Solution of spread, prevention, cure and logistic methods for ebola virus infection based on mathematical model

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Abstract. As the requirements of the question, all study we have done is about EVD pathology, characteristic of EVD spread, and set up EVD spread model and medical production logistic optimal model which are based on these knowledge. By using traditional epidemic model with innovation of considering the population age structure as part of the model, we solved the first model which mentioned above.The model is able to combine the patients contagious distribution with age distribution in mathematical way,thus people can know more about the epidemic trend of EVD. Setting up transfer stations is our way to solve the second model. Drugs get into transfer stations ,then divided into every patients' homes. The transfer stations are set up according to the location of airport. We divided them into large-scale ,middle-scale and small-scale transfer stations. The drugs are delivered according to the size of stations decreasing step by step so that people can keep the transport order , save energy as well as refrain from disturbing the airline. Picking out the line and ensuring the location of transfer stations are our main problems. Shortest path problem model and the transportation linear programming .Model is the tool to solve the problems.We hope our models can have a little effect on EVD prevention and treatment, so as to controlling the disease spreading.

Introduction

Ebola virus disease (EVD) was first identified in 1976,in two simultaneous outbreaks in Sudan and the Democratic Republic of the Congo.It is not completely understood why this epidemic has expanded to such an unprecedented scale compared to previous outbreaks,although regional instability,urbanization,and lack of capacity have all been suggested as potential factors. EVD is transmitted by contact with body fluids.Healthcare workers are at particular risk for transmission due to their frequent contact with patients and body fluids,and burial ceremonies in which mourners contact the body of the deceased have also been identified as playing an important role in transmission.Ebola has an average incubation period of 8-10days (with a range of 2-21 days),and infectiousness is believed to coincide with symptom onset.EVD progresses in two broad stages.Symptoms in the first stage often include fever,headache,sore throat,fatigue,and muscle pain,and the first stage can often be mistaken for other diseases,such as malaria or includes more intense symptoms such as vomiting,diarrhea,rash,symptoms of impaired kidney from the first stag,with much higher death rates in the second stage (indeed,in some outbreaks all second-stage patients died).As second stage symptoms tend to have more release of body fluids (e.g vomit or diarrhea),transmissibility is likely to be higher as the disease progresses as well.Accounting for the stage structure is thus particularly important when evaluating healthcare capacity and how the timing of hospitalization may affect the outbreak dynamics.[1]

First established the epidemiological model age structure is F.Hoppensteadt[7] Since then, Epidemiological model of the age structure of emerging . Most scholars discussing the model of SIS, SIR, and SEIR, Yao Yong [6] Introduces the SEIR model with age structure, And discusses the stability of the disease-free equilibrium solution. [13-14] Most of them do not take into account the influence of age on the patient's illness disease.

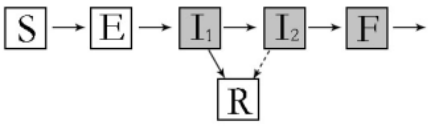

Figure 1 . The flow chart from [1].

Restatement and clarification of the problem

The definition of space debris. This article aims to build a mathematical model about prevention and spread trend,based on the regularity of spread and speed of spread .

Disease spread description

Logistical method and destinations certification

Modeling. Set up spread model according to the detailed data of different region (different density of population)which was provided by WHO and build up a age structure-infection model which is based on the traditional infection model,so that we can establish the optimizing model of drug production quantity and targeted drug delivery.That is setting up intermediate of transport according to the condition of different regions and ensure the quantity of drug transit.

Explain assumptions and rationale/justification

Model 1:

1.Without considering births, deaths, population dynamics factor mobility, etc. This means considering a closed environment and assuming disease over time than birth, death is much significant change over time, so that the latter can be neglected. Thus, the total population of this environment remains a constant, $N(t) \equiv K$ or $S(t) + I(t) + R(t) \equiv K$.

2. Once a patient in contact with the susceptible necessarily have some infectivity. It is assumed that at time t within the unit of time, the number of susceptible and can infect a patient susceptible total number within this environment, $S(t)$ proportional to the scale factor is β ,Thus in unit time at time t is the number of people infected by sick is $\beta S(t)I(t)$.

Model 2:

1. airport location is where the station is, the demand of medical productions increases with the increase of the amount of patients around the zone.

