Influenza vaccine supply chain network design during the COVID-19 pandemic considering dynamical demand

Mehdi Alizadeh
Department of Industrial Engineering, Iran University of Science and Technology
Tehran, Iran, Mehdi8alizadeh@yahoo.com

Mohammad Mahdi Paydar[1]
Department of Industrial Engineering, Babol Noshirvani University of Technology
Babol, Iran, paydar@nit.ac.ir

Seyyed Mehdi Hosseini
Department of Industrial Engineering, Babol Noshirvani University of Technology
Babol, Iran, sm.hosseini33@yahoo.ir

Ahmad Makui
Department of Industrial Engineering, Iran University of Science and Technology
Tehran, Iran, amakui@iust.ac.ir

Abstract

Nowadays, the healthcare industry focuses on the COVID-19 more than any other issues and it uses any approach or solution that is helpful to battle against this pandemic disease. There are many close similarities between the symptoms of the coronavirus and the Influenza (flu) virus, which sometimes make it difficult to distinguish between them. So, it has prompted countries to start flu vaccination to prevent potential problems. As a result, it has caused a significant increase in demand for the flu vaccine. To consider it, this study presents a multi-level supply chain for the flu vaccine during the COVID-19 pandemic. The problem pursues three main goals: cost minimization, maximizing demand allocation based on customer prioritization, and minimizing maximum lost customer demand. Due to the limited number of vaccines, a rate indicating the priority of each group of customers to receive the vaccine in the proposed model is considered. Customer prioritization can undermine justice because a flu patient is in critical condition but has low priority. Therefore, the third objective seeks to create justice and morality by minimizing the maximum lost demand. To evaluate the model, it is conducted based on a case study in Mazandaran province, Iran. The findings illuminate that 79 % of the demand will be met. Besides it shows that by increasing the capacity to 10%, the demand will be satisfied 9 percent more. Finally, some worthwhile and practical managerial insights are suggested.

Keywords: Vaccine supply chain, Dynamical demand, Multi-objective model, COVID-19.

1. Introduction

The pharmaceutical industry is one of the high-tech industries and researchers should take more attention to research and development in this sphere. The pharmaceutical industry includes the process of drug production to its sale, and since this process is long and complex, so research related to this industry should be done with great care and attention. The increasing demand for drugs indicates that the constant need for drugs is an integral part of human life for their health (1). Due to

[1] Corresponding author, Phone: +98 911 3235979

the great and direct impacts of drugs on people's health and lives, many studies are done and still doing in healthcare area (2).

In recent centuries, vaccines have been one of the most important drugs that inject health into society (3). The studies done in the vaccine field reveal that the vaccine production and distribution process is complicated and has its own features. Therefore, it shows the necessity of proper planning and management for the vaccine supply chain. (4).

These days, the world is infected with the coronavirus and it has caused serious troubles for each community in various aspects such as economic, social, educational, and medical. Therefore, all countries, especially the medical community are looking for a helpful, useful, and effective solution to combat this disease. One of the issues that the medical community emphasizes and suggests countries is to vaccinate people with the flu vaccine during the COVID-19 pandemic. As it is clear, the similarities of the symptoms between the flu virus and coronavirus are many and very close. Therefore, it is very difficult to distinguish between these two diseases. So the flu vaccination can be an effective remedy to prevent any possible problem. For example, one of the great problems that the flu causes during this disease is that when a person gets the flu and cannot diagnose these diseases from each other, he or she goes to a medical center to receive medical treatment. Therefore, it is possible to get the COVID-19 disease there. In other words, the flu can indirectly cause to be infected with the COVID-19 disease. Another noteworthy point is that although the medical community has achieved significant success in COVID-19 vaccine production and the vaccination has begun in the world in some countries. But, due to the low production rate of the COVID-19 vaccine and in contrast, the high demand rate for it has caused that many people in many countries have not been vaccinated yet. On the other hand, the cold season is coming in 2021 and the need for the flu vaccine will increase sharply again. Furthermore, there will always be a need for the flu vaccine, even after the COVID-19. Besides, the production and distribution of the flu vaccine have their own characteristics and conditions. For example, the flu vaccine is given over some time in a year. Also, due to its high and fast perishability rate, special conditions are required for its transmission and distribution. Therefore, all of these emphasize the importance of designing a proper supply chain for proper management of this product from production to its supply to customers.

Also, the necessity and importance of our current research are clear. In this study, to consider the topic, a multi-level supply chain network for the flu vaccine during the COVID-19 pandemic is provided. Besides, some important items such as customer prioritization, justice and morality, and dynamical demand are considered in the problem model. To demonstrate the performance of the proposed supply chain, it is implemented in a real case study.

Other parts of this paper include: In the second section, the related literature is reviewed. The third section describes the problem and mathematical model of designing a flu vaccine supply chain network in the COVID-19 epidemic. In the fourth section, a case study is presented and the results of the mathematical model are collected based on its information. In the end, managerial insights are provided and the conclusion of the present study is discussed.

2. Literature review

Drugs are one of the crucial commercial and strategic items in the world because they are important in terms of affecting the health and safety of communities as well as profitability. The pharmaceutical industry is one of the key and most profitable industries in the world so that having a pharmaceutical industry is defined as one of the important indicators of countries' development. The pharmaceutical industry is a futuristic industry, which after the service industry, has the highest percentage of the future-oriented industry. Research plays a key role in healthcare. In recent years, researchers have tried to provide all possible strategies for patients' quick and easy access to medicine. When the drug is produced, the first step is taken, but it is very important that the produced drug reaches the customer quickly or that it is provided to the applicants with the least amount of defects. Vaccines are always an urgent need that must be met immediately. In the context of the COVID-19 epidemic, the distribution of the vaccine has become more sensitive than before. Vaccines usually have special conditions. These conditions include the method of storage, transportation, and allocation. Researchers have also published many articles in this field to play an effective role in improving the health industry.

Vaccines are powerful health tools that save about three million lives each year. Vaccines are temperature-sensitive biological products. The Polio vaccine is crucial sensitive to temperature and should be stored frozen. Vaccines (such as measles and rubella) may be frozen or stored at 2-8 ° C. Other liquid vaccines such as diphtheria, hepatitis B, and tetanus should be stored and transported at 2-8 ° C (5). Exposure to heat reduces the useful life of vaccines (6). Improper storage temperature reduces the strength of vaccines and therefore does not protect patients against disease (7, 8). Improper transportation and storage of the vaccine may reduce the effectiveness of the vaccine. Transportation and storage above 8 ° C have been reported in some countries (9), and vaccine freezing has been reported in many countries (10). A study in Indonesia when monitoring the temperature of the hepatitis B vaccine showed that 75% of these vaccines were frozen during transport. Tunisia, like middle-income countries, used home-built refrigerators and cold boxes to store and transports its vaccines. One of the functional weaknesses of refrigerators is that they are not able to maintain a temperature range of 2-8 degrees Celsius and there is a risk of freezing. This weakness of home refrigerators and its consequences have led to a number of countries to work with refrigerator manufacturers to find solutions to this problem (11). A weak supply chain often results in a loss of vaccine during distribution (12). Most vaccines require a temperature-controlled environment (freezer or refrigerator) (13). In order to maintain the vaccine in the cold chain from the production stage, it is necessary to have sufficient cold chain infrastructure (14), compliance with standards, and effective management. Health care providers need to have enough information to manage the cold chain (15).

On the other hand, an efficient supply chain network can have significant effects on the quality of treatment. Yadava (16) believes that good performance in the supply chain of vaccines, drugs, and medical equipment, which is the backbone of the healthcare system, has given importance to this issue. Weak supply chains in this system jeopardize treatment programs to meet people's needs. In his article, he gives an overview of the structure of the supply chain of medical products in developing countries. Its purpose is to identify key areas for reform to ensure that the supply chain is active or at least that there is no barrier to the supply chain and its objectives. Effective distribution of vaccines is important to reduce the risk of transmitting the disease to the community. A supply chain network including production, packaging, and distribution will reduce costs (17). Lee et al. (18) proposed a mathematical model that examines the impact of a new vaccine on the vaccine supply chain. Their results from this article indicate that the distribution of the new vaccine requires more transport and storage capacity to carry out the vaccination accurately. Shittu et al. (19) in their problem model, concluded that a redesign of the old vaccine supply chain was essential. They believe that capacity is one of the most important points in the vaccine supply chain. They found for their model that 55% needed to increase capacity, and to supply it they could improve the situation to some extent by creating three centers. Previous research has comprehensively reviewed the appropriate distribution and prioritization of vaccines (20-22). Lin et al. (23) believe that the vaccine is sensitive to temperature hence which creates special conditions for transportation and has bad consequences. They presented a vaccine supply chain model involving a distributor and a hospital or clinic. In this article, there is a one-step or two-step inspection and it will be selected based on the cold or non-cold chain problem policies. Finally, they express that the role of the retailer, hospital or clinic, is effective in improving the non-cold chain transportation process. Sajadi et al. (24) designed a vaccine supply chain network. They took into account cost and demand uncertainties. Moreover, they consider other conditions such as limited capacity. For more deep reviews, some related papers could be considered (Hogan et al. (25), Spicknall et al. (26), Pourmehdi et al. (27), Kartoglu et al. (28), Farajzadeh et al. (29), Hosseini et al. (30), Beraud (31), and White et al. (32)).

