

A DYNAMIC ALLOCATION MODEL FOR MEDICAL RESOURCES IN THE CONTROL OF INFLUENZA DIFFUSION

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Abstract

In this paper, we develop a unique time-varying forecasting model for dynamic demand of medical resources based on a susceptible-exposed-infected-recovered (SEIR) influenza diffusion model. In this forecasting mechanism, medical resources allocated in the early period will take effect in subduing the spread of influenza and thus impact the demand in the later period. We adopt a discrete time-space network to describe the medical resources allocation process following a hypothetical influenza outbreak in a region. The entire medical resources allocation process is constructed as a multi-stage integer programming problem. At each stage, we solve a cost minimization sub-problem subject to the time-varying demand. The corresponding optimal allocation result is then used as an input to the control process of influenza spread, which in turn determines the demand for the next stage. In addition, we present a comparison between the proposed model and an empirical model. Our results could help decision makers prepare for a pandemic, including how to allocate limited resources dynamically.

Keywords: Time-varying demand, medical resources, influenza diffusion, time-space network

1. Introduction

A serious influenza can test the ability of a nation to effectively protect its population, to reduce human loss and to rapidly recover. Meanwhile, it can also cause a great economic loss. For example, during the period from 1997 to 2002, more than 3,400,000 chickens were killed in Hong Kong, to prevent the avian influenza from transmitting to human. Generally, it is difficult to predict when an unexpected influenza outbreaks, and our security measures

against such problem rest largely on consequence management, i.e., what can be done after the influenza outbreak occurs? How to ensure the supply of medical resources so that the efficiency of medical care can be maximized? Unfortunately, the available medical resources in the control of influenza are usually limited. Therefore, government decision makers must understand how the influenza spreads and then determine how to allocate the limited medical resources.

Most mathematic models for influenza diffusion analysis are compartmental models (Mishra and Saini 2007, Sun and Hsieh 2010, Li et al. 1999, Zhang et al. 2006, Zhang and Ma 2003). In these models, the total population is divided into several classes and each class of individuals is closed into a compartment. The mixing of members is homogeneous, meaning these models are constructed with the assumption of both homogeneous infectivity and homogeneous connectivity of each individual. Another stream of research is focused on the development of influenza diffusion models by applying simulation methods, including computer simulation and numerical computation (Wein et al. 2005, Craft et al. 2005, Germann et al. 2006, Halloran et al. 2008). Recently, Aleman et al. (2011) proposed an agent-based simulation model that treated each individual as unique, with non-homogeneous transmission and infection rates correlated to demographic information and behavior. Kim et al. (2010) described the transmission of avian influenza among birds and humans. Liu and Zhang (2011) presented a SEIRS epidemic model based on the scale-free networks, where the active contact number of each vertex was assumed to be either constant or proportional to its degree in their model. Samsuzzoha et al. (2010) used a diffusive epidemic model to describe the transmission of influenza. The equations were solved numerically by using the splitting method under different initial distribution of population density. Further, Samsuzzoha et al. (2012) presented a vaccinated diffusive compartmental epidemic model to explore the impact of vaccination as well as diffusion on the transmission dynamics of influenza. The above

mentioned works provide numerous and significant references to research the influenza diffusion. Although the emphasis of this paper is focused on how to allocate the limited medical resources, a basic component of our model, the forecasting mechanism for the dynamic demand, utilizes one of such epidemic diffusion models.

So far, influenza vaccination policy is one of the most effective strategies to prevent a wide spread influenza occurs. However, the level of influenza vaccination coverage in all age groups is suboptimal, even in the majority of developed countries. There are several reasons for this phenomenon, where mismatch between the vaccine supply and the demand side of is one of them. Recently, some significant papers on the subject are focused on the coordination of the influenza vaccine supply chain. For example, Adida et al. (2013) considered how a central policy-maker can induce socially optimal vaccine coverage through the use of incentives to both consumers and vaccine manufacturer in a monopoly market for an imperfect vaccine. The result shows that a fixed two-part subsidy is unable to coordinate the market. Deo and Corbett (2009) examined the interaction between yield uncertainty of influenza vaccine and firms' strategic behavior and found that yield uncertainty can contribute to a high degree of concentration in an industry and a reduction in the industry output and the expected consumer surplus in equilibrium. Further, Arifoğlu et al. (2012) studied the impact of yield uncertainty (supply side) and self-interested consumers (demand side) on the inefficiency in the influenza vaccine supply chain. The result shows that the equilibrium demand can be greater than the socially optimal demand after

accounting for the limited supply due to yield uncertainty and manufacturer's incentives, which is contrast to the previous economic studies. To break the negative feedback loop between the retailer and the manufacturer in influenza vaccine industry, Dai et al. (2012) introduced two coordinating contracts, the Delivery time dependent Quantity Flexibility (D-QF) contract and the Buyback-and-Late-Rebate (BLR) contract. Furthermore, Yamin and Gavius (2013) built a theoretical epidemiological game model to find the optimal incentive for vaccination and the corresponding expected level of vaccination coverage.

