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Epidemic-logistics Modeling: A New Perspective on Operations Research



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Beijing



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Preface

Infectious disease outbreaks have unfortunately been very real threats to the general population and economic development in the past decades whether they are caused by nature or bioterrorism. A typical example was the H1N1 outbreak in 2009, which spread quickly around the world and ultimately affected millions of people in 214 countries, including 128,033 confirmed cases in China. In 2010, more than 600,000 infected cases were reported, and 8000 lives were lost because of the cholera outbreak in Haiti. A more recent example of an epidemic outbreak was the 2014–2015 Ebola pandemic in West Africa, which infected approximately 28,610 individuals, and approximately 11,300 lives were lost in Guinea, Liberia, and Sierra Leone. Therefore, it can be observed that the global burden of epidemics has tremendously increased in recent years.

To our knowledge, many countries have drafted emergency response plans and operational frameworks for immediately implementing the related strategies within 24 hours after the severity of an unexpected pandemic is confirmed. In China, a certain amount of emergency budget will be allocated for quick response according to the severity level of the unexpected epidemic. Emergency medical center will designate several local hospitals to treat infected individuals. Usually, this means a certain section of the appointed hospital will be isolated for quarantining and treating the infectious patients, but not the entire hospital. However, determining the optimal resource allocation to control an unexpected epidemic is a complex optimization problem. On the one hand, managers should understand how the disease propagates and how to model the epidemic dynamics. On the other hand, managers need to know how to bridge the gap between epidemic dynamics and resource allocation. Therefore, an integrated model for epidemic control should foresee the impacts of different resource allocation scenarios on epidemic development, simultaneously and interactively. This is the focus and main contribution of our book. The objective of this book is to develop a general optimization modeling framework to help decision makers minimize infections and death due to an epidemic. The model provides information on the spread dynamics of infections, and where and when to allocate limited resources. To facilitate readers understanding of this book, we briefly introduce all contents as follows:

In Chap. 1, we introduce the basic concept of epidemic-logistics, including the basic knowledge of epidemic dynamics, literature review of epidemics control and logistics operations, and several future directions for epidemic-logistics research.

In Chap. 2, we present epidemic dynamics modeling and analysis, including epidemic dynamics in anti-bioterrorism system, epidemic dynamics modeling for influenza, and epidemic dynamics considering population migration.

In Chap. 3, we design a mixed distribution mode for emergency resources in anti-bioterrorism system, which can find a trade-off between the point-to-point delivery mode and the multi-depot, multiple traveling salesmen delivery systems.

In Chaps. 4 and 5, we propose a discrete time–space network model for allocating medical resource following an epidemic outbreak. It couples a forecasting mechanism for dynamic demand of medical resource based on an epidemic diffusion model and a multistage programming model for optimal allocation and transport of such resource. In Chap. 4, we consider the scenario of that emergency medical resource is enough. While in Chap. 5, we conduct the scenario of that emergency medical resource is limited.

In Chaps. 6 and 7, we research the integrated optimization models for epidemic-logistics network. With the consideration of emergency resources allocated to the epidemic areas in the early rescue cycles will affect the demand in the following periods, we construct two integrated and dynamic optimization model with time-varying demand based on the epidemic diffusion rule.

In Chap. 8, we present a novel FPEA model for medical resources allocation in epidemic control. It couples a forecasting mechanism, constructed for the demand of medicine in the course of such epidemic diffusion and a logistics planning system to satisfy the forecasted demand and minimize the total cost. The model is built as a closed-loop cycle, comprising forecast phase, planning phase, execution phase, and adjustment phase.

In Chap. 9, we modify the proposed epidemics-logistics model in Büyüktaktakın et al. (2018) by changing capacity constraint and then apply it to control the 2009 H1N1 outbreak in China. We formulate the problem to be a mixed-integer non-linear programming model and simultaneously determine when to open the newly isolated wards and when to close the unused isolated wards.

In Chap. 10, we conduct the logistics planning for hospital pharmacy trusteeship under a hybrid of uncertainties. We present two medicine logistics planning models by using a time–space network approach, one with deterministic variables and the other with stochastic variables.

In Chap. 11, we propose two optimal models for medical resources order and shipment in community health service centers, with a dual emphasis on minimizing the total operation cost and improving the operation level in practice. The first planning model is a deterministic planning model. It considers constraints including the lead time of the suppliers, the storage capacity of the medical institutions, and the integrated shipment planning in the dimensions of time and space. Considering the stochastic demand, the second model is constructed as a stochastic programming model.

In Chap. 12, we continuously use time–space network technologies to conduct the problem of medical resources order and shipment. The optimization models are mixed 0-1 integer programming model and chance-constrained programming model, respectively.

In Chap. 13, we present two optimization models for optimizing the epidemic-logistics network. In the first one, we formulate the problem of emergency materials distribution with time windows to be a multiple traveling salesman problem. While in the second one, we propose an improved location allocation model with an emphasis on maximizing the emergency service level.

Although there are only three names on the cover of this book, we want to thank all contributors for their excellent contributions without which this book is impossible. Specifically, we would like to thank Prof. Lindu Zhao from Southeast University (China), Prof. Ding Zhang from State University of New York, Oswego (USA), Prof. Jennifer Shang from University of Pittsburgh (USA), and Prof. Hans-Jürgen Sebastian from RWTH Aachen University (Germany). We thank them for their suggestions and comments when we write the initial manuscripts. Of course, we would like to acknowledge the support of National Natural Science Foundation of China (No. 71771120), National Social Science Foundation of China (No. 16ZDA054), MOE (Ministry of Education) Project of Humanities and Social Sciences (No. 17YJA630058), and Six Major Talents Peak Project of Jiangsu Province (XYDXXJS-CXTD-005). Without financial support, this book cannot be published. Finally, we wish to thank the staff at Science Press and Springer Press for their support, encouragement, and assistance.

There is an old Chinese saying that states “May you live in interesting times.” For both academics and practitioners of emergency management, those times are now, and we should take full advantage of the opportunity, and enjoy it while doing so!

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Chapter 1

Basic Concept of Epidemic-Logistics



The goal of this book is to introduce a part of research directions on epidemic dynamics investigated by our research group and our main results during the past several years. Before this, some basic knowledge on epidemic dynamics will be introduced which may be helpful to those readers who are not familiar with the mathematical modeling on epidemiology.

1.1 Basic Knowledge of Epidemic Dynamics

Epidemic dynamics is an important method for studying the spread of infectious disease, either qualitatively or quantitatively. It is based on the specific property of population growth, the spread rules of infectious diseases, and the related social factors, etc., to construct mathematical models reflecting the dynamic properties of infectious diseases, to analyze the dynamical behavior and to do some simulations. The research results are helpful to predict the developing tendency of the infectious disease, to determine the key factors of the spread of infectious disease and to seek the optimum strategies of preventing and controlling the spread of infectious diseases. In contrast with classic biometrics, dynamical methods can show the transmission rules of infectious diseases from the mechanism of transmission of the disease, so that people may know some global dynamic behaviors of the transmission process. Combining statistics methods and computer simulations with dynamic methods could make modeling and the original analysis more realistic and more reliable.

The popular epidemic dynamic models are compartmental models which were constructed by Kermack and Mckendrick [1] and were developed by many other bio-mathematicians. In the classic K-M model, the population is divided into three compartments: susceptible compartment (S), in which all individuals are susceptible to the disease; infected compartment (I), in which all individuals are infected by the disease and have infectivity; removed compartment (R), in which all the individuals recovered from the compartment (I) and have permanent immunity. There are three assumptions for the proposed SIR model:

- (1) The disease spreads in a closed environment, no emigration and immigration, and no birth and death in population, so the total population remains a constant k , i.e. $S(t) + I(t) + R(t) \equiv k$.
- (2) The infective rate of an infected individual is proportional to the number of susceptible individuals, and the coefficient of the proportion is a constant β , so that the total number of new infected people at time t is $\beta S(t)I(t)$.
- (3) The recovered rate is proportional to the number of infected individuals and the coefficient of proportion is a constant γ . So, the recovered rate at time t is $\gamma I(t)$.

According to the three assumptions above, it is easy to establish the epidemic model as follows

$$\begin{cases} \frac{dS}{dt} = -\beta SI \\ \frac{dI}{dt} = \beta SI - \gamma I, S(t) + I(t) + R(t) \equiv k \\ \frac{dR}{dt} = \gamma I \end{cases} \quad (1.1)$$

In what follows, let us explain some basic concepts on epidemiological dynamics.

1.1.1 Adequate Contact Rate and Incidence

It is well-known that the infections are transmitted through the contact. The number of times an infective individual contacts the other members in unit time is defined as **contact rate**, which often depends on the number N of individuals in the total population, and is denoted by function $U(N)$. If the individuals contacted by an infected individual who are susceptible, then they may be infected. Assume that the probability of infection by every time contact is β_0 , then function $\beta_0 U(N)$ is called **the adequate contact rate**, which shows the ability of an infected individual infecting others (depending on the environment, the toxicity of the virus or bacterium, etc.). Except the susceptible individuals, the individuals in other compartments of the population can't be infected when they contact with the infective, and the fraction of the susceptible in total population is S/N , so the mean adequate contact rate of an infective person to the susceptible individuals is $\beta_0 U(N)S/N$, which is called **the infection rate**. Further, the number of new infected individuals yielding in unit time at time t is $\beta_0 U(N)S(t)I(t)/N(t)$, which is called the **incidence of the disease**.

When $U(N) = kN$, that is, the contact rate is proportional to the size of total population, the incidence is $\beta_0 k N S(t)I(t)/N(t) = \beta S(t)I(t)$ (where $\beta = \beta_0 k$ is defined as the transmission coefficient), which is called **bilinear incidence or simple mass-action incidence**. When $U(N) = k'$, that is, the contact rate is a constant, and the incidence is $\beta_0 k' S(t)I(t)/N(t) = \beta S(t)I(t)/N(t)$ (where $\beta = \beta_0 k'$) which is called **standard incidence**. For instance, the incidence formulating the sexually transmitted disease is often of standard type. Two types of incidence mentioned

above are often used, but they are special for the real cases. In recent years, some contact rates with saturate feature between them are proposed, such as $U(N) = \alpha N / (1 + \omega N)$ [2], $U(N) = \alpha N / (1 + bN + \sqrt{1 + 2bN})$ [3]. In general, the saturate contact rate $U(N)$ satisfies the following conditions:

$$U(0) = 0, U'(N) \geq 0, (U(N)/N)' \leq 0, \lim_{n \rightarrow \infty} U(N) = U_0 \quad (1.2)$$

Moreover, some incidences, which are much more plausible for some special cases, are also introduced, such as $\beta S^q I^q$ [4] and $\beta S^q I^q / N$ [5].

1.1.1.1 Basic Reproduction Number

Basic reproduction number, denoted by R_0 , represents the average number of secondary infectious infected by an individual of infective during whose whole course of disease in the case that all the members of the population are susceptible. According to this definition, it is easy to understand that if $R_0 < 1$ then all the infective individuals will decrease so that the disease will go to extinction; otherwise, if $R_0 > 1$ then all the infective individuals will increase so that the disease can not be eliminated and usually develop into an endemic.

From the mathematical perspective, when $R_0 < 1$, the model has only disease free equilibrium $E_0(S_0, 0)$ in the SOI plane, and E_0 is globally asymptotically stable; when $R_0 > 1$, the equilibrium becomes unstable and usually a positive equilibrium $E^*(S^*, I^*)$ appears. E^* is called an endemic equilibrium and in this case it is stable. Hence, if all the members of a population are susceptible in the beginning, then $R_0 = 1$ is usually a threshold whether the disease go to extinction or go to an endemic. For example, considering the following model:

$$(M_1) \begin{cases} \frac{dS}{dt} = \Delta - \beta SI - bS \\ \frac{dI}{dt} = \beta SI - bI - \gamma I \\ \frac{dR}{dt} = \gamma I - bR \end{cases} \quad (1.3)$$

where b is the natural death rate, γ is the recovered rate, Δ is recruitment. Let $\Delta/b = k$, consider the first two equations we have:

$$(M'_1) \begin{cases} \frac{dS}{dt} = bk - \beta SI - bS \\ \frac{dI}{dt} = \beta SI - (b + \gamma)I \end{cases} \quad (1.4)$$

Let $R_0 = \frac{\beta k}{b + \gamma}$, it is easy to see that when $R_0 < 1$, the system has only one disease free equilibrium $E_0(k, 0)$ and it is stable; when $R_0 > 1$, besides E_0 there is a positive

equilibrium $E^* (\frac{b+\gamma}{\beta}, \frac{b[\beta k - (b+\gamma)]}{\beta(b+\gamma)})$. In this case, E_0 is unstable, E^* is stable, and the endemic appears.

From model (M'_1) we can see that:

$$\frac{dN}{dt} = b(k - N), \quad N(t) = S(t) + I(t) + R(t) \quad (1.5)$$

Hence, the total number of the population is k , and βk should be the number of secondary infectious infected by an individual of infective per unit time when the number of susceptible is k . From the second equation of the system (M'_1) , we can see that $1/(b + \gamma)$ is the average course of the disease. Therefore, $R_0 = \beta k/(b + \gamma)$ is the average secondary infectious infected by an individual of the infective during whose whole course of disease, which is just the reproduction number. It is worth mentioning that the reproduction number is not always equivalent to the threshold mentioned above.

1.2 Epidemics Control and Logistics Operations

According to Dasaklis et al. [6], governmental agencies and health institutions should be prepared in advance for the control of epidemic outbreaks. This means that they should have in place robust contingency plans addressing issues like the availability of emergency medical stocks and well-trained personnel, their appropriate deployment, the availability of different types of vehicles for the transportation of essential medical supplies and commodities etc. Generally, it remains very difficult to define whether the needs for producing and distributing vaccines in the case of e.g. a possible pandemic influenza outbreak can be met [7, 8] by existing capacities. Consequently, any attempt to contain an epidemic outbreak demands real-time solutions that should ensure the effective management of all the logistics activities taking place, since sometimes these activities may become a real nightmare if not managed properly [9]. In the sequence, an inventory of all the logistics operations taking place during the various phases of an epidemic's containment effort is provided. Generally, these phases could be classified as follows [10, 11]:

- Preparedness
- Outbreak investigation
- Response
- Evaluation.

1.2.1 Preparedness

Many organizations around the world have established preparedness plans in the case of epidemic or pandemic outbreaks. Such plans range from community to national level and they include all the measures required for the successful containment of an outbreak. The World Health Organization has published several pandemic preparedness guidelines since 1999 and it updates them in the light of new developments regarding increased understanding of past pandemics, strengthened outbreak communications, greater insight on disease spread etc. [12].

Epidemic preparedness aims at maintaining a certain level of available resources so as to reduce morbidity and mortality when an epidemic outbreak occurs. This means that pharmaceuticals and supplies should remain accessible or kept in large quantities [13] in order to assist a prompt response, if necessary. Procurement of vaccines and medical supplies and their exact storing location play a crucial role for the outcome of any containment effort. For instance, the Strategic National Stockpile (SNS) program in the United States is an indicative preparedness program with the objective to maintain large quantities of medicine and medical supplies and to provide these materials to states and communities within twelve hours in the event of a large-scale public health emergency [14]. In addition, a certain amount of vaccines should be available for the immunization of control teams and health-care workers. This is of great importance as medical personnel will treat the very first infected persons and should be protected against the disease that causes the outbreak. Among the most important logistics operations taking place and relevant logistics-oriented decisions to be made during the phase of preparedness are the following [10–12]:

- Identification of sources for the procurement of medical supplies and relevant commodities.
- Contract management for all the materials procured.
- Inventory management for all the essential medical supplies (vaccines, antibiotics, antiretroviral drugs) and supplementary medical commodities (personal protective supplies) kept.
- Periodical review and updating of medical supplies.
- Facility location and capacity determination for stockpiling centers.
- Network design for transportation/distribution activities and selection of appropriate means for transportation/distribution activities.
- Selection of appropriate vaccination facilities/health care systems and their capacity (size, availability of rooms and designated areas, availability and scheduling of personnel etc.).
- Availability of funds.

1.2.2 *Outbreak Investigation*

Outbreak investigation consists of the detection of any suspected outbreak and its confirmation through laboratory testing. In order to detect and confirm a suspected outbreak, surveillance systems must be put in place in order to provide the decision makers of the health agencies in charge with the essential information regarding any unexplained infection increases seen over a period of time through the systematic analysis of data collected. Surveillance systems provide adequate information that facilitates the development of an initial response framework where the type and magnitude of the containment effort could be determined once epidemic thresholds have been reached. The term epidemic threshold refers to the level of disease above which an urgent response is required. It is specific for each disease and depends on the infectiousness, other determinants of transmission and local endemicity levels [11].

Leading world health organizations have developed surveillance systems covering cases like pandemic outbreaks [15], epidemic outbreaks following natural disasters [11] or even possible disease outbreaks during mass gatherings [12]. Additionally, surveillance systems have been developed by the scientific community [16–18] and many researchers have studied relevant issues arising during the detection and confirmation of diseases outbreaks attributed to bioterrorist attacks [19–22] or epidemic outbreaks related to specific agents [23, 24]. It is worth mentioning that the development of a surveillance system to detect epidemic outbreaks that occur during emergency situations (like a humanitarian crisis) may necessitate taking into consideration some context-specific features like the target population, the political context, the poor infrastructure and, finally, the presence of multiple partners in the field. Among the logistics activities that support the detection and confirmation mechanisms of a suspected outbreak are [11, 25]:

- The provision of all the appropriate materials like report sheets to hospitals, emergency medical services and local public health departments that will be used for the collection of primary data regarding initial cases.
- The training of clinical workers to recognize unexpected patterns of the occurrence of specific diseases and to promptly identify and report suspected cases using standard definitions.
- The provision of all the necessary commodities and resources to the outbreak response team that will facilitate and ensure its operational deployment.
- The collection of specimens and their labeling.
- The secure transportation of specimens to the appropriate laboratory (using cold boxes and coolant blocks).
- The appropriate storage of specimens in the laboratory (kept within a specific temperature range).
- The procurement, handling, storing and distribution of laboratory commodities, their classification, their quality assurance and quality control etc.

It is clear that any successful attempt to contain an epidemic outbreak is closely related to the services provided by laboratories. These services rely on a huge number

of materials and commodities that laboratories utilize and they necessitate increased inventory management capabilities. Additionally, during epidemic outbreaks laboratories must ensure that they have the capacity to cope with increased testing demands [26]. A good reference regarding laboratory logistics can be found in U.S. Agency for International Development [25].

1.2.3 Response

Once leading health agencies have confirmed an epidemic outbreak, measures and control strategies must be implemented as soon as possible at a regional or national level. Treatment centers should be established and available resources such as medical supplies and personnel should be deployed rapidly in order to contain the epidemic before it reaches uncontrollable proportions. Vaccination of susceptible groups or isolation and quarantine of those infected are considered standard interventions for the containment of an epidemic. All measures taken must be based on a clear understanding of the agent's nature triggering the outbreak as some diseases necessitate specific control protocols to be followed [11]. This in turn calls for the availability of additional infrastructure and medical supplies within health care premises such as isolation rooms with good ventilation systems, respiratory equipment etc. The logistics operations and relevant decisions to be made during the phase of response to a confirmed outbreak refer to [10, 12]:

- The selection of facilities to serve as PODs.
- The periodical review and updating of supplies and commodities needed.
- The transportation/distribution of supplies and commodities from central warehouses to local POD.
- The procurement of supplies/resources once depleted.
- The dispensing of medical supplies, supplementary materials and commodities to the public.
- The establishment of a cold supply chain for the provision of essential medical supplies like vaccines.
- The daily/weekly capacity of available personnel to perform mass vaccination campaigns (for example the maximum number of people that can vaccinate per day).
- The scheduling of available vehicles to be used for transportation and distribution purposes.
- Adjustments to the capacity of health care facilities to hospitalize infected people.
- The management of patients in triage centers (clinical flow logistics).

During the phase of response laboratory logistics activities take place as it is very important for the parties involved to have a clear understanding of how the epidemic evolves over space and time (rate of spread among subpopulations). This will allow them to proceed to the necessary adjustments or modifications of the measures initially adopted in order for the new measures to be compliant with the data

analysis from laboratories tests [11]. Other logistics-oriented activities necessitated during this phase may be the safe disposal of body fuels or even the handling of dead bodies, the presence of troops to keep order etc.

1.2.4 Evaluation

After the epidemic has been contained, decision makers and public health policy makers engaged in the control efforts should proceed to evaluate all the measures undertaken during the previous phases. Generally, the evaluation phase is very useful as it provides strong insights towards a series of modifications that need to be made in order to increase the resilience of the control mechanisms in future epidemic outbreaks. Despite the fact that the evaluation phase entails limited physical movement of medical supplies and complementary commodities, it remains important from a logistical point of view. Many useful conclusions can be drawn with respect to logistics control operations such as [10]:

- The identification and assessment of possible bottlenecks or delays that hindered the deployment of the available medical supplies.
- The evaluation of the timeliness that should have been respected during the control of the epidemic.
- The follow-up and monitoring of patients for antibiotic effectiveness or vaccine immunoresponse.
- The identification of patients requiring dose modification or alternative treatment regimen due to adverse effects.
- The development of indicators regarding the performance of the logistics control operations.
- The assessment of coordination issues risen among the parties involved.
- The establishment and operation of rehabilitation procedures in the case of epidemic outbreaks in the aftermath of natural disasters.

All the above should lead to clear conclusions and, therefore, recommendations that will enhance the capabilities of the parties involved and will reduce vulnerabilities of the control mechanisms. Finally, the dissemination of knowledge and the lessons learned should take place among all the parties involved, from public health policy makers and health agencies to local communities.

1.3 Future Directions for Epidemic-Logistics Research

An effective epidemic management requires the combination of managerial decisions such as planning and resource allocation. Epidemiologic modeling provides useful insights for planning and mitigating against a possible disaster. However, the

absence of any significant academic contribution to disaster planning and implementation issues for the suggested control policies and intervention strategies remains a major gap in the literature. It is therefore the purpose of this book to emphasize the importance of logistics decisions at every stage of disaster management. As to the literature review of epidemic logistics, authors can go to Dasaklis et al. [6] and Adivar and Selen [27]. Despite the fact that some logistical considerations have already been incorporated into epidemics control approaches, the area of epidemics control supply chain still remains a promising research area. Following the insights provided in Dasaklis et al. [6], the authors proposed many opportunities for future research efforts, which include:

- (1) Multidisciplinary synergies
- (2) End-to-End approaches
- (3) More realistic assumptions for epidemic control logistics modeling
- (4) Inventory replenishment policies
- (5) Evaluation of models and large scale exercises
- (6) Development of harmonized approaches
- (7) Stochasticity
- (8) Quantification of contingency plans
- (9) Reverse logistics
- (10) Performance metrics
- (11) Responding to complex emergencies
- (12) Cross-functional drivers
- (13) Coordination issues.

Different from these directions, Adivar and Selen [27] considered the following decisions related to epidemic logistics: capacity planning for treatment or isolation facilities, bed capacities, resource allocation, including workforce and health care service, medical supply planning and corresponding make or buy decisions, the distribution and administration of drugs and vaccines, disaster information and communication management, and finally critical inventory management under turbulent disaster environment, i.e. for deteriorating items such as vaccines.

The chemical nature of vaccines and some drugs make their storage challenging. In addition, the handling, location and relocation of large quantities of medical supplies are associated with high costs which might cause inefficiency in overall aftermath effort. On the other hand, it is quite possible that medical resources will be limited at the very beginning of an epidemic. Timely and accurate distribution of medical supplies and health care services is essential in times of disaster. One practical example would be the prioritization of vaccine distribution among the population. This decision addresses cost minimization issues as well as issues that relate to maximizing the effectiveness of control policy. Some research indirectly engages with such logistical considerations whereas other considerations are addressed in more direct ways.

Vaccine production is also a critical issue due to its socio-economic importance. Especially for smallpox, vaccine production depends on international agreements

and relations. It is also important that vaccine is produced under governmental control to ensure the cost is equal and affordable for the whole population. Increased globalization and a growing number of transportation routes mean that re-emerging infectious diseases could have a serious impact on any country. Therefore, authorities in both developed and developing countries should ensure preparedness for a possible epidemic by promoting academic research. In spite of this need, as pointed out in our review, only a limited number of countries are investing in epidemic disaster surveillance.

It is well known that demographic and cultural factors significantly affect dispersion of an epidemic among population. Infection rates for elderly and young are different for many diseases. Countries with a younger, and therefore more socially and economically active population such as Turkey, are more prone to faster epidemic dispersion than, for example, western European countries where the population growth rate is lower and populations are older. Therefore, it is necessary to develop epidemiological models differentiating population by age and immunity level, and to prioritize the population for health care service delivery. Unfortunately, there is no mention of population differentiation in the models of any of the research articles reviewed.

In addition, Chen et al. [28] also proposed several directions for future research. From a view of disease, first, lots of models failed to combine some factors which can impact the number of casualties, such as the different periods in which the patients transfer into the current disease stage. Second, not all the papers studying the response to the diseases were based on real cases and the real emergency management plans. For example, most of the authors assume the recovery rate remains the same for the patients in the same stage while in reality, the recovery rate will decrease when the patients stay in the stage longer. Third, the number of infected individuals will affect the adopted response policy. If the development of the disease follows different disease development probability functions, the number of infected individuals will change. But many authors failed to consider about how disease development probability functions affect the medical interventions.

From a view of disease prevention and control plans, first, the side effect of the medical interventions are neglected by most of the authors. For example, the side effect of the mass vaccination of smallpox has often been neglected. Second, some key important logistics factors, such as the distribution capacity, are not taken into account. The medical intervention can work well only when the medical resources can be delivered in time with the right amount. Though some papers take, into account, the limitation of the medical treatment capacity, they do not address logistics questions like the number and the size of the antibiotic distribution centers. Moreover, most of the papers consider only one factor, which may affect the medical intervention, such as the vaccination coverage rate, but neglect the national stockpile. However, the sudden occurrence of epidemic may be more transmissible than we predicted and more people will be infected. So the national stockpile may be exhausted and a lot of individuals cannot get the medical help in time. In other words, the vaccination coverage policy cannot be executed well without enough medical resources. So, how to dispense medical resources sparingly to avoid exhausting the stockpile should be

studied as well. Third, some individuals, such as the old and the young, have the high possibilities to be infected and need special help. But most of the authors focus their attention on the general population, and neglected them who need the special help. Fourth, it can be found that most of the papers study the vaccination policy because vaccination is one of the most effective ways to prevent and control disease. However, the quarantine policy and isolation policy should also get enough attention.

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Chapter 2

Epidemic Dynamics Modeling and Analysis



Disastrous epidemic such as SARS, H1N1, or smallpox released by some terrorists can significantly affect people's life. The outbreak of infections in Europe in 2011 is another example. The infection, from a strain of *Escherichia coli*, can lead to kidney failure and death and is difficult to treat with antibiotics. A recent example of epidemic outbreak was the 2014–2015 Ebola pandemic in West Africa, which infected approximately 28,610 individuals and approximately 11,300 lives were lost in Guinea, Liberia, and Sierra Leone. It is now widely recognized that a large-scale epidemic diffusion can conceivably cause many deaths and more people of permanent sequela, which presents a severe challenge to the local or regional health-care systems. When an epidemic outbreaks, public officials face with many critical and complex issues, the most important of which is to make certain how the epidemic diffuses. This is the focus of this chapter.

2.1 Epidemic Dynamics in Anti-bioterrorism System

2.1.1 Introduction

Bioterrorism is the intentional use of harmful biological substances or germs to cause widespread illness and fear. It is designed to cause immediate damage and release dangerous substances into the air and surrounding environment. Because it would not usually be signaled by an explosion or other obvious cause, a biological attack may not be recognized immediately and may take local health care workers time to discover that a disease is spreading in a particular area.

Over the past few years, the world has been growing increasingly concerned about the threat that bioterrorists pose to societies, especially after the September 11 attacks and the fatal delivery of anthrax via the US Mail in 2001. Henderson [1] pointed out that the two most feared biological agents in a terrorist attack were smallpox and anthrax. Radosavljević and Jakovljević [2] proposed that biological

attacks can cause an epidemic of infectious disease. Thus, epidemiological triangle chain models can be used to present these types of epidemic. Bouzianas [3] presented that the deliberate dissemination of *Bacillus anthracis* spores via the US mail system in 2001 confirms their potential use as a biological weapon for mass human casualties. This dramatically highlights the need for specific medical countermeasures to enable the authorities to protect individuals from a future bioterrorism attack.

Actually, many recent research efforts have been devoted to understanding the prevention and control of epidemics, such as those of Wein et al. [4], Wein et al. [5], Craft et al. [6], Kaplan et al. [7, 8], Mu and Shen [9], Hiroyuki et al. [10], Tadahiro et al. [11], Michael et al. [12]. Various mathematical models have been proposed to analyze and study the general characteristics of each epidemic, such as SI, SIR, SIS, SIRS, SEI, SEIR, and others. It is worth mentioning that the major purpose of these articles is to compare the performance of the following two strategies, the traced vaccination (TV) strategy and the mass vaccination (MV) strategy. Furthermore, the epidemic diffusion models which they adopted are based on the traditional compartment model, while the complex topological structure of the social contact network is not considered.

As is well known, a class of network with a topology interpolating between that of lattices and random graphs is proposed by Watts and Strogatz [13]. In these models, a fraction of the links of the lattice is randomized by connecting nodes, with probability p , with any other node. For a range of p the network exhibits ‘small world’ behavior, where a local neighborhood (as in lattices) coexists with a short average path length (as in random graphs). Analysis of real networks reveals the existence of small worlds in many interaction networks, including networks of social contacts [14]. Recently, attention has been focused on the impact of network topology on the dynamics of the processes running on it with emphasis on the spreading of infectious diseases. For many infectious diseases, a small-world network on an underlying regular lattice is a suitable simplified model for the contact structure of the host population. It is well known that the contact network plays an important role in both the short term and the long term dynamics of epidemic spread [15]. Thus, one of the major motivations for studying the complex network in this work is to better understand the structure of social contact network, because there is a natural link between the epidemiological modeling and the science of complex network.

Jari and Kimmo [16] propose an SIR model for modeling the spreading process of randomly contagious diseases, such as influenza, based on a dynamic small-world network. A study by Masuda and Konno [17] presents a multi-state epidemic process based on a complex network. They analyze the steady states of various multi-state disease propagation models with heterogeneous contact rates. In many models, heterogeneity simply decreases epidemic thresholds. Xu et al. [18] present a modified SIS model based on complex networks, small-world and scale-free, to study the spread of an epidemic by considering the effect of time delay. Based on two-dimension small-world networks, a susceptible-infected (SI) model with epidemic alert is proposed by Han [19]. This model indicates that the broadcasting of a timely epidemic alert is helpful and necessary in the control of epidemic spreading, and is in agreement with the general view of epidemic alert. Shi et al. [20] propose a new

susceptible-infected-susceptible (SIS) model with infective medium. The dynamic behaviors of the model on a homogeneous network and on a heterogeneous scale-free network are considered respectively. Furthermore, it is shown that the immune density of nodes depends not only on the infectivity between individual persons, but also on the infectivity between persons and mosquitoes. Zhang and Fu [21] study the spreading of epidemics on scale-free networks with infectivity which is nonlinear in the connectivity of nodes. The result shows that nonlinear infectivity is more appropriate than a constant or a linear one. With unit recovery rate and nonlinear irrational infectivity, the epidemic threshold is always positive.

As mentioned in Craft et al. [6], deterrence is not a reliable strategy to against the terrorists, and it is difficult to get the biological agents out of the hands of terrorists before they attack. Our security against a biological attack rests largely on consequence management, i.e., how to ensure the availability and supply of emergency resource so that the loss of life can be minimized and the efficiency of each rescue can be maximized? Considering the relationship between an unexpected bioterror attack and the associated emergency logistics decisions, Liu and Zhao [22] focus on how to deliver emergency resources to the epidemic areas when a bioterror attack is suffered, and propose a mixed-collaborative distribution model for the emergency resources distribution based on the epidemic diffusion rule. A very recent research effort by Wang et al. [23] constructs a multi-objective stochastic programming model with time-varying demand for the emergency logistics network based on epidemic diffusion rule. It is worth mentioning that majority of the existing studies relies on different kinds of differential equations. For instance, first-order partial differential equations are used to integrate the age structures; second-order partial differential equations are suitable when a diffusion term exists; and integral differential equations or differential equations are often used when time delay or delay factors are considered.

2.1.2 *SIQRS Epidemic Diffusion Model*

(1) *Modeling assumptions and notations specification*

To facilitate the model formulation in the following section, three assumptions are specified as follows:

- (1) Once a bioterror attack is suffered, the epidemic area can be isolated from other areas to avoid the spread of the disease.
- (2) Natural birth and death coefficient of the population in the epidemic area are not considered.
- (3) Epidemic diffusion will not be disrupted by itself, which means the infection rate is a constant.

In this section, we consider the situation that epidemic diffusion without incubation period. Notations used in the following model are specified as follows (Table 2.1).

Table 2.1 Parameters specification

Parameters	Specification
N	The whole nodes in the affected area
$S(t)$	Susceptible nodes in the affected area which may become infected. $s(t) = S(t)/N$ represents its density
$I(t)$	Infected nodes in the affected area which are infective with strong infectivity, but have not yet been quarantined. $i(t) = I(t)/N$ represents its density
$Q(t)$	Quarantined nodes in the affected area which have been infected, and have been quarantined. $q(t) = Q(t)/N$ represents its density
$R(t)$	Recovered nodes in the affected area which have recovered from the disease. $r(t) = R(t)/N$ represents its density
$\langle k \rangle$	Average degree distribution of the network
β	Infection rate of the biological epidemic
γ	Rate of the recovered nodes transform to the susceptible nodes
δ	Rate of the infective nodes which will be found and quarantined
μ	Rate of quarantined nodes transform to the recovered nodes
d_1	Death rate of the infective nodes
d_2	Death rate of the quarantined nodes

Furthermore, $S(t) + I(t) + Q(t) + R(t) = N, s(t) + i(t) + q(t) + r(t) = 1$.

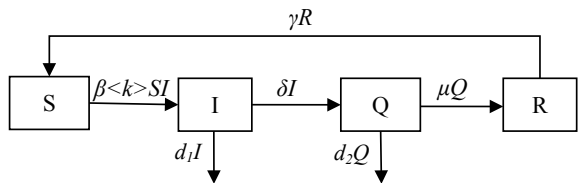
(2) **Model formulation**

Since quarantine is a common response measure when an epidemic outbreaks, here we divide people in the epidemic area into four groups: susceptible people (S), infected people (I), quarantined people (Q) and recovered people (R). The survey by Tham [24] shows that some of the recovered people who are discharged from the emergency department will be re-infected again. Thus, epidemic diffusion model in this section can be illustrated as Fig. 2.1.

For epidemic diffusion, models based on a small-world network match the actual social network much better. A great deal of attention has been paid to studying these models. Therefore, based on the mean-field theory [25], the time-based parameter $s(t)$ meets the following equation from time t to $t + \Delta t$:

$$s(t + \Delta t) - s(t) = -\beta \langle k \rangle s(t) i(t) \Delta t + \gamma r(t) \Delta t. \tag{2.1}$$

Fig. 2.1 Framework of SIQRS model



Thus, we get:

$$\frac{ds(t)}{dt} = -\beta \langle k \rangle s(t)i(t) + \gamma r(t). \quad (2.2)$$

Similarly, we have the other three ordinary differential equations as follows:

$$\frac{di(t)}{dt} = \beta \langle k \rangle s(t)i(t) - d_1 i(t) - \delta i(t). \quad (2.3)$$

$$\frac{dq(t)}{dt} = \delta i(t) - d_2 q(t) - \mu q(t). \quad (2.4)$$

$$\frac{dr(t)}{dt} = \mu q(t) - \gamma r(t). \quad (2.5)$$

Thus, the following SIQRS epidemic diffusion model can be formulated:

$$\begin{cases} \frac{ds(t)}{dt} = -\beta \langle k \rangle s(t)i(t) + \gamma r(t) \\ \frac{di(t)}{dt} = \beta \langle k \rangle s(t)i(t) - d_1 i(t) - \delta i(t) \\ \frac{dq(t)}{dt} = \delta i(t) - d_2 q(t) - \mu q(t) \\ \frac{dr(t)}{dt} = \mu q(t) - \gamma r(t) \end{cases}. \quad (2.6)$$

Here, $\beta, \langle k \rangle, \gamma, \delta, \mu, d_1, d_2 > 0$. Initial conditions for this epidemic diffusion model are demonstrated as follows:

$$i(0) = i_0 \ll 1, \quad s(0) = s_0 = 1 - i_0, \quad q(0) = r(0) = 0.$$

(3) Analysis of the epidemic diffusion model

As is well known, $i(0) = i_0 \ll 1$ and $s(0) = s_0 = 1 - i_0$, are initial percentage of infected people and susceptible people in the population, respectively. Obviously, when wide spread of the epidemic takes place, the following condition should be satisfied:

$$\left. \frac{di(t)}{dt} \right|_{t=0} > 0. \quad (2.7)$$

Considering Eq. (2.3), we have:

$$s_0 > \frac{d_1 + \delta}{\beta \langle k \rangle}. \quad (2.8)$$

Equation (2.8) means that epidemic diffusion will take place when s_0 meets the above condition. Generally, it is difficult to get the analytic solution for Eq. (2.6). Thus, we consider the stable state of Eq. (2.6). As $s(t) + i(t) + q(t) + r(t) = 1$, and considering Eqs. (2.2), (2.3) and (2.4), then we have:

$$\begin{cases} \frac{ds(t)}{dt} = -\beta \langle k \rangle s(t)i(t) + \gamma[1 - s(t) - i(t) - q(t)] \\ \frac{di(t)}{dt} = \beta \langle k \rangle s(t)i(t) - (d_1 + \delta)i(t) \\ \frac{dq(t)}{dt} = \delta i(t) - (d_2 + \mu)q(t) \end{cases}. \quad (2.9)$$

Let $\frac{ds(t)}{dt} = 0$, $\frac{di(t)}{dt} = 0$ and $\frac{dq(t)}{dt} = 0$, we can get an obvious equilibrium point for the epidemic diffusion model I as follows:

$$P_1 = (s, i, q) = (1, 0, 0). \quad (2.10)$$

Equation (2.10) shows that both the number of infected people and the number of quarantined people are equal to zero, which indicates that epidemic diffusion in the disaster area does not happen. All people in the area are susceptible at last. Thus, we refer to this as the disease-free equilibrium point.

Furthermore, according to Eq. (2.9), we can get another equilibrium point for the epidemic diffusion system as follows:

$$P_2 = (s, i, q) = \left(\frac{d_1 + \delta}{\beta \langle k \rangle}, \frac{\gamma[\beta \langle k \rangle - (d_1 + \delta)](d_2 + \mu)}{\beta \langle k \rangle [(d_1 + \delta + \gamma)(d_2 + \mu) + \gamma\delta]}, \frac{\gamma\delta[\beta \langle k \rangle - (d_1 + \delta)]}{\beta \langle k \rangle [(d_1 + \delta + \gamma)(d_2 + \mu) + \gamma\delta]} \right). \quad (2.11)$$

Equation (2.11) shows that when the epidemic diffusion system is stable, a certain amount of infected people and a certain amount of quarantined people exist in the epidemic area. Thus, we refer to this as the endemic equilibrium point.

Lemma 2.1 *Disease-free equilibrium point P_1 in the epidemic diffusion network is stable when $\beta < \frac{d_1 + \delta}{\langle k \rangle}$.*

Proof Considering $P_1 = (s, i, q) = (1, 0, 0)$, we can obtain the Jacobi matrix of Eq. (2.9) as follows:

$$J_{P_1} = \begin{bmatrix} \frac{\partial P_{11}}{\partial s} & \frac{\partial P_{11}}{\partial i} & \frac{\partial P_{11}}{\partial q} \\ \frac{\partial P_{12}}{\partial s} & \frac{\partial P_{12}}{\partial i} & \frac{\partial P_{12}}{\partial q} \\ \frac{\partial P_{13}}{\partial s} & \frac{\partial P_{13}}{\partial i} & \frac{\partial P_{13}}{\partial q} \end{bmatrix} = \begin{bmatrix} -\gamma & -\beta \langle k \rangle - \gamma & -\gamma \\ 0 & \beta \langle k \rangle - (d_1 + \delta) & 0 \\ 0 & \delta & -(d_2 + \mu) \end{bmatrix}. \quad (2.12)$$

Here P_{11} , P_{12} and P_{13} represent the three differential equations in Eq. (2.9), respectively. Thus, it is easy to get the secular equation for the Jacobi matrix as follows:

$$(\lambda + \gamma)(\lambda - \beta \langle k \rangle + d_1 + \delta)(\lambda + d_2 + \mu) = 0. \quad (2.13)$$

Obviously, three characteristic roots for this secular equation are $-\gamma$, $\beta \langle k \rangle - d_1 - \delta$, and $-d_2 - \mu$. Based on Routh-Hurwitz stability criterion, when $\beta < \frac{d_1 + \delta}{\langle k \rangle}$, real parts of these three characteristic roots will be negative at the same time. Thus, the disease-free equilibrium point $P_1 = (s, i, q) = (1, 0, 0)$ is stable when $\beta < \frac{d_1 + \delta}{\langle k \rangle}$.

Lemma 2.2 *Endemic equilibrium point P_2 in the epidemic diffusion network is stable when $\beta > \frac{d_1+\delta}{\langle k \rangle}$.*

Proof Similarly as Lemma 2.1, coupling with Eq. (2.11), we can get the Jacobi matrix of Eq. (2.9) again as follows:

$$J_{P_2} = \begin{bmatrix} -\frac{\gamma[\beta \langle k \rangle - (d_1 + \delta)](d_2 + \mu)}{[(d_1 + \delta + \gamma)(d_2 + \mu) + \gamma\delta]} - \gamma & -(d_1 + \delta) - \gamma & -\gamma \\ \frac{\gamma[\beta \langle k \rangle - (d_1 + \delta)](d_2 + \mu)}{[(d_1 + \delta + \gamma)(d_2 + \mu) + \gamma\delta]} & 0 & 0 \\ 0 & \delta & -(d_2 + \mu) \end{bmatrix}. \quad (2.14)$$

Then, the secular equation for Eq. (2.14) is

$$a_0\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0. \quad (2.15)$$

Here, $a_0 = 1$, $a_1 = (d_2 + \mu) + (A + \gamma)$, $a_2 = (d_2 + \mu)(A + \gamma) + (d_1 + \delta + \gamma)A$, $a_3 = (d_2 + \mu)(d_1 + \delta + \gamma)A + \gamma\delta A$, and $A = \frac{\gamma[\beta \langle k \rangle - (d_1 + \delta)](d_2 + \mu)}{[(d_1 + \delta + \gamma)(d_2 + \mu) + \gamma\delta]}$.

Obviously, when $\beta > \frac{d_1 + \delta}{\langle k \rangle}$, we have $A > 0$. Then, we have $a_1 > 0$, $a_2 > 0$, $a_3 > 0$. Therefore,

$$\begin{aligned} a_1a_2 - a_0a_3 &= (d_2 + \mu)(A + \gamma)(d_2 + \mu + A + \gamma) \\ &\quad + (d_1 + \delta + \gamma)A^2 + \gamma A(d_1 + \gamma) > 0 \end{aligned}$$

According to Routh-Hurwitz stability criterion, Eq. (2.11) contains three characteristic roots with negative real part. Thus, the endemic equilibrium point P_2 is stable when $\beta > \frac{d_1 + \delta}{\langle k \rangle}$.

Remark 2.1 From Lemmas 2.1 and 2.2, we have the first conclusion: without consideration of incubation period, threshold of the epidemic diffusion not only depends on topological structure of the small-world network ($\langle k \rangle$), but also relies on other two key parameters, the quarantined rate (δ) and the death rate of infected people (d_1).

2.1.3 SEIQRS Epidemic Diffusion Model

(1) Model formulation

In this section, we consider the situation that epidemic diffusion with incubation period, and thus, we divide people in the epidemic area into five groups: susceptible people (S), exposed people (E), infected people (I), quarantined people (Q) and recovered people (R). Similarly, epidemic diffusion model in this section can be illustrated as Fig. 2.2.

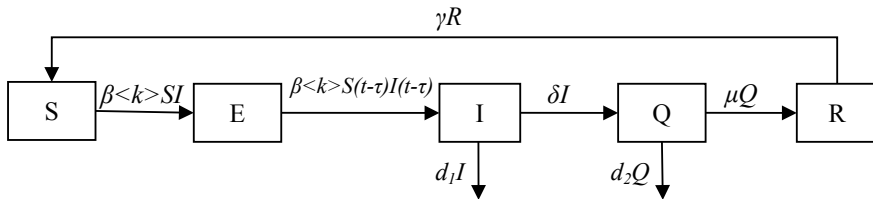


Fig. 2.2 Framework of SEIQRS model

Likewise, the SEIQRS epidemic diffusion model can be formulated as follow:

$$\begin{cases} \frac{ds(t)}{dt} = -\beta \langle k \rangle s(t)i(t) + \gamma r(t) \\ \frac{de(t)}{dt} = \beta \langle k \rangle s(t)i(t) - \beta \langle k \rangle s(t-\tau)i(t-\tau) \\ \frac{di(t)}{dt} = \beta \langle k \rangle s(t-\tau)i(t-\tau) - d_1 i(t) - \delta i(t) \\ \frac{dq(t)}{dt} = \delta i(t) - d_2 q(t) - \mu q(t) \\ \frac{dr(t)}{dt} = \mu q(t) - \gamma r(t) \end{cases} \quad (2.16)$$

Here, $E(t)$ stands for the number of exposed people. $e(t) = E(t)/N$. $s(t) + e(t) + i(t) + q(t) + r(t) = 1$. Moreover, $\beta, \langle k \rangle, \gamma, \delta, \mu, d_1, d_2, \tau > 0$. Initial conditions for the epidemic diffusion model are demonstrated as follows:

$$i(0) = i_0 \ll 1, \quad e(0) = \langle k \rangle i(0), \quad s(0) = 1 - e_0 - i_0, \quad q(0) = r(0) = 0.$$

(2) Analysis of the epidemic diffusion model

Likewise, it is also difficult to get the analytic solution for Eq. (2.16). Thus, we consider the stable state of Eq. (2.16). When the epidemic diffusion system is stable, that means the number of people in each group is unchanged. Then, we have $s(t) = s(t-\tau)$, $i(t) = i(t-\tau)$ and

$$\frac{de(t)}{dt} = \beta \langle k \rangle s(t)i(t) - \beta \langle k \rangle s(t-\tau)i(t-\tau) = 0. \quad (2.17)$$

Equation (2.17) means that the number of exposed people is a constant when the epidemic diffusion system is stable. As $s(t) + e(t) + i(t) + q(t) + r(t) = 1$, and considering Eq. (2.16), we have:

$$\begin{cases} \frac{ds(t)}{dt} = -\beta \langle k \rangle s(t)i(t) + \gamma [1 - s(t) - e(t) - i(t) - q(t)] \\ \frac{di(t)}{dt} = \beta \langle k \rangle s(t-\tau)i(t-\tau) - (d_1 + \delta)i(t) \\ \frac{dq(t)}{dt} = \delta i(t) - (d_2 + \mu)q(t) \end{cases} \quad (2.18)$$

Let $\frac{ds(t)}{dt} = 0$, $\frac{di(t)}{dt} = 0$ and $\frac{dq(t)}{dt} = 0$, we get the following two equilibrium points for the SEIQRS epidemic diffusion model:

$$P_3 = (s, i, q) = (1 - e, 0, 0). \quad (2.19)$$

$$P_4 = (s, i, q) = \left(\frac{d_1 + \delta}{\beta \langle k \rangle}, B, \frac{\delta}{d_2 + \mu} B \right). \quad (2.20)$$

Here, $B = \frac{\gamma[\beta \langle k \rangle (1-e) - (d_1 + \delta)](d_2 + \mu)}{\beta \langle k \rangle [(d_1 + \delta + \gamma)(d_2 + \mu) + \gamma \delta]}$. Similarly, P_3 is the disease-free equilibrium point and P_4 is the endemic equilibrium point.

Lemma 2.3 *Disease-free equilibrium point P_3 is stable when $\beta < \frac{d_1 + \delta}{\langle k \rangle (1-e)}$.*

Lemma 2.4 *Endemic equilibrium point P_4 is stable when $\beta > \frac{d_1 + \delta}{\langle k \rangle (1-e)}$.*

The proof process of Lemmas 2.3 and 2.4 are similar as introduced in Sect. 2.1.2. Thus, it is trivial to prove Lemmas 2.3 and 2.4.

Remark 2.2 From Lemmas 2.3 and 2.4, we get the second conclusion: with the consideration of incubation period, threshold of the epidemic diffusion not only depends on key parameters $\langle k \rangle$, δ and d_1 , but also relies on the number of exposed people when the system is stable.

2.1.4 Computational Experiments and Result Analysis

To test how well the model may be applied in a real world, we exhibit a case study to demonstrate the efficiency of the proposed two different models. To facilitate the calculation process, we assume that a bioterror attack is suffered. The initial values of the parameters in these two epidemic diffusion models are given as follows: $\beta = 10^{-6}$, $\langle k \rangle = 6$, $\gamma = 2 \times 10^{-4}$, $\delta = 0.3$, $\mu = 0.1$, $d_1 = 5 \times 10^{-3}$, $d_2 = 1 \times 10^{-3}$, $\tau = 5$, $N = 10^5$ and $i(0) = 2 \times 10^{-4}$. We use the MATLAB 7.0 mathematical programming solver to simulate these two models. The tests are performed on an Intel(R) Core(TM) 2 CPU 1.66 GHz with 1.5 GB RAM under Microsoft Windows XP. Figure 2.3 is the numerical simulation of these two epidemic models. The curves respectively represent the different groups of people over time.

From Fig. 2.3, we observe that threshold of the epidemic diffusion exists in both Model I and Model II. Comparing these two Figures, we find the peak of $I(t)$ in Model II appears later than it in Model I. It is worth mentioning that the largest number of infected people in Model II is also smaller than it in Model I. This result is reasonable, because the incubation period is considered in Model II. Thus, the number of infected people in Model II would be divided into two parts. On the other hand, it confirms that incubation time plays an important role in epidemic diffusion network.

During an actual emergency rescue process, the time-based parameter $I(t)$, which represents the number of infected people, is much more concerned. Thus, a short sensitivity analysis of the three key parameters (β , $\langle k \rangle$ and δ) is conducted in the following.

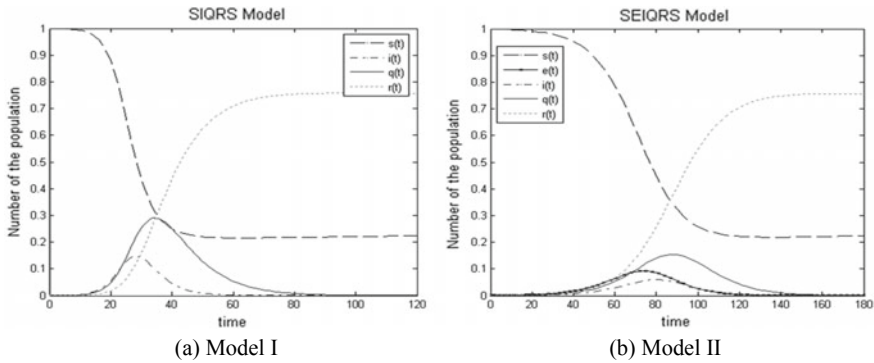


Fig. 2.3 Diffusion profile of the biological epidemic models

Holding all the other parameters fixed as in the numerical example given above, except that β takes on four different values ranging from 10^{-6} to 4×10^{-6} with an increment of 10^{-6} . Figure 2.4 shows that the number of infected people is changed over time. From this figure, we observe that no matter in Model I or Model II, there almost get no distinguish among these curves in the first 40 days. However, distinguish is obvious in the following days. The larger the initial size of β is, the faster the increments speed is. Note that though initial size of β is varied, peaks of different curves in Model I appear almost at the same time. However, situation in Model II is different. The larger β is, the later the peak appears. This phenomenon enlightens us again that the incubation time is an important factor in an anti-bioterrorism system.

Holding all the other parameters fixed as in the numerical example given above, except that $\langle k \rangle$ takes on four different values ranging from 4 to 10 with an increment of 2. Figure 2.5 shows that the number of infected people is changed as time goes by. As before, no matter in Model I and Model II, there almost get no distinguish among these curves in the first 40 days. After then, the number of infected people shows a positive proportional to parameter $\langle k \rangle$. From Fig. 2.5, we get a conclusion that

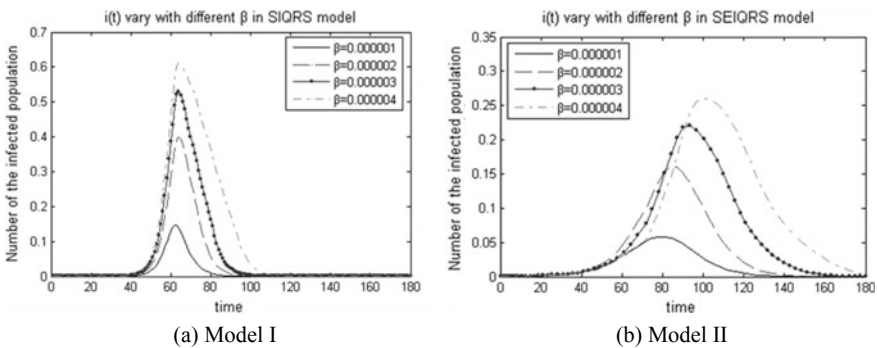


Fig. 2.4 Regularity of the infected nodes with different initial size of β

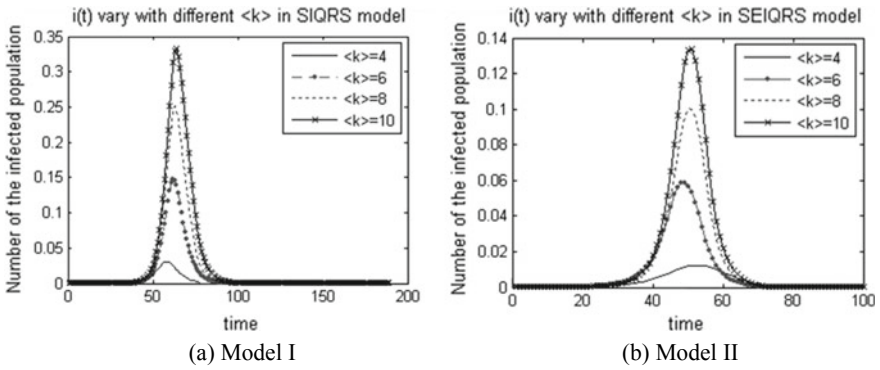


Fig. 2.5 Regularity of the infected nodes with different initial size of $\langle k \rangle$

self-quarantine is an effective strategy for controlling the epidemic diffusion. And this is why Chinese government implements a series of strict quarantine measures when SARS outbreaks. Note that peaks of different curves appear almost at the same time in Model II. This is different from Fig. 2.4b.

Similarly, holding all the other parameters fixed as in the numerical example given above, except that δ takes on four different values ranging from 0.2 to 0.5 with an increment of 0.1. Figure 2.6 shows that the number of infected people is changed over time. Exactly same as our expected, we get the similar conclusion as the former two parameters. Moreover, we get the delay phenomenon again as Fig. 2.4b. Figure 2.6 means that to quarantine the infected people as early as possible is also very important during an actual emergency rescue process.

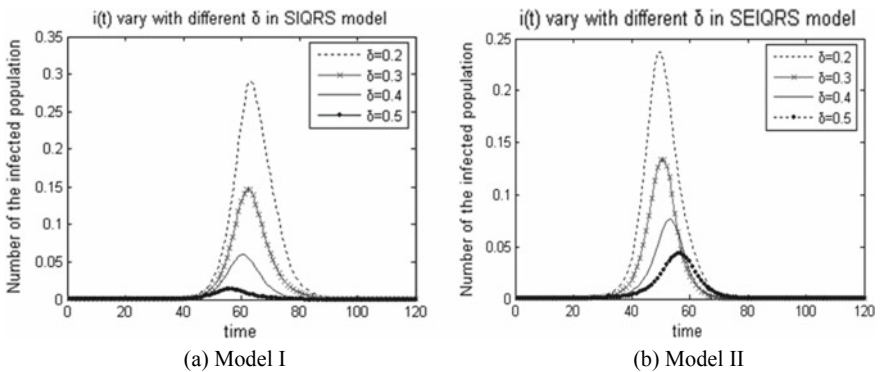


Fig. 2.6 Regularity of the infected nodes with different initial size of δ

2.2 Epidemic Dynamics Modeling for Influenza

2.2.1 Introduction

The first mathematical model that could be used to describe an influenza epidemic was developed early in the 20th century by Kermack and McKendrick [26]. This model is known as the Susceptible-Infectious-Recovered (SIR) model. To simulate an influenza epidemic, the model is analyzed on a computer and one infected individual (I) is introduced into a closed population where everyone is susceptible (S). Each infected individual (I) transmits influenza, with probability β , to each susceptible individual (S) they encounter. The number of susceptible individuals decreases as the incidence (i.e., the number of individuals infected per unit time) increases. At a certain point the epidemic curve peaks, and subsequently declines, because infected individuals recover and cease to transmit the virus. Only a single influenza epidemic can occur in a closed population because there is no inflow of susceptible individuals. The severity of the epidemic and the initial rate of increase depend upon the value of the Basic Reproduction Number (R_0). R_0 is defined as the average number of new infections that one case generates, in an entirely susceptible population, during the time they are infectious. If $R_0 > 1$ an epidemic will occur and if $R_0 < 1$ the outbreak will die out. The value of R_0 for any specific epidemic can be estimated by fitting the SIR model to incidence data collected during the initial exponential growth phase. The value of R_0 may also be calculated retroactively from the final size of the epidemic. If the SIR model is used, R_0 for influenza is equal to the infectivity/transmissibility of the strain (β) multiplied by the duration of the infectious period. Therefore once the value of R_0 has been obtained, the value of β can be determined.

The SIR model has been used as a basis for all subsequent influenza models. The simplest extension to the SIR model includes demographics; specifically, inflow and outflow of individuals into the population. Analysis of this demographic model shows that influenza epidemics can be expected to cycle, with damped oscillations, and reach a stable endemic level [27]. By modifying the basic SIR model in a variety of ways (e.g., by including seasonality [28, 29]) influenza epidemics can be shown to have sustained cycles. The SIR model has also been extended so that it can be used to represent and/or predict the spatial dynamics of an influenza epidemic. The first spatial-temporal model of influenza was developed in the late 1960s by Rvachev [30]. He connected a series of SIR models in order to construct a network model of linked epidemics. He then modeled the geographic spread of influenza in the former Soviet Union by using travel data to estimate the degree of linkage between epidemics in major cities. In the 1980s, he and his colleagues Baroyan and Longini extended his network model and evaluated the effect of air travel on influenza pandemics [31, 32]. Since then other modeling studies have quantified the importance of air travel on geographic spread [33, 34]. For example, a recent study has modeled the potential for influenza epidemics to move through nine European cities: Amsterdam, Berlin, Budapest, Copenhagen, London, Madrid, Milan, Paris, and Stockholm. The authors estimate that, due to a high degree of connectedness through air travel, it would take

less than a month for an epidemic beginning in any one of these cities to spread to the other eight [33]. Network models have also been use to understand the temporal and spatial synchrony of influenza epidemics within the United States (US) [35].

In this section, SEIRS model based on small-world network is formulated for depicting the spread of infectious diseases. The existence and global stability of the disease-free equilibrium and the endemic equilibrium for the epidemic system is proved by differential equations knowledge and Routh-Hurwitz theory. A numerical example, which includes key parameters analysis and critical topic discussion (e.g. medicine resources demand forecasting) is presented to test how well the proposed model may be applied in practice.

2.2.2 SEIRS Model with Small World Network

(1) Basic introduction

For the compartment model of epidemic diffusion is a mature theory, herein we omit the verbose introduction of the framework process. In this section, we consider the situation that infected person will not be quarantined, and divide people in epidemic area into four groups: susceptible people (S), exposed people (E), infected people (I) and recovered people (R). A survey by Tham [24] shows that part of recovered people who are discharged from the healthcare department will be re-infected again. Thus, considering the small world network of the social contact, the structure of Susceptible–Exposure–Infective–Recovered–Susceptible (SEIRS) model is shown as Fig. 2.7.

Notations used in following sections are specified as follows:

- N Population size in epidemic area.
- $S(t)$ Number of susceptible people, $s(t) = S(t)/N$.
- $E(t)$ Number of exposed people, $e(t) = E(t)/N$.
- $I(t)$ Number of infected people, $i(t) = I(t)/N$.
- $R(t)$ Number of recovered people, $r(t) = R(t)/N$.
- $\langle k \rangle$ Average degree distribution of small world network.
- β Propagation coefficient of the epidemic.
- γ Re-infected rate of recovered people.

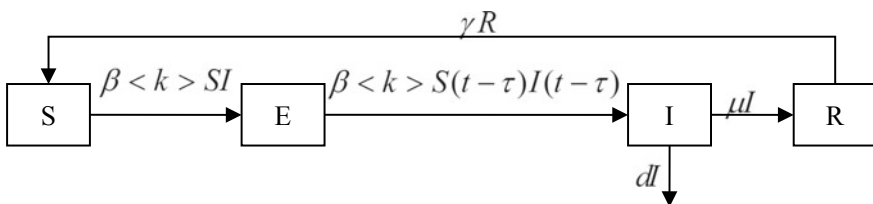


Fig. 2.7 Framework of SEIRS model

- μ Recovered rate.
 τ Incubation period of the epidemic.
 d Death rate of infected people.

Intuitively, we have the first two equations:

$$S(t) + E(t) + I(t) + R(t) = N \quad (2.21)$$

$$s(t) + e(i) + i(t) + r(t) = 1 \quad (2.22)$$

Based on mean-field theory, the time-based parameter $s(t)$ meets the following equation from time t to $t + \Delta t$:

$$s(t + \Delta t) - s(t) = -\beta \langle k \rangle s(t) i(t) \Delta t + \gamma r(t) \Delta t. \quad (2.23)$$

Thus, we get:

$$\frac{s(t + \Delta t) - s(t)}{\Delta t} = -\beta \langle k \rangle s(t) i(t) + \gamma r(t). \quad (2.24)$$

It can be rewritten as:

$$\frac{ds(t)}{dt} = -\beta \langle k \rangle s(t) i(t) + \gamma r(t). \quad (2.25)$$

Similarly, we have the other three ordinary differential equations as follows:

$$\frac{de(t)}{dt} = \beta \langle k \rangle s(t) i(t) - \beta \langle k \rangle s(t - \tau) i(t - \tau) \quad (2.26)$$

$$\frac{di(t)}{dt} = \beta \langle k \rangle s(t - \tau) i(t - \tau) - di(t) - \mu i(t) \quad (2.27)$$

$$\frac{dr(t)}{dt} = \mu i(t) - \gamma r(t) \quad (2.28)$$

Thus, the SEIRS epidemic diffusion model which considers small world network effect can be formulated as follows:

$$\begin{cases} \frac{ds(t)}{dt} = -\beta \langle k \rangle s(t) i(t) + \gamma r(t) \\ \frac{de(t)}{dt} = \beta \langle k \rangle s(t) i(t) - \beta \langle k \rangle s(t - \tau) i(t - \tau) \\ \frac{di(t)}{dt} = \beta \langle k \rangle s(t - \tau) i(t - \tau) - di(t) - \mu i(t) \\ \frac{dr(t)}{dt} = \mu i(t) - \gamma r(t) \end{cases} \quad (2.29)$$

Here, $\beta, \langle k \rangle, \gamma, \mu, d, \tau > 0$. Initial conditions for this epidemic diffusion model are demonstrated as follows:

$$\begin{cases} i(0) = i_0 \ll 1 \\ e(0) = \langle k \rangle i(0) \\ s(0) = 1 - e_0 - i_0 \\ r(0) = 0 \end{cases} \quad (2.30)$$

(2) Analysis of the SEIRS model

As to SEIRS model, while such an epidemic diffusion system is stable, number of people in different groups will be unchanged. Hence, we have $s(t) = s(t - \tau)$, $i(t) = i(t - \tau)$, and we get:

$$\frac{de(t)}{dt} = \beta \langle k \rangle s(t)i(t) - \beta \langle k \rangle s(t - \tau)i(t - \tau) = 0. \quad (2.31)$$

$$\frac{di(t)}{dt} = \beta \langle k \rangle s(t)i(t) - di(t) - \mu i(t) \quad (2.32)$$

Equation (2.31) means that number of exposed people is a constant when epidemic diffusion system is stable. As we all know, if an epidemic is wide spread, it should satisfy the following condition:

$$\left. \frac{di(t)}{dt} \right|_{t=0} > 0. \quad (2.33)$$

Together this equation with Eq. (2.32), we can get:

$$s_0 > \frac{d + \mu}{\beta \langle k \rangle}. \quad (2.33)$$

Equation (2.33) shows that the spread of epidemic outbreaks only when s_0 meets the above condition. As $s(t) + e(t) + i(t) + r(t) = 1$, and combine with Eq. (2.29), we get:

$$\begin{cases} \frac{ds(t)}{dt} = -\beta \langle k \rangle s(t)i(t) + \gamma(1 - s(t) - e(t) - i(t)) \\ \frac{di(t)}{dt} = \beta \langle k \rangle s(t)i(t) - di(t) - \mu i(t) \end{cases}. \quad (2.34)$$

Let $\frac{ds(t)}{dt} = 0$ and $\frac{di(t)}{dt} = 0$, we can get an obvious equilibrium point for such an epidemic diffusion model as follows:

$$P_1 = (s, i) = (1, 0). \quad (2.35)$$

As Eq. (2.35) shows, number of infected people is zero, which indicates that spread of epidemic in such an area does not happened. All people are susceptible individuals. Herein, we refer to such a point as the disease-free equilibrium point.

On the other side, according to Eq. (2.31), number of exposed people is a constant. Thus, combine with Eq. (2.34), we can get another equilibrium result as follows:

$$P_2 = (s, i) = \left(\frac{d + \mu}{\beta \langle k \rangle}, \frac{\gamma[\beta \langle k \rangle (1 - e) - (d + \mu)]}{\beta \langle k \rangle (\gamma + d + \mu)} \right) \quad (2.36)$$

Such a result shows that when epidemic diffusion system is stable, a certain amount of infected people exist in disaster area. Herein, we refer it as the endemic equilibrium point.

Lemma 2.5 *Disease-free equilibrium point P_1 is stable only when $\beta < \frac{d+\mu}{\langle k \rangle}$.*

Proof As $P_1 = (s, i) = (1, 0)$, we can obtain the Jacobi matrix of Eq. (2.34) as follows:

$$J_{P_1} = \begin{bmatrix} \frac{\partial \Pi_1}{\partial s} & \frac{\partial \Pi_1}{\partial i} \\ \frac{\partial \Pi_2}{\partial s} & \frac{\partial \Pi_2}{\partial i} \end{bmatrix} = \begin{bmatrix} -\gamma & -\beta \langle k \rangle - \gamma \\ 0 & \beta \langle k \rangle - d - \mu \end{bmatrix}. \quad (2.37)$$

Here, Π_1 and Π_2 are the two differential equations in Eq. (2.34). The secular equation for the Jacobi matrix is:

$$(\lambda + \gamma)(\lambda - \beta \langle k \rangle + d + \mu) = 0. \quad (2.38)$$

It is easy to get the two characteristic roots for this secular equation, which are $-\gamma$ and $\beta \langle k \rangle - d - \mu$. Based on Routh-Hurwitz stability criterion, when $\beta < \frac{d+\mu}{\langle k \rangle}$, real parts of the two characteristic roots are negative. Thus, the disease-free equilibrium point $P_1 = (s, i) = (1, 0)$ is stable only when $\beta < \frac{d+\mu}{\langle k \rangle}$.

Lemma 2.6 *Endemic equilibrium point P_2 is stable only when $\beta > \frac{d+\mu}{\langle k \rangle (1-e)}$.*

Proof Similarly as Lemma 2.1, coupling with Eq. (2.31), the Jacobi matrix of Eq. (2.29) can be rewritten as follow:

$$J_{P_2} = \begin{bmatrix} \frac{\gamma[-\beta \langle k \rangle (1-e) - \gamma]}{(\gamma + d + \mu)} & -d - \mu - \gamma \\ \frac{\gamma[\beta \langle k \rangle (1-e) - (d + \mu)]}{(\gamma + d + \mu)} & 0 \end{bmatrix}. \quad (2.39)$$

The secular equation for Eq. (2.39) can be expressed as follows:

$$a\lambda^2 + b\lambda + c = 0. \quad (2.40)$$

Herein, $a = 1$, $b = \frac{\gamma[\beta \langle k \rangle (1-e) + \gamma]}{(\gamma + d + \mu)}$ and $c = \gamma[\beta \langle k \rangle (1 - e) - (d + \mu)]$. Based on the quadratic equation theory, such a secular equation contains two characteristic roots λ_1 and λ_2 , and satisfies:

$$\lambda_1 + \lambda_2 = -\frac{b}{a} = -\frac{\gamma[\beta \langle k \rangle (1 - e) + \gamma]}{(\gamma + d + \mu)} < 0. \quad (2.41)$$

$$\lambda_1 \cdot \lambda_2 = \frac{c}{a} = \gamma[\beta \langle k \rangle (1 - e) - (d + \mu)]. \quad (2.42)$$

According to Routh-Hurwitz stability criterion, if we want to get two negative characteristic roots λ_1 and λ_2 again, the Eq. (2.42) should be constant greater than zero, which means, $\beta > \frac{d+\mu}{\langle k \rangle (1-e)}$ should be satisfied. Thus, only when $\beta > \frac{d+\mu}{\langle k \rangle (1-e)}$, the endemic equilibrium point P_2 is stable.

Remark 2.3 From these two lemmas, we can get the first conclusion that threshold of the epidemic diffusion depends on some key parameters, such as average degree distribution of the small world network $\langle k \rangle$, recovered rate μ , death rate of infected people d , also number of exposed people when the system is stable.

2.2.3 Emergency Demand Base on Epidemic Diffusion Model

In this section, we are going to discuss how to forecast the time-varying demand in disaster area. Let $D(t)$ represents demand for medicine resources in disaster area at time t . Obviously, the more people infected, the more resources demanded. Thus, it can be rewritten as:

$$D(t) \propto f[I(t)]. \quad (2.43)$$

We assume that each infected person should be cured for a certain time (the cure cycle), e.g. 10 days, and during these days he/she needs for medicine presents a law of decreasing. Hence, the total demand of medicine resources for each infected/quarantined person is:

$$\psi = \int_0^c \varphi(t) dt, \quad (2.44)$$

where $\varphi(t)$ is a decreasing function in the First Quartile. c is the cure cycle. To the SEIRS model, the average demand for medicine resources in time t can be formulated as follows:

$$D_I(t) = \frac{I(t) \cdot \psi}{c} = \frac{N}{c} \int_0^c \varphi(t) dt \int_0^t \beta \langle k \rangle s(t - \tau) i(t - \tau) - di(t) - \mu i(t) dt. \quad (2.45)$$

Hence we get that:

$$\frac{dD_I(t)}{dt} = \Lambda[\beta \langle k \rangle s(t - \tau) i(t - \tau) - di(t) - \mu i(t)], \tag{2.46}$$

where Λ is a constant.

2.2.4 Numerical Test

In this section, we take a numerical simulation to test how well the proposed model may be applied in practice. The initial values of relative parameters in the proposed epidemic diffusion models are given as follows: $\beta = 2 \times 10^{-5}$, $\langle k \rangle = 6$, $\gamma = 2 \times 10^{-4}$, $\delta = 0.3$, $\mu = 0.2$, $d = d_1 = 5 \times 10^{-3}$, $d_2 = 1 \times 10^{-3}$, $\tau = 5$ (day), $N = 10^4$ and $i(0) = 1 \times 10^{-3}$. We use MATLAB 7.0 mathematical solver together with Runge-Kutta method to simulate the propose model. The tests are performed on an Intel(R) Core(TM) i3 CPU 2.4 GHz with 2 GB RAM under Microsoft Windows XP. Figure 2.8 is the numerical simulation of the smallpox epidemic models. The curves respectively represent the different groups of people over time.

From this Figure we can find that there is a threshold value of epidemic diffusion. The rush of the infected curve in such a Model is around on the 32–33 day. Based on the above theory analysis, we find that some factors, such as β and $\langle k \rangle$, are key parameters in epidemic diffusion system. Herein, we present a short sensitivity analysis for them. Holding all the other parameters fixed as in the numerical example given above, except that β takes on four different values ranging from $\beta = 2 \times 10^{-5}$ to

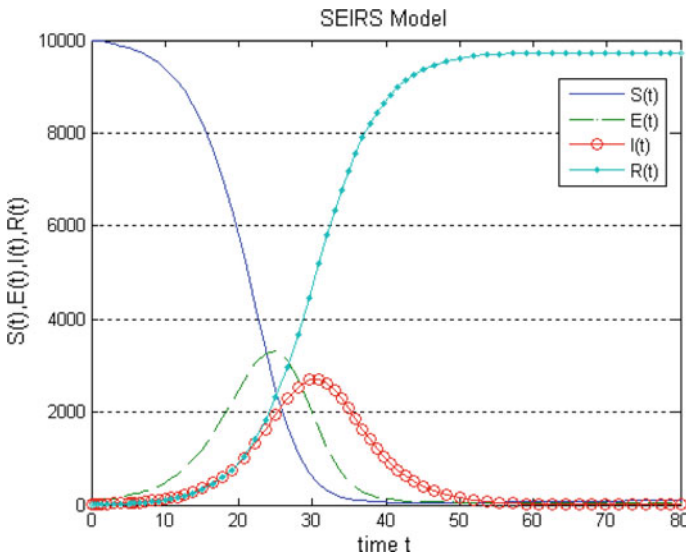


Fig. 2.8 Numerical simulation for SEIRS model

8×10^{-5} with an increment of 2×10^{-5} , Fig. 2.9 shows that number of infected people changed over time. From this figure, we observe that there almost get no distinguish among these curves in the first 15–20 days. However, distinguish is obvious in the following days. The larger initial size of β is, the faster increments speed is. From this figure we know that propagation coefficient controlling is a very important and effective method to prevent the smallpox epidemic diffusion.