The critical situation facing the present century is the presence of an unknown virus that has highlighted the importance of designing a powerful network to deal with it. Mahajan and Tomar (33) investigated the disruption effects of COVID-19 on the food supply chain. Decreased access to vegetables and fruits is one of the important issues that have disrupted the chain. They conducted a case study on an online food sales company to analyze the economic effects of COVID-19 on the food chain network. COVID-19 has exposed the shortcomings in the decision to distribute resources. By defining a problem, they try to decide by a central controller to which center to send the test kits (34). Vaccines are often rare (35). Given the importance of health and treatment, governments and public health organizations generally decide whether to allocate vaccines (36). The complexity of vaccine allocation also has an ethical dimension, as justice and efficiency must also be considered in vaccine allocation (37). Kaufmann et al. (38) expressed that the vaccine supply chain network is divided into two parts: the first segment, moves the vaccine to the receiving countries, and the second segment, distributes the vaccines in the recipient countries. In most cases, the main purpose of vaccination is to prevent the spread of the virus (39). Maureen et al. (40) stated that so far, articles in the field of the COVID-19 vaccine have generally been qualitative, and less attention has been paid to the flexibility of the COVID-19 vaccine supply chain while being of great importance (41). They proposed a comprehensive and quantitative flexibility approach in the vaccine supply chain. Abbasi et al. (42) stated that allocation and distribution during COVID-19 vaccination is a complex and dynamic operation, especially on a large scale (43). They described an effective model for their problem. They provided a mathematical model based on exposure risk, sensitivity rate, and constraints such as transshipment capacity. Rastegar et al. (44) presented a mathematical inventory-allocation model for influenza vaccine and stated that equitable distribution of the vaccine plays a very important role in developing countries. They demonstrated the effectiveness of the model by implementing the model in a case study. In their article, they considered that the flu vaccine belongs to the cold chain and that keeping it at the wrong temperature will affect its quality. On the other hand, they believe that ignoring vulnerable groups in the population can lead to disaster. Tsuzuki et al. (45) stated that the most common transmission of the influenza virus is through children and that if the main focus of vaccination programs is on children, the epidemiological impact will be greater than when the focus of vaccination is on the elderly. In addition, vaccinating children is more effective and economical. Esmizadeh et al. (46) presented a hierarchical hub network in the cold supply chain. They tried to formulate a stochastic demand and multi-level freshness time window by expressing an integer multi-objective mathematical model. The model was solved with a genetic algorithm. For more deep reviews, consider the below articles. (e.g., Duijzer et al. (47), Dai et al. (48) and Sarley et al. (49)). Moreover, Table 1 shows a general literature review of the vaccine supply chain.

*****Please insert Table 1*****

2.1. Research gap

Few papers investigated the flu vaccine supply chain, especially during the COVID-19 pandemic. Also, it is claimed that the flu vaccine is a helpful solution to tackle the COVID-19 disease. So, it is important to study and evaluate its supply chain during this pandemic. Therefore, we consider this topic and design a competent supply chain for it during the pandemic. So, it distinguishes our work from others. Two issues are very important in the flu vaccine supply chain. The first one is the time period and the other is the prioritization of applicants due to the limited number of vaccines. Therefore, both issues are taken into account in our work. To show the priority of each applicant, first, the applicants are classified into different groups and then a degree of importance was allocated to each group. Moreover, based on the literature review, the research done germane to the vaccine supply chain has just paid attention to maintenance conditions and has not considered these important subjects. The contributions of this paper are as follows:

- Designing influenza vaccine supply chain network in the pandemic diseases
- Categorizing the customers into different groups and ascribing a degree of importance to each of them.
- Dynamical demand
- Considering a real case study.

3. Problem formulation

3.1. Problem description

One of the most important crises that people face is influenza and its cure. The main step in treating the disease is prevention. Therefore, countries attempt to prevent people from being involved with the flu. Demand for influenza vaccine in Iran has been high in recent years and the emergence advent of the COVID-19 has caused a significant increase in demand for influenza vaccine compared with before. In addition to providing vaccines, the government should try to prevent the spread of the virus by optimal allocation. Some individuals believe that if they get influenza, they are more likely to get the COVID-19 because they have to go to a health center for treatment, which leads them to enter an environment where the COVID-19 patients are also present. That's why so many people want to get the vaccine. Therefore, the distribution and allocation of influenza vaccines to appropriate people are considered necessary.

It should be noted that there are different groups of people in society that require receiving the influenza vaccine. Receipt of sufficient doses of influenza vaccine for the maximum demand is the first thing the vaccine storage center is obliged to purchase from the distributor. In this study, customers are categorized into six groups: 1) Treatment staff, 2) specific patients, 3) babies, 4) elderly, 5) pregnant women and 6) other people. Since the flu vaccine has not been produced in Iran so far, they must import the required vaccine. The vaccine storage center initially imports the flu vaccine from some countries in specific doses. The flu vaccine is also divided into trivalent and quaternary. The quaternary covers more than trivalent virus strains.

Vaccines are delivered as quickly as possible according to the demand of each region. The *Food and Drug organization* of each region receives the vaccines sent from the central vaccine storage center. The main task of distributing the vaccine is the responsibility of the *Food and Drug organization*. There are six groups of applicants for the vaccine, but due to the sensitivity of the vaccine distribution, the desired goods are sent to three centers, so that the vaccine customers can refer to the intended centers. Hospitals, health centers, and pharmacies are the three centers where the distribution center is required to send the flu vaccine according to customer demand and their degree of importance. Hospitals only cover the demand for medical staff, health centers meet the demand of special patients and infants, and the demand for the elderly, pregnant women, and other people is provided by the pharmacy.

One of the most important parameters of the problem is time period. The demand of customers before the distribution of influenza vaccine is clear and all customers intend to receive the vaccine at the first distribution, but it is very important for the *Food and Drug organization* to first allocate the vaccine to the treatment staff that is prone to the disease. Therefore, at this stage, customers will be prioritized then vaccines will be allocated with the customer's degree of importance. The model covers the demand for medical staff in the first time period. In the second stage, there are special patients and infants for whom vaccination is very important, and in the end. Finally, the elderly, pregnant women, and ordinary people are given priority.

The flu vaccine must be stored under certain and particular conditions otherwise it will not affect. On the other hand, it should be noted that the percentage of vaccines in different centers are discarded due to transportation, operator error during transfer, etc.

All customer demands are in the first period, but the vaccines are imported in different periods, and so the distribution center should distribute it in each period. Therefore, the demand is requested in the first period and due to the fact that a significant part of it is not answered, it will be transferred to the next period. Attempts are made to respond to the demand as much as possible in the next time period, otherwise, it will be postponed to the next period and even some customer requests may remain unanswered due to the small amount of vaccine input.

On the other hand, there is a psychological burden among people to inject different vaccines. In other words, vaccine applicants believe that the quaternary or trivalent, as well as the country that produced it, will be very effective. This psychological burden can be due to the advertisements of various companies, conversations between people in the community and many other things that lead applicants to inject quaternary vaccine produced by a particular company; thus psychological burden can be positive or negative. It should be noted that the problem model is based entirely on a case study, so the following factors are considered in the problem:

- The problem is multi-period.
- The demands of medical staff are met by the hospital, special patients and infants by health centers and the elderly, pregnant women, and individuals by the pharmacy.
- A percentage of the vaccines received are discarded due to defects
- Definition of the significant factor for the type of vaccine
- Prioritization of applicants for influenza vaccine
- Demand is certain. Part of the demand may be lost and the issue may be shortage.
- The capacity of the centers is limited.

- Special patients are assumed to be all types of cancer patients, heart patients, etc.
- Babies are 6 to 59 months old.

What is defined in this study is the role of unanswered demand as total demand in the next period. Demand is requested in the first period and if it is not met, it will be saved as a lost request. The demand lost in the first period is defined as the demand in the next period and this operation will continue until the end of the period. Lost demand in the final period will be expressed as a lack of expression. Dynamical demand means that demand does not exist in each period separately, but at the beginning of the period the amount of demand is specified. Therefore, the lost demand at the end of each period is considered as the demand of the next period. The four-level supply chain network which includes the vaccine storage center, the distribution center, customers includes hospital, health center, and pharmacy and waste centers can be seen in Figure 1.

*****Please insert Figure 1*****

The problem is modeled from the perspective of the central vaccine storage center. In the present study, a multi-objective model is proposed and they are cost minimization, maximizing demand coverage based on customer importance and minimizing the maximum of unanswered demand, respectively.
In recent years, the distribution of the influenza vaccine has not been as sensitive as it uses today. The COVID-19 virus has been one of the greatest crises of the century, affecting all medical activities. On the other hand, one of the most dangerous diseases that cause the death of many people in the world during recent years is the flu. The vaccine has been around for years and is updated every year due to the mutation of the virus, but the flu is still dangerous and deadly. The importance of this issue is quite clear and researchers need to get more and more involved in health issues. The mathematical model that is stated below is defined based on a case study and intends to take an important step in the country's healthcare industry by implementing it, because, in the next step, the model can be expanded for the distribution of the Coronavirus vaccine.

3.2. Mathematical model

First, the indices, parameters, and decision variables are defined. Then the mathematical model of the problem is explained according to the assumptions.

Indices

w Vaccine storage center
o Distribution center
h Hospital
e Health center
p Pharmacy
r Waste center
n Product
t Time period
c Customer

Parameters

$V1_{wo}$ Shipping cost from vaccine storage center w to organization o
$V2_{oh}$ Shipping cost from organization o to hospital h
$V3_{oe}$ Shipping cost from organization o to health center e
$V4_{oe}$ Shipping cost from organization o to pharmacy p
$V5_{hr}$ Shipping cost from hospital h to waste center r
$V6_{er}$ Shipping cost from health center e to waste center r

$V7_{pr}$	Shipping cost from pharmacy p to waste center r
D'_{ch}	Demand for costumer c at hospital h
D''_{ce}	Demand for costumer c at health center e
D'''_{cp}	Demand for costumer c at pharmacy p
X_{cn}	The importance degree of product n for customer c
α_{hnt}	The percentage of the defective product n that transporting to hospital h during period t
β_{ent}	The percentage of the defective product n that transporting to health center e during period t
γ_{pnt}	The percentage of the defective product n that transporting to pharmacy p during t
Dis'_{hr}	1, if the hospital h is within the coverage radius of the waste center r
Dis''_{er}	1, if the health center e is within the coverage radius of the waste center r
Dis'''_{pr}	1, if the pharmacy p is within the coverage radius of the waste center r
Cap_{wt}	The capacity of the vaccine storage center w in period t
Cap'_{ot}	The capacity of the organization o in period t
Cap''_{ht}	The capacity of the hospital h in period t
Cap'''_{et}	The capacity of the health center e in period t
$cappt_{pt}$	The capacity of the pharmacy p in period t
Ds'_{oh}	1, if the hospital h is covered by the organization o
Ds''_{oe}	1, if the health center e is covered by the organization o
Ds'''	1, if the pharmacy p is covered by the organization o