Motivated by the supply chain coordination concept, we study an interactive coordination problem between influenza diffusion and medical resources allocation. This paramount life-saving and costly logistics problem opens up a wide range of applications of OR/MS techniques and has motivated many researches in the past decades (Stinnett and Paltiel 1996, van Zon and Kommer 1999, Zaric and Brandeau 2001, 2002, Brandeau et al. 2003). These models, however, are not applicable to epidemics with discrete rates of growth and are restricted by several assumptions like the number of interventions or independence of populations. Recent mathematical approaches for healthcare resources allocation, on the other hand, suggest advanced models of disease prevalence among several populations, and consider more general forms of cost function for the prevention programs (Zaric et al. 2008, Duintjer Tebbens et al. 2010, Vlah and Rui 2012, Savachkin and Uribe 2012). Furthermore, Rottkemper et al. (2012) designed a mixed integer programming model for distribution and inventory relocation

under uncertainty in humanitarian operations. Rachaniotis et al. (2012) presented a resources scheduling model in epidemic control with limited resources. The objective is to minimize the total infected people in a certain time horizon under consideration by effectively relocating the available resources over several regions. Sun et al. (2013) built a mathematical model to optimize the patient allocation considering two objectives: to minimize the total travel distance by patients to hospitals; and the maximum distance a patient travels to a hospital. In addition, it is worth mentioning that a concise survey of OR/MS contribution to epidemics control can be found in Brandeau (2005). The popular techniques that have been used for resources allocation in epidemics control are linear and integer programming models, numerical analysis procedures, cost-effectiveness analysis, simulation, non-linear optimization and control theory techniques. Recently, Dasaklis et al. (2012) focused on defining the role of logistics operations and their management that may assist the control of epidemic outbreaks. They reviewed the literature and pointed out the research gaps critically.

In summary, this section does not aim to be an exhaustive review of the literature; rather, we introduce an illustrative subset of existing models. In our previous work (Liu and Zhao 2012), we divided influenza diffusion process into three stages. The first stage is the inception of influenza in very limited population. If the infectious disease is noticed in time and treated properly, the epidemic can be controlled without causing a wide spread. Otherwise, influenza diffusion develops into the second widespread

diffusion stage. The third stage is the recovery stage that influenza diffusion is under controlled. In this paper, we attempt to model the interactive coordination process between influenza diffusion and medical resources allocation in the second response stage. The model couples a forecasting mechanism for dynamic demand of medical resources based on the classical SEIR epidemic model (Brauer and Castillo-Chavez 2012). As shown in Figure 1, we decompose the whole interactive coordination process into n correlated sub-problems (n decision-making cycles). Each sub-problem includes three phases, which are influenza diffusion analysis, demand forecasting and medical resources allocation. We briefly introduce the connections among these three phases as below.

i) Initially, we employ a SEIR model to depict the dynamic epidemic diffusion process. The model gives us a forecast of the growing (or decreasing) number of the infected population in the course of the epidemic diffusion, which will be embedded in the following demand forecasting model.

ii) Secondly, we define a difference factor to illustrate the change in the number of infected population. Coupling with this factor and medical resources allocation result in the current decision cycle, we can get the demand of medical resources for the next decision cycle.

iii) Based on the forecasting demand for the next decision cycle, we solve an integer programming problem for the optimized allocation of medical resources in a supportive logistics system to meet the dynamic demand.

The latter two phases are executed iteratively. The details of the demand forecasting model are presented in Section 2.2. It is worth mentioning that medical resources allocated in current

period will take effect in subduing the spread of influenza and thus impact the demand in the next period. To the best of our knowledge, such an operational procedure is different from any existing influenza response operations, which have always been carried out under the assumption that demand is deterministic or stochastic. When the proposed method is adopted, we can take a fixed time interval (i.e. one day) as the decision-making cycle and then update the allocation result for each epidemic area periodically. Moreover, we believe the proposed model should serve for the benefit of a centralized decision maker, usually a local or regional governmental agent, in control of the influenza diffusion, who needs an analytic model to plan for the logistics and to revise and update such plan in the actual implementation.

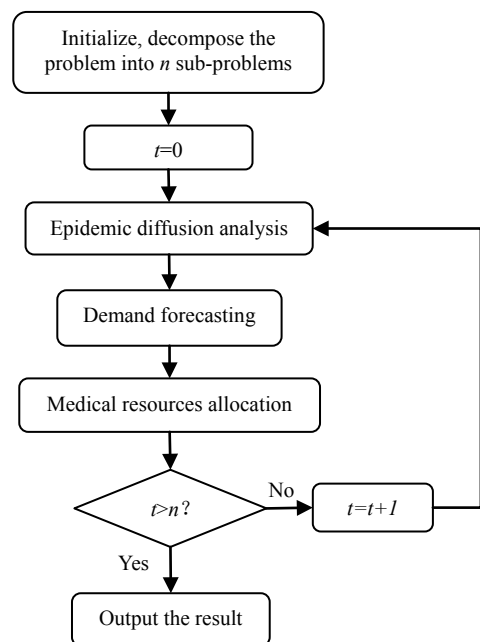


Figure 1 The dynamic operational procedure of medical resources allocation

The remainder of the article is organized as follows. Section 2 is the epidemic diffusion analysis and demand forecasting. A dynamic medical resources allocation model is proposed in Section 3. Numerical example and a short sensitivity analysis are presented in Section 4. Finally, conclusions are given in Section 5.

2. Epidemic Diffusion Analysis and Demand Forecasting

2.1 Influenza Diffusion Analysis

In 1927, W. O. Kermack and A. G. McKendrick created the first SIR model in which they considered a fixed population with only three compartments, the susceptible, the infected, and the removed (Kermack and McKendrick 1927). $S(t)$ is used to represent the number of individuals not yet infected with the disease at time t . $I(t)$ denotes the number of individuals who have been infected with the disease and are capable of spreading the disease to those in the susceptible category. $R(t)$ is the compartment used for those individuals who have been recovered from the disease, either due to immunization or due to death. Since that time, theoretical epidemiology has witness numerous developments. Some of the recent studies can be found in (Liu and Chen 2015, Harko et al. 2014).

Although the deterministic SIR model is successful in predicting the behavior of outbreaks very similar to which observed in many recorded epidemics (Brauer and Castillo-Chavez 2012), the SIR model discussed above takes into account only those diseases which cause an individual to be able to infect others immediately upon their infection. In fact,

many diseases, such as influenza, have what is termed a latent or exposed phase, during which the individual is said to be infected but not infectious. Therefore, the host population N should be broken into four compartments: the susceptible, the exposed, the infectious, and the recovered, with the number of individuals in a compartment, or their densities denoted respectively by $S(t)$, $E(t)$, $I(t)$ and $R(t)$. That means, $N = S(t) + E(t) + I(t) + R(t)$. The SEIR model is proved to be a more suitable model to match the influenza diffusion (Zhang and Ma 2003).