Holding all the other parameters fixed as in the numerical example given above, except that $\langle k \rangle$ takes on four different values ranging from 4 to 10 with an increment of 2. Figure 2.10 shows that number of infected people is changed as time goes by. As before, number of infected people shows a positive proportional to such a parameter $\langle k \rangle$. From this figure, we know that self-quarantine and decreasing the contact with people around is an effective strategy for controlling epidemic diffusion. Hence, during the SARS period, governments implement a series of strict quarantine measures.

To facilitate the process in the following section, here we given that $\Lambda = 1$ directly. Such an operation will not affect the final compare result. According to Eq. (2.27), holding all the parameters fixed as in the above numerical example, we can get the demand for medicine resources by the proposed model, which are shown in Fig. 2.11.

Form this figure, we can decompose the entire smallpox emergency rescue process into three mutually correlated stages, and we present three corresponding controlling strategies for them.

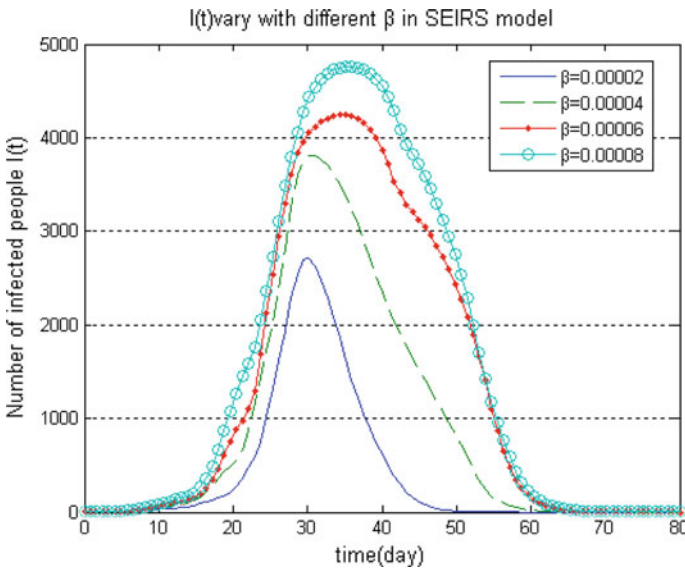


Fig. 2.9 Number of $I(t)$ with different β

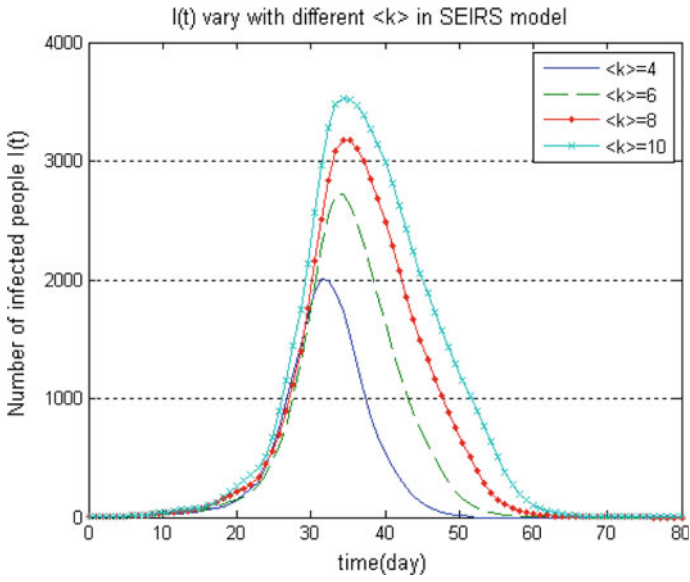


Fig. 2.10 Number of $I(t)$ with different $\langle k \rangle$

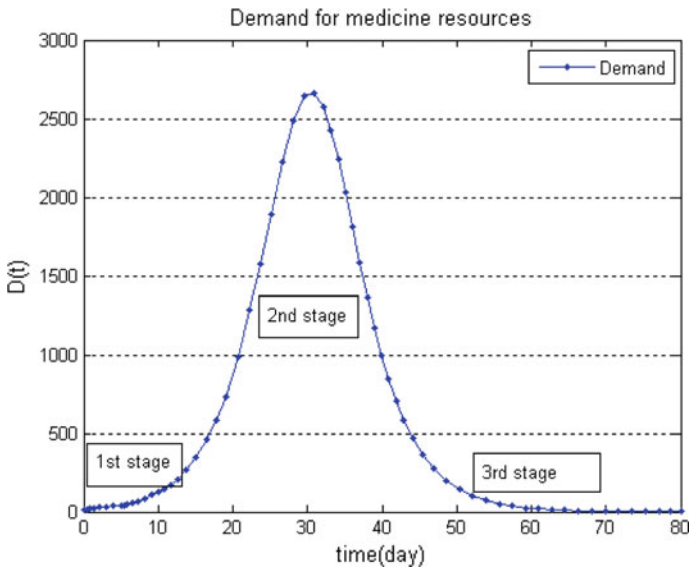


Fig. 2.11 Demand for medicine resources

- (1) At the first stage (e.g. 0–15 days), epidemic has just outbreak, and it has not yet caused a widespread diffusion. Such a period is the best emergency rescue time. The demand for medicine resources during this period keeps in low level. Hence, medicine resources inventory in local health departments should be distributed to the infected people's hands as quickly as possible.
- (2) If we miss the opportunities in the first stage, epidemic would cause a widespread diffusion, which makes us face to the second stage. In such a stage (e.g. 15–70 days), demand for medicine resources is dynamic and time-varying. Thus, resources distribution program in such a stage should also be varied over time.
- (3) At the third stage (e.g. 70-more days), epidemic diffusion goes to be stable, and demand for medicine resources shows decreasing. Hence, we can replenish the inventory of medicine resources for these local health departments, and allocate some other medicine resources to the remaining infected areas, simultaneously.

2.3 Epidemic Dynamics Considering Population Migration

2.3.1 Introduction

As mentioned in Rachaniotis et al. [36], a serious epidemic is a problem that tests the ability of a nation to effectively protect its population, to reduce human loss and to rapidly recover. Sometime such a problem may acquire worldwide dimensions. For example, during the period from November 2002 to August 2003, 8422 people in 29 countries were infected with SARS, 916 of them were dead at last for the effective medical resources appeared late. Other diseases, such as HIV, H1N1 can also cause significant numbers of direct infectious disease deaths. Epidemic diffusion is a typical complex dynamic system problem in Gao et al. [37], for we don't know what kind of epidemic outbreaks, when it outbreaks, and how it diffuses. Generally, after an epidemic outbreak, public officials are faced with many critical and complex issues, the most important of which is to make certain how the epidemic diffuses so that the rescue operation efficiency maximized.

Traditionally, analytical works on epidemic diffusion are concentrated on the compartmental epidemic models of ordinary differential equations [38–42]. In these models, the total population is divided into several independence classes and each class of individuals is closed into a compartment. The sizes of the compartments are large enough and the mixing of members is homogeneous. In other words, the models based on the differential equations are always under the assumption of both homogeneous infectivity and homogeneous connectivity of each individual. However, the traditional models do not consider the population migration among different compartments.

The other stream of related research to our work is on the epidemic diffusion with population migration. For instance, Hethcote [43] proposed that deterministic communicable disease models were initial value problems for a system of ordinary

differential equations, and thus he considered the asymptotic stability for the equilibrium points for models involving temporary immunity, disease-related fatalities, carriers, migration, dissimilar interacting groups, and transmission by vectors. In his work, both susceptible individuals and infected individuals in each population could migrate (only equal rates were considered), which led to different equilibriums. Another model that considers two interacting populations undergoing SIS dynamics was presented in Kribs-Zaleta and Velasco-Hernandez [44]. The authors considered that the two groups may have different values for model parameters especially those dealing with vaccination. Liebovitch and Schwartz [45] proposed that classical disease models always use a mass action term as the interaction between infected and susceptible people in separate patches and they derived the equations when this interaction is a migration of people between patches. Sani and Kroese [46] formulated various mathematical control problems for HIV spread in mobile heterosexual populations. They applied the cross-entropy method to solve these highly multi-modal and non-linear optimization problems, and demonstrated the effectiveness of the method via a range of experiments and illustrated how the form of the optimal control function depends on the mathematical model used for the HIV spread. Yang et al. [47] considered SIR and SIS epidemic models with bilinear incidence and migration between two patches, where infected individuals cannot migrate from one patch to another due to medical screening. They found the thresholds classifying the global dynamics of the models in terms of the model parameters, and they obtained the global asymptotical stability of the disease free and the disease endemic equilibrium. Wolkewitz and Schumacher [48] pointed out that the main limitation of the compartmental models is that several parameters are based on uncertain expert guesses (default values) and are not estimated from the study data. Lee et al. [49] extended the SEIR model to incorporate population migration between cities and investigated the effectiveness of travel restrictions as a control against the spread of influenza.

As a continued work, this section presents an SIS epidemic model with population migration between two cities. We consider unequal migration rates for these two populations and only susceptible individuals can migrate, which is different from the whole existing works.

2.3.2 Epidemic Model with Population Migration

As the compartment model of epidemic diffusion is a mature theory, herein we omit the verbose introduction of the framework process. In this section, we divide people in epidemic areas into two groups: susceptible individuals (S) and infected individuals (I). The transfer diagram of individuals in the epidemic areas can be illustrated as Fig. 2.12.

To smooth the formulation progress of the SIS epidemic diffusion model in the following subsections, some assumptions and parameters are specified as follows:

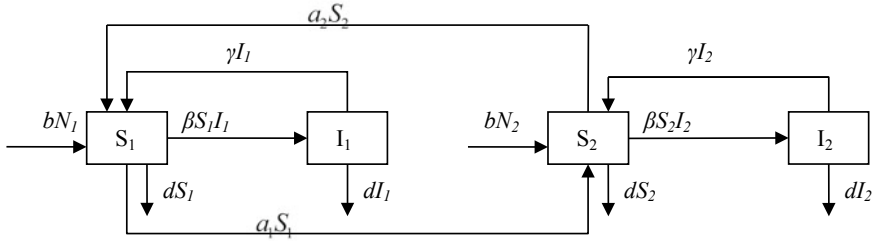


Fig. 2.12 The transfer diagram of SIS model with population migration

- (1) The susceptible individuals and the infected individuals in city i at time t are denoted as $S_i(t)$ and $I_i(t)$, respectively. Thus, the total individuals in city i is $N_i(t) = S_i(t) + I_i(t)$, $i = 1, 2$.
- (2) b and d are the natural birth rate and the natural death rate, respectively. γ is the recovery rate. β is the propagation coefficient. To facilitate the process in the following sections, we assume that $b = d$. Moreover, disease-related death rate is not considered in this work.
- (3) Only the susceptible individuals can migrate in this paper. a_i represents the migrating-out rate of susceptible individuals in city i ($a_i > 0$ for $i = 1, 2$ and $a_1 \neq a_2$).
- (4) Using the notation N to represent the total number of the population in these two cities $N = N_1 + N_2$. Note that N is a constant.

Hence, the ordinary differential equations for the SIS epidemic diffusion model can be formulated as:

$$\begin{cases} \frac{dS_1}{dt} = bN_1 - a_1S_1 + a_2S_2 - dS_1 - \beta S_1 I_1 + \gamma I_1 \\ \frac{dI_1}{dt} = \beta S_1 I_1 - \gamma I_1 - dI_1 \\ \frac{dS_2}{dt} = bN_2 + a_1S_1 - a_2S_2 - dS_2 - \beta S_2 I_2 + \gamma I_2 \\ \frac{dI_2}{dt} = \beta S_2 I_2 - \gamma I_2 - dI_2 \end{cases} \quad (2.47)$$

ODE (2.47) describes the following dynamics of epidemic diffusion among the population groups. (1) The change rate of the susceptible population in both city 1 and city 2 are determined by the entry population, the exiting population, and the losing population who actually gets exposed to the disease and thus is counted towards the class of infected population. The last one is in proportion to the propagation coefficient β , and both of the current mass of the susceptible individuals and the current mass of the infected individuals. (2) The change rate of the infected population is determined by the difference between the entering population, those of the susceptible population who get sick, the exiting population, and the losing population. All parameters β , b , γ , a_1 , a_2 are positive and initial conditions for the model are demonstrated as follows:

$$I_1(0) = i_1^0 \ll N, \quad I_2(0) = i_2^0 \ll N, \quad S_1(0) = s_1^0, \quad S_2(0) = N - s_1^0 - i_1^0 - i_2^0. \quad (2.48)$$

2.3.3 Model Analysis

(1) Condition of the epidemic diffusion

As shown in above, $I_1(0) = i_1^0 \ll N$, $I_2(0) = i_2^0 \ll N$, $S_1(0) = s_1^0$ and $S_2(0) = N - s_1^0 - i_1^0 - i_2^0$ are initial conditions for the proposed model, which symbolize the initial number of susceptible and infected individuals. Then, it is easy to obtain the initial condition for epidemic diffusion, which should satisfy the following premise:

$$\frac{dI_1}{dt}|_{t=0} > 0 \text{ or } \frac{dI_2}{dt}|_{t=0} > 0. \quad (2.49)$$

Taking it into Eq. (2.47), we can obtain the initial condition of the susceptible individuals in city 1 and city 2:

$$s_1^0 > \frac{b + \gamma}{\beta} \text{ or } s_2^0 < N - i_1^0 - i_2^0 - \frac{b + \gamma}{\beta}. \quad (2.50)$$

Equation (2.50) shows that the spread of epidemic only when s_1^0 and s_2^0 meet the above initial conditions.

(2) Existence of the system equilibrium solution

Generally, it is difficult to obtain the analytic solution of the Eq. (2.47). To analyze the epidemic diffusion, we consider the stable state of Eq. (2.47). Considering that $b = d$ and expunging S_2 , Eq. (2.47) can be rewritten as:

$$\begin{cases} \frac{dS_1}{dt} = -a_1 S_1 + a_2(N - S_1 - I_1 - I_2) - \beta S_1 I_1 + (b + \gamma)I_1 \\ \frac{dI_1}{dt} = \beta S_1 I_1 - (b + \gamma)I_1 \\ \frac{dI_2}{dt} = \beta(N - S_1 - I_1 - I_2)I_2 - (b + \gamma)I_2 \end{cases}. \quad (2.51)$$

Let $\frac{dI_1}{dt} = 0$, we can get $I_1 = 0$ or $S_1 = \frac{b+\gamma}{\beta}$. Similarly, let $\frac{dI_2}{dt} = 0$, we can obtain $I_2 = 0$ or $S_1 + I_1 + I_2 = N - \frac{b+\gamma}{\beta}$. With the partial derivative $\frac{dS_1}{dt} = 0$, $\frac{dI_1}{dt} = 0$ and $\frac{dI_2}{dt} = 0$, we can obtain one equilibrium point of the SIS epidemic diffusion system intuitively when $I_1 = 0$ and $I_2 = 0$:

$$P_1 = (S_1, I_1, I_2) = \left(\frac{a_2}{a_1 + a_2} N, 0, 0 \right). \quad (2.52)$$

From Eq. (2.52) we can see that both number of infected individuals in city 1 and city 2 are zero, which indicate that epidemic diffusion in these two cities does not happened, and all the individuals in these two cities are susceptible individuals at last. Herein, we call it disease-free equilibrium point.

When $I_1 = 0$ and $S_1 + I_1 + I_2 = N - \frac{b+\gamma}{\beta}$, we can obtain the second equilibrium point of the SIS epidemic diffusion system:

$$P_2 = (S_1, I_1, I_2) = \left(\frac{a_2}{a_1} \cdot \frac{b+\gamma}{\beta}, 0, N - \frac{a_1+a_2}{a_1} \cdot \frac{b+\gamma}{\beta} \right). \quad (2.53)$$

From Eq. (2.53), when the SIS epidemic diffusion system is stable, the number of infected individuals in city 1 is zero, and some infected individuals in city 2 still exist. In this condition, we call it the endemic equilibrium point.

Likewise, when $S_1 = \frac{b+\gamma}{\beta}$ and $I_2 = 0$, we can obtain the third equilibrium point of the SIS epidemic diffusion system:

$$P_3 = (S_1, I_1, I_2) = \left(\frac{b+\gamma}{\beta}, N - \frac{a_1+a_2}{a_2} \cdot \frac{b+\gamma}{\beta}, 0 \right). \quad (2.54)$$

In line with the above work, when the SIS epidemic diffusion system is stable, the number of infected individuals in city 2 is zero, and some infected individuals in city 1 still exist. So it is called endemic equilibrium point as well.

It is worth mentioning that when $S_1 = \frac{b+\gamma}{\beta}$ and $S_1 + I_1 + I_2 = N - \frac{b+\gamma}{\beta}$, there is $\frac{dS_1}{dt} = (a_2 - a_1) \cdot \frac{b+\gamma}{\beta} \neq 0$ for that $a_1 \neq a_2$. That means, under the conditions of $S_1 = \frac{b+\gamma}{\beta}$ and $S_1 + I_1 + I_2 = N - \frac{b+\gamma}{\beta}$, there is no solution for the simultaneous Equations $\frac{dS_1}{dt} = 0$, $\frac{dI_1}{dt} = 0$ and $\frac{dI_2}{dt} = 0$.

(3) Stability of the system equilibrium solution

Lemma 2.7 *Disease-free equilibrium point P_1 in the SIS epidemic diffusion system is stable only when $\beta < \min\{\frac{(a_1+a_2)(b+\gamma)}{a_1N}, \frac{(a_1+a_2)(b+\gamma)}{a_2N}\}$.*

Proof Let $P = \frac{dS_1}{dt}$, $Q = \frac{dI_1}{dt}$ and $R = \frac{dI_2}{dt}$, the Jacobi matrix of Eq. (2.51) can be obtained as follows:

$$\begin{aligned} J &= \begin{pmatrix} \frac{\partial P}{\partial S_1} & \frac{\partial P}{\partial I_1} & \frac{\partial P}{\partial I_2} \\ \frac{\partial Q}{\partial S_1} & \frac{\partial Q}{\partial I_1} & \frac{\partial Q}{\partial I_2} \\ \frac{\partial R}{\partial S_1} & \frac{\partial R}{\partial I_1} & \frac{\partial R}{\partial I_2} \end{pmatrix} \\ &= \begin{pmatrix} -a_1 - a_2 - \beta I_1 & b + \gamma - a_2 - \beta S_1 & -a_2 \\ \beta I_1 & \beta S_1 - (b + \gamma) & 0 \\ -\beta I_2 & -\beta I_2 & \beta(N - S_1 - I_1 - 2I_2) - (b + \gamma) \end{pmatrix}. \end{aligned} \quad (2.55)$$

For $P_1 = (S_1, I_1, I_2) = \left(\frac{a_2}{a_1+a_2}N, 0, 0\right)$, the Jacobi matrix J can be rewritten as follows:

$$J_{P_1} = \begin{pmatrix} -a_1 - a_2 & b + \gamma - a_2 - \frac{a_2 N}{a_1+a_2} \beta & -a_2 \\ 0 & \frac{a_2 N}{a_1+a_2} \beta - (b + \gamma) & 0 \\ 0 & 0 & \frac{a_1 N}{a_1+a_2} \beta - (b + \gamma) \end{pmatrix}.$$

According to the Jacobi matrix J_{P_1} , it is easy to obtain the secular equation of Eq. (2.51):

$$(\lambda + a_1 + a_2)(\lambda + b + \gamma - \frac{a_2 N}{a_1 + a_2} \beta)(\lambda + b + \gamma - \frac{a_1 N}{a_1 + a_2} \beta) = 0. \quad (2.56)$$

The three latent roots of this secular equation are $-a_1 - a_2$, $\frac{a_2 N}{a_1+a_2} \beta - b - \gamma$ and $\frac{a_1 N}{a_1+a_2} \beta - b - \gamma$. Based on Routh-Hurwitz stability criterion, only when $\beta < \frac{(a_1+a_2)(b+\gamma)}{a_1 N}$ and $\beta < \frac{(a_1+a_2)(b+\gamma)}{a_2 N}$, three latent roots of the secular equation would have negative real part, simultaneously, and then $P_1 = (S_1, I_1, I_2) = \left(\frac{a_2}{a_1+a_2}N, 0, 0\right)$ is the stable solution of the differential equations.

Lemma 2.8 *Endemic equilibrium point P_2 in the SIS epidemic diffusion system is stable only when $a_2 < a_1$ and $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_1 N}$.*

Proof As far as we concerned, if the endemic equilibrium point $P_2 = (S_1, I_1, I_2) = \left(\frac{a_2}{a_1} \cdot \frac{b+\gamma}{\beta}, 0, N - \frac{a_1+a_2}{a_1} \cdot \frac{b+\gamma}{\beta}\right)$ exists, it should satisfy condition $I_2 > 0$ firstly. Namely, the propagation coefficient β should satisfy $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_1 N}$. Then, similar as Lemma 2.7, we can obtain the Jacobi matrix for P_2 as follows:

$$J_{P_2} = \begin{pmatrix} -a_1 - a_2 & b + \gamma - a_2 - \frac{a_2}{a_1}(b + \gamma) & -a_2 \\ 0 & \frac{a_2}{a_1}(b + \gamma) - (b + \gamma) & 0 \\ \frac{a_1+a_2}{a_1}(b + \gamma) - \beta N & \frac{a_1+a_2}{a_1}(b + \gamma) - \beta N & \frac{a_1+a_2}{a_1}(b + \gamma) - \beta N \end{pmatrix}.$$

According to the Jacobi matrix J_{P_2} , we can obtain the secular equation of Eq. (2.51) again:

$$[\lambda + b + \gamma - \frac{a_2}{a_1}(b + \gamma)](\lambda^2 + A_1 \lambda + A_0) = 0. \quad (2.57)$$

where $A_0 = a_1[\beta N - \frac{a_1+a_2}{a_1}(b + \gamma)]$ and $A_1 = a_1 + a_2 + \beta N - \frac{a_1+a_2}{a_1}(b + \gamma)$. Obviously, one of the latent roots of Eq. (2.57) is $\lambda_1^* = \frac{a_2 - a_1}{a_1}(b + \gamma)$. Only when $a_2 < a_1$, the latent root λ_1^* is negative. On the other hand, when $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_1 N}$, there is $A_0 > 0$ and $A_1 > 0$. Based on Routh-Hurwitz stability criterion, the other

two latent roots of Eq. (2.57) will be with negative real part. Therefore, P_2 is the stable solution of the simultaneous differential equations only when $a_2 < a_1$ and $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_1N}$.

Lemma 2.9 *Endemic equilibrium point P_3 in the SIS epidemic diffusion system is stable only when $a_1 < a_2$ and $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_2N}$.*

Proof Similarly as Lemma 2.8, if the endemic equilibrium point $P_3 = (S_1, I_1, I_2) = \left(\frac{b+\gamma}{\beta}, N - \frac{a_1+a_2}{a_2} \cdot \frac{b+\gamma}{\beta}, 0\right)$ is exist, it should satisfy condition $I_1 > 0$. That is, the propagation coefficient β should satisfy $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_2N}$. Then, we can obtain the Jacobi matrix for P_3 as follows:

$$J_{P_3} = \begin{pmatrix} -a_1 - a_2 - \beta N + \frac{a_1+a_2}{a_2}(b+\gamma) & -a_2 & -a_2 \\ \beta N - \frac{a_1+a_2}{a_2}(b+\gamma) & 0 & 0 \\ 0 & 0 & \frac{a_1-a_2}{a_2}(b+\gamma) \end{pmatrix}.$$

Again, according to the Jacobi matrix J_{P_3} , we can obtain the secular equation of Eq. (2.51):

$$\left[\lambda - \frac{a_1 - a_2}{a_2}(b + \gamma)\right](\lambda^2 + B_1\lambda + B_0) = 0. \quad (2.58)$$

where $B_0 = a_2[\beta N - \frac{a_1+a_2}{a_2}(b+\gamma)]$ and $B_1 = a_1 + a_2 + \beta N - \frac{a_1+a_2}{a_2}(b+\gamma)$. Obviously, one of the latent roots of Eq. (2.58) is $\lambda_1^* = \frac{a_1-a_2}{a_2}(b+\gamma)$. Only when $a_1 < a_2$, the latent root λ_1^* is negative. On the other hand, when $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_2N}$, there is $B_0 > 0$ and $B_1 > 0$. Based on Routh-Hurwitz stability criterion, the other two latent roots of Eq. (2.58) will be with negative real part. Therefore, P_3 is the stable solution of the simultaneous differential equations only when $a_1 < a_2$ and $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_2N}$.

Remark 2.4 From Lemmas 2.7, 2.8 and 2.9, we can draw a conclusion that the diffusion threshold of the SIS epidemic diffusion model relies on the migrating-out coefficients of susceptible individuals of the two cities $a_i (i = 1, 2)$, also depends on the three key parameters: the total individuals of the two cities N , the birth rate b and the recovery rate γ .

2.3.4 Numerical Test

In this section, we take a numerical simulation to test how well the proposed model may be applied in practice. The initial values of parameters in the proposed epidemic diffusion model are listed as follows: $\beta = 8 \times 10^{-6}$, $b = 2 \times 10^{-4}$, $\gamma = 0.4$,

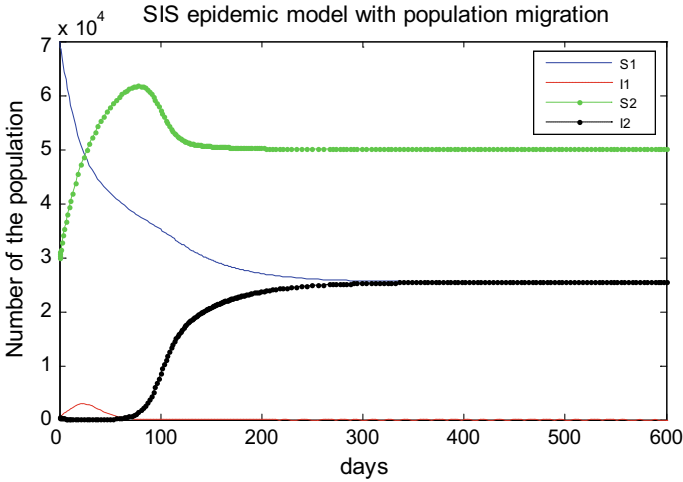


Fig. 2.13 Evolution trajectories of the SIS epidemic model

$a_1 = 0.02$, $a_2 = 0.01$, $N = 10^5$, $S_1(0) = 0.7 \times 10^5$, $I_1(0) = 600$ and $I_2(0) = 400$. We use MATLAB 7.0 mathematical solver together with Runge-Kutta method to simulate the epidemic model. The test is performed on an Intel(R) Core(TM) i3 CPU 2.4 GHz with 2 GB RAM under Microsoft Windows XP. Figure 2.13 is the evolution trajectories of the epidemic model. The curves respectively represent the different groups of people over time in these two cities.

From Fig. 2.13, one can see that the evolution trajectories of the SIS epidemic model with population migration between two cities are complicated. The number of susceptible individuals in city 1 decreases gradually with time increasing, while the number of susceptible individuals in city 2 increases at first and then decreases. On the other hand, the number of infected individuals in city 1 increases at first and then decreases; while the number of infected individuals in city 2 increases gradually with time increasing. However, all the susceptible individuals and infected individuals in city 1 and city 2 tend to the fixed values when time is long enough ($t > 300$). Meanwhile, the limit value of the SIS epidemic diffusion model with population migration between two cities is $Q_1 = (S_1, S_2, I_1, I_2) = (2.5013 \times 10^4, 5.0025 \times 10^4, 0, 2.4961 \times 10^4)$.

In line with the initial values we defined above, we have $a_2 < a_1$ and $\beta > \frac{(a_1+a_2)(b+\gamma)}{a_1 N}$. According to Lemma 2.8, one can get that the number of susceptible and infected individuals will be converged at $Q_2 = (S_1^*, S_2^*, I_1^*, I_2^*) = (2.50125 \times 10^4, 5.00245 \times 10^4, 0, 2.4963 \times 10^4)$. One can see that Q_1 is very close to Q_2 , which is not a surprise, as it is consistent with the analytical conclusion in the last section. Once an epidemic outbreak, we are more concerned with the change regularity of the infected individuals in practice. Therefore, in the following subsections, we will discuss the relationship between the key parameters and the number of the infected individuals.

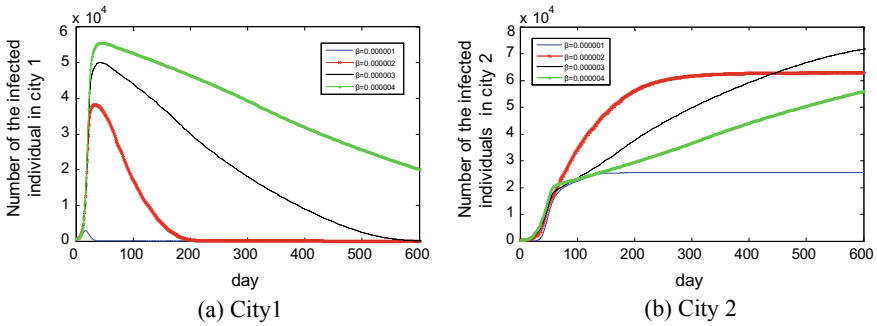


Fig. 2.14 Number of the infected individuals versus different β

Figure 2.14 demonstrates the change of the number of the infected individuals in both cities with different propagation coefficient. It is easy to know that the evolution trajectories of infected individuals in city 1 are different from that in city 2 for any certain propagation coefficient β . From Fig. 2.14a, we can see that in the first some days, the larger β is, the faster spread of the epidemic in city 1 is. However, from Fig. 2.14b, we can't get the similar conclusion. Number of infected individuals in city 2 is not in direct proportion to the propagation coefficient β . It is worth mentioning that when the number of infected individuals in city 1 reach zero, the number of infected individuals in the other city is still positive when the epidemic diffusion system is stable. This is consistent with the Lemma 2.8. Similarly, if the initial conditions changed, we can also test and verify the other lemmas.

Figure 2.15 demonstrates the change of the number of the infected individuals in both cities with different recovery rate γ . As shown in Fig. 2.15a, when $\gamma = 0.2$, the maximum number of infected individual in city 1 is about 3.3×10^4 . When $\gamma = 0.3$, the number is about 1.5×10^4 . When $\gamma = 0.4$, the maximum number of infected individual in city 1 is less than 0.5×10^4 . It informs us that the larger the recovery rate constant is, the smaller of the maximum number of infected individuals in city 1 is. Similar phenomenon can also be observed from Fig. 2.15b in city 2. Such figure

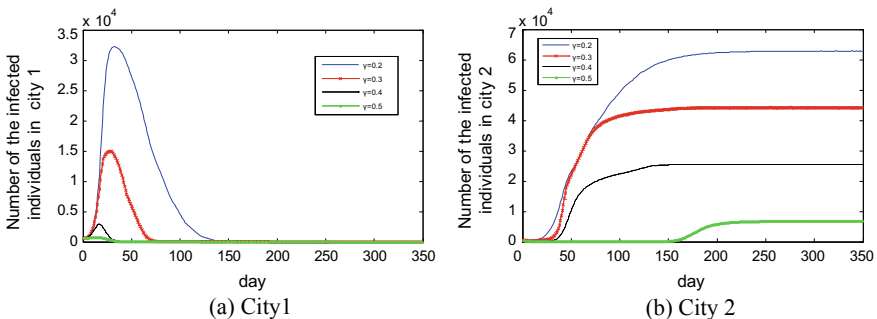


Fig. 2.15 Number of the infected individuals versus different γ

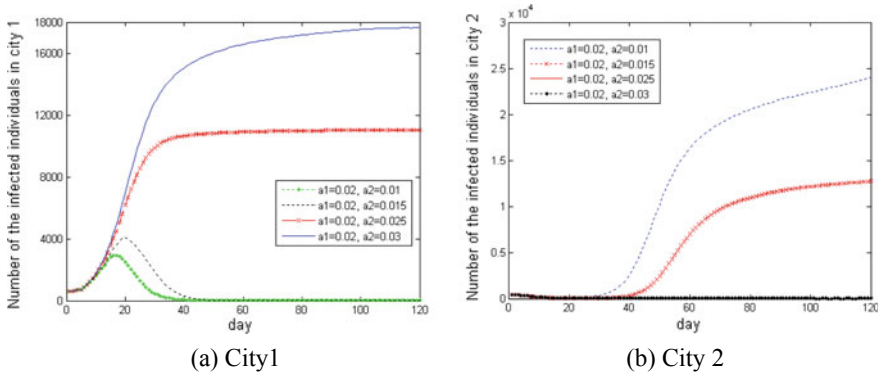


Fig. 2.16 Number of the infected individuals versus different a_1 and a_2

informs us it is important to improve the recovery rate as much as possible when in controlling an epidemic spread.

Figure 2.16 shows the change of the number of infected individuals in both cities with different migrating-out coefficients a_1 and a_2 . According to Fig. 2.16, one can observe that no matter in city 1 or in city 2, the evolution trajectories of the infected individuals may generate a serious change when the migrating-out coefficient of susceptible individuals changed. For example, in city 1, when $a_2 < a_1$ ($a_1 = 0.02, a_2 = 0.01$ and $a_1 = 0.02, a_2 = 0.015$), the number of infected individual tends to be zero. However, when $a_1 < a_2$ ($a_1 = 0.02, a_2 = 0.025$ and $a_1 = 0.02, a_2 = 0.03$), the number of infected individuals tends to be a positive constant above 1×10^4 . In other words, with the increment of migrating-out coefficient in city 2, the limit number of infected individuals in city 1 may become positive from zero. The larger the migrating-out coefficient in city 2 is, the larger the limit number of infected individuals in city 1 is. Opposite to city 1, when $a_2 < a_1$, the number of infected individuals in city 2 tends to be a positive constant above 1×10^4 . When $a_1 < a_2$, the number of infected individuals is very small and tends to be zero at last. It informs us that with the increment of migrating-out coefficient in city 2, the limit number of infected individuals in city 2 may become zero from a positive value. The larger the migrating-out coefficient in city 2 is, the smaller the limit number of infected individuals in city 2 is. To summarize, decreasing the migration population in only one city is not as effective as improving the recovery rate for controlling the epidemic diffusion. However, we can find a trade-off between the migrating-out coefficients in these two cities, and hence can control the infected individuals in both cities at last.

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Chapter 3

Mixed Distribution Mode for Emergency Resources in Anti-bioterrorism System



In this chapter, we construct a unique forecasting model for the demand of emergency resources based on the epidemic diffusion rule when suffering a bioterror attack. In what follows, we focus on how to deliver emergency resources to the epidemic areas. We find that both the pure point-to-point delivery mode and the pure multi-depot, multiple traveling salesmen delivery system are difficult to operate in an actual emergency situation. Thus, we propose a mixed-collaborative distribution mode, which can equilibrate the contradiction between these two pure modes. A special time window for the mixed-collaborative mode is designed. A genetic algorithm is adopted to solve the optimization model. To verify the validity and the feasibility of the mixed-collaborative mode, we compare it with these two pure distribution modes from both aspects of total distance and timeliness.

3.1 Introduction

The threat of bioterrorism, which is the deliberate use of viruses, bacteria, toxins, or even insects to harm civilian populations. Over the past few years, a number of bioterror events have been witnessed by the world, e.g. the attempt to disseminate anthrax in Japan in 1993, the frequent occurrence of bioterrorist hoaxes, revelations about the bio-weapon programs in the former Soviet Union and Iraq, and the anthrax-related exposures in Florida, New York City, and Washington, DC [1]. As such, bioterrorism has become one of the strongest enemies, threatening human health and life, and the well-being of national economics. Henderson [2] points out that the two most feared biological agents in a terrorist attack are smallpox and anthrax. Of these two, anthrax does not spread from person to person, and we focus on analyzing the response to a smallpox attack in a large city, with an eye towards how to deliver emergency resources to the epidemic areas.

After a bioterror attack occurs, public officials are faced with many critical issues, the most important of which is how to ensure the availability and supply of emergency resources so that the loss of life can be minimized and the efficiency of each rescue

operation can be maximized [3]. As mentioned in Craft et al. [4], deterrence is not a reliable strategy against terrorists, and because it is difficult to get biological agents out of the hands of terrorists before they attack, our security against a biological attack rests largely on consequence management, i.e., what can be done following a bioterror attack. The particularity of the problem opens up a wide range of applications of Operations Research/Management Science techniques. Actually, many recent research efforts have been devoted to applying Operations Research/Management Science techniques in emergency decision-making. For example, Altay and Green [5] offer a summary of literature survey that identifies potential research directions in disaster operations which make use of Operations Research/Management Science techniques. Moreover, a survey of operation research models and applications in homeland security is proposed by Wright et al. [6]. However, only a limited amount of Operations Research/Management Science techniques is adopted in the context of anti-bioterrorism.

Generally, emergency distribution in an anti-bioterrorism system is more complex, and differs from business logistics. Liu and Zhao [7] divide the emergency distribution problem in an anti-bioterrorism system into three stages. At the first stage, the disaster area has just suffered a bioterror attack, and the bio-virus (smallpox) has not yet caused a widespread diffusion. Thus, emergency resources from the local health department should be delivered to the epidemic area as quickly as possible. However, the following two important problems must be solved before the emergency distribution: (1) How should demand for emergency resources in the epidemic area be forecasted? It is often very difficult to predict the actual demand based on historical data (and for many disasters, historical data may not even exist). (2) What kind of distribution mode should be adopted to deliver the emergency resources?

So far, emergency distribution planning in China has traditionally been done manually and individually, based on the decision makers' experience. The following two distribution modes are frequently used: the pure point-to-point delivery mode (we refer to this as PTP mode), and the multi-depot, multiple traveling salesmen shipment system (we refer to this as MMTS mode). However, research on this topic shows that both of these two pure delivery modes are difficult to operate in an actual emergency situation. Thus, we propose a mixed-collaborative mode, which allows both of these two pure shipment systems to coexist. Furthermore, as mentioned before, the demand for emergency resources in an anti-bioterrorism system is different from that in other disasters (e.g. flood, typhoon and earthquake). It is closely related to the epidemic diffusion rule when a bioterror attack is suffered. Thus, we propose a unique forecast mechanism to predict the demand in the epidemic area. The model is expected to be an effective decision-making tool that can help to improve the efficiency of emergency distribution when a bioterror attack has taken place.

3.2 Literature Review

Considering the relationship between an unexpected bioterror attack and the associated emergency distribution decisions, we review two aspects of recent research efforts here: one is focused on the modeling methods for prevention and control of epidemics, and the other is related to emergency distribution.

3.2.1 *Literature Related to Epidemic Prevention and Control*

Many recent research efforts have been devoted to understanding the prevention and control of epidemics, such as those of Wein et al. [8, 9], Craft et al. [4], Kaplan et al. [10, 11], Kaplan and Wein [12]. Various mathematical models have been proposed to analyze and study the general characteristics of each epidemic, such as SI, SIR, susceptible–infected–susceptible (SIS), SIRS, SEI, SEIR and so on. It is worth mentioning that the major purpose of these articles is to compare the performance of the following two strategies, the traced vaccination (TV) strategy and the mass vaccination (MV) strategy, but not to focus on how to deliver emergency resources to the epidemic areas. Furthermore, the epidemic models which they addressed are based on the traditional compartment model, and the complex topological structure of the real world is not considered.

Jari and Kimmo [13] present a SIR model for modeling the spreading process of randomly contagious diseases, such as influenza, based on a dynamic small-world network. A study by Masuda and Konno [14] presents a multi-state epidemic process based on a complex network. They analyze the steady states of various multi-state disease propagation models with heterogeneous contact rates. In many models, heterogeneity simply decreases epidemic thresholds. Xu et al. [15] present a modified SIS model based on complex networks, small-world and scale-free, to study the spread of an epidemic by considering the effect of time delay. Based on two-dimension small-world networks, a susceptible-infected (SI) model with epidemic alert is proposed by Han [16]. This model indicates that the broadcasting of a timely epidemic alert is helpful and necessary in the control of epidemic spreading, and is in agreement with the general view of epidemic alert. Shi et al. [17] propose a new susceptible-infected-susceptible (SIS) model with infective medium. The dynamic behaviors of the model on a homogeneous network and on a heterogenous scale-free network are considered respectively. Furthermore, it is shown that the immune density of nodes depends not only on the infectivity between individual persons, but also on the infectivity between persons and mosquitoes. Zhang and Fu [18] study the spreading of epidemics on scale-free networks with infectivity which is nonlinear in the connectivity of nodes. The result shows that nonlinear infectivity is more appropriate than a constant or a linear one. With unit recovery rate and nonlinear irrational infectivity, the epidemic threshold is always positive.

It is worth mentioning that the majority of the previous work relies on different kinds of differential equations. For instance, first-order partial differential equations are used to integrate the age structures; second-order partial differential equations are suitable when a diffusion term exists; and integral differential equations or differential equations are often used when a time delay or delay factors are considered [3]. Although the epidemic diffusion rule is not the emphasis of our research, it is a necessary component when depicting the emergency demand.

3.2.2 Literature Related to Emergency Distribution

As mentioned before, PTP mode and MMTS mode are the two frequently used distribution modes in reality. Thus, there exists a great deal of research on emergency distribution that uses these two distribution modes. However, only a limited amount of the literature is dedicated to the mixed-collaborative shipment system. We shall now give a brief review of the existing studies.

Kemball-Cook and Stephenson [19] were among the first group of scholars to point out that logistics management is needed to improve transportation efficiency when rescue materials are being transported. Since then, a lot of articles pertinent to emergency distribution have been published. Some typical literature about the emergency distribution in the recent years are shown as follows: Yi and Kumar [20] present a meta-heuristic of ant colony optimization for solving the logistics problem arising in disaster relief activities. The logistics planning involves the following two aspects: to distribute emergency resources to the distribution centers in the affected areas and to evacuate the wounded people to medical centers. Tzeng et al. [21] construct a relief-distribution model using the multi-objective programming method for designing relief delivery systems in a real case. The model features three objectives: minimizing the total cost, minimizing the total travel time, and maximizing the minimal satisfaction during the planning period. Chang et al. [22] develop a decision-making tool that can be used by government agencies in planning for flood emergency logistics. In this article, the flood emergency resources distribution problem is formulated as two stochastic programming models. A study by Sheu [23] presents a hybrid fuzzy clustering-optimization approach to the operation of an emergency resources distribution in response to the time-varying demand during the crucial rescue period. Yan and Shih [24] consider how to minimize the length of time required for emergency roadway repair and relief distribution, as well as the related operating constraints. The weighting method is adopted and a heuristic algorithm is developed to solve the actual emergency relief problem, such as the Chi-Chi earthquake in Taiwan. For more recent results on this topic, we refer readers to Laurent and Hao [25].

It is worth mentioning that all the previous works are not in the context of anti-bioterrorism. In order to optimize the process of materials distribution in an anti-bioterrorism system, and to improve the emergency relief timeliness, the emergency materials distribution problem in a system of anti-bioterrorism is constructed as

a multiple traveling salesman problem with time window in Liu and Zhao [7]. A very recent research effort by Wang et al. [3] constructs a multi-objective stochastic programming model with time-varying demand for the emergency logistics network based on the epidemic diffusion rule. The genetic algorithm coupled with Monte Carlo simulation is adopted to solve the optimization model.

Though a great deal of literature on emergency distribution has been published, only little attention has been paid to the mixed-collaborative shipment system. Liu et al. [26] propose a heuristic algorithm for scheduling vehicles in a mixed truck delivery system with both hub-and-spoke and direct shipment delivery modes. The experiment’s results show that the mixed system can save around 10% of total traveling distance on average as compared with either of the two pure systems. The focus of Grünert and Sebastian [27] is on models for long-haul transportation in postal and package delivery systems, and a mixed network, which combines both direct flights and hub flights, is applied. However, these works were not carried out under emergency conditions. To the best of our knowledge, there has not yet been any research which has used a mixed-collaborative shipment system to deliver emergency resources in the context of anti-bioterrorism.

Therefore, in this chapter, we construct a unique forecasting model of the demand for emergency resources based on the epidemic diffusion rule when a bioterror attack is suffered. Then we propose three different distribution models based on different constraints. A special time window for the mixed-collaborative model is designed. A genetic algorithm is adopted to solve the optimization model.

3.3 Demand Forecasting Based on Epidemic Dynamics

3.3.1 SEIQRS Model Based on Small-World Network

Most epidemics divide people into five classes: susceptible people (S), people during the incubation period (E), infected people (I), quarantined people (Q) and recovered people (R). The survey by Tham [28] shows that some of the recovered people who are discharged from the emergency department will be re-infected. Thus, as Fig. 3.1

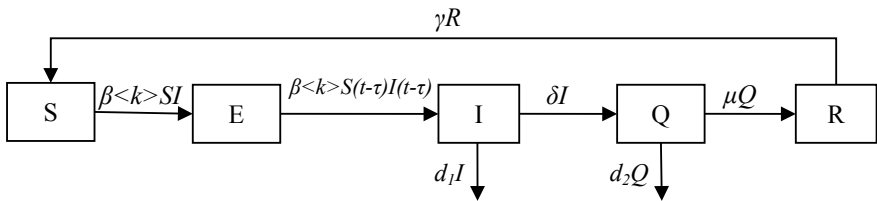


Fig. 3.1 SEIQRS model based on small-world network

shows, without consideration of the population migration, we can use a SEIQRS model based on small-world network to describe the developing epidemic process.

For epidemic diffusion models based on small-world network match the actual social network much better, a great deal of attention has been paid to studying these models. Therefore, the following SEIQRS model [7] is adopted in this chapter:

$$\begin{cases} \frac{dS}{dt} = -\beta \langle k \rangle S(t)I(t) + \gamma R(t) \\ \frac{dE}{dt} = \beta \langle k \rangle S(t)I(t) - \beta \langle k \rangle S(t - \tau)I(t - \tau) \\ \frac{dI}{dt} = \beta \langle k \rangle S(t - \tau)I(t - \tau) - (d_1 + \delta)I(t) \\ \frac{dQ}{dt} = \delta I(t) - (d_2 + \mu)Q(t) \\ \frac{dR}{dt} = \mu Q(t) - \gamma R(t) \end{cases} \quad (3.1)$$

In such an epidemic diffusion model, the time-based parameters $S(t)$, $E(t)$, $I(t)$, $Q(t)$ and $R(t)$, represent the number of susceptible people, the number of people during the incubation period, the number of infected people, the number of quarantined people and the number of recovered people, respectively. Other parameters include: $\langle k \rangle$ is the average degree distribution of the small-world network; β is the propagation coefficient of the bio-virus (smallpox); γ represents the rate of the recovered people who will be re-infected; δ is the quarantined rate of the infected people; d_1 is the death rate of the infected people caused by the disease; d_2 is the death rate of the quarantined people caused by the disease; μ is the recovered rate of the infected people; τ stands for the incubation period. Furthermore, $\langle k \rangle$, β , γ , δ , d_1 , d_2 , μ , $\tau > 0$.

From Eq. (3.1), we can see that $I(t)$ and $Q(t)$, which denote the number of infected people and the number of quarantined people, can be calculated by solving the ordinary differential equations when the initial values of $S(t)$, $E(t)$, $I(t)$, $Q(t)$ and $R(t)$ are given. It is desired that these two parameters stay at a value as low as possible, which implies that the situation is stable and the spread of the epidemic is under control.

3.3.2 Demand for Emergency Resources

Demand for emergency resources has been devoted to variety of forms in the previous literature, such as a time-varying value [23], or obeying some stochastic distribution [24]. These forecasting models are not suitable when a bioterror attack is suffered. As mentioned above, demand for emergency resources is closely related to the epidemic diffusion rule. Intuitively, the more people infected by the bio-virus, the more emergency resources will be demanded. To facilitate the calculation process in the following sections, and based on Eq. (3.1), demand for emergency resources can be formulated as follows:

$$d_t = \langle k \rangle I(t) + Q(t), \quad (3.2)$$

where d_t represents demand for emergency resources in the epidemic area at time t . Thus, with the partial derivative of d_t , we get

$$\begin{aligned} \frac{dd}{dt} = & \langle k \rangle [\beta \langle k \rangle S(t - \tau) I(t - \tau)] \\ & - [\langle k \rangle (d_1 + \delta) - 1] I(t) - (d_2 + \mu) Q(t). \end{aligned} \quad (3.3)$$

According to the above formulas, demand for emergency resources in the epidemic area can be forecasted when the initial values of relative parameters are given. In what follows, we will propose the three different distribution models based on the forecasting demand.

3.4 Model Formulations

3.4.1 Point-to-Point Distribution Mode with no Vehicle Constraints

Intuitively, PTP mode with no vehicle constraints would result in the best delivery efficiency, because each demand node obtains the replenishment directly. If all emergency resources are distributed by PTP mode, then the problem is simple and can be formulated as a linear programming model as follows.

Suppose the emergency distribution network can be constructed as a digraph $G(O, V, E, \omega)$, where $O = \{1, 2, \dots, m\}$ represents the emergency stockpile depots, and $V = \{1, 2, \dots, n\}$ stands for the emergency demand nodes. $E = \{e_{ij} | i \in O, j \in V\}$ represents the distribution arcs, where e_{ij} is the arc from the stockpile depot i to the emergency demand node j . ω_{ij} is characterized as the Euclidean distance from stockpile depot i to emergency demand node j . $E Q_i \{i \in O\}$ means the original inventory of emergency resources in stockpile depot i . I_j and $Q_j \{j \in V\}$ stand for the number of infected people and the number of quarantined people in the demand node j , respectively. $d_j \{j \in V\}$ is the demand for emergency resources in node j and can be calculated by Eq. (3.2). And last, the decision variable $z_{ij} = 1$ if the demand node j will be serviced by stockpile depot i ; otherwise, $z_{ij} = 0$. Suppose that capacity of the vehicle is large enough for each demand node to be satisfied in one trip. Thus, it is easy to formulate the linear programming model for the PTP mode with no vehicle constraints as follows (M1):

$$(M1) \quad \min \sum_{i \in O} \sum_{j \in V} 2\omega_{ij} z_{ij} \quad (3.4)$$

$$\text{s.t.} \quad \sum_{j=1}^n d_j z_{ij} \leq E Q_i, \quad \forall i \in O \quad (3.5)$$

$$\sum_{i=1}^m EQ_i z_{ij} \geq d_j, \forall j \in V \quad (3.6)$$

$$\sum_{i=1}^m z_{ij} \geq 1, \forall j \in V \quad (3.7)$$

$$\omega_{ij} = \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2}, \forall i \in O, j \in V \quad (3.8)$$

$$d_j = \langle k \rangle I_j + Q_j, \forall j \in V \quad (3.9)$$

$$z_{ij} = 0 \text{ or } 1, \forall i \in O, j \in V. \quad (3.10)$$

Here, Eq. (3.4) is the objective function, searching for the minimum total delivery distance. Equations (3.5) and (3.6) are constraints for flow conservation and guarantee that there are enough emergency resources. Equation (3.7) ensures that all demand nodes would be supplied. Equation (3.8) is the Euclidean distance from stockpile depot i to emergency demand node j , where x and y represent the X-coordinate and Y-coordinate, respectively. Equation (3.9) denotes the demand for emergency resources in demand node j (as introduced in the Sect. 3.3.2). And last, Eq. (3.10) is the decision variable. The above model is a simple 0–1 integer programming model, and can be solved by some programming tools (e.g. Matlab, Lingo) directly.

Due to various constraints (such as the number of vehicles is limited, etc.), such a pure point-to-point distribution mode may be infeasible in an actual emergency rescue situation. In reality the delivery mode of the emergency resources is much more complex and difficult. For making a comparison between different emergency distribution modes, we propose a relative evaluation function as follows.

Supposing that the speed of the vehicle is a constant v , we can obtain the minimum waiting time set $T_{wait}^{PTP} = \{t_1^{PTP}, t_2^{PTP}, \dots, t_n^{PTP}\}$ for all demand nodes in the pure PTP mode based on the optimal solution of (M1). We define the relative timeliness of all demand nodes in this mode as equal to the standard value 1. Meanwhile, we define ϕ_j^{else} as representing the timeliness of demand node j in other distribution modes as follows:

$$\phi_j^{else} = \frac{t_j^{PTP}}{t_j^{else}}, \forall j \in V. \quad (3.11)$$

Herein, t_j^{else} is the minimum waiting time of the demand node j in other shipment systems before it gets the emergency replenishment. Therefore, the relative evaluation function of the timeliness in other distribution modes can be formulated as follows:

$$\Phi_{else} = \frac{1}{n} \sum_{j \in V} \phi_j^{else}, \forall j \in V. \quad (3.12)$$

3.4.2 The Multi-depot, Multiple Traveling Salesmen Distribution Mode with Vehicle Constraints

In this section, we analyze the problem from another point of view. We assume that both the capacity and the number of vehicles are limited. Thus, an inevitable problem for distribution in such a situation is scheduling for all the demand nodes. Under the assumption that each demand point would be satisfied after one replenishment, the problem can be transformed to a multi-depot, multiple traveling salesmen distribution problem, which is characterized as a NP-hard problem.

Suppose that the shipment system can be constructed as a digraph $G(O \cup V, E, \omega)$, where $O = \{1, 2, \dots, m\}$ represents the emergency stockpile depots, and $V = \{m + 1, m + 2, \dots, m + n\}$ stands for the emergency demand nodes. $E = \{e_{ij} | i, j \in O \cup V, i \neq j\}$ represents the distribution arcs, where e_{ij} is the arc from point i to j in the network (if $i \in O, j \in V$, that means from the stockpile depot i to the demand node j ; if $i \in V, j \in O$, that means from the demand node i back to the stockpile depot j ; if $i, j \in V, i \neq j$, that means from the demand node i to the demand node j ; And last, if $i, j \in O, i \neq j$, that means from the stockpile depot i to the stockpile depot j). ω_{ij} is the Euclidean distance from point i to point j . Specially, in order to depict that there is no distribution arc between any two stockpile depots, ω_{ij} is defined as a large number while $i, j \in O, i \neq j$. R represents the feasible path set, and r_l stands for the feasible path in R . $EQ_k\{k \in O\}$ means the original inventory of the emergency resource in stockpile depot k . $S_k(k \in O)$ means the demand nodes set that is supplied by stockpile depot k , and it meets the constraint $\bigcup_{k \in O} S_k = V$. I_j and $Q_j\{j \in V\}$ stand for the number of people who are infected, and the number of people who are quarantined, respectively. $d_j\{j \in V\}$ is the demand for emergency resources in node j . $N_k(k \in O)$ is the least number of vehicles we needed in depot k , and Q_{cap} represents the capacity of the vehicle. And last, the decision variable, $z_{ij} = 1$ if the vehicle travels from point i to point j ; otherwise, $z_{ij} = 0$. Thus, the multi-depot, multiple traveling salesmen distribution problem can be formulated as follows (M2):

$$(M2) \quad \min \sum_{i \in O \cup V} \sum_{j \in O \cup V, i \neq j} \omega_{ij} z_{ij} \quad (3.13)$$

$$\text{s.t.} \quad \sum_{i \in O \cup V} x_{ij} = 1, \forall j \in V, i \neq j \quad (3.14)$$

$$\sum_{j \in O \cup V} x_{ij} = 1, \forall i \in V, i \neq j \quad (3.15)$$

$$\sum_{i \in O} \sum_{j \in V} z_{ij} = \sum_{i \in V} \sum_{j \in O} z_{ij} \quad (3.16)$$

$$\sum_{j \in S_k} d_j \leq EQ_k, \forall k \in O \quad (3.17)$$

$$\sum_{j \in r_i} d_j \leq Q_{cap}, \forall r_i \in R \quad (3.18)$$

$$\sum_{i \notin S} \sum_{j \in S} z_{ij} \geq 1, \forall S \subseteq V, |S| \geq 2 \quad (3.19)$$

$$N_k = \left\lceil \frac{\sum_{j \in S_k} d_j}{Q_{cap}} \right\rceil, \forall k \in O \quad (3.20)$$

$$\omega_{ij} = \begin{cases} \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2}, & \forall i \in O, j \in V, \\ \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2}, & \text{or } i \in V, j \in O, \\ \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2}, & \text{or } i, j \in V, i \neq j \end{cases} \quad (3.21)$$

$$\omega_{ij} = M, \forall i, j \in O, i \neq j \quad (3.22)$$

$$d_j = \langle k \rangle I_j + Q_j, \forall j \in V \quad (3.23)$$

$$z_{ij} = 0 \text{ or } 1, \forall i, j \in O \cup V, i \neq j \quad (3.24)$$

Herein, Eq. (3.13) is the objective function, searching for the minimum total distribution distance. Equations (3.14) and (3.15) ensure that each demand node would be supplied once. Equation (3.16) means all vehicles leaving the stockpile depots must return to them afterwards. Equation (3.17) means there are enough emergency resources for the demand nodes. Equation (3.18) is a constraint for the feasible path, which warrants that the total emergency requirement on the feasible path does not exceed the capacity of the vehicle. Equation (3.19) ensures that there is no sub-loop in the optimal solution. Equation (3.20) is used for calculating the number of vehicles required in each depot. Equations (3.21) and (3.22) are the distance constraints. Equation (3.23) is used for forecasting the demand for emergency resources in each demand node. Finally, Eq. (3.24) is the variable constraint. The above model is a typical NP problem, and would thus be difficult to optimally solve, especially for realistically large-scale problems. Therefore, we should design an algorithm to get the approximate optimal solution.

3.4.3 The Mixed-Collaborative Distribution Mode

In the above two Sects. (3.4.1) and (3.4.2), we discussed the problem from two different directions. In fact, both of these two pure distribution modes may be infeasible in an actual situation. On the one hand, we may have not enough vehicles to implement all the emergency services by PTP mode. On the other hand, if we adopt the MMTS mode, some of the vehicles may be unused, which reduces the emergency timeli-

ness. Thus, a mixed-collaborative mode, which allows both of these two distribution modes to coexist, is proposed in the following, with the objective of equilibrating the total rescue distance and timeliness. Similarly as before, this problem can also be depicted as follows.

at_j represents the time when the distribution vehicle arrives at the demand node $j \{j \in V\}$. $[e_j, l_j]$ represents the time window for demand node $j \{j \in V\}$, where e_j means the earliest arrival time (result of the PTP mode), and l_j is the latest arrival time (result of the MMTS mode). Here, we design a special time window for such a mixed-collaborative mode using the computational results of the former two pure modes, which guarantee that the outcome of the mixed-collaborative mode will be maintained at a high level. $N_i, i \in O$ means the number of vehicles in stockpile depot i . Suppose that the speed of the vehicle is an invariable constant, then $t_{ij} = \omega_{ij}/v, \forall i, j \in O \cup V$ would be the time consumed from point i to point j . Other parameters are specified in the same way as MMTS mode.

Such a mixed system can be understood as a MMTS mode which allows some requirements to be delivered directly when the constraints are much stricter. Thus, combined with Eq. (3.12) in Sect. 3.4.1, the mixed distribution problem can be formulated as follows (M3):

$$(M3) \quad \max \sum_{i \in O} \Phi_i \quad (3.25)$$

$$\text{s.t.} \quad \sum_{i \in O \cup V} x_{ij} = 1, \forall j \in V, i \neq j \quad (3.26)$$

$$\sum_{j \in O \cup V} x_{ij} = 1, \forall i \in V, i \neq j \quad (3.27)$$

$$\sum_{j \in V} z_{ij} = N_i, \forall i \in O \quad (3.28)$$

$$\sum_{i \in V} z_{ij} = N_j, \forall j \in O \quad (3.29)$$

$$\sum_{j \in S_k} d_j \leq EQ_k, \forall k \in O \quad (3.30)$$

$$\sum_{j \in r_l} d_j \leq Q_{cap}, \forall r_l \in R \quad (3.31)$$

$$\sum_{i \notin S} \sum_{j \in S} x_{ij} \geq 1, \forall S \subseteq V, |S| \geq 2 \quad (3.32)$$

$$\omega_{ij} = \sqrt{(x_i - x_j)^2 + (y_i - y_j)^2}, \quad \begin{array}{l} \forall i \in O, j \in V \\ \text{or } i \in V, j \in O \\ \text{or } i, j \in V, i \neq j \end{array} \quad (3.33)$$

$$\omega_{ij} = M, \forall i, j \in O, i \neq j \quad (3.34)$$

$$d_j = \langle k \rangle I_j + Q_j, \forall j \in V \quad (3.35)$$

$$e_j \leq at_j \leq l_j, \forall j \in V \quad (3.36)$$

$$at_i + t_{ij} + (1 - z_{ij})T \leq at_j, \forall i \in O \cup V, j \in V, i \neq j \quad (3.37)$$

$$at_i = 0, \forall i \in O \quad (3.38)$$

$$at_j > 0, e_j > 0, l_j > 0, \forall j \in V \quad (3.39)$$

$$t_{ij} > 0, \forall i \in O \cup V, j \in V, i \neq j \quad (3.40)$$

$$z_{ij} = 0 \text{ or } 1, \forall i, j \in O \cup V, i \neq j. \quad (3.41)$$

Equation (3.25) is the objective function, searching for the maximizing timeliness. Equations (3.28) and (3.29) mean that all vehicles leaving from the stockpile depot must finally return to the depot. Equations (3.35)–(3.39) are the time window constraints, T means a large enough number. Other constraints are defined in the same way as in Sect. 3.4.2.

3.5 Solution Procedures

The ‘dde23 function’ in MATLAB coupled with Eqs. (3.2) and (3.3) is adopted to calculate the demand in Eqs. (3.9), (3.23) and (3.35). The linear programming tool in MATLAB is implemented to solve the first model (M1). Thus, in this section, we focus on the solution methodology for the following two models (M2) and (M3). Since the available techniques for solving the mixed integer programming problems are still limited, and a genetic algorithm is commonly used, we adopt a genetic algorithm to solve the two models. Liu and Zhao [7] have designed a modified GA for such a problem, the major difference from Carter and Ragsdale [29] being that the former have designed a special set order operator, a crossover operator and a mutation operator. Based on this previous work, we make a further improvement to the GA in order to meet the requirements of the models in this chapter.

3.5.1 Operating Instructions for Genetic Algorithms

3.5.1.1 Chromosome Coding

The first step, which is also characteristic of the new “genetic algorithms”, is to define the chromosome coding as follows.

Figure 3.2 presents the three-part chromosome in this chapter (for example, 3 emergency stockpile depots, 27 demand nodes, $n = 9$ and $m = 3$). The first part of the chromosome represents the serial number of the emergency stockpile depot. The second part means the demand nodes which are supplied by the stockpile depot in the first part. The third part stands for the number of demand nodes to which each vehicle will be assigned. This part should meet the following two constraints: (i) Each element in this part should be a positive integer; (ii) The sum of all elements in this part should be equal to the length of the second part.

3.5.1.2 Other Steps

The fitness of each individual is obtained by computing the objective function. The selection process is based on the rule ‘the best one copy strategy’. Order crossover is selected for the second part because it is commonly used by TSP operator. The third part of the chromosome uses an asexual crossover method. We mutate the individual use of the custom mutation operator in Liu and Zhao [7]. As we cannot get the optimal result exactly for a NP-Hard problem, a max iteration is given for the termination.

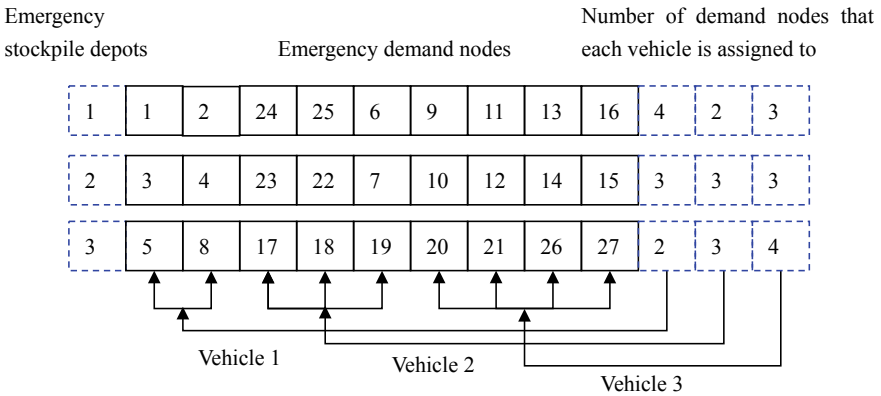


Fig. 3.2 The three-part chromosome

3.5.2 The Solution Procedure

We present the solution procedure in Table 3.1.

As mentioned before, the mixed-collaborative mode can be understood as a special case of MMTS mode. Thus, a solution algorithm of this kind can also be similarly applied for solving the model (M3) with suitable modifications as follows (Table 3.2).

Table 3.1 The solution procedure for model (M2)

Step 1	Initialize the population according to the chromosome coding rule and the related constraints (M2)
Step 2	Evaluation. Calculate fitness values of all the chromosomes
Step 3	Selection. Execute selection operation according to the selection rule
Step 4	Crossover. Execute crossover operation according to the crossover operator, 70% probability
Step 5	Verify validity of the two children's chromosomes using constraints in (M2), if true, compare the two children's chromosomes and the two parents' chromosomes, and reserve the best two of them
Step 6	Mutation. Execute mutation operation according to the mutation operator, 1% probability
Step 7	Verify validity of the children's chromosome using constraints in (M2), if true, compare the children's chromosome and the parents' chromosome, and reserve the better one
Step 8	Gen = gen + 1, if the termination condition is satisfied, end the GA program and output the optimal result, and then go to the next step. otherwise, go back to Step 2
Step 9	Output the results

Table 3.2 The solution procedure for model (M3)

Step 1	Initialize the population according to the chromosome coding rule and the related constraints (M3)
Step 2	Evaluation. Calculate fitness values of all the chromosomes (Evaluation function changed)
Step 5	Verify validity of the two children's chromosomes using constraints in (M3), if true, compare the two children's chromosomes and the two parents' chromosomes, and reserve the best two of them
Step 7	Verify validity of the children's chromosome using constraints in (M3), if true, compare the children's chromosome and the parents' chromosome, and reserve the better one

3.6 Computational Experiments and Result Analysis

To test how well the model may be applied in the real world, we exhibit a case study to demonstrate the efficiency of the proposed three different distribution models. To facilitate the calculation process, we assume that a city is suffering from a smallpox attack. There are 3 stockpile depots and 27 demand nodes (27 epidemic areas) in the city. The coordinates of these points are randomly selected from the Solomon benchmark data set. To further verify the validity and the feasibility of the solution procedure, we repeat this work 3 times, respectively for the 3 different kinds of the data R, C and RC subset in the Solomon benchmark problem.

The first step in the solution procedure is to forecast the demand for emergency resources in each demand node. We assume that each infected area can be isolated from the other areas to avoid the spread of the disease. The values of the parameters in the epidemic diffusion model are given as follows. $\beta = 1 \times 10^{-5}$, $\langle k \rangle = 6$, $d_1 = 5 \times 10^{-3}$, $d_2 = 1 \times 10^{-3}$, $\gamma = 2 \times 10^{-3}$, $\delta = 0.3$, $\mu = 0.1$, $\tau = 5$. As mentioned in Sect. 3.3.1, the number of infected people and the number of quarantined people, can be calculated by solving the ordinary differential equations when the initial values of $S(t)$, $E(t)$, $I(t)$, $Q(t)$ and $R(t)$ are given. Taking the first demand node as an example, we assume that $S(0) = 9940$, $E(0) = 50$, $I(0) = 10$, $Q(0) = R(0) = 0$, and that Fig. 3.3 is a numerical simulation of the epidemic diffusion model for this epidemic area. The five curves respectively represent the five groups of people (S, E, I, Q, R) over time. Thus, demand of the emergency resources in such node is shown in Fig. 3.4.

After getting the demand in each epidemic node by repeating the above work 27 times, in what follows, we will compare the mixed-collaborative mode with the two pure distribution modes, from both aspects of total distance and timeliness.

Fig. 3.3 An example of the SEIQRS epidemic diffusion model

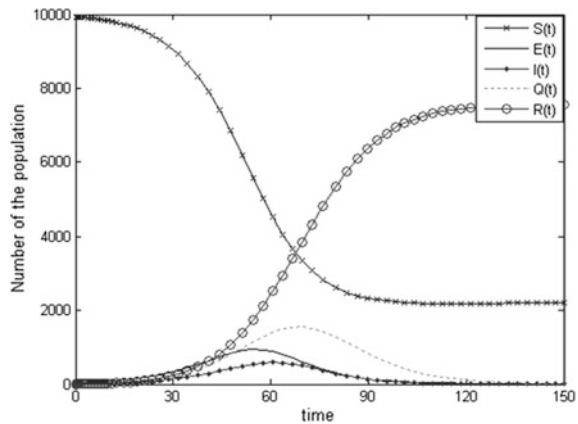
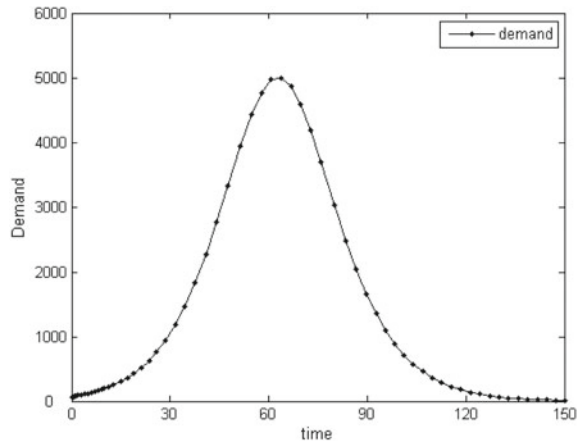


Fig. 3.4 An example of the demand for emergency resources



3.6.1 Comparison and Analysis for Each Stockpile Depot

As mentioned in Sect. 3.4, this chapter focuses on the first stage of responding to a bioterror attack, thus we take the distribution results at time $t = 3$ as our example. Furthermore, we assume that the emergency rescue cost is directly proportional to the total distance.

Comparing the two Figs. 3.5 and 3.6 (for detailed information about Figs. 3.5 and 3.6, please go to Appendix A in the end of this book), although we declare that the PTP mode often results in the best delivery efficiency, we also observe that the total distance in this mode is the largest one, whether in C, R, or RC subset. Thus, the total emergency rescue cost in this mode will also be the largest one. As to MMTS mode, we can observe that the total distance in this mode is always the minimum one when compared with the other two modes, whether to C, R, or RC subset. Although the total emergency rescue cost in this mode is the lowest one, it is worth mentioning that timeliness in MMTS mode is also the minimal one too, compared with the other two modes.

Thus, we reach the conclusion that both of these two pure distribution modes are difficult to operate in an actual situation. For the pure point-to-point delivery mode, there is a risk of raising the total rescue cost (Fig. 3.5), while the multi-depot, multiple traveling salesmen delivery system holds the risk of decreasing the total timeliness (Fig. 3.6), whether to C, R, or RC subset.

From these two Figs. 3.5 and 3.6, we also observe that the efficiency of the mixed-collaborative mode is always situated between these two pure modes. In the mixed-collaborative mode, we utilize the PTP mode to deliver the emergency resources to the demand node when the time window is very strict. For the demand node with loose time window, the MMTS mode is adopted. Thus, the contradiction between these two pure modes can be equilibrated. For example, when the mixed-collaborative mode

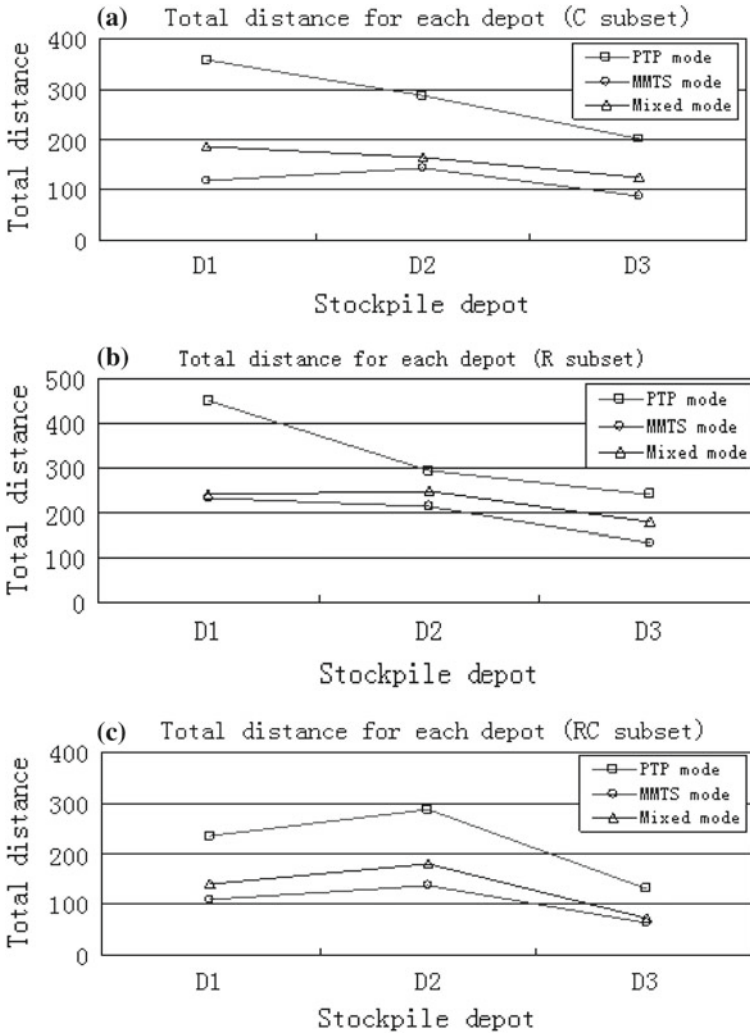


Fig. 3.5 Total distance of each depot

is adopted, the total distance of the three depots in C subset is respectively increased by 19, 7 and 18.5%, as opposed to MMTS mode (Fig. 3.5a). However, timeliness for those three depots is respectively improved by 8.3, 6.4 and 19%, too (Fig. 3.6a).