Decisions variables

QWO_{wont}	The amount of product n transmitted from vaccine storage center w to organization o in period t
QOH_{ohntc}	The amount of product n transmitted from organization o to hospital h in period t for customer c
QOE_{oentc}	The amount of product n transmitted from organization o to health center e in period t for customer c
QOP_{opntc}	The amount of product n transmitted from organization o to pharmacy p in period t for customer c
SHR_{hrnt}	The amount of product n transmitted from hospital h to waste center r in period t
SER_{ernt}	The amount of product n transmitted from health center e to waste center r in period t
SPR_{prnt}	The amount of product n transmitted from pharmacy p to waste center r in period t
JOH_{ohntc}	The amount of unanswered demand product n that should be transmitted from organization o to hospital h in period t for customer c
JOE_{oentc}	The amount of unanswered demand product n that should be transmitted from organization o to health center e in period t for customer c
JOP_{opntc}	The amount of unanswered demand product n that should be transmitted from organization o to pharmacy p in period t for customer c

Objective functions

$$Min\ Z_1 = \sum_{w,o,n,t} V1_{wo}QWO_{wont} + \sum_{o,h,n,t,c} V2_{oh}QOH_{ohntc} + \sum_{o,e,n,t,c} V3_{oe}QOE_{oentc} + \sum_{o,p,n,t,c} V4_{oe}QOP_{opntc} + \sum_{h,r,n,t} V5_{hr}SHR_{hrnt} + \sum_{e,r,n,t} V6_{er}SER_{ernt} + \sum_{p,r,n,t} V7_{pr}SPR_{prnt} \quad (1)$$

$$Max\ Z_2 = \sum_{o,h,n,t,c} X_{cn}QOH_{ohntc} + \sum_{o,e,n,t,c} X_{cn}QOE_{oentc} + \sum_{o,p,n,t,c} X_{cn}QOP_{opntc} \quad (2)$$

$$Min\ Z_3 = \underset{h}{Max}\left\{\sum_{o,n,t,c} JOH_{ohntc}\right\} + \underset{e}{Max}\left\{\sum_{o,n,t,c} JOE_{oentc}\right\} + \underset{p}{Max}\left\{\sum_{o,n,t,c} JOP_{opntc}\right\} \quad (3)$$

The first objective function in Eq. (1) is to minimize the transportation cost. It considers the cost of shipping the vaccine storage center to the distribution center, from the distribution center to customers, and finally from the customers to the waste center.

In Eq. (2), the second objective function is to maximize the amount of delivered product to the customer based on its importance degree. In other words, customers are prioritized and those customers for whom vaccination is necessary are given higher priority. In this case, the modeling was based on the real world, and it can even be said that it was a look at the sensitivity of the distribution of the COVID-19 vaccine in the future. Therefore, according to this objective function, the vaccine will first be injected into people who have a higher degree of importance, for example, the treatment staff has a much higher priority than a normal person because they face the disease directly and if they get the disease will have worse consequences.

In Eq. (3), the third objective function also seeks to minimize the maximum unfulfilled demand at hospitals, health centers, and pharmacies. In the third objective, the model tries to balance the lost demand for customers. In other words, the problem model does not meet only one customer that has the biggest range of importance because the second objective is to prioritize customers. The third objective serves the purpose of justice among customers.

Constraints

$$\sum_{w} QWO_{wont} = \sum_{h}\sum_{c} QOH_{ohntc} + \sum_{e}\sum_{c} QOE_{oentc} + \sum_{p}\sum_{c} QOP_{opntc} \qquad \forall o,n,t \quad (4)$$

$$\sum_{o}\sum_{c} \alpha_{hnt} QOH_{ohntc} Dis'_{hr} = SHR_{hrnt} \qquad \forall h,r,n,t \quad (5)$$

$$\sum_{o}\sum_{c} \beta_{ent} QOE_{oentc} Dis''_{er} = SER_{ernt} \qquad \forall e,r,n,t \quad (6)$$

$$\sum_{o}\sum_{c} \gamma_{pnt} QOH_{opntc} Dis'''_{pr} = SPR_{prnt} \qquad \forall p,r,n,t \quad (7)$$

$$\sum_{o}\sum_{n} (1-\alpha_{hnt}) QOH_{ohntc} Ds'_{oh} + \sum_{o}\sum_{n} JOH_{ohntc} = D'_{ch} \qquad \forall c,h,t=1 \quad (8)$$

$$\sum_{o}\sum_{n} JOH_{ohn(t-1)c} = \sum_{o}\sum_{n} \left((1-\alpha_{hnt}) QOH_{ohntc} Ds'_{oh} + JOH_{ohntc}\right) \qquad \forall c,h,t>1 \quad (9)$$

$$\sum_{o}\sum_{n} (1-\beta_{ent}) QOE_{oentc} Ds''_{oe} + \sum_{o}\sum_{n} JOE_{oentc} = D''_{ce} \qquad \forall c,e,t=1 \quad (10)$$

$$\sum_{o}\sum_{n} JOE_{oen(t-1)c} = \sum_{o}\sum_{n} \left((1-\beta_{ent}) QOE_{oentc} Ds''_{oe} + JOE_{oentc}\right) \qquad \forall c,e,t>1 \quad (11)$$

$$\sum_{o}\sum_{p} (1-\gamma_{pnt}) QOP_{opntc} Ds'''_{op} + \sum_{o}\sum_{p} JOP_{opntc} = D'''_{cp} \qquad \forall c,p,t=1 \quad (12)$$

$$\sum_{o}\sum_{n} JOP_{opn(t-1)c} = \sum_{o}\sum_{n} \left((1-\gamma_{pnt}) QOP_{opntc} Ds'''_{op} + JOP_{opntc}\right) \qquad \forall c,p,t>1 \quad (13)$$

$$\sum_{o}\sum_{n} QWO_{wont} \le Cap_{wt} \qquad \forall w,t \quad (14)$$

$$\sum_{w}\sum_{n} QWO_{wont} \leq Cap'_{ot} \qquad \forall o,t \qquad (15)$$

$$\sum_{o}\sum_{n}\sum_{c}(1-\alpha_{hnt})QOH_{ohntc} \leq Cap''_{ht} \qquad \forall h,t \qquad (16)$$

$$\sum_{o}\sum_{n}\sum_{c}(1-\beta_{ent})QOE_{oentc} \leq Cap'''_{et} \qquad \forall e,t \qquad (17)$$

$$\sum_{o}\sum_{n}\sum_{c}(1-\gamma_{pnt})QOP_{opntc} \leq cappt_{pt} \qquad \forall p,t \qquad (18)$$

Constraint (4) represents the balance between the input and output currents of the distribution center. This organization is obliged to transfer all the vaccines it receives from the vaccine storage center to the hospital, health center, and pharmacy. In this constraint, it is clear that no vaccine will remain in stock for the next period. Constraints (5)- (7) indicate that some vaccines cannot be used due to defects and must be shipped to a waste center. There is a different percentage of defective vaccines for hospitals, health centers, and pharmacies, and this is because the storage and transportation of the vaccine have certain conditions that can lead to corruption. Constraint (8) states that a healthy vaccine will meet customer demand if it is within a coverage radius and transported to a hospital. If part of the request is not answered, constraint 9 indicates that it will be replaced as a request. In this way, the unanswered demand at each stage is defined as the demand for the next period. In other words, demand in each period is updated by the lost demand of the previous period. Vaccine demand for customers is initially fixed and is allocated at different time periods based on the model. Constraints (10) and (11) do the same for health centers, and Constraints (12) and (13) do the same for pharmacy demand. Constraints (14)- (18) indicate limited capacity determination. Each level can store a certain level.

3.3. Linearization of the third objective function

Since the third objective function is nonlinear, the following constraints are used for linearization. y_h, y_e and y_p are free variable that replaces the maximum lost demand. Since y_h, y_e and y_p must get the maximum value possible, Constraints (20)- (22) make this condition.

$$Min\ Z_3 = \sum_{h} y_h + \sum_{e} y_e + \sum_{p} y_p \qquad (19)$$

$$y_h \geq \sum_{h}\sum_{n}\sum_{t}\sum_{c} JOH_{ohntc} \qquad \forall h \qquad (20)$$

$$y_e \geq \sum_{e}\sum_{n}\sum_{t}\sum_{c} JOE_{oentc} \qquad \forall e \qquad (21)$$

$$y_p \geq \sum_{p}\sum_{n}\sum_{t}\sum_{c} JOP_{opntc} \qquad \forall p \qquad (22)$$

3.4 Multi-objective optimization approach

In the real world, issues have different goals and managers want to optimize all their goals (50). There are many approaches to dealing with multi-objective issues, some of which depend on the decision-maker to prioritize (51), while others try to minimize deviations from all goals (52). In this research, the lexicographic method will be applied .This approach will be described below. Multi-objective optimization problems have more than one goal, which can be minimization or maximization. Goals conflict with each other, meaning that improving one goal makes the other worse or does not change the other. The general form of a multi-objective optimization problem is as follows:

$min/\max\ f_m(x) \qquad \forall\, m \in M \qquad (25)$

Subject to: $\quad g_j(x) > 0 \qquad \forall\, j \in J \qquad (26)$

$\qquad h_k(x) = 0 \qquad \forall\, k \in K \qquad (27)$

One method of solving multi-objective optimization is the lexicographic approach. In this method, the decision-maker prioritizes the objective functions and according to that, the problem solving operation begins. Assume that the importance and priority of the objectives are according to their indices, f_1 the most important and f_m the least important. Then, the problem is solved as follows:

$$\max\ f_1 \tag{25}$$

$$\text{Subject to:} \quad g_j(x) \leq 0 \qquad \forall\, j \in J \tag{26}$$

$$h_k(x) \leq 0 \qquad \forall k \in K \tag{27}$$

$$x \geq 0 \tag{28}$$

So, f_1^* is the optimal answer to the model written above. By taking into account f_1^*, the model below is formulated by considering the second most important objective function.

$$\max f_2 \tag{29}$$

$$\text{Subject to:} \quad g_j(x) \leq 0 \qquad \forall\, j \in J \tag{30}$$

$$f_1(x) = f_1^* \tag{31}$$

This process continues respectively until considering the last objective function. When several conflicting objectives are of importance, there is no single optimal answer that minimizes or maximizes all desired objective functions at the same time. The solution output of a multi-objective optimization problem is a set of alternate answers with corresponding values for the desired purposes called Pareto. The answers in the Pareto sets do not differ in mathematical terms. If f_1 the first priority object, optimal range answer would be $x_b \leq x \leq x_c$. Due to the minimizing $f_1(x)$, in this circumstance, the $f_2(x)$ will be minimized at the point x_c, accordingly x_c is the answer to the problem. This method is sensitive to the prioritizing by the decision-maker, and it is evident that the optimal solution of the model changes if the ranking of goals alters. During the vaccination allocation process, the order of priority of customers is most important because it can prevent the spread of disease and mortality, which is defined in the second objective function. The next priority is to minimize the maximum lost demand, and finally, the cost to the *ministry of health and medical education* (MOHME) is the priority, which is the third and first goals of the problem model, respectively. There are many approaches to multi-objective optimization solution methods, in this problem the lexicographic approach is used.