Even though people travel across regions and the population of any region is of a fluid nature, it is reasonable to believe that the population size does not change significantly over a short period of time without a social economic reason. Therefore, during the course of influenza spread-to-control, which usually lasts no longer than three months, there should not be significant difference between the in-flow and out-flow number of people. We note that this is the basic rationale based on which most SEIR literatures assume a constant population size as is in this paper. For future research, the basic framework proposed here can be extended to incorporate such factors as people's hesitation to visit the epidemic outbreak region and/or government's quarantining policy in controlling people from traveling out of the region.

Therefore, without considering the natural birth rate and death rate of the population, we can use a simple deterministic compartmental model (SEIR) to describe the influenza spread process, which is described by the following system of ordinary differential equations (ODE).

$$\begin{cases} S'(t) = -\beta S(t)I(t), \\ E'(t) = \beta S(t)I(t) - \beta S(t-\tau)I(t-\tau), \\ I'(t) = \beta S(t-\tau)I(t-\tau) - (\alpha + \delta) I(t), \\ R'(t) = \delta I(t). \end{cases} \quad (1)$$

In ODE(1), $S(t)$, $E(t)$, $I(t)$ and $R(t)$ represent the number of susceptible people, the number of exposed people, the number of infected people, and the number of recovered people, respectively. β is the propagation coefficient of the influenza; δ is the recovery rate; α is the loss rate; and τ represents the incubation period of the disease. $\beta, \delta, \alpha, \tau > 0$. ODE (1) states the following: (i) The decrease rate of the susceptible population is in proportion to the propagation coefficient, β , and both of the current mass of the susceptible population and the current mass of the infected population. (ii) The growth rate of the exposed population is determined by the difference between the entering population, those of susceptible people who actually get exposed to the disease, and the exiting population, those of exposed population who get sick after the incubation period of the disease; (iii) The growth rate of the infected population is determined by the difference between the entering population, those of exposed population who get sick, and the exiting population who are either recovered or dead; Finally (iv) the growth rate of the recovered population is determined by the joining population of the newly recovered.

According to ODE(1), improving the recovery rate, δ , and reducing the propagation coefficient, β , are two effective measures to take in suppressing the growth of $I(t)$. That means, on one hand, local government should execute some quarantining policies in controlling people from traveling in (or out) of

the region. Meanwhile, self-quarantine and decreasing the contact with people around are also effective strategies for controlling influenza diffusion. On the other hand, a sufficient medical resources supply should be allocated to the emergent designated hospitals (EDH), to guarantee or improve the recovery rate of infected persons.

2.2 Demand Forecasting

Generally, demand forecasting for medical resources in epidemic area is formulated as a linear or non-linear function with the number of infected people, which can be illustrated as follows:

$$d_t^* = f[I(t)]. \quad (2)$$

Herein, we refer it as the demand forecasting mode I (DFM-I). It is obvious that the demand has some functional relationship with the number of infected people. The deficiency is that it ignores the interactive effect between the influenza spread and medical resources allocation. Actually, the demand is discrete and independent. We use a schematic diagram to illustrate the evolution trajectory of the time-varying demand (see Figure 2). Herein, we refer it as the demand forecasting mode II (DFM-II).

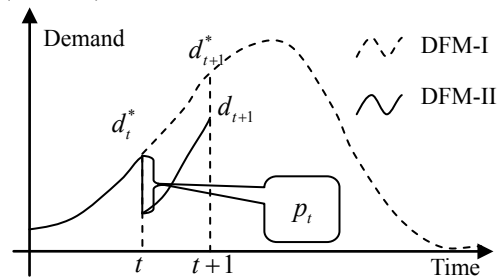


Figure 2 Schematic diagram of the demand forecasting

In this figure, the horizontal axis represents the decision-making cycle, and the vertical axis stands the demand for medical resources. The dotted curve depicts the forecasting demand which is obtained by using Equation (2), and the solid curve represents the actual time-varying demand. For example, we get the results d_t^* and d_{t+1}^* , respectively for the two difference decision cycles t and $t+1$, when we use Equation (2) to predict the demand. However, a certain amount of medical resources, p_t , would have been allocated to the disaster area during decision cycle t . These medical resources would affect in curing infected patients in hospitals and thus subduing influenza diffusion on decision cycle $t+1$. Therefore, instead of d_{t+1}^* , the expected demand on decision cycle $t+1$ is d_{t+1} . To reflect the dynamic property of the time-varying demand, we define a difference factor to depict the change in demand for each decision-making cycle, which is formulated as:

$$\eta_t = \frac{(d_{t+1}^* - d_t^*)}{d_t^*}. \quad (3)$$

The linear factor η_t can be either positive (increasing demand) or negative (decreasing demand), and may vary in the different cycles. To facilitate the model formulation in the following sections, herein we define the decision making cycle as λ , and we suppose that each infected person needs ω units of medical resources in each decision making cycle. Considering that each infected person needs a period of time to get cured, herein we denote the treatment cycle as Γ . Generally, to guarantee the efficiency of decision-making, decision cycle is always set to be a small time interval, e.g., one day. The shorter the time interval is, the more accurate the decision-making is. In another

side, treatment cycle in actual practice is always a long time. It may be several weeks or more. Suppose that a certain amount of medical resources p_t is allocated to the epidemic area during cycle t , thus the commuted recovery rate at decision cycle t can be formulated as $\lambda p_t / \omega \Gamma$. Thus, we have the following recursion formulas:

$$\text{when } t=1, \quad d_1 = (1 + \eta_0)(d_0 - \frac{\lambda p_0}{\omega \Gamma}), \quad (4)$$

$$\text{when } t=2, \quad d_2 = (1 + \eta_1)(d_1 - \frac{\lambda p_1}{\omega \Gamma}), \quad (5)$$

.....

$$\text{when } t=n, \quad d_n = (1 + \eta_{n-1})(d_{n-1} - \frac{\lambda p_{n-1}}{\omega \Gamma}). \quad (6)$$

The recursion formulas (4-6) are our prescribed demand forecasting model. Specially, $d_0 = \omega \cdot I(0)$ is the initial demand for medical resources, and p_0 is the best allocation result on decision cycle $t=0$, which can be obtained by solving the programming model in the following Section 3. After that, we can forecast the demand for medical resources on decision cycle $t=1$ by using Equation (4). Similar works are executed iteratively to obtain the demand information for each decision cycle during the entire medical resources allocation process.

