5-1-3. The fitting curve and accurate expression of Liberia




```
General model:
     f(x) = a*exp(b*x)+c
Coefficients (with 95% confidence bounds):
       a =   1.251e+05  (-5.502e+06, 5.752e+06)
       b =   0.005837  (-0.2209, 0.2326)
       c =  -1.381e+05  (-5.829e+06, 5.552e+06)
```

Figure 5-1-4. The fitting curve and accurate expression of Sierra Leone

5.2 The Error Analysis of ARIMA Model

(1) SSE: Sum of squares for error. Reflect the discrete situation of each sample of each observation value, also known as the sum squared error or the residual sum of squares.

(2) R-square: The correlation coefficient. While R^2 is closer to 1, the fitting results should be closer to the data, and the fitting result is better.

(3) Adjust R-square: The correlation coefficient after correction. In the multiple linear regression equations, the number of independent variables will increase R_2 (although some independent variables not significant). Therefore, in order to eliminate this effect, introduced the adjusted R-square, $R_2 = 1 - \dfrac{(n-1)(1-R^2)}{n-k-1}$

(4) RMSE: Root mean square error or RMS error. In a limited number of measurements, the root mean square error of common formula is

$$\sqrt{\frac{\sum d_i * 2}{n-1}} = \mathrm{Re} \tag{20}$$

Where the measuring number is denoted as n, a group of measurement deviation and average value is denoted as d_i.

Country	SSE	R-square	Adjusted R-square	RMSE
Guinea	9.287e+04	0.9244	0.8992	124.4
Liberia	1.221e +05	0.9584	0.9445	142.6
Sierra Leone	2.9e+06	0.8953	0.8604	695.3

TABLE 5-2-1. SSE, R-square, Adjusted R-square, RMSE of Guinea, Liberia and Sierra Leone

Even though the RMSE or R-square of Sierra Leone is a little bit disappointed, but since our data is not large enough, ARIMA model is actually the best method we can use to forecast and fit the trend of data.

5.3 The Stability Analysis of Tree Structure

First, in our drugs distribution and transportation model, we have assumed that the transportation route rules to the fact that bigger cities are surrounded by the neighbor middle size cities and recursive step by step like the figure.(see fig.5-3-1) However, the real map should be like the figure.(see fig.5-3-2)

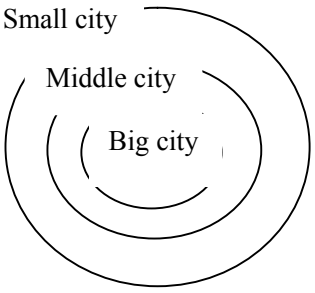


FIGURE 5-3-1. Our assumed transportation route

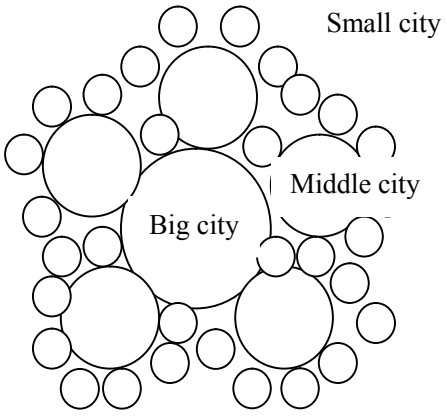


FIGURE 5-3-2. The real map

Therefore, there are several situations we should consider.

(1) If there exists another path that is shorter between the not neighbor level city *A* and *B*, we should change the recursive relationship between *a* and *b*.

(2) If the distance between the city *A* and two bigger cities *B* or *C* is the same, then we should rebuild a better standard of the level judgment or consider the number of this kind of group.

(3) If there exists the worst case of the tree structure, which is a straight line, the

time complexity will be higher and this mode of transportation will be just waste of time. Therefore a better region distribution method should be applied.

In conclusion, our drugs distribution and transportation model is qualified in the case of Ebola in the West Africa, because of the poor transport condition and urbanization level.

7. Strengths and Weaknesses

Strengths:

(1) Our solution of how to restrict the spreading or deterioration of Ebola is divided into two parts which depends on the supply of medicines. Therefore, the result of our drug distribution and transportation will be better and closer to the reality.

(2) The time series model we have used when the medical supply is adequate is capable of forecasting trend and data in a short term. Therefore, our calculation of the medical demanded production will be an accurate approximate value, which can reduce the risk of over production or lack of production. In addition, since we can nip in the bud and provide enough medicines before the explosion happens, the restraint of the spread of Ebola will be the optimal.

(3) In our multi-goal programming model, we conclude the emigration of the infective that are anxious about the lack of supply or rug medical environment in county or small city. It is closer to the reality since humans won’t await one's doom, especially when they are about to die. So with the consideration the emigration of infective, our modeling will be the most practical one.

Weaknesses:

(1) Because we have considered the financial and social situation of West Africa in reality, our transportation of medical aids are assumed that can only be in the capital city, and the rest infected regions are divided into several levels. The emigration of each level can only be from bottom to top as a tree structure. However, the time complexity of transportation in some cities is not the least since there are not always the completed tree structures or the orders of different levels are not always from bottom to top.

(2) The prediction in our time series model requires the data to be large enough. However, the real time data is hard to be collected and therefore, our prediction of the incomplete data may be in low accuracy.

8. A Non-technical Letter

Dear the world medical association,

Thank you for reading our article, we are a student group who study on the optimal strategy of drug's distribution and transportation in the case of Ebola. Now based on our studying, it is our honor to share our findings on how to restrict the spreading of Ebola with you.

We all know that 2014 is a desperate year to lots of people, because a new spreading epidemic called Ebola has exploded in the West Africa. It is not only fatal but also urgent. No matters the gender or age, male and female, kids and adults are sharing the same chances of catching this disease, which is with the 30 to 90 percent possibility of death. Due to the destruction of Ebola, the poor financial and medical conditions in West Africa are worse. However, thanks to the aid of drugs from the world health organization and many other medical organizations, Ebola is now being eliminated step by step. Based on the existing technology and medical resources, can we figure out the optimal way to fight with the disease?

The answer is yes. In our studying, we focus on the drug's distribution and transportation as our constraint conditions. If the drugs are adequate, we can use the Time Series model for forecasting and fitting the short-term predicted value of the sick, and therefore, after calculating the sum of each in need region, we can nip in the bud before the next explosion of disease. In addition, since the virus mutates frequently, with the accurate needed quantity of drugs will prevent the over-product as well.

Otherwise, when the drugs are in short supply, there will be no use to predict or fit the needed quantity. Our top priority is now turning to restrict the spreading of the disease and prevent it turning into the eternal epidemic. Therefore, we have emphasized on the optimal strategy of drug's distribution and transportation instead.

Firstly, based on the SEIS model, we have estimated the point that represents whether the disease is eternal or not. And then with the combination of thoughts of composite population model, we construct a multi-goal drug's distribution and transportation model with the tree structure.

Because of the lack of medical resources, there is no doubt that the patients or the people carrying virus will leave the county or small city and be crowded into the bigger city for better medical condition. As a result, we take the emigration caused by the shortage of drugs into consideration and select both the ratio of infected and the distance to the eternal point as our affected factors of distribution.

To restraint the spread of Ebola virus, there are still lots of works needed to do. It is a long way to invest more on the emergency site or create the medicine with higher efficiency.

We hope our article can do some help to deal with this epidemics.

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