4. Case study

4.1. Case description and input parameters

Today, academic research is defined in terms of the real problems of organizations. Therefore, the effectiveness of research can be evaluated in a real case study. In this study, the problem is defined based on a real case, which is one of the biggest problems of the treatment system in special COVID-19 conditions.

Mazandaran is located in the north of Iran and because of having the most beautiful scenery in Iran, it always attracts many travelers. The arrival of travelers to an area is always considered positive because it causes the economic prosperity of the area, but this time we must look at it from another angle. The arrival of non-natives to visit the sights, if viewed from the perspective of the health system, causes the entry of different diseases into a province. Imagine a sick tourist entering an area and spreading the virus. Clearly, the health system of that region will be in crisis for a long time and the people of that region will have to pay for the beauty of their province in this way. On the other hand, when many travelers enter a province, they naturally use the health care system there as well. In other words, the health facilities of the people of one province are shared by others, and sometimes these areas also face shortages. During the COVID-19 arrival period, Mazandaran province has always been one of the most affected by coronavirus disease in the country.

Influenza vaccine has always had many applicants during its implementation period, and now that the COVID-19 is the main health crisis of the current century, the demand for influenza vaccine among the people has multiplied. Humans have been exposed to many viruses during their lifetimes, such as plague and tuberculosis, and in the present age, the COVID-19 has caused the death of many people around the world. The flu vaccine, despite the efforts of scientists to produce it for many years and is updated every year due to changes in the virus, but still could not prevent the death of some patients with the flu. One of the challenges that the health system of any country faces is fair and priority distribution to prevent the Prevalence of disease and death of patients as much as possible.

In this study, the *ministry of health and medical education* (MOHME) is in charge of receiving the vaccine and distributing it. Since the flu vaccine has not yet been produced in the country, it must be purchased from other countries. The purchased vaccine is collected in the vaccine storage center of the ministry of health and medical education, and from there the vaccine is allocated to the food and drug organization of each province according to the amount of demand. Some provinces have several organizations due to their population and area. In this article, the issue is to distribute the flu vaccine among the applicants in Mazandaran province with a fair and priority distribution. According to the above explanations, the first level of the supply chain is the Ministry of Health's vaccine storage center, and the problem, as stated in the modeling section, is the three goals of cost minimization, maximization of allocation based on priority, and minimization of maximum lost demand in hospitals, health centers, and pharmacies is included. Three types of trivalent and quaternary vaccines are sent by the vaccine storage center. Customers have different views on each of these three vaccines based on personal information, which affects their significance. The cities for the case study are shown in Figure 2.

*****Please insert Figure 2*****

There are two Iran Food and Drug Organizations (IFDOs) in Mazandaran province and each of them covers different cities. The IFDO number 2 covers two cities of Babol and Babolsar and IFDO number 1 covers other cities of Mazandaran province. In each city of Mazandaran province, a hospital, health center, and pharmacy are defined as a reference for receiving vaccines. Each customer refers to each of the mentioned centers according to the defined mechanism. The amount of vaccine allocated by the vaccine storage center is shown in Table2. Tables (3) to (6) show the capacity of each center.

*****Please insert Table 2*****

*****Please insert Table 3*****

*****Please insert Table 4*****

*****Please insert Table 5*****

*****Please insert Table 6*****

The demand for influenza vaccine is summarized in Tables (7) to (9). Table 7 shows the total customer demand in the hospital. The hospital only meets the demand of the medical staff. Table 8 shows the level of customer demand from health centers. The clients of the health center are special patients and infants from 6 to 59 months. Table 9 also shows the demand for pharmacy customers. Pharmacy customers include the elderly, pregnant women, and the general public.

*****Please insert Table 7*****

*****Please insert Table 8*****

*****Please insert Table 9*****

It is worth mentioning that 2% of the items sent by the IFDO could not be used for reasons such as corruption, breakage, and others and will be sent to the waste center. Table 10 shows how important the type of vaccine is for each client. On the other hand, it is clear that customers also have priority over each other. As shown in Table 10, the treatment staff has the highest priority for receiving the type 1 vaccine, and normal people have the lowest priority in this regard. Each hospital, health center, and pharmacy can only move their defective product to their city waste center.

*****Please insert Table 10*****

4.2. Computational results

The definitive model of the flu vaccine supply chain network has been solved by considering the input parameters in GAMS software, MIP model was resolved with CPLEX by a computer with Intel Core i5 and 4 GB specification. Since the problem has three goals, one of the multi-objective optimization approaches must be considered to solve the problem. The problem is presented using a lexicographic approach. The optimal values of the problem after solving with the lexicographic approach are given in Table 11. The second goal has the first priority, the third goal has the second priority and the first goal has the last priority.

*****Please insert Table 11*****

As expected, the second objective gets its best value by prioritizing the problem objectives based on the method of solving the function. Then the third objective function according to the answer to the problem by the second objective function gets a worse answer than the ideal answer expressed through the single objective function and so for the first objective function. The third objective function has deteriorated by 13% and the first objective function by 33%, and this is in exchange for the second objective function having its best value.

The problem model, according to the objective functions, tries to meet the restrictions of the problem and allocate the vaccine accordingly to the customers and centers. In this study, 6 groups of customers received the vaccine from the intended centers. As stated in the second goal, the treatment staff has a high priority, and then special patients and infants are given priority. The problem model has met all the demands of the medical staff through the hospital. On the other hand, 85% of customers 'requests are met from the health center and 54% of customers' requests are met from pharmacies that shown in Figure 3. In total, 79% of flu vaccine demands have been answered and only 21% of demands have been lost.

*****Please insert Figure 3*****

Figure 4 shows what percentage of each customer's demand is met. As mentioned earlier, all the demands of the medical staff have been met. Given the objectives of the issue and its limitations, Figure 4 shows what percentage of other customers' demands have been met.

*****Please insert Figure 4*****

Tables (12)-(13) show how much of each vaccine is given to customers in each time period. Tables 12 and 13 show how much vaccine is delivered from the IFDO to the hospital to meet the demand of the first client, the treatment staff.

*****Please insert Table 12*****

*****Please insert Table 13*****

Tables (14)-(17) show how much vaccine is delivered from IFDO to health centers to meet second and third customer demand.

*****Please insert Table 14*****

*****Please insert Table 15*****

*****Please insert Table 16*****

*****Please insert Table 17*****

Tables (18)-(23) show how much vaccine is delivered from IFDO to the pharmacy to meet customer demand.

*****Please insert Table 18*****

*****Please insert Table 19*****

*****Please insert Table 20*****

*****Please insert Table 21*****

*****Please insert Table 22*****

*****Please insert Table 23*****

In the third section, the problem was precisely defined and its hypotheses were explained. Then, by presenting a multi-objective mathematical model of the conceptual model of the problem and solving it using the lexicographic method, the model answer was presented quite accurately.

4.3. Sensitivity analyses and managerial implications

Mathematical modeling and its implementation are very important in a case study, but what better shows the output of research is the sensitivity analysis and the proposed management packages. Sensitivity analysis means what effect changes will have on the parameters of the problem, and to what extent these changes can improve the situation. Then, by analyzing and presenting a managerial package insight to the manager, it leads to the efficiency and effectiveness of research. In addition to defining the problem and solving it from real problems, the academic environment should have a comprehensive analysis of the situation so that managers can try to solve it by raising the issue. In the following, several cases of sensitivity analysis regarding the problem model are collected.

4.3.1. The effects of changing the percentage of defective vaccine

The effect of decreasing or increasing the percentage of vaccine defects on the Objective Functions (OFs) is shown in Figure 5. As it is observed, if the percentage of the defective products increases for various reasons, the second OF, the importance range of each vaccine type for customers, will have a sharp decrease. If the percentage of defective items increases, the lost demand increases, it is natural that the amount of second OF decreases. Increasing or decreasing the spoiled vaccine percentage has a direct effect on lost demand, hence the third OF, minimizing maximum lost demand, will change; an increasing the percentage of vaccine defect cause to increase this OF. On the other hand, if the percentage of defective items is reduced, it will have a significant impact on reducing the first OF.

*****Please insert Figure 5*****

4.3.2. Sensitivity analysis of assigning the IFDO to customers under different scenarios

Figure 6 demonstrates that if the main scenario of the IFDOs are allocated to customer changes, how much changing the response to the problem will have. In this regard, three different scenarios are defined: the first scenario is in accordance with the main problem form; The second scenario is when there are no restrictions on sending from the IFDOs to customers in all cities; The third one is that the first IFDO should meet the demand of customers in cities 1 to 5, and the second IFDO should be responsible for the demand of other remaining cities.

Obviously, it is expected that in the second scenario by eliminating the allocation of cities to IFDOs, the total costs of the problem will be reduced; because if each IFDO meets the demand for vaccines according to its distance from the centers, the costs will be reduced. It should be noted that the goals of customer prioritization (the second OF) and minimizing the maximum lost demand of each center (the third OF) have a higher priority than the first OF, and it represents the significant results of this sensitivity analysis shown in Figure 6.

*****Please insert Figure 6*****

4.3.3. Sensitivity analysis of increasing the capacity of the MOHME

Figure 7 reveals that if the MOHME can increase the initial capacity, it will improve the OFs and increase the percentage of demand response. In this regard, three different scenarios are defined to examine the changes in the OFs. The first scenario describes the current situation of the problem. The second scenario states that the capacity of the MOHME increases by 5% and in the third scenario it increases by 10%. In the current situation, 79% of the demand is answered. Under the second scenario, 84% of the demand is met, and the second and third OFs will be improved. As more vaccines are delivered across the supply chain network, the first OF, reducing the costs, increased. All the outcomes of the second and the third scenario are identical except when 88% of the demand will be met.