2.the distance from stations to each patient is not far, thus the delivery cost from station to patients is not under consideration.

3.the medical production could only be transferred directly from manufacture to high medical transfer stations, and directly from high to middle, and then from middle to small. It is banned to deliver across this level structure.

4.the candidate locations of each station is assumed to be known for discrete network selecting location.

5.the cost of delivery is simply linear positive correlative with the distance.

6.all stations is capable of handling the delivery process.

models

Model 1

Model structure

This model, taking into account the different stages have different infection rates,Ebola often progresses through multiple stages of illness—an initial infectious stage in which symptoms tend to by milder (such as fever, headache, sore throat, muscle aches), often progressing to diarrhea, vomiting, and a second, more intense stage during which the more advanced symptoms (such as hemorrhaging and multi-organ failure) manifest [1,3,7]， The second stage is usually fatal.This model is based on *SIR* model， We also consider the age structure， We divided the total population: $S(a,t)$ is susceptible, $E(a,t)$ is expose, $R(a,t)$ is removal, $I(a,b,t)$ is infective .Assume $N(a), 0 \le a \le A$ as populatio n density function depend on age. a,b represent the physiological age and infected age separately, and A is the maximum physiological age a individual could live with. R represents the cured group of people, and they have the immunity of ebola virus infection.

Table1. Variables and their meanings

Variable	Meanings
S	The fraction of the population which is susceptible
E	The fraction exposed
I_1	The population in the first stage of infection
I_2	The second stage of infection
R	The fraction of the population which who are recently recovered
F	The fraction of the population who hace died

Ebola virus infection equation：

$$\frac{\partial S}{\partial a}+\frac{\partial S}{\partial t}=-[(\mu_1(a)+\beta_{1(a,t)})+(\mu_2(a)+\beta_2(a,t)+(\mu_1(a)+\beta_F(a,t))]S(a,t)+\gamma_R R(a,t)$$

$$\frac{\partial E}{\partial a}+\frac{\partial E}{\partial t}=[(\mu_1(a)+\beta_1(a,t)+(\mu_2(a)+\beta_2(a,t)+(\mu_1(a)+\beta_F(a,t))]S(a,t)-(\mu_E(a)+\alpha)E(a,t)$$

$$\frac{\partial I_1}{\partial a}+\frac{\partial I_1}{\partial b}+\frac{\partial I_1}{\partial t}=(\mu_E(a)+\alpha)E(a,t)-(\mu_1(a)+\gamma_1)I_1(a,b,t)$$

$$\frac{\partial I_2}{\partial a}+\frac{\partial I_2}{\partial b}+\frac{\partial I_2}{\partial t}=\delta(\mu_1(a)+\gamma_1)I_1(a,b,t)-(\mu_2(a)+\gamma_2)I_2(a,b,t)$$

$$\frac{\partial F}{\partial t}=\delta_2\gamma_2 I_2-\gamma_F F$$

$$\frac{\partial R}{\partial a}+\frac{\partial R}{\partial t}=-(\mu_R(a)+\gamma_R)R(a,t)+\gamma_1\int_0^B I_1(a,b,t)db+\gamma_2\int_0^B I_2(a,b,t)db$$

Parameter Estimation

Table2.From Wikipedia http://en.wikipedia.org/wiki/List_of_countries_and_dependencies_by_population

National	Population	Information Date	Proportion	Source
Guinea	9,982,000	2010	0.14%	UN estimate for 2010
Liberia	3,994,000	2010	0.06%	UN estimate for 2010
Sierra leone	5,868,000	2010	0.08%	UN estimate for 2010

Table3.This data source [1]

	Meaning	Units	Range	Source
β_1	The first phase of the prevalence	1/people.day	Estimated	Estimated
$\frac{\beta_2}{\beta_1}$	The prevalence ratio of the second phase vs. first stage of the prevalence	Unitless	1.5-5	[8,9]
$\frac{\beta_F}{\beta_1}$	The prevalence ratio of the funeral transmission vs first stage of the prevalence	Unitless	1.5-5	[8,9,10]
α^{-1}	The average incubation period	Days	8-10	[2,5]
γ_1^{-1}	The first phase of the cycle of illness	Days	5-7	[2,3]
γ_2^{-1}	The second phase of the cycle of illness	Days	1-2	[2,3]
γ_F^{-1}	Time from death until burial	Days	1-3	[2,4]
γ_R^{-1}	From recovery to the time spent susceptible	Days	5-15	[5],*
δ	Total mortality	Unitless	Estimated	Estimated
δ_2	The second phase of mortality	Unitless	0.9-1	[3]