3. The Dynamic Medical Resources Allocation Model

3.1 Model Specification

Time-space network approach has been popularly employed to solve scheduling/routing problems, as it is efficient to represent the result in dimensions of time and space (Yan and Shih 2009, Yan et al. 2013, Yan et al. 2014). To depict the dynamic process of medical resources allocation, we employ such network flow

technique to develop a dynamic and multi-stage programming model, with the objective of cost minimization subject to some related operating constraints.

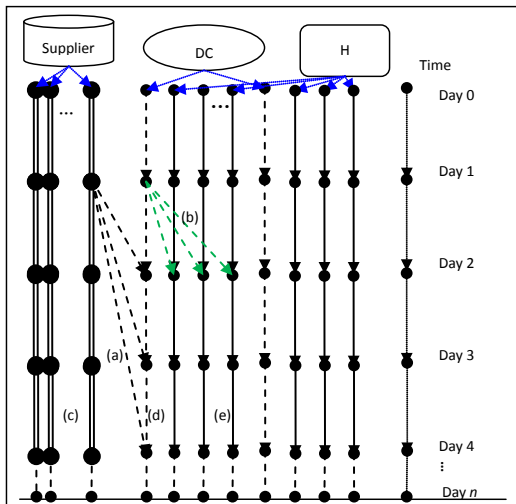


Figure 3 Time-space network of medical resources allocation

Figure 3 describes the time-space network of medical resources allocation. The vertical axis stands for time duration. The horizontal axis represents medical resources suppliers, distribution centers (DC) and local designated hospitals (H). There are several suppliers, $i = 1, 2, \dots, I$, who can produce and ship the medical resources to the epidemic area. Surely, each supplier has a production capacity. Also, there are several distribution centers, $j = 1, \dots, J$, and many local hospitals, $k = 1, 2, \dots, K$, geographically located in the area that are designated to host and treat the infected people. Allocation arcs are defined as follows: (a) represents that medical resources are delivered from supplier to DC; (b) denotes that medical resources are allocated from DC to the

designated hospitals; (c)~(e) are time duration arcs. The distribution centers transship the medical resources and distribute them to the local hospitals based on the forecasting demand. As mentioned in Section 1, the local government or an agent designated by the government would take the role of centralized decision making and control the relevant resources in a burst of influenza spread. The objective of the decision making is to minimize the total logistics cost in terms of medicine supply and distribution. To minimize it, medicine distribution scheduling should be coordinated, forming a just-in-time mechanism for the two-echelon medicine supply chain. Therefore, inventory level in the DCs and the local hospitals should be as lower as possible and thus inventory costs in both DCs and local hospitals can be ignored in our model.

3.2 Notation

Before introducing the model's formulation, the notation and symbols are listed below:

Sets

T : Set of decision cycle.

S : Set of supplier.

D : Set of DC.

H : Set of hospital.

Parameters

c_{ij} : Unit transportation cost for medical resources from supplier i to DC j .

r_{jk} : Unit transportation cost for medical resources from DC j to local hospital k .

a_{it} : The production capacity of supplier i on decision cycle t .

z_{jt} : The available quantity of medical resources in DC j on decision cycle t .

d_{kt} : Demand for medical resources in hospital k on decision cycle t .

Decision variables

x_{ijt} : Quantity of medical resources transported from supplier i to DC j on decision cycle t .

y_{jkt} : Quantity of medical resources transported from DC j to hospital k on decision cycle t .

3.3 Model Formulation

Let $F(x, y)$ be the objective function, the dynamic medical resources allocation model can be formulated as follows:

$$\text{Min } F(x, y) = \sum_{i \in T} \sum_{i \in S} \sum_{j \in D} x_{ijt} c_{ij} + \sum_{i \in T} \sum_{j \in D} \sum_{k \in H} y_{jkt} r_{jk} \quad (7)$$

s.t.

$$z_{jt} = \{z_{j(t-1)} + \sum_{i \in S} x_{ijt} - \sum_{k \in H} y_{jkt}\}^+, \forall j \in D, t \in T \quad (8)$$

$$\sum_{j \in D} x_{ijt} \leq a_{it}, \forall i \in S, t \in T \quad (9)$$

$$\sum_{j \in D} y_{jkt} \leq d_{kt}, \forall k \in H, t \in T \quad (10)$$

$$\sum_{j \in D} \sum_{k \in H} y_{jkt} = \min \left\{ \sum_{k \in H} d_{kt}, \sum_{i \in S} a_{it} \right\}, \forall t \in T \quad (11)$$

$$d_{kt} = (1 + \eta_{k(t-1)}) \left(d_{k(t-1)} - \frac{\lambda \sum_{j \in D} y_{jk(t-1)}}{\omega \Gamma} \right), \forall k \in H, t \in T \quad (12)$$

$$x_{ijt}, y_{jkt} \in I, \forall i \in S, j \in D, k \in H, t \in T \quad (13)$$

The objective function in Equation (7) minimizes the total logistics cost of medical resources allocation. Constraint (8) is the flow conservation constraint. Constraint (9) is the production capacity constraint. Constraints (10)-(12) are the demand constraints. At last, constraint (13) ensures that all decision variables are integers.