*****Please insert Figure 7*****

4.3.4. Conflict of the objectives

Figure 8 indicates the conflict between the OFs and Figure 9 denotes the conflict between the second and third OF. The second OF prioritizes the customers based on their urgent need for vaccines and the third OF is justice among the customers. The second OF increases, the third OF also increases, so this indicates the conflict.

*****Please insert Figure 8*****

*****Please insert Figure 9*****

The main purpose of this study is to present a practical mechanism helping the healthcare system in epidemic conditions such as COVID-19, which vehemently affects the treatment process. The flu virus has endangered the health of many people globally in recent years, and even though its vaccine has been developed, people who become infected with the disease are still in danger of dying. During an epidemic like COVID-19, which has flu-like symptoms, the demand for the flu vaccine increases as people try to prevent any disease, and the need for proper management and planning in medical and health dominations are more necessary than any other times. Therefore, to cover this issue, special attention must be paid to social justice.

4.4. Managerial insights

This study provides useful suggestions for the government and managers of medical departments and other related institutions from different perspectives. Considering the findings, some of the recommendations are presented:

1. One of the critical issues in health is preventing the spread of diseases in the community. Hence, the effort to improve the performance of medical product supply chain by prioritizing applicants would help this cause. Nowadays, when the shadow of COVID-19 is on all health issues, the demand for the flu vaccine has also increased. Therefore, distribution centers can play an essential role in this chain. In this study, it has been observed that changing the radius of coverage of distribution centers, IFDO, can significantly influence the answer to the problem.
2. Improper management in the health network can have irreparable consequences. The rate of transmission of influenza can increase the number of people with the disease in a short time.

Furthermore, each vaccine not only saves one life but can prevent many people from becoming infected. Therefore, with efficient management, it will be possible to reduce the percentage of spoiled vaccines during transfers.

3. Using experts to calculate sufficient capacity for centers can significantly reduce the risk of catching the flu. In section 4.3.3, it has been observed that managers can transfer more vaccines by considering more capacity for their centers. In this study, the importance of capacity is quite tangible. In the present study, by increasing the input capacity by 10%, the satisfied demand changes from 79% to 88%.
4. In this research, it has been shown that the considered supply chain had the highest productivity with the lowest cost. Effective and efficient supply chain network design in this study made the minimization of costs possible.

5. Conclusion

The current study presents a mathematical model for the influenza vaccine supply chain network during the COVID-19 epidemic. In this study, the problem faces limitations such as grouping vaccinations, prioritizing individuals and their degree of importance, vaccine shortages, and covering lost demand as quickly as possible. The designed network is a multi-level supply chain including vaccine storage center, distribution center, customer groups, and waste center. Also, the model is a multi-objective one including minimizing costs, prioritizing vaccine applicants, and establishing justice and morality. The first objective minimizes the cost of transportation. The second objective function categorizes customers into different groups and ranks them based on their degree of importance, the likelihood of being infected with the virus, and its spread. In this research, it was stated that the demand is equal to the requested vaccine at the beginning of the period. Due to the conditions of the problem and the arrival of the vaccine during different periods, the demand in each period is updated according to the lost demand of the previous period. The third objective function minimizes the maximum lost demand for each center, hospital, health center, and pharmacy. In the second objective function, customers have priority and it causes that some customers who have emergency conditions and are placed in a lower category to be ignored. Therefore, the third OF tries to solve this problem. Significant conflict is formed between the second and third OFs leads to optimal Pareto responses.

- One of the suggestions of the present study is to examine the strategic and tactical decisions of the supply chain. The vaccine is maintained under special conditions, and in this regard, such as maintenance and transmission conditions can be considered.
- The issue of scheduling the movement of vehicles on the network route is critical. Given that vaccines are also a perishable commodity.
- Define the mechanism after vaccination. Medical products can lead to the spread of infection in the community after consumption. Therefore, centers should be considered for sterilization before using medical products. Biological risk is always lurking, so considering a reverse supply chain network is essential too.
- Routing under different scenarios can also make this research more interesting. In this research, the COVID-19 epidemic has been considered, and in other researches, this issue can be evaluated in some other critical situations such as earthquakes.

References

1. Meng Y, Jin M, Tang X, Xu J. "Drug repositioning based on similarity constrained probabilistic matrix factorization: COVID-19 as a case study". *Applied soft computing*. (2021).
2. Garai A, Chowdhury S, Sarkar B, Roy TK. "Cost-effective subsidy policy for growers and biofuels-plants in closed-loop supply chain of herbs and herbal medicines: An interactive bi-objective optimization in T-environment". *Applied Soft Computing*.(2021).
3. Shahparvari S, Hasanizadeh B, Mohammadi A, Kiani B, Lau KH, Chhetri P, et al. "A Decision Support System for Prioritised COVID-19 Two-dosage Vaccination Allocation and Distribution". *Available at SSRN* 3762826. (2021).

4. Fong SJ, Li G, Dey N, Crespo RG, Herrera-Viedma E. "Composite Monte Carlo decision making under high uncertainty of novel coronavirus epidemic using hybridized deep learning and fuzzy rule induction". *Applied soft computing*. (2020).
5. Tobin-West C. "EFFECTS OF HEALTH WORKERS TRAINING ON THE PROPORTIONS OF MISSED OPPORTUNITIES FOR CHILDHOOD IMMUNIZATION IN KHANA LOCAL GOVERNMENT AREA OF RIVERS STATE". *PUBLIC HEALTH*. (2008).
6. Galazka A, Milstien J, Zaffran M. "Thermostability of vaccines" (WHO document ref. WHO/GPV/98.07). *Geneva: WHO*. (1998).
7. Adu F, Adedeji A, Esan J, Odusanya O. "Live viral vaccine potency: an index for assessing the cold chain system". *Public health*. (1996).
8. Hanjeet K, Lye M, Sinniah M, Schnur A. "Evaluation of cold chain monitoring in Kelantan, Malaysia". *Bulletin of the World Health Organization*. (1996).
9. Thakker Y, Woods S. "Storage of vaccines in the community: weak link in the cold chain?" *British medical journal*. (1992).
10. Casto DT, Brunell PA. "Safe handling of vaccines". *Pediatrics*. (1991).
11. Ferguson NM, Keeling MJ, Edmunds WJ, Gani R, Grenfell BT, Anderson RM, et al. "Planning for smallpox outbreaks". *Nature*. (2003).
12. Setia S, Mainzer H, Washington ML, Coil G, Snyder R, Weniger BG. "Frequency and causes of vaccine wastage". *Vaccine*. (2002).
13. Omilabu S, Oyefolu A, Ojo O, Audu R. "Potency status and efficacy of measles vaccine administered in Nigeria: a case study of three EPI centres in Lagos, Nigeria". *African journal of medicine and medical sciences*. (1999).
14. Oyefolu A, Nwaeke A, Audu R, Akinyemi K, Salu O, Muller C, et al. "Evaluation of Measles vaccine cold chain in Lagos state, Nigeria". *African Journal of Clinical and Experimental Microbiology*. (2007).
15. Zuckerman JN. "Protective efficacy, immunotherapeutic potential, and safety of hepatitis B vaccines". *Journal of medical virology*. (2006).
16. Yadav P. "Health product supply chains in developing countries: diagnosis of the root causes of underperformance and an agenda for reform". *Health Systems & Reform*. (2015).
17. Health UDo, Services H. "HHS pandemic influenza plan". *Washington (DC): The Department*. (2005).
18. Lee BY, Assi T-M, Rookkapan K, Wateska AR, Rajgopal J, Sornsrivichai V, et al. "Maintaining vaccine delivery following the introduction of the rotavirus and pneumococcal vaccines in Thailand". *PloS one*. (2011).
19. Shittu E, Harnly M, Whitaker S, Miller R. "Reorganizing Nigeria's vaccine supply chain reduces need for additional storage facilities, but more storage is required". *Health Affairs*. (2016).
20. Huang H-C, Singh B, Morton DP, Johnson GP, Clements B, Meyers LA. "Equalizing access to pandemic influenza vaccines through optimal allocation to public health distribution points". *PloS one*. (2017).
21. Chen X, Li M, Simchi-Levi D, Zhao T. "Allocation of COVID-19 vaccines under limited supply". *Available at SSRN* 3678986. (2020).
22. Buccieri K, Gaetz S. "Ethical vaccine distribution planning for pandemic influenza: Prioritizing homeless and hard-to-reach populations". *Public Health Ethics*. (2013).
23. Lin Q, Zhao Q, Lev B. "Cold chain transportation decision in the vaccine supply chain". *European Journal of Operational Research*. (2020).
24. Sadjadi SJ, Ziaei Z, Pishvaee MS. "The design of the vaccine supply network under uncertain condition". *Journal of Modelling in Management*. (2019).
25. Hogan AB, Campbell PT, Blyth CC, Lim FJ, Fathima P, Davis S, et al. "Potential impact of a maternal vaccine for RSV: a mathematical modelling study". *Vaccine*. (2017).