Table4.This data source [1]

	Parameter	Best estimate	Range of LHS Estimates
All Countries	β_1	0.11	0.079-0.18(0.12)
	δ	0.56	0.55-0.6(0.57)
	R_0	1.6	1.43-1.64(1.53)
Guinea	β_1	0.16	0.078-0.18(0.11)
	δ	0.65	0.64-0.72(0.68)
	R_0	1.79	1.47-1.79(1.61)
Liberia	β_1	0.12	0.0725-0.17(0.10)
	δ	0.63	0.63-0.72(0.67)
	R_0	1.81	1.34-2.75(1.47)
Sierra Leone	β_1	0.12	0.085-0.17(0.12)
	δ	0.38	0.36-0.38(0.37)

	R_0	1.32	1.39-1.37(1.25)

Fitting and forecasting results Because we did not find data on the age structure is changing infection rate, We did not have to carry out further graphical analysis.

Model 2

Transfer station is based on the airport station, the locations of transfer stations and distributions of supply of the medical products depends on medical production demand, delivery time, delivery speed. The distribution of the infection is shown as below:

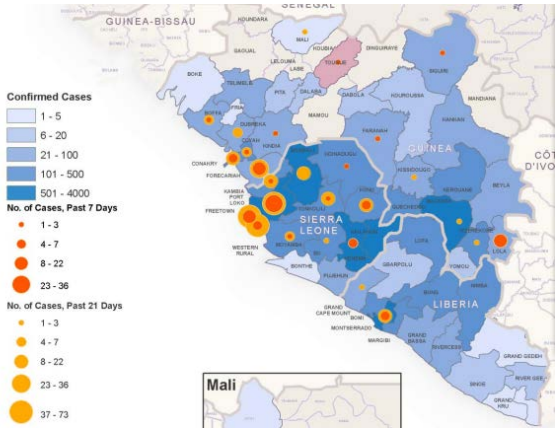

Figure 2 . The distribution of the infection

In consideration of setting up the path road, budget of cost and logistical efficiency are two main factors, thus the short-path method is selected with the program Lingo to make the short-path model, and decide the path road.The distribution of airport stations are shown as below:

Figure 3 . The distribution of airport stations

Figure 4 . Sierra leone middle transfer station

Table5.Distance and amount of medical production

Distance	X_1	X_2	X_3	X_4	X_5	Supply
X_1	0	176	268	343	407	7000
X_4	343	167	75	0	103	8000
Demand	4000	3000	2000	4000	2000	

Table6. Result of medical production distribution

Amount	Y_1	Y_2	Y_3	Y_4	Y_5
Y_1	4000	3000	0	0	0
Y_4	0	0	2000	4000	2000

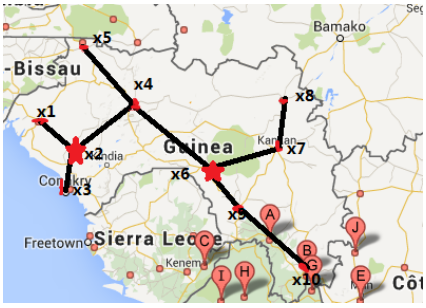

Figure 5 . Guinea middle transfer station

Even though the demand in guinea is relatively lower, but the area is spread and bigger, thus two middle stations are needed.

Table7. Distance and amount of medical production form:

Distance	X_1	X_2	X_3	X_4	X_5	X_6	X_7	X_8	X_9	X_{10}	Supply
X_2	102	0	85	180	219	401	571	680	524	742	1300
X_6	503	401	486	221	260	0	170	280	123	341	2700
Demand	100	500	200	200	300	500	500	200	1000	500	

Table8. Result of medical production distribution:

Amount	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}
Y_2	100	500	200	500	0	0	0	0	0	0
Y_6	0	0	0	0	0	500	700	0	1500	0
Y_4	0	0	0	200	300	0	0	0	0	0
Y_7	0	0	0	0	0	0	500	200	0	0
Y_9	0	0	0	0	0	0	0	0	1000	500