3.4 Solution Procedure

For any $t \in T$, the proposed model is a standard transshipment programming problem. The feature of such a programming problem is

that both the input quantity and the output quantity of medical resources in each DC are unknown. Hence, we design a heuristic algorithm to solve the proposed model, which is presented as follows:

Procedure:

Input: parameters of the SEIR model, c_{ij}, r_{ij} and a_{it} .

Output: the final optimal allocation result

Begin

Solve the ODE and decompose the problem into n correlated sub-problems (n decision-making cycles);

$t \leftarrow 0$;

while (not termination condition) do

Forecast the demand d_{kt} ;

Solve the programming model on decision cycle t ;

Obtain the allocation result p_t ;

$t \leftarrow t + 1$;

end

Output the medical resources allocation result and the cost for each decision-making cycle.

End

4. Numerical Example and Discussion

4.1 Numerical Example

In this section, we rely on a numerical example to demonstrate the efficiency of the proposed method. The tests are performed on a personal computer equipped with a Intel (R) Core (TM) 3.10 GHz CPU and 4.0 Gb of RAM in the environment of Microsoft Window 7. Since the proposed programming model is

formulated as a multi-stage integer programming model, we can solve it by MATLAB coupled with the optimal software CPLEX 12.4.

An area, with 2 medicine suppliers that supply the medicine for the influenza, 4 distribution centers (DC) that store and distribute the medicine to the local hospitals based on their demand, and 8 local hospitals(H) that are designated to host and treat the infected individuals, is assumed to be the hypothetical influenza outbreaks area. Initial values of the related parameters for the SEIR model are given in Table 1.

Taking region 1 as our example, Figure 4 depicts the numerical simulation result if no medical resources could be allocated. The computation time to solve the ODE is less than 10 seconds. The four curves respectively represent the number of four groups of people (S, E, I, R) over time. As a numerical test, we extract the time interval from the 15th day (decision-making cycle $t=0$) to the 45th day (decision-making cycle $t=30$) to be the second response stage of the influenza diffusion process according to our previous works (Liu et al. 2011,

Liu and Zhao 2012). Of course, the time range for the response stage can be adjusted correspondingly when different influenza outbreak occurs.

Let $\lambda = 1$ and $\omega = 1$, there are 30 iterations for the test and we can rewrite the demand for medical resources as $d_t^* = I(t), t \in T$. Meanwhile, we can obtain the difference factor η_t for each decision cycle. Moreover, let $\Gamma = 15$ (days) and suppose the production capacity of each supplier is 2,000 units of medical resources daily. Therefore, with the given coefficient matrix of transportation cost between the different nodes (i.e. the suppliers, the DCs and the local hospitals), we can obtain the medical resources allocation result for the first decision cycle. Coupling with the result, we can forecast the demand for the second decision cycle by using Equation (5). After that, we can solve the programming model for the second decision cycle and acquire the medical resources allocation result p_2 . Such phase is executed iteratively and the computation time to get the final optimal solution of the whole test is 457.81 seconds.

Table 1 Initial values of the relative parameters

Hospital(H)	Region 1	Region2	Region3	Region4	Region5	Region6	Region7	Region8
$S(0)$ (person)	5×10^3	4.5×10^3	5.5×10^3	5×10^3	6×10^3	4.8×10^3	5.2×10^3	4×10^3
$E(0)$ (person)	30	35	30	40	25	40	50	45
$I(0)$ (person)	5	6	7	8	4	7	9	10
$R(0)$ (person)				0				
β				4×10^{-5}				
δ				0.3				
α				1×10^{-3}				
τ (day)				5				

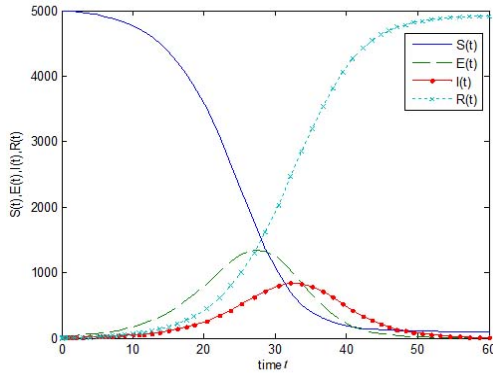


Figure 4 Numerical simulation of the SEIR model

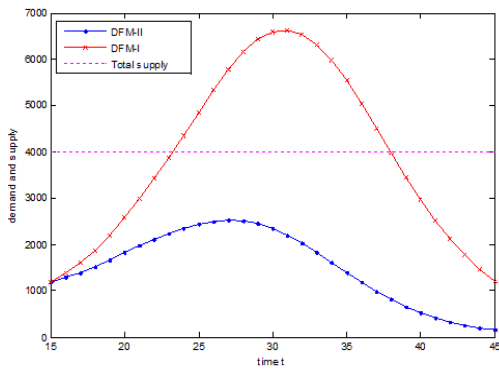


Figure 5 Demand for medical resources over time

Figure 5 shows the changes in demand for medical resources during the entire testing response stage. While DFM-I is adopted to forecast the demand, medical resources supply is not enough from the 24th day to the 38th day. To avoid the stock-out situation, the suppliers should either improve their production capacity or replenish medical resources from other emergency suppliers. Whatever, the effect that medical resources allocated in early periods takes effect in subduing the spread of influenza and thus impacts the demand in the later period is ignored. While DFM-II is adopted, the above stock-out problem is no longer a problem. That

means, the assumption that each supplier has a production capacity of 2,000 is feasible for the entire process. The second observation from Figure 5 is that both curves exhibit similar trends, namely, the demand will first increase along with the spread of influenza, and then decrease after it is under control. However, it is magnified while DFM-I is adopted to predict the demand, and the proposed DFM-II is superior to the first one in less waste of medical resources.