26. Spicknall IH, Looker KJ, Gottlieb SL, Chesson HW, Schiffer JT, Elmes J, et al. "Review of mathematical models of HSV-2 vaccination: Implications for vaccine development". *Vaccine*. (2019).
27. Pourmehdi M, Paydar MM, Asadi-Gangraj E. "Reaching sustainability through collection center selection considering risk: using the integration of Fuzzy ANP-TOPSIS and FMEA". *Soft Computing*. (2021).
28. Kartoglu UH, Moore KL, Lloyd JS. "Logistical challenges for potential SARS-CoV-2 vaccine and a call to research institutions, developers and manufacturers". *Vaccine*. (2020).
29. Farajzadeh F, Moadab A, Valilai OF, Houshmand M. "A Novel Mathematical Model for a Cloud-Based Drone Enabled Vehicle Routing Problem considering Multi-Echelon Supply Chain". *IFAC-PapersOnLine*. (2020).
30. Hosseini SM, Paydar MM, Alizadeh M, Triki C. "Ecotourism supply chain during the COVID-19 pandemic: A real case study". *Applied Soft Computing*. (2021).
31. Béraud G. "Mathematical models and vaccination strategies". *vaccine*. (2018).
32. White MT, Verity R, Churcher TS, Ghani AC. "Vaccine approaches to malaria control and elimination: Insights from mathematical models". *Vaccine*. (2015).
33. Mahajan K, Tomar S. "COVID-19 and Supply Chain Disruption: Evidence from Food Markets in India". *American journal of agricultural economics*. (2021).
34. Thul L, Powell W. "Stochastic Optimization for Vaccine and Testing Kit Allocation for the COVID-19 Pandemic". *arXiv preprint arXiv*:210101204. (2021).
35. Westerink-Duijzer E, Schlicher L, Musegaas M. "Fair allocations for cooperation problems in vaccination". (2019).
36. Keeling MJ, Shattock A. "Optimal but unequitable prophylactic distribution of vaccine. Epidemics". (2012).
37. Teytelman A, Larson RC. "Multiregional dynamic vaccine allocation during an influenza epidemic". *Service Science*. (2013).
38. Kaufmann JR, Miller R, Cheyne J. "Vaccine supply chains need to be better funded and strengthened, or lives will be at risk". *Health Affairs*. (2011).
39. Seib K, Pollard AJ, de Wals P, Andrews RM, Zhou F, Hatchett RJ, et al. "Policy making for vaccine use as a driver of vaccine innovation and development in the developed world". *Vaccine*. (2017).
40. Golan MS, Trump BD, Cegan JC, Linkov I. "The Vaccine Supply Chain: A Call for Resilience Analytics to Support COVID-19 Vaccine Production and Distribution". *arXiv preprint arXiv*:201114231. (2020).
41. Ezzat D, Hassanien AE, Ella HA. "An optimized deep learning architecture for the diagnosis of COVID-19 disease based on gravitational search optimization". *Applied Soft Computing*. (2020).
42. Abbasi B, Fadaki M, Kokshagina O, Saeed N, Chhetri P. "Modeling Vaccine Allocations in the COVID-19 Pandemic: A Case Study in Australia". *Available at SSRN* 3744520. (2020).
43. Mishra AR, Rani P, Krishankumar R, Ravichandran K, Kar S. "An extended fuzzy decision-making framework using hesitant fuzzy sets for the drug selection to treat the mild symptoms of Coronavirus Disease 2019 (COVID-19)". *Applied Soft Computing*. (2021).
44. Rastegar M, Tavana M, Meraj A, Mina H. "An inventory-location optimization model for equitable influenza vaccine distribution in developing countries during the COVID-19 pandemic". *Vaccine*. (2021).
45. Tsuzuki S, Baguelin M, Pebody R, van Leeuwen E. "Modelling the optimal target age group for seasonal influenza vaccination in Japan". *Vaccine*. (2020).
46. Esmizadeh Y, Bashiri M, Jahani H, Almada-Lobo B. "Cold chain management in hierarchical operational hub networks". *Transportation Research Part E: Logistics and Transportation Review*. (2021).

47. Duijzer LE, Van Jaarsveld W, Dekker R. "Literature review: The vaccine supply chain". *European Journal of Operational Research*. (2018).
48. Dai T, Cho S-H, Zhang F. "Contracting for on-time delivery in the US influenza vaccine supply chain". *Manufacturing & Service Operations Management*. (2016).
49. Sarley D, Mahmud M, Idris J, Osunkiyesi M, Dibosa-Osadolor O, Okebukola P, et al. "Transforming vaccines supply chains in Nigeria". *Vaccine*. (2017).
50. Alizadeh M, Sharbafi F, Paydar MM. "A bi-objective natural disaster blood supply chain network considering blood transfusion: A case study in Babol". I*nternational Journal of Industrial Engineering and Management Science*. (2020).
51. Pourmehdi M, Paydar MM, Asadi-Gangraj E. "Scenario-based design of a steel sustainable closed-loop supply chain network considering production technology". *Journal of Cleaner Production*. (2020).
52. Alizadeh M, Makui A, Paydar MM. "Forward and reverse supply chain network design for consumer medical supplies considering biological risk". *Computers & Industrial Engineering*. (2020).
53. Bozorgi A, Fahimnia B. "Transforming the vaccine supply chain in Australia: Opportunities and challenges". *Vaccine*. (2021).
54. Sun X, Andoh EA, Yu H. "A simulation-based analysis for effective distribution of COVID-19 vaccines: A case study in Norway". *Transportation Research Interdisciplinary Perspectives*. (2021).
55. Chandra D, Vipin B, Kumar D. "A fuzzy multi-criteria framework to identify barriers and enablers of the next-generation vaccine supply chain". *International Journal of Productivity and Performance Management*. (2021).
56. Golan MS, Trump BD, Cegan JC, Linkov I. "The vaccine supply chain: A call for resilience analytics to support COVID-19 vaccine production and distribution". *COVID-19: Systemic Risk and Resilience*: Springer; (2021).
57. Bulula N, Mwiru DP, Swalehe O, Mori AT. "Vaccine storage and distribution between expanded program on immunization and medical store department in Tanzania: a cost-minimization analysis". *Vaccine*. (2020).
58. de Carvalho MI, Ribeiro D, Barbosa-Povoa AP. "Design and Planning of Sustainable Vaccine Supply Chain". *Pharmaceutical Supply Chains-Medicines Shortage*s: Springer; (2019).
59. Chandra D, Kumar D. "Prioritizing the vaccine supply chain issues of developing countries using an integrated ISM-fuzzy ANP framework". *Journal of Modelling in Management*. (2019).
60. Chandra D, Kumar D. "Analysis of vaccine supply chain issues using ISM approach". *International Journal of Logistics Systems and Management*. (2018).
61. Lee BY, Haidari LA, Prosser W, Connor DL, Bechtel R, Dipuve A, et al. "Re-designing the Mozambique vaccine supply chain to improve access to vaccines". *Vaccine*. (2016).

List of Figures:

List of Tables:

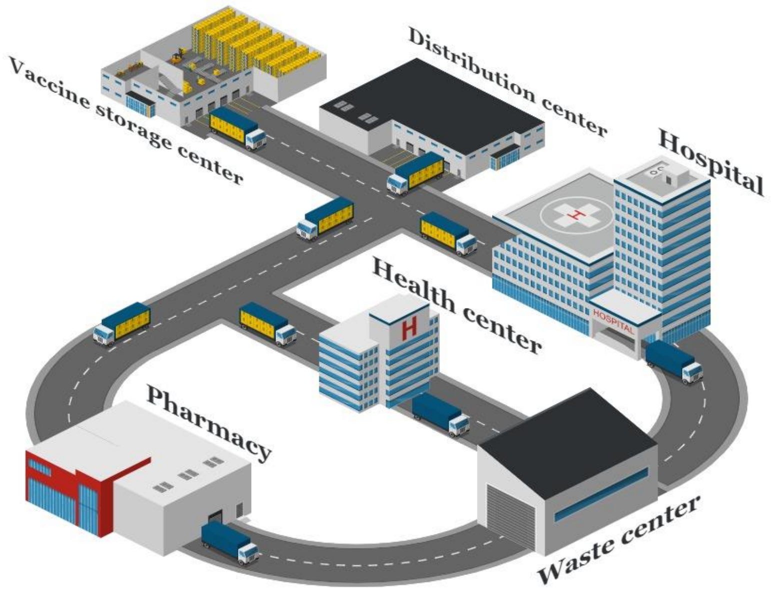

Figure 1. The proposed supply chain network problem

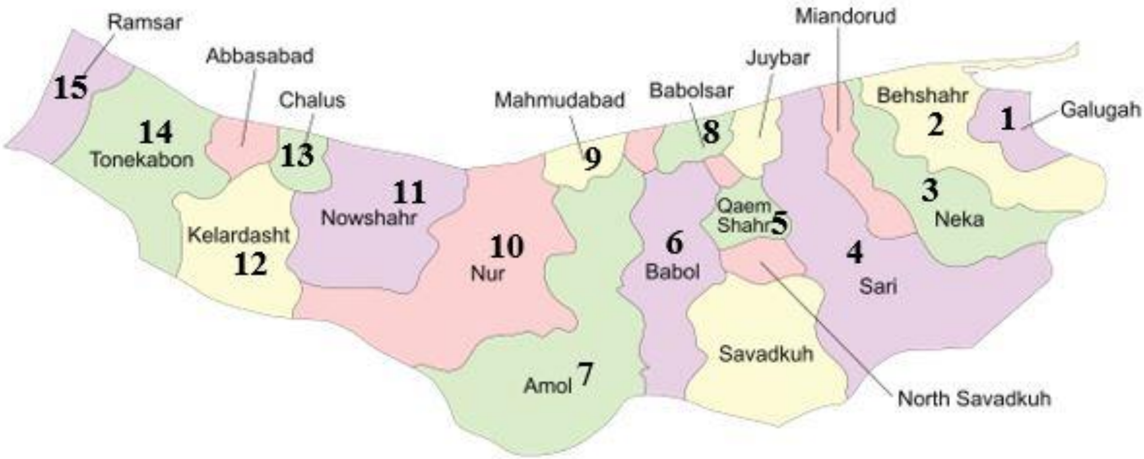

Figure 2. Cities for the case study

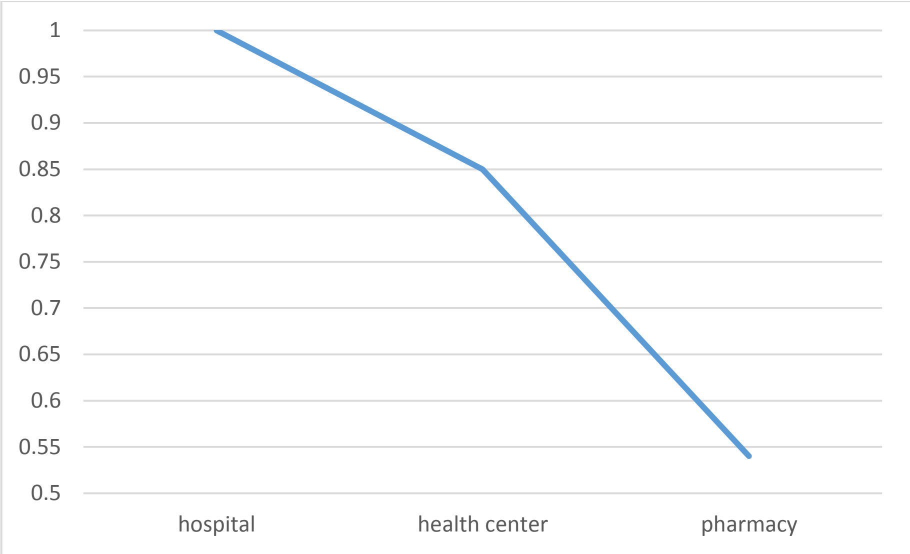

Figure 3. Percentage of demand met for each center

Figure 4. Percentage of demand met for each type of customer

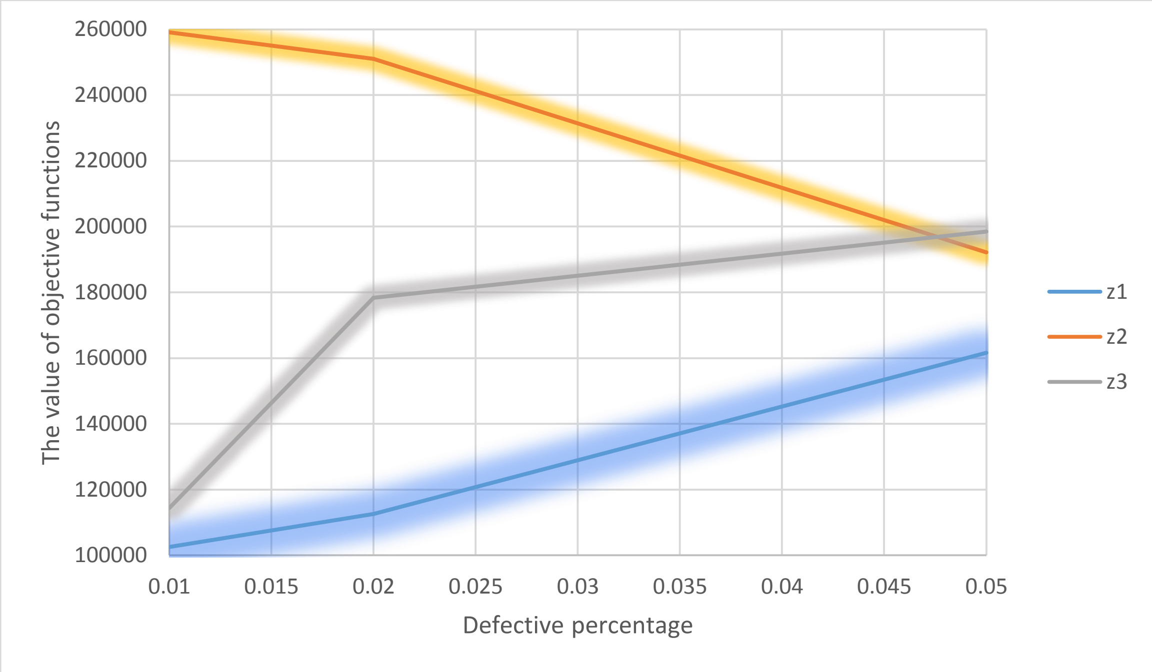

Figure 5. Effect of defect percentage on objective functions

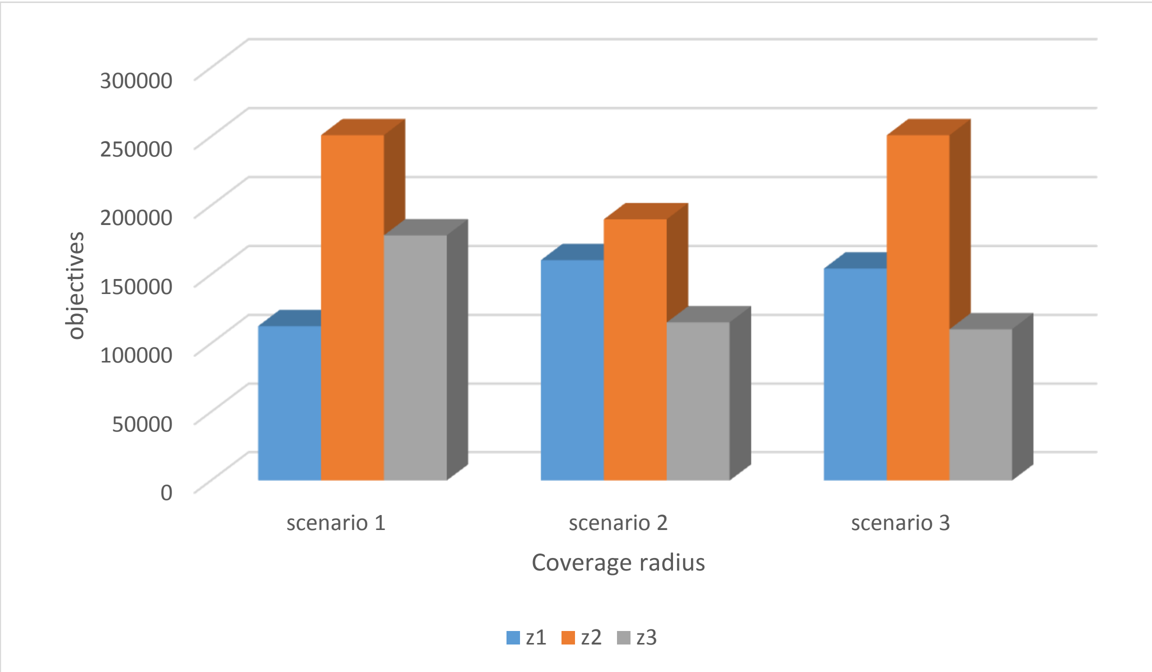

Figure 6. Amount of the objectives due to a changing allocation

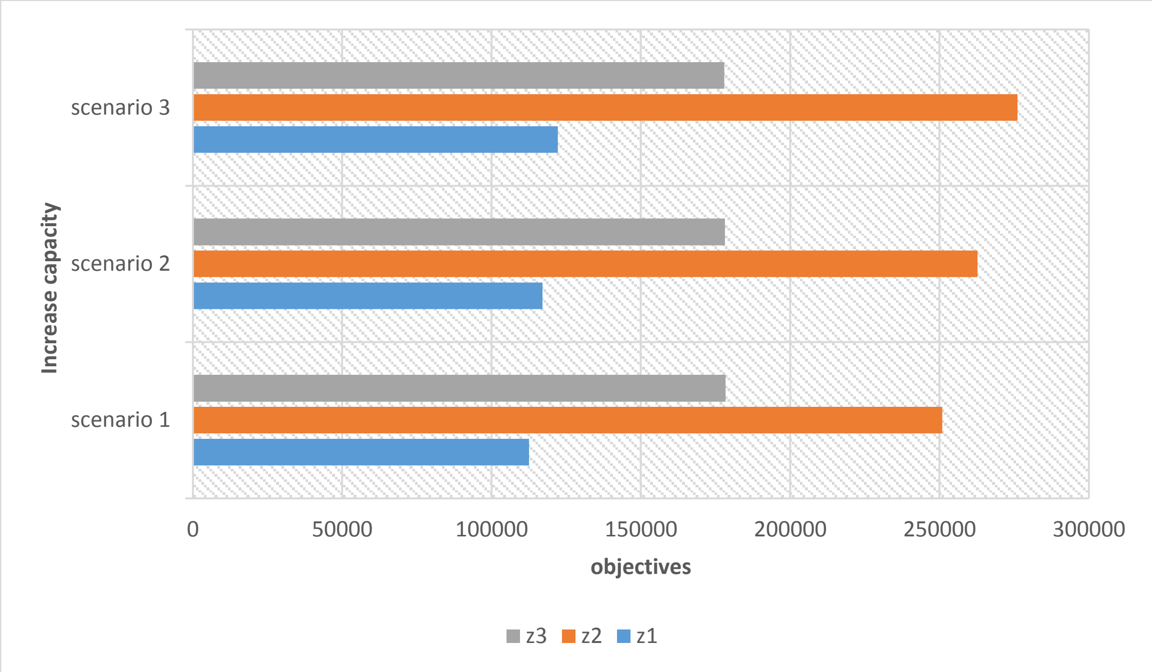

Figure 7. Impact of increasing input capacity by the MOHME

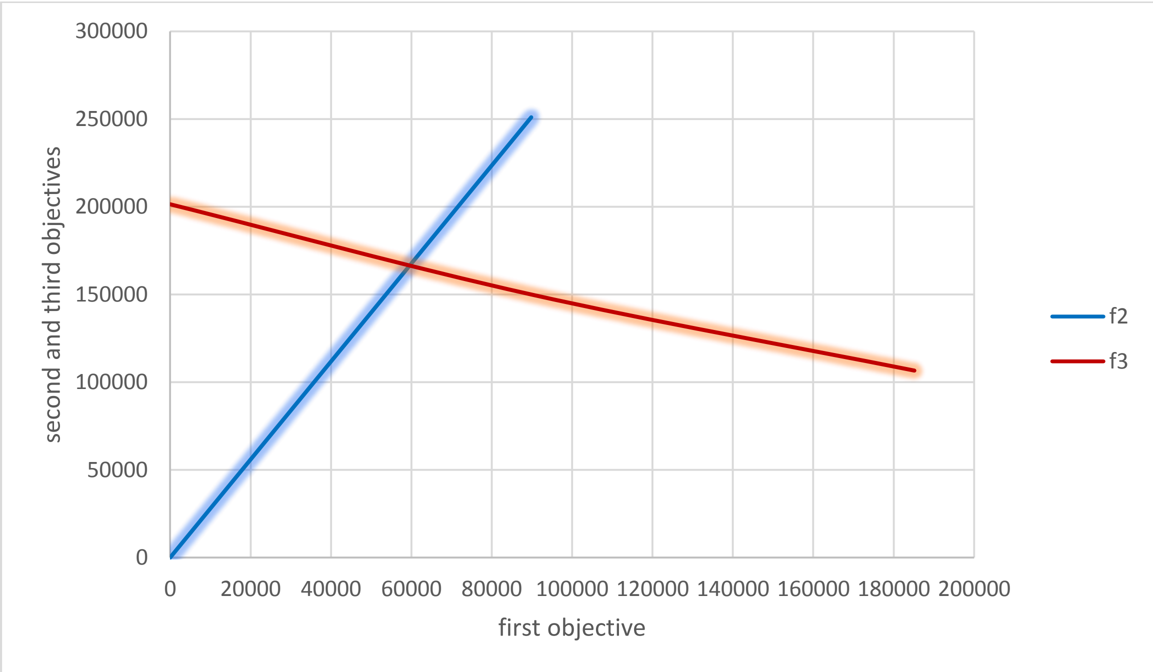

Figure 8. Conflict of the first objective with the second and third objectives

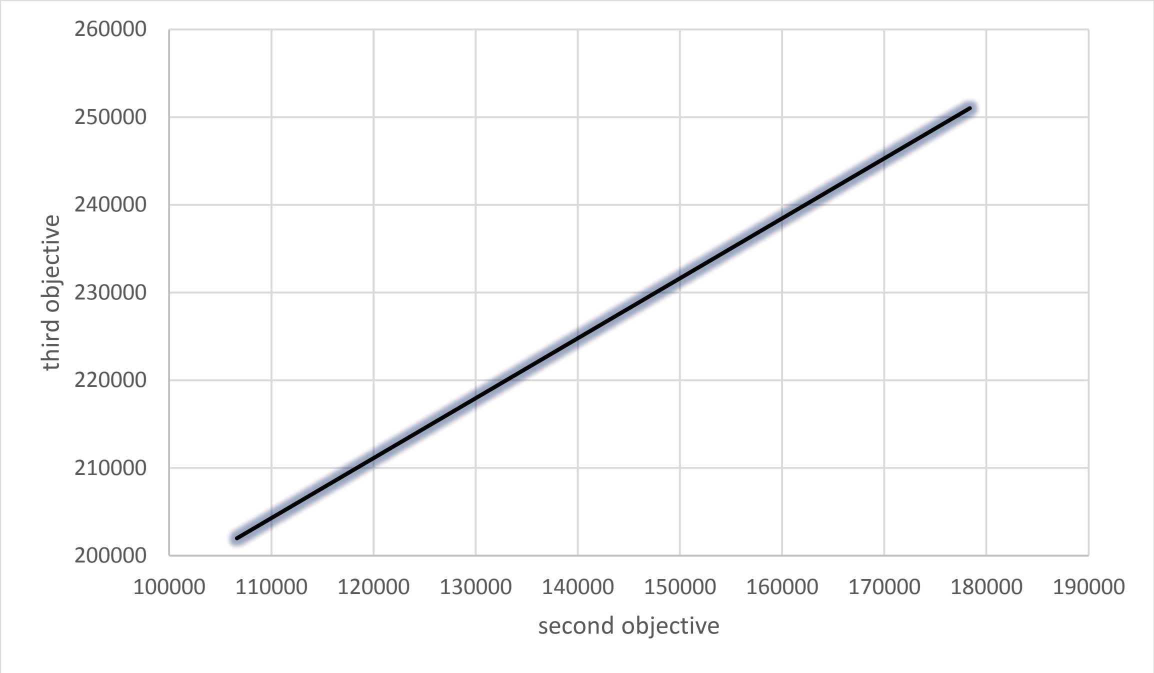

Figure 9. Conflict of the second objective with the third objective

Table 1. Literature review

Author(s) name	Year	Main discussion	Tools, methods, or approaches	Case study
Bozorgi and Fahimnia (53)	2021	Vaccine supply chain	-	Australia
Sun et al. (54)	2021	Analysis for effective vaccine distribution	Simulation	Norway
Rastegar et al. (44)	2021	Inventory-allocation influenza vaccine	Mathematical model	Iran
Chandra et al. (55)	2021	next-generation vaccine supply chain	fuzzy analytical hierarchical process (FAHP)	-
Golan et al. (56)	2021	Analyzing vaccine supply chain resilience	Mathematical model	-
Tsuzuki et al. [45]	2020	vaccination programs	Markov Chain, Monte Carlo	Japan
Abbasi et al. (42)	2020	Allocation and distribution vaccination	Mathematical model	Australia
Bulula et al. (57)	2020	Vaccine storage and distribution	Micro-costing approach	Tanzania
de Carvalho et al. (58)	2019	Design and Planning of Sustainable Vaccine Supply Chain	Mathematical model	European company
Chandra and Kumar (59)	2019	Prioritizing the vaccine supply chain	Fuzzy ANP	-
Chandra and Kumar (60)	2018	Analysis of vaccine supply chain	ISM approach	-
Lee et al. (61)	2016	Re-designing vaccine supply chain	Simulation	Mozambique
Lee et al. [18]	2011	Maintaining vaccine delivery	Simulation	Thailand

Table 2. The MOHME capacity

Vaccine type	Period				
	1	**2**	**3**	**4**	**5**
1	2000	2000	2000		
2	2000	2000	2000	1000	
3				2000	1000
4				3000	1000
5				2000	1000
6				2000	2000

Table 3. The capacity of IFDO

cap'_{ot}					
IFDO	**Period**				
	1	**2**	**3**	**4**	**5**
1	15000	15000	15000	15000	15000
2	12000	12000	12000	12000	12000

Table 4. The capacity of the hospitals

cap''_{ht}					
Hospital	**Period**				
	1	**2**	**3**	**4**	**5**
1	10000	10000	10000	10000	10000
2	10000	10000	10000	10000	10000
3	10000	10000	10000	10000	10000
4	20000	20000	20000	20000	20000
5	10000	10000	10000	10000	10000
6	20000	20000	20000	20000	20000
7	20000	20000	20000	20000	20000
8	10000	10000	10000	10000	10000
9	10000	10000	10000	10000	10000
10	10000	10000	10000	10000	10000
11	10000	10000	10000	10000	10000
12	10000	10000	10000	10000	10000
13	10000	10000	10000	10000	10000
14	10000	10000	10000	10000	10000
15	10000	10000	10000	10000	10000

Table 5. The capacity of the health center

cap'''_{et}					
Health center	**Period**				
	1	**2**	**3**	**4**	**5**
1	10000	10000	10000	10000	10000
2	10000	10000	10000	10000	10000
3	10000	10000	10000	10000	10000
4	20000	20000	20000	20000	20000
5	10000	10000	10000	10000	10000
6	20000	20000	20000	20000	20000
7	20000	20000	20000	20000	20000
8	10000	10000	10000	10000	10000
9	10000	10000	10000	10000	10000
10	10000	10000	10000	10000	10000
11	10000	10000	10000	10000	10000
12	10000	10000	10000	10000	10000
13	10000	10000	10000	10000	10000
14	10000	10000	10000	10000	10000
15	10000	10000	10000	10000	10000

Table 6. The capacity of pharmacy

$cappt_{pt}$					
Pharmacy	**Period**				
	1	**2**	**3**	**4**	**5**