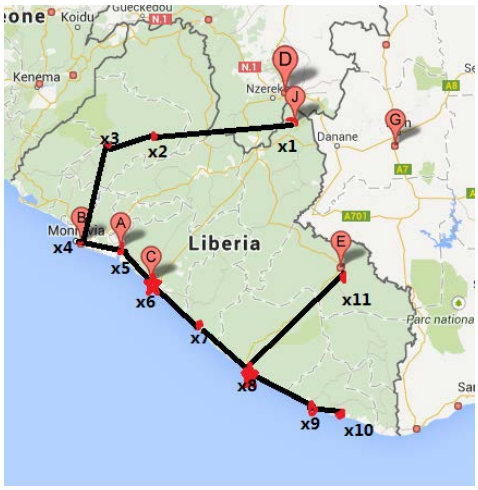

Figure 6 . Liberia middle transfer station

Table9. Distance and amount of medical production form:

Distance	X_1	X_2	X_3	X_4	X_5	X_6	X_7	X_8	X_9	X_{10}	X_{11}	Supply
X_5	357	207	153	40	0	48	119	191	271	301	338	8000
X_8	518	368	314	201	161	113	72	0	80	110	147	1000
Demand	500	400	100	500	4000	2000	500	200	200	200	400	

Table10. Result of medical production distribution:

Amount	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_{10}	Y_{11}
Y_5	0	0	0	1500	4000	2500	0	0	0	0	0
Y_4	0	0	1000	500	0	0	0	0	0	0	0
Y_3	0	900	100	0	0	0	0	0	0	0	0
Y_2	500	400	0	0	0	0	0	0	0	0	0
Y_6	0	0	0	0	0	2000	500	0	0	0	0
Y_8	0	0	0	0	0	0	0	200	300	0	500
Y_9	0	0	0	0	0	0	0	0	100	200	0

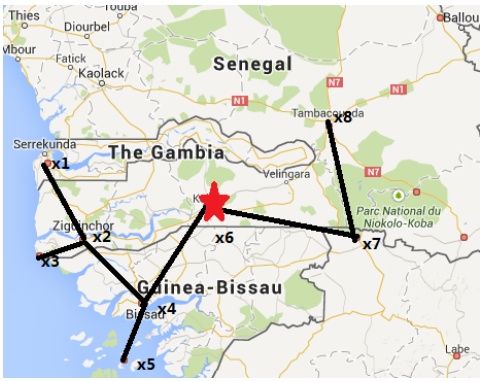

Figure 7 .Middle transfer stations of other areas

Table11. Distance and amount of medical production form:

Distance	X_1	X_2	X_3	X_4	X_5	X_6	X_7	X_8	Supply
X_4	193	99	145	0	60	130	298	423	1200
Demand	100	100	100	500	100	100	100	100	

Table12. Result of medical production distribution

Amount	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8
Y_4	0	300	0	500	100	300	0	0
Y_2	100	100	100	0	0	0	0	0
Y_6	0	0	0	0	0	100	200	0
Y_7	0	0	0	0	0	0	100	100

Figure 8 .High transfer station path road

Table13.Distance and amount of medical production form

Distance	X_1	X_2	X_3	X_4	X_5	X_6	X_7	Supply
X_4	1026	487	745	0	310	660	860	29200
Demand	1200	1300	2700	7000	8000	8000	1000	

Table14.Result of medical production distribution

Amount	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7
Y_4	0	2500	0	7000	19700	0	0
Y_2	1200	1300	0	0	0	0	0
Y_5	0	0	2700	0	8000	9000	0
Y_6	0	0	0	0	0	8000	1000

Describe model testing and sensitivity analysis. Guinea, Sierra leone and Liberia are the worst-hit areas of the ebola virus infection, in order to achieve the purpose of high efficiency and feasible budget control, the model suggests to set up one high level transfer station for the whole heat area, two middle transfer stations for each country, and small stations for all rest of the airports. The logistical logic is that the middle transfer stations could only receive the medical production from high station, and the small station could only receive the production from middle station. According to the information of resources, the cure medical production would be sent from their manufactures in American and Canada to the high station. It would be much better than directly deliver the production from manufactures to each zone of each countries, not just because of capital resources and budgets but also for realistic flight planning. In this model it is assumed that the high station is built to have the capability to store and deliver huge amount packages. The model would solve the problem that where this station would be located and the path road of delivery.

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