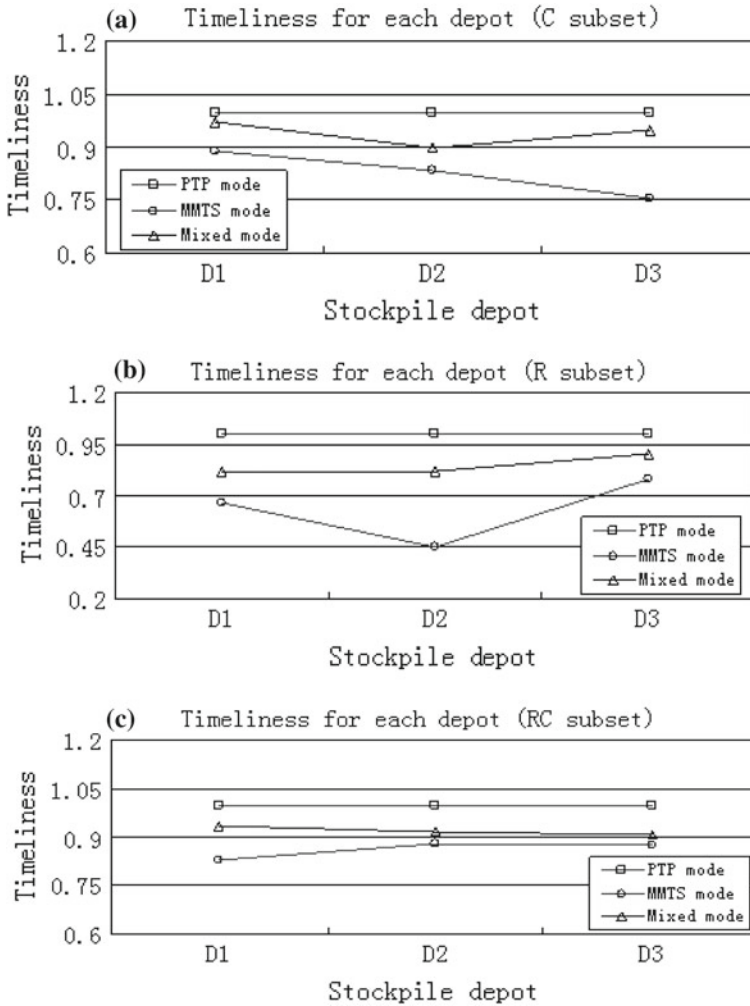


Fig. 3.6 Timeliness of each depot

3.6.2 Comparison and Analysis for Total Distance and Timeliness

In this section, we compare and analyze the three distribution models from the perspectives of total distance and timeliness. The results are shown as the following two tables.

From these two tables, we reach a similar conclusion as before: the PTP mode results in the best delivery efficiency and the largest distance, while the MMTS mode results in the worst delivery efficiency and the lowest distance. And finally, the contra-

Table 3.3 Total distance for the three modes

	C subset	R subset	RC subset
PTP mode	848.393	986.365	654.8171
MMTS mode	352.8543	581.8270	311.9578
Mixed mode	477.8886	665.5658	395.03989

Table 3.4 Total timeliness for the three modes

	C subset	R subset	RC subset
PTP mode	1	1	1
MMTS mode	0.8264	0.6310	0.8602
Mixed mode	0.9393	0.8478	0.9188

diction between these two pure modes can be equilibrated in the mixed-collaborative mode. For instance, the total average of the timeliness in the MMTS mode is merely 77.3%. To the three subsets C, R and RC, when the mixed-collaborative mode is adopted, the total distance is respectively increased by 14.7, 8.49 and 12.7%, as compared to the MMTS mode (Table 3.3). However, the total timeliness is respectively improved by 11.29, 21.68 and 5.86% (Table 3.4), which makes the total average of the timeliness in the mixed-collaborative mode 90.2%, and achieves a 12.9% improvement compared to the MMTS mode. This will be a much more appropriate solution for the actual relief activities.

As introduced in Sect. 3.3.1, emergency distribution in an anti-bioterrorism system is more complex, and differs from business logistics. Computational experiments and result analysis in this section show that the mixed-collaborative distribution model is expected to be an effective decision-making tool when a bioterror attack is suffered. Both of the two problems have been solved by such a mixed-collaborative method. Therefore, this method can be adopted by the emergency command center, and the traditional emergency distribution planning based on the decision makers’ experience would be improved.

3.7 Conclusions

In this chapter, we focus on how to deliver emergency resources to epidemic areas as fast as possible after a bioterror attack, and we propose three different distribution models, each based on different constraints. The main differences that distinguish this chapter from the past literature are presented as follows:

- (1) We construct a unique forecast mechanism to predict the demand in the epidemic area, which has just suffered a bioterror attack, based on epidemic diffusion rule. This is one of the basic constraints in the following three models, and a method of this kind is different from all past reports.

- (2) As both of these two pure distribution modes may be infeasible in a real-life situation, we propose a mixed-collaborative mode, which can equilibrate the contradiction between these two pure modes. To verify the validity and the feasibility of the mixed-collaborative mode, we compare it with the two pure distribution modes from both aspects of distance and timeliness.
- (3) To facilitate the comparison process, we propose a relative measure method of timeliness for the different distribution modes.

Besides, we offer a newly modified GA for solving the problems. To obtain more accurate results, we can increase the number of generations and the population size so as to expand the coding scale and search the optimization solution in a larger space.

It's also necessary to point out some limitations of this research. First of all, the programming models in this chapter are discrete, and do not consider that emergency resources distributed at an earlier stage will affect the demand later. Second, only homogeneous vehicle and hard time windows are considered in this chapter, which limits the practical implications of the method. Third, we assume that the infected area can be isolated from other areas to avoid the spread of the disease. Actually, this is very difficult. All these areas of improvement represent our future research directions.

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Chapter 4

Epidemic Logistics with Demand Information Updating Model I: Medical Resource Is Enough



In this chapter, we present a discrete time-space network model for allocating medical resource following an epidemic outbreak. It couples a forecasting mechanism for dynamic demand of medical resource based on an epidemic diffusion model and a multi-stage programming model for optimal allocation and transport of such resource. In this chapter, we present a discrete time-space network model for allocating medical resource following an epidemic outbreak. It couples a forecasting mechanism for dynamic demand of medical resource based on an epidemic diffusion model and a multi-stage programming model for optimal allocation and transport of such resource. At each stage, the linear programming solves for a cost minimizing resource allocation solution subject to a time-varying demand that is forecasted by a recursion model. The rationale that the medical resource allocated in early periods will take effect in subduing the spread of epidemic and thus impact the demand in later periods has been incorporated in such recursion model. We compare the proposed medical resource allocation mode with other operation modes in practice, and find that our model is superior to any of them in less waste of resource and less logistic cost. The results may provide some practical guidelines for a decision-maker who is in charge of medical resource allocation in an epidemics control effort.

4.1 Introduction

Over the past few years, the world has grown increasingly concerned about the threat of different epidemics. Disastrous epidemic events such as SARS and H1N1 significantly impacted people's life. The outbreak of infections in Europe is another recent example. The infection, from a strain of *Escherichia coli*, can lead to kidney failure and death and is difficult to treat with antibiotics. It is now widely recognized that a large-scale epidemic diffusion can conceivably cause many deaths and more people of permanent sequela, which presents a severe challenge to local or regional health-care systems.

After an epidemic outbreak, public officials are faced with many critical issues, the most important of which being how to ensure the availability and supply of medical resource so that the loss of life may be minimized and the rescue operation efficiency maximized. The medicine logistics in an epidemics controlling system is often complex and difficult. Hu et al. [1] compared public-health management mechanisms in both US and China from the following three aspects: organizational structure, management system and logistics network, and pointed out some deficient areas in the Chinese public-health management mechanism. To date, medicine logistics operation in epidemic control activities in China has traditionally been done unsystematically and separately, based on the decision-makers' experience and disregarding the interrelationship between the time-varying demand and the logistics operation planning from a systematic perspective. Thus, this paramount life-saving and costly logistics problem opens up a wide range of applications of Operations Research/Management Science techniques and has motivated many recent research works.

In this chapter, a time-space network model for the medical resource allocation problem in controlling epidemic diffusion is proposed. It couples a forecasting mechanism for the dynamic demand of the medical resource based on the epidemic diffusion pattern of susceptible-exposed-infected-recovered (SEIR) model [2] and a multi-stage programming model for optimal allocation and transport of such resource. The two dynamic processes are woven together and interactively proceed to model the epidemic diffusion and the medical resource allocation. Particularly, given the dynamic demand for the medical resource at each stage predicted by the forecasting mechanism, the linear programming problem solves the cost minimizing resource allocation pattern subject to related operating constraints. The optimal solution of the resource allocation will then determine their availability at each emergent district hospital, upon which the efficiency of rescuing effort is conditioned (assuming the other needed health care technologies and human resource are guaranteed). The efficiency of the rescuing effort will determine the recovering rate of the infected population, which, in turn, will generate the new forecast of the demand for medical resource by updating the SEIR diffusion model. The above described model is expected to be an effective decision-making tool that can help improve the efficiency of medicine logistics when an epidemic outbreaks.

4.2 Literature Review

Considering the relationship between the epidemic diffusion and the associated medical resource allocation, we review two streams of recent research efforts here: one is focused on the epidemic diffusion modeling, and the other is related to the medical resource allocation modeling.

4.2.1 Epidemic Diffusion Modeling

Most analytical works on epidemic diffusion are concentrated on the compartmental epidemic models described by ordinary differential equations [3–5]. In these models, the total population is divided into several classes and each class of people is closed into a compartment. The sizes of the compartments are assumed to be large enough and the mixing of members to be homogeneous.

The second stream of research is on the development of epidemic diffusion models by applying complex network theory to the traditional compartment models [6–8]. Jung et al. [9] extended the previous studies on the prevention of the pandemic influenza to evaluate time-dependent optimal prevention policies, and they found that the quarantine policy was very important, and more effective than the elimination policy, during the disease spread period. Wang et al. [10] presented some suggestions for the epidemic prevention and infection control in the Wenchuan earthquake areas, Sichuan Province, China.

The third stream of research is on the development of epidemic diffusion models by applying simulation methods, including computer simulation and numerical computation [11–13]. For example, Samsuzzoha et al. [14] 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. [15] presented a vaccinated diffusive compartmental epidemic model to explore the impact of vaccination as well as diffusion on the transmission dynamics of influenza.

Recently and importantly, a robust data-driven fault detection approach is proposed with application to a wind turbine benchmark [16, 17]. The main challenges of the wind turbine fault detection lie in its nonlinearity, unknown disturbances as well as significant measurement noise. Sometimes the relative data may be missed [18, 19]. These works are constructive and helpful to understand and model the epidemic diffusion process in a very different way.

The above mentioned works represent some of the research on various differential equation models for epidemic diffusion and control. Although the emphasis of this chapter is on the efficient allocation of medical resource, a basic component of our model, the forecasting mechanism for their dynamic demand utilizes one of such epidemic diffusion models.

4.2.2 Medical Resource Allocation Modeling

To the best of our knowledge, a great deal of researches has been published with the topic on optimal allocation of medical resource [20–24]. To optimize the process of materials distribution in an epidemic diffusion system and to improve the distribution timeliness, Liu and Zhao [25] modeled the emergency materials distribution problem as a multiple traveling salesman problem with time window. Wang et al.

[26] constructed a multi-objective stochastic programming model with time-varying demand for the emergency logistics network based on the epidemic diffusion rule. A genetic algorithm coupled with Monte Carlo simulation was adopted to solve the optimization model. Qiang and Nagurney [27] proposed a humanitarian logistic model for supply/distribution of critical needs in a disruption caused by a natural disaster. They considered a general network structure and disruptions that may have an impact on both network link capacities and product demand. The problem was studied in a bi-criteria system optimization framework for network performance. Recently, Rachaniotis et al. [28] presented a deterministic resource scheduling model in epidemic control. In their work, a deterministic model, appropriate for large populations, where random interactions could be averaged out, was used for the epidemic's rate of spread. Besides, a case of the mass vaccination against H1N1 influenza in the Attica region, Greece and a comparative study of the model's performance versus the applied random practice were presented.

To deal with the complexity and difficulty in solving the medical resource allocation problem, we observe a trend in solution methodologies, that is, decomposing the original problem, which can be a multi-commodity, -modal, or -period model, into several mutually correlated sub-problems, and then solve them systematically in same decision scheme. For instance, Barbarosoglu et al. [29] proposed a bi-level hierarchical decomposition approach for helicopter mission planning during a disaster relief operation. The top-level model was formulated to deal with the tactical decisions, covering the issues of helicopter fleet management, crew assignment, and the number of tours undertaken by each helicopter. The base-level model aimed to address the corresponding operational decisions, including routing, loading/unloading and re-fueling scheduling. Yan and Shih [30] was more recent work following this line.

Furthermore, we note that most of the previous works were carried out under the assumption that the relief demand is not time sensitive. While in reality, the demand for medical resource is dynamic, and the medical resource allocated in early cycles will affect the demand in later periods. In this chapter, we will use a discrete time-space network to model the medical resource allocation problem when an epidemic outbreaks. In each decision cycle, the problem is constructed as a linear programming model to solve for the cost minimizing allocation solution subject to the time-varying demand that is predicted by the epidemic diffusion rule. As such, this study attempts to bridge the two streams of literature, the epidemic diffusion and the medicine logistics, which were studied separately in existing literature.

4.3 The Mathematical Model

Epidemic diffusion process can be divided according to its development into three stages [31]. The first stage is the inception of the epidemic in very limited population, which if noticed in time and treated properly can be controlled effectively without causing a wide spread. In the second stage, the epidemic has broken out into a widespread diffusion. An important part of epidemic control and rescue campaign is

to ensure the timely delivery of the needed medical resource according to the dynamic demand as determined by the progress of the epidemic spread. In the third stage, the epidemic diffusion has been controlled and the demand for medical resource has significantly declined. Liu et al. [32] proposed a model for studying medical resource distribution in the first stage. In this study, we will concentrate on the logistics problem of medical resource allocation in the second stage. Particularly, we will study how the Area Distribution Centers (ADC) should supply the District Distribution Centers (DDC), and how the DDCs should deliver the needed medical resource to the Emergency Designated Hospitals (EDH) in the most efficient and cost-effective way. Here we assume there are several ADCs in the epidemic spread area, which can be divided into several municipal districts or towns. Each district will have one or more DDCs which supply the needed medical resource to the EDHs in that district.

Since demand from each EDH is determined by the number of patients hospitalized there and varies according to the progress of epidemic diffusion, the allocation of medical resource need to chase the demand over time. Figure 4.1 gives a diagram of operations outlining the execution of the proposed model. The sequential operational routine continues until the epidemic diffusion gets under control. As Fig. 4.1 shows, medical resource allocation process is decomposed into n decision-making cycles. Each decision-making cycle includes three phases: epidemic diffusion analysis, demand forecasting, and medical resource allocation. These three phases are executed iteratively. The effect of the medical resource allocation is analyzed, and the number of infected people is updated at each cycle during the entire distribution process.

In the sequel, we will introduce SIERS model, a well-recognized epidemic diffusion model, in Sect. 4.3.1. Then we propose a forecasting model for the dynamic

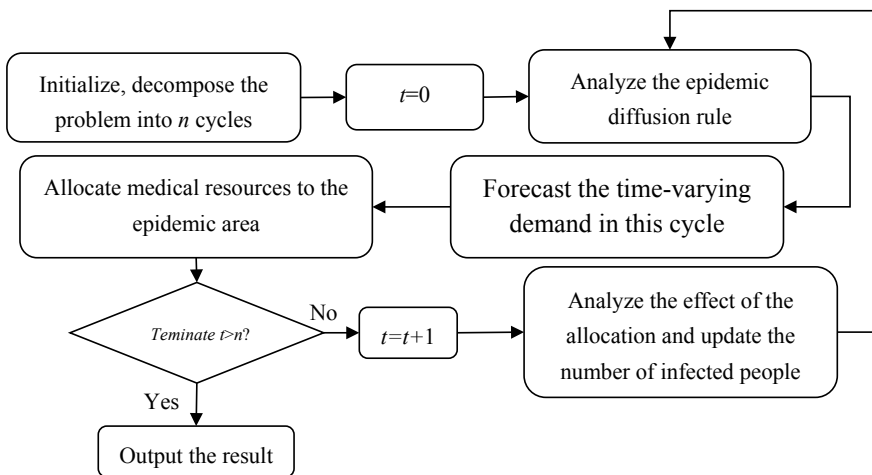


Fig. 4.1 Operational procedure of the dynamic medicine logistics network

demand for the medical resource during the epidemic diffusion in Sect. 4.3.2, and a linear programming model for distribution of medical resource according to the forecasted dynamic demand.

4.3.1 SEIRS Epidemic Diffusion Model

The SEIR model has been widely adopted by researchers to study epidemic diffusion. It is based on small-world network theory and provides a good match to the actual social network. Generally, the total population is divided into four classes, susceptible people (S), exposed people (E), infected people (I), recovered people (R), and each class of people is closed into a compartment. Tham [33] showed that some of the recovered people who were discharged from hospitals might be re-infected. Figure 4.2 shows, without consideration of migration, the natural birth rate and death rate of the population, the epidemic process can be described by a SEIRS model based on a small-world network.

The dynamic system for the SEIRS diffusion model can be rewritten by the following ordinary differential equations:

$$\begin{cases} \frac{dS}{dt} = -\beta k S(t)I(t) + \gamma R(t) \\ \frac{dE}{dt} = \beta k S(t)I(t) - \beta k S(t-\tau)I(t-\tau) \\ \frac{dI}{dt} = \beta k S(t-\tau)I(t-\tau) - (\alpha + \delta)I(t) \\ \frac{dR}{dt} = \delta I(t) - \gamma R(t). \end{cases} \quad (4.1)$$

In the above system of equations, $S(t)$, $E(t)$, $I(t)$ and $R(t)$ represent respectively the number of susceptible people, the number of exposed people, the number of infected people, and the number of recovered people. k is the average degree of distribution for this small-world network, which can be interpreted as the average contact number of susceptible people of each infected person; β is the propagation coefficient of the epidemic; γ is the rate of the recovered people who are not immune and thus may be re-infected; δ is the recovery rate; α is the death rate; τ represents the incubation period of the disease. $k, \beta, \gamma, \delta, \alpha, \tau > 0$.

ODE (4.1) states the following: (i) The growth rate of the susceptible population is determined by the returning population who are recovered but not immune and

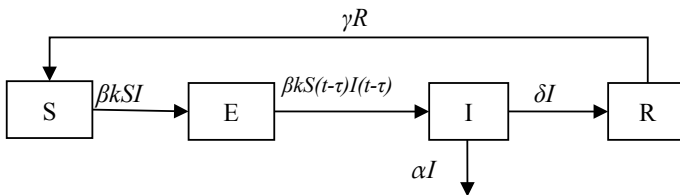


Fig. 4.2 SEIRS model based on a small-world network

the losing population who actually get exposed to the disease and thus are counted towards the class of $E(t)$. The latter is in proportion to the propagation coefficient β , the average contact number of susceptible people of each infected person, k , 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; And, finally (iv) the growth rate of the recovered population is determined by the difference between the joining population of the newly recovered and the losing population of the re-infected people.

Particularly, as we noted in (iii), the number of infected people, $I(t)$, is determined by the population of the recovered people and the onset exposed people at the end of the incubation period. Hence, improving the recovery rate, δ , and reducing the propagation coefficient, β , are the two effective measures to take in suppressing the growth of $I(t)$. In the context of epidemic controlling operation, that means sufficient medical resource should be allocated to the emergent designated hospitals (EDH).

4.3.2 The Forecasting Model for the Time-Varying Demand

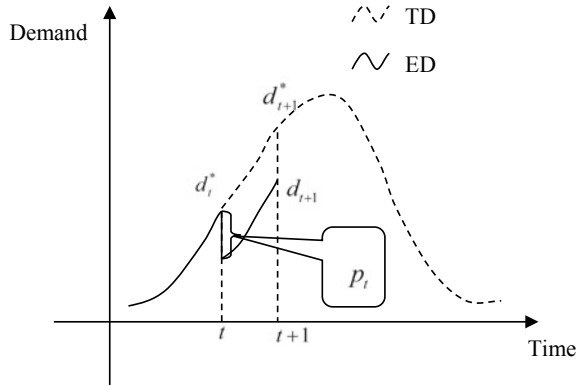
Demand for medical resource has been studied in a variety of forms in the literature, such as a time-varying value [34], or obeying some stochastic distribution [30]. However, the impact of earlier resource allocation to the demand in later periods has basically been ignored in these approaches.

To address this deficiency, we propose the following linear relationship between the demand for medical resource and the number of infected people at time t based on the SEIRS epidemic diffusion model:

$$d_t = aI(t), \quad (4.2)$$

where d_t refers to the demand for medical resource at time t , and a is the proportionality coefficient. In our interviews with the public health care administrative personnel about controlling the epidemic spread, we found this linear forecasting function is the one they commonly adopted. Here we define it as the traditional demand (TD). However, a lag effect of earlier medicine allocation should be taken into account in the current demand forecast. As shown in Fig. 4.3, the horizontal axis represents the decision-making cycle, and the vertical axis stands for demand in an epidemic area. The dotted line is a trajectory of Eq. (4.2), and the solid curve is the expected demand (ED). For instance, if the demand for medical resource at cycle t is d_t^* , and according to Eq. (4.2), the demand at cycle $t + 1$ would have been d_{t+1}^* . However, a certain amount of medical resource, p_t , had been allocated to the disaster area during

Fig. 4.3 Diagrammatic sketch of the time-varying demand



cycle t , and it would be taking effect in cycle $t + 1$ in curing the infected patients in hospitals and thus subduing the diffusion. Hence, the expected demand for medical resource at cycle $t + 1$ should be d_{t+1} , instead of d_{t+1}^* .

The following growth factor is introduced by the above observation to account for the lag effect.

$$\eta_t = (d_{t+1}^* - d_t^*) / d_t^*. \tag{4.3}$$

Herein, the growth factor η_t can be either positive (increasing demand) or negative (decreasing demand), and may vary in different cycles for the different demand d_t^* . As mentioned before, part of the recovered people who are discharged from the healthcare department may be re-infected. Thus, we define the effective cure rate as θ as the percent of recovered people who are not re-infected. Considering that each infected person needs a period of time to receive treatment and get cured, herein we denote the treatment cycle as Γ and we assume it to be an integral multiple of the decision cycle. Then, the commuted effective cure rate in each decision cycle can be obtained as $\frac{\theta}{\Gamma}$. Such an assumption would be feasible if the decision cycle is small enough, e.g. one day. Hence, it helps us get the following recursion formulas:

$$\text{When } t = 1, \quad d_1 = (1 + \eta_0) \left(1 - \frac{\theta}{\Gamma}\right) d_0; \tag{4.4}$$

$$\text{When } t = 2 \quad d_2 = (1 + \eta_1) \left(1 - \frac{\theta}{\Gamma}\right) d_1 = (1 + \eta_0)(1 + \eta_1) \left(1 - \frac{\theta}{\Gamma}\right)^2 d_0; \tag{4.5}$$

...

$$\text{When } t = n \quad d_n = \prod_{i=0}^{n-1} (1 + \eta_i) \left(1 - \frac{\theta}{\Gamma}\right)^n d_0. \tag{4.6}$$

Herein, $\prod_{i=0}^{n-1} (1 + \eta_i) = (1 + \eta_0)(1 + \eta_1) \dots (1 + \eta_{n-1})$. $d_0 = aI(0)$ is the initial demand for medical resource in the epidemic area, and $I(0)$ is the initial number of infected people in the epidemic area. Recursion formulas (4.4)–(4.6) are our prescribed forecast model for the demand of medical resource. In what follows, we will propose a medicine logistics operation model to minimize the total allocation cost based on the forecasting model.

4.3.3 Time-Space Network of the Medicine Logistics

In this subsection, a multi-stage programming model for cost minimizing allocation of the medical resource is built upon a time-space network. Figure 4.4 is the schematic diagram of the network. The vertical axis represents the time duration. The horizontal axis represents the Area Distribution Center (ADC), the District Distribution Center (DDC), and the Emergency Designated Hospital (EDH), respectively. The allocation arcs are defined as follows: (a) represents that medical resource is transported from ADC to DDC; (b) stands for that medical resource is allocated from DDC to EDH in the same district; (c) refers to that medical resource is allocated from DDC to EDH in the other district; (d)–(f) are time duration arcs for different departments.

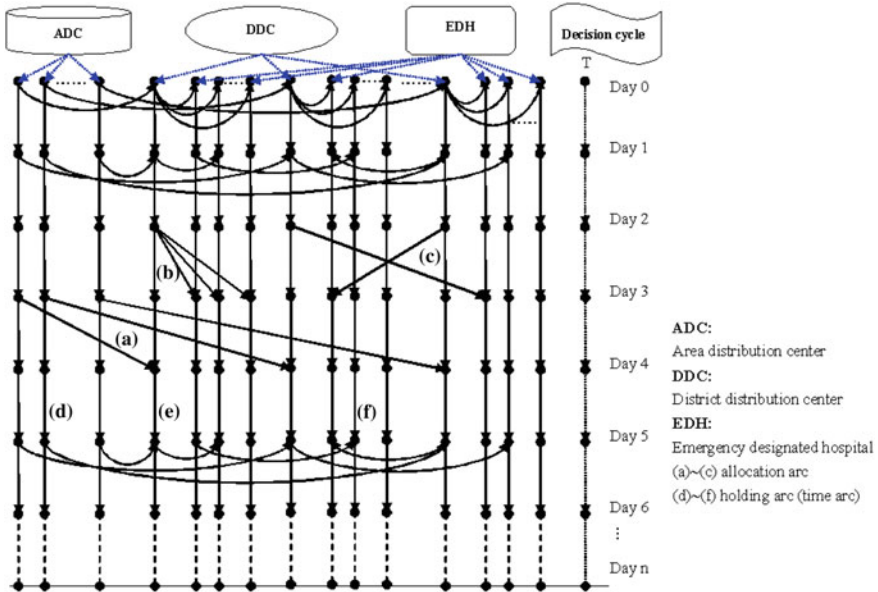


Fig. 4.4 Time-space network of medical resource allocation

(1) Assumptions

The following assumptions are needed to facilitate the model formulation in the following sections:

- (i) In the event of an epidemic outbreak, it is paramount for the government and the entire society to control the spread and rescue the infected. Thus it is reasonable to assume that the government can ensure the adequate supply of the needed medical resource either from domestic pharmaceutical companies or imported. Hence, there is enough medical resource in ADCs during the entire operation process.
- (ii) Once an epidemic outbreak, the government will take strict control measures so that each epidemic area can be isolated from other areas to avoid the cross spread of the disease. In each epidemic area, the government will appoint a hospital to be the EDH, to be responsible for the rescue work in such an isolated area.
- (iii) Medical resource in this study is an assembled product, which may includes water, vaccine, antibiotic, etc.

(2) Notations

Notations used in the following programming model are specified as follows:

- cc_{ij} : Unit transportation cost of medical resource from ADC i to DDC j .
 cr_{ij} : Unit transportation cost of medical resource from DDC i to EDH j .
 es_{it} : The available quantity of medical resource in ADC i in decision cycle t .
 zr_{it} : Quantity of medical resource allocated to DDC i in decision cycle t .
 x_{ijt} : Medical resource transported from ADC i to DDC j in decision cycle t .
 y_{ijt} : Medical resource transported from DDC i to EDH j in decision cycle t .
 d_{it} : Demand for medical resource in EDH i in decision cycle t .
 T : Set of decision cycles.
 C : Set of ADCs.
 R : Set of DDCs.
 H : Set of EDHs.

(3) Model formulation

Let $F(x, y)$ be the objective function of the total cost of medical resource allocation. Based on the above assumptions and descriptions, the proposed problem can be formulated as follows:

$$\text{Min } F(x, y) = \sum_{t \in T} \sum_{i \in C} \sum_{j \in R} x_{ijt} cc_{ij} + \sum_{t \in T} \sum_{i \in R} \sum_{j \in H} y_{ijt} cr_{ij} \quad (4.7)$$

$$\text{s.t. } \sum_{i \in C} x_{ijt} = zr_{jt}, \quad \forall j \in R, \quad t \in T \quad (4.8)$$

$$\sum_{j \in R} x_{ijt} \leq es_{it}, \quad \forall i \in C, \quad t \in T \quad (4.9)$$

$$\sum_{i \in R} y_{ijt} = d_{jt}, \quad \forall j \in H, \quad t \in T \quad (4.10)$$

$$\sum_{j \in H} y_{ijt} \leq zR_{it}, \quad \forall i \in R, \quad t \in T \quad (4.11)$$

$$d_{i0} = aI_i(0), \quad \forall i \in H \quad (4.12)$$

$$d_{it} = \prod_{t=0}^{t-1} (1 + \eta_{it}) \left(1 - \frac{\theta}{\Gamma}\right)^t d_{i0}, \quad \forall i \in H, \quad t \in \{T, t \neq 0\} \quad (4.13)$$

$$x_{ijt} \geq 0, \quad \forall i \in C, \quad j \in R, \quad t \in T \quad (4.14)$$

$$y_{ijt} \geq 0, \quad \forall i \in R, \quad j \in H, \quad t \in T \quad (4.15)$$

In this optimization model, x_{ijt} and y_{ijt} are the decision variables. The objective function (4.7) is to minimize the total cost of medical resource allocation, which is the transportation cost for delivering the medical resource from ADCs to DDCs and from DDCs to EDHs. Constraints (4.8)–(4.11) are the flow conservation equations. Particularly, constraint (4.8) suggests that each DDC can obtain medical resource from all ADCs. Constraint (4.9) ensures that the total shipments from any ADC cannot exceed the available amount of the resource in this ADC. Constraint (4.10) states that the period demand generated by the forecasting model in Sect. 4.3.2 at each EDH must be satisfied. That is, the shipments from all DDCs to each EDH must be equal to the demand at this EDH. Constraint (4.11) implies that the total shipments from any DDC cannot exceed the available stock in this DDC. Constraints (4.12) and (4.13) are forecasting model for the time-varying demand (Sect. 4.3.2). Herein, η_{it} is the growth factor (can be either positive or negative) of the demand for medical resource in EDH i in decision cycle t . Finally, (4.14) and (4.15) are the non-negativity of the flows. Such model is a dynamic and multi-stage programming model.

4.4 Solution Methodology

To solve the above optimization model, Eqs. (4.12)–(4.14) are adopted to calculate the time-varying demand firstly. After that, to $\forall t \in T$, the research model can be converted as a two-stage linear programming model. The feature of such a two-stage programming problem is that both the input quantity and the output quantity of the medical resource in the DDCs are unknown. There are many available techniques for solving such a problem, and a genetic algorithm is commonly used. Hence, a genetic algorithm coupled with MATLAB 7.0 mathematical programming solver is adopted to solve the model.

(1) Chromosome coding and population initializing

The first step of a genetic algorithm is to define the coding method of the chromosome. As is well known, the real number coding is superior to the binary coding in both aspects of quality and efficiency of the solution. Besides, the real number coding is closer to the actual problem findings and easier to interpret in the real world problem. Herein, the real number coding is adopted. For $\forall t \in T$, each chromosome contains R bit gene, where R is the number of DDC. The value of each bit refers to the available amount of medical resource in each DDC, which is also the quantity of medical resource replenished from all ADCs. Each individual in the initial population is generated by a random method, subject to the related resource constraints in the programming model.

(2) Fitness definition

The fitness of each individual is obtained by computing the objective function

$$F(x, y) = \sum_{t \in T} \sum_{i \in C} \sum_{j \in R} x_{ijt} cc_{ij} + \sum_{t \in T} \sum_{i \in R} \sum_{j \in H} y_{ijt} cr_{ij}.$$

Herein, the fitness function contains two parts. The first part is the total transportation cost between ADCs and DDCs. The second part is the total transportation cost between DDCs and EDHs. Obviously, the lower the total cost is, the better the fitness of the individual is.

(3) Selection operator

The best individual copy strategy is adopted in selection section. That means, each time when selection operator is iterated, the worst chromosome in the population will be replaced by the best one.

(4) Crossover operator

A crossover operator is one of the most important operators in a genetic algorithm. Different crossover operators are suitable for different kinds of chromosomes. According to the real number coding in this study, an arithmetic crossover is adopted. Let P_1 and P_2 represent the two parent chromosomes, and P_{c1} and P_{c2} stand for the two children chromosomes, respectively. The linear relationship between the parent and the children chromosomes can be formulated as:

$$\begin{cases} P_{c1} = \mu P_1 + (1 - \mu) P_2 \\ P_{c2} = (1 - \mu) P_1 + \mu P_2 \end{cases}$$

Herein, $\mu = U(0, 1)$ is a uniform random number between 0 and 1. Note that both of these two children chromosomes automatically satisfy the resource constraints in the multi-stage programming model. The range of the crossover probability p_c is 0.2–0.8.

(5) Mutation operator

A mutation operator is intended to simulate genetic mutation during biological evolution. Mutation is operated on some bits of individuals at a probability of p_m . This probability is generally very small and is set in the range of $0.001 \leq p_m \leq 0.1$. When mutating, we exchange a pair of genes in the individual.

(6) Termination condition

As the optimal result is unpredictable, a max iteration is given for the termination.

4.5 Numerical Tests

4.5.1 A Numerical Example

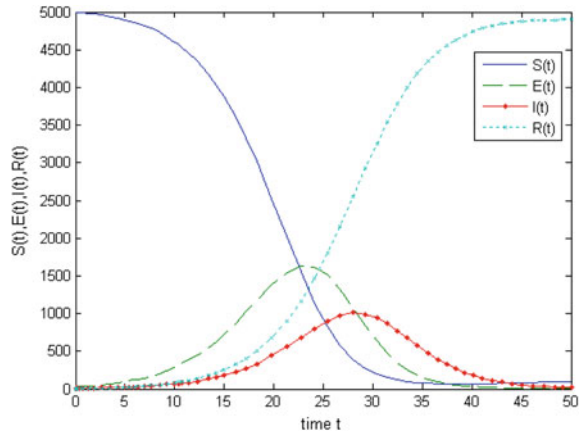
We present a numerical example to illustrate the efficiency of the proposed model. Assume there is a smallpox outbreak in a city, which has two ADCs and four DDCs. Two hospitals are designated in each district, and each EDH can service a certain amount of patients. The values of the parameters in the epidemic diffusion model are given in Table 4.1.

Figure 4.5 depicts a numerical simulation of the epidemic model at EDH1 in this effected region. The four curves respectively represent the number of four groups of people (S, E, I, R) over time. As mentioned in Sect. 4.3, the process of epidemic diffusion is divided into three stages and our work in this study is focus on the second stage. According to Fig. 4.5, such a stage can be ranged from the 10th day (decision-making cycle $t = 0$) to the 40th day (decision-making cycle $t = 30$). Of course, when different emergency outbreak, the result can be adjusted correspondingly.

Table 4.1 Values of parameters in the SEIRS model

	ADC1				ADC2			
	DDC1		DDC2		DDC3		DDC4	
	EDH1	EDH2	EDH3	EDH4	EDH5	EDH6	EDH7	EDH8
$S(0)$	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
$E(0)$	30	35	30	40	25	40	50	45
$I(0)$	5	6	7	8	4	7	9	10
$R(0)$	0							
β	5×10^{-5}							
$\langle k \rangle$	6							
δ	0.3							
d	1×10^{-3}							
γ	1×10^{-3}							
τ	5							

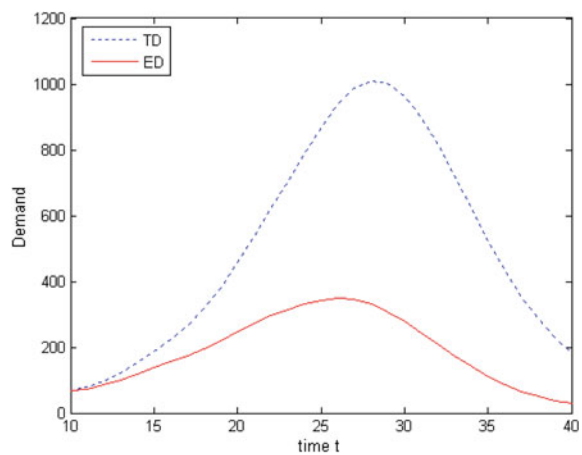
Fig. 4.5 Solution of the SEIRS epidemic diffusion model (EDH1)



To facilitate the calculate process in the following sections, the decision-making cycle is assumed to be one day. Let $a = 1$, MATLAB 7.0 mathematical programming solver coupled with Eqs. (4.1) and (4.2) are adopted to calculate the TD for medical resource in each EDH. Furthermore, given that $\theta = 90\%$ and $\Gamma = 15$ (days), the growth factor η_{it} in each decision-making cycle can be obtained. Then, the ED for medical resource in each EDH in each decision cycle can be forecasted according to Eqs. (4.12) and (4.13). Taking EDH1 as an example, the demand for medical resource in each decision-making cycle by these two different methods is compared as shown in Fig. 4.6.

One can observe in Fig. 4.6 that ED is way below TD, suggesting that the allocation of medical resource in the early periods will significantly reduce the demand in the following periods. The second observation is that both curves exhibit similar trends,

Fig. 4.6 Demand in EDH1 by the two different methods



namely, the demand will first increase along with the spreading the epidemic, and then will decrease after the epidemic is brought under control.

We now proceed to illustrate the optimal allocation of the resource at each EDH. Table 4.2 shows the unit operation cost of medicine between two different departments.

Let $n = 200$, $p_c = 0.75$ and $p_m = 0.01$. The algorithm is set to terminate in 200 generations. Taking the allocation at cycle $t = 0$ as the initial example, we solve the above programming model (4.7)–(4.15) according to the solution procedure. The convergent allocation scheme is reported in Table 4.3 and the total operation cost is 2663.22.

To test the accuracy and stability of the algorithm, the computation process has been repeated for six times independently. As shown in Table 4.4, the convergent results in these six times are very close and the deviation is less than 0.065%. This proves the proposed algorithm is stable and accurate. We execute the solution procedure (Table 4.1) to find the dynamic allocation result of medical resource and show in Fig. 4.7 the total cost at each decision-making cycle.

Comparing Fig. 4.7 with Fig. 4.6, one can find that the curve of the total operation cost matches well with the demand curves in their variation pattern, suggesting that the cost of medical resource allocation mainly depends on the demand. The characteristics also reflect the hysteresis effect in an epidemic controlling system that medicine logistics lags behind the epidemic diffusion.

In next subsection, we will compare the proposed model with the two traditional allocation measurements that have been used in practice.

4.5.2 Model Comparison

Based on our interviews with the public healthcare administrative personnels in China, there are two traditional measurements in practice to predict the demand for medical resource in case of an epidemic outbreak. Both of them utilize Eq. (4.2) as the basic forecasting method. In the first traditional measurement, referred as Traditional 1, the medical resource will only be allocated through administrative distribution. That is, an ADC will only service the DDCs in its own area, and a DDC will only service the EDHs in its own district. For instance, as Table 4.1 shows, ADC1 will only service DDC1 and DDC2, and DDC1 will only replenish medical resource to EDH1 and EDH2. The second traditional measurement, referred here as Traditional 2, is based on the same forecasting method of Eq. (4.2), but allows cross-area distribution. The total costs of these three different models are compared and illustrated in Fig. 4.8.

Several interesting observations can be drawn from Fig. 4.8. First, the total operation costs by model Traditional 2 are all time lower than those by Traditional 1, although the difference is not large, suggesting that cross area distribution has a definite advantage in saving allocation cost, which is of course not surprising from an optimization perspective. Secondly, the two cost curves by Traditional 1 and

Table 4.2 Unit operation cost between two different departments (Unit: \$)

Cost	ADC1	ADC2	EDH1	EDH2	EDH3	EDH4	EDH5	EDH6	EDH7	EDH8
DDC1	3.5	2	1	2	4	2.5	5	5	2.5	1.5
DDC2	1.5	2	2	2.5	2	3	5	4	2.5	2
DDC3	3	1.5	2.5	3	5	2	1	3	1.5	4
DDC4	2.5	3	4	4	1.5	2.5	3	2	2	1.5

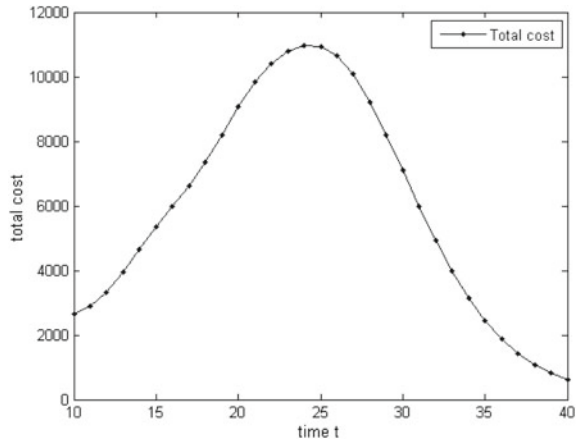
Table 4.3 Medical resource allocation result at decision-making cycle $t = 0$ (Unit: \$)

	DDC1		DDC2		DDC3		DDC4	
ADC1	0		186.6901		0		163.759	
ADC2	188.8323		0		191.9134		0	
	EDH1	EDH2	EDH3	EDH4	EDH5	EDH6	EDH7	EDH8
DDC1	67.1588	43.0695	0	31.1464	0	0	0	47.4576
DDC2	0	23.5330	82.9355	22.1931	0	0	31.4635	26.5650
DDC3	0	0	0	38.6671	74.9403	0	78.3061	0
DDC4	0	0	28.1169	14.6546	0	86.9697	18.6328	15.3849

Table 4.4 Total cost in cycle $t = 0$ (Unit: \$)

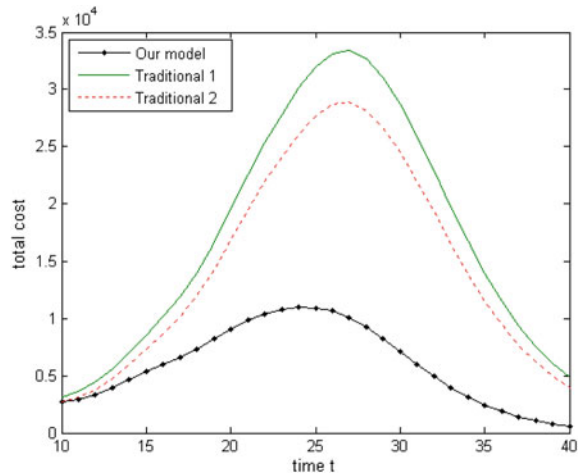
Run	1	2	3	4	5	6
Total cost	2664.97	2663.22	2663.22	2663.22	2664.97	2663.22

Fig. 4.7 Total cost in each decision-making cycle (Unit: \$)



Traditional 2 behave consistently in their rising and falling trend and arrive at their maximum at the exact same time $t = 26$. This is because these two traditional models are based on the same demand forecasting mechanism for the medical resource, and the allocation cost is mainly determined by the allocation volume, i.e., the demand. Thirdly, the cost curve generated by our time-space network model is the all time minimum and much lower than that by the two traditional measurements. The allocation cost generated by our model is obvious less than the traditional methods in most of the time. We attribute this significant cost reduction to our proactive forecasting that takes into account the positive impact of the early allocation of medical resource to the demand in following periods. Finally and most importantly, one can notice that the cost curve by our model reaches its maximum at $t = 24.5$, comparing the two traditional measurements at $t = 26$. This suggests that by using our proposed

Fig. 4.8 Total cost in three different patterns (Unit: \$)



model we can get control of the epidemic spread earlier, which stands for an invaluable social merit on top of the economic savings. To conclude our findings in this example, the cross area distribution that features our proposed model and Traditional 2 can reduce the logistic part of the allocation cost. The proactive forecasting model coupled with our time-space optimal allocation programming proposed in this study can subdue the epidemic diffusion and thus significantly reduce the demand for the medical resource, resulting greater saving in the total operation cost.

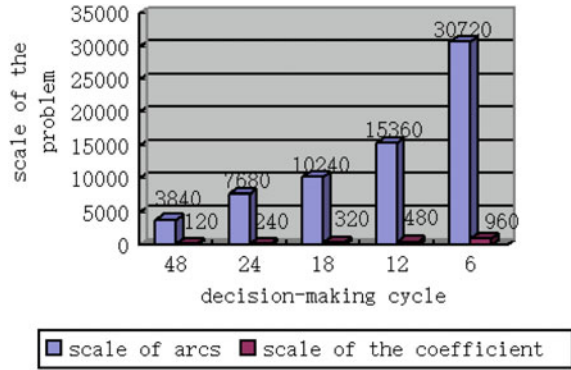
4.5.3 Sensitivity Analysis

In this section, a sensitivity analysis of the three key parameters (η , θ and Γ) in the time-varying demand forecast model is conducted. According to the definition in Sect. 4.3.2, the parameter η is closely related to the decision-making cycle. In this study, the decision-making cycle is set to be one day (24 h), so we get a total of 240 η and 7680 arcs in the experiment. Figure 4.9 shows the relationship between the scale of the problem and the decision-making cycle (unit: h).

In practice, the decision-maker can choose the decision-making cycle according to the actual situation. Generally speaking, the shorter the cycle is, the better the forecast accuracy, but the larger the scale of the problem and its complexity. On the other hand, if the decision-making cycle is set too short to let the actual distribution operations un-complete, then the accuracy of the model might be adversely affected. Therefore, the decision-making cycle should be selected appropriately in a practical problem.

As total cost of the proposed medicine logistics network mainly depends on the demand for medical resource, these two variables get a similar variation tendency. Thus, taking EDH1 as an example, we can hold all the parameters fixed, as in the

Fig. 4.9 Relationship between the scale of problem and decision-making cycle



numerical example given in Sect. 4.5.1, and let θ and Γ take on five different values, respectively. The demand for medical resource in each decision-making cycle is shown in Figs. 4.10 and 4.11.

As Fig. 4.10 shows, θ takes on five values ranging from 60 to 100%. The larger θ is, the lower the demand is. Accordingly, the lower the total cost would be. As Fig. 4.11 shows, Γ takes on five values ranging from 10 to 20. The shorter Γ is, the lower the demand is, and thus the lower the total cost would be. The above analysis confirms that both of these two key parameters play important roles in medical resource allocation decisions. For a small change of θ and Γ , the final allocation decisions and the total operation costs in each cycle can change significantly. Unfortunately, the precise values for these two parameters in an epidemic control are difficult to get. As the accuracy of these two parameters is vital to the success of medicine logistics operation, it calls for more research work to scientifically estimate these two parameters for different epidemics.

Fig. 4.10 Demand in EDH1 with different value of θ

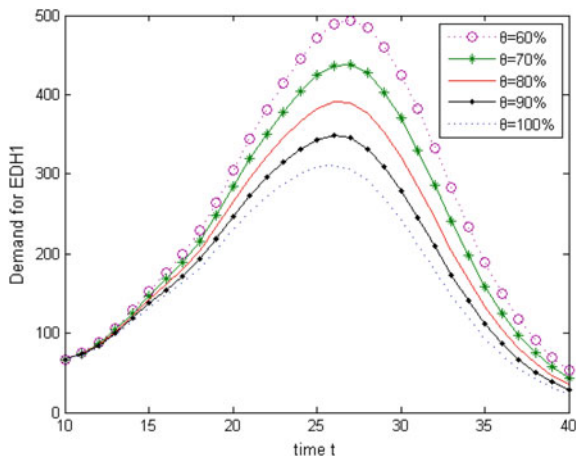
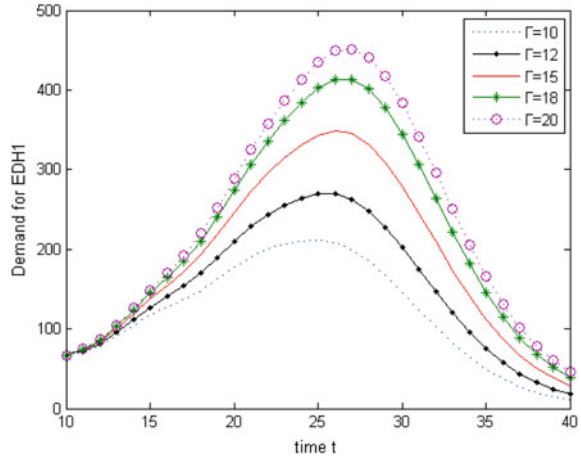


Fig. 4.11 Demand in EDH1 with different value of Γ



4.6 Conclusions

In this chapter, we develop a discrete time-space network model to study the medical resource allocation problem in an epidemic outbreak. In each decision-making cycle, the allocation of medical resource across the region from ADCs through DDCs to EDHs is determined by a linear programming model with the dynamic demand that is forecasted by an epidemic diffusion rule. The novelty of our model against the existing works in literature is characterized by the following three aspects:

- (i) While most research on medical resource allocation studies a static problem which takes no consideration of the time evolution and dynamic nature of the demand, the model proposed in this study addresses a time-series demand that is forecasted in match of the course of an epidemic diffusion.
- (ii) The model couples a multi-stage linear programming for optimal allocation of medical resource with a proactive forecasting mechanism cultivated from the epidemic diffusion dynamics. The two dynamic processes are woven together and interactively proceed to model the epidemic diffusion and the medical resource allocation. The rationale that the medical resource allocated in early periods will take effect in subduing the spread of the epidemic spread and thus impact the demand in later periods has been for the first time incorporated into our model.
- (iii) The computational results show that the proposed model remarkably outperforms the traditional measurements in both terms of cost reduction and epidemic control. Our model can significantly reduce the total operation cost of the medical resource allocation and may get the epidemic diffusion in control earlier than the traditional measurements.

Furthermore, the medicine logistics operation problem has been decomposed into several mutually correlated sub-problems, and then be solved systematically in the

same decision scheme. Thus, the result will be much more suitable for a real operation. As the limitation of the model, it is developed for the medical resource allocation in a geographic area where an epidemic disease has been spreading and it does not consider possible cross area diffusion between two or more geographic areas. We assume that once an epidemic outbreak, the government has effective means to separate the epidemic areas so that cross-area spread can be basically prevented. However, this cannot always be guaranteed in reality.

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Chapter 5

Epidemic Logistics with Demand Information Updating Model II: Medical Resource Is Limited



This chapter is a continuous work of Chap. 4. In this chapter, 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.

5.1 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 transfers from animals to human. Generally, it is difficult to predict when an unexpected influenza outbreaks, and our security measures to 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 [1–5]. 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 [6–11] 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. [12] described the transmission of avian influenza among birds and humans. Liu and Zhang [13] 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. [14] 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. [15] 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 study 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 studies on the subject are focused on the coordination of the influenza vaccine supply chain. For example, Adida et al. [16] 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 [17] 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. Arifoğlu et al. [18] 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. [19] introduced two coordinating contracts, the Delivery-time-dependent Quantity Flexibility (D-QF) contract and the Buyback-and-Late-Rebate (BLR) contract, and

connected them to those used in practice. Furthermore, Yamin and Gavious [20] 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 much research works in the past decades [21–25]. 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 [26–30] designed a mixed-integer programming model for distribution and inventory relocation under uncertainty in humanitarian operations. Rachaniotis et al. [31] 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. [32] 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 [33]. 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. [34] 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 [35], 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 study, 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 [36]. As shown in Fig. 5.1, 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.

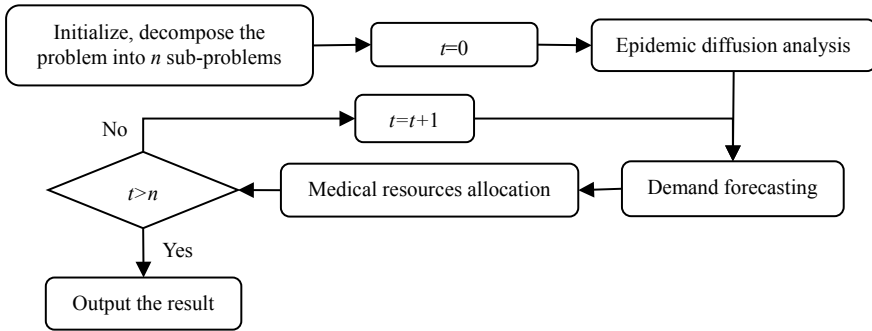


Fig. 5.1 The dynamic operational procedure of medical resources allocation

- (i) Initially, we employ a SEIR model to depict the dynamic epidemic diffusion process. The model will give 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 Sect. 5.2.2. 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. While 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.

5.2 Epidemic Diffusion Analysis and Demand Forecasting

5.2.1 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 [37]. $S(t)$ 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 [38, 39].

Although the deterministic SIR model is successful in predicting the behavior of outbreaks very similar to that observed in many recorded epidemics [36], 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 numbers 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.

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 literature assumes a constant population size as is in this study. 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).

$$\begin{cases} S'(t) = -\beta S(t)I(t) \\ E'(t) = \beta S(t)I(t) - \beta S(t-\tau)I(t-\tau) \\ I'(t) = \beta S(t-\tau)I(t-\tau) - (\alpha + \delta)I(t) \\ R'(t) = \delta I(t) \end{cases} \quad (5.1)$$

In ODE (5.1), $S(t)$, $E(t)$, $I(t)$ 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 (5.1) 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 (5.1), 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.

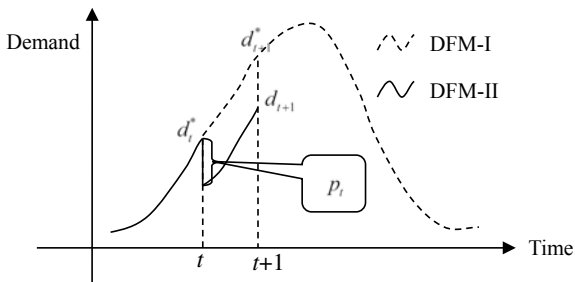
5.2.2 Demand Forecasting

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:

$$d_t^* = f[I(t)]. \tag{5.2}$$

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 Fig. 5.2). Herein, we refer it as the demand forecasting mode II (DFM-II). 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 Eq. (5.2), 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

Fig. 5.2 Schematic diagram of the demand forecasting



Eq. (5.2) 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:

$$\eta_t = (d_{t+1}^* - d_t^*) / d_t^*. \tag{5.3}$$

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:

$$\text{When } t = 1, \quad d_1 = (1 + \eta_0) \left(d_0 - \frac{\lambda p_0}{\omega \Gamma} \right). \tag{5.4}$$

$$\text{When } t = 2, \quad d_2 = (1 + \eta_1) \left(d_1 - \frac{\lambda p_1}{\omega \Gamma} \right). \tag{5.5}$$

...

$$\text{When } t = n, \quad d_n = (1 + \eta_{n-1}) \left(d_{n-1} - \frac{\lambda p_{n-1}}{\omega \Gamma} \right). \tag{5.6}$$

The recursion formulas (5.4)–(5.6) 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 Sect. 5.3. After that, we can forecast the demand for medical resources on decision cycle $t = 1$ by using Eq. (5.4). Similar works are executed iteratively to obtain the demand information for each decision cycle during the entire medical resources allocation process.

5.3 The Dynamic Medical Resources Allocation Model

5.3.1 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 [40–42]. 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 5.3 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) stands for 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 Sect. 5.1, 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.

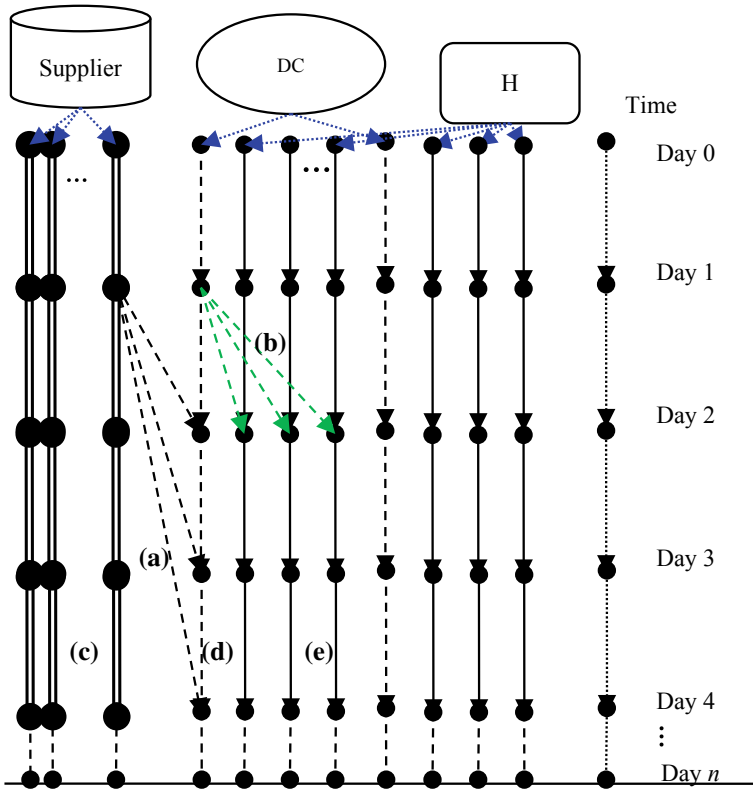


Fig. 5.3 Time-space network of medical resources allocation

5.3.2 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 .

5.3.3 Model Formulation

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

$$\text{Min } F(x, y) = \sum_{t \in T} \sum_{i \in S} \sum_{j \in D} x_{ijt} c_{ij} + \sum_{t \in T} \sum_{j \in D} \sum_{k \in H} y_{jkt} r_{jk} \quad (5.7)$$

$$\text{s.t. } z_{jt} = \left\{ z_{j(t-1)} + \sum_{i \in S} x_{ijt} - \sum_{k \in H} y_{jkt} \right\}^+, \quad \forall j \in D, t \in T \quad (5.8)$$

$$\sum_{j \in D} x_{ijt} \leq a_{it}, \quad \forall i \in S, t \in T \quad (5.9)$$

$$\sum_{j \in D} y_{jkt} \leq d_{kt}, \quad \forall k \in H, t \in T \quad (5.10)$$

$$\sum_{j \in D} \sum_{k \in H} y_{jkt} = \min \left\{ \sum_{k \in H} d_{kt}, \sum_{i \in S} a_{it} \right\}, \quad \forall t \in T \quad (5.11)$$

$$d_{kt} = (1 + \eta_{k(t-1)}) \left(d_{k(t-1)} - \frac{\lambda \sum_{j \in D} y_{jk(t-1)}}{\omega \Gamma} \right), \quad \forall k \in H, t \in T \quad (5.12)$$

$$x_{ijt}, y_{jkt} \in I, \quad \forall i \in S, j \in D, k \in H, t \in T \quad (5.13)$$

The objective function in Eq. (5.7) minimizes the total logistics cost of medical resources allocation. Constraint (5.8) is the flow conservation constraint. Constraint (5.9) is the production capacity constraint. Constraints (5.10)–(5.12) are the demand constraints. At last, constraint (5.13) ensures that all decision variables are integers.

5.3.4 Solution Procedure

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

5.4 Numerical Example and Discussion

5.4.1 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 5.1.

Taking region 1 as our example, Fig. 5.4 depicts the numerical simulation result if no medical resources could be allocated. The computation time to solve the ODE is less than 10 s. 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 [13, 35]. 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 2000 units of medical resources

Table 5.1 Initial values of the relative parameters

Hospital(H)	Region 1	Region 2	Region 3	Region 4	Region 5	Region 6	Region 7	Region 8
$S(0)$ (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							

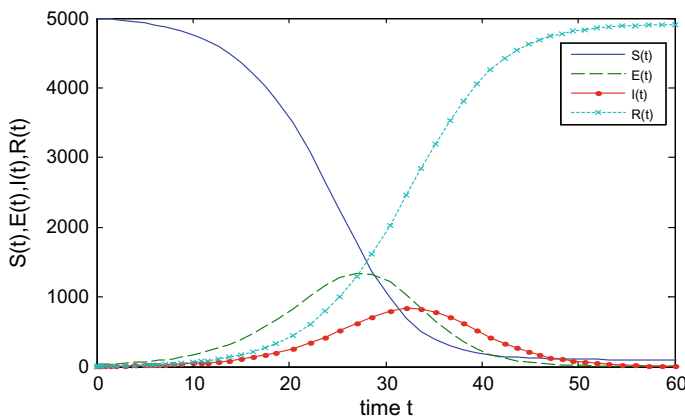


Fig. 5.4 Numerical simulation of the SEIR model

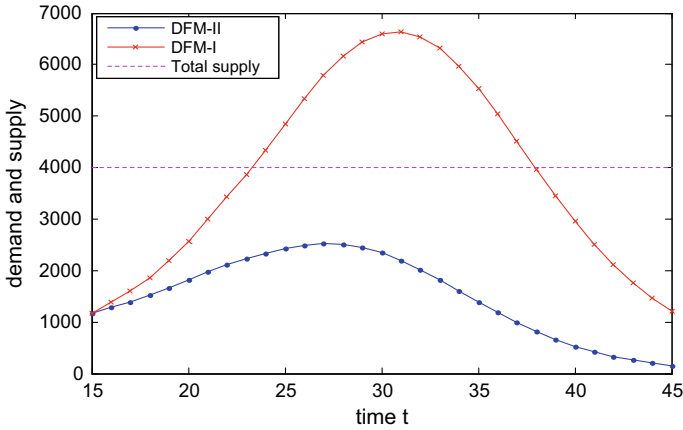


Fig. 5.5 Demand for medical resources over time

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 Eq. (5.5). 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 s.

Figure 5.5 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 impact 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 2000 is feasible for the entire process. The second observation from Fig. 5.5 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.

5.4.2 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 1000 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, 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.

$$p_{kt} = \begin{cases} d_{kt}, & \text{if } \sum_{k \in H} d_{kt} \leq \sum_{i \in S} a_{it} \\ \frac{d_{kt} \sum_{i \in S} a_{it}}{\sum_{k \in H} d_{kt}} & \text{if } \sum_{k \in H} d_{kt} > \sum_{i \in S} a_{it} \end{cases}, \forall k \in H, t \in T. \quad (5.17)$$

Holding all the other parameters fixed as in numerical example given in Sect. 5.4.1, except that production capacity of each supplier, which is limited as 1000 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 Fig. 5.6. 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.

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 Fig. 5.7. While 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 Fig. 5.7a). The total allocation cost on this decision cycle is 6475 RMB. However, while we implement the equilibrium allocation mode to assign the medical resources, significant gaps between supply and demand for each

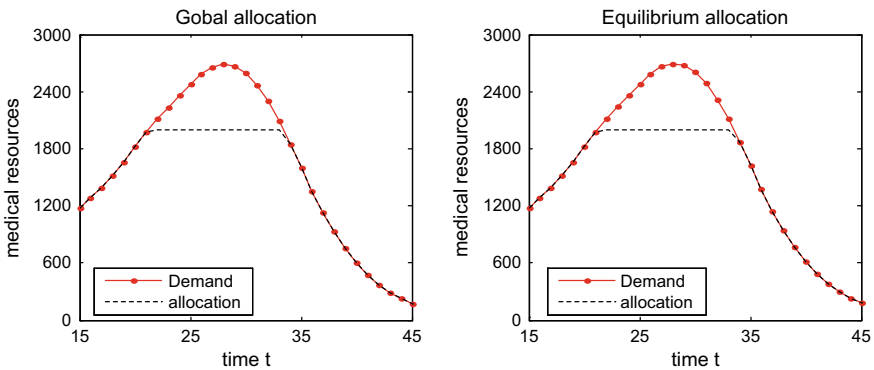


Fig. 5.6 Total demand of medical resources in each decision cycle

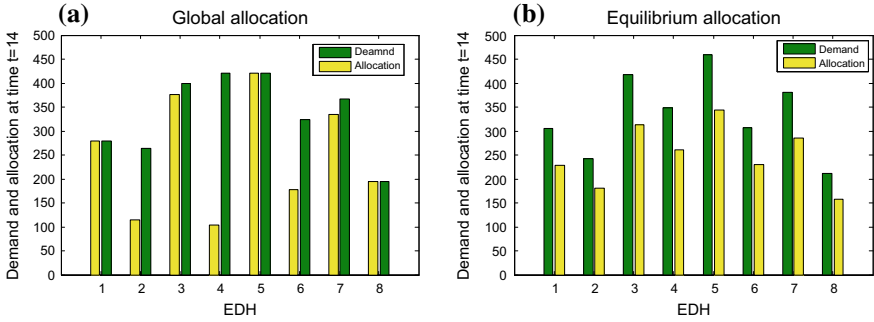


Fig. 5.7 Supply and demand on decision cycle $t = 14$ (the 29th day)

EDH are presented (see Fig. 5.7b). 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 6642 RMB. Therefore, it can be concluded that the equilibrium allocation mode, which is always adopted as an empirical method in practice, is uneconomical.

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 Fig. 5.8. 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 Fig. 5.8 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

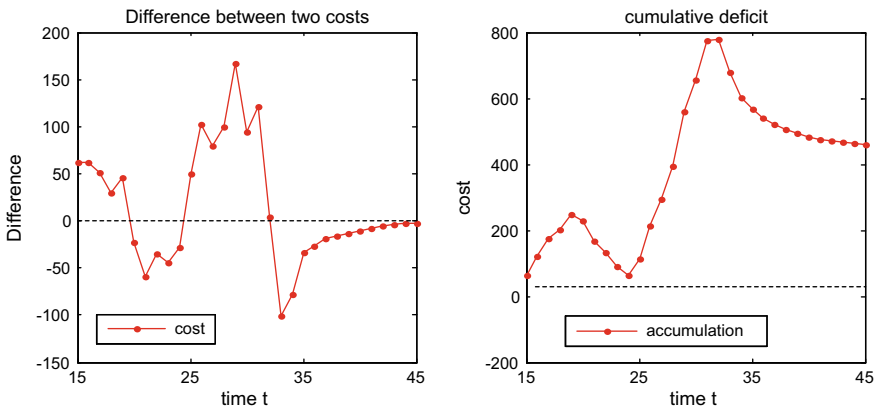


Fig. 5.8 Cost comparison between the two modes

more efficient, because it assigns more medical resources within less cost during the same time interval.

5.4.3 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 Sect. 5.4.1, 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 Fig. 5.9. As Fig. 5.9 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 Fig. 5.9 is that occurrence time and 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 such 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.

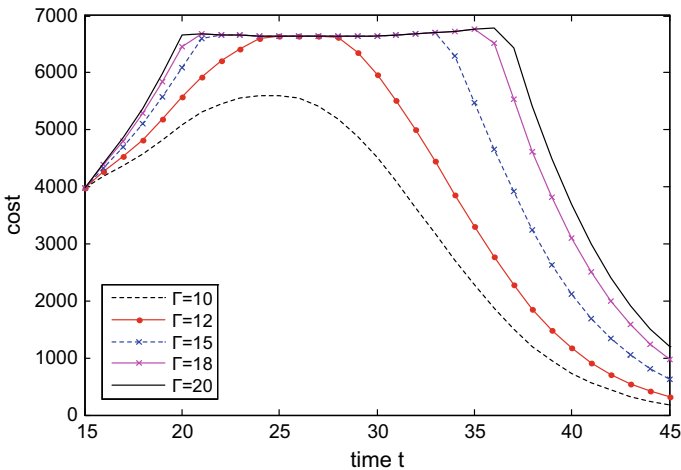


Fig. 5.9 Total cost with different value of Γ

5.5 Conclusions

In this study, 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 SEIR diffusion rule. The three main differences that distinguish this work from the past literature are presented as follows.

Firstly, the model proposed in this study 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 both 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 solve. In this study, 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 study 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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Chapter 6

Integrated Optimization Model for Two-Level Epidemic-Logistics Network



As mentioned in the above chapters, the demand of emergency resource is usually uncertain and varies quickly in anti-bioterrorism system. With the consideration of emergency resources allocated to the epidemic areas in the early rescue cycles will affect the demand in the following periods, we construct an integrated and dynamic optimization model with time-varying demand for the emergency logistics network based on the epidemic diffusion rule. The heuristic algorithm coupled with ‘DDE23 tool’ in MATLAB is adopted to solve the optimization model, and the application of the model as well as a short sensitivity analysis of the key parameters in the time-varying demand forecast model is presented by a numerical example. The win-win emergency rescue effect is achieved by such an optimization model. Thus, it can provides some guidelines for decision makers when coping with emergency rescue problem with uncertain demand, and offers an excellent reference when issues are pertinent to bioterrorism.

6.1 Introduction

Bioterrorism is the intentional use of harmful biological substances or germs to cause widespread illness and fear. It is designed to cause immediate damage and release dangerous substances into the air and surrounding environment. Because it would not usually be signaled by an explosion or other obvious cause, a biological attack may not be recognized immediately and may take local health care workers time to discover that a disease is spreading in a particular area.

Over the past few years, the world has grown increasingly concerned about the threat bioterrorists pose to the societies, especially after the September 11 attacks and the fatal delivery of anthrax via the US Mail in 2001. Henderson [1] points out that the two most feared biological agents in a terrorist attack are smallpox and anthrax. Radosavljević and Jakovljević [2] propose that biological attacks can cause an epidemic of infectious disease, thus, epidemiological triangle chain models can be used to present these types of epidemic. Bouzianas [3] presents that the

deliberate dissemination of *Bacillus anthracis* spores via the US mail system in 2001 confirm their potential use as a biological weapon for mass human casualties. This dramatically highlights the need for specific medical countermeasures to enable the authorities to protect individuals from a future bioterrorism attack.

Generally, emergency logistics in anti-bioterrorism system is more complex and difficult, and differs from business logistics in the following aspects. First of all, a bioterror attack usually happens suddenly and causes a surge of demand for a particular medicine during a very short period of time. Hence, emergency resources must be allocated to the epidemic areas as quickly as possible. Second, the demand information is quite limited and varies rapidly with time. It is often very difficult to predict the actual demand based on historical data [4]. Third, unlike logistics management in which all the activities are triggered based on customer orders, emergency logistics network in the anti-bioterrorism system is derived from the epidemic diffusion network.

Considering the relationship between an unexpected bioterror attack and the associated emergency logistics decisions, Liu and Zhao [5, 6] focus on how to control the emergency resources and divide the whole emergency rescue process into three stages. In the first stage, for the disaster area is just suffered from a bioterror attack, and the bio-virus (such as smallpox, *Bacillus anthracis* and so on) hasn't cause a widespread diffusion, thus, we should deliver the existing emergency resources in the local health departments to the disaster areas as quickly as possible. Then, objective of the second stage is that emergency resources can be allocated to the disaster areas along with the spreading of the bio-virus, continually. Thus in this study, we focus on the third rescue stage, and the following problem should be answered: how to replenish emergency resources to the local health departments, and simultaneously, how to allocate emergency resource to the infected areas? To accomplish such objective, we employ network flow techniques to develop an integrated and dynamic optimization model, with the objective of minimizing the total rescue cost and subject to related operating constraints. The model is expected to be an effective decision-making tool that can help improve the efficiency of emergency rescue when suffered from a bioterror attack.

6.2 Problem Description

As mentioned before, we have divided the entire emergency rescue process into three stages in Liu and Zhao [5], and this study focuses on the optimization of the emergency logistics network in the third rescue stage. In such stage, situation of the epidemic diffusion tends to be stable and the spread of the epidemic goes to under control. Thus, optimization goal in such stage is to construct an integrated, dynamic and multi-level emergency logistics network, which includes the national strategic storages, the urban health departments and the epidemic areas. The research idea of the third emergency rescue stage is shown in Fig. 6.1.

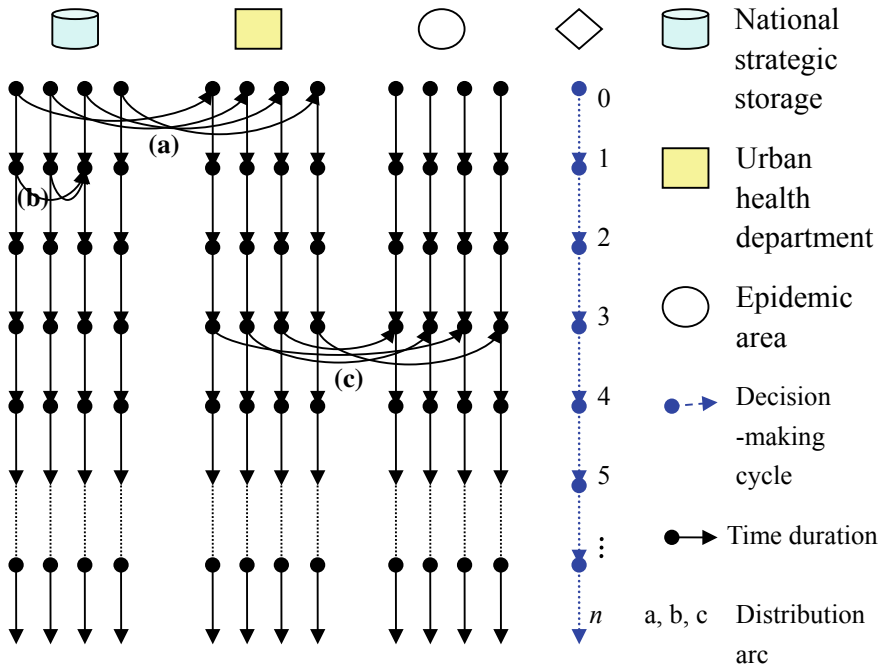


Fig. 6.1 Research idea of the third emergency rescue stage

As Fig. 6.1 shows, the entire rescue process in the third emergency rescue stage is decomposed into several mutually correlated sub-problems (i.e. n decision-making cycles). To each decision-making cycle, there exist two sub-problems. In the upper level, we consider the problem how to replenish emergency resources to the urban health departments. Besides, we adjust the replenishment arcs by a heuristic algorithm, and construct a mixed-collaborative delivery system. Thus, the total rescue cost of the upper level sub-problem would be minimized. In the lower level, we present the problem how to allocate emergency resources to the infected areas. We propose a forecasting model for the time-varying demand in the epidemic areas based on the epidemic diffusion rule. Such two phases are executed iteratively. Besides, at the end of each rescue cycle, effect of emergency resources allocated is analyzed and the number of infected people is updated. Such a sequential operational routine is continued until the bio-virus diffusion is under control.