4.2 Comparison and Discussion

It is easy to obtain the global optimal solution of the programming model in the above test, since medical resources are provided enough. Herein, we refer it as ‘the global allocation mode’. An obvious question is that what will happen when the production capacity is limited? For example, if each supplier can only provide 1,000 units of medical resources in each decision cycle, does the global allocation mode still efficient to assign the medical resources? Moreover, based on our interviews with the public healthcare administrative personnel in China, an empirical method has always been adopted in practice. In such manual method, if medical resources supply is adequate, the demand in each hospital would be satisfied. Otherwise, while medical resources are limited provided, they would be allocated to each hospital according to the proportion of its demand in the total demand. Herein, we call it “the equilibrium allocation mode”, which can be formulated as follows.

$$p_{kt} = \begin{cases} d_{kt}, & \text{if } \sum_{k \in H} d_{kt} \leq \sum_{i \in S} a_{it}, \\ \frac{d_{kt} \sum_{i \in S} a_{it}}{\sum_{k \in H} d_{kt}}, & \text{if } \sum_{k \in H} d_{kt} > \sum_{i \in S} a_{it}, \end{cases} \quad \forall k \in H, t \in T \quad (14)$$

Holding all the other parameters fixed as in numerical example given in Section 4.1, except that production capacity of each supplier, which is limited as 1,000 for each decision cycle. We calculate the whole test again and obtain the new final allocation results for each decision cycle. The comparison of supply and demand matching between these two methods is shown in Figure 6. Both allocation modes cannot avoid the problem of stock-out, and medical resources supply is not enough from the 22th day to the 34th day.

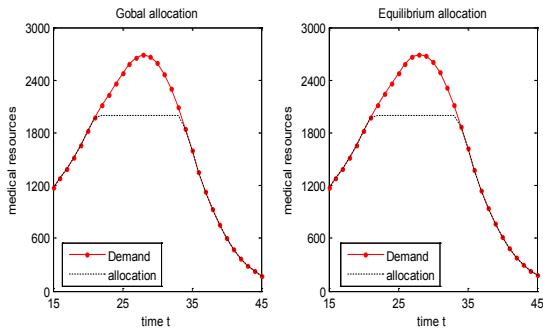
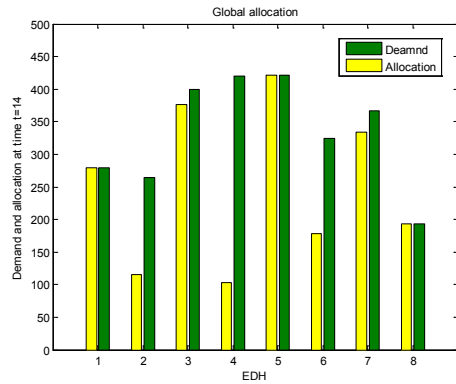


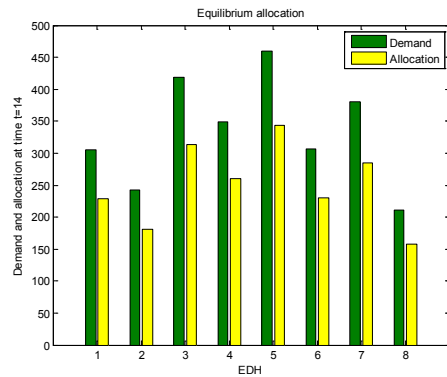
Figure 6 Total demand of medical resources in each decision cycle

To make a clear comparison between these two allocation results, we extract the final result on the decision cycle $t=14$ (the 29th day) as our example. The comparison result is shown in Figure 7. When we adopt the global allocation mode to assign the restricted medical resources, hospitals 1, 5 and 8 are supplied adequately, and the others are provided partially (see Figure 7(a)). The total allocation cost on this decision cycle is 6,475RMB. However, when we implement the equilibrium allocation mode to assign the medical resources, significant gaps between supply and demand for each EDH are presented (see Figure 7(b)). The reason is that medical resources are allocated to each hospital

according to the proportion of its demand in the total demand. The larger the demand is, the larger the shortage is. The total allocation cost for this mode is 6,642 RMB. Therefore, it can be concluded that the equilibrium allocation mode, which is always adopted as an empirical method in practice, is uneconomical.



(a)



(b)

Figure 7 Supply and demand on decision cycle $t=14$ (the 29th day)

In addition, we calculate the difference between the two total costs for these two modes. We also present the cumulative deficit for the cost difference. The results are shown in Figure 8. Superficially, it is difficult to distinguish

which mode is the better one; but on the whole, the total allocation cost by using equilibrium allocation mode is the higher one. The second observation from Figure 8 is that the total quantity of medical resources allocated by using the equilibrium allocation mode is 44,741 units, and the total allocation cost is 150,076 RMB for the whole 30 decision cycles. However, these two values in global allocation mode are 44,760 units and 149,615 RMB, respectively. It can be concluded that the global allocation mode is more efficient, because it assigns more medical resources within less cost during the same time interval.