It is worth mentioning that the optimal result of the upper level sub-problem affects the result of the lower level sub-problem, directly; on the other side, the optimal result of the lower level sub-problem will affect the result of the upper level sub-problem in the next emergency rescue cycle. Therefore, this is different to the bi-level programming method. In what follows, we will present the SEIR epidemic diffusion model and the forecasting models for the time-varying demand and inventory.

6.2.1 SEIR Epidemic Diffusion Model

Since most epidemics divide people into four classes: the susceptible people (S), the people during the incubation period (E), the infected people (I), and the recovered people (R). Thus, as Fig. 6.2 shows, without consideration of the population migration, and the natural birth and death rate of the population, we can use a SEIR model based on small-world network to describe the developing epidemic process.

Therefore, the following SEIR model [6] is adopted in this study.

$$\begin{cases} \frac{dS}{dt} = -\beta\langle k \rangle S(t)I(t) \\ \frac{dE}{dt} = \beta\langle k \rangle S(t)I(t) - \beta\langle k \rangle S(t-\tau)I(t-\tau) \\ \frac{dI}{dt} = \beta\langle k \rangle S(t-\tau)I(t-\tau) - (d + \delta)I(t) \\ \frac{dR}{dt} = \delta I(t) \end{cases} \quad (6.1)$$

In such epidemic diffusion model, the time-based parameters $S(t)$, $E(t)$, $I(t)$ and $R(t)$, represent the number of susceptible people, the number of people during the incubation period, the number of infected people, and the number of recovered people, respectively. Other parameters include: $\langle k \rangle$ is the average degree distribution of the small-world network; β is the propagation coefficient of the bio-virus (small-pox); δ is the recovered rate of the infected people; d is the death rate caused by the disease; τ stands for the incubation period. Furthermore, $\langle k \rangle, \beta, \delta, d, \tau > 0$.

From the Eq. (6.1), we can see that $I(t)$, which denotes the number of infected people, can be calculated by solving the ordinary differential equations when the initial values of $S(t)$, $E(t)$, $I(t)$ and $R(t)$ are given. Actually, this parameter is one of the most important concerns during the emergency rescue process, and it is desired that $I(t)$ stays at a value as low as possible, which implies that the situation is stable and the spread of the epidemic is under control. Wang et al. [4] propose that the change of $I(t)$ mainly depends on the population of the recovered people and the onset people at the end of the incubation period. And thus, we should improve the recovered rate δ and reduce the propagation coefficient β , thereby decreasing the value of $I(t)$ effectively.

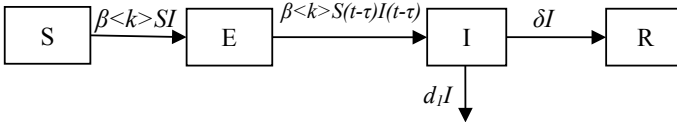


Fig. 6.2 SEIR epidemic diffusion model

6.2.2 Forecasting Model for the Time-Varying Demand

As mentioned before, for both upper and lower sub-problems are existed in each emergency rescue cycle, thus, the time-varying demand in each sub-problem should be the forecasted respectively.

(1) Forecasting model for the time-varying demand in the epidemic area

As introduced in Sect. 6.1, the demand information is quite limited and varies rapidly with time when suffered from a bioterror attack. Thus, it is often difficult to predict the actual demand based on historical data. Xu et al. [7] propose that demand forecasting after a disaster is especially important in emergency management, and present an EMD-ARIMA (empirical mode decomposition and autoregressive integrated moving average) forecasting methodology to predict the agricultural products demand after the 2008 Chinese winter storms. Other related works can be found in [8, 9]. Note that emergency demand in the previous literature has always been formulated as a stochastic or deterministic variable, while the effectiveness that emergency resource allocated in the early rescue cycle will affect the demand in the later rescue cycle has not been considered. Based on the previous works ([5]), the following forecasting model for the time-varying demand in the epidemic area is adopted in this study.

$$d_t^* = aI(t), \quad t \in 0, 1, 2, \dots, n \quad (6.2)$$

$$\eta_t = (d_{t+1}^* - d_t^*)/d_t^*, \quad t \in 0, 1, 2, \dots, n-1 \quad (6.3)$$

$$\text{When } t = 0, \quad d_0 = aI(0) \quad (6.4)$$

$$\text{When } t = 1, \quad d_1 = (1 + \eta_0) \left(1 - \frac{\theta}{\Gamma}\right) d_0 \quad (6.5)$$

$$\text{When } t = 2, \quad d_2 = (1 + \eta_1) \left(1 - \frac{\theta}{\Gamma}\right) d_1 = (1 + \eta_0) \left(1 + \eta_1\right) \left(1 - \frac{\theta}{\Gamma}\right)^2 d_0 \quad (6.6)$$

...

$$\text{When } t = n, \quad d_n = \prod_{i=0}^{n-1} (1 + \eta_i) \left(1 - \frac{\theta}{\Gamma}\right)^n d_0 \quad (6.7)$$

Herein, $\prod_{i=0}^{n-1} (1 + \eta_i) = (1 + \eta_0)(1 + \eta_1) \dots (1 + \eta_{n-1})$. Equation (6.2) is the traditional forecasting model for the time-varying demand. d_t^* means demand of the emergency resources in the epidemic area at time t , $t \in 0, 1, 2, \dots, n$. $I(t)$ is the number of infected people in the epidemic area at time t . a is the proportionality coefficient. Equation (6.3) is used to calculate the linear scale factor of the change in demand for each rescue cycle. Furthermore, $\eta_t \leq 0$. d_0 in the Eq. (6.4) is the initial

demand of emergency resources in the epidemic area, and $I(0)$ represents the initial number of infected people in the epidemic area. d_1, d_2, \dots, d_n in Eqs. (6.5)–(6.7) represent the demand of emergency resources in emergency rescue cycle 1, 2, \dots , n . Other parameter include: θ is the effective rescue rate in each cycle; Γ is the treatment cycle for each infected person. To facilitate the calculation process in the following sections, we assume that Γ is an integral multiple of the rescue cycle.

According to the above recursion formulas, the change of emergency demand mainly depends on these two important parameters. Thus, in the context of emergency rescue, there should be enough emergency resources to cure the infected people, so that the effective rescue rate θ can be improved and the treatment cycle Γ can be reduced, thereby, decreasing the total emergency rescue cost.

(2) Forecasting model for the time-varying demand in urban health department

As introduced before, in the upper level sub-problem, we consider the problem how to replenish emergency resources to the urban health departments. Thus, the urban health departments, which are the emergency suppliers in the lower level sub-problem, have been changed to be the demand nodes in the upper level replenishment network. Note that time-varying demand in the urban health department mainly depends on the unsatisfied capacity. Hence, to facilitate the calculation process in the following sections, we assume that the initial inventory in each urban health department is equal to zero. Besides, we suppose that capacity of each urban health department is equal to V_{cap} . Supposing that d_t^v represents the demand of emergency resources in urban health department at rescue cycle t , P_t represents the total supply of the emergency resources in urban health department at rescue cycle t (Such value is obtained by solving the lower level sub-problem in the previous rescue cycle). Thus, the forecasting model for time-varying demand in urban health department can be formulated as follows.

$$d_t^v = \begin{cases} V_{cap}, & t = 0 \\ P_{t-1}, & t = 1, 2, \dots, n \end{cases} \quad (6.8)$$

6.2.2.1 Forecasting Model for the Time-Varying Inventory

As mentioned in Sect. 6.1, the focus of this study is placed on replenishing emergency resources to the urban health departments and distributing them to the epidemic areas, simultaneously. Thus, the urban health departments play the role of the link in the multi-level emergency logistics network. Intuitively, inventory of the emergency resources in the urban health department should also be changed as time goes by. Supposing that V_t is the inventory of the emergency resources in the urban health department at rescue cycle t , and we can get the following equation.

$$V_t = \begin{cases} 0, & t = 0 \\ V_{cap} - P_{t-1}, & t = 1, 2, \dots, n \end{cases} \quad (6.9)$$

6.3 Optimization Model and Solution Methodology

6.3.1 The Integrated Optimization Model

To facilitate the model formulation in the following section, we make the following four assumptions.

- (1) Once suffered from a bioterror attack, each epidemic area can be isolated from other areas to avoid the spread of the disease.
- (2) The locations of the national strategic storages, and urban health departments are known. Practically, the number of storage places to be used can be preset by a national disaster plan.
- (3) Holding cost of the emergency resources is not considered.
- (4) Capacity of the national strategic storage is large enough, and in each rescue cycle, each one of them can supply a certain amount of emergency resources.

Notations used in the following integrated and dynamic optimization model are specified as follows.

nc_{ij} : Unit replenishment cost of the emergency resource from the nation strategic storage i to the urban health department j .

ce_{jk} : Unit distribution cost of the emergency resource from the urban health department j to the epidemic area k .

ns_i : The certain amount of emergency resources that can be supplied by the nation strategic storage i in each rescue cycle.

V_{cap} : Capacity of the urban health department.

d_{kt} : Demand of the emergency resources in epidemic area k at rescue cycle t .

d_{jt}^v : Demand of the emergency resources in urban health department j at rescue cycle t .

P_{jt} : Total supply of the emergency resources in urban health department j at rescue cycle t .

V_{jt} : Inventory of the emergency resources in the urban health department j at rescue cycle t .

x_{ijt} : Amount of the emergency resources that transport from the national strategic storage i to the urban health department j at rescue cycle t .

y_{jkt} : Amount of the emergency resources that transport from the urban health department j to the epidemic area k at rescue cycle t .

TC : Total cost of the multi-level emergency logistics network.

N : Set of the national strategic storages.

C : Set of the urban health departments.

E : Set of the epidemic areas.

T : Set of the decision-making cycles.

According to the above explanation and assumptions, the integrated and dynamic optimization model for the multi-level emergency logistics network can be formulated as follows:

$$\text{Min } TC = \sum_{t \in T} \sum_{i \in N} \sum_{j \in C} x_{ijt} n c_{ij} + \sum_{t \in T} \sum_{j \in C} \sum_{k \in E} y_{jkt} c e_{jk} \quad (6.10)$$

$$\text{s.t. } \sum_{j \in C} x_{ijt} \leq n s_i, \quad \forall i \in N, \quad t \in T \quad (6.11)$$

$$\sum_{i \in N} x_{ijt} = d_{jt}^v, \quad \forall j \in C, \quad t \in T \quad (6.12)$$

$$d_{jt}^v = V_{cap}, \quad \forall j \in C, \quad t = 0 \quad (6.13)$$

$$d_{jt}^v = P_{jt-1}, \quad \forall j \in C, \quad t = 1, 2, \dots, T \quad (6.14)$$

$$P_{jt} = \sum_{k \in E} y_{jkt}, \quad \forall j \in C, \quad t \in T \quad (6.15)$$

$$\sum_{k \in E} y_{jkt} \leq V_{cap}, \quad \forall j \in C, \quad t \in T \quad (6.16)$$

$$\sum_{j \in C} y_{jkt} = d_{kt}, \quad \forall k \in E, \quad t \in T \quad (6.17)$$

$$d_{kt} = a I_k(t), \quad \forall k \in E, \quad t = 0 \quad (6.18)$$

$$d_{kt} = \prod_{i=0}^{t-1} (1 + \eta_{ki}) \left(1 - \frac{\theta}{\Gamma}\right)^t d_{k0}, \quad \forall k \in E, \quad t = 1, 2, \dots, T \quad (6.19)$$

$$\prod_{i=0}^{t-1} (1 + \eta_{ki}) = (1 + \eta_{k0})(1 + \eta_{k1}) \dots (1 + \eta_{k(t-1)}), \quad \forall k \in E, \quad t = 1, 2, \dots, T \quad (6.20)$$

$$x_{ijt} \geq 0, \quad \forall i \in N, \quad j \in C, \quad t \in T \quad (6.21)$$

$$y_{jkt} \geq 0, \quad \forall j \in C, \quad k \in E, \quad t \in T \quad (6.22)$$

Herein, the objective function in Eq. (6.10) is to minimize the total cost of the multi-level emergency logistics network. Equations (6.11) and (6.12) are constraints for flow conservation in the upper level sub-problem. Equations (6.13)–(6.15) are the time-varying demand models in the upper level sub-problem. Equations (6.16)

and (6.17) are constraints for flow conservation in the lower level sub-problem. Equations (6.18)–(6.20) are the time-varying demand models in the lower level sub-problem. At last, Eqs. (6.21) and (6.22) ensure all the arc flows in the emergency logistics network within their bounds.

Our model is formulated as an integrated, dynamic and multi-stage programming model, and could thus be difficult to solve directly, especially for realistically large-scale problems. Therefore, as mentioned in Sect. 6.2, we should decompose the problem into several mutually correlated sub-problems, and then solve them systematically in the same decision scheme. In what follows, we will develop a heuristic algorithm to efficiently solve the problem.

6.3.2 Solution Methodology

(1) Solution procedure for the optimization model

As introduced before, we decompose the entire emergency process in the third rescue stage into n sub-problems (i.e. n decision-making cycles or n rescue cycles). Thus, to each rescue cycle, the research problem has been become a two correlated programming problems and simple to solve. The ‘DDE23’ tool in MATLAB coupled with the forecasting model for the time-varying demand (As introduced in Sect. 6.2.2) is adopted to calculate the dynamic demand. Then, the solution procedure can be presented as follows.

Step 1. Preset the decision-making cycle, and decompose the entire emergency process in the third rescue stage into n decision-making cycles.

Step 2. Let $t = 0$, and initialize parameters in the SEIR epidemic diffusion model.

Step 3. Analyze the epidemic diffusion rule, and calculate the initial demand of the emergency resources in each epidemic area according to the Eq. (6.18).

Step 4. Solve the two correlated programming problems in rescue cycle $t = 0$ and obtain the initial solution.

Step 5. Improve the initial solution by heuristic algorithm (Detail about the heuristic algorithm is introduced in Sect. 6.3.2).

Step 6. Get the final solution of the emergency allocation in such rescue cycle.

Step 7. Set $t = t + 1$, if the termination condition for the rescue cycle is not satisfied, update the demand in each epidemic area and urban health department, and update the inventory level of the emergency resources in each urban health department, go back to Step 3. Else, go to the next step.

Step 8. End the programme and output the final result.

(2) Heuristic algorithm for improving the initial solution

It is not difficult to find that only two types of distribution arcs (type (a) and (c) in Fig. 6.1) have been optimized in the above model, while the collaborative arcs (type (b) in Fig. 6.1) have not been considered. In other words, the collaborative

effect among the national strategic storages has not been considered. Zhao and Sun [10] propose that emergency rescue system with a supply source can results in better performance in both aspects of operational efficiency and operating cost. Thus, to improve the performance of the emergency rescue system without supply source, as Fig. 6.3 shows, we can select an adjacent national strategic storage in the network as the HUB location, and then take the national strategic storages which are at some distance from the epidemic area as the supply sources. As a result, a mixed-collaborative replenishment system is constructed.

Obviously, such mixed-collaborative replenishment system allows both hub-and-spoke and direct shipment (we call it point to point mode) delivery modes. Thus, both advantages of the economies of scale in hub-and-spoke system and the effectiveness in direct shipment system can be taken account. It is worth mentioning that some previous works are related (e.g. [11, 12]), and the experiment results in these works show that the mixed system can save total traveling distance or delivery cost as compared with either of the two pure systems. Therefore, such mixed-collaborative system can improve the initial solution in the last section. Besides, the heuristic algorithm in Liu et al. [12] can be applied in this study with suitable modified as follows (The flowchart of the procedure is also given in the Fig. 6.4).

Step 1. Solve the pure point to point replenishment mode, and let the distribution arc set be D^d . By solving the objective Eq. (6.10), we can get the total emergency replenishment cost at rescue cycle t . Let $TC^d = \sum_{i \in N} \sum_{j \in C} x_{ij} n c_{ij}$.

Step 2. Solve the pure hub-and-spoke problem. This is done as follows: select a national strategic storage $h(h \in N)$ which is adjacent to the epidemic areas as the HUB location, and then, solve a programming problem with the depot located at h

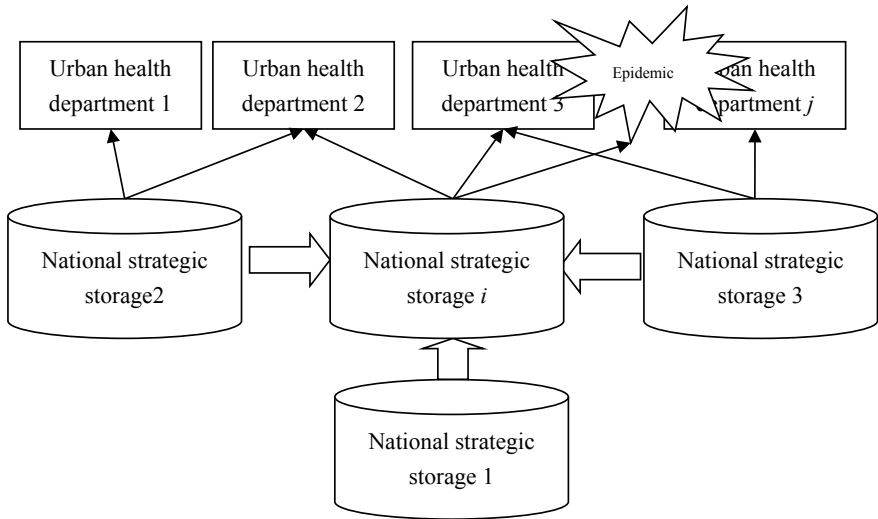


Fig. 6.3 Mixed-collaborative replenishment system

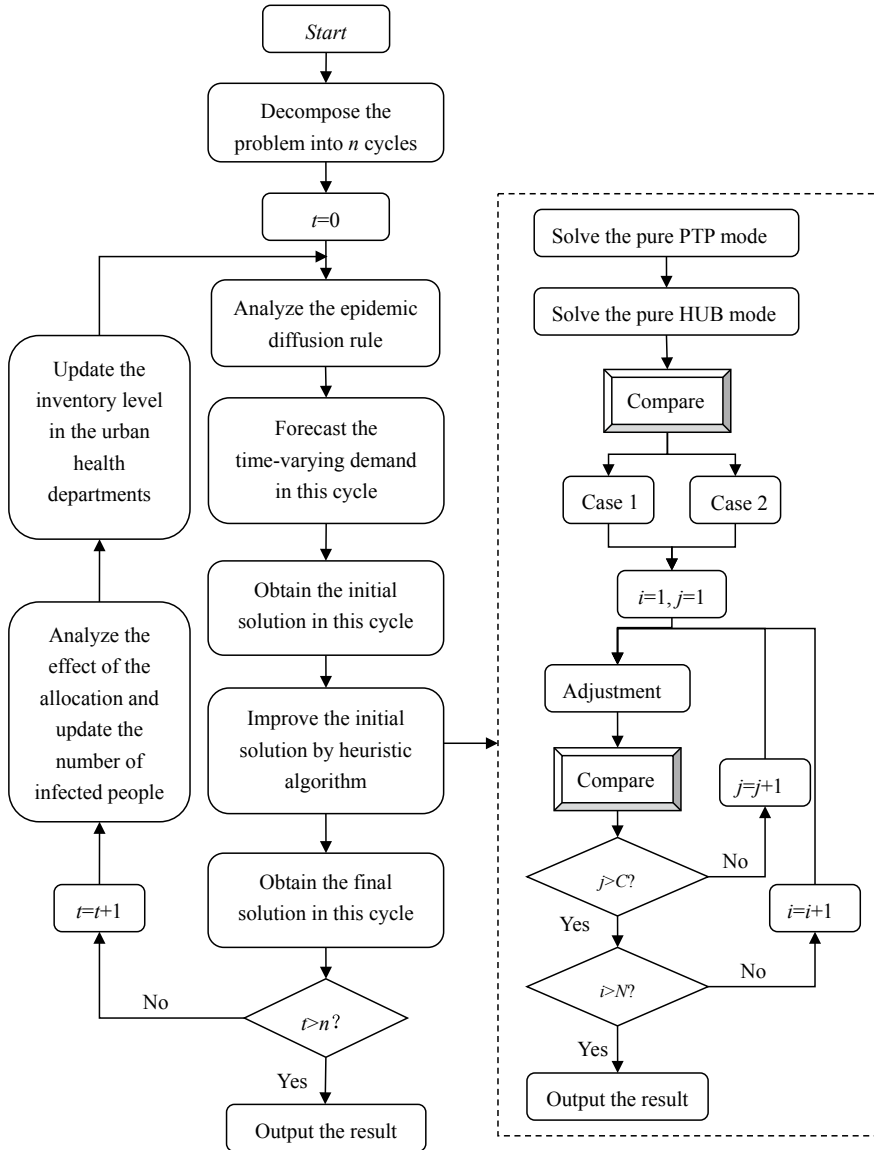


Fig. 6.4 The flowchart of the solution procedure

to collect the emergency resources from all the other storages and to distribute the emergency resources to the urban health departments. Let the distribution arc set be D^h . q_{ih} represents amount of emergency resources that transport from national strategic storage i to the HUB, and the unit transportation cost is nz_{ih} . Thus, $TC^h = \sum_{i \in N \setminus h} z_{ih}q_{ih} + \sum_{h \in N} \sum_{j \in C} x_{hj}nc_{hj}$ is the total emergency replenishment cost at rescue cycle t .

Step 3. Compare TC^d and TC^h , if $TC^d < TC^h$, let $D^d = D$, $D^h = \emptyset$, record it as the case 1; else if $TC^d \geq TC^h$, let $D^h = D$, $D^d = \emptyset$ and record it as the case 2. Let $TC^s = \min\{TC^d, TC^h\}$ and $TC^m \leftarrow TC^s$.

Step 4. Adjust the distribute arc according to the following two situations.

Step 4.1. If case 1 appears, then for every replenishment arc $(N_i, C_j) \in D^d$, compute S_{ij}^{dh} , which is an estimate of the improvement in the solution value if the replenishment arc is transferred from D^d to D^h . Transfer all those pairs with positive S_{ij}^{dh} from direct shipment delivery to hub-and-spoke delivery, and set $D^d \leftarrow D^d \setminus \{(N_i, C_j) | S_{ij}^{dh} \geq 0\}$, $D^h \leftarrow D^h \cup \{(N_i, C_j) | S_{ij}^{dh} \geq 0\}$.

Step 4.2. If case 2 appears, then for every replenishment arc $(N_i, C_j) \in D^h$, compute S_{ij}^{hd} , which is an estimate of the improvement in the solution value if the replenishment arc is transferred from D^h to D^d . Transfer all those pairs with positive S_{ij}^{hd} from direct shipment delivery to hub-and-spoke delivery, and set $D^h \leftarrow D^h \setminus \{(N_i, C_j) | S_{ij}^{hd} > 0\}$, $D^d \leftarrow D^d \cup \{(N_i, C_j) | S_{ij}^{hd} > 0\}$.

Step 5. Solve the mixed-collaborative delivery problem with demand partition $\{D^d, D^h\}$, and record the total emergency rescue cost as TC' .

Step 6. Compare the TC^s and TC' , if $TC' < TC^s$, let $TC^s \leftarrow TC'$ and record the partition $\{D^d, D^h\}$. Thus, TC^s is the value of the best solution obtained so far, if $TC^s < TC^m$, let $TC^m \leftarrow TC^s$.

Step 7. Let $j = j + 1$, go back to the Step 4, if top limit of j is satisfied, go to the next step.

Step 8. Let $i = i + 1$, go back to the Step 4, if top limit of i is satisfied, go to the next step.

Step 9. End the programme and output the optimal result.

Since S_{ij}^{dh} or S_{ij}^{hd} are updated at every iteration and for more results on this topic, we refer readers to Liu et al. [12]. In what follows, we will test how well the model may be applied in the real world.

6.4 A Numerical Example and Implications

6.4.1 A Numerical Example

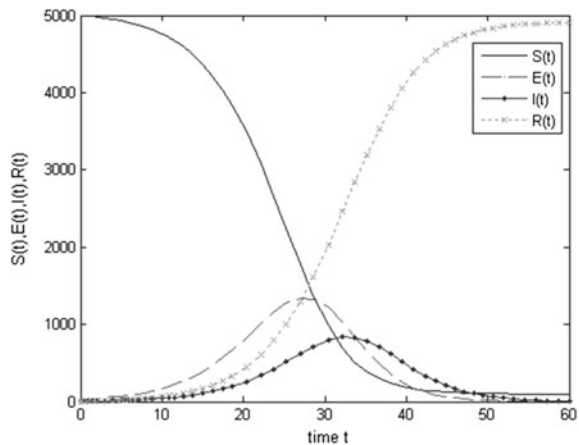
In this section, we rely on a numerical analysis to demonstrate the efficiency of the proposed method for the multi-level emergency logistics network when suffered a bioterror attack. Since the focus of this study is placed on the third emergency rescue stage, and goal of the optimization model is to better control the total emergency rescue cost and the inventory level in the local health departments, thus, the subsequent numerical example will be focused on the analysis of these two objectives. We assume that a region is suffered from a smallpox attack. There are 8 epidemic areas, 6 urban health departments and 3 national strategic storages in such region. The values of the parameters in the epidemic diffusion model are given in Table 6.1.

Taking the epidemic area 1 as the example, Fig. 6.5 is the numerical simulation of the epidemic model in this disaster area. The four curves respectively represent the

Table 6.1 Values of the parameters in SEIR epidemic diffusion model

Area	1	2	3	4	5	6	7	8
$S(0)$	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
$E(0)$	30	35	30	40	25	40	50	45
$I(0)$	5	6	7	8	4	7	9	10
$R(0)$	0							
β	4×10^{-5}							
$\langle k \rangle$	6							
δ	0.3							
d	1×10^{-3}							
τ	5							

Fig. 6.5 Solution of the SEIR epidemic diffusion model (epidemic area 1)



number of four groups of people (S, E, I, R) as time goes by. As this study focuses the third emergency rescue, we assume that it runs from the 45th day (rescue cycle $t = 0$) to the 55th day (rescue cycle $t = 10$). Meanwhile, the rescue cycle is set to be one day. Thus, a total of 8640 arcs are generated and used in the experiment).

Let $a = 1$, $\theta = 90\%$ and $\Gamma = 15$ (days), the 'DDE23 tool' in MATLAB coupled with Eqs. (6.18)–(6.20) are adopted to forecast the time-varying demand for each epidemic area from time $t = 0$ to $t = 10$. As before, taking the epidemic area 1 as the example, demand of the emergency resources at each rescue cycle by both of the time-varying and traditional forecast models are shown in the Fig. 6.6.

As Fig. 6.6 shows, the forecasting model for time-varying demand can reflect the effectiveness that emergency resources allocated in the early rescue cycle will affect the demand in the following periods efficiently. The time-varying demand of emergency resources is reduced obviously when compared with the traditional demand in the following periods. It is worth to mentioning that both these two curves get a similar variation tendency, which represents the epidemic is going to be controlled. After getting demand of emergency resources in each rescue cycle, in what follows, we will focus on how to allocate emergency resources to the epidemic areas, and at the same time, how to replenish emergency resources to each urban health department, with the objective of minimizing the total emergency rescue cost. Table 6.2 shows the unit transportation cost from the supply point to the demand point in the emergency logistics network (Suppose that national strategic storage 1 is preset as the HUB location).

As mentioned before, we assume that each national strategic storage can supply a certain amount of emergency resources in each rescue cycle. Let them be 400, 420 and 450, and let the capacity of the urban health department be 210. Take the emergency allocation result at time $t = 0$ as the example, we can solve the programming model according to the solution procedure (As introduced in Sect. 6.4). The initial solution is reported in Table 6.3 (Total cost 6576.24). Then, the heuristic algorithm is adopted

Fig. 6.6 Demand of the emergency resources in epidemic area 1

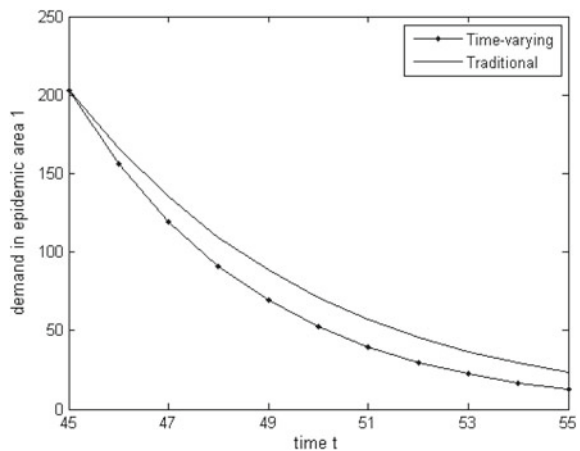


Table 6.2 Unit transportation cost between two different points

Cost	N1	C1	C2	C3	C4	C5	C6	
N1	–	2	9	1	3	10	2	
N2	4	7	2	10	8	9	8	
N3	5	10	8	2	9	2	8	
	E1	E2	E3	E4	E5	E6	E7	E8
C1	6	2	6	7	4	2	5	9
C2	4	9	5	3	8	5	8	2
C3	5	2	1	9	7	4	3	3
C4	7	6	7	3	9	2	7	1
C5	2	3	9	5	7	2	6	5
C6	5	5	2	2	8	1	4	3

Table 6.3 Solution of the optimization model at time $t = 0$

Amount		N1	C1	C2	C3	C4	C5	C6
Before the adjustment	N1	–	106	–	–	94	–	200
	N2	–	104	210	–	106	–	–
	N3	–	–	–	210	10	210	10
After the adjustment	N1	–	210	–	–	210	–	210
	N2	210	–	210	–	–	–	–
	N3	20	–	–	210	–	210	–
	E1	E2	E3	E4	E5	E6	E7	E8
C1	–	81.8	–	–	128.2	–	–	–
C2	29.3	–	–	117.5	–	–	–	12.8
C3	–	114.3	55.8	–	–	–	39.9	–
C4	–	–	–	–	–	35.4	–	174.6
C5	173.4	36.6	–	–	–	–	–	–
C6	–	–	38.2	–	–	124.7	47	–

to adjust and improve the solution, and thus, the final solution is obtained (Total cost 6346.24).

As Table 6.3 shows, while the replenishment arcs $(N_2, C_1) \in D^d$, $(N_2, C_4) \in D^d$, $(N_3, C_4) \in D^d$ and $(N_3, C_6) \in D^d$ are transferred from the direct shipment delivery system to the hub-and-spoke delivery system, the total rescue cost can be reduced. Our test on the selected problem instance shows that the mixed-collaborative system can save 5.9% of the rescue cost compared with the cost before the adjustment. And at last, a mixed-collaborative replenishment system is conducted for the upper level sub-problem. Actually, to better control the total emergency rescue cost, the decision

maker can adjust and improve the initial solution of the lower level sub-problem as similar to the above way.

In a similar way, we can complete the whole operations according to the solution procedure (Fig. 6.4), then we can obtain the optimal initial solution for each rescue cycle. Then, the heuristic algorithm is adopted to adjust and improve the solution for each cycle. Replenishment arcs which need to be transferred in each cycle are shown in Table 6.4. At last, the final solution and the total emergency rescue cost for each cycle can be obtained.

Figure 6.7 shows the change in total rescue cost as time goes by. From this figure, we can get the following two conclusions: (1) Coupled with Fig. 6.6, we can see that demand of emergency resources becomes less and less, which implies that the epidemic diffusion situation is going to be stable and the spread of the epidemic is going to be under control. (2) Coupled with Table 6.4, we can see that the total rescue cost can be reduced by the proposed heuristic algorithm in a certain degree. It is worth mentioning that there is no adjustment after the rescue cycle $t = 4$, that's because the national strategic storages which are adjacent to the epidemic areas will have stored

Table 6.4 Transferred arcs in each cycle

Cycle	Arcs need to be transferred		Cycle	Arcs need to be transferred	
	Before	After		Before	After
$t = 0$	$N2 \rightarrow C1$ $N2 \rightarrow C4$ $N3 \rightarrow C4$ $N3 \rightarrow C6$	$N2 \rightarrow N1 \rightarrow C1$ $N2 \rightarrow N1 \rightarrow C4$ $N3 \rightarrow N1 \rightarrow C4$ $N3 \rightarrow N1 \rightarrow C6$	$t = 1$	$N2 \rightarrow C1$ $N2 \rightarrow C4$	$N2 \rightarrow N1 \rightarrow C1$ $N2 \rightarrow N1 \rightarrow C4$
$t = 2$	$N2 \rightarrow C1$ $N2 \rightarrow C4$	$N2 \rightarrow N1 \rightarrow C1$ $N2 \rightarrow N1 \rightarrow C4$	$t = 3$	$N2 \rightarrow C1$ $N2 \rightarrow C4$	$N2 \rightarrow N1 \rightarrow C1$ $N2 \rightarrow N1 \rightarrow C4$

Note There is no adjustment when $t = 4, 5, 6, 7, 8, 9, 10$

Fig. 6.7 Total rescue cost for each rescue cycle

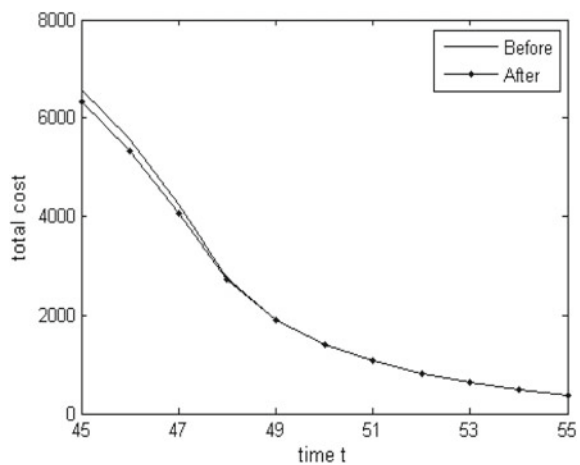
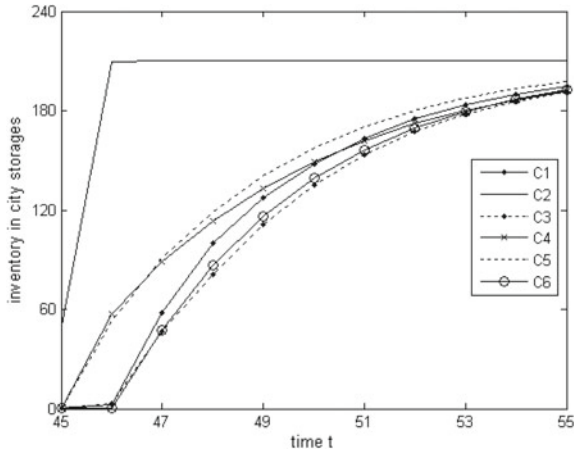


Fig. 6.8 Inventory level in different urban health departments as time goes by



enough emergency resources at that time, and thus, the emergency logistics network will be simplified greatly by then.

As mentioned before, the other control target of the optimization model is to better control the inventory level of the local urban health departments. Figure 6.8 implies that inventory level in each urban health department has been improved and raised as time goes by. Therefore, with the application of the integrated and dynamic optimization model, the total emergency rescue cost can be controlled effectively, and meanwhile, inventory level in each urban health department can be restored and raised gradually. Thus, such optimization model achieves a win-win emergency rescue effect in anti-bioterrorism system.

6.4.2 A Short Sensitivity Analysis

From the previous analysis we can see that the change in total rescue cost mainly depends on the change in demand. In this section, a short sensitivity analysis of the key parameters (θ and Γ) in the forecasting model for the time-varying demand is conducted.

Taking the total rescue cost at time $t = 10$ as the example, holding all the other parameters fixed as in the numerical example given in Sect. 6.4.1, except that θ and Γ take on five different values, respectively. The changes in total rescue cost are shown in Figs. 6.9 and 6.10. As Fig. 6.9 shows, θ takes on five values ranging from 60% to 100% with an increment of 10%, we can obtain the following conclusion: the larger the θ is, the higher of the actual effective rescue rate in each cycle is, thus, the less of demand is, and finally, the lower of the total rescue cost is. Similarly, as Fig. 6.10 shows, Γ takes on five values ranging from 9 to 21 with an increment of 3. Conversely, the larger of Γ is, the longer of the treatment cycle is, thus, the larger of the demand of emergency resources is, and finally, the higher of the total rescue

Fig. 6.9 Change in total rescue cost with different value of θ ($t = 10$)

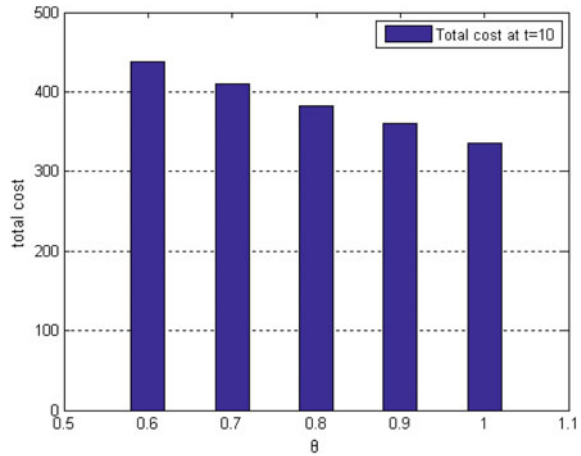
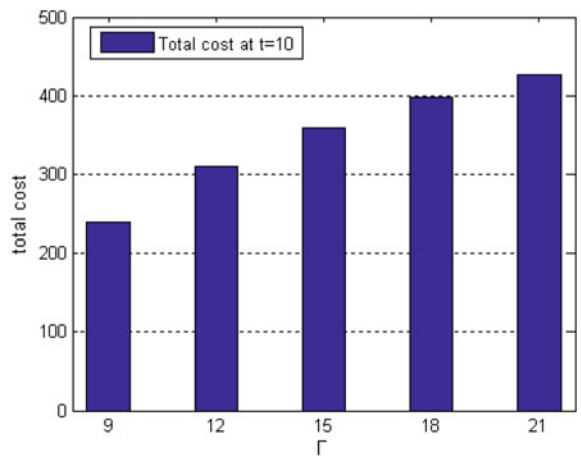


Fig. 6.10 Change in total rescue cost with different value of Γ ($t = 10$)



cost is. The above analysis confirms that both of the two key parameters play an important role in the emergency decisions. For a small change of θ and Γ , the total rescue cost at each cycle can change significantly. Unfortunately, precise value of these two parameters for an epidemic is difficult to get. As the accuracy of these two parameters is vital to the success of emergency rescue, a great deal of effort needs to be devoted to scientifically estimating these two parameters of different epidemics.

Overall, to enhance the emergency rescue effectiveness in the anti-bioterrorism system, we should improve our rescue work from the following aspects:

- (1) Once suffered from a bioterror attack, the epidemic area should be isolated from other areas to avoid the spread of the disease as far as possible.

- (2) Demand of the emergency resources in the epidemic area should be forecasted quickly and precisely, for medicine in such emergency period is precious and should not be wasted.
- (3) An effective, integrated and dynamic optimization model should be conducted for the emergency logistics network so that a win-win emergency rescue effect will be achieved.
- (4) There should be enough emergency resources to cure the patients so that the actual effective rescue rate and the treatment time for each infected person can be improved, and then, the epidemic diffusion can be controlled effectively.

6.5 Conclusions

In this chapter, the optimal decision of the multi-level emergency logistics network with uncertain demand is investigated. An integrated and dynamic optimization model is developed, and an effective solution procedure is designed. To verify the validity and the feasibility of the solution procedure, we have presented a numerical example and an accurate result is obtained in a short amount of time. The main differences distinguish this study to the past literature are presented as follows.

- (1) With the consideration of that emergency resources allocated in the early rescue cycle will affect the demand in the following periods, a unique forecast mechanism to predict the demand in the epidemic area is proposed. Furthermore, we construct two forecasting models for the time-varying demand and inventory level in urban health department.
- (2) A win-win emergency rescue effect is achieved by the integrated and dynamic optimization model. The total emergency rescue cost is controlled effectively, and meanwhile, inventory level in each urban health department is restored and raised gradually.
- (3) Emergency planning has always been formulated as vehicle routing problem (VRP), or vehicle routing problem with time windows (VRPTW) in the precious literature, which includes many sub-tour constraints and is difficult to solve. Further more, time duration factor is not incorporated into the decision, resulting in incomplete decisions in real operations. In this study, the emergency problem has been decomposed into several mutually correlated sub-problems, and then be solved systematically in the same decision scheme. Thus, the result will be suitable to the real operations much better.

To summarize, in this study, emergency logistics network in the anti-bioterrorism system has been optimized from the perspective of integration. And we have achieved the win-win rescue goal. However, it's also necessary to point out some limitations of this research. First of all, we assume that once suffered from a bioterror attack, each epidemic area can be isolated from other areas to avoid the spread of the disease. Second, emergency resources in the anti-bioterrorism system may include vaccine,

antibiotics, masks and so on, thus, the emergency logistics problem should be a multi-commodity problem. Third, to facilitate the calculation process, initial inventory and capacity of the urban health departments are assumed ideally. The situations in actual operations would be much more complex. All these areas represent our future research directions.

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Chapter 7

Integrated Optimization Model for Three-Level Epidemic-Logistics Network



This chapter is a continuous work of Chap. 6. In this chapter, a three-level and dynamic linear programming model for allocating medical resources based on epidemic diffusion model is proposed. The epidemic diffusion model is used to construct the forecasting mechanism for dynamic demand of medical resources. Heuristic algorithm coupled with MATLAB mathematical programming solver is adopted to solve the model. A numerical example is presented for testing the model's practical applicability. The main contribution of the present study is that a discrete time-space network model to study the medical resources allocation problem when an epidemic outbreak is formulated. It takes consideration of the time evolution and dynamic nature of the demand, which is different from most existing researches on medical resources allocation. In our model, the medicine logistics operation problem has been decomposed into several mutually correlated sub-problems, and then be solved systematically in the same decision scheme. Thus, the result will be much more suitable for real operations. Moreover, in our model, the rationale that the medical resources allocated in early periods will take effect in subduing the spread of the epidemic spread and thus impact the demand in later periods has been for the first time incorporated. A win-win emergency rescue effect is achieved by the integrated and dynamic optimization model. The total rescue cost is controlled effectively, and meanwhile, inventory level in each urban health departments is restored and raised gradually.

7.1 Introduction

As mentioned in Rachaniotis et al. [1], a serious epidemic is a problem that tests the ability of a nation to effectively protect its population, to reduce human loss and to rapidly recover. Sometime such a problem may acquire worldwide dimensions. For example, during the period from November 2002 to August 2003, 8422 people in 29 countries were infected with SARS, 916 of them were dead at last for the

effective medical resources appeared late. Other diseases, such as HIV, H1N1 also cause significant numbers of direct infectious disease deaths.

Actually, many recent research efforts have been devoted to understanding the prevention and control of epidemics, such as Wein et al. [2], Craft et al. [3] and Kaplan et al. [4]. The major purpose of these articles is to compare the performance of the following two strategies, the traced vaccination (TV) strategy and the mass vaccination (MV) strategy, but not address how to optimize the allocation of medical resources.

Another stream of research is on the development of epidemic diffusion models by applying complex network theory to traditional compartment models. For example, Saramäki and Kaski [5] proposed a susceptible-infected-recovered (SIR) model for the spreading of randomly contagious diseases, such as influenza, based on a dynamic small-world network. Xu et al. [6] presented a modified susceptible-infected-susceptible (SIS) model based on complex networks, small-world and scale-free, to study the spread of an epidemic by considering the effect of time delay. Based on two-dimensional small-world networks, a susceptible-infected (SI) model with epidemic alert is proposed in [7]. This model indicates that to broadcast an epidemic alert timely is helpful and necessary in the control of epidemic spreading. Jung et al. [8] extended the previous studies on the prevention of the pandemic influenza to evaluate the time-dependent optimal prevention policies, and they found that the quarantine policy is very important, and more effective than the elimination policy. After determining the epidemiologic features of an Escherichia coli O157:H7 outbreak in Xuzhou, Jiangsu Province, China, Zhu et al. [9] provided a scientific approach for establishing prevention and control strategies in local areas. These above mentioned works represent some of the research on various differential equation models for epidemic diffusion and control.

However, after an epidemic outbreak, public officials are faced with many critical issues, one of the most important of which being how to ensure the availability and supply of medical resources so that the loss of life may be minimized and the rescue operation efficiency maximized. Sheu [10] presented a hybrid fuzzy clustering-optimization approach to the operation of medical resources allocation in response to the time-varying demand during the crucial rescue period. Yan and Shih [11] considered how to minimize the length of time required for emergency roadway repair and relief distribution, as well as the related operating constraints. The weighting method is adopted, and a heuristic algorithm is developed to solve a real emergency relief problem, the Chi-Chi earthquake in Taiwan. To optimize the process of materials distribution in an epidemic diffusion system and to improve the distribution timeliness, Liu and Zhao [12] modeled the emergency materials distribution problem as a multiple traveling salesman problem with time window. Wang et al. [13] constructed a multi-objective stochastic programming model with time-varying demand for the emergency logistics network based on the epidemic diffusion rule. A genetic algorithm coupled with Monte Carlo simulation is adopted to solve the optimization model. Qiang and Nagurney [14] proposed a humanitarian logistic model for supply/distribution of critical needs in a disruption caused by a nature disaster. They consider a general network structure and disruptions that may have an impact to both

network link capacities and product demand. The problem is studied in a bi-criteria system optimization framework for network performance.

In this study, a three-level and dynamic linear programming model for allocating medical resources based on epidemic diffusion model is proposed. The epidemic diffusion model introduced here is to construct the forecasting mechanism for the dynamic demand of medical resources. Heuristic algorithm coupled with MATLAB mathematical programming solver is adopted to solve the model.

7.2 Problem Description

7.2.1 The Research Ideas and Way to Achieve

As work in Liu and Zhao [15], this study focus on the recovered stage of epidemic rescue. In such a stage, epidemic diffusion tends to be stable. Thus, optimization goal in such stage is to construct an integrated, dynamic and multi-level emergency logistics network, which includes the national strategic storages (NSS), the urban health departments (UHD), the area disease prevention and control centers (ADPC), and the emergency designated hospitals (EDH). Herein, we introduce a time-space network to depict the network structure relationship of these elements, which is shown as Fig. 7.1. In such figure, the vertical axis represents the time duration, and the horizontal axis represents different emergency departments.

The entire recovered stage of epidemic rescue process is decomposed into several mutually correlated sub-problems (i.e. n decision-making cycles). To each decision-making cycle, there exist two sub-problems. In the upper level, we consider the problem how to replenish medical resources to the UHDs. Besides, we adjust the replenishment arcs among these NSSs by a heuristic algorithm, and construct a mixed-collaborative delivery system. Thus, the total rescue cost of the upper level

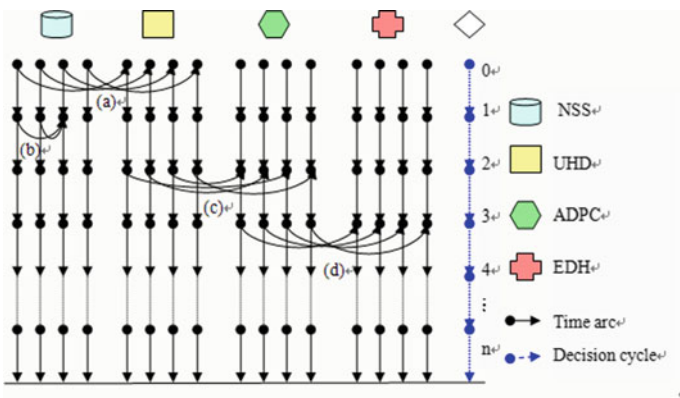


Fig. 7.1 Time-space network of medical resources allocation

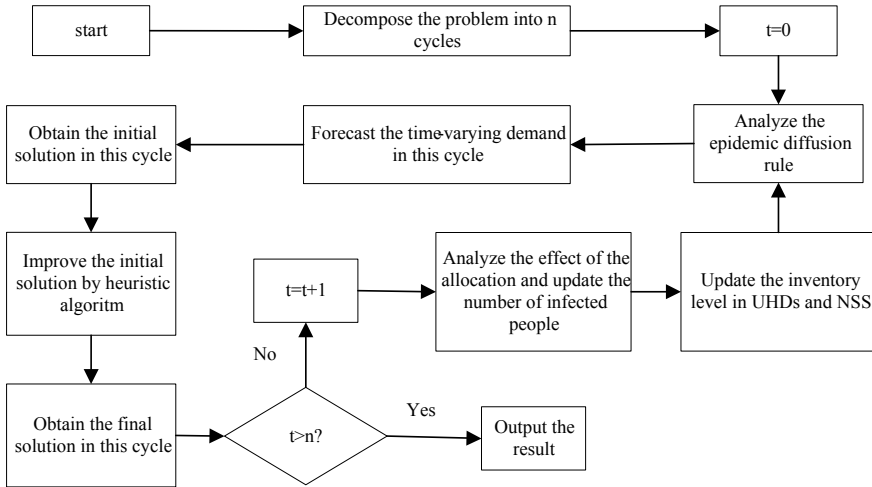


Fig. 7.2 Operational procedure of the dynamic medicine logistics network

sub-problem would be minimized. In the lower level, we present the problem how to distribute medical resources to the ADPCs and then allocate medical resources to EDHs. We propose a forecasting model for the time-varying demand in EDHs based on a SEIR epidemic diffusion model. Such two phases are executed iteratively. Besides, at the end of each rescue cycle, effect of medical resources allocated is analyzed and the number of infected people is updated. The research idea of such rescue stage is shown in Fig. 7.2.

7.2.2 Time-Varying Forecasting Method for the Dynamic Demand

In this study, we divide people into four classes: the susceptible people (S), the exposed people (E), the infected people (I), and the recovered people (R). The following SEIR epidemic diffusion model in Liu and Zhao [16] is adopted to depict the epidemic diffusion rule.

$$\begin{cases} \frac{dS}{dt} = -\beta\langle k \rangle S(t)I(t) \\ \frac{dE}{dt} = \beta\langle k \rangle S(t)I(t) - \beta\langle k \rangle S(t - \tau)I(t - \tau) \\ \frac{dI}{dt} = \beta\langle k \rangle S(t - \tau)I(t - \tau) - (d + \delta)I(t) \\ \frac{dR}{dt} = \delta I(t) \end{cases} \tag{7.1}$$

Herein, $\langle k \rangle$ is the average degree distribution of the small-world network; β is the propagation coefficient; δ is the recovered rate of the infected people; d is the death rate caused by the disease; τ stands for the incubation period. Furthermore, $\langle k \rangle, \beta, \delta, d, \tau > 0$. Traditionally, a simple linear function is used to formulated the demand for medical resources as follows:

$$d_t^* = aI(t), \quad t \in 0, 1, 2, \dots, n \quad (7.2)$$

Herein, $I(t)$ is the number of infected people in the epidemic area at time t . a is the proportionality coefficient. Note that emergency demand for medical resources is closely related to the number of infected people, and medical resources allocated in the early rescue cycle will affect the demand later, here we propose a time-varying forecasting method for the demand in each EDH as follows:

$$\eta_t = (d_{t+1}^* - d_t^*)/d_t^*, \quad t \in 0, 1, 2, \dots, n-1 \quad (7.3)$$

$$\text{When } t = 0, \quad d_0 = aI(0) \quad (7.4)$$

$$\text{When } t = 1, \quad d_1 = (1 + \eta_0) \left(1 - \frac{\theta}{\Gamma}\right) d_0 \quad (7.5)$$

$$\text{When } t = 2, \quad d_2 = (1 + \eta_1) \left(1 - \frac{\theta}{\Gamma}\right) d_1 = (1 + \eta_0)(1 + \eta_1) \left(1 - \frac{\theta}{\Gamma}\right)^2 d_0 \quad (7.6)$$

$$\text{When } t = n, \quad d_n = \prod_{i=0}^{n-1} (1 + \eta_i) \left(1 - \frac{\theta}{\Gamma}\right)^n d_0 \quad (7.7)$$

Herein, $\prod_{i=0}^{n-1} (1 + \eta_i) = (1 + \eta_0)(1 + \eta_1) \cdots (1 + \eta_{n-1})$. θ is the effective rescue rate; Γ is the treatment cycle for each infected person. To facilitate the calculation process in the following sections, we assume that Γ to be an integral multiple of rescue cycle. Equation (7.3) is used to calculate the linear scale factor of the change in demand. Equation (7.4) is the initial demand in the epidemic area, and $I(0)$ represents the initial number of infected people in the epidemic area. Equations (7.5)–(7.7) represent demand for medical resources in rescue cycle 1, 2, \dots , n , respectively.

7.2.3 Dynamic Demand and Inventory for the UHD

To facilitate the calculation process in the following sections, we assume that initial inventory of medical resources in each UHD is zero. Besides, we suppose that capacity of each UHD is V_{cap} . d_t^v represents demand for medical resources in UHD in rescue cycle t . P_t represents the total output of medical resources in UHD in rescue cycle t . Thus, the forecasting model for dynamic demand in UHD can be formulated

as follows:

$$d_t^v = \begin{cases} V_{cap}, & t = 0 \\ P_{t-1}, & t = 1, 2, \dots, n \end{cases} \quad (7.8)$$

Correspondingly, suppose that V_t is inventory of medical resources in UHD in rescue cycle t , we can get the following equation:

$$V_t = \begin{cases} 0, & t = 0 \\ V_{cap} - P_{t-1}, & t = 1, 2, \dots, n \end{cases} \quad (7.9)$$

7.3 Optimization Model and Solution Procedure

7.3.1 Optimization Model

The following assumptions are needed to facilitate the model formulation in the following sections:

- (1) Once an epidemic outbreak, each EDH can be isolated from other areas to avoid the spread of the disease.
- (2) It is reasonable to assume that the government can ensure the adequate supply of the needed medicines either from domestic pharmaceutical companies or imported. Hence, there are enough medical resources during the entire operation process.
- (3) Holding cost of medical resources is not considered in this study.
- (4) Medical resources in this section are an assembled product, which may includes water, vaccine, antibiotic, etc.

Notations used in the following optimization model are specified as follows.

nc_{ij}	Unit replenishment cost of medical resources from NSS i to UHD j .
ce_{jk}	Unit distribution cost of medical resources from UHD j to ADPC k .
eh_{kl}	Unit distribution cost of medical resources from ADPC k to EDH l .
ns_i	Amount of medical resources supplied by NSS i in each rescue cycle.
V_{cap}	Capacity of UHD.
d_{lt}	Demand for medical resources in EDH l in rescue cycle t .
d_{jt}^v	Demand for medical resources in UHD j in rescue cycle t .
P_{jt}	Total output of medical resources in UHD j in rescue cycle t .
V_{jt}	Inventory of medical resources in UHD j in rescue cycle t .
x_{ijt}	Amount of medical resources that will be transported from NSS i to UHD j in rescue cycle t .
y_{jkt}	Amount of medical resources that will be transported from UHD j to ADPC k in rescue cycle t .

- z_{klt} Amount of medical resources that will be transported from ADPC k to EDH l in rescue cycle t .
- TC Total rescue cost of the three-level medical logistics network.
- N Set of NSSs.
- C Set of UHDs.
- E Set of ADPCs.
- H Set of EDHs.
- T Set of decision-making cycles.

According to the above explanations and assumptions, the three-level and dynamic linear programming model for allocating medical resources based on epidemic diffusion model can be formulated as follows:

$$\text{Min } TC = \sum_{t \in T} \sum_{i \in N} \sum_{j \in C} x_{ijt} n c_{ij} + \sum_{t \in T} \sum_{j \in C} \sum_{k \in E} y_{jkt} c e_{jk} + \sum_{t \in T} \sum_{k \in E} \sum_{l \in H} z_{klt} e h_{kl} \quad (7.10)$$

$$\text{s.t. } \sum_{j \in C} x_{ijt} \leq n s_i, \quad \forall i \in N, t \in T \quad (7.11)$$

$$\sum_{i \in N} x_{ijt} = d_{jt}^v, \quad \forall j \in C, t \in T \quad (7.12)$$

$$d_{jt}^v = V_{cap}, \quad \forall j \in C, t = 0 \quad (7.13)$$

$$d_{jt}^v = P_{jt-1}, \quad \forall j \in C, t = 1, 2, \dots, T \quad (7.14)$$

$$P_{jt} = \sum_{k \in E} y_{jkt}, \quad \forall j \in C, t \in T \quad (7.15)$$

$$\sum_{k \in E} y_{jkt} \leq V_{cap}, \quad \forall j \in C, t \in T \quad (7.16)$$

$$\sum_{j \in C} \sum_{k \in E} y_{jkt} = \sum_{k \in E} \sum_{l \in H} z_{klt}, \quad \forall t \in T \quad (7.17)$$

$$\sum_{k \in E} z_{klt} = d_{lt}, \quad \forall l \in H, t \in T \quad (7.18)$$

$$d_{lt} = a I_l(t), \quad \forall l \in H, t = 0 \quad (7.19)$$

$$d_{lt} = \prod_{i=0}^{t-1} (1 + \eta_i) \left(1 - \frac{\theta}{\Gamma}\right)^t d_{l0}, \quad \forall l \in H, t = 1, 2, \dots, T \quad (7.20)$$

$$\prod_{i=0}^{t-1} (1 + \eta_{li}) = (1 + \eta_{l0})(1 + \eta_{l1}) \cdots (1 + \eta_{lt-1}), \quad \forall l \in H, t = 1, 2, \dots, T \quad (7.21)$$

$$x_{ijt} \geq 0, \quad \forall i \in N, j \in C, t \in T \quad (7.22)$$

$$y_{jkt} \geq 0, \quad \forall j \in C, k \in E, t \in T \quad (7.23)$$

$$z_{klt} \geq 0, \quad \forall k \in E, l \in H, t \in T \quad (7.24)$$

Herein, the objective function in Eq. (7.10) is to minimize the total rescue cost of the three-level medical distribution network. Equations (7.11) and (7.12) are constraints for flow conservation in the upper level sub-problem. Equations (7.13)–(7.15) are the dynamic demand models in the upper level sub-problem. Equations (7.16)–(7.18) are constraints for flow conservation in the lower level sub-problem. Equations (7.19)–(7.21) are the time-varying demand models in the lower level sub-problem. At last, Eqs. (7.21)–(7.23) ensure all the arc flows in the time-space network within their bounds.

7.3.2 Solution Procedure

As Fig. 7.2 shows, the solution procedure for the proposed optimization model is presented as follows:

Step 1. Decompose the entire recovered stage of epidemic rescue process into n decision-making cycles.

Step 2. Let $t = 0$, and initialize parameters in the SEIR epidemic diffusion model.

Step 3. Analyze the epidemic diffusion rule, and calculate the initial demand for medical resources in each EDH according to Eqs. (7.3)–(7.7).

Step 4. Solve the programming model in rescue cycle $t = 0$ and obtain the initial solution.

Step 5. Improve the initial solution by heuristic algorithm. Detail about the heuristic algorithm, please go to Liu et al. [17].

Step 6. Get the final solution for medical resources allocation in this rescue cycle.

Step 7. Let $t = t + 1$, if the termination condition for the rescue cycle has not been satisfied, update the demand in each EDH, and update the inventory level of medical resources in each UDH, go back to Step 3. Else, go to the next step.

Step 8. End the program and output the final result.

7.4 Numerical Example

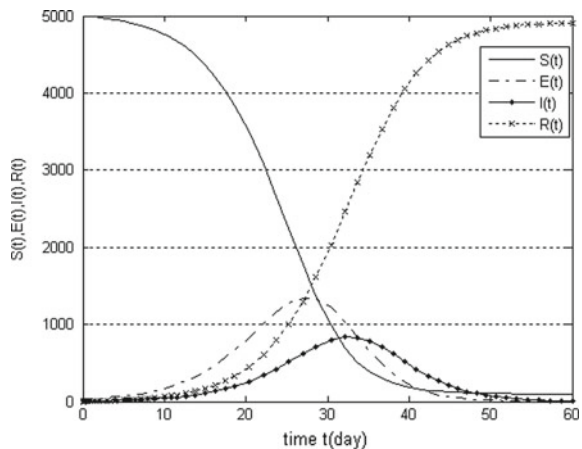
To test how well the proposed model may be applied in an actual event, we present a numerical example to illustrate its efficiency. Assume there is a smallpox outbreak in a city, which has 3 NSSs, 4 UHDs, 6 ADPCs and 8 EDHs. The values of parameters in SEIR epidemic diffusion model are given in Table 7.1.

Figure 7.3 depicts a numerical simulation of the epidemic model at EDH 1 in this effected region. The four curves respectively represent the number of four groups of people (S, E, I, R) over time. As mentioned in Liu and Zhao [16], the process of epidemic diffusion is divided into three stages and our research focus on the recovered one. According to the above figure, we assume that such stage range from the 45th day (decision-making cycle $t = 0$) to the 55th day (decision-making cycle $t = 10$). For simplicity, the decision-making cycle is assumed to be one day. A total

Table 7.1 Values of parameters in SEIR epidemic diffusion model

	EDH1	EDH2	EDH3	EDH4	EDH5	EDH6	EDH7	EDH8
$S(0)$	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
$E(0)$	30	35	30	40	25	40	50	45
$I(0)$	5	6	7	8	4	7	9	10
$R(0)$	0							
β	4×10^{-5}							
$\langle k \rangle$	6							
δ	0.3							
d	1×10^{-3}							
τ	5							

Fig. 7.3 Solution of the SEIRS epidemic diffusion model (EDH 1)



of 138,240 variations are generated in the experiment. During an actual epidemic activity, decision makers can adjust these parameters according to the actual situation.

Let $a = 1$, $\theta = 90\%$ and $\Gamma = 15$, the MATLAB mathematic solver coupled with Eqs. (7.2)–(7.7) is adopted to forecast the time-varying demand for each EDH. Taking the EDH 1 as an example, the demand for medical resources in each rescue cycle is shown in Fig. 7.4. One can observe in Fig. 7.4 that time-varying demand is way below traditional demand, suggesting that the allocation of medical resources in the early periods will significantly reduce the demand in the following periods. The second observation is that both curves exhibit similar trends, namely, the demand will decrease after the epidemic is brought under control.

After getting the demand for medical resources in each rescue cycle, in what follows, we are going to discuss how to allocate these medical resources to the epidemic areas, and at the same time, how to replenish medical resources to each UHD, with the objective of minimizing the total rescue cost. Table 7.2 shows the unit cost from the supply points to the demand points (Here, we suppose that NSS 1 has been preset as the HUB location).

Assume that three NSS can supply 400, 420 and 450 unit of medical resources in each rescue cycle, and suppose that capacity of each UHD is 320. Let us take the allocation result at cycle $t = 0$ as example, we can solve the programming model according to the solution procedure. The initial solution is reported in Table 7.3.

Then, we can improve the initial solution by heuristic algorithm in Liu et al. [17]. As Table 7.3 shows, when replenishment arcs $(N_2, C_1) \in D^d$ and $(N_3, C_1) \in D^d$ are transferred from the direct shipment delivery system to the hub-and-spoke delivery system, such as $N_2 \rightarrow N_1 \rightarrow C_1$ and $N_3 \rightarrow N_1 \rightarrow C_1$, the total rescue cost will be reduced 10.75% when compared with the cost before adjustment (4090/3650). Similarly, we can complete the whole operations according to the solution procedure. Replenishment arcs that need to be transferred in each cycle are shown in Table 7.4. Total rescue cost at each cycle is presented in Fig. 7.5.

Fig. 7.4 Demand in EDH 1 by the two different methods

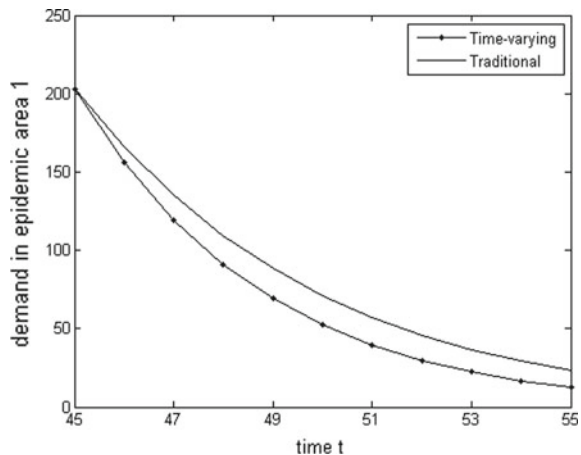


Table 7.2 Unit cost of medical resources between two different departments

Cost	N1	C1	C2	C3	C4			
N1	–	2	2	1	3			
N2	3	7	2	10	9			
N3	4	8	9	2	10			
	E1	E2	E3	E4	E5	E6		
C1	1	3	4	2	5	5		
C2	2	1	2	3	5	4		
C3	2	3	5	4	1	3		
C4	4	4	1	2	3	2		
	H1	H2	H3	H4	H5	H6	H7	H8
E1	6	2	6	7	4	2	5	9
E2	4	9	5	3	8	5	8	2
E3	5	2	1	9	7	4	3	3
E4	7	6	7	3	9	2	7	1
E5	2	3	9	5	7	2	6	5
E6	5	5	2	2	8	1	4	3

Table 7.3 Solution of the optimization model at cycle $t = 0$

Amount		C1	C2	C3	C4	
Before adjustment	N1	100	0	0	320	
	N2	110	320	0	0	
	N3	110	0	320	0	
	N1	C1	C2	C3	C4	
After adjustment	N1	–	320	0	0	320
	N2	110	0	320	0	0
	N3	110	0	0	320	0

Table 7.4 Transferred arcs in each rescue cycle

Cycle	Arcs need to be transferred		Cycle	Arcs need to be transferred	
	Before	After		Before	After
$t = 0$	N2 → C1 N3 → C1	N2 → N1 → C1 N3 → N1 → C1	$t = 1$	N2 → C1 N3 → C1	N2 → N1 → C1 N3 → N1 → C1
$t = 2$	N2 → C1	N2 → N1 → C1	$t = 3$	N2 → C1	N2 → N1 → C1

Note There is no adjustment when $t = 4, 5, 6, 7, 8, 9, 10$

Fig. 7.5 Total rescue cost at each rescue cycle

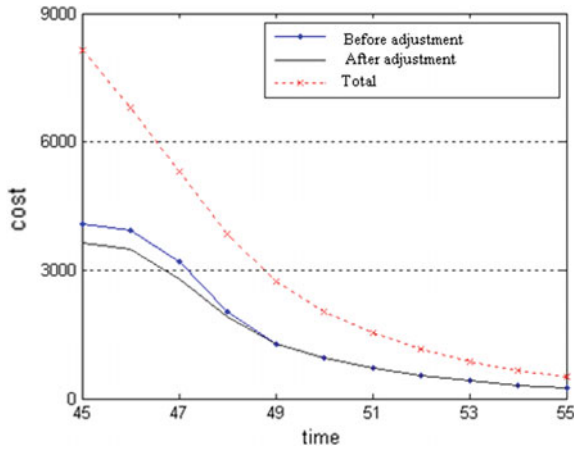
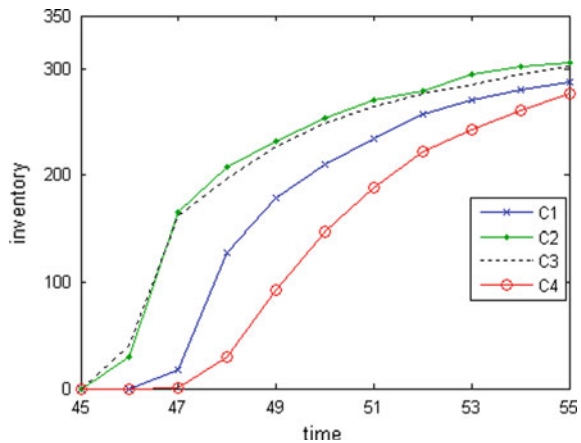


Figure 7.5 shows the change in total rescue cost over time. From this figure, we can get the following two conclusions: (1) Coupled with Fig. 7.4, we can see that demand for medical resource is decreasing, which implies that epidemic diffusion is on the recovered stage. (2) Coupled with Table 7.4, we can see that the total rescue cost can be reduced in a certain degree by using the proposed heuristic algorithm. It is worth mentioning that there is no adjustment after rescue cycle $t = 4$, for that NSSs and UHDs which are adjacent to the epidemic areas will have stored enough resources at that time.

Figure 7.6 shows the inventory level in different UHDs. It shows that inventory level in each UHD has been improved and raised as time goes by. Therefore, with the application of the three-level and dynamic optimization model, the total rescue

Fig. 7.6 Inventory level in different UHD over time



cost can be controlled effectively, and meanwhile, inventory level in each UHD can be restored and raised gradually. Thus, such optimization model achieves a win-win rescue effect.

7.5 Conclusions

In this chapter, we develop a discrete time-space network model to study the medical resources allocation problem in the recovered stage when an epidemic outbreak. In each decision-making cycle, the allocation of medical resources across the region from NSSs through UHDs and ADPCs to EDHs is determined by a linear programming model with the dynamic demand that is forecasted by an epidemic diffusion rule. The novelty of our model against the existing works in literature is characterized by the following three aspects:

- (1) While most research on medical resources allocation studies a static problem taking no consideration of the time evolution and dynamic nature of the demand, the model proposed in this chapter addresses a time-series demand that is forecasted in match of the course of an epidemic diffusion. The model couples a multi-stage linear programming for optimal allocation of medical resources with a proactive forecasting mechanism cultivated from the epidemic diffusion dynamics. The rationale that the medical resources allocated in early periods will take effect in subduing the spread of the epidemic spread and thus impact the demand in later periods has been for the first time incorporated into our model.
- (2) A win-win emergency rescue effect is achieved by the integrated and dynamic optimization model. The total rescue cost is controlled effectively, and meanwhile, inventory level in each UHD is restored and raised gradually.
- (3) In this chapter, the medicine logistics operation problem has been decomposed into several mutually correlated sub-problems, and then be solved systematically in the same decision scheme. Thus, the result will be much more suitable for real operations.

As the limitation of the model, it is developed for the medical resources allocation in a geographic area where an epidemic disease has been spreading and it does not consider possible cross area diffusion between two or more geographic areas. We assume that once an epidemic outbreaks, the government will have effective means to separate the epidemic areas so that cross-area spread can be basically prevented. However, this cannot always be guaranteed in reality.

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Chapter 8

A Novel FPEA Model for Medical Resources Allocation in an Epidemic Control



This chapter presents a dynamic logistics model for medical resources allocation that can be used to control an epidemic diffusion. It couples a forecasting mechanism, constructed for the demand of a medicine in the course of such epidemic diffusion, and a logistics planning system to satisfy the forecasted demand and minimize the total cost. The forecasting mechanism is a time discretized version of the SEIR model that is widely employed in predicting the trajectory of an epidemic diffusion. The logistics planning system is formulated as a mixed 0–1 integer programming problem characterizing the decision-making at various levels of hospitals, distribution centers, pharmaceutical plants, and the transportation in between them. The model is built as a closed-loop cycle, comprising forecast phase, planning phase, execution phase, and adjustment phase. The parameters of the forecasting mechanism are adjusted in reflection of the real data collected in the execution phase by solving a quadratic programming problem. A numerical example is presented to verify efficiency of the model.

8.1 Introduction

In the past two decades, the world has been aware of the threat of various epidemics. According to WHO's annual report in 2002, the world was confronted with an infectious disease crisis of global proportions. A fact was that more than 4 million people worldwide were infected with HIV in 2002 [1]. This number became 36.9 million at the end of 2014. In that year, 2 million people became newly infected, and 1.2 million died of AIDS-related causes [2].

There are two separate streams of modeling work in the operations research and management science discipline on the topic of epidemic spread and control that will be briefly overviewed below. One of the compartmental models studies on the diffusion dynamics and the other studies on medical resources allocation problems. The intended contribution of this study is to bridge these two streams of research by presenting a hybrid model that embeds a periodic forecast update of the epidemic

spread, based on a SEIR compartmental model, into a dynamic logistics planning of medical resources allocation and distribution. Such endeavor is not solely of academic challenge but also bring our modeling work in this subject one step closer to the real world application.

The first stream of research studies epidemic diffusion dynamics. A great number of analytical works on epidemic diffusion have focused on the compartmental epidemic models formulated as ordinary differential equations (cf. [3–6], and the references therein). In these models, the total population is divided into several classes and each class of people is closed into a compartment. The size of the compartment is assumed to be large enough and the mixing of members is homogeneous. The models are built upon differential equations and assume both homogeneous infectivity and homogeneous connectivity of each individual. Recently, Kim et al. [7] described the transmission of avian influenza between birds and humans. Liu and Zhang [8] presented a Susceptible-Exposed-Infected-Recovered-Susceptible (SEIRS) epidemic model based on a scale-free network. Samsuzzoha et al. [9] proposed a diffusive epidemic model to describe the transmission of influenza. The ordinary differential equations were solved numerically by the splitting method under different initial distribution of population density. Further, Samsuzzoha et al. [10] developed a vaccinated diffusive compartmental epidemic model to explore the impact of vaccination as well as diffusion on the transmission dynamics of influenza.

The second stream of the relevant research is on medical resources allocation or stockpiling for emergent needs in the wake of a nature disaster, a terrorist attack, or in a case of influenza prevalence (c.f., [11–14], and the references therein). The modeling work in these articles is characterized with a background of emergency that calls for urgent actions. Zaric and Brandeau studied resource allocation problems in an effort to control infectious diseases in multiple independent populations using cost-effectiveness analysis and methods [15–17]. As indicated in the review of Brandeau [18], cost-effectiveness analysis, linear integer programming, nonlinear optimization, optimal control methods, simulation techniques and heuristic approaches were adopted as modeling tools in studying such problems. More recent works in this stream include Tebbens et al. [19] on vaccine stockpile policy, Rachaniotis et al. [20] on optimal resource scheduling, and the review by Dasaklis et al. [21].

Although there are many publications on the topic of medical resources allocation, the interaction between the course of epidemic diffusion and the dynamic medical resources allocation, has not been well addressed until recently. Liu et al. [22] presented a time-space network model for studying the dynamic impact of medical resource allocation in controlling an epidemic spread. The medical resources allocated in the early period would take effect in subduing the spread of influenza and thus impact the medicine demand in the later period, and such impact was estimated by a so-called linear growth factor in that study. However, the linear-growth factor is artificially created but not real data justified as the forecast adjustment proposed in that study. While the former is a simple and quick corrector, the latter is a data supported adjustment and thus more scientific. The time-space network model of Liu et al. [22] is also deficient in the logistic planning and does not address many practical and important features of a logistic system that are explicitly modeled in this study

such as lead times, order sizes, warehouse capacities, as well as the switch-on and switch-off costs of the pharmaceutical plants.

In this study, we will present a dynamic logistics model for medical resources allocation in reflection of the time varying demand that synchronizes with epidemic spread. A four-phase closed loop model, comprised of a forecast phase, a planning phase, an execution phase and an adjusted forecast phase (FPEA), is built to design the logistics system for medical resources allocation to control an epidemic diffusion. The framework of the FPEA model is introduced as follows.

- (i) For the first forecast phase, we employ a time discretized version of the SEIR model to forecast the growing (or decreasing) of the infected population in the course of the epidemic diffusion, and thus give a forecast of the dynamic demand for the needed resources in the next few days, which is termed as a decision cycle.
- (ii) According to the demand forecast for the next decision cycle, the second planning phase will solve a mixed 0–1 integer programming problem for the best allocation of the medical resources in a supportive logistics system to meet the dynamic demand. The logistics system is characterized with decision making at three tiers, i.e., the local hospitals, the area distribution centers and the pharmaceutical plants, and is incorporated with decision variables such as the number of beds allocated in each hospital, the daily shipment pattern from the DCs to the hospitals, the inventory levels at the DCs, order quantities and order times of the DCs, and the production levels of the plants. Capacity constraints are explicitly considered in this health care and medical logistics system.
- (iii) The execution phase is designed as an exogenous part of the model where the plan is implemented in the real world and the data is collected in practice.
- (iv) The real world data will be utilized in the fourth phase to close the loop of the decision cycle. In this phase, we adjust the parameters in the forecast model to better reflect the diffusion course and control the effect by using the real data collected in the implementation of phase three. For this purpose, the model will solve a series of sub-problems to minimize the forecast error and update the parameters for the forecast for the next decision cycle.

We believe the proposed model should serve for the benefit of a centralized decision making system, usually a local or regional governmental agent, in control of the epidemic diffusion that needs an analytic model to plan for the logistics and to revise and update such plan in the actual implementation. It also stands for the first attempt to incorporate the well-studied epidemic diffusion model as a forecast in the logistic planning.

8.2 The Mathematical Model

As introduced above, the FPEA model is constructed as a closed loop of forecast, planning, execution, and adjustment, as it proceeds in the endeavor of planning medical resources to control the epidemic diffusion in an effective way.

There are two time notation in our model, one for the cycle serial number and the other for the time within a cycle. Let T denote the length of a cycle, $t = 1, \dots, T$ denote a particular day in the cycle (in this study, “day” is a modeling term for the basic time unit within a cycle, which can be two days to a week in actual time depending on actual need), and $s = 1, 2, \dots$ denote the cycle serial number. Each cycle begins with the first phase of a forecast for the number of infected people in each day of this cycle. This determines the need for medical resources in the second phase of the cycle when the model plans for the best allocation of hospital beds, the best distribution and transport of the medicine. The third phase (exogenous part of the model) is the execution of the plan. In the fourth phase, we adjust the parameters of the forecast model based on the actual result from the execution and solve an optimization sub-problem to determine the best fit of the parameters for the forecast phase in the next cycle. Therefore, the forecast in the next cycle has a reflection of the actual happening in the execution of this cycle.

In the sequel, we describe and explain the technical details for each part of the forecast-planning-execution-adjustment (FPEA) model.

8.2.1 Forecasting Phase

The forecast in the first phase utilizes a SEIR model. The SEIR model has been widely used for epidemic diffusion in the literature, which is based on a compartment theory and is proved to be a good match to the actual epidemic diffusion. In such a model, people are divided into four classes: the susceptible individuals S , the exposed individuals E , the infected individuals I , and the recovered individuals R . As illustrated in Fig. 8.1, individuals enter the compartment through $S(t)$ at rate λN and exit the compartment at rate $\lambda(S(t) + E(t) + I(t) + R(t))$.

Although 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

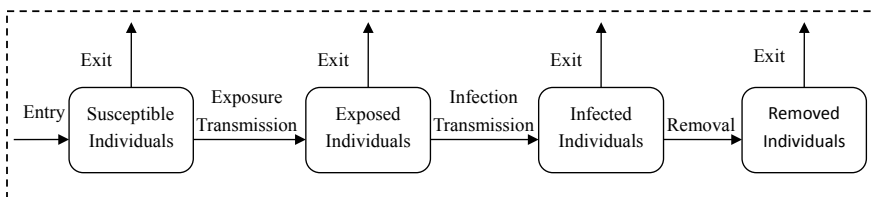


Fig. 8.1 Schematic diagram of SEIR model

over a short period of time without a social economic reason. Therefore, during the course of an epidemic spread-to-control, which usually lasts no longer than six 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 literature assumes a constant population size as is in this study. 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. Hence, without consideration of the natural birth rate and death rate of the population, we can use a simple deterministic compartmental model to describe the epidemic spread process, which can be described by the following system of ordinary differential equations (ODE).

$$\begin{cases} S'(t) = \lambda N - \beta S(t)I(t) - \lambda S(t) \\ E'(t) = \beta S(t)I(t) - \gamma E(t) - \lambda E(t) \\ I'(t) = \gamma E(t) - \lambda I(t) - \delta I(t) \\ R'(t) = \delta I(t) - \lambda R(t) \\ N = S(t) + E(t) + I(t) + R(t) \end{cases} \quad (8.1)$$

In the above system of equations, $S(t)$, $E(t)$, $I(t)$ and $R(t)$ represent respectively the number of susceptible individuals, the number of exposed individuals, the number of infected individuals, and the number of recovered individuals. β is the propagation coefficient of the epidemic. γ is the transmission rate between the exposed subpopulation and the infected subpopulation. δ is the rate of infected individuals who will be recovered. λ is the entry or exit rate of the population. All the parameters, β , γ , δ and λ , are greater than zero.

ODE (8.1) describes the following dynamics of epidemic diffusion among the population groups. (i) The change rate of the susceptible population is determined by the entering population, the exiting population, and the transitioning population who actually get exposed to the disease and thus are counted towards the class of $E(t)$. The size of transitioning population is in proportion to the propagation coefficient β , and both of the current number of the susceptible individuals and the current number of the infected individuals. (ii) The change 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, the exiting population, and the transitioning population, those of exposed population who get sick after the incubation period of the disease; (iii) The change rate of the infected population is determined by the difference between the entering population, those of exposed population who get sick, the exiting population, and the transitioning population who are recovered; And, finally (iv) the change rate of the recovered population is determined by the difference between the joining population of the newly recovered and the exiting population of the recovered people.

When the parameters are determined and input to the ODE (8.1), the evolution trajectories of $S(t)$, $E(t)$, $I(t)$ and $R(t)$ are determined. These trajectories can be

approximated by time-discrete algorithm such as Runge-Kutta method (cf. e.g. [26, 27]). Usually, the shorter the time horizon is, the better the approximation of discrete-time algorithm is. As noted above, let T be the cycle length, that is, the time horizon for medical resources distribution and logistics planning, which in practice can be one to two weeks depending on the emergency of the case. Then ODE (8.1) can be time discretized into the following system of difference equations, for any $t = 0, 1, \dots, T - 1$:

$$\begin{cases} S(t+1) = S(t) + \lambda N - \beta S(t)I(t) - \lambda S(t) \\ E(t+1) = E(t) + \beta S(t)I(t) - \gamma E(t) - \lambda E(t) \\ I(t+1) = I(t) + \gamma E(t) - \lambda I(t) - \delta I(t) \\ R(t+1) = R(t) + \delta I(t) - \lambda R(t) \\ N = S(t+1) + E(t+1) + I(t+1) + R(t+1) \end{cases} \quad (8.2)$$

The difference equations (8.2) can be used to forecast the number of susceptible, exposed, infected and recovered individuals given the initial values of $S(0)$, $E(0)$, $I(0)$, $R(0)$. In fact, to forecast $S(t)$, $E(t)$, $I(t)$, $R(t)$ for the next cycle $s + 1$, the initial condition of $S(0)$, $E(0)$, $I(0)$, $R(0)$ is set to be the actual observed population size of the susceptible, exposed, infected and recovered individuals on the last day of the current cycle s . For simplicity, we may denote the forecast of the susceptible, exposed, infected, and recovered population on day $t + 1$, that is, the right-hand sides of the difference equations (8.2) by

$$\hat{S}(t)(\beta, \lambda) = S(t) + \lambda N - \beta S(t)I(t) - \lambda S(t) \quad (8.3)$$

$$\hat{E}(t)(\beta, \gamma, \lambda) = E(t) + \beta S(t)I(t) - \gamma E(t) - \lambda E(t) \quad (8.4)$$

$$\hat{I}(t)(\gamma, \lambda, \delta) = I(t) + \gamma E(t) - \lambda I(t) - \delta I(t) \quad (8.5)$$

$$\hat{R}(t)(\delta, \lambda) = R(t) + \delta I(t) - \lambda R(t) \quad (8.6)$$

Therefore, the difference equations (8.2) can be rewritten as

$$\begin{cases} S(t+1) = \hat{S}(t)(\beta, \lambda) \\ E(t+1) = \hat{E}(t)(\beta, \gamma, \lambda) \\ I(t+1) = \hat{I}(t)(\gamma, \lambda, \delta) \\ R(t+1) = \hat{R}(t)(\delta, \lambda) \end{cases} \quad (8.7)$$

8.2.2 Planning Phase

In this subsection, we will describe the planning phase of our FPEA model and present a 0–1 mixed integer programming problem for the optimal planning of hospital resources and medicine distribution and transportation, based on the forecasted number of infected individuals in the next cycle. Suppose that there are several pharmaceutical plants, $i = 1, 2, \dots, I$, which can produce and ship the medicine to the epidemic area. There are several distribution centers or district warehouses, $j = 1, \dots, J$, in this area, and several hospitals, $k = 1, 2, \dots, K$, geographically located in the area that are designated to host and treat the infected people. A critical medicine is used on a daily basis in these hospitals as the main treatment for this disease. This medicine can be obtained from any and all of the plants, which produce and ship the ordered quantity to each of the distribution centers upon receiving an order. The distribution centers will hold an inventory of the medicine and distribute it to the local hospitals based on their demand, and will order from the plants a certain amount to refill their inventory from time to time so that they maintain an adequate supply for the need of the local hospitals. Theoretically, every distribution center can send the medicine to any hospital upon request regardless whether the hospital is in the same district or not, but the shipping cost varies with the location of the hospitals.

Assume that the local government or an agent designated by the government will take the role of centralized decision making and control of the relevant resources in a burst of epidemic spread. The objective of the decision making is to minimize the total operation and logistics cost in terms of medicine supply and distribution and the allocation of available hospital beds. In what follows, we will describe the logistics part of our model in the tier of local hospitals, the tier of district distribution centers, and the tier of pharmaceutical plants, as well as the decision variables, parameters, and pertinent costs in each tier.

(1) Logistics part of hospital tier

Assume that prior to the epidemic burst the government has made a contingency plan that describes which local hospitals may be designated for hosting infected patients in case of any possible epidemic spread, and their designated capacity in terms of the number of beds for the allocation and medical treatment of infected patients. Usually this means a certain section of the hospital but not the entire hospital is dedicated to the epidemic use, and this should be understood in our model when we refer to the number of available beds in a designated hospital. Also, a designated hospital can but not must be used at a certain time or in any time at all during the course of epidemic spread and control, and when it is not in operation for this exclusive use, it will be open to the general public. Thereafter a designated hospital is said to be in operation at a certain time when it is used for epidemic treatment in that time. Thus, for any designated hospital k , we can define a 0–1 variable $\alpha_k(t)$, $\forall t = 1, 2, \dots, T$.

$$\alpha_k(t) \begin{cases} = 1, & \text{if hospital } k \text{ is in epidemic operation on time } t \\ = 0, & \text{otherwise} \end{cases} .$$

We define $x_k(t)$ to be the number of beds assigned for epidemic patients in hospital k at time t , which must be under the designated capacity X_k , i.e.,

$$x_k(t) \leq X_k, \quad \forall k = 1, 2, \dots, K, \quad t = 1, 2, \dots, T. \quad (8.8)$$

Since no bed can be used to host any epidemic patient in a designated hospital unless it is chosen to operate for that day, one has the following relationship

$$x_k(t) \leq \alpha_k(t)X_k. \quad (8.9)$$

Various costs could occur at a designated hospital during the course of the epidemic control and treatment. First, there will be a fixed cost h_{1k} that may account for administrative manpower overhead, utilities, and other resources allocated. The resources include patient rooms and facilities allocated exclusively for treating the epidemic patients and thus not available for any other use. Such cost does not change daily during the time when the hospital is in operation of epidemic treatment. Secondly, there is a variable cost that is represented by doctor-hours, nurse-hours, medicine cost (including medicine expense and medicine inventory cost) meals etc., which is in proportion to the number of patients hospitalized. Let h_{2k} indicate the rate of the variable cost in hospital k during epidemic operation, then the variable cost for day t is $h_{2k}x_k(t)$. Thirdly, when a designated hospital is opened for treating epidemic patients, there is a switch-on cost, including such costs for storing up needed medicines, preparing of equipment, separating the ward, etc. Likewise, when a hospital from operational in one period changes to non-operational in the following period, there will be a switch-off cost related to such processes as sterilization. Denote h_{3k} the switch-on cost and h_{4k} the switch-off cost for hospital k . We define another set of auxiliary 0–1 variables $\phi_k^{01}(t)$, $\phi_k^{10}(t)$, $\forall t = 1, 2, \dots, T$.

$$\begin{cases} \phi_k^{01}(t) = 1, & \text{if hospital } k \text{ is non-operational on day } t-1 \text{ and operational on day } t; \\ \phi_k^{01}(t) = 0, & \text{otherwise} \end{cases};$$

$$\begin{cases} \phi_k^{10}(t) = 1, & \text{if hospital } k \text{ is operational on day } t-1 \text{ and non-operational on day } t; \\ \phi_k^{10}(t) = 0, & \text{otherwise} \end{cases};$$

The following relationships between the 0–1 variables $\alpha_k(t)$, $\forall t = 1, 2, \dots, T$ and the auxiliary 0–1 variables $\phi_k^{01}(t)$, $\phi_k^{10}(t)$, $\forall t = 1, 2, \dots, T$ must hold in accordance with the definitions:

$$\phi_k^{01}(t) \leq \alpha_k(t); \quad \phi_k^{01}(t) \leq 1 - \alpha_k(t-1); \quad \phi_k^{01}(t) \geq \alpha_k(t) - \alpha_k(t-1); \quad (8.10)$$

$$\phi_k^{10}(t) \leq \alpha_k(t-1); \quad \phi_k^{10}(t) \leq 1 - \alpha_k(t); \quad \phi_k^{10}(t) \geq \alpha_k(t-1) - \alpha_k(t); \quad (8.11)$$

As a matter of fact, the values of the 0–1 variables $\alpha_k(t-1)$ and $\alpha_k(t)$ together will uniquely determine the values of $\phi_k^{01}(t)$, $\phi_k^{10}(t)$ by the inequalities of Eqs. (8.10) and (8.11), and thus introducing the auxiliary variables $\phi_k^{01}(t)$, $\phi_k^{10}(t)$ does not

actually increasing the computational complexity of our model. The aggregated cost at hospital k on day t , $h_k(t)$, is given by

$$h_k(t) = h_{2k}x_k(t) + h_{1k}\alpha_k(t) + \phi_k^{01}(t)h_{3k} + \phi_k^{10}(t)h_{4k},$$

$$\forall t = 1, \dots, T, k = 1, \dots, K. \quad (8.12)$$

Inventory cost at the hospital level is not explicitly addressed in our model but reflected as a part of the variable cost h_{2k} . The foremost reason is that, although there is inventory cost for carrying the medicine at the hospital level, there is no separate decision making at this level. The hospitals are not allowed to carry excessive inventory during this special time because the medicine resource is critically important and tightly controlled to prevent spoilage and waste. Holding an excessive amount of medicine at one hospital may cause shortage at another hospital, which is detrimental to the overall effort in treating the patients and controlling the epidemic. On the other hand, no hospital wants to run any risk of medicine supply shortage in exchange of carrying cost advantage. This assumption is made in contrast to most inventory models dealing with consumer commodities. In practice, hospitals are supplied a just-right amount of medicine according to the number of their inpatients for their usage in a very short period of time (one to three days). Our model includes the medicine inventory cost in the variable cost, which is in proportion to the number of the inpatients, but does not model the ordering point and/or ordering quantity as decision variables. Secondly, the time t in our model, although referred to a day in a modeling term, can actually be two or three days in application as a decision time within which some inventory holding cost is insignificant but the guarantee of supply is paramount.

(2) Logistics part of distribution center tier

The district distribution centers (DCs) are used to store the medicine and distribute them to the local hospitals based on their demand. Theoretically, we assume any distribution center can send the needed amount of medicine to any hospital on any day. Let $y_k^j(t)$ be the amount of medicine shipped from distribution center j to hospital k on day t , $v_j(t)$ be the inventory of distribution center j on day t , V_j be the storage capacity at DC j and v_j^s be the safety stock at DC j . Then, DC j must satisfy the upper bound and the lower bound on each day, i.e.,

$$v_j^s \leq v_j(t) \leq V_j, \quad \forall t = 1, \dots, T, j = 1, \dots, J. \quad (8.13)$$

Suppose that each distribution center has a fixed order size and it can order from any of the medicine suppliers. Let v_j^0 be the order size of DC j and let L^i be the lead time of pharmaceutical plant i , and define the 0–1 variable:

$$\varepsilon_j^i(t) \begin{cases} = 1, & \text{if DC } j \text{ orders from supplier } i \text{ on day } t \\ = 0, & \text{otherwise} \end{cases},$$

then the orders received by DC j on day t is $\sum_{i=1}^I \varepsilon_j^i(t - L^i)^+ v_j^0$ and it should hold the following relationship between the ending inventories of two consecutive days at DC j :

$$v_j(t + 1) = v_j(t) - \sum_{k=1}^K y_k^j(t) + \sum_{i=1}^I \varepsilon_j^i(t - L^i)^+ v_j^0, \\ \forall t = 1, \dots, T, \quad j = 1, \dots, J. \quad (8.14)$$

Suppose that the inventory carrying cost rate (per day) is g_{2j} and the ordering cost is g_{1j} at DC j . Then the total daily operation cost incurred at DC j is:

$$g_j(t) = g_{2j}v_j(t) + g_{1j} \sum_{i=1}^I \varepsilon_j^i(t), \quad \forall t = 1, \dots, T. \quad (8.15)$$

Meanwhile, we can relate the number of patients in hospital k on day t , $x_k(t)$, with the medicine supplies that are distributed from the DCs to the hospital on day t , $y_k^j(t)$, which are given as below:

$$mx_k(t) = \sum_{j=1}^J y_k^j(t), \quad (8.16)$$

where m is the average daily dose for a patient across the area in this epidemic spread.

(3) Logistics part of supplier tier

We now consider the pharmaceutical plants at the top tier of this medical supply chain network. Since the plants are not necessarily located in the area and they need a production plan to acquire the raw materials and reset the facilities to make this medicine, we suppose each pharmaceutical plant has an independent and possibly different lead time for the order of the distribution centers, namely L^i , $\forall i = 1, \dots, I$. Also, each supplier has a production capacity, D_i , $\forall i = 1, \dots, I$. The operation cost for supplier i , $\forall i = 1, \dots, I$, is comprised of two parts, as in most manufacturing firms, a constant fixed cost f_{1i} that is incurred whenever the production of this medicine takes place and is regardless of the output level, and a variable cost that is in proportion to the production output, with the unit cost being denoted by f_{2i} . The aggregated order that supplier i receives on day t is:

$$d_i(t) = \sum_{j=1}^J \varepsilon_j^i(t) v_j^0, \quad (8.17)$$

which forms the dynamic demand for its production plan. We can get the following constraint pertaining to production capacity and the aggregated orders:

$$d_i(t) = \sum_{j=1}^J \varepsilon_j^i(t) v_j^0 \leq D_i. \quad (8.18)$$

The production cost for supplier i , $\forall i = 1, \dots, I$ can be formulated as:

$$f_i(t) = f_{1i} \omega_i(t) + f_{2i} d_i(t), \quad \forall t = 1, \dots, T. \quad (8.19)$$

where $\omega_i(t)$ is a 0–1 variable for plant i pertaining to its operation schedule on day t and is defined as:

$$\omega_i(t) \begin{cases} = 1, & \text{if supplier } i \text{ runs its operation on time } t \\ = 0, & \text{otherwise} \end{cases}.$$

Since any order from a distribution center will trigger the production operation of the plant who receives the order, the following relationship between the 0–1 variables of DC order schedule and the supplier operation schedule must be satisfied:

$$\varepsilon_j^i(t) \leq \omega_i(t), \quad \forall j = 1, \dots, J, \quad i = 1, \dots, I. \quad (8.20)$$

Namely, $\omega_i(t)$ cannot be zero unless all $\varepsilon_j^i(t)$'s are zero. On the other hand, since the production cost Eq. (8.19) is eventually to be minimized, $\omega_i(t)$ will be zero in the optimal solution if all $\varepsilon_j^i(t)$'s are zero, although not directly implied by Eq. (8.20). Note that Eqs. (8.19) and (8.20) imply a pull system in which the production system will be turned on by any order received from a distribution center, which is not unreasonable in an urgent rescue campaign such as an epidemic spread. One sees that in Eq. (8.19), $f_i(t)$ is zero if and only if all $\varepsilon_j^i(t)$, $\forall j = 1, \dots, J$ are zero, i.e., no order is received on day t , and that even a small size ordered by one DC will trigger the production system to bear the fixed cost. Such a system may result in a higher supplier cost. However, the problem is modeled as a centralized control system to minimize the overall social cost, and therefore, all the costs regardless at which tier they occur are equally accounted for in the minimization. Consequently, the 0–1 decision variables, $\varepsilon_j^i(t)$, $\forall j = 1, \dots, J$, defined for the distribution centers tier will eventually take into account of the production cost minimization too. That is, the central agent shall consider coordinating the ordering times of various distribution centers so that they will pool together a larger size of aggregated orders to trigger the production system of a supplier. This can be observed in the numerical example.

(4) Transportation costs and objective function

We now turn to look at the shipments both between the supplier tier and the DC tier, and between the DC tier and the location hospital tier. By the definition of $\varepsilon_j^i(t)$ and the lead time L^i , the shipment from supplier i to arrive at DC j on day t is:

$$z_j^i(t) = \varepsilon_j^i(t - L^i)^+ v_j^0, \quad (8.21)$$

which is zero if DC j didn't place an order on day $t - L^j$. Let our model employ a general function for the transportation cost so that it can take a special form in a particular application. Note that a line haul cost is the major part of this transportation cost because the suppliers in our model may be located outside of the area and thus geographically far away from the distribution centers that are within the epidemic spread area. Therefore, some types of consolidation in truck load can take effect in reducing the transportation cost. For instance, shipments from the same supplier to several DC's in the area can be consolidated in transportation and result in significant saving, or two close-by suppliers can also consolidate their shipments. Let $u^i(t)$ denote the general transportation cost for supplier i on day t , which is a general function of $z^i(t) = (z_1^i(t), \dots, z_J^i(t)) \in R_+^J$, namely

$$u^i(t) = u^i(z^i(t)). \quad (8.22)$$

Likewise, let $w^j(t)$ denote the general transportation cost for DC j on day t , which is a function of $y^j(t) = (y_1^j(t), \dots, y_K^j(t)) \in R_+^K$, namely

$$w^j(t) = w^j(y^j(t)). \quad (8.23)$$

The system optimization problem is to minimize the total cost of operations occurring at the tier of local hospitals, district distribution centers, the pharmaceutical plants as well as the transportation costs for shipping the medicine from the suppliers to the distribution centers and shipping the medicine from the distribution centers to the local hospitals. Let Π denote the total cost, i.e.,

$$\Pi(x, y, \alpha, \varepsilon, \omega) = \sum_{t=1}^T \left(\sum_{k=1}^K h_k(t) + \sum_{j=1}^J (g_j(t) + w^j(t)) + \sum_{i=1}^I (f_i(t) + u^i(t)) \right). \quad (8.24)$$

Given the forecasted number of infected people in the next cycle $I(t)$, $t = 1, \dots, T$ provided by the forecast phase of the model, we can now define a feasible region:

$$\Omega = \left\{ (x, y, \alpha, \varepsilon, \omega) : \sum_{k=1}^K x_k(t) = I(t), \right. \\ \left. \text{and (9-11), (13-14), (16-18), (20-21) hold} \right\} \quad (8.25)$$

Then, the optimal planning for hospital resource allocation, medicine distribution and transport for the next cycle can be obtained by solving the following optimization problem:

$$\text{Min}_{(x, y, \delta, \varepsilon, \omega) \in \Omega} \Pi(x, y, \alpha, \varepsilon, \omega). \quad (8.26)$$

Since all the constraints in this optimization problem are linear, and the cost functions defined in the model are linear, so the system minimization problem (8.26) is a mixed 0–1 linear integer programming problem. Such a problem can be solved by some available optimization software such as CPLEX for an optimal solution.

8.2.3 Execution Phase

This phase is an exogenous part of the model that will implement the developed plan in practice to allocate the hospital resources and medicine distribution. In terms of hospital resources, even though our optimization problem (8.26) explicitly addresses only the number of beds in each hospital in operation, other critical resources such as patient rooms, examination facility hours, doctor-hours, nurse-hours, clinic material items, meals etc., must all be included in the allocation planning, which mostly can be determined by the number of patients hospitalized. During the execution of the plan, the actual number of infected individuals, recovered individuals, and deaths, will be collected, recorded and analyzed. These numbers may not be equal to the forecasted numbers in practice. Therefore, some adjustments must be made in reality during the execution of the plan. What actual measures are to be taken for the adjustment and how they are implemented go beyond of our research scope. Another part of the exogenous decision making involves with the initial inventory stocking policy at each DC for each decision cycle. We leave this part to the role of a central coordinator (local government or its designated agent) outside of our model for the sake of application flexibility. A common practice is to fill up the stock to a certain capacity at the beginning of each cycle in order to prevent any possible stock-out during the lead time when a new decision cycle begins. We call this preventive stocking policy between cycles.

8.2.4 Loop Closed

To close the loop in phase four of our FPEA model, we will adjust the parameters of the forecast model in reflection of the most recent data that are collected during the execution of the current cycle regarding the population size of susceptible, exposed, infected and recovered people. There are four parameters in the SEIR model. λ is the entry and exit rate of the population, which may vary slightly over time. For the individuals who enter $S(t)$ at rate λN and exit at rate $\lambda(S(t) + E(t) + I(t) + R(t))$, one sees that the total number of the compartment population is a constant. β is the propagation coefficient of the epidemic, which is determined by medical studies especially for a known epidemic type but can vary slightly over time accounting for the climate change and other factors. γ is the transmission rate between the exposed subpopulation and the infected subpopulation. It may vary slightly from case to case even for a same epidemic type and is thus subject to update in our

model. Finally δ is the rate of infected individuals who will recover. This parameter will evolve in the course of the control and the treatment of the epidemic disease over time when more cases are treated and experience is learned, as the hospitals cumulating more observation and knowledge of the recovery pattern in an individual case. To summarize, we will adjust the parameters $\beta, \gamma, \delta, \lambda$ in each cycle to update our forecasting model in reflection of the most recently observed data so that we can have the “best” forecast for the next cycle. The constraints of the optimization sub-problem require $\beta, \gamma, \delta, \lambda$ (regarded now as the variables) to generate perfect forecast for the last day when evaluated at the observed data, i.e.,

$$\begin{cases} S(T) - [S(T-1) + \lambda N - \beta S(T-1)I(T-1) - \lambda S(T-1)] = 0 \\ E(T) - [E(T-1) + \beta S(T-1)I(T-1) - \gamma E(T-1) - \lambda E(T-1)] = 0 \\ I(T) - [I(T-1) + \gamma E(T-1) - (\lambda + \delta)I(T-1)] = 0 \\ R(T) - [R(T-1) + \delta I(T-1) - \lambda R(T-1)] = 0 \end{cases} \quad (8.27)$$

Note that Eq. (8.27) is a system of linear equations for $\beta, \gamma, \delta, \lambda$ where all $S(T), E(T), I(T), R(T), S(T-1), E(T-1), I(T-1), R(T-1)$ are observed data. In light of Eqs. (8.3)–(8.7), the constraints (8.27) can be also be expressed by

$$\begin{cases} S(T) - \hat{S}(T-1)(\beta, \lambda) = 0 \\ E(T) - \hat{E}(T-1)(\beta, \gamma, \lambda) = 0 \\ I(T) - \hat{I}(T-1)(\gamma, \lambda, \delta) = 0 \\ R(T) - \hat{R}(T-1)(\delta, \lambda) = 0 \end{cases} \quad (8.28)$$

The objective function of the optimization sub-problem is to minimize the weighted forecast errors for all the days in the current cycle except the last day, which has zero forecast error ensured by the constraints already, with a higher weight assigned to a more recent day. That is, we want to find the $\beta, \gamma, \delta, \lambda$ satisfying constraints (8.28) and minimize

$$\begin{aligned} \min \sum_{t=1}^{T-1} w_t \{ & [S(T-t) - \hat{S}(T-t-1)(\beta, \lambda)]^2 + [E(T-t) - \hat{E}(T-t-1)(\beta, \gamma, \lambda)]^2 \\ & + [I(T-t) - \hat{I}(T-t-1)(\gamma, \lambda, \delta)]^2 + [R(T-t) - \hat{R}(T-t-1)(\delta, \lambda)]^2 \}. \end{aligned} \quad (8.29)$$

Herein, $w_t, t = 1, \dots, T-1$ are the weight coefficients satisfying

$$\sum_{t=1}^{T-1} w_t = 1, \quad 0 < w_{T-1} < \dots < w_1. \quad (8.30)$$

Sub-problem (8.28) and (8.29) are designed to be solved for the best parameters β , γ , δ , λ so that they reflect the observed data collected in the current cycle in order to generate accurate forecast for the next cycle. The objective function is in spirit of a weighted moving average method, a widely used forecasting method in reflection of a fundamental forecast principle that the more recent data are more reliable (cf. [23]). Note that the rank of the coefficient matrix is equal to the rank of the augmented matrix, and it is smaller than the number of variables ($r_A = r_{(A|B)} = 3 < 4$) in the system of linear equations (8.28), therefore the existence of solutions for the system of linear equations (8.28) can be ensured. The special structure (8.28) will yield a feasible region, the set of the feasible solutions for the optimization sub-problem. By solving the quadratic programming problem (8.28)–(8.29), we can find the optimal β^* , γ^* , δ^* , λ^* for the next decision cycle. The loop is closed in our mathematical model.

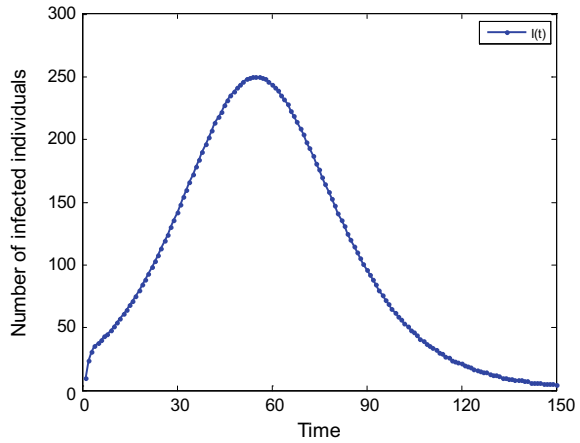
8.3 Numerical Example

In this section, we will present a numerical example to show the applicability of the model and to demonstrate the performance and computational results of the proposed FPEA method. The numerical example is constructed upon a hypothetical case of an epidemic diffusion, and for this illustrative purpose, the number of infected people over time is generated by a simulation of SEIR model. Such an approach is taken by other researchers in studying and testing their relevant models when no actual data is available (see, e.g., [20, 24–26]). This is particularly necessary for the adjustment phase in our model, which requires real time information about the number of infected people by the end of each decision cycle to adjust the parameters. The computation of this numerical example is conducted on a personal computer equipped with an Intel (R) Core (TM) 3.10 GHz CPU and 4.0 Gb of RAM in the environment of Microsoft Windows 7. The proposed FPEA model involves with a mixed 0–1 integer programming problem and a quadratic programming problem, both can be solved within a reasonable time, by using the MATLAB compiler coupled with commercial software CPLEX 12.4.

8.3.1 Test for Forecasting Phase

In line with Arenas et al. [27] and Rachaniotis et al. [20], the initial value of the parameters in the SEIR model are chosen as: $S(0) = 9955$, $E(0) = 40$, $I(0) = 5$, $R(0) = 0$, $N = 10,000$, $\beta = 4 \times 10^{-5}$, $\gamma = 0.6$, $\delta = 0.3$, and $\lambda = 1 \times 10^{-3}$. Figure 8.2 shows the number of infected people over time generated by the difference equations (8.7) in Sect. 2.1 (the forecasting phase). Initially, the number of infected individuals grows exponentially, reaching the maximum 250. However, there is a turning point when more infected individuals depart the infected compartment than

Fig. 8.2 Number of infected individuals over time



enter it. The epidemic ends when the number of infected individuals drops to 0, which often happens before all susceptible individuals in the populations are infected. The entire course has 150 days and is divided into 5 closed loop decision cycles of 30 days each cycle.

8.3.2 Test for Logistic Planning Phase

(1) Parameters setting

Supposing that in a hypothetical influenza outbreaks area, there are 3 pharmaceutical plants (S) which supply a critical medicine for the epidemic, 4 distribution centers (DC) that store and distribute the medicine, and 8 local hospitals (H) that are designated to host and treat the infected individuals. Assume that all the transportation costs from the pharmaceutical plants to the DCs and from the DCs to the local hospitals are linear. The coefficient matrix is given by Table 8.1.

Particularly, the transportation cost for S1 on day t is a linear function of the shipment quantities from this pharmaceutical plant to the four DCs, namely

$$u^1(t) = 2 \cdot z_1^1(t) + 4 \cdot z_2^1(t) + 6 \cdot z_3^1(t) + 8 \cdot z_4^1(t).$$

Table 8.1 Transportation cost between different departments (dollar)

	S1	S2	S3	H1	H2	H3	H4	H5	H6	H7	H8
DC1	2	4	3	6	2	6	7	4	2	5	9
DC2	4	3	5	4	9	5	3	8	5	8	2
DC3	6	2	2	5	2	1	9	7	4	3	3
DC4	8	1	3	7	6	7	3	9	2	7	1

For instance, the operation cost for the H3 on day t , is:

$$h_3(t) = 2.7 \times x_3(t) + 33 \times \alpha_3(t) + 40 \times \phi_3^{01}(t) + 33 \times \phi_k^{10}(t), \quad \forall t = 1, \dots, T.$$

Since the number of patients that can be hosted by H3 on day cannot exceed its capacity 40 and only when it is chosen to operate on day t , the following constraint must hold

$$x_3(t) \leq \alpha_3(t) \times 40$$

Table 8.2 describes the operation cost parameters of the local hospitals.

Table 8.3 summarizes the capacity, the operation cost parameters, and initial inventory at each of the four distribution centers.

For example, the daily operation cost for the DC1 is:

$$g_1(t) = 1.4 \times v_1(t) + 6 \times \sum_{i=1}^3 \varepsilon_1^i(t), \quad \forall t = 1, \dots, T,$$

Table 8.2 Hospital parameters

Parameter value $k = 1, 2, \dots, 8$	Capacity X_k (person)	Fixed cost h_{1k} (dollar)	Variable cost h_{2k} (dollar)	Switch-on cost h_{3k} (dollar)	Switch-off cost h_{4k} (dollar)
H1	40	35	2.5	40	35
H2	45	34	2.6	45	34
H3	40	33	2.7	40	33
H4	45	32	2.8	45	32
H5	40	31	2.9	40	31
H6	35	30	3.0	35	30
H7	35	29	3.1	35	29
H8	40	28	3.2	40	28

Table 8.3 DC parameters

Parameter value $j = 1, 2, 3, 4$	Capacity V_j (dose)	Initial inventory (dose)	Ordering cost g_{1j} (dollar)	Carrying cost g_{2j} (dollar)	Order size v_j^0 (dose)	Safety stock v_j^s (dose)
DC1	120	70	6	1.4	40	10
DC2	150	70	6.5	1.3	30	10
DC3	120	80	7	1.2	40	10
DC4	150	80	7.5	1.1	30	10

where

$$v_1(1)=70 \text{ and } v_1(t+1) = v_1(t) - \sum_{k=1}^8 y_k^1(t) + \sum_{i=1}^3 \varepsilon_i^1(t - L^i)^+ \times 40, \forall t = 1, \dots, T.$$

The daily inventory in DC1 must not be less than the safety stock and must not exceed its capacity, or mathematically expressed as:

$$10 \leq v_1(t) \leq 120, \quad \forall t = 1, \dots, T.$$

Table 8.4 gives the lead time, the production capacity, the fixed cost and the variable cost for each of the three pharmaceutical plants.

For example, the production cost for S1 is:

$$f_1(t) = 120 \times \omega_1(t) + 6 \times d_1(t), \quad \forall t = 1, \dots, T,$$

where the aggregated orders $d_1(t)$ should satisfy the production capacity constraint,

$$d_1(t) = \sum_{j=1}^4 \varepsilon_j^1(t) \times v_j^0 \leq 80.$$

Since any order from a distribution center will trigger the production operation of the pharmaceutical plant S1, we have

$$\varepsilon_j^1(t) \leq \omega_1(t), \quad \forall j = 1, \dots, 4.$$

(2) Test results

The computation results are summarized in following tables and figures. Initially, Table 8.5 reports the cumulative number of the daily infected people, the maximum daily infected people, and the computation time, in each of the five cycles.

Following the preventive stocking policy between cycles as discussed in Sect. 8.2, Fig. 8.3 shows the inventory level over time in each of four DCs during the entire 150 days. They all begin with a certain stock for the lead time of the first order as required by the policy and then are maintained at the minimum level (equal to the safety stock) in most of the days in the cycle except for the necessary reorder point. We accredit this low inventory-carrying performance to the merit of the model

Table 8.4 Parameters of pharmaceutical plants

Parameter value $i = 1, 2, 3$	Lead time L^i (day)	Capacity D_i (dose)	Fixed cost f_{1i} (dollar)	Variable cost f_{2i} (dollar)
S1	1	80	120	6
S2	2	90	110	7
S3	1	100	115	6.5

Table 8.5 Computation time and daily infected people

Decision cycle	Cumulative daily infected people	Maximum daily infected people	Computation time (s)
Cycle 1	2233	142	17.0
Cycle 2	6506	250	47.5
Cycle 3	5151	241	24.1
Cycle 4	1465	91	6.9
Cycle 5	305	21	1.4

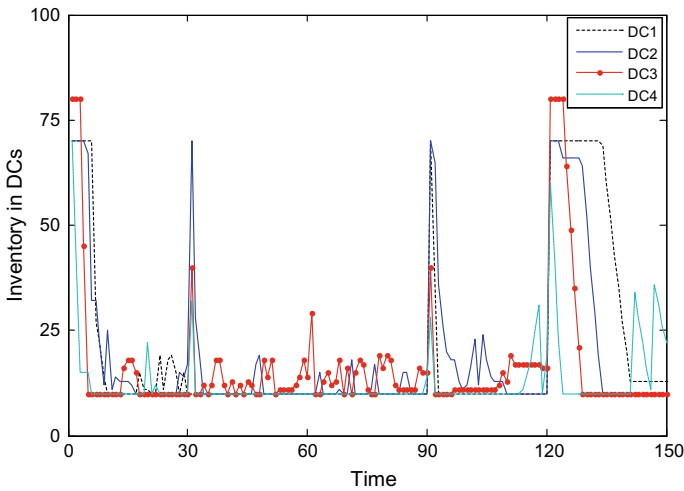


Fig. 8.3 Inventory level in the DCs

that minimizes the inventory ordering and carrying cost while meeting the hospitals’ need.

Namely, in the first place, the DCs are deposited a certain level of initial inventory, for ensuring supply to the hospitals during the lead time of their first order. In the second place, they are operated to minimize the total logistics cost, therefore the inventory level in the DCs should be as low as possible while coordinated with the medicine order planning and the medicine distribution scheduling. The trajectory in Fig. 8.3 illustrates an almost just-in-time mechanism in the medicine supply chain of our model.

Figure 8.4 exhibits the daily production level of the three pharmaceutical plants over time in the solution of our model. It can be seen that the production patterns of all the suppliers are similar where the output levels are high in the second and third cycle, but low in the first, fourth and fifth cycle. This is well expected because in the first cycle when the epidemic just bursts, the infected population size is small and the need for medicine is relatively low. In the second and third cycle when the

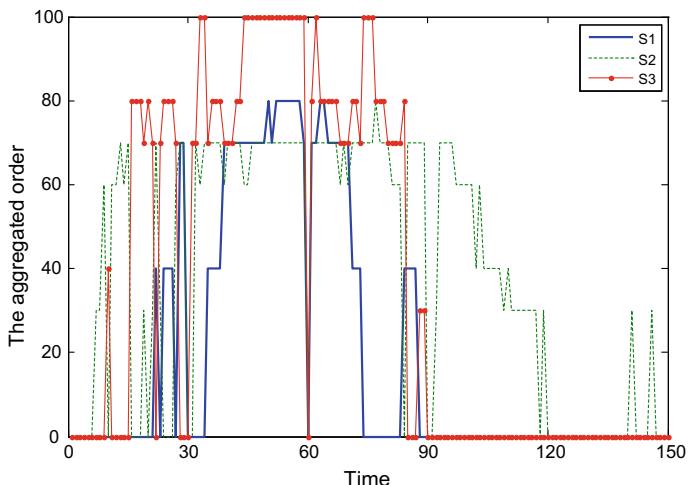


Fig. 8.4 Production level in the pharmaceutical plants (S)

epidemic diffusion is at its maximum scale, the number of infected people reaches the peak and the demand for the medicine is at the highest level, thus so would be the production level. In the fourth and fifty cycle, when the epidemic diffusion is brought under control and the infected population diminishes, the medicine demand decreases and the production slows down.

The solution of our model provides a dynamic assignment of patients at each hospital over the entire 150 days in this numerical example. As a snapshot, Fig. 8.5 shows the number of patients assigned to each hospital on the 36th day. On this particular day, Hospital 2, 3, 6 and 8 are operated at capacity, Hospital 4 is used to treat the infected on that day but is not filled up, while Hospital 1, 5 and 7 are not in

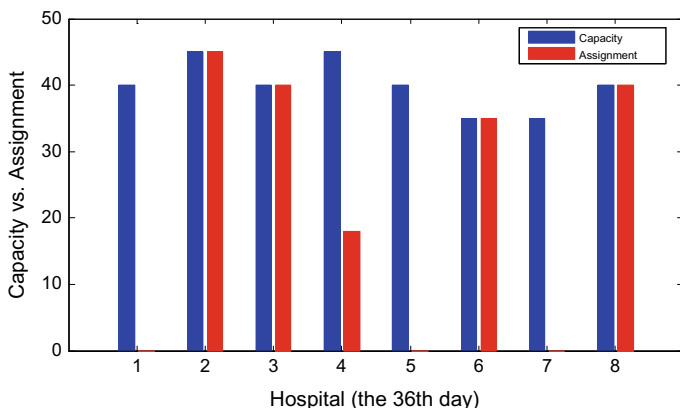


Fig. 8.5 Hospital assignment on 36th day

operation. Considering the cost structure of the hospitals, such assignment explains for avoiding as much as possible the fixed cost, the turning on and turning off costs in the optimal solution. It makes a common sense that it is not desired to have more than one hospital operated under capacity in such a cost structure.

8.3.3 Test for Adjustment Phase

Epidemiological models are only as good as their parameter values. Therefore, an accurate forecasting and understanding of influenza dynamics mainly depend on finding and using the realistic epidemiological parameters in the forecasting equations [28]. As a hypothetical case, we adopt the mature Runge-Kutta method, which has been widely used in simulating the evolution trajectories of $S(t)$, $E(t)$, $I(t)$ and $R(t)$ (see, e.g., [26, 29, 30]), to simulate the epidemic diffusion and generate the assumed actual number of infected people over time. In the adjustment phase, we solve a quadratic programming problem for the best parameters β^* , γ^* , δ^* , λ^* to fit in the assumed actual data and use them for forecasting the infected number in the next cycle.

Table 8.6 shows the number of infected people by the end of each cycle respectively of the assumed actual data (AA in the 2nd column), by difference Eq. (8.7) without adjustment of the parameters (WO in the 3rd column), and by our FPEA model (WA in the 5th column). The deviation of WO from AA in percentage is reported in the 4th column and the deviation of WA from AA in percentage is reported in the 6th column. It is apparent that our FPEA model with periodically adjusted parameters matches much better to the assumed actual data than that of the difference Eq. (8.7) without adjustment of the parameters.

In turn, Fig. 8.6 shows the absolute deviation of FPEA forecasted number of the infected people off the assumed actual data, compared with the absolute deviation of the difference Eq. (8.7) with original parameters (i.e., without adjustment) off the assumed actual data, in the entire course of 150 days. It is not surprising that the forecast with adjustment is much closer to the assumed actual data and serves for the purpose of adjustment phase to be implemented in our FPEA model. In practice,

Table 8.6 Numerical comparison by using different methods

Time	Assumed actual (AA)	Without adjustment (WO)	WO versus AA (%)	With adjustment (WA)	WA versus AA (%)
30th day	142	138	-2.8	141	-0.7
60th day	244	250	2.4	243	-0.4
90th day	96	98	2.1	96	0.0
120th day	21	20	-4.7	20	-4.7
150th day	4	4	0.0	4	0.0

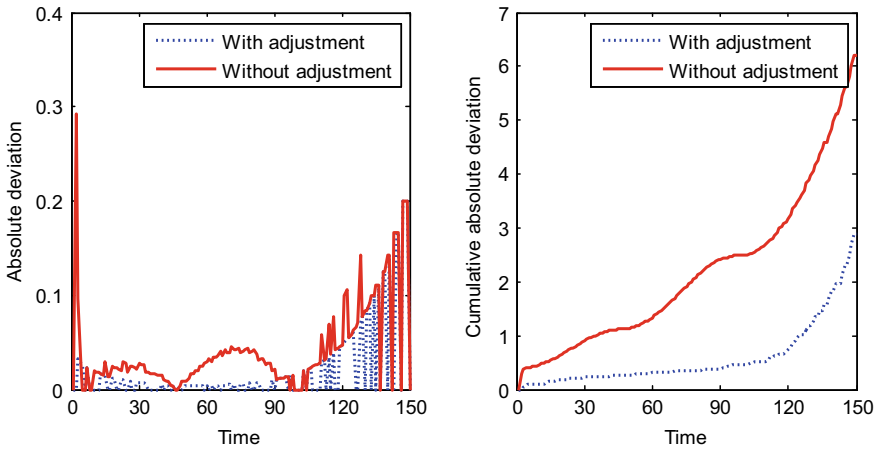


Fig. 8.6 Comparison of the simulated results

this adjustment can help us to track the disease spread in a real world case and to provide a more accurate forecast of the number of infected people.

8.4 Conclusions

In this chapter, a FPEA model is presented to study the dynamic allocation of medical resources in the control of an epidemic diffusion. The model is constructed as a closed loop consisting of a forecast phase, a planning phase, an execution phase and an adjusted forecast phase, as it proceeds to control the epidemic spread and to plan for medical resources allocation. The novelties of our model against the existing works are characterized by the following aspects.

Firstly, while most research on medical resources allocation studies a static problem taking no consideration of the time evolution and especially the dynamic demand for such resources, the proposed FPEA model integrates a forecast of a time-series demand, in match of the course of an epidemic diffusion, with a dynamic logistics planning for ordering, shipping, and allocating the needed resources.

In the second place, the forecasting mechanism is designed to simulate the epidemic diffusion dynamics, as a time-discretized version of the widely accepted SEIR model, which provides a more suitable prediction of the demand for the resources, and serves for a proactive purpose for the logistics planning.

Thirdly, the dynamic logistics planning for resources allocation and distribution in response to the forecast is constructed as a 0–1 mixed linear integer programming model, which characterizes the decision making at the local hospitals, the area distribution centers and the medicine suppliers. The optimal solution can minimize the total operation cost of the whole medicine supply chain.

In addition, to close the loop of our FPEA model and minimize the forecast error, the parameters of the forecasting model are adjusted periodically, by solving a quadratic programming sub-problem, which can reflect the most recent data that are collected during the execution of the current cycle.

Last but not least, the computation results of a numerical example show that the proposed model can be well applied to a real world problem of epidemic control for a centralized system, with detailed operational implications for suppliers' production planning, distribution centers' distribution and transportation, and hospital beds allocation.

As for the limitation of the model, it has yet to consider possible cross area diffusion between two or more geographic areas. Future studies may also address other realistic concerns such as stock-out of the critical medicine and different exit rates of the population groups.

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Chapter 9

Integrated Planning for Public Health Emergencies: A Modified Model for Controlling H1N1 Pandemic



Infectious disease outbreaks have occurred many times in the past decades and are more likely to occur in the future. Recently, Büyüктаhtakın et al. [1] proposed a new epidemics-logistics model to control the 2014 Ebola outbreak in West Africa. Considering that different diseases have dissimilar diffusion dynamics and can cause different public health emergencies, we modify the proposed model by changing capacity constraint, and then apply it to control the 2009 H1N1 outbreak in China. We formulate the problem to be a mixed-integer non-linear programming model (MINLP) and simultaneously determine when to open the new isolated wards and when to close the unused isolated wards. The test results reveal that our model could provide effective suggestions for controlling the H1N1 outbreak, including the appropriate capacity setting and the minimum budget required with different intervention start times.

9.1 Introduction

Infectious disease outbreaks have unfortunately been very real threats to the general population and economic development in the past decades, whether they are caused by nature or bioterrorism. A typical example was the H1N1 outbreak in 2009, which spread quickly around the world and ultimately affected millions of people in 214 countries, including 128,033 confirmed cases in China [2]. In 2010, more than 600,000 infected cases were reported and 8000 lives were lost because of the cholera outbreak in Haiti [3]. A recent example of epidemic outbreak was the 2014–2015 Ebola pandemic in West Africa, which infected approximately 28,610 individuals and approximately 11,300 lives were lost in Guinea, Liberia, and Sierra Leone [4]. Therefore, it can be observed that the global burden of epidemics has tremendously increased in recent years.

To our knowledge, many countries have drafted emergency response plans and operational frameworks for immediately implementing the related strategies within 24 h after the severity of an unexpected pandemic is confirmed [5]. In China, a

certain amount of emergency budget will be allocated for quick response according to the severity level of the unexpected epidemic. Emergency medical center (EMC) will designate several local hospitals to treat the infected individuals. Usually, this means a certain section of the appointed hospital will be isolated for quarantining and treating the infectious patients, but not the entire hospital.

Determining the optimal budget allocation to control an unexpected epidemic is a complex optimization problem. On the one hand, managers should understand how the disease propagates and how to model the epidemic dynamics [6]. Conventionally, epidemiology researchers use compartmental models to depict the dynamics of epidemic due to its ease of modeling and short computation time. However, they cannot capture spatial and social heterogeneities and lack the ability to adapt to government interventions. On the other hand, we need to know how to bridge the gap between epidemic dynamics and budget allocation. An integrated model for epidemic control should foresee the impacts of different resource-allocation scenarios on epidemic development, simultaneously and interactively.

The model framework in this study is inspired by Büyüktaktın et al. [1], which proposed a new mixed-integer programming (MIP) model to determine the optimal amount, timing and location of resources for controlling the Ebola outbreak in West Africa. Since different infectious diseases have dissimilar epidemic dynamics and can cause different degrees of public health emergencies, we modify the epidemic-logistics model by changing the capacity constraint, and then we apply the modified model to control the H1N1 outbreak in China. More precisely, we consider: (1) How to allocate the limited emergency budget to the affected areas? (2) What is the impact on epidemic dynamics with different budget scale? (3) What is the amount of capacity established at each period? (4) What is the amount of capacity reduced at each period? (5) How does the intervention starting time impact the budget allocation? The problems (1), (2), (3) and (5) have been conducted in Büyüktaktın et al. [1], while the problem (4) is new incorporated. Therefore, the modified model can simultaneously determine when to open the new isolated wards and when to close the unused isolated wards.

9.2 Literature Review

Although several studies try to combine medical response with emergency logistics [7], only a few studies exist on emergency medical logistics for epidemic control, despite its importance and particularity. The main body of this literature could be classified into the following two main streams.

The first stream consists of disease transmission modeling approaches that are utilized for depicting epidemic dynamics and assessing the possible effects of control interventions. Previous research includes a great number of analytical works on epidemic diffusion [8–11]. In these models, the total population was divided into several classes (susceptible, exposed, infected, treated, deceased, recovered, etc.) and each class of people was placed in an enclosed compartment. For example, Tan

et al. [12] used H1N1 epidemic data of Guangdong Province, China, in conjunction with a susceptible-exposed-infectious-recovered model (SEIR) to estimate the basic reproduction number of the epidemic. Saito et al. [13] proposed an extended SEIR model to describe the immigration of infected people and validated it with the 2009 H1N1 pandemic in Japan. Samsuzzoha et al. [14, 15] proposed a vaccinated diffusive compartmental epidemic model (SVEIR) to describe the transmission of influenza. The ordinary differential equations were solved numerically by the splitting method under different initial distributions of population density. González-Parra et al. [16] proposed a nonlinear fractional order model to explain and understand the H1N1 outbreak based on the classical SEIR model. Note that the articles from this stream incorporate novel features of biological interest, and most of them have been published in epidemiologic/medical scientific journals. These mathematical models can not only be used to depict the dynamics of different epidemics, but also be used to facilitate demand forecasting for public health emergencies [17].

The second stream of relevant researches focused on medical resource allocation for emergency response in the wake of a terrorist attack or in the case of a natural epidemic outbreak. For example, bioterror response logistics, a special case in emergency medical logistics, was frequently discussed at the beginning of this century [18–21]. Meanwhile, Zaric and Brandeau studied resource allocation problems in an effort to control infectious diseases in multiple independent populations by using the cost-effectiveness analysis method [22–24]. In recent years, this topic has attracted more and more attention. The approaches involve compartmental model-based simulation [25, 26], network model [27, 28], simulation optimization [29, 30], and mathematical programming [31, 32]. By using different approaches, scholars have evaluated the performance of different control measures for different infectious diseases. A number of surveys regarding operations research and management science contributions to epidemic and disaster control can be found in Dasaklis et al. [33] and Dimitrov and Meyers [34].

In particular, several extremely relevant papers that study the integration of epidemic control and logistics planning are summarized as follows. Rachaniotis et al. [35] proposed a deterministic resource scheduling model in H1N1 control. The problem of scheduling limited available resource for several areas was presented. A case where a large-scale smallpox attack was considered in Dasaklis et al. [36]. A linear programming (LP) model for optimally distributing a predetermined vaccine stockpile to several affected subpopulations was presented. Furthermore, given the available number of mobile medical teams, Rachaniotis et al. [37] proposed an integer programming (IP) model to minimize the total number of new infections. Ekici et al. [38] developed a disease spread model to estimate the spread pattern of the disease, and combined it with a facility location and resource allocation network model for food distribution. Chen et al. [39] proposed a model which linked the disease progression, the related medical intervention actions and the logistics deployment together to help crisis managers extract crucial insights on emergency logistics management from a strategic standpoint. Ren et al. [40] presented a multi-city resource allocation model to distribute a limited amount of vaccine to minimize the total number of fatalities due to a smallpox outbreak. He and Liu [41] proposed a time-varying forecasting

model based on a modified SEIR model and used a linear programming model to facilitate distribution decision-making for quick responses to public health emergencies. Anparasan and Lejeune [42] proposed an integer linear programming model, which determined the number, size, and location of treatment facilities, deployed medical staff, located ambulances to triage points, and organized the transportation of severely ill patients to treatment facilities. In 2012, Liu and Zhao [43] integrated a SEIR epidemic model and an emergency optimization model to allocate the limited resources for an anti-bioterrorism problem. After that, Liu et al. [44] proposed a time-space network model for studying the dynamic impact of medical resource allocation in controlling the spread of an epidemic. Furthermore, Liu and Zhang [45] presented a dynamic decision-making framework, which coupled a forecasting mechanism based on the SEIR model and a logistics planning system to satisfy the forecasted demand and minimize the total operation costs. Table 9.1 shows the summary and comparison of the studies mentioned in this paragraph.

9.3 Model Formulation

9.3.1 Epidemic Compartmental Model

As shown in Fig. 9.1, we construct a compartment model for analyzing epidemic dynamics based on the 2009 H1N1 pandemic. In each affected area j , $\forall j \in J$, individuals are classified as: susceptible (S), exposed (E), infected (I), hospitalized (H), recovered (R), and asymptomatic and partially infectious (A). We call it SEIHR-A model. In this model, each compartment represents the corresponding health status of people with regard to the H1N1, while the connected arc shows epidemic transmission between two compartments. Note that deceased individuals are not considered in our model, because H1N1 has become a seasonal flu with very low mortality rates due to the advance in medical technologies.

There are several assumptions for the proposed SEIHR-A model. First, compared to the traditional bilinear transfer rates among compartments S , E and I [14], the single-linear transfer rate assumption, except the variable transfer rate from I to H , is the foundation for modeling a mixed-integer linear programming (MIP) in Büyükahtakin et al. [1]. Otherwise, we cannot alleviate the non-linearity of epidemic model and thus the integrated epidemic-logistics model is always non-linear. Second, we assume that individuals who are infected will go into a latent (exposed) stage, during which they may have a low level of infectivity (we define a reduction factor q for transmissibility of the exposed class in following paragraph). After that, some proportion of the exposed individuals go into the infected compartment and then to the recovered compartment through treatment. Meanwhile, some proportion of the latent individuals never develop symptoms and go directly from the latent class to the asymptomatic and partially infectious class and then to the recovered class [12]. Whatever, we assume that individuals in the recovered class receive lifelong

Table 9.1 Summary of the relevant studies

References	Logistics attribute			Minimize total new infections	Objective			Methodology			Solution
	Allocation	Distribution	Location		Minimize unsatisfied demand	Minimize total deaths	Minimize cost	IP	LP	MIP	
Rachamiotis et al. [35]	X			X				X			Heuristic
Rachamiotis et al. [37]	X			X				X			Heuristic
Dasaklis et al. [36]		X			X				X		Simulation
Ekcici et al. [38]			X							X	CPLEX
Chen et al. [39]		X		X					X		CPLEX
Ren et al. [40]	X						X			X	Heuristic
He and Liu [41]		X			X		X		X		MATLAB

(continued)

Table 9.1 (continued)

References	Logistics attribute			Minimize total new infections	Objective			Methodology			Solution	
	Allocation	Distribution	Location		Minimize unsatisfied demand	Minimize total deaths	Minimize cost	IP	LP	MIP		
Anparasan and Lejeune [42]	X		X	X	X			X			CPLEX	
Büyüktaktakın et al. [1]	X		X	X		X				X	CPLEX	
Liu and Zhao [43]		X					X	X			MATLAB	
Liu et al. [44]		X					X	X			CPLEX	
Liu and Zhang [45]		X	X				X			X	CPLEX	
This study	X		X		X						X	MATLAB

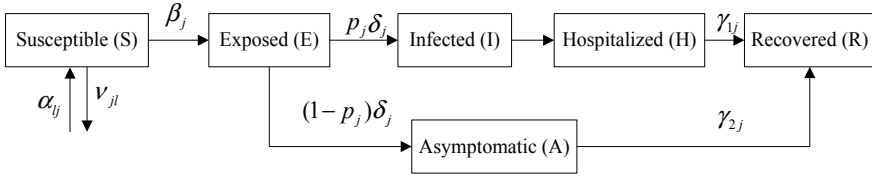


Fig. 9.1 Framework of the epidemic compartment model

immunity. Third, similar to Büyüктаhtakin et al. [1], we assume that transfer rate from compartment I to H is a variable parameter, which is determined by the available number of isolated wards. Correspondingly, infected persons who are not quarantined will continue to spread disease in the outside. Since the H1N1 outbreak only last for several months, natural birth/death rates are excluded from the epidemic model because they normally affect the dynamics of disease over several years.

To facilitate epidemic model formulation, we give the notations used as follows:

Parameters:

- T Set of time, $t = \{0, 1, 2, \dots, T\}$.
- J Set of affected areas, $j = \{1, 2, \dots, J\}$.
- L Set of all surrounding affected regions of area j , $l = \{1, 2, \dots, J\} \setminus j$.
- β_j Transmission rate of the H1N1 in area j .
- q_j Reduction factor of infectiousness for the class E_j .
- p_j Proportion of symptomatic infection in area j .
- δ_j Infected rate in area j .
- γ_{1j} Recovery rate for infectious class in area j .
- γ_{2j} Recovery rate for asymptomatic class in area j .
- α_{lj} Migration rate of susceptible individuals from surrounding areas to area j .
- v_{jl} Migration rate of susceptible individuals from area j to surrounding areas.

State variables:

- $S_j(t)$ Number of susceptible individuals in area j at time t .
- $E_j(t)$ Number of exposed individuals in area j at time t .
- $I_j(t)$ Number of infected individuals in area j at time t .
- $H_j(t)$ Number of hospitalized individuals in area j at time t .
- $R_j(t)$ Number of recovered individuals in area j at time t .
- $A_j(t)$ Number of asymptomatic individuals in area j at time t .
- $\hat{S}_j(t)$ Number of susceptible individuals migrate into area j at time t .
- $\bar{S}_j(t)$ Number of susceptible individuals travel out from area j at time t .
- $\bar{I}_j(t)$ Number of patients that can be accepted for treatment in area j at time t .

Based on the above notations, we can use the following time discretized equations to demonstrate the epidemic dynamics.

$$S_j(t+1) = S_j(t) + \widehat{S}_j(t) - \overline{S}_j(t) - \beta_j[q_j E_j(t) + I_j(t) + A_j(t)],$$

$$\forall j \in J, t \in T. \quad (9.1)$$

$$E_j(t+1) = E_j(t) + \beta_j[q_j E_j(t) + I_j(t) + A_j(t)] - \delta_j E_j(t),$$

$$\forall j \in J, t \in T. \quad (9.2)$$

$$I_j(t+1) = I_j(t) + p_j \delta_j E_j(t) - \overline{I}_j(t), \quad \forall j \in J, t \in T. \quad (9.3)$$

$$H_j(t+1) = H_j(t) + \overline{I}_j(t) - \gamma_{1j} H_j(t), \quad \forall j \in J, t \in T. \quad (9.4)$$

$$R_j(t+1) = R_j(t) + \gamma_{1j} H_j(t) + \gamma_{2j} A_j(t), \quad \forall j \in J, t \in T. \quad (9.5)$$

$$A_j(t+1) = A_j(t) + (1 - p_j) \delta_j E_j(t) - \gamma_{2j} A_j(t), \quad \forall j \in J, t \in T. \quad (9.6)$$

According to He and Liu [41], we assume that all individuals who move in and out of the area are susceptible. Therefore, following the formulation of Büyüktaktın et al. [1], we use Eq. (9.7) to define the immigration of susceptible individuals from all surrounding regions to area j at time t , and use Eq. (9.8) to represent the outmigration of susceptible individuals from area j to all surrounding areas at time t .

$$\widehat{S}_j(t) = \sum_{l \in L} \alpha_{lj} S_l(t), \quad \forall j \in J, t \in T. \quad (9.7)$$

$$\overline{S}_j(t) = \sum_{l \in L} \nu_{jl} S_j(t), \quad \forall j \in J, t \in T. \quad (9.8)$$

The above eight difference equations describe that the change rate of each compartment is determined by the entering and exiting population in the corresponding compartment. For example, Eq. (9.6) shows that the number of asymptomatic individuals at time $t + 1$ is equal to the number of asymptomatic individuals on the previous time plus the new individuals transferring from the exposed compartment, and minus individuals who are recovered. These equations can be used to forecast the number of susceptible, exposed, infected, hospitalized, asymptomatic and recovered individuals by giving the initial values of each compartment and the corresponding parameters. The only problem need to be determined is the state variable $\overline{I}_j(t)$, which means the number of infected individuals that can be accepted for treatment in area j at time t .

As we all know, the quantity of how many infected individuals can be treated depends on the scale of emergency budget. If emergency budget is enough, all infected people can be hospitalized [44]. However, if emergency budget is limited, policymakers must consider how to effectively use the limited budget to maximize the emergency service level [45], to minimize the total number of infections and fatalities [1], or to minimize the total unsatisfied demand [41]. With the different

optimization objectives, the state variable $\bar{I}_j(t)$ will be correspondingly changed. Considering that H1N1 is now a seasonal flu with very low mortality rates, we use the minimization of total unsatisfied demand as our optimization objective in this study. The detail of the resource allocation model is introduced in the following section.

9.3.2 Resource Allocation Model

Similar to Sect. 9.3.1, we give the notations that will be used to formulate the resource allocation model as follows:

Parameters:

- f_j Fixed cost for establishing an isolated ward in area j .
- \bar{f}_j Fixed cost for closing an unused ward in area j .
- g_j Unit variable cost for treating a patient in area j .
- Ω Total available budget.
- $C_j(0)$ Initial number of isolated wards in area j .

State variables:

- $C_j(t)$ Cumulative number of isolated wards in area j at time t .

Decision variables:

- $C_j^v(t)$ New increased number of isolated wards in area j at time t .
- $\bar{C}_j^v(t)$ New closed number of isolated wards in area j at time t .

Following the convention of Büyüktaktın et al. [1], we formulate the resource allocation model as follows:

$$\text{Min } \sum_{t \in T} \sum_{j \in J} \max\{[I_j(t) + H_j(t) - C_j(t)], 0\}. \quad (9.9)$$

Subject to:

Equations (9.1)–(9.8);

$$\sum_{t \in T} \sum_{j \in J} [f_j C_j^v(t) + \bar{f}_j \bar{C}_j^v(t) + g_j H_j(t)] \leq \Omega; \quad (9.10)$$

$$C_j(t) = \sum_{r=0}^t C_j^v(r) - \sum_{r=0}^t \bar{C}_j^v(r) + C_j(0), \quad \forall j \in J, t \in T; \quad (9.11)$$

$$C_j(t) \geq C_j(0), \quad \forall j \in J, t \in T; \quad (9.12)$$

$$\bar{I}_j(t) = \min\{C_j(t) - H_j(t), I_j(t)\}, \quad \forall j \in J, t \in T; \quad (9.13)$$

$$S_j(t), E_j(t), I_j(t), \bar{I}_j(t), H_j(t), R_j(t), A_j(t) \geq 0, \quad \forall j \in J, t \in T; \quad (9.14)$$

$$C_j^v(t), \bar{C}_j^v(t) \in Z^+, \quad \forall j \in J, t \in T. \quad (9.15)$$

The objective function in Eq. (9.9) is to minimize the total unsatisfied demand in all affected areas over the finite planning horizon. In addition to the epidemic dynamics constraints (Eqs. 9.1–9.8), the resource constraints are introduced as follows. Equation (9.10) provides a budget limitation on the sum of the fixed costs for establishing and closing isolated wards and the variable cost for hospitalizing the infected individuals over all affected areas. Obviously, we can not establish and close the isolated wards at the same time. Therefore, if $C_j^v(t) > 0$, which means we need to open several new isolated wards in area j at time t , we have $\bar{C}_j^v(t) = 0$. Correspondingly, if $C_j^v(t) = 0$, we may have $\bar{C}_j^v(t) \geq 0$, which means we may close some unused isolated wards or maintain the number of isolated wards unchanged. Equation (9.11) illustrates how to calculate the capacity (cumulative number of isolated wards) in affected area j at time t . Equation (9.12) shows that the cumulative number of isolated wards should not be less than its initial size $C_j(0)$ at any time. Similar to Büyükahtakın et al. [1], Eq. (9.13) provides the number of infected individuals that can be hospitalized based on the number of available isolated wards in area j at time t . Intuitively, if the number of infected individuals $I_j(t)$ is more than the remaining capacity in affected area j at time t , then only $C_j(t) - H_j(t)$ of infected individuals can be accepted for treatment. Otherwise, if there are enough isolated wards in affected area j at time t , all infected individuals $I_j(t)$ can be accepted for treatment. Equation (9.14) requires that all state variables are non-negative. Finally, Eq. (9.15) shows that both $C_j^v(t)$ and $\bar{C}_j^v(t)$ are non-negative integer variables, corresponding to the number of isolated wards to be opened or closed.

9.3.3 Model Solution

The proposed model is a mixed-integer non-linear programming (MINLP) model due to the non-linear term in the objective function (Eq. 9.9) and the available treatment constraint (Eq. 9.13). Following the convention of Büyükahtakın et al. [1], we need to transfer the MINLP model to be an equivalent MIP. By introducing a binary variable $z_j(t)$ and two auxiliary variables ($U_j(t)$ and $W_j(t)$), Büyükahtakın et al. [1] provided several linear constraints to replace the non-linear constraint (9.13). In their paper, $z_j(t)$ took a value of 1 when only $C_j(t) - H_j(t)$ of infected individuals can be accepted for treatment, and zero when there were enough isolated wards for all infected individuals $I_j(t)$. Since the detail of linearization could be found in Büyükahtakın et al. [1], we omit it in this study.

The second non-linear term in our model is the objective function. Similarly, we can linearize it in the same way. Let $NC_j(t) = \max\{[I_j(t) + H_j(t) - C_j(t)], 0\}$. Then the objective function could be rewritten as:

$$\text{Min} \sum_{t \in T} \sum_{j \in J} NC_j(t) \quad (9.16)$$

By introducing a binary variable $\omega_j(t)$, $NC_j(t)$ could be reformulated as:

$$NC_j(t) = [I_j(t) + H_j(t) - C_j(t)] \cdot \omega_j(t) \quad (9.17)$$

Herein, $\omega_j(t)$ is a binary variable, which takes a value of 1 when the current isolated wards are not enough and thus we need to establish new ones, and zero when all infected individuals can be hospitalized. To ensure that the value of $NC_j(t)$ is equal to the maximum one between $[I_j(t) + H_j(t) - C_j(t)]$ and zero, we add the following two constraints:

$$NC_j(t) \geq I_j(t) + H_j(t) - C_j(t), \quad \forall j \in J, t \in T \quad (9.18)$$

$$NC_j(t) \geq 0, \quad \forall j \in J, t \in T \quad (9.19)$$

Note that Eq. (9.17) is still nonlinear as it involves multiplication of two variables. Let UB_j and LB_j be the upper and lower bounds for $[I_j(t) + H_j(t) - C_j(t)]$. According to Büyükahtakın et al. [1], we add the following constraints (9.20)–(9.23) to the proposed model. Herein, the upper bound UB_j is an estimate of the maximum number of unsatisfied beds in affected area j . In this study, we set it to be the initial number of susceptible individuals $S_j(0)$ minus the initial number of isolated wards $C_j(0)$ in such area. The lower bound LB_j for $[I_j(t) + H_j(t) - C_j(t)]$ is set to be $-C_j(0)$, which represents there are no more infected individuals in area j .

$$NC_j(t) \leq \omega_j(t)UB_j, \quad \forall j \in J, t \in T \quad (9.20)$$

$$NC_j(t) \geq \omega_j(t)LB_j, \quad \forall j \in J, t \in T \quad (9.21)$$

$$NC_j(t) \leq [I_j(t) + H_j(t) - C_j(t)] - LB_j(1 - \omega_j(t)), \quad \forall j \in J, t \in T \quad (9.22)$$

$$NC_j(t) \geq [I_j(t) + H_j(t) - C_j(t)] - UB_j(1 - \omega_j(t)), \quad \forall j \in J, t \in T \quad (9.23)$$

Again, following the convention of Büyükahtakın et al. [1], the proposed MINLP model can be replaced by an equivalent MIP model, which is defined in Eqs. (9.1)–(9.8), (9.10)–(9.16), and (9.18)–(9.23). Therefore, we can solve it directly by use MATLAB2017 or CPLEX.