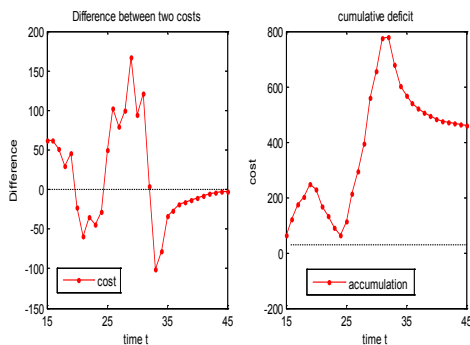


Figure 8 Cost comparison between the two modes

4.3 A Short Sensitivity Analysis

In this section, we present a short sensitivity analysis of the parameter Γ in time-varying demand forecasting model. Holding all the other parameters fixed as in numerical example given in Section 4.1, except that Γ takes on five different values (10, 12, 15, 18 and 20), respectively. The total allocation cost on each decision cycle is shown in Figure 9. As Figure 9 shows, the shorter Γ is, the lower allocation cost is. It is worth mentioning that such a phenomenon only appears when medical resources are supplied adequately. The second

observation from Figure 9 is that the occurrence time and the duration time of the stock-out are earlier and longer respectively as the growth of Γ . The reason is that more medical resources would be required to treat the infected people if the treatment cycle is extended. Therefore, the total allocation cost would be increased and the duration time of stock-out would be extended. The above analysis confirms that this parameter plays an important role in medical resources allocation decisions. For a small change of Γ , the final allocation decisions and the total operation cost will be changed significantly.

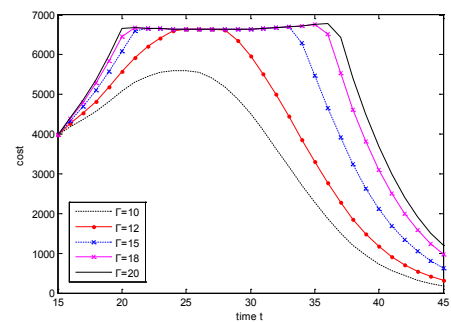


Figure 9 Total cost with different value of Γ

5. Conclusions

In this paper, we rely on a discrete time-space network to describe medical resources allocation problem when an unexpected influenza is outbreak. We formulate the problem as a multi-stage integer programming model with time-varying demand based on the SEIR diffusion rule. The three main differences that distinguish this work from the past literatures are presented as follows.

Firstly, the model proposed in this paper addresses a time-series demand that is forecasted in match of the course of influenza diffusion. The model couples a multi-stage integer

programming for optimal allocation of medical resources with a proactive forecasting mechanism cultivated from influenza diffusion dynamics. The rationale that medical resources allocated in early periods take effect in subduing the spread of influenza and thus impact demand in later periods has been for the first time incorporated into our model.

Secondly, the computational results based on a numerical example show that the proposed model is superior to the general measures in terms of cost reduction and medical resources control. Our model can reduce the total operation cost of medical resources allocation and may get influenza diffusion in control earlier than general measures.

Last but not least, medical resources allocation problem has always been formulated as vehicle routing problem (VRP), or vehicle routing problem with time windows (VRPTW) in precious literatures, which includes many sub-tour constraints and is difficult to be solved. In this paper, we decompose medical resources allocation problem into several mutually correlated sub-problems, and solve them systematically in the same decision scheme subsequently. Therefore, the proposed method is more suitable for an actual decision-making support.

The next research steps of this paper incorporate a more realistic influenza diffusion model including features such as subdivision of the population by risk group and disease stage. It can also include the cross area diffusion between two or more geographic areas, and the incorporation of purchase lead time of medical resources. In addition, the utilization of multiple resources in model is another important topic for

the further research.

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References

- [1] Adida, E., Dey, D. & Mamani, H. (2013). Operational issues and network effects in vaccine markets. *European Journal of Operational Research*, 231(2): 414-427.
- [2] Aleman, D.M., Wibisono, T.G. & Schwartz, B. (2011). A nonhomogeneous agent-based simulation approach to modeling the spread of disease in a pandemic outbreak. *Interfaces*, 41(3): 301-315.
- [3] Arifoğlu, K., Deo, S. & Irvani, S. (2012). Consumption externality and yield uncertainty in the influenza vaccine supply chain: interventions in demand and supply sides. *Management Science*, 58(6): 1072-1091.
- [4] Brandeau, M. (2005). Allocating resources to control infectious diseases. *Operations Research and Health Care*, 70(3): 443-464.
- [5] Brandeau, M.L., Zaric, G.S. & Richter, A. (2003). Resources allocation for control of infectious diseases in multiple independent

- populations: beyond cost-effectiveness analysis. *Journal of Health Economics*, 22(4): 575-598.
- [6] Brauer, F. & Castillo-Chávez, C. (2012). *Mathematical Models in Population Biology and Epidemiology*. Springer, New York.
- [7] Craft, D.L., Wein, L.M. & Alexander, H.W. (2005). Analyzing bioterror response logistics: the case of anthrax. *Management Science*, 51(5): 679-694.
- [8] Dai, T.L., Cho, S.H. & Zhang, F.Q. (2014). Contracting for on-time delivery in the U.S. influenza vaccine supply chain. Available at SSRN: <http://dx.doi.org/10.2139/ssrn.2178157>. 6 May, 2014.
- [9] Dasaklis, T.K., Pappis, C.P. & Rachaniotis, N.P. (2012). Epidemics control and logistics operations: a review. *International Journal of Production Economics*, 139(2): 393-410.
- [10] Deo, S. & Corbett, C. J. (2009). Cournot competition under yield uncertainty: the case of the U.S. influenza vaccine market. *Manufacturing & Service Operations Management*, 11(4): 563-576.
- [11] Duintjer Tebbens, R.J., Pallansch, M.A., Alexander, J.P. & Thompson, K.M. (2010). Optimal vaccine stockpile design for an eradicated disease: application to polio. *Vaccine*, 28(26): 4312-4327.
- [12] Elizabeth Halloran, M., Ferguson, N.M., Eubank, S., et al. (2008). Modeling targeted layered containment of an influenza pandemic in the United States. *Proceedings of the National Academy of Sciences*, 105(12): 4639-4644.
- [13] Germann, T.C., Kadau, K., Longini, I.M. & Macken, C.A. (2006). Mitigation strategies for pandemic influenza in the United States. *Proceedings of the National Academy of Sciences*, 103(15): 5935-5940.
- [14] Harko, T., Lobo, F. & Mak, M.K. (2014). Exact analytical solutions of the Susceptible-Infected-Recovered (SIR) epidemic model and of the SIR model with equal death and birth rates. *Applied Mathematics and Computation*, 236, 184-194.
- [15] Kermack, W.O. & McKendrick, A.G. (1927). A contribution to the mathematical theory of epidemics. *Proceedings of the Royal Society A: containing papers of a mathematical and physical character*, 115(772): 700-721.
- [16] Kim, K.I., Lin, Z.G. & Zhang, L. (2010). Avian-human influenza epidemic model with diffusion. *Nonlinear Analysis: Real World Applications*, 11(1): 313-322.
- [17] Li, M.Y., Graef, J.R., Wang, L.C. & Karsai, J. (1999). Global dynamics of a SEIR model with varying total population size. *Mathematical Biosciences*, 160(2): 191-213
- [18] Liu, J.L. & Zhang, T.L. (2011). Epidemic spreading of an SEIRS model in scale-free networks. *Communications in Nonlinear Science and Numerical Simulation*, 16(8): 3375-3384.
- [19] Liu, M. & Zhao, L.D. (2012). An integrated and dynamic optimisation model for the multi-level emergency logistics network in anti-bioterrorism system. *International Journal of Systems Science*, 43(8): 1464-1478.
- [20] Liu, Q. & Chen, Q.M. (2015). Analysis of the deterministic and stochastic SIRS epidemic models with nonlinear incidence. *Physica A: Statistical Mechanics and Its*

- Applications, 428, 140-153.
- [21]Mishra, B.K. & Saini, D.K. (2007). SEIRS epidemic model with delay for transmission of malicious objects in computer network. *Applied Mathematics and Computation*, 188(2): 1476-1482.
- [22]Rachaniotis, N.P., Dasaklis, T.K. & Pappis, C.P. (2012). A deterministic resources scheduling model in epidemic control: a case study. *European Journal of Operational Research*, 216(1): 225-231.
- [23]Rottkemper, B., Fischer, K. & Blecken, A. (2012). A transshipment model for distribution and inventory relocation under uncertainty in humanitarian operations. *Socio-Economic Planning Sciences*, 46(1): 98-109.
- [24]Samsuzzoha, M., Singh, M. & Lucy, D. (2010). Numerical study of an influenza epidemic model with diffusion. *Applied Mathematics and Computation*, 217(7): 3461-3479.
- [25]Samsuzzoha, M., Singh, M. & Lucy, D. (2012). A numerical study on an influenza epidemic model with vaccination and diffusion. *Applied Mathematics and Computation*, 219(1): 122-141.
- [26]Savachkin, A. & Uribe, A. (2012). Dynamic redistribution of mitigation resources during influenza pandemics. *Socio-Economic Planning Sciences*, 46(1), 33-45.
- [27]Stinnett, A.A. & Paltiel, A.D. (1996). Mathematical programming for the efficient allocation of health care resources. *Journal of Health Economics*, 15(5): 641-653.
- [28]Sun, C.J. & Hsieh, Y.H. (2010). Global analysis of an SEIR model with varying population size and vaccination. *Applied Mathematical Modelling*, 34(10): 2685-2697.
- [29]Sun, L., DePuy, G.W. & Evans, G.W. (2013). Multi-objective optimization models for patient allocation during a pandemic influenza outbreak. *Computers & Operations Research*, 51, 350-359.
- [30]Van Zon, A.H. & Kommer, G.J. (1999). Patient flows and optimal health-care resources allocation at the macro-level: a dynamic linear programming approach. *Health Care Management Science*, 2(2): 87-96.
- [31]Vlah, J.S. & Rui, F.J. (2012). Multi-objective scheduling and a resources allocation problem in hospitals. *Journal of Scheduling*, 15(5), 513-535.
- [32]Wein, L.M., Liu, Y.F. & Leighton, T.J. (2005). Evaluation of a HEPA/vaccine plan for indoor remediation after an airborne anthrax attack. *Emerging Infectious Diseases*, 11(1): 69-76.
- [33]Yamin, D. & Gaviou, A. (2013). Incentives' Effect in Influenza Vaccination Policy. *Management Science*, 59(12): 2667-2686.
- [34]Yan, S.Y., Lin, C.K. & Chen, S.Y. (2014). Logistical support scheduling under stochastic travel times given an emergency repair work schedule. *Computers & Industrial Engineering*, 67, 20-35.
- [35]Yan, S.Y., Lin, J.R. & Lai, C.W. (2013). The planning and real-time adjustment of courier routing and scheduling under stochastic travel times and demands. *Transportation Research Part E: Logistics and Transportation Review*, 53, 34-48.
- [36]Yan, S.Y. & Shih, Y.L. (2009). Optimal scheduling of emergency roadway repair

and subsequent relief distribution. *Computers and Operations Research*, 36(6): 2049-2065.

[37]Zaric, G.S. & Brandeau, M.L. (2001). Resources allocation for epidemic control over short time horizons. *Mathematical Biosciences*, 171(1): 33-58.

[38]Zaric, G.S. & Brandeau, M.L. (2002). Dynamic resources allocation for epidemic control in multiple populations. *Journal of Mathematics Applied in Medicine and Biology*, 19(4): 235-255.

[39]Zaric, G.S., Bravata, D.M., Cleophas Holty, J.E., McDonald, K.M., Owens, D.K. & Brandeau, M.L. (2008). Modeling the logistics of response to anthrax bioterrorism. *Medical Decision Making*, 28(3): 332-350.

[40]Zhang, J., Li, J.Q. & Ma, Z.E. (2006). Global Dynamics of an SEIR epidemic model with immigration of different compartments. *Acta Mathematica Scientia*, 26(3): 551-567.

[41]Zhang, J. & Ma, Z.E. (2003). Global dynamics of an SEIR epidemic model with saturating contact rate. *Mathematical Biosciences*, 185(1): 15-32.

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