9.4 Case Study

In this section, we present a case study to demonstrate the performance of the proposed model. All computational processes are conducted on a personal computer with a 2.4 Hz CPU and 8G RAM in the Microsoft Windows 10 environment.

9.4.1 Background and Parameters Setting

The proposed model is employed on a real case study concerning the 2009–2010 H1N1 pandemic in Jiangsu Province, China. Data are gathered from the Data-center of China Public Health Science (DCPHS), the World Health Organization (WHO) and the literature regarding the H1N1 outbreak [12, 13]. Jiangsu Province is located on the coast of the East China Sea. It is among the most populous provinces in China and registers more than 78 million permanent residents on 39,614 m² of land. These numbers account for 5.69% of mainland China's population and only 1.06% of the national land area. After the first H1N1 patient was confirmed on June 12, 2009, the epidemic quickly spread across the entire province because no control intervention was implemented at the beginning.

When the severity of this public health emergency was determined, the local government started the emergency response plan on July 1, 2009. As illustrated in Fig. 9.2, the province was divided into three affected areas, North-Jiangsu (JS-N), Center-Jiangsu (JS-C) and South-Jiangsu (JS-S). The JS-N area includes the prefectures of Xuzhou, Lianyungang, Suqian and Huaian. The JS-C area covers the cities of Yancheng, Yangzhou, Taizhou and Nantong. The JS-S area includes the cities of Nanjing, Zhenjiang, Changzhou, Wuxi and Suzhou. Most regions in the JS-N area are rural villages and more than 1/3 of the people in these areas travel out as migrant workers throughout the year. Therefore, the JS-N area is a typical population output area. In contrast, most regions in the JS-S area are modern cities with numerous job opportunities. Therefore, the JS-S area is a typical population input area. Correspondingly, the JS-C area in the middle position is a population equilibrium area. The population data for each affected area is given in Table 9.2. The immigration rate and emigration rate between different areas are estimated in Table 9.3. These data are extracted from the Sixth Population Census Report of China in 2010 [46]. Emergency budget is allocated to help establish isolated wards in all three affected areas. The fixed cost for establishing a new isolated room is estimated to be ¥10,000 and the fixed cost for closing an unused isolated ward is estimated to be ¥1500 (i.e., a fixed cost accounts for administrative manpower, overhead, utilities, and sterilization of the patient rooms and facilities allocated exclusively for treating H1N1 patients). Finally, the unit variable cost for treating a patient is approximately ¥1000 (i.e., a variable cost includes doctor-hours, nurse-hours, medicine cost, meals, etc.).

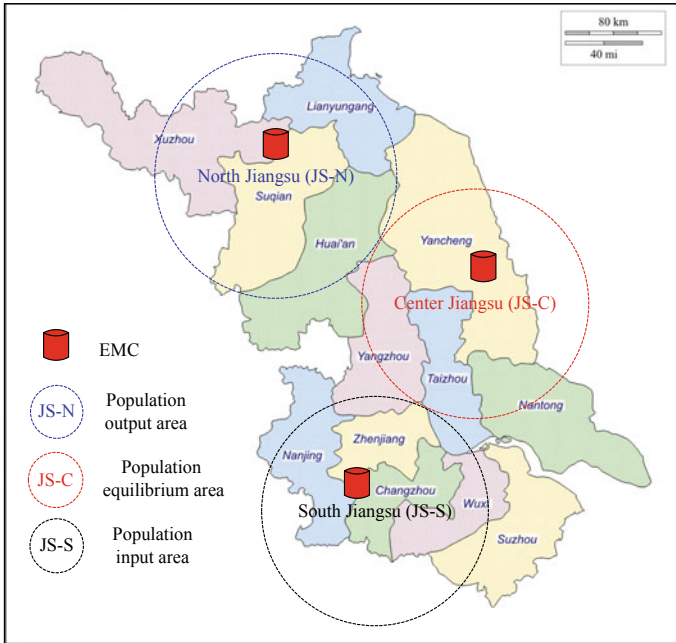


Fig. 9.2 Map of 3 affected areas in Jiangsu Province

Table 9.2 Population size in affected areas [46]

Affected areas	Population size	Ratio
JS-N	22,489,856	0.29
JS-C	23,621,393	0.30
JS-S	32,548,654	0.41
Total	78,659,903	1.00

Table 9.3 Migration rate between areas [46]

Affected areas	JS-N	JS-C	JS-S
JS-N	–	0.1	0.25
JS-C	0.05	–	0.1
JS-S	0.05	0.1	–

Although the whole province is divided into three affected areas, we believe that there is no difference in the values of epidemic parameters. The parameters are given as follows. First, because the age distribution profile in Jiangsu Province is similar to that in Guangdong Province of China [12], the mean latent period of the exposed stage $E(t)$ is assumed to be 2.62 days (95% confidence interval, (CI) 2.28–3.12). Therefore, the infected rate δ is considered to be $\delta = 1/2.62$. Second, of all the cases in Jiangsu Province, most symptomatic individuals are characterized by mild

infections and symptoms. According to Tuite et al. [47], the same rates are used to reflect recovery rates of symptomatic and asymptomatic cases. Therefore, we have $1/\gamma_1 = 1/\gamma_2 = 3.38$ (95% CI, 2.06–4.69). Moreover, the possibility of transmission from exposed class q is fixed at $1/8$ in a rather crude way [48]. The proportion of symptomatic infectious cases p is fixed at 60.2% according to the serological survey conducted by the Jiangsu Center for Disease Control and Prevention. Finally, the transmission rate β is set to be 0.411 according to Tan et al. [12], which has a confidence interval of 95% (0.390–0.432). Using these initialized parameters, it is revealed that the basic reproduction number (R_0 , the expected number of secondary infections produced by an index case in a completely susceptible population) is 1.525 (95% CI, 1.448–1.602), which is consistent with most analyses of data from Mexico (R_0 : 1.2–1.6, Davoudi et al. 2010) [49] and Vietnam (R_0 : 1.5–1.6, Hien et al. [50]).

9.4.2 Test Results

Because Chinese Center for Disease Control and Prevention (CCDCP) requires local government to report the H1N1 data every three days, our test data is a time-series data with an interval of three days. The actual cumulative number of isolated wards in each area j from July 1st, 2009, to December 27th, 2009, are adopted and fed into the model. Therefore, the proposed model can be solved with fixed $C_j(t)$ values based on the actual data. Similar to the verification process in Büyükahtakin et al. [1], we validate our predicted data against the actual outbreak data in terms of the cumulative number of infected individuals on these days. The result is shown in Appendix B.1.

(1) Optimization results with different budget sizes

When facing an unexpected epidemic outbreak, managers want to know how to allocate the limited budget to different affected areas and what the impact on epidemic dynamics with different budget scales is. Following the convention of Büyükahtakin et al. (2018) [1], we conduct these two questions and demonstrate the results in Appendix B.2. The CPU times for the four scenarios are 1268.24, 1326.31, 1194.12, and 1378.56 s, respectively.

Initially, when budget allocation is inadequate (i.e., ¥100 M), the effect of emergency response is extremely limited. More than half of people in Jiangsu Province will be infected by the disease and most of them can not be hospitalized for treatment. As the budget grows, one can see that the unsatisfied demand sharply decreased. When a budget limitation of ¥250 M is given, the unsatisfied demand is only 2821. The cumulative number of infected individuals decreases by approximately 99.9% when compared to the scenario of a budget limitation of ¥100 M. The above results demonstrate that an ample emergency budget is very important when response to an unexpected epidemic outbreak. In that case, managers can implement several effective intervention measures, i.e. quarantine and treatment, which can effectively

reduce the contact between susceptible people and infected people, and thus decrease the possibility of disease transmission among the population.

Second, Fig. 9.3 shows budget allocation proportions for the three affected areas. One can see that the test results are pretty stable (22.8–23.7%, 28.2–30.2% and 46.8–48.4%, respectively). Combined with the population ratio in these three areas (29, 30 and 41%, respectively), one can see that budget allocation is always partial to the JS-S area and prejudice to the JS-N area. The core reason is that the JS-N area is a population output area and the JS-S area is a population input area. During the entire planning horizon, thousands of people move from the JS-N area to the JS-S area for study, work or business. Therefore, budget allocation is not consistent with the population proportion for these affected areas.

(2) The optimal number of isolated wards

Figure 9.4 provides model results regarding the number of isolated wards that should be added and removed at each period with the budget of ¥250 M. First, when intervention starts on July 1, one can see that hundreds of isolated wards should be immediately opened in all three affected areas (156, 187, and 311, respectively).

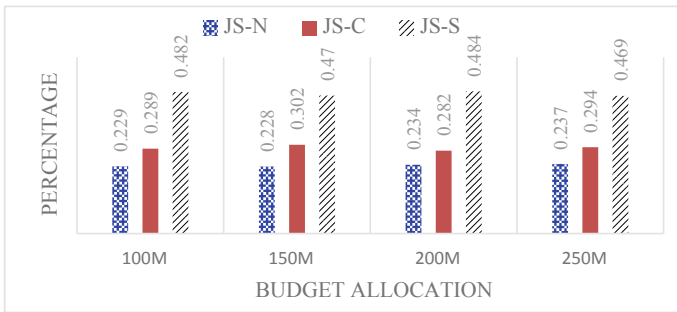
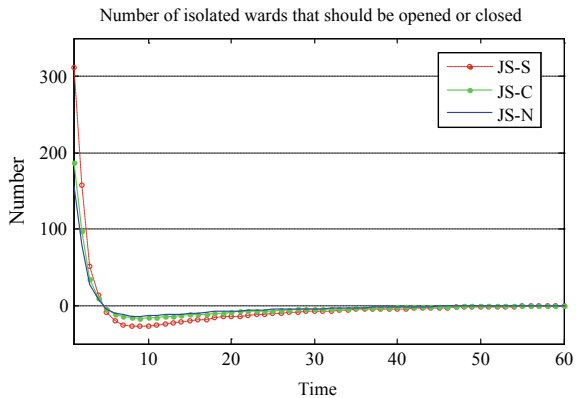


Fig. 9.3 Percentage of budget allocation in different areas

Fig. 9.4 Number of isolated wards that should be opened or closed with ample budget



This can help accept as many patients as possible who were infected in the period from the outbreak date (June 12) to the intervention start time (July 1). Second, we need to continuously open new isolated wards in the following 5 periods, which means 15 days in our test. Although infected individuals can be obviously reduced when control intervention starts, there are still numerous exposed individuals who will become new infected persons and thus we still need to establish new isolated wards for them. Finally, after the first 5 periods, the opened isolated wards will be gradually closed until the final planning horizon.

9.4.3 Discussion

Again, following the convention of Büyüктаhtakın et al. [1], we solve our model with five different intervention starting dates (July 1, July 16, July 31, August 15 and August 30). After that, we discuss the impact of different intervention starting dates from the following three aspects: (1) the number of infected individuals; (2) the optimal allocation of emergency budget; and (3) the available capacity required. The impact of different intervention starting dates on the number of infected individuals is illustrated in Appendix B.3. In what follows, we introduce the test results of the above questions (2) and (3).

The impact of different intervention starting dates on the optimal allocation of emergency budget is demonstrated in Table 9.4. First, it can be observed that the major cost for H1N1 intervention is the fixed cost, which is expended for establishing isolated rooms in the appointed hospitals. This is different from Büyüктаhtakın et al. [1], which suggested a major cost of the variable treatment cost and followed by the fixed cost and the burial cost for controlling the shocking Ebola. Second, the test

Table 9.4 Budget allocation with different intervention starting dates

Budget allocation (Million)	Cost	July 1	July 16	July 31	August 15	August 30
JS-N	Fixed cost	55.8	112.4	258.5	610.8	1458.2
	Variable cost	3.4	6.3	16.9	44.6	105.2
	Area total cost	59.2	118.7	275.4	655.4	1563.4
JS-C	Fixed cost	67.5	135.8	316.3	748.1	1786.0
	Variable cost	6.1	8.7	21.9	54.3	126.7
	Area total cost	73.6	144.5	338.2	802.4	1912.7
JS-S	Fixed cost	109.4	216.2	508.5	1214.2	2901.7
	Variable cost	7.8	15.2	36.8	90.6	215.6
	Area total cost	117.2	231.4	545.3	1304.8	3116.3
Total cost		250	494.6	1158.9	2762.6	6592.4
Total unsatisfied demand		2821	7012	25,428	70,124	194,680

result shows that emergency budget required could be significantly increased with each 15 days of delay in intervention. For example, if intervention starts on July 1st and an emergency budget of ¥250 M is allocated, the cumulative unsatisfied demand is only 2821. However, if we postpone the intervention by half a month (July 16), the model solution requires an optimal budget of ¥494.6 M with an unsatisfied demand of 7012. What is worse, although there is ample emergency budget, the values of total unsatisfied demand in the following three scenarios are considerably large.

The impact of different intervention starting dates on the isolated wards capacity required is illustrated in Fig. 9.5. It can be observed that the capacity required in all three areas show similar change trajectories. The capacity required increases sharply in the first several days. Beyond its peak, it decreases until the final planning horizon. The later the intervention starts, the more isolated rooms will be required to suppress the disease spread. In summary, we suggest that intervention to an unexpected epidemic should start as early as possible. This can significantly reduce the number of infected individuals, shrink the scale of isolated wards required, and finally save the valuable emergency budget.

Furthermore, we also conduct sensitivity analysis for three key parameters in our epidemic model. The results suggest that local government should try its best to reduce the transmission rate. Meanwhile, shorting the treatment time for infected persons could also reduce the total number of infected individuals. To reduce the transmission rate, several forcible quarantine measures should be carried out. In the meantime, self-quarantine for the exposed people and decreasing the contact with other susceptible individuals around are also effective strategies for controlling epidemic diffusion. Other monitoring measures such as taking a temperature test before boarding airplane or train could also help to alleviate epidemic diffusion risk. As to short the treatment time, it could be realized by improving the corresponding medical techniques and this beyond our research scope.

9.5 Conclusion

In this study, we present a modified epidemic-logistics model for controlling H1N1 in China. Our model is inspired by the modeling framework of Büyüktaktakın et al. [1]. We get several similar conclusions from our test. For example, managers should start intervention strategy as early as possible when response to an unexpected epidemic outbreak. Otherwise, the consequence would be very serious even with ample emergency budget and strong intervention efforts. We also obtain several different viewpoints from our test. For instance, we demonstrate that budget allocation proportion for the three affected areas is pretty stable. However, it is not consistent with population ratio. Managers should allocate more budget to the population input area (i.e. JS-S area). We also suggest that managers should do their best to open enough number of isolated wards at the beginning of intervention, to receive as many patients as possible who were infected in the period from the outbreak date to the intervention

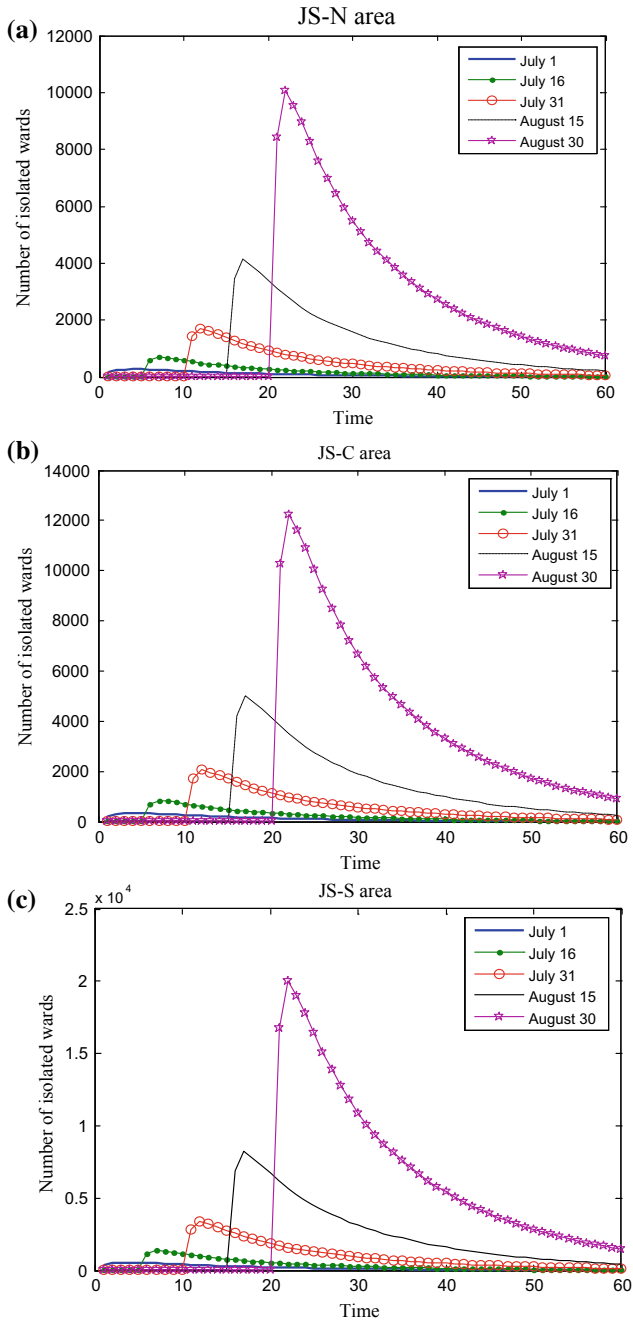


Fig. 9.5 Capacity required with different intervention starting dates

start time. This can effectively help control the epidemic diffusion. Other differences between Büyükahtakin et al. [1] and this study are listed as follows.

- (1) Different infectious diseases have dissimilar diffusion dynamics, and thus we have different constraints for the integrated epidemic-logistics model. For example, individuals infected by H1N1 will first go into a latent (exposed) stage, during which they may have a low level of infectivity. However, the transmission dynamics of Ebola is totally different in Büyükahtakin et al. [1]. Moreover, we consider a compartment of asymptomatic and partially infectious (see Fig. 9.1), but we do not consider the deceased individuals because H1N1 is now a seasonal flu. While in the Ebola pandemic, funerals and how to bury the deceased individuals are important and unavoidable problems. Therefore, when we address the time discretized epidemic compartment model as the linear constraints, there will be total different constraints for the integrated epidemic-logistics model.
- (2) Different infectious diseases can cause different public health emergencies, and thus we have different optimization objectives for the integrated epidemic-logistics model. As one can see, Büyükahtakin's objective is to minimize the total number of infected individuals and deaths of infected people who do not receive treatment. While in our study, the objective function is to minimize the total unsatisfied demand in all affected areas.
- (3) In Büyükahtakin et al. [1], the authors preset two kinds of ETC, 50-bed and 100-bed, and thus the capacity decision is a combinatorial optimization problem. While in this study, we focus on when to open the new isolated wards and when to close the unused isolated wards. Moreover, our test demonstrates that the major cost for H1N1 intervention is the fixed cost. This is also different from Büyükahtakin et al. [1], which suggested the major cost is the variable treatment cost and followed by the fixed cost. We think the difference of cost structure is caused by the different characteristics of the two diseases. As we all know, the treatment for Ebola patients is more complex and dangerous, and thus the variable treatment cost should be the major one. As to H1N1, it is now a seasonal flu with very low mortality rates due to advances in medical technologies. Therefore, the major cost for treating the infected individuals is the fixed cost.

Note that although there are several papers that study the integration of epidemic control and logistics planning in recent 5 years (i.e., [33, 39, 41, 45]), many of them divide the continuous time into several independent decision-making periods and update forecasting for the number of infected individuals at the beginning of each period. Thus in essentially, the epidemic compartment model and the planning model are still independent from each other. Different from that, Büyükahtakin et al. [1] integrated epidemic dynamics and the corresponding emergency logistics considerations into one optimization model. The key component was that no constant transition rate from compartment I to H . In this study, we retain the advantage of this modeling framework and thus our model could also forecast the development of H1N1 and depict the impact on different resource-allocation scenarios on the disease progression.

Future research could address some of the limitations in both the epidemiological and resource allocation portions of the proposed model. For example, other epidemics with other transmission characteristics could be incorporated into the optimization model. Moreover, cross-regional transmission with different transition rates and population structures could also be incorporated into the model. As to the resource allocation portion, future studies could also consider the influence of unsatisfied demand, the emergency service level, or the potential delay in arrival time of the intervention budget.

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Chapter 10

Logistics Planning for Hospital Pharmacy Trusteeship Under a Hybrid of Uncertainties



This chapter presents two medicine logistics planning models by using a time-space network approach, one with deterministic variables and the other with stochastic variables. Flow dependent variable costs, random demand and random service time are featured in our models in addressing economies of scale and uncertainties in a real-world medical logistics problem. Effective computational schemes are designed, and an evaluation method is proposed to derive and assess a solution to the models. Numerical tests are conducted and show promising results for applications to a real-world problem.

10.1 Introduction

Medicine logistics planning is a major part of operations management in a hospital that is responsible for the procurement of medicine, setting order quantities and order times, scheduling shipping, the in-house distribution of medicine, and determining the safety stock and service level for the medicine. This study is partly motivated by the concerns of practical medicine logistics operations in many hospitals in China. Because of the culture and the current prevailing health insurance plans in China, most people go to the hospital to see a doctor and obtain prescriptions from the hospital pharmacy rather than going to a community health care center for even mild illnesses, such as a cold. The statistics show that more than 90% of patients purchase their medicine in a hospital pharmacy with a doctor's prescription instead of using retail pharmacies outside of the hospital. Therefore, medicine inventory levels in most hospitals remain high year round, blocking capital flow and increasing the risk of medicine expiration.

In the past decades, two main capital sources were presented in maintaining a high-level inventory of medicines in hospitals: government funding and medicine revenue generated by hospital pharmacies. Government authorities allow hospitals to make a 15–20% profit on medicine sales. For example, the wholesale price of a box of amoxicillin capsules is 15 CNY, and the retail price in the hospital's pharmacy

may be 16–18 CNY. However, due to the lack of supervision, the actual retail price of amoxicillin capsules can reach 26–30 CNY in some hospitals.

The Chinese government has been in the process of implementing medical and healthcare system reform, which prohibits hospitals from profiting from medication sales, which means that a hospital's pharmacy will become a not-for-profit department and can no longer generate medicine-related revenue. This is the reason why many hospitals are looking for outsourcing solutions, such as the hospital pharmacy trusteeship (HPT) scheme. HPT is a vendor-managed inventory approach. In this scheme, the internal pharmacy of a hospital will be outsourced to and managed by a pharmaceutical company, which is responsible for ensuring the timely replenishment of the hospital pharmacy's stock and maintaining the required medical service level [1]. Therefore, it is in the core mission of HPT to develop a stable and economic medicine logistics plan to minimize operation costs while ensuring supply maintenance and managing a combination of uncertainties. However, a stable logistics plan is always disrupted by the following factors.

- (1) The first influencing factor is uncertain demand. Although electronic purchase systems and decision support systems are used in medicine inventory management in most Chinese medical institutions, important parameters for decision-making, such as the order quantity, order point, and safety stock, are manually determined by staff members based upon his/her experience. Since most patient requests in a hospital are stochastic and time-varying, experience-based schedules are often insufficient or ineffective in meeting the actual demand. In lacking a systematic analysis and optimal decision making mechanism, the fear of stock-out drives the stock level to be consistently high.
- (2) The second factor is the uncertain service time. "Service time" in this study is a general term (similar to the lead time) that is defined as the total time from when an order is placed until the order is received. This includes the order processing time, sorting time, packaging time, loading and unloading time, and transportation time. Many of these operation links can experience unexpected delays, such as traffic congestion, resulting in the actual receipt time being far from the planned service time. Therefore, designing robust medicine logistics planning entails explicitly addressing the uncertainty in the service time.
- (3) The third factor is the variable service cost. Although the price of a medicine does not vary, its cost varies because of the wholesale discount price. Therefore, there are economies of scale in production and distribution. The unit service cost is not a fixed constant but is dependent on the flow in the service arc.

This study develops two medicine logistics planning models based on a time-space network approach, one for deterministic variables and the other for stochastic variables. Most research on this topic in the existing literature tends to either address demand uncertainty or only service time uncertainty. The SPM model proposed in this study addresses both uncertainties in a unified framework. Meanwhile, the penalty for the time error between the planned service time and actual service time is also introduced into our model for the first time. Incorporating the penalty on an early or late arrival of a delivery into the objective function can effectively reduce excessive

holding and shortage costs, as shown in our numerical examples, and further yield an optimal solution as a more robust logistics plan. Our models employ variable service costs accounting for possible economies of scale, such as wholesale price, consolidation in order processing and transportation. This is another step forward toward the reality of modeling with flow independent service costs in the previous works.

10.2 Literature Review

10.2.1 VMI in Hospital

The VMI strategy originated in the U.S. in the 1980s; early adopters of this strategy included large retailers such as Wal-Mart and JC Penney [2]. However, most of the existing studies addressing the issue of VMI have focused on manufacturing firms and retailers [3]. The literature has largely ignored the application of the VMI system within the healthcare domain.

In recent years, some studies highlight the advantages of implementing the VMI system in the hospital's pharmacy. Kim [4] discussed the adoption of the VMI system between a wholesaler and a hospital warehouse in South Korea. The VMI system has several advantages, the most significant one being a reduction of the inventory level. Furthermore, it decreases the workload of the pharmacy staff in the hospital and facilitates information integration between the wholesaler and the hospital. Tsui et al. [5] also stated that the VMI can help the hospital reduce the number of required staff members, reduce stock holdings and improve customer service. According to their report, 3.5 full-time equivalent staff members were redeployed to clinical pharmacy support duties, and the stock holding decreased by \$352,000. Lin and Sun [6] developed a mathematical model based on VMI to describe the supply chain in a hospital. They proposed a quantitative model of a two-stage supply chain to compare the inventory cost of hospitals and their suppliers before and after the adoption of VMI. Through a quantitative comparison, it is confirmed that the adoption of VMI can effectively reduce the overall inventory cost of the hospitals and the supply chain. Mustaffa and Potter [7] also suggested that the application of a VMI system leads to higher customer service levels (i.e., delivering the correct quantity of the product to the clinic) and improvements in key supply chain variables such as decreasing stock-outs and eliminating the bullwhip effect.

More recent works in this stream include Liang et al. [8], Bhakoo et al. [9] and Govindan [10]. For example, Liang et al. [8] focused on the establishment of a VMI pattern in medicine storage management. Through a comparison between the traditional ABC analysis method and VMI pattern, an optimization strategy was established. Bhakoo et al. [9] showed how VMI works by discussing the application of a VMI system downstream in the supply chain, particularly from the hospital's perspective. Govindan [10] proposed the optimal replenishment policy for time-

Table 10.1 Summary of the studies with respect to VMI in the hospital

Reference	Goal	Methodology	VMI's benefit(s)
Kim [4]	Inventory optimization	Case study	(1), (2), (3)
Tsui et al. [5]	Inventory optimization	Case study	(1), (2), (4)
Lin and Sun [6]	Cost minimization	Mathematical model	(5)
Mustaffa and Potter [7]	Inventory management	Case study	(4), (5)
Liang et al. [8]	Inventory management	ABC versus VMI	(1), (5)
Bhakoo et al. [9]	Inventory management	Case study	(1), (4), (5)
Govindan [10]	Cost minimization	Mathematical model	(4), (5)

(1) Reduce inventory level; (2) decrease the workload; (3) facilitate information integration; (4) improve customer service; (5) reduce inventory cost

varying stochastic demand under VMI. The models are applied in both the traditional system and VMI supply chain based on pharmaceutical industry data. Table 10.1 shows a summary of the studies mentioned in this section with respect to several factors, such as goals, methodology and the benefit(s) of VMI.

10.2.2 *Logistics Planning with Different Influence Factors*

As mentioned in Sect. 10.1, stable logistics planning is always disrupted by the following factors: uncertain demand, uncertain service time and variable service cost. The related literature is briefly introduced below.

There are three common ways to model uncertain demand: (1) stochastic distribution [32], (2) time-varying function [11–13], and (3) the information updating mode [14, 15]. A stochastic distribution means that the demand is defined as a random function, i.e., uniform distribution, normal distribution and Poisson distribution. The time-varying function indicates that the demand has a time-varying characteristic. For example, Wang and his colleagues constructed a time-varying function for forecasting the demand in hospitals, where the time-varying function was designed based on an epidemic diffusion rule [16, 17]. The last information updating mode allows the demand information to be updated as the decision-making process evolves. Because this mode can effectively reduce the mismatch between the supply side and demand side, it is adopted in this study in the following sections.

Regarding uncertain service times, researchers tend to use the average service time in drug delivery scheduling [18–21]. For example, Yan et al. [21] proposed a logistical support scheduling model in humanitarian relief. In this model, an average service time is adopted for each delivery trip, and stochastic factors during the vehicle travel stage may have a significant influence on logistics planning. When real stochastic service time is not considered in traditional deterministic models, medical resources in hospitals will be used excessively, resulting in an overly optimistic “optimal” schedule [22, 23, 33]. Therefore, Yan and his colleagues employed network flow

techniques to construct a logistical support scheduling model with uncertain service times. The concept of time inconsistency is proposed to precisely estimate the impact of stochastic disturbances arising from variations in vehicle trip service times during the planning stage [24]. This helps us design an unanticipated penalty cost to penalize the time inconsistency in the following sections.

Motivated by the importance of uncertain demand and service times, which are key elements of scheduling strategy, scholars have developed models to guide optimal logistics support for medicine order and delivery with hybrid uncertainties [25, 26]. For example, Lapierre and Ruiz [25] presented an innovative approach for improving hospital logistics by coordinating procurement and distribution operations while respecting inventory capacities. In recent years, Liu and his colleagues have also worked extensively in this domain. They employed time-space network and different optimization techniques to construct logistical scheduling models for optimization medicine order and delivery [27–30].

Table 10.2 shows a summary of the studies mentioned in this section. These works give us constructive inspiration for managing the various uncertainties in this study. As introduced in Sect. 10.1, this study differs from previous studies by addressing a much more realistic environment with uncertain demand, service time and service cost. To the best of our knowledge, so far, no model has been formulated to solve this type of problem. Moreover, logistics planning for medicine order and delivery involves numerous time and space constraints that are highly correlated with each other. Therefore, it is difficult to use traditional integer programming techniques to formulate and efficiently solve this type of problem. On the other hand, the time-space network method has been popularly employed to solve various scheduling problems because it provides a natural and efficient way to represent the relative network nodes in the dimensions of time and space. Although the resulting model scale generally enlarges due to the extension in the dimension of time, complicated time-related constraints can normally be easily modeled for realistic problems, particularly in comparison to the space network models [31]. Coupled with the development of efficient algorithms, the time-space models (usually formulated as multiple commodity network flow problems) can be effectively solved; see Yan et al. [24, 31] and Liu et al. [27].

Based on the analysis mentioned above, the time-space network technique may be a suitable way to solve the logistics planning issue for HPT under a hybrid of uncertainties. Therefore, this study employs it to develop models to help a pharmaceutical company manage a hospital's pharmacy with several types of medicine. Certainly, the development of other models to solve this type of problem and comparing the results with those of our model could be a direction of future research.

Table 10.2 Summary of the studies with respect to logistics planning

Reference	Goal		Model/methodology	Questions addressed		
	Cost min.	Profit max.		(1)	(2)	(3)
Mcguire and Hughes [32]	✓		Case study	✓		
Sheu [11]	✓	✓	Hybrid fuzzy clustering optimization	✓		
Sheu [12]		✓	Data fusion, fuzzy clustering, TOPSIS	✓		
Rachaniotis et al. [13]		✓	System dynamics model	✓		
Liu et al. [14]	✓		Dynamic programming	✓		
Liu and Zhang [15]	✓		Dynamic programming	✓		
Wang and Wang [16]	✓		Stochastic programming	✓		
Xu and Wang [17]	✓		Dynamic programming	✓		
Zhen et al. [18]		✓	Stochastic programming		✓	
Gonsalves and Itoh [19]	✓		Simulation optimization		✓	
Hui et al. [20]		✓	Case study		✓	
Yan et al. [21]	✓		Integer programming		✓	
Zhang et al. [22]		✓	Queuing model		✓	
Dessouky et al. [33]		✓	Mixed 0–1 integer programming		✓	
Harper et al. [23]		✓	Mixed 0–1 integer programming		✓	
Yan et al. [24]	✓		Mixed-integer programming		✓	
Lapierre and Ruiz [25]	✓		0–1 programming	✓	✓	
Mete and Zabinsky [26]	✓		Stochastic programming	✓	✓	
Liu et al. [27]	✓		Stochastic programming	✓	✓	
Zhang and Liu [28]	✓		Chance-constrained programming	✓	✓	

(continued)

Table 10.2 (continued)

Reference	Goal		Model/methodology	Questions addressed		
	Cost min.	Profit max.		(1)	(2)	(3)
Zhang and Liu [29]	✓		Mixed 0–1 integer programming	✓	✓	
Liu et al. [30]	✓		Mixed 0–1 integer programming	✓	✓	
Our study	✓		Multi-stage stochastic programming	✓	✓	✓

(1) Uncertain demand; (2) uncertain service time; (3) variable service cost

10.3 Time-Space Network Model

This section presents a time-space network model for a healthcare logistics planning problem with uncertain demand, uncertain service time and variable cost. First, a deterministic planning model (DPM) is developed for the supply chain planning with constant demand and deterministic service time. After that, a stochastic logistics planning model (SPM) is developed to incorporate the uncertainties in demand, service cost and service time. A network structure will be introduced as the common platform for these two models in the next subsection.

10.3.1 Network Structure

In a real-world medicine logistics supply chain, operations management is responsible for planning, controlling, collecting feedback from implementation, updating the parameters and re-planning. The time-space network model proposed here is a rolling horizon of a dynamic decision making process for a periodical adjustment process. In Fig. 10.1, the horizontal axis stands for the time duration, and the vertical axis stands for the decision-making round. In each round of decision-making, the planning horizon (PH) is divided into two parts: the execution phase (EP) and the reference phase (RP). In each round of decision making, an optimization problem is solved for the planning horizon, of which only its EP will be implemented in decision variables, and its RP will not be executed but open for reference updating. When implementation of the EP is completed, the planning horizon is rolled into the next round of decision making, in which the information regarding demand, service time, and inventory level, etc., from the execution will be updated and feedback sent to the next PH. For instance, suppose that the entire planning horizon lasts 12 days and each execution phase lasts 2 days. There will then be 6 rounds of decision making. In the 1st round, a scheduling problem for the whole 12 days needs to be solved, but

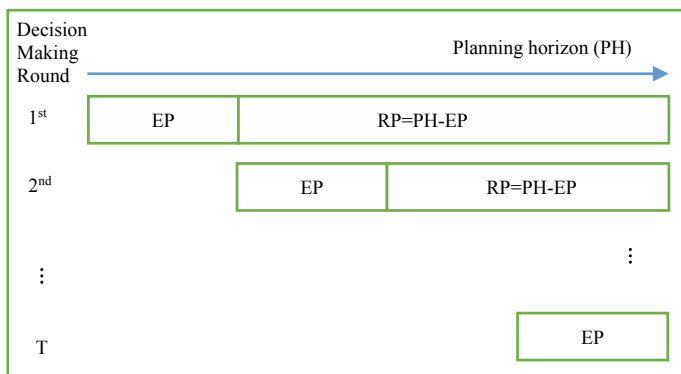


Fig. 10.1 Schematic diagram of a dynamic decision-making framework

only the optimal solution for the first 2 days will be adopted as our executive phase. After that, the planning will be updated with new information on the demand and service time and then go to the 2nd round of decision-making. In the 2nd round, the planning horizon is rolled into the remaining 10 days. Optimal scheduling will be conducted for the last 10 days, but will be executed for 2 days (i.e., day 3 and day 4 in the original calendar). The planning horizon is rolled into the remaining 8 days for the 3rd round of decision making and so forth until the 6th round, which is the last two days.

As shown in our previous works [14, 15], this periodical adjustment can help track the actual demand and service time in the real world and provide a more accountable logistics plan than only planning without adjustment. It is worth mentioning that “day” here is a modeling term for the basic time unit for planning, which can be an hour or week in actual time for a practical problem.

Figure 10.2 illustrates a time-space network for the logistics planning of medicine delivery and storage within a certain period of time and space. Each layer represents a medicine type. The various tiers in the supply chain, including the pharmaceutical company, the hospital’s pharmacy, and departments in the hospital, are horizontally displayed. The planning horizon is illustrated by the vertical axis. A node in this time-space network indicates an individual party at a certain time in the planning horizon. A vertical link whose length corresponds to the time unit used in the PH, e.g., one day, is used to indicate the evolution of medicine flow or storage in each party. Therefore, if a shorter time unit is employed in an application, the time-space network will display more nodes that are vertically aligned. An arc represents an operation activity in the medicine supply chain. There are four types of arcs that are defined below.

(1) External service arc

An external service arc (arc (1) in Fig. 10.2) represents a shipment of medicine from a pharmaceutical company to the hospital’s pharmacy. The arc cost consists of the procurement cost and the shipping cost of the medicine, both having economies of

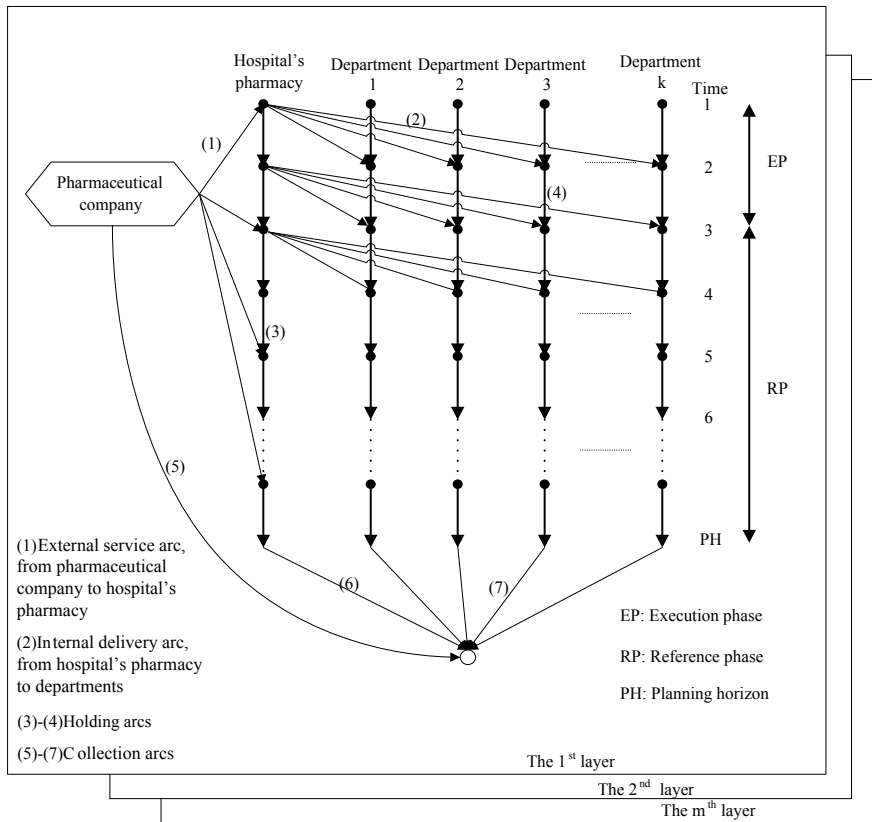


Fig. 10.2 Time-space network of the logistics planning

scale. For simplicity of expression and modeling convenience, these two costs are combined into a general arc cost for an external service arc, which should reflect the corresponding economies of scale, such as a quantity discount in a purchasing strategy. In a real-world application, there are usually two price schedules. One is a fixed unit price that is negotiated by the pharmaceutical company and the hospital when they sign the medicine supply contract. In this case, the supplier would consider the quantity discount and the price fluctuation in advance. The other is a dynamic pricing strategy, which has a basic charge set in the contract and a dynamic price that will be adjusted according to the actual medicine flow. The latter method is more flexible and widely adopted. This study adopts the dynamic pricing strategy, which can be expressed mathematically by:

$$f(x_{ij}^m) = \begin{cases} p_1^m, & 0 < x_{ij}^m \leq X_1^m \\ p_2^m, & X_1^m < x_{ij}^m \leq X_2^m \\ p_3^m, & X_2^m < x_{ij}^m \leq X_3^m \\ \dots & \dots \\ p_p^m, & X_{p-1}^m < x_{ij}^m \leq X_p^m \end{cases} \quad (10.1)$$

Herein, $f(x_{ij}^m)$ is the unit service cost for medicine type m on service arc (i, j) , which is a piecewise function of arc flow x_{ij}^m .

(2) Internal delivery arc

An internal delivery arc (arc (2) in Fig. 10.2) represents the delivery of a medicine type from the hospital's pharmacy to various departments in the hospital, and the arc cost reflects the labor and overhead cost involved in this operation. The upper bound of the flow in this arc is the inventory capacity of the hospital's pharmacy.

(3) Holding arc

A holding arc, shown as (3–4) in Fig. 10.2, represents the operation of holding a stock of medicine at the hospital's pharmacy or departments. The arc cost reflects the inventory carrying cost, which is in proportion to the flow amount (inventory level) in the arc. The upper bound of the arc flow is the inventory capacity of the corresponding node (hospital's pharmacy or a department), and the lower bound is the safety stock, specified as the minimum level that should be kept for the hospital or department to guarantee the emergency medical need.

(4) Collection arc

The collection node at the bottom of Fig. 10.2 is the sink of this network that is created for flow conservation. A collection arc (arc (5–7) in Fig. 10.2) does not represent any substantial operation in the supply chain but is an artificial link that connects every party node to the collection node by the end of the PH so that the unused medicines (at the pharmaceutical company, the hospital's pharmacy, and hospital departments) "flow" to the collection node in the model. Therefore, the arc cost is zero for a collection arc.

10.3.2 Deterministic Planning Model

The deterministic planning model (DPM) assumes that the dynamic demand at each node is known in advance and that the service times from the pharmaceutical company to the hospital's pharmacy and from the hospital's pharmacy to the departments are known constants. For the convenience of the presentation of the model, the pharmaceutical company ships the medicines to the hospital's pharmacy every two days, and the hospital's pharmacy delivers the medicines to its departments every day. The notations in the DPM formulation are introduced below:

Sets

- M Set of all medicine types in the time-space network.
 N^m Set of all nodes in the m th layer of the time-space network.
 A^m Set of all arcs in the m th layer of the time-space network.
 S^m Set of all external service arcs in the m th layer of the time-space network.
 D^m Set of all internal delivery arcs in the m th layer of the time-space network.
 H^m Set of all holding arcs in the m th layer of the time-space network.

Parameters

- ct_{ij}^m Unit cost for internal delivery arc (i, j) in the m th layer of the time-space network.
 ch_{ij}^m Unit cost for holding arc (i, j) in the m th layer of the time-space network.
 l_{ij}^m Lower bound for flow on arc (i, j) .
 u_{ij}^m Upper bound for flow on arc (i, j) .
 um_{ij} Inventory capacity of the arc (i, j) .
 a_i^m Supply or demand of node i in the m th layer of the time-space network ($a_i^m > 0$: indicates a supply node, $a_i^m \leq 0$: indicates a demand node).

Decision variables

- x_{ij}^m Arc (i, j) flow in the m th layer of the time-space network.

The DPM is to solve for the following optimizing problem to determine the optimal arc flows subject to the flow conservation, upper bound and lower bound of the arc flows to minimize the total logistical cost for the planning horizon.

$$\text{Min } z = \sum_{m \in M} \left(\sum_{ij \in S^m} f(x_{ij}^m) x_{ij}^m + \sum_{ij \in D^m} ct_{ij}^m x_{ij}^m + \sum_{ij \in H^m} ch_{ij}^m x_{ij}^m \right) \quad (10.2)$$

$$\text{s.t.} \quad \sum_{j \in N^m} x_{ij}^m - \sum_{k \in N^m} x_{ki}^m = a_i^m, \quad \forall i \in N^m, m \in M \quad (10.3)$$

$$\sum_{m \in M} x_{ij}^m \leq um_{ij}, \quad \forall ij \in H^m \quad (10.4)$$

$$l_{ij}^m \leq x_{ij}^m \leq u_{ij}^m, \quad \forall ij \in A^m, m \in M \quad (10.5)$$

$$x_{ij}^m \in INT, \quad \forall ij \in A^m, m \in M \quad (10.6)$$

The objective function (10.2) minimizes the total logistics cost, including the external service cost, the internal delivery cost and the holding cost. The constraints at (10.3) are the flow conservation equations for each node in the time-space network. The constraints at (10.4) are the capacity constraints for the hospital's pharmacy and the departments in the hospital. The constraints at (10.5) guarantee that all arc flows are within their bounds. The constraints at (10.6) ensure that all flow variables are

integers. Because the service costs in the objective function are piecewise functions, the optimization problem (10.2)–(10.6) is a nonlinear integer programming problem.

The DPM works well if the demand at each node in the time-space network can be known for certain in advance. However, in reality, a large part of the demand is uncertain and is difficult to accurately forecast. In addition, the shipping time, as a part of the external service cost, is subject to the traffic congestion and delay. This calls for an extension of the model that can address these uncertainties and is the motivation for developing the Stochastic Planning Model in the next subsection.

10.3.3 Stochastic Planning Model

In the stochastic planning model (SPM), the demand at each node in the time-space network is assumed to be a random variable, the service time from a dispatch node to an arrival node is also set at a random variable, and both obey a normal distribution. In fact, the SPM proposed here can accommodate any other distributions, but the normal distribution is chosen for implementation in our computation in this study as a specific demonstration of the model. It is worth noting that SPM is designed to address the uncertainties in daily operation, namely, events that were observed and recorded in the past under normal conditions but not to capture extraordinary events or disasters such as an earthquake or an epidemic, which instead fall into the category of emergency logistics research.

(1) Penalty for plan time deviation

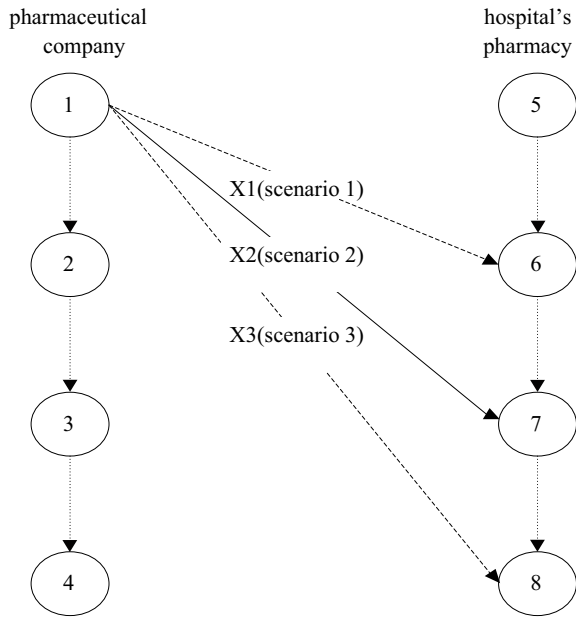
SPM is designed to minimize the expected deviation of the service time for all delivery links in the time-space network for the best planning effect. If the actual time of a medicine delivery is longer or shorter than the plan time of the activity in this link, there is an error in the service time estimate, which is to be penalized in the model.

As shown in Fig. 10.3, suppose that the actual service time is a random variable that can be 1, 2, or 3 days, respectively, with a probability of 0.2, 0.5 and 0.3 and that the planned time for this delivery is 2 days. If $X_1 = 1$, $X_2 = 2$, $X_3 = 3$, then the delivery time is one day less than the plan time in scenario 1, equal to the plan time in scenario 2, and one day more than the plan time in scenario 3. Therefore, in scenarios 1 and 3, the plan time has an error of time estimate and will be penalized for the estimate deviation. While an early arrival of the delivery may cause stocking problem and increase holding cost, a late arrival may affect the downstream workflows or even a shortage of this medicine in the hospital.

Let γ_{ij}^m be the penalty on arc (i, j) in the m th layer of the time-space network for each unit time deviation from the planned time. The expected penalty cost on arc (i, j) is:

$$pc_{ij}^m = \sum_{\omega \in \Omega} P_{ij}^m(\omega) |\Delta t_{ij}^m(\omega)| \gamma_{ij}^m \quad (10.7)$$

Fig. 10.3 Random service time in various scenarios



where $p_{ij}^m(\omega)$ is the probability of an early or late arrival in scenario ω for arc (i, j) and $\Delta t_{ij}^m(\omega)$ is the time deviation in scenario ω on service arc (i, j) . Therefore, the expected penalty cost for the previous example is:

$$pc_{X2}^m = 0.2 \times 1 \times \gamma_{X1}^m + 0.5 \times 0 \times \gamma_{X2}^m + 0.3 \times 1 \times \gamma_{X3}^m.$$

Note that the time deviation in the second term is zero, meaning that the second term can be removed.

(2) Mathematical formulation for SPM

The following is a list of the notations that will be employed in the formulation of SPM.

Sets

- C^m Set of the arcs in the execution stage in the m th layer of the time-space network.
- U^m Set of the arcs in the reference stage in the m th layer of the time-space network.
- CN^m Set of the nodes in the execution stage in the m th layer of the time-space network.
- UN^m Set of the nodes in the reference stage in the m th layer of the time-space network.
- CS^m Set of all arcs from pharmaceutical company to hospital's pharmacy in the C^m .

- US^m Set of the arcs from the pharmaceutical company to the hospital's pharmacy in the U^m .
- CZ^m Set of the arcs from the hospital's pharmacy to the departments in the C^m .
- UZ^m Set of the arcs from the hospital's pharmacy to the departments in the U^m .
- CH^m Set of the holding arcs in the C^m .
- UH^m Set of the holding arcs in the U^m .
- Ω Set of all scenarios ω .

Parameters

- $\Delta t_{ij}^m(\omega)$ Time deviation for the service arc (i, j) in scenario ω in the U^m .
- Δt_{ij}^m Time deviation for the service arc (i, j) in the C^m .
- $a_i^m(\omega)$ Supply or demand of node i in scenario ω in the m th layer of the time-space network ($a_i^m > 0$: indicates a supply node, $a_i^m \leq 0$: indicates a demand node).

Decision variables

- x_{ij}^m Arc flow on arc (i, j) in the C^m .
- $y_{ij}^m(\omega)$ Arc flow on arc (i, j) in scenario ω in the U^m .

Based on the notations, the SPM is defined by the following nonlinear stochastic integer programming problem:

$$\begin{aligned}
 \text{Min } z = & \sum_{m \in M} \sum_{ij \in CS^m} (f(x_{ij}^m) + |\Delta t_{ij}^m| \gamma_{ij}^m) x_{ij}^m \\
 & + E \left(\sum_{m \in M} \sum_{ij \in US^m} (f(y_{ij}^m(\omega)) + |\Delta t_{ij}^m(\omega)| \gamma_{ij}^m) y_{ij}^m(\omega) \right) \\
 & + \sum_{m \in M} \sum_{ij \in CZ^m} (ct_{ij}^m + |\Delta t_{ij}^m| \gamma_{ij}^m) x_{ij}^m \\
 & + E \left(\sum_{m \in M} \sum_{ij \in UZ^m} (ct_{ij}^m + |\Delta t_{ij}^m(\omega)| \gamma_{ij}^m) y_{ij}^m(\omega) \right) \\
 & + \sum_{m \in M} \sum_{ij \in CH^m} ch_{ij}^m x_{ij}^m + E \left(\sum_{m \in M} \sum_{ij \in UH^m} ch_{ij}^m y_{ij}^m(\omega) \right) \quad (10.8)
 \end{aligned}$$

$$\begin{aligned}
 \text{s.t.: } & \sum_{j \in CN^m} x_{ij}^m + \sum_{r \in UN^m} y_{ir}^m(\omega) - \sum_{p \in CN^m} x_{pi}^m \\
 & - \sum_{c \in UN^m} y_{ci}^m(\omega) = a_i^m(\omega), \quad \forall i \in N^m, m \in M, \omega \in \Omega \quad (10.9)
 \end{aligned}$$

$$\sum_{m \in M} x_{ij}^m \leq um_{ij}, \quad \forall ij \in CH^m \quad (10.10)$$

$$\sum_{m \in M} y_{ij}^m(\omega) \leq um_{ij}, \quad \forall ij \in UH^m, \omega \in \Omega \quad (10.11)$$

$$l_{ij}^m \leq x_{ij}^m \leq u_{ij}^m, \quad \forall ij \in C^m, m \in M \quad (10.12)$$

$$l_{ij}^m \leq y_{ij}^m(\omega) \leq u_{ij}^m, \quad \forall ij \in U^m, m \in M, \omega \in \Omega \quad (10.13)$$

$$x_{ij}^m \in INT, \quad \forall ij \in C^m, m \in M \quad (10.14)$$

$$y_{ij}^m(\omega) \in INT, \quad \forall ij \in U^m, m \in M, \omega \in \Omega \quad (10.15)$$

The objective function (10.8) minimizes the sum of the total expected logistics cost on all the arcs and the expected penalty cost of the plan. The constraints at (10.9) are the flow conservation equations for each node in the time-space network. The constraints at (10.10) and (10.11) are the capacity constraints. The constraints at (10.12) and (10.13) guarantee all the arc flows within their bounds. The constraints at (10.14) and (10.15) ensure that all flow variables are integers. Because the service costs in the objective function are piecewise functions, the optimization problem is a nonlinear stochastic integer programming problem.

10.4 Solution Algorithms and Evaluation Methods

This section develops efficient and effective algorithms for the DPM and the SPM. In both models, the arc costs are expressed by a piecewise linear function in the objective function, which increases the computational difficulty and complexity in solving these models. For a small problem, the costs can be found in a reasonable time using commercial software such as MATLAB and CPLEX. When the problem size becomes close to the practical one in the real world, it is impossible to be solved in a reasonable amount of time by using commercial software. Therefore, a suitable and effective procedure should be designed.

10.4.1 Solution Method for DPM

There are m medicine types, P service price schedules and T rounds of decision making ($T = PH/EP$) in DPM. Because these parameters increase, the complexity of the problem increases exponentially and it will make the model practically unsolvable by commercial software such as CPLEX directly.

A genetic algorithm (GA) can be an effective computational method to solve an optimization problem for which little is known. It can usually derive a highly qualified solution if it has been coded in the search criteria. A GA will then evolve

itself until the termination condition is satisfied, incorporating a cyclical process with successive operations of selection, crossover, mutation, and improvement.

The generic algorithm for the DPM is described as follows:

Step 1. There are 2 types of service prices for the parameter $f(x_{ij}^m)$, p and $0.9 \times p$. Herein, binary coding is adopted for the chromosome. 0 represents the service price p^m and the flow constraint $x_{ij}^m \leq X^m$. 1 denotes the service price $0.9 \times p^m$ and the flow constraint $x_{ij}^m > X^m$. Because there are m medicine types and T rounds of decision-making in a planning horizon, the length for a chromosome is $m \cdot T$.

Step 2. The fitness of each chromosome is obtained by calculating the objective function of the DPM, which means $f_i = fitness(pop_i(t))$.

Step 3. The selection operator is critically important since it can improve the average quality of the population by giving the high-quality chromosomes a better chance to be copied in the next generation [34]. There are two basic types of selection schemes that are widely used in practice: proportionate selection and ordinal-based selection. Proportionate selection selects chromosomes according to their fitness values relative to the fitness of other chromosomes, while ordinal-based selection selects chromosomes based on their fitness values compared to certain chromosomes in the population. In this study, a classic proportionate selection, the roulette wheel selection, is used to choose the new population. The probability distribution for the roulette wheel selection is calculated as follows:

$$p_i = \frac{f_i}{\sum_{i=1}^{Popsize} f}, \quad i = 1 \dots Popsize.$$

Step 4. Pairs of parents are selected for crossover in the population according to the crossover rate p_c . The crossover procedure exchanges the genes in pairs of parents in a random position to produce offspring. After that, the fitness of the parents and the offspring are compared, and then the best two chromosomes are adopted from them to replace the original parents in the population.

Step 5. Parents are selected for mutation in the population according to the mutation rate p_m . The mutation procedure uses a single-point mutation method, which mutates the gene (from 0 to 1 or from 1 to 0) in a random position to produce offspring. After that, the fitness of the paternal chromosome and the offspring will be compared, and the better one will be reserved. The mutation expands the search space for good solutions.

10.4.2 Solution Method for SPM

The heuristic procedure for the SPM is introduced below.

Step 1. Initialization; set all parameters in the SPM.

Step 2. Set $\lambda = 1$.

Step 3. Generate Ω groups of data as the demand data for all nodes in the time-space network according to the given distribution functions. Relax the constraints in the SPM and disassemble the stochastic model into Ω deterministic models.

Step 4. Solve the deterministic models with GA and compare the results for each arc. Choose the arcs with constant flow quantity or minor changes. Calculate the average value and use it as the arc flow quantity.

The pick method is illustrated as follows. First, calculate the average value and standard deviation of the arc flow quantity on the same arc with different scenarios. Then, filtrate the arc with the statistical constraint $|X_\omega - \bar{X}| \leq \alpha \cdot \sigma$. Herein, X_ω is the arc flow quantity on the same arc with a different scenario, \bar{X} is the average value, σ is the standard deviation, and α is a coefficient of determination.

Step 5. If $\lambda = \Lambda$, where Λ is a given number, go to Step 6; otherwise, $\lambda = \lambda + 1$, and return to Step 3.

Step 6. Input the information of average demand at each node and the arc flows, which have been confirmed in Step 4, into the deterministic model, solve it again and obtain the arc flows for these unconfirmed arcs.

10.4.3 Evaluation Method

According to the dynamic decision-making framework in Sect. 3.1, an evaluation method is designed to assess the performance of the DPM and the SPM. The rationale of this evaluation method is introduced below. When the planning time is at an end, the actual demand information in each node and the actual service time between any two nodes will be collected. These data will be used as the input data, and the deterministic model will be solved again. Intuitively, an optimal logistics planning result with the complete information will be obtained. Herein, it is referred as the ideal planning model (IPM). In theory, the logistics planning result in IPM is the optimized result. Therefore, it can be used as a reference standard to evaluate the performance of the DPM and the SPM.

10.5 Numerical Tests

To test the practicality and efficiency of the proposed models and algorithms, numerical tests use operating data from Gulou Hospital in Nanjing with reasonable simplifications are performed in this section. MATLAB software is used as the development environment, coupled with CPLEX 12.4. The tests are performed on an Intel Pentium 1.87 GHz desktop computer with 6 GB RAM in a Microsoft Windows 7 environment.

10.5.1 Data Setting

As a numerical example, 5 departments and 3 medicine types in Gulou Hospital are chosen as our sample. The planning horizon is set at 12 days. The execution phase is 2 days. Six rounds of decision-making are constructed for this numerical test. Demand information from these medicines over the past 5 years is adopted as our basic data. For each node in the time-space network, the average demand with the basic data is used as the deterministic demand information in the DPM. The mean value of Δt in the SPM is 0, and the variance is set at 2. The determination coefficient α is set at 0.6. Of course, it can be other values in an actual operation depending on the actual need. The unit time penalty costs are 1 and 0.5 CNY, respectively, for the external service arc and the internal delivery arc. The service prices for the 3 types of medicines are 20, 30 and 10 CNY, and the order quantities for the price discount are 770, 1232 and 2170, respectively. The holding cost is set at 20% of the service cost. The unit internal delivery cost for each type of medicine is 3 CNY. The safety stock in the hospital's pharmacy is set at 5 times its daily demand. The safety stock in the department is set at its daily demand. The capacity of the hospital's pharmacy and the department are set at 20 times its their daily demand.

10.5.2 Test Results

(1) Performance of the GA

The crossover probability is set at 0.6, and the mutation probability is set at 0.1. The population size is set at 30. To test the best iteration number, the maximum iteration number is set at 20, 30, 40, 50, 70, and 100, respectively. The results are shown in Fig. 10.4. When the iteration number is more than 70, the optimal result is stable. Therefore, the iteration number is set at 70 in the following test. As introduced in Sect. 4.1, for each permutation and combination of the three parameters m , P and T , the DPM will be an integer programming, and it can be solved with the CPLEX software directly. The performance of the proposed GA and the CPLEX software is compared in Table 10.3.

In the 1st round of decision-making, there are 262,144 possibilities for the permutation and combination, which means it should be delayed for a long period of time (6591 s, 1 h and 50 min) to obtain the optimal result when the CPLEX software is used to solve the model directly. However, when the proposed GA is applied, a near-optimal solution can be obtained in less than 2 min (110 s). The result with GA may be slightly inferior. However, the performance of the calculation time shows that its calculation ability outperforms the commercial software, particularly when the problem scale is large.

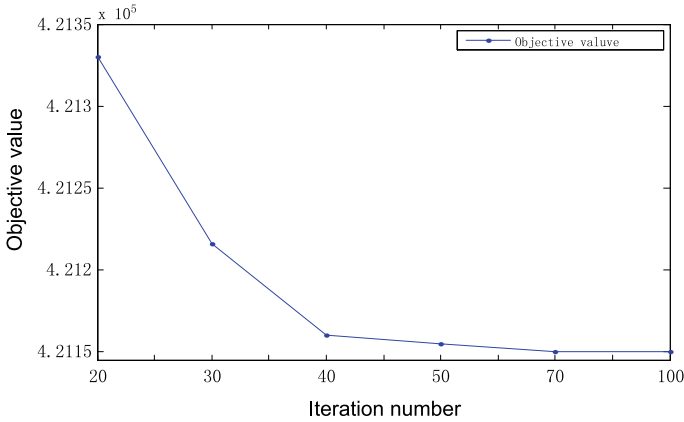


Fig. 10.4 Test of the maximum iteration number

Table 10.3 Comparison of the solution results

Round	Objective value			Solution time		
	CPLEX (CNY)	GA (CNY)	Gap (%)	CPLEX (s)	GA (s)	Gap (%)
1	419,991	421,180	-0.28	6591	110	98
2	312,923	313,385	-0.15	829	90	89
3	263,878	264,079	-0.07	129	56	57
4	190,551	190,655	-0.05	5.9	5.6	5
5	98,769	98,790	-0.02	0.8	0.78	2.5
6	10,618	10,618	0.00	0.1	0.1	0

$$\text{GAP} = (\text{CPLEX} - \text{GA}) / \text{CPLEX} * 100\%$$

(2) Performance of the proposed two models

To compare the performances of the DPM and the SPM, the test results are collected together in Table 10.4. First, it can be observed that the objective value shows a decreasing tendency as the decision-making round increases because the dynamic decision making framework is applied in this work. In the 1st round of decision making, logistics planning for the whole 12 days is solved. Additionally, in the last round, planning for only 2 days is solved. Second, it can be observed that the SPM shows better performance most of time because the objective values in the SPM are always smaller than in the DPM, except for the 1st round. The planning results should not mislead the reader into believing that the DPM performs more poorly than the SPM. The actual performance of these planning methods can be evaluated after their application to actual operations. In this test, it is observed that the solution time using the SPM is much longer than the DPM, which is the weakness of the SPM.

According to the dynamic decision making framework in Sect. 3.1, when a decision is made in each round, an optimal result is solved for its planning time (notice

Table 10.4 Comparison of the DPM and the SPM

Round		1	2	3	4	5	6
DPM	Objective value (CNY)	421,150	313,322	277,746	190,551	98,769	10,618
	Solution time (s)	111.92	90.00	56.47	5.91	0.72	0.11
SPM	Objective value (CNY)	462,268	262,373	211,041	118,327	45,360	11,866
	Solution time (s)	2237	1923	1184	179	18	2
Gap	Objective value (%)	8.89	-19.42	-31.61	-61.04	-117.74	10.52
	Solution time (%)	95	95	95	97	96	95

$$\text{Gap} = ((\text{SPM} - \text{DPM})/\text{SPM}) * 100\%$$

that the planning time is variable), and only the schedules during the execution stage are adopted because this stage is a short period and the demand and service time at this stage are relatively clear and unchanged. After that, the demand information and service time will be updated. Therefore, the optimal result for each execution stage can be collected whether it is in the DPM or the SPM. When the planning time is at an end, the actual demand information in each node and the actual service time between any two nodes can be collected. These data are used as the input data for the IPM. The results are shown in Table 10.5.

It can be observed that logistics cost in each execution stage is a fluctuating value. Generally, in the 1st execution stage, managers will order a larger quantity of the required medicine to obtain the discount of the service cost and decrease the delivery trips. Therefore, the logistics costs in the following two execution stages can remain at a relatively low level. After this, the medicine should be ordered again to guarantee the demand, and thus the logistics cost increases again in the 4th execution stage. The difference is shown in the 5th execution stage. The medicine should be ordered once more in this stage when the DPM is applied. However, the order quantity in the 4th stage can satisfy the last two stages when the SPM is adopted. The total logistics cost obtained from the SPM (with a value of 395,290 CNY) is 0.56% higher than the IPM (with a value of 393,071 CNY). This proportion for the DPM is 1.88%. It

Table 10.5 Test results for each execution stage

Round	1	2	3	4	5	6	Total cost	Gap (%)
DPM (CNY)	102,406	66,671	48,021	81,427	81,167	20,759	400,451	1.88
SPM (CNY)	151,766	43,525	59,702	91,427	32,806	16,064	395,290	0.56
IPM (CNY)	151,435	43,218	59,304	91,143	32,310	15,661	393,071	-

$$\text{Gap} = ((\text{DPM} - \text{IPM})/\text{IPM}) * 100\% \text{ or } ((\text{SPM} - \text{IPM})/\text{IPM}) * 100\%$$

appears that the SPM yields the better solution. The main reason is that uncertain disruptions have been considered in the SPM, while the demand and service time in the DPM are deterministic.

10.5.3 Sensitivity Analysis

The proposed models and solution methods described in Sects. 10.3 and 10.4 provide several key parameters that may affect the solution: the average demand, the standard deviation and the safety stock. A sensitivity analysis of these parameters is performed as follows.

First, the ratio of the average demand is set with 5 different values (-50 , -25 , 0 , $+25$ and $+50\%$) to see the influence in the final solution. As shown in Table 10.6, the sum of the logistics cost increases as the value of the ratio increases, regardless of which planning model is used. This suggests that the higher the average demand is, the higher the total logistics cost becomes. If the manager can find a way to reduce the average demand, the sum of the logistics cost can be reduced. However, this requires further investigation and could be a topic of future research. Another interesting result is the gaps between the two proposed models and the IPM. The gaps between the DPM and the IPM change from 3.56 to 1.24%, while the gaps between the SPM and the IPM vary from 1.33 to 0.2%. Both decrease as the value of the ratio increases.

To examine the impact of the standard deviation changes on the models' performance, 5 different values (-50 , -25 , 0 , $+25$ and $+50\%$) of the standard deviation in both average demand and the uncertain service time are tested. As shown in Table 10.7, the sum of the logistics cost in SPM increases slightly as the standard deviation of the average demand increases (with a value from 393,894 to 396,586 CNY). However, the values in IPM almost show no changes. Therefore, the gaps between the SPM and the IPM gradually increase (with a value from 0.22 to 0.88%), while the gaps between the DPM and the IPM show almost no change. Table 10.8 shows a similar variation trend. According to these two tables, it can be concluded that the standard deviation changes only have a small influence on the models' performance. However, the SPM's performance becomes unstable with the increase of the standard deviation.

Table 10.6 Sensitivity analysis of the ratio of average demand

Ratio (%)	-50	-25	0	+25	+50
DPM (CNY)	195,420	300,338	400,451	500,964	601,477
SPM (CNY)	191,203	296,467	395,290	496,088	595,307
IPM (CNY)	188,702	294,029	393,071	494,590	594,085
DPM versus IPM (%)	3.56	2.15	1.88	1.29	1.24
SPM versus IPM (%)	1.33	0.83	0.56	0.30	0.20

Table 10.7 Sensitivity analysis of the ratio of standard deviation (average demand)

Ratio (%)	-50	-25	0	+25	+50
DPM (CNY)	-	-	400,451	-	-
SPM (CNY)	393,894	394,642	395,290	395,887	396,586
IPM (CNY)	393,025	393,110	393,071	393,192	393,126
DPM versus IPM (%)	1.89	1.87	1.88	1.85	1.86
SPM versus IPM (%)	0.22	0.39	0.56	0.69	0.88

Table 10.8 Sensitivity analysis of the ratio of the standard deviation (service time)

Ratio (%)	-50	-25	0	+25	+50
DPM (CNY)	-	-	400,451	-	-
SPM (CNY)	394,731	394,996	395,290	395,672	396,025
IPM (CNY)	393,075	393,019	393,071	393,138	393,151
DPM versus IPM (%)	1.88	1.89	1.88	1.86	1.86
SPM versus IPM (%)	0.42	0.50	0.56	0.64	0.73

Table 10.9 Sensitivity analysis of the ratio of safety stock

Ratio (%)	-50	-25	0	+25	+50
DPM (CNY)	396,452	391,282	400,451	409,661	419,266
SPM (CNY)	383,170	380,198	395,290	404,381	416,628
IPM (CNY)	373,037	378,703	393,071	402,139	410,293
DPM versus IPM (%)	6.28	3.32	1.88	1.87	2.19
SPM versus IPM (%)	2.72	0.39	0.56	0.56	1.54

The impact of the changes in the safety stock is also examined. As shown in Table 10.9, the total logistics cost decreases first and then increases as the safety stock increases, regardless of which planning model is adopted. The gaps between the two proposed models and the IPM show the same tendencies. The optimal result can be obtained when the safety stock is 75% of the present setting. This means that when the safety stock in the departments is set at 75% of their daily demand in the test, better logistics planning can be designed.

10.6 Conclusions

Two medicine logistics planning models are developed in this study based on a time-space network approach for daily logistics operations in medicine management for a hospital. The deterministic planning model (DPM) is designed for logistics problems whose demand and service time can be known for certain in advance. The

stochastic planning model (SPM) is developed to address uncertain demand and uncertain service time. Efficient computational schemes are specially designed for each of the models to effectively find an optimal solution. An evaluation method is presented to compare the performance of these two models through numerical tests running on the data for Gulou Hospital in Nanjing, China. The test results show that SPM outperforms DPM in terms of both cost minimization and robustness. A sensitivity analysis is conducted to see how the parameters affect the performance of the proposed models.

The contribution of this work to the literature can be recognized in three aspects: (1) Most research on medicine logistics planning focuses either on the demand uncertainty or only on service time uncertainty. The SPM model in this study addresses both certainties at the same time. (2) Variable service costs are incorporated in a model that accounts for realistic concerns such as price discount strategies, transportation consolidation, economies of scale, etc. for the first time. (3) Penalties have been introduced in our model to penalize early or late arrival of scheduled medicine deliveries that may generate additional costs for medicine logistics, such as increased stocking and holding costs or the shortage of a medicine in the downstream flow.

The application prospects of the model are particularly promising now given China's current medical and healthcare system reform process. Traditionally, most patients in China go to hospitals to see a doctor and obtain their prescriptions from the hospital pharmacy because of the culture and the current prevailing health insurance plans in China. Hospitals earn most of their revenue from medicine sales by marking up the price. Consequently, medicine inventory levels in most hospitals remain high year round, blocking capital flow and increasing the risk of medicine expiration. The proposed models in this study are in support of a hospital pharmacy trusteeship (HPT) that would outsource hospital pharmacy services to a major pharmaceutical company using a vendor managed inventory system. Our research is from the standpoint of a major medicine supplier (a pharmaceutical company) that acts as a vendor manager for a hospital in generating an optimal logistic plan to minimize the operational cost and logistical risk of stock-out. As is explicitly factored into the objective function, our model aims to provide a stable and economic medicine logistic plan that addresses the uncertainties in demand and service time and minimizes the total operational costs, including in external and internal delivery, inventory holding, and distribution. The potential benefit for the hospital in such HPT practice is apparent and enormous. By outsourcing the pharmacy to supplier, a hospital severs a large portion of their payroll costs in labor and management, inventory costs, the costs of expired medicine and liability cost of lawsuits. More importantly, by outsourcing the pharmacy business, a hospital can concentrate on its mission of diagnosing and treating patients, which is one of the main purposes of the medical system reform. Since 2013, the Chinese government has been in the process of enforcing a zero mark-up price policy as part of the medical and health care system reform. For the implementation of this policy, hospitals must surrender their for-profit pharmacy business, willingly or otherwise, and outsourcing has been widely recognized as a feasible and effective solution.

There are several directions that can be extended and enhanced. First, hospitals can collaborate in their medicine logistics planning, such as consolidating their shipments from the same pharmaceutical company and reducing expensive medicine inventory units in the hospitals to reduce the carrying costs and reduce the risk of supply shortage. Second, a mechanism of penalty weight adjustment can be proposed and studied to find the most effective penalty weights based on the cost structure of the service arcs and distribution of service times. Third, it will be interesting on a practical level to study the measures to avoid stock outs of critical medicines and incorporate such measures into a medicine logistics plan.

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Chapter 11

Medical Resources Order and Shipment in Community Health Service Centers



Medical resources scheduling affects the medical institution's operation cost, customer satisfaction and medical service quality. Therefore, a lean arrangement of medical resources order and shipment is quite necessary and important. In this chapter, we propose two optimal models for medical resources order and shipment in community health service centers (CHSCs), with a dual emphasis on minimizing the total operation cost and improving the operation level in practice. The first planning model is a deterministic planning model (DM). Systematically, it considers constraints including the lead time of the suppliers, the storage capacity of the medical institutions, and the integrated shipment planning in the dimensions of time and space. The problem is a multi-commodities flow problem and is formulated as a mixed 0–1 integer programming model. Considering the stochastic demand, the second model is constructed as a stochastic programming model (SM). A solution procedure is developed to solve the two models and a simulation-based evaluation method is presented to compare the performances of the proposed models. The main contributions of this study include the following two aspects: (1) most research on medical resources allocation studies a static problem taking no consideration of the time evolution and the time-varying demand. In this study, time-space network technique is adopted to depict the logistics situation in CHSCs from both time and space dimensions. (2) The logistics plans in response to the deterministic demand and the time-varying demand are constructed as a 0–1 mixed integer programming model and a stochastic integer programming model, respectively. The optimal solutions can not only minimize the total operation cost, but also improve the order and shipment operation in practice. Generally, medical resources in CHSCs are purchased by telephone or e-mail. The important parameters in decision making, i.e., order/shipment frequency and order quantity, are manually determined by the decision maker based upon his/her experience. The planned schedules may not be efficient or feasible to satisfy all demands since a large portion of customer requests are uncertain and time-varying. The proposed methods in this chapter could be effective in solving the problems in actual operations.

11.1 Introduction

In 2014, we conducted a research on medicine supply chain situation in CHSCs in Nanjing, China, by using the questionnaire survey method. The result shows that most CHSCs currently in this city do not use any electronic purchase systems or decision support systems to help optimize the ordering and scheduling work. Medical resources are always purchased by telephone or e-mail. The important parameters in decision making, i.e., order/shipment frequency and order quantity, are manually determined by the decision maker based on his/her experience. The planned schedules may not be efficient, or may not be feasible to satisfy all demands since a large portion of customer service requests in CHSCs are uncertain and time-varying [1]. The result of the questionnaire survey motivates us to improve the situation and to develop a systematic planning approach that takes all these factors into consideration.

In line with our survey, CHSC purchases medical resources from its upstream authorities, the District Center for Disease Control and Prevention (DCDC), and DCDC imports medical resources from the pharmaceutical companies (the suppliers). A lead time is required for the supplier, to produce the required medical resources. Similarly, a lead time is required for the DCDC to check the quality of medical resources. Generally, a compacted scheduling of medical resources order and shipment can not only efficiently reduce the operation cost, but also promote the medical service quality. However, to the best of our knowledge, although many studies have focused on medical resources scheduling, few of them consider the problem of medical resources scheduling problem in CHSCs with uncertain demands, lead time, as well as capacity constraint.

In this chapter, we consider the medical resources scheduling problem in CHSCs with time-varying demand, the lead time of supplier, the capacity constraint. Meanwhile, the scheduling problem integrates the shipment planning in the dimensions of time and space.

11.2 Literature Review

Numerous studies have focused on medical resources scheduling, including medicine ordering, shipment and medical resources allocation. We briefly introduce them in the following paragraphs.

Initially, a most related empirical study is provided by Dib et al. [2]. They investigated 58 community health centers and surveyed 372 residents randomly about their satisfaction towards these centers in Dalian, China. They suggested that the medicine supply chain for the community health centers should be improved and the superior departments support to the community health centers should be augmented.

In the second place, theory research with the topic of medical resources scheduling have been conducted by many experts. For example, Tebbens et al. [3] proposed a mathematical framework for determining the optimal management of a vaccine

stockpile over time. Sun et al. [4] built mathematical models to optimize the patients' allocation considering two objectives related to patients' cost of access to healthcare services: (1) minimizing the total travel distance to hospitals; and (2) minimizing the maximum distance a patient travels to a hospital. Moreover, the models can help decision makers to predict a resources shortage during a pandemic influenza outbreak. Savachkin and Uribe [5] presented a simulation optimization model to generate dynamic strategies for distribution of limited mitigation resources, such as vaccines and antivirals, over a network of regional outbreaks. The model can redistribute the resources remaining from previous allocations in response to changes in the pandemic progress. Jerić and Figueira [6] addressed the issue of scheduling medical treatments for resident patients in a hospital as a multi-objective binary integer programming (BIP) model and three types of heuristics were proposed and implemented to solve it. Rottkemper et al. [7] designed a mixed-integer programming model for distribution and inventory relocation under uncertainty in humanitarian operations. Rachaniotis et al. [8] presented a resources scheduling model in epidemic control with limited resources. The objective is to minimize the total amount of the infected people in a certain time horizon by relocating the available resources over several regions. Dasaklis et al. [9] suggested several future research directions and defined the roles of logistics operations and their management may play in assisting the control of epidemic outbreaks.

Thirdly, as to the variability and uncertainty characteristics of the demand, Holte and Mannino [10] presented that a major difficulty in medical resources allocation stems from the fact that such an allocation must be established several months in advance, and the exact number of patients for each specialty is an uncertain parameter. They modeled the uncertain problem as adjustable robust scheduling problem and developed a row and column generation algorithm to solve it. Beraldi et al. [11] considered the inherent uncertainty in emergency medical services and developed a stochastic programming model with probabilistic constraints, which aims to decide the location of the service sites and the amount of emergency vehicles to be assigned to each site. Zhang and Jiang [12] presented a bi-objective robust program to design a cost-responsiveness efficient emergency medical services (EMS) system under uncertainty. The proposed model simultaneously determined the location of EMS stations, the assignment of demand areas to EMS stations, and the number of EMS vehicles at each station to balance cost and responsiveness. Nikakhtar and Hsiang [13] considered uncertain situations such as epidemic diseases that could affect the patient flow in a healthcare system by developing a discrete-event simulation model for a local community health clinic in Lubbock, Texas. To tackle the uncertain nature of emergency department and improve the resources management, Xu et al. [14] used self-organizing map, k-means, and hierarchical methods to group patients based on their medical procedures, and then discussed how the resulting patient groups can be used to enhance the emergency department resources planning.

In summary, the time-varying demand in CHSCs, with multiple medical resources types and the optimal scheduling of ordering and shipment are highly correlated with each other. It is difficult to use the traditional integer programming techniques to formulate and efficiently solve this type of problem. On the other hand, the time-space

network method has been popularly employed to solve scheduling problems, which provides a natural and efficient way to represent multiple conveyance routings with multiple commodities in the dimensions of time and space. Although the resulting model scale is generally enlarged due to the extension in the dimension of time, complicated time-related constraints can normally be easily modeled for realistic problems, particularly in comparison with the space network models [15]. Coupled with the development of efficient algorithms, the time-space network models (usually formulated as multiple commodity network flow problems) can be effectively and efficiently solved [16–19]. Therefore, time-space network technique could be suitable to solve the medical resources scheduling problem in CHSCs.

11.3 Modeling Approach

In this section, we discuss the network structure and mathematical formulation for the planning of logistical support in CHSCs. A time-space network framework is employed to denote the medical resources order and shipment scheduling. Based on the time-space network, a deterministic planning model (DM) is developed to address the issue of knowing the demand in CHSCs in advance. A stochastic planning model (SM) is then presented to address the issue of stochastic demand in actual operations. In what follows, we will first introduce the time-space network that serves as the basis for our mathematical formulations.

11.3.1 Network Structure

The time-space network of logistical support in CHSCs denotes the potential order and shipment of the medical resources within a certain period and space locations, as shown in Fig. 11.1. The vertical axis represents the supplier, the district center for disease control and prevention (DCDC) and the CHSCs, while the horizontal axis stands for the duration of time. Each node denotes the different department at a specific time. The shorter the time interval is, the more accurate the decision-making is. Three types of arcs are defined below.

(1) Ordering arc

An ordering arc (see (a–b) in Fig. 11.1) represents an order from the DCDC to the supplier, or an order from the CHSC to the DCDC. While an ordering arc exists, an ordering cost is incurred no matter when the order takes place, and how many medical resources are purchased. Note that order operation is always completed by telephone or e-mail in practice, thus there is no physical flow on the ordering arc. The arc flow, which is a binary variable, denotes whether an order is placed or not. The arc flow's upper bound is one, indicating that an order takes place. Intuitively, the arc flow's low bound is zero.

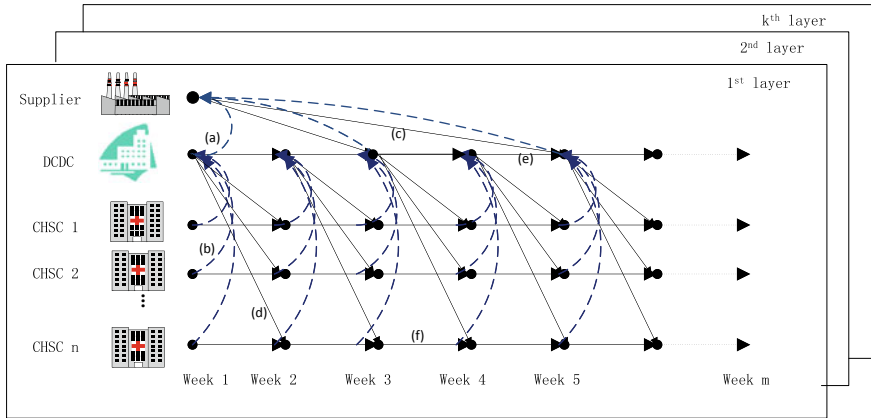


Fig. 11.1 Time-space network of medical resources flows

(2) Shipment arc

A shipment arc (see (c–d) in Fig. 11.1) represents medical resources are delivered from the supplier to the DCDC or from the DCDC to the CHSC. The cost for the shipment arc is also comprised of two parts, which are the constant cost that is incurred whenever the shipment takes place and regardless of the quantity of medical resources, and a variable cost represented by travel distance, carry hours used, meals etc., which is in proportion to the quantity of medical resources shipped. Since the shipment arc connects different depots, the arc flow’s upper bound is the capacity of the DCDC or the CHSC, and the arc flow’s low bound is zero.

(3) Holding arc

A holding arc (see (e–f) in Fig. 11.1) represents the holding of medical resources at DCDC or CHSC. The arc cost denotes the inventory cost incurred by holding medical resources, which is in proportion to the stored quantity of medical resources on the arc. Therefore, the arc flow’s upper bound is also the capacity of the node (DCDC or CHSC), and the arc flow’s low bound is zero.

11.3.2 The Deterministic Planning Model (DM)

Before introducing the model’s formulation, the notations and symbols are listed below:

Sets

- A^k Set of all arcs in the k th layer of the time-space network.
- N^k Set of all nodes in the k th layer of the time-space network.
- K Set of the k th layer of the time-space network.
- H Set of all holding arcs in the time-space network.

Parameters

- c_{ij}^k Arc (i, j) cost in the k th layer of the time-space network; if the arc is a ordering arc, the arc cost is the ordering cost; if the arc is a shipment arc, the arc cost is the shipment cost; if the arc is a holding arc, the arc cost is the inventory cost incurred by holding the medical resources.
- u_{ij}^k Arc (i, j) flow's upper bound in the k th layer of the time-space network.
- l_{ij}^k Arc (i, j) flow's lower bound in the k th layer of the time-space network.
- um_{ij} Storage capacity (DCDC or CHSC) for the holding arc (i, j) flow.
- a_i^k The supply or demand of medical resources at node i in the k th layer of the time-space network; if $a_i^k \geq 0$, the supply of medical resources; if $a_i^k < 0$, the demand of medical resources; at the time slot for beginning dispatching, the supply at the DCDC and the CHSC equals to its storage capacity.

Decision variables

- x_{ij}^k Arc (i, j) flow in the k th layer of the time-space network.

Based on the notations, the mathematical formulation of DM can be formulated as follows:

$$\text{Min: } Z = \sum_{k \in K} \sum_{ij \in A} c_{ij}^k x_{ij}^k, \quad (11.1)$$

$$\text{s.t.: } \sum_{j \in N^k} x_{ij}^k - \sum_{l \in N^k} x_{li}^k = a_i^k, \quad \forall i \in N^k, k \in K, \quad (11.2)$$

$$\sum_{k \in K} x_{ij}^k \leq um_{ij}, \quad \forall ij \in H, \quad (11.3)$$

$$l_{ij}^k \leq x_{ij}^k \leq u_{ij}^k, \quad \forall ij \in A^k, k \in K, \quad (11.4)$$

$$x_{ij}^k \in I, \quad \forall ij \in A^k, k \in K. \quad (11.5)$$

The objective function (11.1) minimizes the sum of the operation cost, including the ordering cost, the shipment cost and the holding cost. Constraint (11.2) is the flow conservation constraint for each node in the time-space network. Constraint (11.3) is the capacity constraints. Constraint (11.4) guarantees that all arc flows are within their bounds. Constraint (11.5) ensures that all flow variables are integers.

Since all constraints and cost functions in this optimization model are linear, the proposed multi-commodity flow problem is formulated as a mixed 0–1 integer programming model. The optimal result can be put to practical use if we can identify the demand at each node in the time-space network in advance. However, a large part of the demand for medical resources are stochastic and are difficult to be accurately forecasted, which make the planned medicine scheduling unable to satisfy all those demands that suddenly pop up. Therefore, we need to improve the model to make it more realistic and practical.

11.3.3 The Stochastic Planning Model (SM)

The network structure of the SM is the same to the network of the DM, except that the demand at each node in the time-space network is uncertain. It is worth mentioning that only the normal stochastic demand is considered in this work. Large-scale disruption of the demand which may be caused by some unexpected public health incidents (i.e., SARS) goes beyond our research scope. To formulate the SM, we set more notations and symbols as follows in addition to those already introduced.

Set

Ω The set of stochastic situations.

Parameters

$a_i^k(\omega)$ The stochastic supply or demand for medical resources at node i in the k th layer of the time-space network; if $a_i^k \geq 0$, the stochastic supply of medical resources; if $a_i^k < 0$, the stochastic demand of medical resources; at the time slot for beginning dispatching, the stochastic supply at the DCDC and the CHSC is still set to be its storage capacity.

$E()$ Excepted cost of the logistics arcs with the stochastic demand.

Decision variables

$x_{ij}^k(\omega)$ Arc (i, j) flow in the k th layer of the time-space network with the stochastic situation ω .

Based on the notations, the SM can be formulated as follows:

$$\text{Min: } Z = E \left(\sum_{k \in K} \sum_{ij \in A} c_{ij}^k x_{ij}^k(\omega) \right), \quad (11.6)$$

$$\text{s.t.: } \sum_{j \in N^k} x_{ij}^k(\omega) - \sum_{l \in N^k} x_{li}^k(\omega) = a_i^k(\omega), \quad \forall i \in N^k, k \in K, \omega \in \Omega, \quad (11.7)$$

$$\sum_{k \in K} x_{ij}^k(\omega) \leq um_{ij}, \quad \forall ij \in H, \omega \in \Omega, \quad (11.8)$$

$$l_{ij}^k \leq x_{ij}^k(\omega) \leq u_{ij}^k, \quad \forall ij \in A^k, k \in K, \omega \in \Omega, \quad (11.9)$$

$$x_{ij}^k(\omega) \in I, \quad \forall ij \in A^k, k \in K, \omega \in \Omega. \quad (11.10)$$

Similarly, the objective function (11.6) minimizes the excepted value of the operation cost. Constraint (11.7) is the flow conservation constraint for each node in the time-space network. Constraint (11.8) is the capacity constraint with stochastic demand. Constraint (11.9) guarantees that all arc flows with stochastic demand are within their bounds. Constraint (11.10) ensures that all flow variables with stochastic

demand are integers. Since all decision variables are time-varying with the stochastic demand, the proposed problem can be processed as a stochastic integer programming model. The optimal result would be more realistic and practical.

11.4 Solution Procedure and Evaluation Method

In this section, we will discuss how to solve the proposed models and how to evaluate them based on a simulation method.

11.4.1 Solution Procedure

The DM is formulated as a mixed 0–1 integer programming model and it can be solved within a reasonable time, by using the mathematical tool MATLAB, coupled with the optimal software CPLEX 12.4. The SM is formulated to depict the stochastic demand at each time point, and the model is constructed as a stochastic integer programming model. Given the demand for each node in the time-space network, the SM can be solved as a deterministic planning model. Therefore, the solution procedure for the SM is described as follows:

Procedure for the SM:

Input: Initial parameters in the SM and the distribution function of demand.

Output: The optimal scheduling and the operation cost of the medical resources order and shipment for the DCDCs and the CHSCs.

Begin

Initialization, set C as the number of simulation times, $c = 1, 2, \dots, n$;

$c \leftarrow 1$;

while (not termination condition) do

1. Randomly generate the demand for each CHSC in the time-space network according to the distribution function;

2. Solve the mixed 0-1 integer programming model by using the MATLAB compiler, coupled with CPLEX 12.4 ;

3. Record the optimal schedules and the operation cost.

$c \leftarrow c + 1$;

end

4. Calculate the average operation cost as the final result.

5. Output optimal scheduling and the operation cost.

End

11.4.2 Evaluation Method

In practice, a classic order strategy, the (t, S) strategy, has always been adopted to manage the medicine inventory in both CHSC and DCDC. That means, the CHSC and the DCDC will import medical resources with a fixed time interval. The purpose of the order is to keep the stock of medical resources at a certain level. Herein, we address it as the actual operations of medical resources scheduling and we abbreviate it as AOM. Similarly in the SM, demand for each node in the time-space network is randomly generated. The first difference between the AOM and the SM is the order quantity, which is equal to the capacity of the node minus the available quantity of medical resources when decision making. The second difference between these two models is the fixed time interval, which is set to be two weeks. Similarly, the AOM can be solved by using the above solution procedure.

The performances of the DM, the SM, and the AOM are evaluated via a simulation test. We first use the average demand of the historical demand data to complete the DM calculation. Next we randomly generate the stochastic demand data based on the average demand with a certain standard deviation, and input them into the SM and then solve it. After that, we fix the ordering time interval and adopt the (t, S) strategy to complete the AOM calculation. Finally, we compare the DM, the SM and the AOM with statistical results.

11.5 Numerical Tests

To test how well the models may be applied in the real world, we perform numerical tests using operating data from 5 CHSCs in Nanjing, China, with reasonable simplifications. 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 Windows 7.

11.5.1 Parameters Setting

This numerical example focuses on the scheduling of logistical support for medical resources order and shipment in CHSCs. The planning period is set to be half a year (26 weeks). Lead time of the supplier is set to be 2 weeks, and lead time of the DCDC is 1 week. Each layer of the time-space network, which represents a kind of the medicine, involves 1 supplier, 1 DCDC and 5 CHSCs. The historical data of the order quantity for each kind of vaccines in the past years, from January 2011 to June 2013, was collected when we conducted the questionnaire survey in the CHSCs in Nanjing, China. For example, the historical data of influenza vaccine during these years in a CHSC is shown in Fig. 11.2. According to the historical data, we can

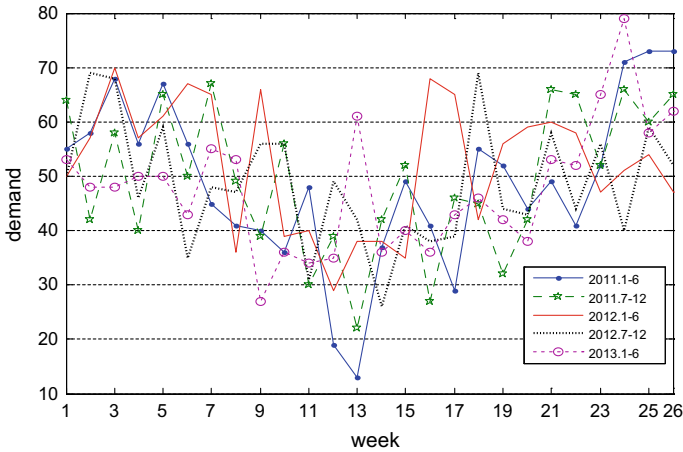


Fig. 11.2 Historical data of influenza vaccine

calculate the average demand for each kind of vaccines at each week. The standard deviation of the stochastic demand is set to be 10. In practice, the decision makers can adjust these parameters according to the actual situation.

11.5.2 Test Results

As introduced above, we use the AOM to simulate the actual operation of the medical resources order and shipment, and we present two other methods, the DM and the SM, to address with different demand situations. DM is designed to deal with the scheduling when demand at each time point is preset in advance, and SM is proposed to complete the planning when demand is uncertain. The performances of these three methods are shown in Table 11.1. The objective value of the SM (638,087.2) is the smallest one, which is 35.4% lower than the operation cost of the AOM (987,950.1). Similarly, the objective value of the DM is 643,167.5, which is 34.8% lower than the cost of the AOM and only 0.78% lower than the value of the SM. It can be observed that both of the two proposed methods are superior to the empirical operations in

Table 11.1 Comparison of different methods

Planning method	DM	SM	AOM
Average objective value	643,167.5	638,087.2	987,950.1*
Average solution time (s)	834.44	314.38	N/A
<i>Gap (%)</i>			
Difference in the total cost between other methods and the AOM	34.8	35.4	0.0

actual operations, and the performance of the DM is a little inferior to the SM. This result is quite suitable and meaningful for the actual operations.

It is worth mentioning that out-of-stock situation occurred during the AOM test (we use the symbol * to label it). A shortage of the third kind of medical resources was appeared at the 7th week and the 25th week, with a quantity of 3 and 6, respectively. However, this phenomenon does not occur in both the DM and the SM. The reason is that both the order time and order quantity in these two models are decision variables and would be systematically optimized, while both the order time and order quantity in AOM are pre-set. As introduced in Sect. 11.1, if the important parameters, such as order/shipment frequency and order quantity, are manually determined by the decision maker based on his/her experience, the planned schedules may not be efficient, or may not be at all feasible to satisfy all demands since a large portion of customer service requests in CHSCs are uncertain and time-varying.

11.5.3 Sensitivity Analysis

To understand the influence of stochastic demand on the solution, we perform sensitivity analysis of the change of demand to the operation cost. The proposed models in Sect. 11.3 provide several key parameters that may affect the final result, i.e., the average demand of medical resources in each planning week, the standard deviation setting, and the capacity of DCDC and CHSC, etc. The sensitivity analyses of these parameters are shown as follows.

To detect the influence of the average demand on the final solution, the value of it is adjusted with four different values (-20 , -10 , 10 and 20%). The results are shown in Table 11.2. The total operation cost is increasing along with the growth of the average demand, regardless of which planning method is used as a basis (from -24.00 to 24.41% , from -24.58 to 24.67% , and from -13.73 to 10.79% , respectively). This suggests us that the higher the average demand of medical resources, the higher the operation cost. If the decision makers can find a way to reduce the average demand, i.e., informing people to prevent the epidemic by using internet, radio and television, and thus reduce the actual demand of medical resources, the total operation cost can be reduced.

It can also be observed that the difference between the DM and the SM is negligible, no matter what the average demand is. However, difference between the DM and the AOM decreases from 42.64 to 26.89% , and it varies from 43.53 to 27.32% when it is compared between the SM and the AOM. This result suggests that the proposed two methods produce better planned results, especially when the average demand is lower.

To investigate the influence of standard deviation on the final solution, we test four values of the standard deviation (8 , 9 , 11 and 12). As the standard deviation increases, the stochastic demand can be generated in a larger range. The results are shown in Table 11.3. The operation cost is increasing along with the standard deviation, whatever in SM or AOM. The difference in the operation cost between

Table 11.2 Sensitivity analysis with the change of average demand

Ratios (%)	-20	-10	+10	+20
<i>DM</i>				
Objective value	488,835.5	566,242.5	721,369	800,174.5
Solution time (s)	273.16	630.48	406.02	120.80
<i>Gap (%)</i>				
Before versus after	-24.00	-11.96	12.16	24.41
<i>SM</i>				
Objective value	481,252.5	588,244	748,945.5	795,494
Solution time (s)	617.25	130.23	157.19	69.33
<i>Gap (%)</i>				
Before versus after	-24.58	-7.81	17.37	24.67
<i>AOM</i>				
Objective value	852,267	917,423.5	1,043,610*	1,094,520*
Solution time (s)	N/A	N/A	N/A	N/A
<i>Gap (%)</i>				
Before versus after	-13.73	-7.14	5.63	10.79
<i>Gap (%)</i>				
DM versus AOM	42.64	38.28	30.88	26.89
SM versus AOM	43.53	35.88	28.24	27.32

Table 11.3 Sensitivity analysis of the standard deviation

Value	8	9	11	12
<i>SM</i>				
Objective value	640,302	644,415	657,644.5	668,352
Solution time (s)	329.98	535.19	720.34	987.69
<i>Gap (%)</i>				
Before versus after	0.35	0.99	3.06	4.74
<i>AOM</i>				
Objective value	985,927.5	985,668	993,108	1,001,154*
Solution time (s)	N/A	N/A	N/A	N/A
<i>Gap (%)</i>				
Before versus after	-0.20	-0.23	0.52	1.34
<i>Gap (%)</i>				
Difference in the total cost between SM and AOM	35.06	34.62	33.78	33.24

the SM and the AOM decreases from 35.06 to 33.24% as the standard deviation increases. Although there are only small differences among these objective values (from 0.35 to 4.74% and from -0.20 to 1.34%, respectively), more time is required to solve the problem as the standard deviation increases (from 329.98 to 987.69 s in SM). This suggests that the more stable of the demand, the lower of the operation cost and the better of the solution performance.

To investigate the influence of the capacity of the organizations on the performances of the three different methods, we test four values of the parameters. As shown in Table 11.4, the operation cost decreases about 0.3% when the capacity of DCDC and CHSCs respectively increases 10%, whatever in DM or SM. It can also be found that only small differences among these objective values. However, 5% of the operation cost increases when the capacity of DCDC and CHSC respectively increases 10% in the AOM. Moreover, difference between the DM and the AOM raises from 39.01 to 47.00% as the value of ratio increases. Similarly, difference between the SM and the AOM is varied from 38.91 to 46.91%. This suggests us that the capacity of the medical institutions can strongly influence the total operation cost in our actual operations. However, when the proposed two methods are applied, such influence decreases greatly.

Table 11.4 Sensitivity analysis of the change ratio of capacity

Ratios (%)	+10	+20	+30	+40
<i>DM</i>				
Objective value	640,790.5	639,078	637,305	635,431
Solution time (s)	110.81	484.59	880.84	476.53
<i>Gap (%)</i>				
Before versus after	-0.37	-0.64	-0.91	-1.20
<i>SM</i>				
Objective value	641,843	639,906	638,134.5	636,508.5
Solution time (s)	1034.36	524.64	145.02	442.52
<i>Gap (%)</i>				
Before versus after	0.59	0.29	0.01	-0.25
<i>AOM</i>				
Objective value	1,050,569	1,099,984	1,149,399	1,198,814
Solution time (s)	N/A	N/A	N/A	N/A
<i>Gap (%)</i>				
Before versus after	6.34	11.34	16.34	21.34
<i>Gap (%)</i>				
DM versus AOM	39.01	41.90	44.55	47.00
SM versus AOM	38.91	41.83	44.48	46.91

11.6 Conclusions

In this study, a time-space network technique is applied to formulate the medical resources order and shipment scheduling in community health service centers. A deterministic planning model is presented to depict medical resources order and shipment with a pre-ascertained demand. A stochastic planning model is then developed to respond to the uncertain demand. A solution procedure is developed to efficiently solve the proposed models and a simulation-based evaluation method is also developed to compare the performances of the models. Numerical tests, relating to some health service departments' operations, are performed to evaluate the proposed models and the actual operations. The main contributions of this work to the literature are as follows:

- (1) While most research on medical resources optimization studies a static problem taking no consideration of the time evolution and especially the dynamic demand for such resources [20, 21], the proposed models in our work integrate time-space network technique, which can find the optimal scheduling of logistical support for medical resources order and shipment in CHSCs effectively.
- (2) The logistics plans in response to the deterministic demand and the time-varying demand are constructed as a 0–1 mixed integer programming model and a stochastic integer programming model, respectively. The optimal solutions not only minimize the operation cost of the logistics system, but also can improve the order and shipment operation in practice.

Future research would be useful in the following directions. Initially, although it is reasonable to assume that the government can ensure the adequate supply of the needed medical resources, out-of-stock situation could be a meaningful topic of future research. Secondly, we did not consider shipment routing in this work. Actually, it would be more useful in application if the model considers these two aspects. Certainly, the development of other models using other methods for solving this type of problem and comparing the results with those of our model could also be a direction of future research.

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Chapter 12

Three Short Time-Space Network Models for Medicine Management



Generally, medicine order and delivery are operated based on the previous experiences. First of all, estimating the average annual demands of hospital storage center. Second, planning a medical goods order and delivery schedule based on the annual average demands as well as establishing the period of ordering and delivering. Third, in the process of operating, medical system supplies goods according to the re-order point and safe stock. In this chapter, we propose three time-space network models for medicine order and shipment, which may help improve the effectiveness when managing the medicine in hospitals.

12.1 Model I: A Basic Time-Space Network Model

12.1.1 Introduction

To minimize the operation cost, Wei [1] applied the concept of JIT and stockless in hospital materials management system. Breen and Crawford [2] pointed out that the use of electronic commerce technology can improve the internal pharmaceutical supply chain. Danas et al. [3] proposed virtual hospital pharmacy (VHP) information system to meet the demands and calculate minimum stock level and reorder point of hospital departments. Zhu et al. [4] designed an improved randomized algorithm for the vehicle routing problem of medical goods for large-scale emergency scenario.

The time-space network approach has been popularly employed to solve medical material transit scheduling problems, because it is natural and efficient to represent conveyance routings in the dimensions of time and space. Liao [5] and Cao [6] employed time-space network techniques with the system optimization perspective to construct a deterministic real-time and stochastic real-time medical goods scheduling model and adopted integer programming method to minimize the total cost of medical system. Yan and his colleagues [7, 8] developed a novel time-space network model with the objective of minimizing the length of time needed for emergency repair.

Steinzen et al. [9] presented a new modeling approach that is based on a time-space network representation of the underlying vehicle-scheduling problem. Yan et al. [10, 11] applied time-space network to present a logistical support scheduling model for the given emergency repair work schedule to minimize the total operating cost.

This study presents a logistics support model for medical goods scheduling to address the uncertain demand in the hospital nodes. The model is a stochastic order and delivery scheduling model, which systematically considers the demand of medical goods for every time slot in different hospital nodes, the storage capacity and other constraints, as well as the integrated delivery plan of medical goods in the dimensions of time and space. The problem is formulated as a mixed 0–1 integer programming model and a heuristic algorithm is proposed to solve it. The test results show the good performance of the proposed model. Hence, it is expected to be a useful planning tool for decision-maker to get effective medical goods supply order and delivery schedules.

12.1.2 The Time-Space Network Model

In this section, we will first introduce the dynamic decision-making structure and the time-space network structure which can help us to understand the logistics support process. After that, we will give the mathematical formulation of the problem.

(1) The dynamic decision-making structure

As Fig. 12.1 shows, we make a dynamic decision-making framework for the whole planning cycle. We operate the model once a week and it will present the scheduling result for the whole remainder planning cycle. For example, in the first week, the optimal result will show the schedules for the whole 26 weeks. However, only the

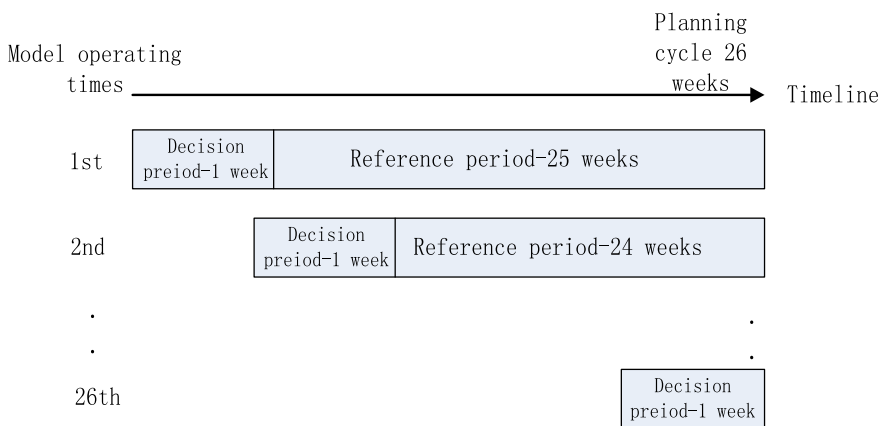


Fig. 12.1 Dynamic decision-making framework

result for the first week will be adopted while the results in the other 25 weeks are used as reference. We do this because the demand information in the recent week is more deterministic and the demand information in further is inaccurate. After that, we will update the demand information in the following weeks and then repeat the above work until the end of the planning cycle.

(2) **Time-space network structure**

As Fig. 12.2 shows, a time-space network is built for supply routing and inventory state at one planning cycle. The horizontal axis represents the manufacturer, the supplier and the hospitals in medical system; the vertical axis stands for the time duration. “Nodes” and “arcs” are the two major components in the network. The nodes include the manufacturer, the supplier, the hospitals and the collection points. The supplier node provides medical goods to hospitals. The hospitals nodes order medical goods from suppliers. The collection node is used to ensure flow conservation. One time point represents one week. The arc flows express the flow of medical goods in the network. The arc flow’s lower and upper bounds are defined as the minimum and

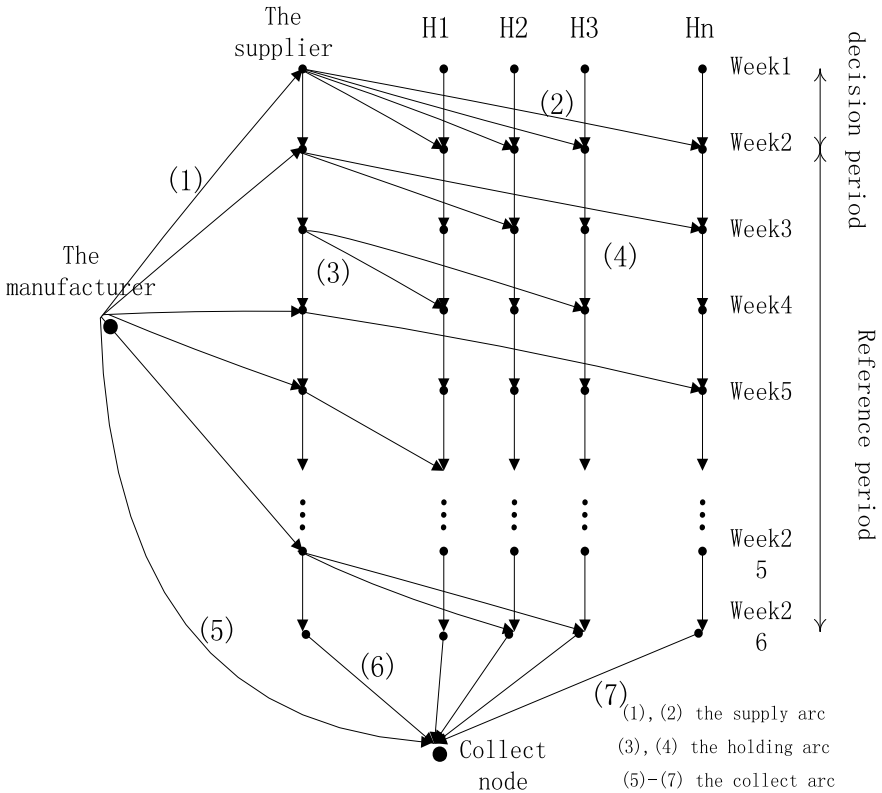


Fig. 12.2 The time-space network

maximum number of flow units allowable on the arc. Three types of arcs are defined as below.

- (i) **Supply arc.** A supply arc (see (1–2) in Fig. 12.2) represents the medical goods are delivered from the manufacturer to the supplier, or from the supplier to the hospital. The arc's cost for (1–2) is the purchase cost of the medical goods plus the fixed ordering cost. The arc flow's upper bound for (1–2) is the inventory capacity of the supplier or the hospital. The arc flow's lower bound is zero.
- (ii) **Holding arc.** A holding arc (see (3–4) in Fig. 12.2) represents the holding of medical goods in the supplier or in the hospital. The arc flow denotes the number of medical goods held in the supplier or the hospital in a moment. The arc's cost is the inventory cost. The arc flow's upper bound is the inventory capacity of the supplier or the hospital. The arc flow's lower bound is safe stock of the supplier or the hospital.
- (iii) **Collection arc.** A collection arc (see (5–7) in Fig. 12.2) connects the last node associated with a supplier, the last node associated with a hospital and the manufacturer node to the collection node. It is used to ensure flow conservation at the last time associated with each supplier and hospital point. The arc flow's upper bound is infinity and the arc flow's lower bound is zero. The arc's cost is zero.

(3) Mathematical formulation

The assumptions for the mathematical formulation are listed below:

1. Demand for each hospital node at every time point is uncertain and obey random distribution. When the model is operated, the demand information will be updated in each decision period.
2. The manufacturer can provide enough medical goods, thus out-of-stock will not take place.
3. Lead time of the order is one week. However, when to order and the order quantity is uncertain, they are the decision variables.
4. For simplicity, only one manufacturer, one supplier and one kind of medical good are considered in the supply network.
5. The initial inventory of every hospital in the first week is the safe inventory plus the maximum demand.

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

Parameters:

- | | |
|-----------|---|
| cb_{ij} | Supply arc (i, j) cost. |
| cs_{ij} | Holding arc (i, j) cost. |
| co_{ij} | Fixed ordering cost for the supply arc (i, j). |
| l_{ij} | Arc (i, j) flow's lower bound. |
| u_{ij} | Arc (i, j) flow's upper bound. |
| S, W, H | The set of all manufacturer, supplier and hospital nodes, respectively. |

- NM Set of all nodes in the network.
 AB, AS Set of all supply arcs and holding arcs, respectively.
 $a_i(w)$ The i th node's supply or demand in the w th random event (if $a_i \geq 0$, supply; else demand).

Decision variables:

- $x_{ij}(w)$ The supply arc (i, j) flow in the w th random event.
 $y_{ij}(w)$ The holding arc (i, j) flow in the w th random event.
 $\delta_{ij}(w)$ A binary variable in the w th random event which indicates whether supply arc (i, j) in the network has flows. If $\delta_{ij}(w) = 1$, then $x_{ij}(w) > 0$; else, $x_{ij}(w) = 0$

Based on the notations, the proposed problem can be formulated as follows:

$$\text{Min } z = \sum_{\forall ij \in AB} cb_{ij}x_{ij}(w) + \sum_{\forall ij \in AS} cs_{ij}y_{ij}(w) + \sum_{\forall ij \in AB} co_{ij}\delta_{ij}(w) \quad (12.1)$$

$$\text{s.t.: } \sum_{j \in W \cup H} x_{ij}(w) + \sum_{r \in W \cup H} y_{ir}(w) - \sum_{p \in S \cup W} x_{pi}(w) - \sum_{c \in W \cup H} y_{ci}(w) = a_i(w), \quad \forall i \in NM \quad (12.2)$$

$$x_{ij}(w) \leq M\delta_{ij}(w), \quad \forall ij \in AB \quad (12.3)$$

$$l_{ij} \leq x_{ij}(w) \leq u_{ij}, \quad \forall ij \in AB \quad (12.4)$$

$$l_{ij} \leq y_{ij}(w) \leq u_{ij}, \quad \forall j \in AS \quad (12.5)$$

$$x_{ij}(w), y_{ij}(w) \in I, \quad \forall j \in AS \quad (12.6)$$

$$\delta_{ij}(w) = 0, 1, \quad \forall ij \in AB \quad (12.7)$$

The objective function (12.1) minimizes the total cost of the medical system. The first item of objective function represents all supply costs; the second item stands for all inventory costs; the third item expresses all order costs. Constraint (12.2) denotes the flow conservation constraint at every node in the network. Constraint (12.3) denotes whether the node orders medical goods or not. Constraint (12.4) and (12.5) holds all the arc flows within their bounds. Constraint (12.6) ensures the integrality of the supply flows and holding flows, and constraint (12.7) denotes all the decision variables are either 0 or 1.

12.1.3 Solution Algorithm

The model is formulated as a mixed 0–1 integer network flow problem that is characterized as NP-hard problem. To efficiently solve this problem we develop a heuristic algorithm, with the assistance of the mathematical programming solver, CPLEX. The procedure is described as follows:

Step 1. Initialization, generate a sequential data follows uniform distribution, which includes 26 data stand for the demand at 26 time points.

Step 2. Set $f = 1$ as the decision period.

Step 3. With the target of minimizing the total cost of the medical system, we solve the medical goods order and delivery schedules for the remainder weeks by CPLEX.

Step 4. Take the schedules of decision period (f) as a certain result. Then we execute it and put the holding situation and the ordering situation in the decision period as the initial conditions of the next decision period.

Step 5. If $f = 26$, then go to Step 6; otherwise, $f = f + 1$, and return to Step 3.

Step 6. Record the optimal schedules and the operations cost.

12.1.4 Numerical Tests

To test how well the proposed model may be applied in the real world, we perform some numerical tests using data in Ref. [5]. The matlab computer language, coupled with the CPLEX 12.4 mathematical programming solver, is used to develop all the necessary programs for building and solving the proposed model. Assume there are five hospitals and thus the model contains 156 nodes, 468 variables and 778 constraints.

(1) The initial data setting

We generate the demands for the hospitals by using `unidrnd()` function in the matlab tool. The average of each hospital demand is 450, 550, 600, 450 and 450, respectively. The variance of each hospital demand is 300, 833, 133, 208 and 300, respectively. The unit procurement price for the supplier is 20 yuan, and it is 22 yuan for the hospital. The unit inventory cost for the supplier and the hospital is 0.3 yuan and 0.5 yuan per week, respectively. The fixed ordering cost for the supplier and the hospital is 3000 and 600 yuan, respectively. Safe stock in each hospital is set as 450, 550, 600, 450 and 500, respectively. The safe stock of the supplier is 3 times of the sum of all hospital's average demand. The inventory capacity of the supplier and the hospital is 5 times of their safe stock, respectively. In practice, relevant data can be set according to the actual situation.

(2) The test results

As shown in Fig. 12.3, the objective value decrease as the dynamic decision-making

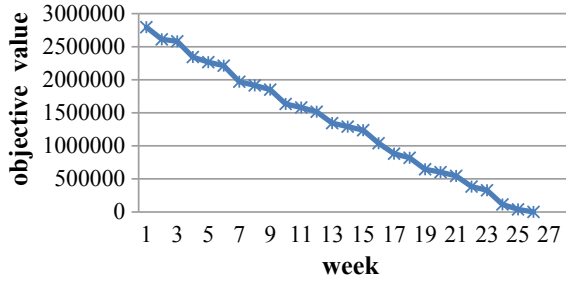


Fig. 12.3 Objective value variation with the solution procedure continuous implement

procedure continuous implement. In the first week, the optimal result will give out the schedules for the whole 26 weeks. Thus the total cost is 2,796,137.7 yuan. As the reference period goes down, the number of decision variables reduce, then the objective values decrease.

To test the stability of the solution result, we adjust the inventory capacity as 2, 3, 4, 5 and 6 times of the safe stock, and then we solve the model respectively. The results are shown in Fig. 12.4. As inventory capacity increases, the total costs reduce. For the frequency of ordering decrease, but the order quantity increases. When the fixed ordering cost and the inventory cost balanced, the inventory capacity will not affect the final result.

We change the variances of the demands to observe the influence on the objective values. When the variances are changed to 1, 4 and 9 times of the original variances, their squared correlation coefficient (R^2 s) are 0.9917, 0.992 and 0.9921 in scatter diagrams, as shown in Fig. 12.5. The results show that variances of demands can only bring slight changes on the objective values.

Furthermore, we evaluate our model with a certain order time model which may always adopted in an actual operation. The order time of the certain order time model is one week. Other parameters are set as the same to proposed model. We adjust the ordering cost for the two models. The comparison results are shown in Fig. 12.6.

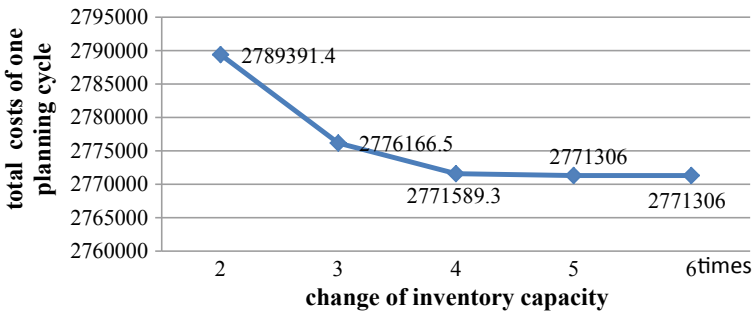


Fig. 12.4 Sensitivity analysis of inventory capacity

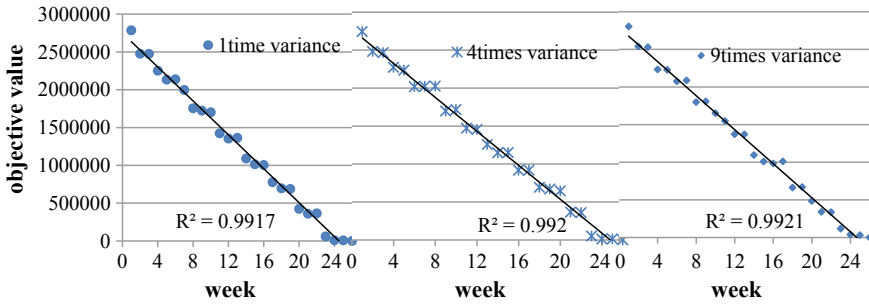


Fig. 12.5 The variance of demands is 1, 4 and 9 times of the original variance

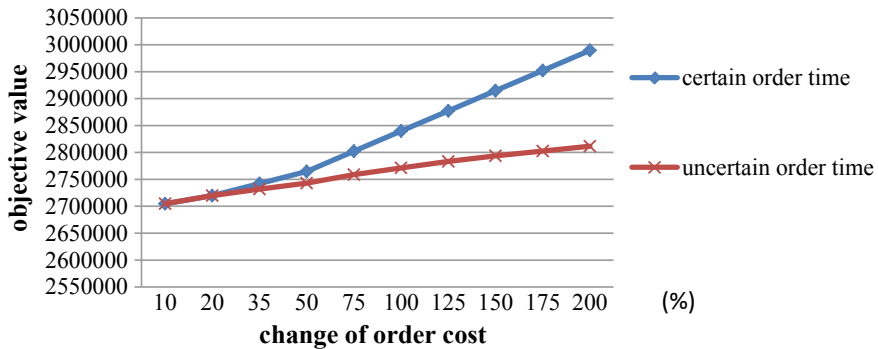


Fig. 12.6 Comparison of certain order time model and uncertain order time model

When the ordering cost is set as no more than 50% of the original costs setting, the two results are similar. However, when the ordering cost is greater than 50% of the original costs setting, the objective values of the proposed model in this work is more optimal.

12.1.5 Conclusions

In this study, the time-space network technique is applied to develop a model to find optimal medical goods order and delivery schedules. The model is a stochastic order and delivery scheduling model, which systematically considers the demand of medical goods for every time slot in different hospital nodes, the storage capacity and other constraints, as well as the integrated delivery plan of medical goods in the dimensions of time and space. The problem is formulated as a mixed 0–1 integer programming model and a heuristic algorithm is proposed to solve it. In an actual practice, the medical goods could be multi-commodities, and lead time of the order would be influenced by many factors and therefore be stochastic. Hence, how to

incorporate a multiple commodity flow and stochastic lead time of the order into the model, to make the schedule more reliable, are our research directions in the future.

12.2 Model II: An Improved Time-Space Network Model

12.2.1 Introduction

Nowadays, most domestic hospitals still make medical resource order plans by experience or according to historical data. In actual operations, this subjective and unscientific method could not only increase inventory level, but also lead to stock-outs sometimes. Hence, how to plan the order and distribution of medical resource, and how to improve hospitals' service quality has become a hot issue in recent years.

To the best of our knowledge, several past studies have focused on the medical resource order and distribution scheduling problem. For example, Shi [12] developed a two stage supply chain inventory or supplier-hospital model with Vendor Managed Inventory (VMI), which could effectively reduce the overall inventory cost of the hospitals and the supply chain. Rachaniotis et al. [13] established a deterministic model to schedule limited available resource under the situation of an epidemic infection with the concept of deteriorating jobs. Zhou et al. [14] built a stochastic dynamic programming model for ordering a perishable medical product, and concluded that the total expected cost was sensitive to changes in the expected demand as well as the regular policy. Nagurney [15] developed a tractable network model and computational approach for the design of medical nuclear supply chains to minimize the total operational cost, the cost associated with nuclear waste discarding, and capacity investment costs. Chen et al. [16] proposed a model based on a relational view, delineating the factors that influence hospital supply chain performance: trust, knowledge exchange, IT integration between hospital and its suppliers, and hospital-supplier integration. Uthayakumar and Priyan [17] presented an inventory model that integrated continuous review with production and distribution for a supply chain to achieve hospital customer service level (CSL) targets with a minimum total cost.

As the time-space network can visually and effectively show the movement both in the dimensions of time and space, this approach has been widely used to solve scheduling problems in many fields. Zhang and Li [18] applied time-space network to establish a dynamic pricing model to maximize manufacturers' profits. To help airport authorities with flight-to-gate reassignments following temporary airport closures, Yan et al. [19] developed a reassignment network model with the objective to minimize the number of gate changes. Steinzen et al. [9] developed a time-space network model to solve the integrated vehicle- and crew-scheduling problem in public transit with multiple depots, and numerical results showed that this approach could perform well. Buhrkal et al. [20] used the time-space concept to develop three main models of the discrete dynamic berth allocation problem, and the results indicate that a generalized set-partitioning model outperforms all other existing models. Yan

et al. [10] developed a logistical support scheduling model for the emergency roadway repair work schedule to minimize the short-term operating cost subject to time constraints and other related operating constraints. Lin et al. [21] developed a planning model and a real-time adjustment model based on a time-space network to plan courier routes and schedules and adjust the planned routes in actual operations for an international express company facing uncertain demands.

But as for medical resource order and distribution scheduling, the time-space network concept has seldom been applied to this problem. Liao [5] and Cao [6] established a deterministic real-time and stochastic real-time medical resource order and transit scheduling model based on the time-space network with the objective of minimizing the total operation costs. However, they did not consider the constant ordering cost (related to ordering frequency), which is not practical. In this work, the ordering cost is taken into consideration, and we employ the time-space network flow technique to develop a model designed to help a hospital to plan the order and distribution of medical resource.

12.2.2 Model Formulation

This section presents the formulation of medical resource order and distribution model. In practice, hospital staff would periodically review the current standards of purchasing plans (e.g. safety inventory, ordering frequency), and adjust the plans to new demands. Therefore, the ‘dynamic decision-making framework’ is introduced into the time axis of the scheduling model to correspond with real-world operations. The time axis is divided into 2 parts: ‘decision period’ and ‘reference period’. To make the scheduling results more consistent with reality, after every decision period, the order and distribution will be rescheduled according to new demands. This operation would be repeated until the end of the scheduling cycle. Besides, the scheduling results during decision period are deterministic scheduling, and results during reference period can be used as a reference for the current scheduling.

For example, if we implement the model every week, the duration of every scheduling is from the time where the implementation starts to the end of scheduling cycle, as shown in Fig. 12.7. The duration of implementation for the first time is 26 weeks. After that, 25 weeks is remained for the second time, and 24 weeks for the third time. It’s worth mentioning that only the scheduling results during the decision period (the first week) would be put to actual use.

(1) Basic assumptions

Only one kind of medical resource is considered in this work. To facilitate the model formulation, we set some assumptions as follows:

1. Demands for medical resource at each time interval can be set to obey a normal distribution according to history data.
2. The scheduling cycle is half a year (26 weeks); both of the order lead time and the distribution lead time are one week.

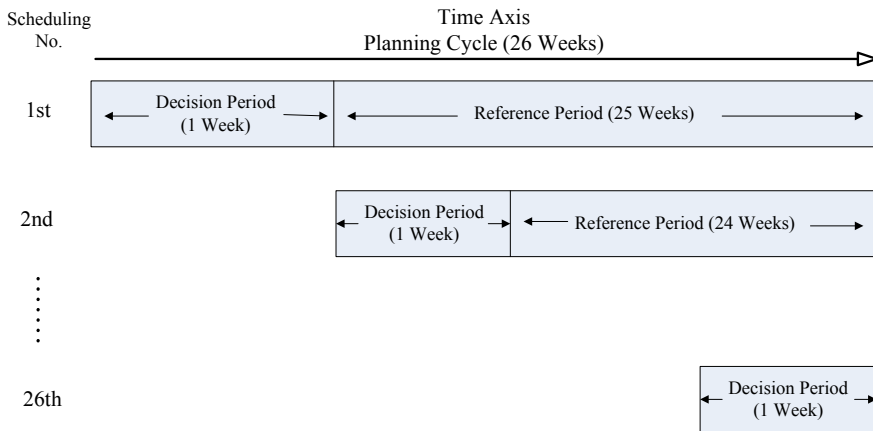


Fig. 12.7 Dynamic decision framework of the scheduling model

3. Medical resource is supplied by one supplier; there is only one warehouse in the hospital.
4. The supplier can meet the market demand completely, and transit medical resources to the hospital warehouse in time and in the right quantity.
5. The storage capacity of the hospital warehouse and departments are known and fixed.

(2) Time-space network of medical resource order and distribution

A time-space network is established to describe the supply of medical resource in the dimensions of time and space, as shown in Fig. 12.8. The horizontal axis represents the supplier, the hospital warehouse and departments. The vertical axis stands for the duration of scheduling. The time interval is one week.

The time-space network contains two basic elements: node and arc. Next, we will introduce them in detail respectively as follows.

1. Node

A node represents the supplier, the hospital warehouse or a department at a specific time. There are 4 types of nodes in this time-space network: the supplier node, the hospital warehouse node, the hospital department node and the collection node. The supplier must convey the medical resource to the warehouse first, and then the resource will be distributed to each department after arrangement. The department nodes will place an order to the warehouse when their inventory cannot afford their demands. The warehouse and each department have an initial amount of medical resource at the beginning of the scheduling cycle, which is the remaining inventory of the previous scheduling cycle. The collection node maintains the flow conservation of the network. All unused medical resource on the nodes will assemble at the collection node at the last week of the scheduling cycle.

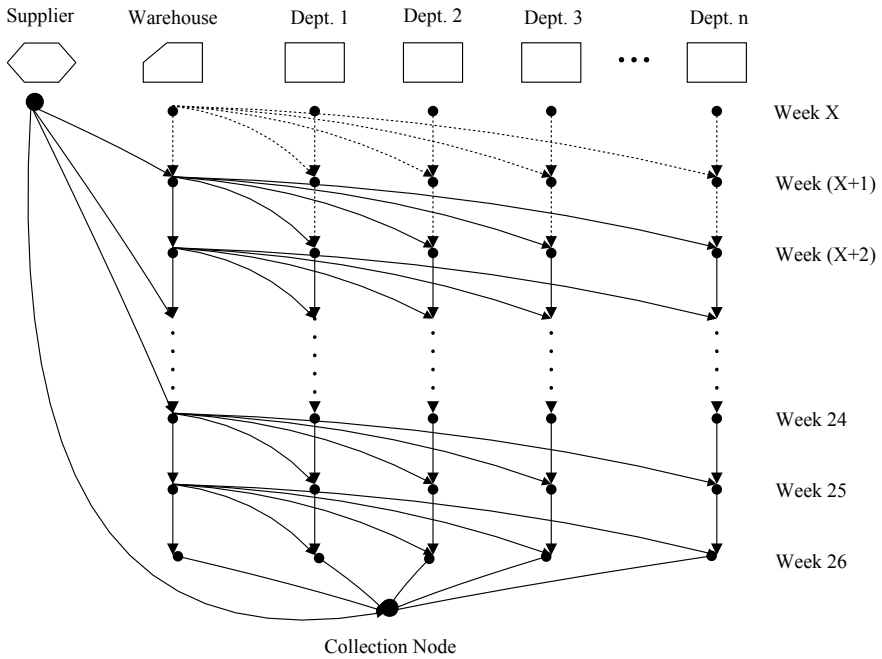


Fig. 12.8 Time-space network of medical resource scheduling

2. Arc

An arc denotes the activity of medical resource distribution in different time and space. The arc flows express the flow of medical resource in the network. There are 4 types of arcs: supply arc, distribution arc, holding arc and collection arc.

- (i) Supply arc: It represents that the supplier delivers medical resource to the hospital. The arc cost is the unit price of medical resource plus a fixed ordering cost. The arc flow's upper bound is the warehouse's storage capacity, and the lower bound is zero.
- (ii) Distribution arc: It represents that the warehouse delivers medical resource to the departments. The arc cost is the unit distribution cost plus a fixed labor cost. The arc flow's upper bound is each department's storage capacity, and the lower bound is zero.
- (iii) Holding arc: It represents the holding of medical resource at the warehouse or departments. The arc cost is the unit inventory-holding cost. The arc flow's upper bound is the storage capacity of the warehouse/departments, and the lower bound is the safety stock of the warehouse/departments.
- (iv) Collection arc: It connects the supplier node, the warehouse node and department nodes to the collection node, and ensures the flow conservation of this network. The arc cost is zero. The supplier collection arc flow's upper bound

is infinity, and the lower bound is zero. The warehouse/departments collection arc flow's upper bound is the storage capacity of the warehouse/departments, and the lower bound is the safety inventory of the warehouse/departments.

(3) Notations used in the model formulation

Parameters:

- Z The total costs of the order and distribution of medical resource;
 a_{jt} The demand for medical resource of the j th department at the time interval of t ;
 p_{SW} Unit purchasing cost from the supplier;
 s_{WD} Unit distribution cost from the warehouse to departments;
 f_1 Constant fixed ordering cost from the supplier to the warehouse;
 f_2 Constant fixed labor cost from the warehouse to departments;
 h_w Unit inventory-holding cost of medical resource in the warehouse;
 h_d Unit inventory-holding cost of medical resource in each department;
 T The set of time interval;
 SW The set of arcs between the supplier and the warehouse;
 WD The set of arcs between the warehouse and the departments;
 D The set of all departments in the hospital;
 LW Minimum inventory level of the warehouse;
 UW Maximum inventory level of the warehouse;
 LD_j Minimum inventory level of the j th department;
 UD_j Maximum inventory level of the j th department.

Decision variables:

- x_{ij} Supply arc (i, j) flow from the supplier to warehouse;
 y_{jk} Distribution arc (j, k) flow from the warehouse to departments;
 z_{wt} Holding flow in the warehouse at the time interval of t ; when $t = 0$, z_{wt} represents the initial inventory of medical resource in the warehouse;
 z_{jt} Holding flow in the j th department at the time interval of t ; when $t = 0$, z_{jt} represents the initial inventory of medical resource in the j th department;
 δ_{ij} A binary variable that indicates whether the hospital warehouse sends an order to the supplier. If $\delta_{ij} = 1$, then $x_{ij} \geq 0$; if $\delta_{ij} = 0$, then $x_{ij} = 0$;
 ξ_{jk} A binary variable that indicates whether the departments send an order to the warehouse. If $\xi_{jk} = 1$, then $y_{jk} \geq 0$; if $\xi_{jk} = 0$, then $y_{jk} = 0$.

(4) The mathematic model

Based on the notations, the scheduling model can be formulated as follows:

$$\text{Min } Z = \sum_{ij \in SW} (p_{SW}x_{ij} + f_1)\delta_{ij} + \sum_{jk \in WD} (s_{WD}y_{jk} + f_2)\xi_{jk} + h_w z_{wt} + \sum_{j \in D} h_d z_{jt} \quad (12.8)$$

Subject to:

$$x_{ij}\delta_{ij} + z_{wt-1} - \sum_{j \in D} y_{jk} = z_{wt}, \quad \forall ij \in SW, \quad jk \in WD, \quad t \in T \quad (12.9)$$

$$y_{jk}\xi_{jk} + z_{jt-1} - z_{jt} = a_{jt}, \quad \forall jk \in WD, \quad j \in D, \quad t \in T \quad (12.10)$$

$$0 \leq x_{ij} \leq UW, \quad \forall ij \in SW \quad (12.11)$$

$$0 \leq y_{jk} \leq UD, \quad \forall jk \in WD \quad (12.12)$$

$$LW \leq z_{wt} \leq UW, \quad \forall t \in T \quad (12.13)$$

$$LD_j \leq z_{jt} \leq UD_j, \quad \forall j \in D, \quad t \in T \quad (12.14)$$

$$x_{ij} \in I, \quad \forall ij \in SW \quad (12.15)$$

$$y_{jk} \in I, \quad \forall jk \in WD \quad (12.16)$$

$$z_{wt} \in I, \quad \forall t \in T \quad (12.17)$$

$$z_{jt} \in I, \quad \forall j \in D, \quad t \in T \quad (12.18)$$

$$\delta_{ij} = 0 \text{ or } 1, \quad \forall ij \in SW \quad (12.19)$$

$$\xi_{jk} = 0 \text{ or } 1, \quad \forall jk \in WD \quad (12.20)$$

The objective function (12.8) denotes the minimization of total costs of medical resource order and distribution, including purchasing cost, distribution cost in hospital and holding cost. Constraints (12.9) and (12.10) indicate the flow conservation in this network. Constraints (12.11) to (12.14) ensure that all arc flows are within their bounds. Constraints (12.15) to (12.20) ensure that all variables are binary number or integers.

12.2.3 The Solution Procedure

In this section, we discuss how to solve the proposed model. The model is formulated as a mixed 0–1 integer network flow problem with NP-hard complexity. Considering the long scheduling cycle and the number of departments in practice, it is almost

impossible to optimally solve this large problem within a limited time. Thus the solution effectiveness and efficiency need to be traded off. To efficiently solve this problem, we develop a heuristic algorithm, with the assistance of the mathematical programming solver, CPLEX. The procedure is described as follows:

Step 1: Initialization. Set parameters of the model, including simulation rounds, the storage capacity, the safety inventory, the initial inventory, cost data and other related data.

Step 2: Set $t = 1$. Solve the model for the first round.

Step 3: Use MATLAB function `normrnd()` to generate N groups of demands for medical resource at each time interval.

Step 4: Call function `cplexmilp()` to solve the model and obtain the scheduling results of the whole scheduling cycle. The results from the previous decision period will be taken as the input data for the current decision period.

Step 5: Continue generating demands of the remaining time intervals. Solve and get the rest of scheduling results.

Step 6: Repeat step 4 and 5, until obtaining the scheduling results at the last time interval of the scheduling cycle. If $t = 26$, then go to Step 7; otherwise, $t = t + 1$, and return to Step 4.

Step 7: Record the optimal schedules and the total operation costs.

12.2.4 Numerical Tests

To test how well the proposed model may be applied in the real world, we perform several numerical tests using historical operating data of a certain kind of medical resource from a hospital in Nanjing, China, with reasonable simplifications. The tests were performed on a personal computer equipped with a Intel (R) Core (TM) 2.13 GHz CPU and 2.00 GB of RAM in the environment of Microsoft Window 7.

(1) Case data

This kind of medical resource has only one supplier. There is one warehouse and five departments in the hospital. The scheduling cycle is 26 weeks. The time interval is one week. We set the demands to obey a normal distribution, and use MATLAB to generate the demands of 26 weeks. The averages of each department's demand are 10, 11, 12, 8 and 13 respectively, and the standard deviations are 2, 2, 2, 1 and 1, respectively. According to the hospital's practical operations in Nanjing, the related cost data and inventory bounds are set as in Tables 12.1 and 12.2.

Table 12.1 Parameter settings

p_{sw}	s_{wD}	f_1	f_2	h_w	h_d
20	8	50	15	0.7	1.4

Table 12.2 Inventory bounds settings

	Warehouse	Dept. 1	Dept. 2	Dept. 3	Dept. 4	Dept. 5
<i>LD</i>	250	12	13	15	10	15
<i>UD</i>	750	36	40	50	30	45

(2) Test results

As shown in Fig. 12.9, we get the total operation costs from one scheduling cycle. The horizontal axis represents the week that is scheduled; the vertical axis represents the objective value at each week. In different rounds of programming, the objective value decreases weekly until it equals zero as the dynamic decision-making procedure continuously proceeds. The objective values are the results during decision period and reference period. In the early decision period, most of supply and distribution arcs are idle, the number of variables in the model is large, and the scope of scheduling is the whole scheduling cycle (26 weeks), so the objective value is high. As time advances, the reference period of dynamic decision framework gets shorter, and the number of variables declines, so the objective value reduces.

Besides, we test the scheduling model for five times and get five groups of objective value data, from whom we select five sets of results of the 1st, 6th, 12th, 18th, 24th week to compare the changes of objective values at the same scheduling interval. As shown in Fig. 12.10, in the vertical direction, the 5 sets of objective values all decrease as the model continues to be implemented, which is in line with the characteristic of the objective value’s changes in each scheduling cycle shown in Fig. 12.9. On the other hand, horizontally, the objective value at the same week is fluctuant for the reason that the demands data are generated randomly by MATLAB function `normrnd()`. But the amplitude of fluctuation is small (the largest rate of change from the 5 sets of results above is 10.70%), which reveals that the randomly generated demands would not influence the objective value, and then proves the stability of the model.

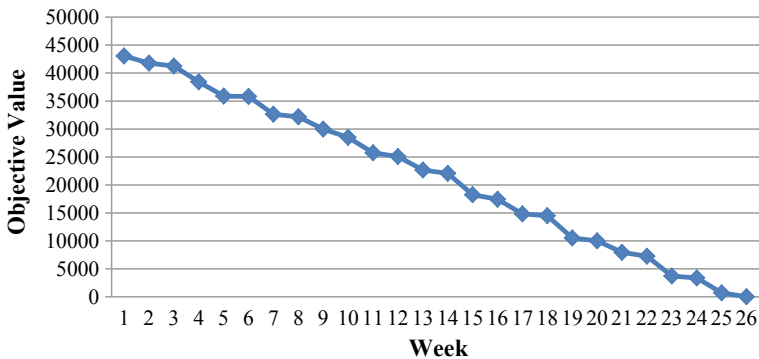


Fig. 12.9 Changes of objective value in one scheduling cycle

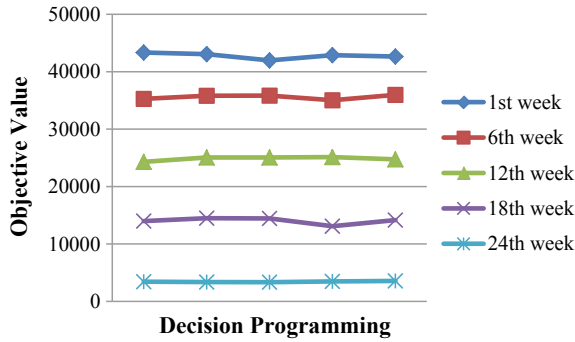


Fig. 12.10 Comparison of objective values at the same scheduling interval in different scheduling cycles

(3) Sensitivity analysis

To understand the influence of the related parameters on the proposed model, several sensitivity analyses are performed here, which could be taken as references for warehouse managers. In consideration of emergencies (e.g., number of patients increases, or overdue supplying), safety inventory is necessary to be set accurately. So we performed the sensitivity analysis on safety inventory of the warehouse to understand its influence on the total operating costs. We tested five situations, 60, 80, 100, 120 and 140% of the original safety inventory. The results are shown in Fig. 12.11. The results show that the objective value grows with the increase of safety inventory. When the safety inventory rises from 60 to 140% of the original, the growth rates of objective value are 4.6, 4.5, 4.4 and 4.3% respectively, from which we can see that the growth is trending down. When the warehouse’s safety inventory increases, the hospital manager would order more medical resource for each time, so the inventory cost increases. But the ordering frequency declines, so the ordering cost declines. The inventory cost and ordering cost would finally achieve a balance and then the objective value would level off and approach a certain constant value. However, in

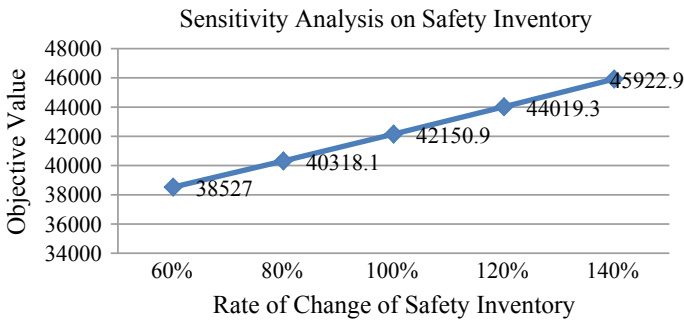


Fig. 12.11 Sensitivity analysis on safety inventory

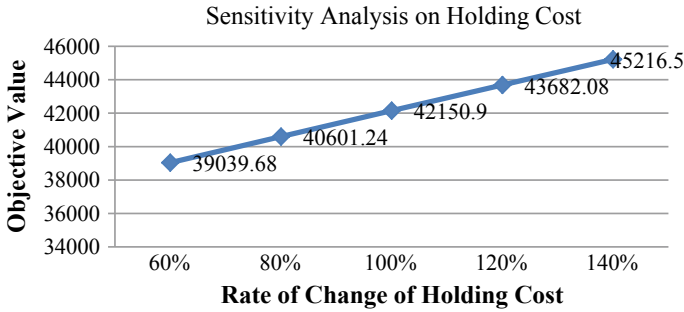


Fig. 12.12 Sensitivity analysis on unit holding cost

actual operations, managers should not reduce safety inventory level without limit to obtain less operation costs. An adequate safety inventory level is indispensable to mitigate risk of stock-outs due to uncertainties in supply and demand, and permit operational activities to proceed according to their plans.

In order to test whether the holding cost is properly set, we performed the sensitivity analysis on it. We tested five situations, 60, 80, 100, 120 and 140% of the original safety inventory. The results are shown in Fig. 12.12. The results show that the objective value grows with the increase of unit holding cost. When the holding cost rises from 60 to 140% of the original, the growth rates of objective value are 4.0, 3.8, 3.6 and 3.5% respectively. So we can conjecture that the objective value would reach to a certain constant value if the unit holding cost keeps increasing. As the unit holding cost increases, the manager would order less medical resource for each time to reduce the total holding cost, but the frequency of ordering gets relatively high, and which increases the ordering cost. When the unit holding cost continues increasing, the ordering cost and total holding cost would be balanced until the objective value reaches to a certain fixed value.

In general, every supplier has different ordering fees and price standards, and the hospital should make a trade-off among them and select a supplier modestly. So there is a need to perform a sensitivity analysis on the shipment cost to understand the influence of different ordering costs on total costs. We tested five situations, 60, 80, 100, 120 and 140% of the original ordering cost. As we can see on Fig. 12.13, the objective value increases as the ordering cost increases. When the constant ordering cost rises from 60 to 140% of the original, the growth rates of objective value are 0.2863, 0.2855, 0.2738 and 0.2603% respectively. With the increasing of the constant ordering cost, the hospital manager would order more medical resource for each time to reduce the ordering frequency, and then to reduce the ordering cost. When the ordering cost keeps rising, it would finally balance with the ordering cost until the objective value reaches to a certain fixed value. Hence, the hospital should select a right supplier for a right ordering fee.

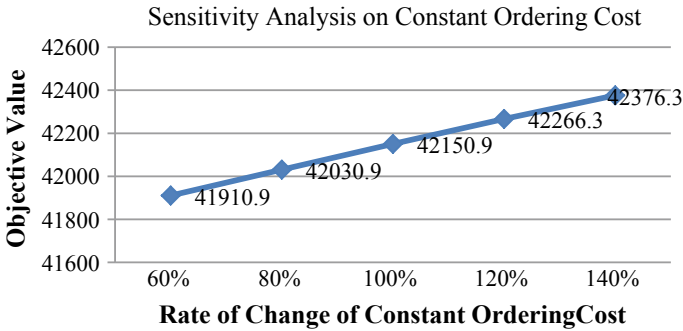


Fig. 12.13 Sensitivity analysis on constant ordering cost

12.2.5 Conclusion

In this work, we creatively take the ordering cost into consideration, and employ the ideas of time-space network and dynamic decision framework to describe the order and distribution of medical resource in a hospital. The problem is formulated as a mixed 0–1 integer programming model. Then a heuristic algorithm is developed to solve it. The test results show the good performance and practicability of the model.

Future research would be useful in at least the following directions. First, since we assume the demands are known and the lead time is certain, the problem to be solved is how to optimize the total cost of medical resource order and distribution under stochastic conditions. Second, only one kind of medical resource is considered in the model, hence it would be more practical and useful to consider multi-variety problem.

12.3 Model III: A Chance-Constrained Programming Model Based on Time-Space Network

12.3.1 Introduction

High operating cost has been a thorny problem for most hospitals in China all the time. Aside of institutional reasons, management method in purchase and inventory should also be responsible for it. Although most major hospitals have adopted electric purchasing management information systems, parameters inside them are often set according to staff's experience. This could give rise to inaccurate decisions due to lack of systematic analysis and overdependence on staff's subjective judgments.

To the best of our knowledge, many studies have focused on the hospital medical resources order and distribution scheduling problem. Lapierre and Ruiz presented an inventory cost oriented model and a balanced schedule model, and used a tabu search

metaheuristic to solve them. The supply schedules generated by this method were efficient and well balanced [22]. Chang et al. [23] established an optimal purchase model to minimize a hospital's drug inventory management cost, and obtained the optimal quantity and frequency to order medicine. Liao and Chang [24] established a simulation model for the supply chain of the hospital logistics system based on the dynamic Taguchi method, and proposed an optimal approach to obtain an optimal robust design in achieving optimal multi-performance. Uthayakumar and Priyan [25] presented an inventory model that considers multiple pharmaceutical products, variable lead time, permissible payment delays, constraints on space availability, and the customer service level (CSL) designed to achieve hospital CSL targets with a minimum total cost for the supply chain. Then they put this problem in a fuzzy-stochastic environment and extended the model [26].

Particularly, Liao [5] and Cao [6] applied the time-space network concept to medical resources order and distribution scheduling, and constructed a deterministic model and a stochastic model respectively. Zhang and Liu [27] developed a mixed 0–1 integer programming model based on time-space network with the assumptions that the demand is known and the supplier can completely meet the market demand.

In this study, we discuss the order and distribution under uncertainty, where the departments' demands are stochastic, and cannot be completely met by the supplier, which may cause a penalty cost due to stock shortage. With time-space network and stochastic programming, a chance-constrained programming model is constructed with the objective to help a hospital to plan the order and distribution of one certain kind of medical resources. Generic algorithm is applied to solve the proposed model.

12.3.2 Model Formulation

(1) Basic assumptions

To facilitate the model formulation, some assumptions are set as follows:

1. Demand for medical resources of every week is stochastic, and obeys a Gaussian distribution.
2. The weekly supply quantity of the supplier is a known value, and the supplier might not completely meet the hospital's demand.
3. The whole scheduling cycle is 52 weeks; the lead time of order and distribution are both one week.
4. The safety stock and stock capacity of the warehouse and departments are known and fixed.
5. There is a certain known amount of initial stock in the warehouse and departments at the beginning of the scheduling cycle.

(2) Time-space network

A time-space network is established to describe the supply of medical resources as shown in Fig. 12.14. The horizontal axis represents the supplier, the hospital

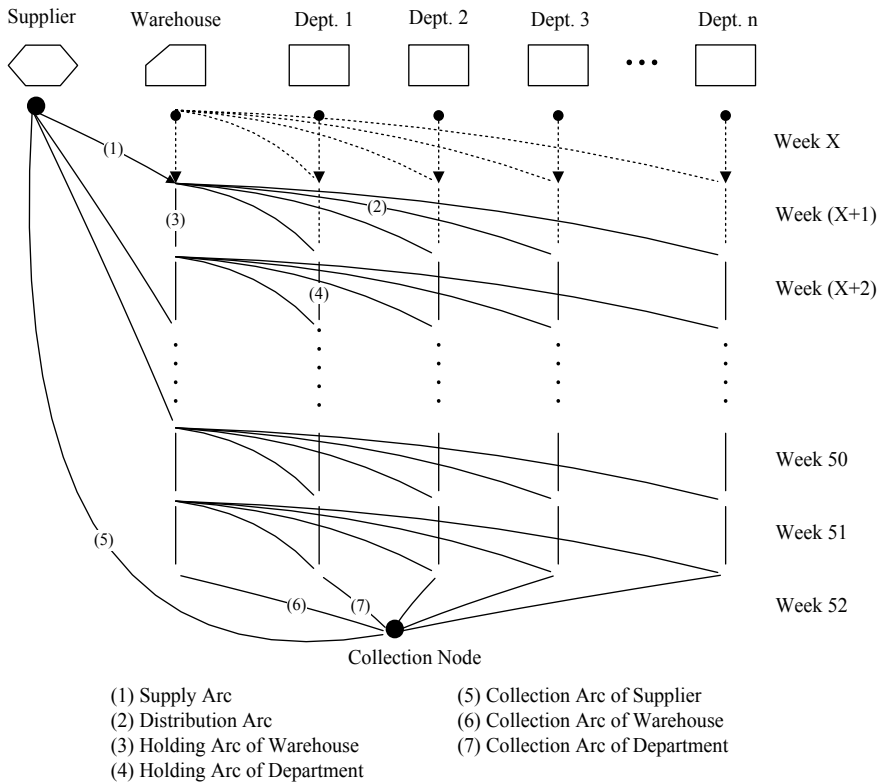


Fig. 12.14 Time-space network for medical resources ordering and distribution

warehouse and departments. The vertical axis stands for the duration of scheduling. The time interval is one week. The time-space network contains two basic elements: node and arc.

1. Node

A node represents the supplier, the hospital warehouse or a department at a specific time. There are 4 types of nodes in this network: (1) Supplier node: It supplies medical resources to the hospital. (2) Warehouse node: It delivers the resources to departments. (3) Department node: They receive the resources from the warehouse node. (4) Collection node: It maintains the flow conservation of the network. All unused medical resources would assemble at this node at the end of the scheduling cycle.

2. Arc

An arc denotes the activity of medical resources distribution in different time and space. The arc flows express the flow of medical resources in the network. There are 4

types of arcs: (1) Supply arc: It represents that the supplier delivers medical resources to the hospital. The arc cost is the unit purchase price of medical resources plus a fixed ordering cost. The arc flow's upper bound is the warehouse's stock capacity, and the lower bound is zero. (2) Distribution arc: It represents that the warehouse delivers medical resources to the departments. The arc cost is the unit distribution cost. The arc flow's upper bound is each department's stock capacity, and the lower bound is zero. (3) Holding arc: It represents the holding of medical resources in the warehouse or departments. The arc cost is the unit stock holding cost. The arc flow's upper bound is their stock capacity, and the lower bound is their safety stock. (4) Collection arc: It connects the supplier node, the warehouse node and department nodes to the collection node, and ensures the flow conservation of this network. The arc cost is zero. The supplier collection arc flow's upper bound is infinity, and the lower bound is zero. The warehouse and departments collection arc flow's upper bound is their stock capacity, and the lower bound is their safety stock.

(3) Notations used in the model formulation

Parameters:

- AM, NM* The set of all arcs and nodes respectively;
- SW* The set of all arcs between the supplier and hospital warehouses;
- WD* The set of all arcs between the hospital warehouses and departments;
- HA* The set of all holding arcs in the network;
- RM* The set of all arcs except *HA*;
- D* The set of all department nodes;
- p* Unit purchase price;
- d* Unit distribution cost from the warehouse to departments;
- h* Unit stock holding cost in the warehouse and departments;
- c* Fixed cost incurred by every ordering;
- t* Unit shortage cost;
- l_{ij}/u_{ij}* The lower/upper bound of the arc (*i, j*)'s flow;
- a_{ij}* The demand quantity of the node *i*;
- α, β, λ* The confidence levels of the corresponding chance constraints.

Decision variables:

- x_{ij}* The flow of arc (*i, j*);
- y_i* The shortage quantity of node *i*, and $y_i = \max \left\{ a_i - \sum_{j \in NM} x_{ji}, 0 \right\}, i \in NM.$
- δ_{ij}* A binary variable that indicates whether the hospital places an order to the supplier. When $\delta_{ij} = 1, x_{ij} > 0$; when $\delta_{ij} = 0, x_{ij} = 0$.

(4) The mathematic model

Based on the notations, the scheduling model can be formulated as follows:

$$\text{Min } \bar{f} \tag{12.21}$$

$$\Pr \left\{ \sum_{ij \in SW} (px_{ij} + c)\delta_{ij} + \sum_{ij \in WD} dx_{ij} + \sum_{ij \in HA} hx_{ij} + \sum_{i \in D} y_i t \leq \bar{f} \right\} \geq \alpha \quad (12.22)$$

$$\Pr \left\{ \sum_{j \in NM} x_{ij}\delta_{ij} - \sum_{k \in NM} x_{ki}\delta_{ki} = a_i \right\} \geq \beta, \quad \forall i \in NM \quad (12.23)$$

$$\Pr \{ l_{ij} \leq x_{ij} \} \geq \lambda, \quad \forall ij \in HA \quad (12.24)$$

$$x_{ij} \leq u_{ij}, \quad \forall ij \in HA \quad (12.25)$$

$$l_{ij} \leq x_{ij} \leq u_{ij}, \quad \forall ij \in RM \quad (12.26)$$

$$x_{ij} \in I, \quad \forall ij \in AM \quad (12.27)$$

$$\delta_{ij} \in 0, 1 \quad \forall ij \in AM \quad (12.28)$$

The objective function (12.21) denotes the minimization of total costs of medical resources order and distribution. Constraint (12.22) means the model obtains the optimal solution under the confidence level α . Constraint (12.23) indicates the flow conservation in this network under the confidence level β . Constraint (12.24) ensures all holding arc flows exceed the corresponding safety stock under the confidence level λ . Constraints (12.25) and (12.26) set bounds for all arc flows. Constraints (12.27) and (12.28) guarantee all variables are binary numbers or integers.

12.3.3 The Solution Procedure

The model is formulated as a chance-constrained stochastic programming problem with NP-hard complexity. Considering the scale of the problem, it is almost impossible to solve it with general enumeration method. Practices have proven that genetic algorithm can solve NP-hard problems effectively by virtue of its superior global optimization search strategy, and is regarded as one of the best tools to find the satisfactory solution. Therefore, genetic algorithm is applied to solve the mathematic model.

12.3.4 Numerical Tests

To test how well the model may be applied in the real world, we performed numerical tests based on operating data of a certain kind of medical resources from a major hos-

pital in Nanjing, China, with reasonable simplifications. We used MATLAB R2012a to build the model and to solve the problems. The tests were performed on a PC equipped with an Intel (R) Core (TM) 2.13 GHz CPU and 2.00 GB of RAM in the environment of Microsoft Windows 7.

(1) Input data

We consider 1 supplier, 1 hospital warehouse and 3 departments in the test case. The input data of the computer program conclude: demand of each department, unit purchase price, fixed ordering cost, unit distribution cost (in hospital), unit stock holding cost, unit shortage cost, safety stock and stock capacity of the warehouse and each departments, and the three confidence levels α , β , λ . As for genetic algorithm parameters, we set population size = 50, maximum evolutionary generations = 200, crossover probability = 60%, and mutation probability = 30%.

(2) Test results

After running the program in the MATLAB environment, we get the scheduling results. As shown in Fig. 12.15, with genetic algorithm “selecting the superior and eliminating the inferior” generation by generation, the objective value decreases until it becomes a fixed value at about 120th generation, which is the model’s optimal value.

Also, we get the order and distribution scheduling results of 52 weeks, including warehouse order quantity and distribution quantity of every department, as shown in Fig. 12.16. We can find that there are some weeks when the hospital doesn’t order medical resources. Because of the fixed ordering cost for every purchase order, the hospital can neither place an order every week, nor order all the needed medical

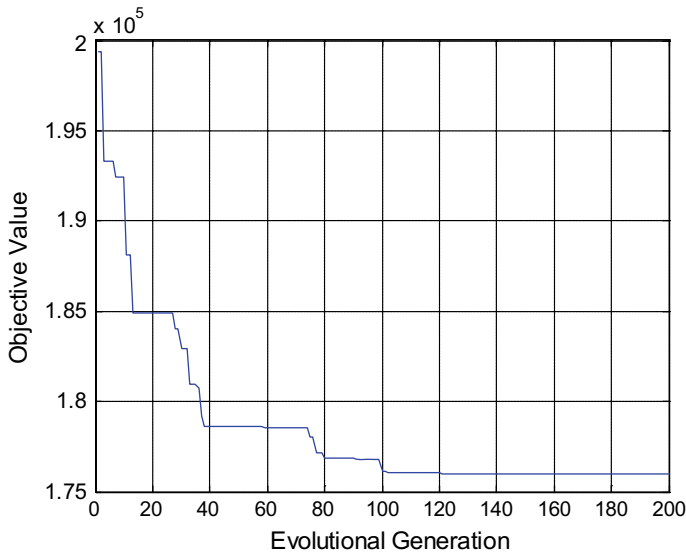


Fig. 12.15 The objective value for every evolutionary generation

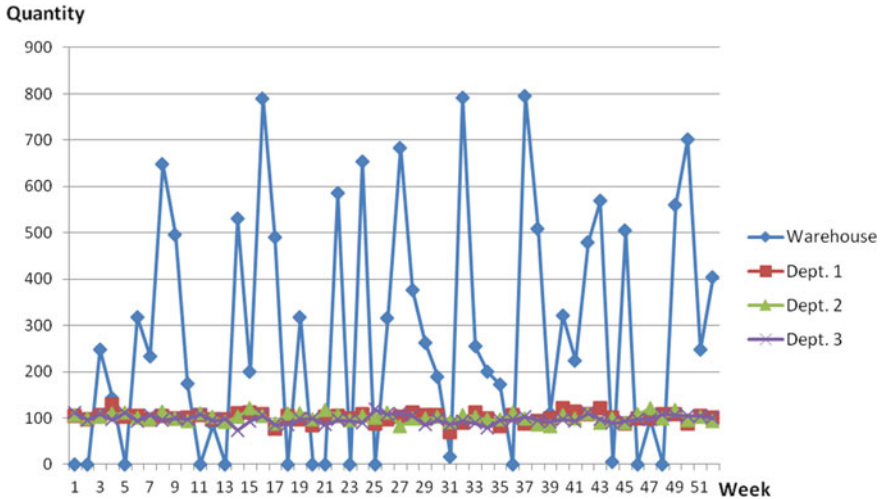


Fig. 12.16 Scheduling results of weekly order and distribution quantity

resources for the whole year at the first week, which could result in huge stock holding cost. The model keeps a good balance between fixed ordering cost and stock holding cost, and obtains the minimum total operating cost.

(3) Sensitivity analyses

With different parameter settings, the scheduling model may get different scheduling results and performance. In order to understand the parameters' influence on the proposed model, several sensitivity analyses are performed in this section. For each rate of change, we run the program 20 times, and take the mean of these 20 objective values as the observation value.

1. Sensitivity analysis on average demand

With other parameters being constant, we change the average of the demand from 80 to 120%. The planning results are shown in Fig. 12.17. As the rate increases, the mean objective value goes up. The reason could be that when the demand rises, the hospital must purchase more medical resources as inventory reserves in response to random disturbances in actual operations.

2. Sensitivity analysis on standard deviation

We change the standard deviation from 80 to 120%. As we can see in Fig. 12.18, the mean objective value grows up as the rate increases. That the RATE of change for standard deviation rises suggests the stochastic disturbances increase. So when the variation range of the demand for every week increases, it leads to the advance of the objective value. Therefore, the more the demand is disturbed in real operations, the more operating cost the hospital will pay.

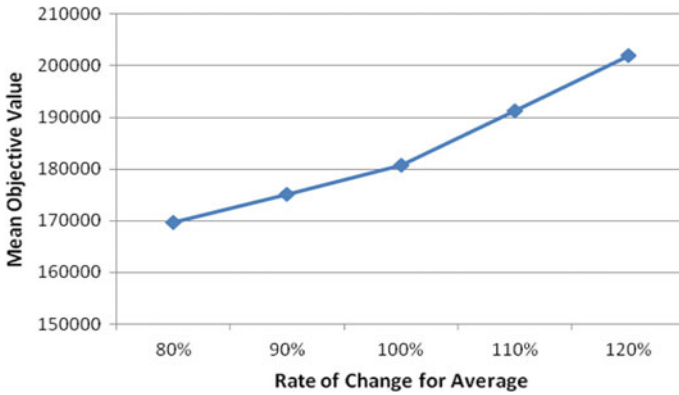


Fig. 12.17 Sensitivity analysis on average demand

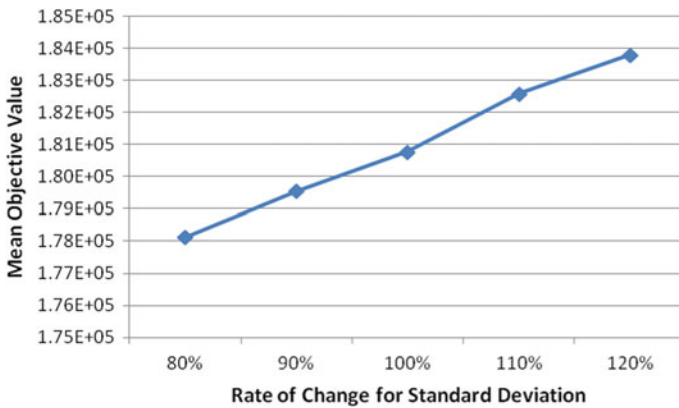


Fig. 12.18 Sensitivity analysis on standard deviation

3. Sensitivity analysis on fixed ordering cost

We change the fixed ordering cost from 50 to 150%. The test results are shown in Fig. 12.19. With the rate increasing, the mean objective value descends until 100% at first, and then goes up. So we can get the optimal objective value with the original fixed ordering cost, which demonstrates the importance of a proper fixed ordering cost.

12.3.5 Conclusions

In this work, we study the order and distribution of medical resources in an environment characterized by stochastic demand and limited supply. A chance-constrained

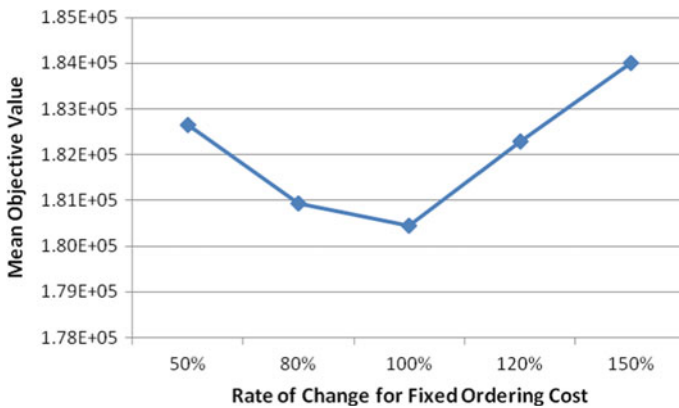


Fig. 12.19 Sensitivity analysis on fixed ordering cost

programming model is constructed based on time-space network. Generic algorithm is applied to solve the model. The test results show the good performance of the proposed model.

Future research would be useful in at least the following directions. First, since we discuss only one kind of medical resources, future work could study multiple kinds of medical resources. Second, the lead time in this model is certain, so it would be more practical and useful to consider an uncertain lead time.

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Chapter 13

Epidemic-Logistics Network Considering Time Windows and Service Level



In this chapter, we present two optimization models for optimizing the epidemic-logistics network. In the first one, we formulate the problem of emergency materials distribution with time windows to be a multiple traveling salesman problem. Knowledge of graph theory is used to transform the MTSP to be a TSP, then such TSP route is analyzed and proved to be the optimal Hamilton route theoretically. Besides, a new hybrid genetic algorithm is designed for solving the problem. In the second one, we propose an improved location-allocation model with an emphasis on maximizing the emergency service level. We formulate the problem to be a mixed-integer nonlinear programming model and develop an effective algorithm to solve the model. In this chapter, we present two optimization models for optimizing the epidemic-logistics network. In the first one, we formulate the problem of emergency materials distribution with time windows to be a multiple traveling salesman problem. Knowledge of graph theory is used to transform the MTSP to be a TSP, then such TSP route is analyzed and proved to be the optimal Hamilton route theoretically. Besides, a new hybrid genetic algorithm is designed for solving the problem. In the second one, we propose an improved location-allocation model with an emphasis on maximizing the emergency service level. We formulate the problem to be a mixed-integer nonlinear programming model and develop an effective algorithm to solve the model.

13.1 Emergency Materials Distribution with Time Windows

13.1.1 Introduction

With rapid development of the global economy, a new biological virus can get anywhere around the world in 24 h. Virus which lurked in the forest or other biological environment before, have been forced to face human ecology when its nature ecology environment destroyed, and this would cause some new type diseases such as Mar-

burg hemorrhagic fevers in Angola, SARS in China, Anthrax mail in USA, Ebola in Congo, smallpox and so on. Bioterrorism threats are realistic and it has a huge influence on social stability, economic development and human health. Without question, nowadays the world has become a risk world, filling with all kinds of threaten from both nature and man made.

Economy would always be the most important factor in normal materials distribution network. However, timeliness is much more important in emergency materials distribution network. To form a timeliness emergency logistics network, a scientific and rational emergency materials distribution system should be constructed to cut down the length of emergency rescue route and reduce economic loss.

In 1990s, America had invested lots of money to build and perfect the emergency warning defense system of public health, aiming to defense the potential terrorism attacks of biology, chemistry and radioactivity material. Metropolitan Medical Response System (MMRS) is one of the important parts, which played a crucial role in the "9.11" event and delivered 50 tons medicine materials to New York in 7 h [1]. In October 2001, suffered from the bioterrorism attack of anthrax, the federal medicine reserve storage delivered a great deal of medicine materials to local health departments [2].

Khan et al. [3] considered that the key challenge of anti-bioterrorism is that people don't know when, where and in which way they would suffer bioterrorism attack, and what they can do is just using vaccine, antibiotics and medicine to treat themselves after disaster happened. Because of this, Venkatesh and Memish [4] mentioned that what a country most needed to do is to check its preparation for bioterrorism attacks, especially the perfect extent of the emergency logistics network which includes the reserve and distribution of emergency rescue materials, and the emergency response ability to bioterrorism attacks. Other anti-bioterrorism response relative researches can be found in Kaplan et al. [5].

Emergency materials distribution is one of the major activities in anti-bioterrorism response. Emergency materials distribution network is driven by the biological virus diffusion network, which has different structures from the general logistics network. Quick response to the emergency demand after bioterrorism attack through efficient emergency logistics distribution is vital to the alleviation of disaster impact on the affected areas, which remains challenges in the field of logistics and related study areas [6].

In the work of Cook and Stephenson [7], importance of logistics management in the transportation of rescue materials was firstly proposed. References Ray [8] and Rathi et al. [9] introduced emergency rescue materials transportation with the aim of minimizing transportation cost under the different constraint conditions. A relaxed VRP problem was formulated as an integer programming model and proved that's a NP-Hard problem in Dror et al. [10] Other scholars have also carried out much research on the emergency materials distribution models such as Fiedrich et al. [11], Ozdamar et al. [12] and Tzeng et al. [13].

During the actual process of emergency material distribution, the Emergency Command Center(ECC) would always supply the emergency materials demand points(EMDP) in groups based on the vehicles they have. Besides, each route

wouldn't repeat, which made any demand point get the emergency materials as fast as possible. To the best of our knowledge, this is a very common experience in China. Under the assumption that any demand point would be satisfied after once replenishment, the question researched would be turn into a multiple traveling salesman problem (MTSP) with an immovable origin. In the work of Bektas [14], the author gave a detailed literature review on MTSP from both sides of model and algorithm. Malik et al. [15], Carter and Ragsdale [16] illustrate some more results on how to solve the MTSP.

To summarize, our model differs from past research in at least three aspects. First, nature disaster such as earthquake, typhoons, flood and so on was always used as the background or numerical simulation in the past research, such kind of disaster can disrupt the traffic and lifeline systems, obstructing the operation of rescue machines, rescue vehicles and ambulances. But situation in anti-bioterrorism system is different, traffic would be normal and the epidemic situation could be controlled with vaccination or contact isolation. Second, to the best of our knowledge, this is the first time to combine research on the biological epidemic model and the emergency materials distribution model, and we assume that emergency logistics network is driven by the biological virus diffusion network. Therefore, it has a different structure from the general logistics network. Third, the new hybrid genetic algorithm we designed and applied in this study is different from all the traditional ways, we improved the two-part chromosome which proposed by Carter and Ragsdale [16], and custom special set order function, crossover function and mutation function, which can find the optimal result effectively.

13.1.2 SIR Epidemic Model

Although rule of the virus diffusion isn't the emphasis in our research, it is the necessary part when depicting the emergency demanded. Figure 13.1 illustrates SIR epidemic model with natural birth and death of the population.

Then we can get the mathematic formulas as follows.

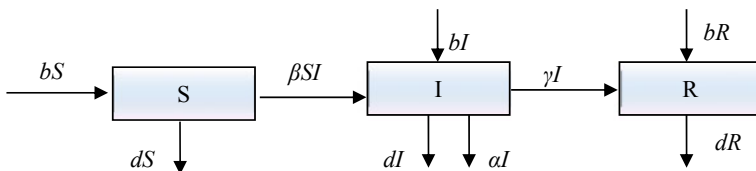


Fig. 13.1 SIR model with natural birth and death

$$\begin{cases} \frac{dS}{dt} = (b - d)S - \beta SI \\ \frac{dI}{dt} = \beta SI + (b - \gamma - d - \alpha)I \\ \frac{dR}{dt} = bR + \gamma I - dR \end{cases} \quad (13.1)$$

where S , I and R , represent number of the susceptible, infective and recovered population, respectively. b and d , stand for the natural birth and death coefficient, α is the death coefficient for disease, β is the proportion coefficient from S to I in unit time, and last, γ is the proportion coefficient from I to R .

Note that number of the susceptible and the infective persons would be gotten via computer simulation with value of the other parameters preset. Then, the emergency materials each point demanded can be also calculated based on the number of sick person.

13.1.3 Emergency Materials Distribution Network with Time Windows

Figure 13.2 is the roadway network of a city in south China, numbers beside the road are the length of the section (unit: km). Point O is the ECC and the other nodes 1–32 are the EMDPs. Now, there are some emergency materials arrived at the ECC by air transport and we need to send it to each demand point as fast as possible. We assumed that all the EMDPs are divided into 4 groups, and any demand point in the network would be satisfied after once replenishment, then the question researched was turn into a MTSP with an immovable origin. However, time windows constraint wasn't considered.

In this study, we use the new hybrid GA to solve the MTSP with time windows. Using SIR epidemic model in Sect. 13.2, number of the susceptible and infective people can be forecasted before emergency distribution. Then symbol t_i is set to show how much time is consumed in demand point i , $i = 1, 2, \dots, 32$. We assume it has a simple linear functional relationship with number of the infective person as follows.

$$t_i = \frac{I_i}{v_{vac}} \quad (13.2)$$

where I_i is number of the infective people in demand point i , v_{vac} is the average speed of vaccination. Another assumption for this research is that vehicle speed is the same as in any roadway section in the network, which noted as a symbol V . So, question researched in this study is: Based on the epidemic model analysis, how can we distribute the emergency materials to the whole EMDPs with a time windows constraint? How many groups should be divided? And, how can we get the optimization route? With the analysis above, objective function model can be formulated as follows.

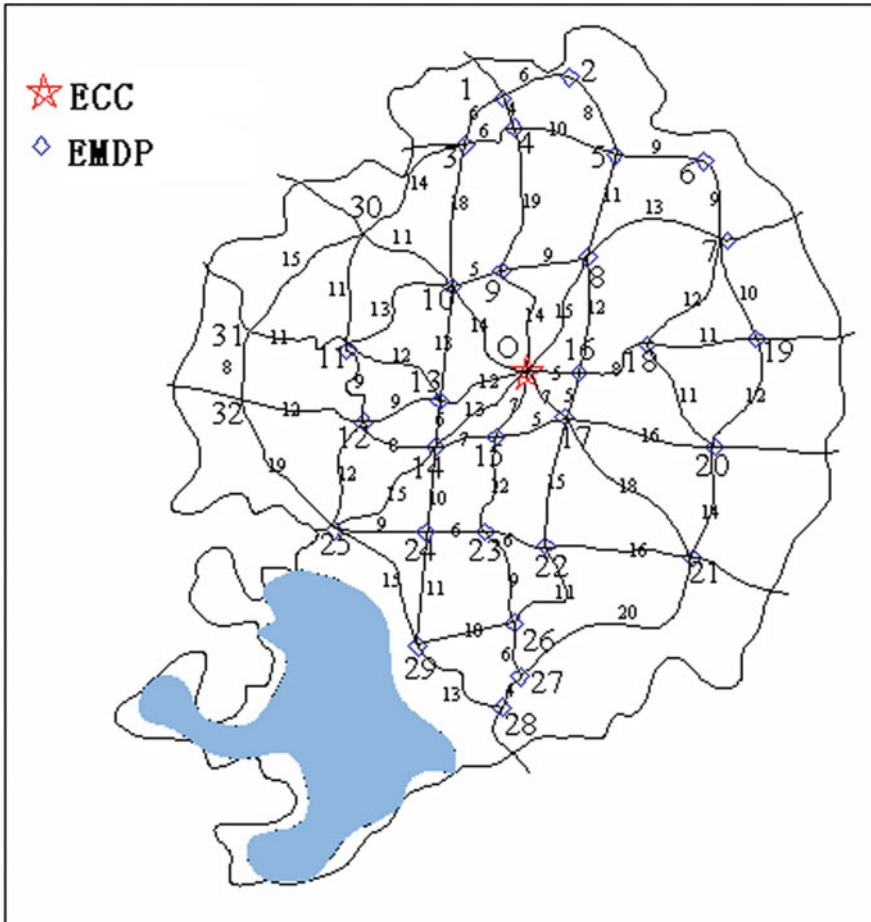


Fig. 13.2 Roadway network of the city

$$\min \sum_{i=1}^{32} \sum_{j=1}^{32} \frac{s_{ij}x_{ij}}{V} + \sum_{i=1}^{32} t_i \tag{13.3}$$

$$s.t. \sum_{j=1}^{32} x_{oj} = n \tag{13.4}$$

$$\sum_{j=1}^{32} x_{jo} = n \tag{13.5}$$

$$\sum_{i=1}^{32} x_{ij} = 1, \forall j = 1, 2, \dots, 32 \tag{13.6}$$

$$\sum_{j=1}^{32} x_{ij} = 1, \forall i = 1, 2, \dots, 32 \quad (13.7)$$

$$\sum_{i \notin S} \sum_{j \in S} x_{ij} \geq 1, \forall S \subseteq V \setminus \{O\}, S \neq \emptyset \quad (13.8)$$

$$T_k \leq T_{TW}, k = 1, 2, \dots, n \quad (13.9)$$

$$x_{ij} \in \{0, 1\}, \forall (i, j) \in G \quad (13.10)$$

where $x_{ij} = 1$ means that the emergency materials is distributed to point j immediately after point i , otherwise, $x_{ij} = 0$. s_{ij} represent the shortest route between point i and j . n is number of the distribution groups. T_k is time consumed in group k . T_{TW} is the time windows. Equations (13.4) and (13.5) are the grouping constraints, (13.6) and (13.7) insure that each demand point would be supplied once. Equation (13.8) assures that there is no sub loop in the optimal route. Equation (13.9) is the time windows constraint. And last, Eq. (13.10) is the parameter specification. The hybrid genetic algorithm are presented as follows.

Step 1: Using SIR epidemic model in Sect. 13.2 to forecast number of the susceptible and infective people, and then, confirm the emergency distribution time in each EMDP;

Step 2: Generate the original population based on the code rule;

Step 3: Using the custom set order function to optimize the original population and make the new population have finer sequence information;

Step 4: Estimate that whether the results satisfy the constraints (4) to (10) in the model, if yes, turn to the next step, if not, delete the chromosome;

Step 5: Using the fitness function to evaluate fitness value of the new population;

Step 6: End one fall and the best one doubled policy are used to copy the population;

Step 7: Crossover the population using the custom crossover function;

Step 8: Mutate the population using the custom mutation function;

Step 9: Repeat the operating procedures (3)–(8) until the terminal condition is satisfied;

Step 10: 10 approximate optimal routes would be found by the new hybrid genetic algorithm and then the best equilibrium solution would be selected by the local search algorithm.

13.1.4 Numerical Tests

In order to evaluate the practical efficiency of the proposed methodology, parameters of the SIR epidemic model are given as follows, $b = d = 10^{-5}$, $\beta = 10^{-5}$, $\alpha = 0.01$, $\gamma = 0.03$, and initializing $S = 10,000$, $I = 100$, $R = 0$. $v_{vac} = 2000$,

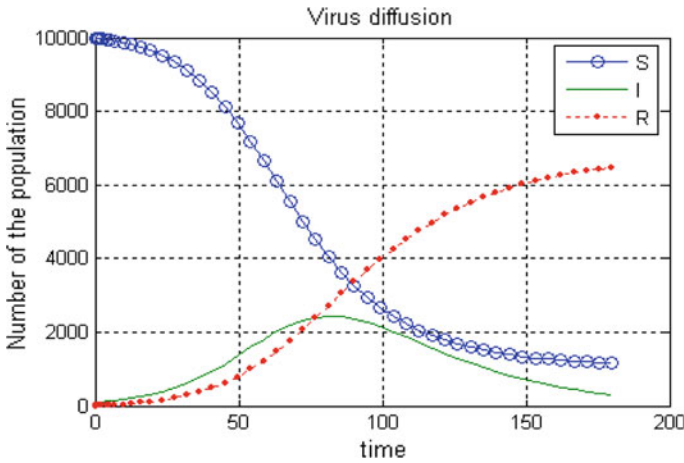


Fig. 13.3 Virus diffusion with time

$T_{TW} = 12$, $V = 40$, $Day = 5$. And we assume that each EMDP has the same situation. Figure 13.3 illustrates that number of the susceptible and infective people changed. Similarly, with different initial value of the S_i and I_i in different EMDP, number of the susceptible and infective people in any EMDP and any time can be forecasted, and then, time consumed in each demand point can be calculated. Figure 13.4 illustrates the magnitude of the differences in the solution spaces for the

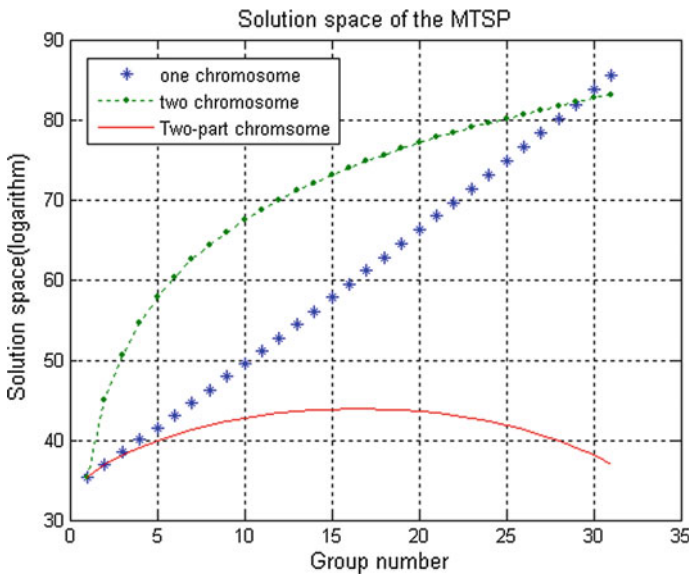


Fig. 13.4 Solution space of the MTSP

three chromosomes for a MTSP with $n = 32$ demand points as the group number is varied from 1 to 32. From this figure we can see that when $n \geq 4$, size of the solution space in Two-part chromosome is distinguish to the other two styles.

Figures 13.5 and 13.6 show the fitness and route length vary with iterate times using the new hybrid GA, respectively. From the figures we can see that each group would be converged effectively, 10 approximate optimal routes would be obtained.

Comparison of the 10 approximate optimal routes is illustrated in Fig. 13.7, and the best equilibrium solution of emergency materials distribution is shown in Fig. 13.8.

From Figs. 13.6 and 13.7, though length of the route in group 9 is the shortest one, it isn't the best equilibrium solution. In other words, some demand points can be supplied immediately but others should wait for a long time. This is not the objective we pursue. From Fig. 13.7, inside deviation of group 7 is the minimum one, which means route in group 7 is the best equilibrium solution, though it isn't the shortest route. In other words, all the demand points can be supplied in the minimum time difference at widest possibility. Another problem worthy to be pointed out is that group 10 is the suboptimal to group 7, and this can be used as a candidate choice for commander under the emergency environment.

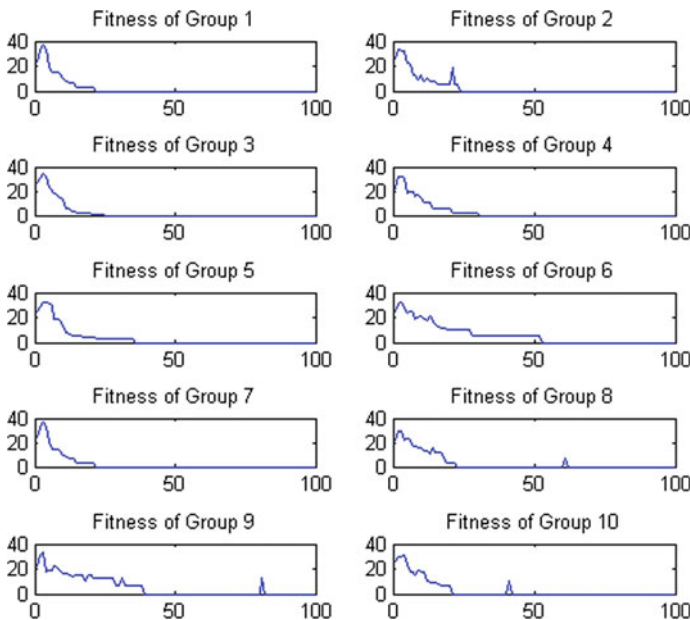


Fig. 13.5 Fitness with iteration

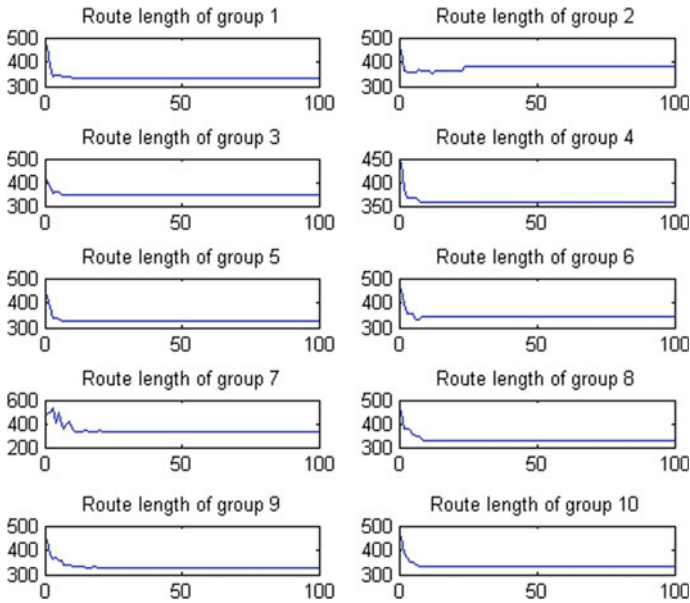


Fig. 13.6 Route length with iteration

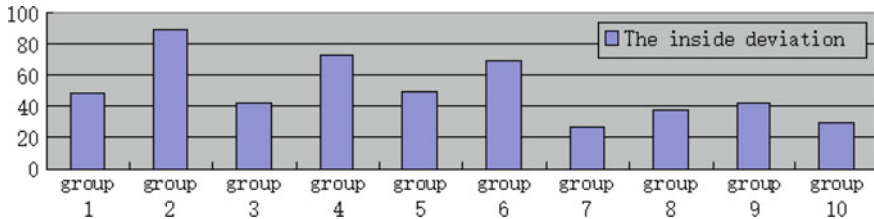


Fig. 13.7 The inside deviation of each group

13.1.5 Discussion

In fact, results in the prior section are too idealized, for we just considered emergency materials distribution at the beginning of the virus diffusion ($Day = 5$) and we assume that each EMDP has the same situation. In fact, it is impossible. Each parameter preset would affect the result at last immensely. Some of them are discussed as follows.

(1) Time consumed with different initial size of S

There are 32 EMDPs in this distribution network, actually, each point has a different number of the susceptible people to others, and we can assume they are distributed from 10,000 to 50,000. With the SIR epidemic model in Sect. 13.1.2, different size

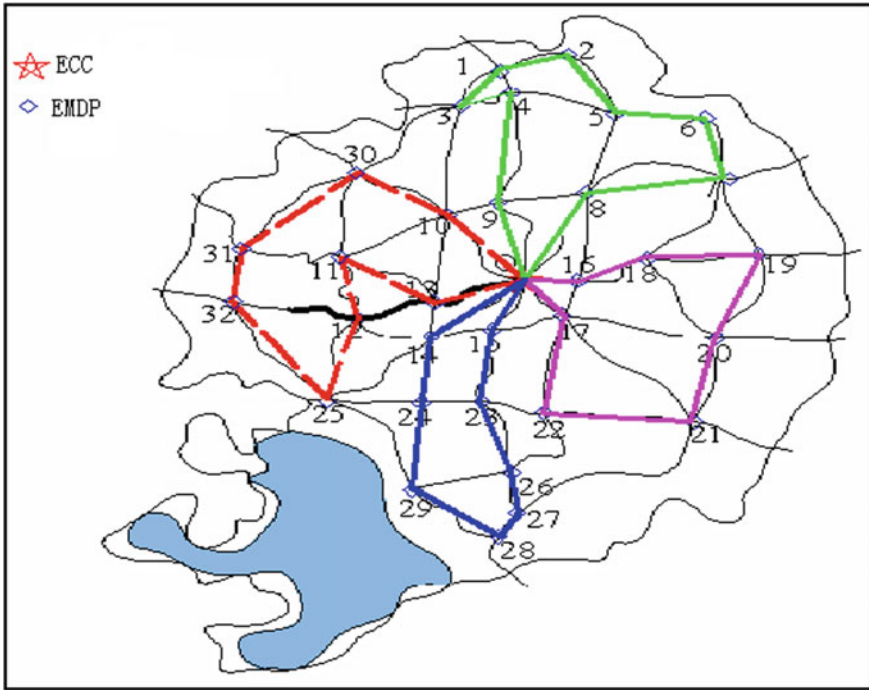


Fig. 13.8 Best equilibrium solution of the MTSP

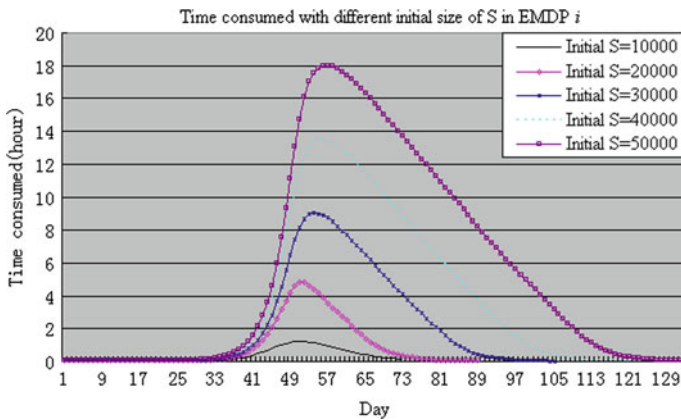


Fig. 13.9 Time consumed with different initial size of S

of the initial susceptible people will bring different size of infective people at last, and then, time consumed in these EMDPs would be varied. Figure 13.9 illustrates that time consumed in one EMDP with different initial size of S as date increased.

There is almost no distinguish among them in the first 30 days (a month), however, distinguish is outstanding in the following days. The larger the initial size of S is, the faster increment speed of the time consumed. In Sect. 13.1.4, $S = 10,000$ is taken for each EMDP and the time consumed almost no more than 1 h, this is a very simple situation, and the optimal route with time windows can be depicted easily. But when initial size of S increased, the problem would become much more trouble for satisfying the time window constraint, and then, we should divided the distribution route in much more groups.

(2) **Time consumed with different initial size of I**

As mentioned before, each EMDP also has a different number of the infective people to others, and we can assume they are distributed from 50 to 200. Figure 13.10 illustrates that time consumed in one EMDP with different initial size of I as date increased. It also can get that time consumed in the first 30 days is smoothly, but distinguish is outstanding in the following days. Similar as before, the larger the initial size of I is, the faster increment speed of the time consumed. Another interesting result is that vary I from 50 to 200, distinguish of the time consumed in each situation isn't very outstanding, and size of the time consumed is around 1 h. In other words, model in Sect. 13.1.3 is still serviceable and we needn't change the grouping design.

(3) **Time consumed with different initial size of β**

β is one of the most important parameters in SIR epidemic model, it affects number of the infective people in the population directly, and then, it affects the time consumed in EMDP accordingly. Vary value of β from 10^{-5} to 5×10^{-5} , and we get time consumed with it changed as show in Fig. 13.11. Still we have conclusion that time consumed in the first 30 days is more or less in different situations, but distinguish is outstanding in the following days. Similar as before, the larger the initial size of β is, the faster increment speed of the time consumed. With initial size of β increased, distribution groups should be adjusted for satisfying the time windows.

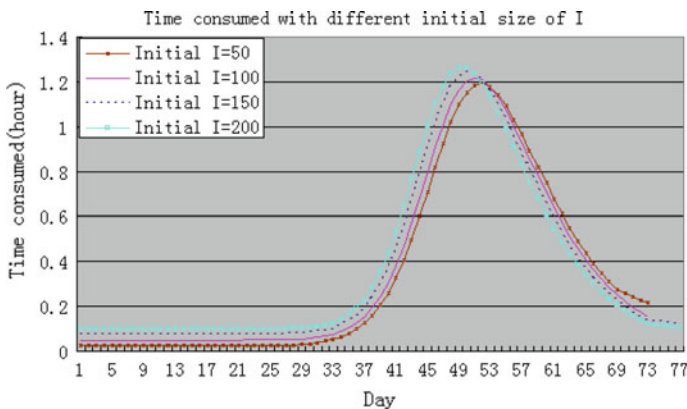


Fig. 13.10 Time consumed with different initial size of I

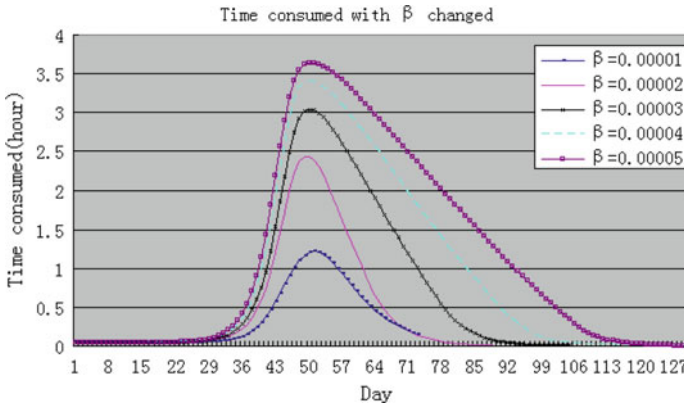


Fig. 13.11 Time consumed with different initial size of β

Based on the analysis above, we can see that time consumed in the first 30 days always stay in a lower level. It is important information for emergency relief in the anti-bioterrorism system, which means the earlier the emergency materials distributed, the less affect would be brought by parameters varied. This also answers the actual question that why emergency relief activities always get the best effectiveness at the beginning.

13.1.6 Conclusions

Emergency materials distribution problem with a MTSP characteristic in the anti-bioterrorism system is researched in this study, and the best equilibrium solution is obtained by the new hybrid GA. Modeling the MTSP using the new two-part chromosome proposed has clear advantages over using either of the existing one chromosome or the two chromosome methods. Besides, combined with the SIR epidemic model, relationship between the parameters and the result are discussed at last, which makes methods proposed in this study more practical.

A problem worthy to be pointed out is that the shortest route between any two EMDPs in the new hybrid GA is calculated by Dijkstra algorithm, so, the optimal result would be gotten even if some sections of the roadway are disrupted, which makes applicability range of the method projected in this study expanded. Research on the emergency materials distribution is a very complex work, only some idealized situations are analyzed and discussed in this study, and some other constraints such as loading capacity of the vehicles, death coefficient for disease, distribution mode and so on, which could be directions of further research.

13.2 An Improved Location-Allocation Model for Emergency Logistics Network Design

Emergency logistics network design is extremely important when responding to an unexpected epidemic pandemic. In this study, we propose an improved location-allocation model with an emphasis on maximizing the emergency service level (ESL). We formulate the problem to be a mixed-integer nonlinear programming model (MINLP) and develop an effective algorithm to solve the model. The numerical test shows that our model can provide tangible recommendations for controlling an unexpected epidemic.

13.2.1 Introduction

Over the past decade, various types of diseases have erupted throughout the world, i.e., SARS (2003), human avian influenza (2004), H1N1 (2009), and Ebola (2014–2015). These unconventional diseases not only seriously endanger humanity's life, but also have significant impacts on economic development. A recent example is the 2014–2015 Ebola pandemic occurring in West Africa, which infected 28,610 individuals, causing 11,300 fatalities and \$32.6 billion in economic losses.

To satisfy the emergency demand of epidemic diffusion, an efficient emergency service network, which considers how to locate the regional distribution center (RDC) and how to allocate all affected areas to these RDCs, should be urgently designed. This problem opens a wide range for applying the OR/MS techniques and it has attracted many attentions in recent years.

For example, Ekici et al. [17] proposed a hybrid model, which estimated the spread of influenza and integrated it with a location-allocation model for food distribution in Georgia. Chen et al. [18] proposed a model which linked the disease progression, the related medical intervention actions and the logistics deployment together to help crisis managers extract crucial insights on emergency logistics management from a strategic standpoint. Ren et al. [19] presented a multi-city resource allocation model to distribute a limited amount of vaccine to minimize the total number of fatalities due to a smallpox outbreak. He and Liu [20] proposed a time-varying forecasting model based on a modified SEIR model and used a linear programming model to facilitate distribution decision-making for quick responses to public health emergencies. Liu and Zhang [21] proposed a time-space network model for studying the dynamic impact of medical resource allocation in controlling the spread of an epidemic. Further, they presented a dynamic decision-making framework, which coupled with a forecasting mechanism based on the SEIR model and a logistics planning system to satisfy the forecasted demand and minimize the total operation costs [22]. Anparasan and Lejeune [23] proposed an integer linear programming model, which determined the number, size, and location of treatment facilities, deployed medical staff, located ambulances to triage points, and organized the transportation of severely ill patients

to treatment facilities. Büyüktaşkın et al. [24] proposed a mixed-integer programming (MIP) model to determine the optimal amount, timing and location of resources that are allocated for controlling Ebola in West-Africa. Moreover, literature reviews on OR/MS contributions to epidemic control were conducted in Dasaklis et al. [25], Rachaniotis et al. [26] and Dasaklis et al. [27].

In this study, we propose an improved location-allocation model for emergency resources distribution. We define a new concept of emergency service level (ESL) and then formulate the problem to be a mixed-integer nonlinear programming (MINLP) model. More precisely, our model (1) identifies the optimal number of RDCs, (2) determines RDCs' locations, (3) decides on the relative scale of each RDC, (4) allocates each affected area to an appropriate RDC, and (5) obtains ESL for the best scenario, as well as other scenarios.

13.2.2 Model Formulation

(1) Definition of ESL

In this study, ESL includes two components. ESL_1 is constructed to reflect the level of demand satisfaction and ESL_2 is proposed for the relative level of emergency operation cost. These two aspects are given by the weight coefficient α and $1 - \alpha$ respectively. The influence of these two factors on the ESL is illustrated in Fig. 13.12. Figure 13.12a represents that ESL_1 increases as the level of demand satisfaction raised. As we can see that it is a piecewise curve. Before demand is completely met, it is an S-shape curve from zero to α . After that, it becomes a constant, which means the additional emergency supplies cannot improve the ESL. Figure 13.12b identifies that ESL_2 decreases as the relative total cost increases. When emergency operation cost is minimized, the ESL_2 arrives at its best level of $1 - \alpha$. Similarly, when emergency operation cost is maximized, the ESL_2 is zero.

(2) Mathematic Model

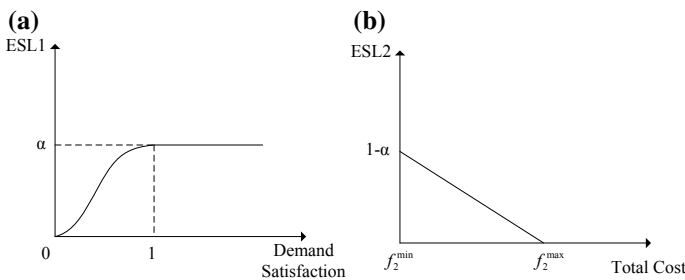


Fig. 13.12 Schematic diagram of ESL

Our model depicts the problem of location and allocation for emergency logistics network design. The network is a three-echelon supply chain of strategic national stockpile (SNS), RDCs, and affected areas. The core problem is to determine the number and locations for the RDCs. In each affected area, there is a point of dispensing (POD). To model the problem, we first present the relative parameters and variables as follows.

Parameters:

I : Set of SNSs, $i \in I$.

J : Set of RDCs, $j \in J$.

K : Set of affected areas, $k \in K$.

α : Weight coefficient for the two parts of ESL.

d_k : Demand for emergency supplies in affected area k .

(x_k, y_k) : Coordinates of affected area k .

(x_i, y_i) : Coordinates of SNS i .

C_{TL} : Unit transportation cost from SNS to RDC.

C_{LTL} : Unit transportation cost from RDC to affected area.

C_j^{RDC} : Cost for operating a RDC. It is decided by the relative size of the RDC j .

U_i : Supply capacity of SNS i .

Variables:

D_{ij} : Distance from SNS i to RDC j . For simplify, the Euclidean distance is adopted.

D_{jk} : Distance from RDC j to affected area k .

ε_{jk} : Binary variable. If RDC j provides emergency supplies to affected area k , $\varepsilon_{jk} = 1$; otherwise, $\varepsilon_{jk} = 0$.

z_j : Binary variable. If RDC j is opened, $z_j = 1$; otherwise, $z_j = 0$.

x_{jk} : Amount of emergency supplies from RDC j to affected area k .

y_{ij} : Amount of emergency supplies from SNS i to RDC j .

(x_j, y_j) : Coordinates of RDC j .

According to the above notations, we can define the optimization model as follows.

$$Max\ ESL = ESL_1 + ESL_2 \tag{13.11}$$

Herein, ESL_1 is defined as (13.12)–(13.14). These equations reflect that the less the unsatisfied demand is, the higher ESL_1 is.

$$ESL_1 = \alpha \frac{1}{K} \sum_{k=1}^K p_k(h) \tag{13.12}$$

$$p_k(h) = e^{\frac{-h_k}{1-h_k}} \tag{13.13}$$

$$h_k = 1 - \frac{\sum_{j=1}^J \varepsilon_{jk} x_{jk}}{d_k} \tag{13.14}$$

ESL_2 is defined as follows. First, we formulate the total operation cost as (13.15):

$$f_2 = C_{TL} \sum_{j=1}^J \sum_{i=1}^I z_j y_{ij} D_{ij} + C_{LTL} \sum_{j=1}^J \sum_{k=1}^K \varepsilon_{jk} x_{jk} D_{jk} + \sum_{j=1}^J z_j C_j^{RDC} \quad (13.15)$$

where C_j^{RDC} is the operating cost for RDC j when it is opened. It is decided by the relative size of the RDC, which can be expressed as:

$$C_j^{RDC} = f(s_j) \quad (13.16)$$

$$s_j = \frac{\sum_{k=1}^K x_{jk}}{\sum_{j=1}^J \sum_{k=1}^K x_{jk}}, \forall j \quad (13.17)$$

Second, to non-dimensionalize the cost function f_2 , we calculate the following two extreme values for Eq. (13.15).

$$\text{Min}_{\text{var} \in S} f_2(\text{var}) = f_2^{\min}, \text{Max}_{\text{var} \in S} f_2(\text{var}) = f_2^{\max} \quad (13.18)$$

$$F_2 = 1 - \frac{f_2(\text{var}) - f_2^{\min}}{f_2^{\max} - f_2^{\min}} = \frac{f_2^{\max} - f_2(\text{var})}{f_2^{\max} - f_2^{\min}} \quad (13.19)$$

$$ESL_2 = (1 - \alpha) F_2 \quad (13.20)$$

where var represents all variables and S represents the following constraints. f_2^{\min} and f_2^{\max} are the minimum and maximum values obtained by solving (13.15) without considering the ESL_1 . The definition of ESL_2 means that the lower the total operation cost is, the higher the ESL is. The constraints for the optimization model are given as follows:

$$\text{s.t. } \sum_{j=1}^J \varepsilon_{jk} = 1, \forall k \in K \quad (13.21)$$

$$\sum_{j=1}^J \varepsilon_{jk} x_{jk} \leq d_k, \forall k \in K; \quad (13.22)$$

$$\sum_{i=1}^I z_j y_{ij} = \sum_{k=1}^K \varepsilon_{jk} x_{jk}, \forall j \in J \quad (13.23)$$

$$\varepsilon_{jk} \leq z_j, \forall j \in J, k \in K \quad (13.24)$$

$$\sum_{j=1}^J z_j \leq J \quad (13.25)$$

$$\sum_{j=1}^J y_{ij} \leq U_i, \forall i \in I \quad (13.26)$$

$$z_j, \varepsilon_{jk} = \{0, 1\}, \forall j \in J, k \in K \quad (13.27)$$

$$x_{jk}, y_{ij} \in \mathbb{Z}_0^+, \forall i \in I, j \in J, k \in K \quad (13.28)$$

$$(x_j, y_j), \forall j \in J \text{ are continuous variables.} \quad (13.29)$$

Constraint (13.21) indicates that each affected area is serviced by a single RDC. Constraint (13.22) specifies that the supplies to each affected area should not be more than its demand. Constraint (13.23) is a flow conservation constraint. Constraint (13.24) shows that only the opened RDC can provide distribution service. Constraint (13.25) specifies the upper bound of RDC number. Constraint (13.26) is the supply capacity constraint of each SNS. Finally, constraints (13.27)–(13.29) are variables constraints.

13.2.3 Solution Procedure

The proposed model for emergency services network design is a MINLP model as it involves multiplication of two variables (i.e., $\varepsilon_{jk}x_{jk}$). More importantly, the optimization model includes a continuous facility location-allocation model with unknown number of RDCs. To avoid the complexity of such MINLP model, we modify it by adding two auxiliary variables. The detail of the modification was introduced in McCormick [28]. Our solution procedure integrates an enumeration search rule and a genetic algorithm (GA), which are applied iteratively. As GA is a mature algorithm [29], details of the GA process are omitted here. We summarize the proposed solution methodology as below.

Step 1: Data input and parameters setting, which includes $I, J, K, \alpha, d_k, (x_k, y_k), (x_i, y_i), C_{TL}, C_{LTL}$, and C_j^{RDC} and the related parameters for GA.

Step 2: Initialization. Generate the original population according to the constraints.

Step 3: Evaluation. Fitness function is defined as the reciprocal of ESL.

Step 4: Selection. Use roulette as the select rule.

Step 5: Crossover. Single-point rule is used.

Step 6: Mutation. A random mutation is applied.

Step 7: If termination condition is met, go to the next Step; else, return to Step 4.

Step 8: Output the results.

13.2.4 Numerical Test

(1) Data Setting

To clarify the effect of the model, we conduct a numerical test. Assuming there is an unexpected epidemic outbreak in a 100×100 square region with 10 affected areas in it. In the square region, only three SNSs can provide emergency supplies. Because at the early stage of the outbreak, there is a large demand for emergency supplies. The supply capacity of these SNSs is less than the total demand in affected areas, which are set at 700, 600 and 400 respectively. The coordinates of the SNSs and the affected areas are obtained in advance. The upper bound of RDC number is set to be 8. The cost of operating a RDC is defined as $6760 \times \sqrt{s_j}$. The demand in each affected area is randomly generated. Finally, unit transportation cost from SNS to RDC is set to be 80 and unit transportation cost from RDC to affected area is 160.

(2) Test Results

Based on the above data setting, we solve our model by using MATLAB software and obtain the results in Fig. 13.13. As it shows in this figure, one can observe that there is a trade-off between the two components of the ESL. In our example, we test the parameter α from 0.4 to 0.9, which means the demand satisfaction is more and more important in our decision making. The result shows that when α is equal to 0.6, the total ESL can arrive at its best value (0.9258). Beyond which it decreases again. In practice, the decision makers may have different value of α according to the actual needs. Correspondingly, it will lead to different ESL.

Our model also determines the optimal number, locations and relative sizes for the RDCs. The test results are shown in Table 13.1. For example, RDC1 deliver emergency supplies to affected areas 2, 7 and 9. Its relative size is 33.23%, which means emergency supplies transshipped in this RDC occupies the corresponding proportion in total emergency distribution.

Table 13.2 illustrates the proportion of demand satisfaction for each affected area. For an example, demand for emergency supplies in affected area 2 is 149, and all this area's demand is totally satisfied. However, one can also observe that demands in some areas are partly supplied due to the supply capacity limitation. For example, only 69.5% of the demand in affected area 1 is delivered.

Fig. 13.13 ESL with different scenario of α

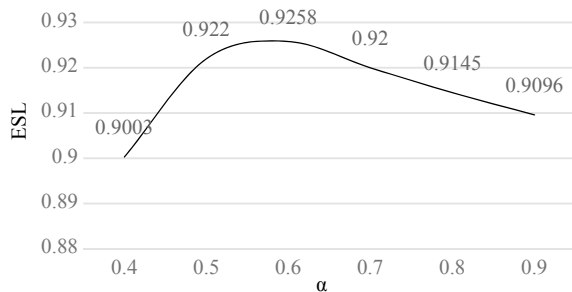


Table 13.1 Location and relative scale of each RDC

RDC	Location	Relative scale (%)	Affected area
1	(18.1651, 33.8696)	33.23	2, 7, 9
2	(38.2318, 39.6607)	10.24	10
3	(75.9550, 37.1063)	21.24	4, 6
4	(61.6731, 93.3449)	13.41	1, 5
5	(48.1101, 84.0045)	21.88	3, 8

Table 13.2 The proportion of demand satisfaction in each affected area

Number	Affected areas	Demand	Supply	Proportion (%)
1	(81.5, 15.7)	141	98	69.5
2	(90.6, 89)	149	149	100
3	(31.7, 85.7)	158	158	100
4	(48.5, 31.3)	170	170	100
5	(3.2, 70)	188	130	69.15
6	(8.7, 4.2)	191	191	100
7	(27.8, 42.1)	208	208	100
8	(54.7, 91.6)	214	214	100
9	(55.8, 79.2)	208	208	100
10	(36.4, 26)	233	174	74.68

(3) Sensitivity Analysis

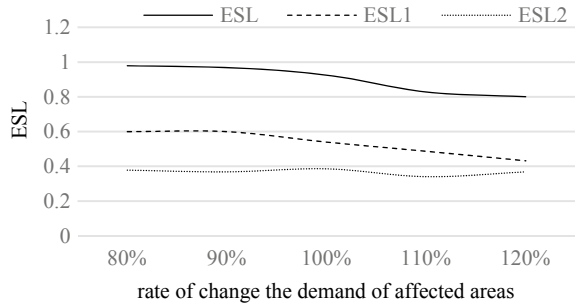
(1) Impact of α on the ESL

To understand the impact of α on the ESL, we solve our model with 6 different values of this parameter, meaning that decision makers have different considerations of the two components of the ESL. We compare the test result in Table 13.3. It can be observed that ESL_1 increases along with the emphasis on demand satisfaction. However, the actual proportion of ESL_1 is always staying at 90% of the setting of α .

Table 13.3 Sensitivity analysis on weight of ESL

α	ESL_1	Proportion (%)	ESL_2	Proportion (%)	ESL
0.4	0.3537	88.425	0.5466	91.1	0.9003
0.5	0.4381	87.62	0.4839	96.78	0.9220
0.6	0.5398	89.96	0.386	96.5	0.9258
0.7	0.6378	89.99	0.2822	94.07	0.9200
0.8	0.7269	90.86	0.1876	93.8	0.9145
0.9	0.8182	90.91	0.0914	91.4	0.9096

Fig. 13.14 ESL with different demand in affected areas



As to the ESL_2 , one can note that it increases at first and then decreases as α varied from 0.4 to 0.9.

(2) Sensitivity analysis on different demand in each affected area

We also examined the impact of different demand in each affected area. The test results are shown in Fig. 13.14. We change the original demand in each affected area for five scenarios. That means different demand situations when an unexpected infectious epidemic happened. One can easily observe the more the demand is, the lower the optimal ESL is. That is because when the demand increases, the supplies of SNSs remain original, which leads a reduction in ESL_1 . When the demand in each affected area changes, ESL_2 varies slightly. Which shows that the change of the total operation cost for the emergency logistics is not obvious when the scale of disease becomes smaller.

13.2.5 Conclusions

In this study, we propose an improved location-allocation model with an emphasis on maximizing the emergency service level (ESL). We formulate the problem to be a mixed-integer nonlinear programming model and develop an effective algorithm to solve the model. Moreover, we test our model through a case study and sensitivity analysis. The main contribution of this research is the function of ESL, which considers demand satisfaction and emergency operation cost simultaneously. Our definition of ESL is different from the existing literature and has a significant meaning for guiding the actual operations in emergency response. Future studies could address the limitations of our work in both the disease forecasting and logistics management. For example, the dynamics of epidemic diffusion could be considered and thus our optimization problem can be extended to a dynamic programming model.

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Appendix A

Total distance for three depots (C subset)

	<i>D1</i>	<i>D2</i>	<i>D3</i>
PTP mode	357.278	288.473	202.642
MMTS mode	119.3851	145.0218	88.4474
Mixed mode	187.36958	164.4879	126.0311

Total timeliness for three depots (C subset)

	<i>D1</i>	<i>D2</i>	<i>D3</i>
PTP mode	1	1	1
MMTS mode	0.88821901	0.83309162	0.75788615
Mixed mode	0.97178651	0.89720673	0.94884224

Total distance for three depots (R subset)

	<i>D1</i>	<i>D2</i>	<i>D3</i>
PTP mode	452.153	293.746	240.466
MMTS mode	233.8722	215.4168	132.5380
Mixed mode	238.6701	248.54435	178.3513

Total timeliness for three depots (R subset)

	<i>D1</i>	<i>D2</i>	<i>D3</i>
PTP mode	1	1	1
MMTS mode	0.662748	0.452693	0.777507
Mixed mode	0.816888	0.820834	0.905773

Total distance for three depots (RC subset)

	<i>D1</i>	<i>D2</i>	<i>D3</i>
PTP mode	234.556	288.473	131.7881
MMTS mode	109.0158	137.5527	65.3893
Mixed mode	141.13521	181.61341	72.29127

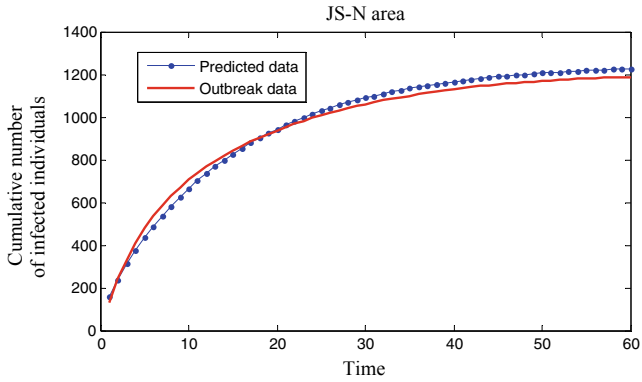
Total timeliness for three depots (RC subset)

	<i>D1</i>	<i>D2</i>	<i>D3</i>
PTP mode	1	1	1
MMTS mode	0.830251	0.87731	0.872961
Mixed mode	0.936154	0.914882	0.90525

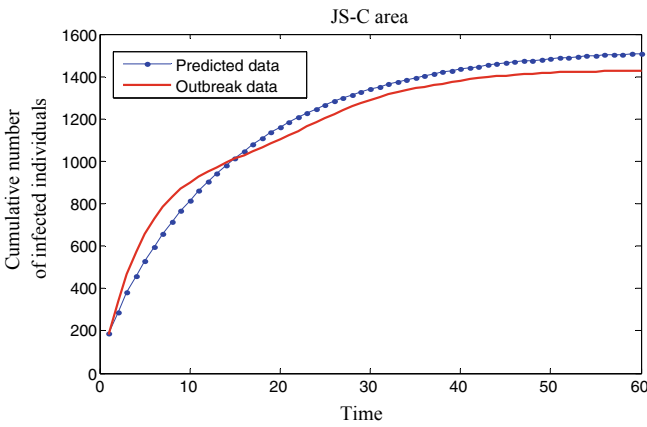
Appendix B

B.1 Model Validation

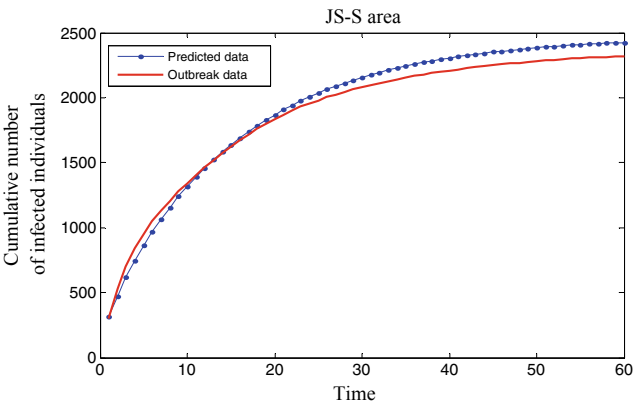
Following the verification process in Büyükahtakın et al. [1], we validate our predicted data against the actual outbreak data in terms of the cumulative number of infected individuals on these days (from July 1st to December 27th), which includes a planning horizon of 180 days and contains 60 time-series data. Figure B.1 shows that our predicted data is slightly underestimated at the initial 15 time-series data and then marginally overestimated than the actual outbreak data in later. The paired-t-test results in Table B.1 prove that our model provides statistically similar results with respect to the outbreak data for the time period (from July 1st, 2009 to December 27th, 2009). As we all know, the paired-t-test, sometimes called the dependent sample t-test, is a statistical procedure used to compare the mean difference between two sets of observations. Since all p -values in Table B.1 are greater than 0.05, it illustrates that there is no significant difference between the predicted data and the actual outbreak data.



(a) JS-N area



(b) JS-C area



(c) JS-S area

Fig. B.1 Comparison of the cumulative number of infected individuals between the predicted data and the outbreak data [1]

Table B.1 Statistical test of our predicted data and outbreak data [1]

	Area	Mean		Two-tailed paired-t-test	
		Outbreak data	Predicted data	t-stat	p-value
Infected areas	JS-N	19.78	20.35	-0.1476	0.8826
	JS-C	23.81	24.57	-0.2932	0.8125
	JS-S	40.42	38.23	-0.1793	0.8355

B.2 Optimization Results With Different Budget Sizes

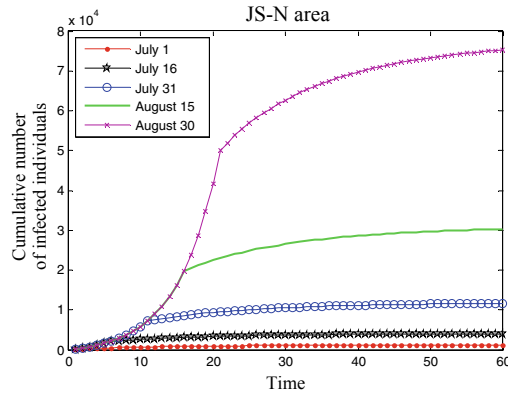
The columns of Table B.2 report the objective value, affected areas, optimal budget allocations, cumulative capacity, cumulative number of infected individuals and cumulative number of hospitalized individuals in each affected area, by solving our model with different budget limitations.

Table B.2 Optimization results with different budget sizes [1]

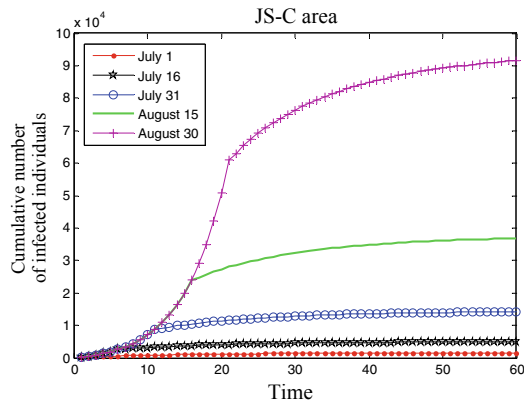
Budget (Million)	Objective	Affected area	Budget allocation	Capacity	Infected	Hospitalized
100	44,412,018	JS-N	22.9 M (22.9%)	1911	10,931,678	1474
		JS-C	28.9 M (28.9%)	2253	13,933,064	1738
		JS-S	48.2 M (48.2%)	3768	19,552,069	2907
		Total	100 M	7932	44,416,812	6120
150	10,902,400	JS-N	34.2 M (22.8%)	2903	2,983,946	2240
		JS-C	45.3 M (30.2%)	3635	3,216,222	2804
		JS-S	70.5 M (47.0%)	5359	4,717,945	4135
		Total	150 M	11,897	10,918,113	9179
200	853,285	JS-N	46.8 M (23.4%)	3895	239,426	3005
		JS-C	56.4 M (28.2%)	4475	264,531	3453
		JS-S	96.8 M (48.4%)	7685	395,144	5930
		Total	200 M	16,056	899,101	12,388
250	2821	JS-N	59.2 M (23.7%)	4396	5218	4178
		JS-C	73.6 M (29.4%)	5943	6590	5153
		JS-S	117.2 M (46.9%)	8908	10,298	6310
		Total	250 M	19,247	22,106	15,641

B.3 Impact of Different Intervention Starting Dates

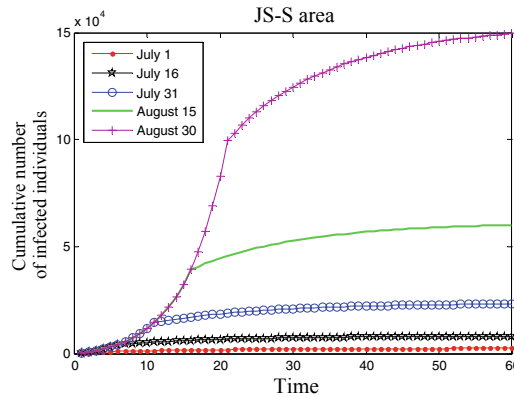
The impact of different intervention starting dates on the number of infected individuals is shown in Fig. B.2. Although all intervention strategies can help reduce the number of infections and lessen the exponential growth of the disease [1], one can see that the earlier the intervention starts, the fewer the infected individuals there are. It is worth mentioning that starting intervention on August 30 is too late because it leads to an outstandingly higher number of infected individuals when compared to the other four scenarios. Such result is consistent with Büyüktaktın et al. [1], which suggests that the number of infected cases can



(a) JS-N area



(b) JS-C area



(c) JS-S area

Fig. B.2 Impact of different intervention starting dates [1]

increase significantly if starting intervention is too late, even with ample emergency budget and strong intervention efforts. Therefore, this result implies us that applying an early intervention strategy is particularly important when response to an unexpected epidemic outbreak.

Reference

Büyüktaktın İE, Des-Bordes E, Kızı EY. A new epidemics-logistics model: insights into controlling the Ebola virus disease in West Africa. *Eur J Oper Res.* 2018;265(3):1046–63.