1	10000	10000	10000	10000	10000
2	10000	10000	10000	10000	10000
3	10000	10000	10000	10000	10000
4	20000	20000	20000	20000	20000
5	10000	10000	10000	10000	10000
6	20000	20000	20000	20000	20000
7	20000	20000	20000	20000	20000
8	10000	10000	10000	10000	10000
9	10000	10000	10000	10000	10000
10	10000	10000	10000	10000	10000
11	10000	10000	10000	10000	10000
12	10000	10000	10000	10000	10000
13	10000	10000	10000	10000	10000
14	10000	10000	10000	10000	10000
15	10000	10000	10000	10000	10000

Table 7. The amount of customer demand from the hospital

D'_{ch}															
Customer	**Period**														
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
1	300	300	300	500	300	400	300	300	300	300	300	300	300	300	300

Table 8. The amount of customer demand from the health center

D''_{ce}															
Customer	**Pharmacy**														
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
2	500	500	500	700	500	700	600	500	500	500	500	500	500	500	500
3	500	500	500	700	500	700	600	500	500	500	500	500	500	500	500

Table 9. The amount of customer demand from the pharmacy

D'''_{cp}															
Customer	**Period**														
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
4	400	400	400	600	400	600	500	400	400	400	400	400	400	400	400
5	400	400	400	600	400	600	500	400	400	400	400	400	400	400	400
6	400	400	400	600	400	600	500	400	400	400	400	400	400	400	400

Table 10. Importance factor of vaccine type for customer

x_{cn}						
customer	**Vaccine type**					
	1	**2**	**3**	**4**	**5**	**6**
1	10	9	8	7	6	5
2	9	8	7	6	5	4
3	8	7	6	5	4	3
4	7	6	5	4	3	2
5	6	5	4	3	2	1
6	5	4	3	2	1	0.5

Table 11. The optimal values of target functions

	$Minz_1$	$Minz_2$	$Minz_3$
Optimal single objejctive	84302.6	251000	157670
Optimal lexicographic	112558.36	251000	178380

Table 12. The amount of vaccine transferred from the IFDO 1 to the hospital

QOH_{ohntc}

$IFDO = 1 \quad customer = 1$

Vaccine type	**period**	**Hospital**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	1		306		450			306				306			306	
1	2			306		306										
2	1	306			41					306	306		306	22		306

Table 13. The amount of vaccine transferred from the IFDO 2 to the hospital

QOH_{ohntc}

$IFDO = 2 \quad customer = 1$

Vaccine type	**period**	**Hospital**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	1								306							
2	1						408									

Table 14. The amount of vaccine transferred from the IFDO 1 to the health center

QOE_{oentc}

$IFDO = 1 \quad Customer = 2$

Vaccine type	**period**	**Health center**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	2													225		
1	3		510	245	265											
2	2										510					
2	3							510								
4	4											510				
5	4													286		408
5	5	510														

Table 15. The amount of vaccine transferred from the IFDO 1 to the health center

QOE_{oentc}

$IFDO = 1 \quad Customer = 3$

Vaccine type	**period**	**Health center**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	3				714					510						
2	2															510
3	3	163	510													
3	4					225										
3	5											510				
4	3													510	510	
4	4	347														
4	5										510					
5	4					286										

Table 16. The amount of vaccine transferred from the IFDO 2 to the health center

QOE_{oentc}																
$IFDO = 2 \quad Customer = 2$																
Vaccine type	**period**	e														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
4	4								510							

Table 17. The amount of vaccine transferred from the IFDO 2 to the health center

QOE_{oentc}																
$IFDO = 2 \quad Customer = 3$																
Vaccine type	**period**	**Health center**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	3						714									
2	3								510							

Table 18. The amount of vaccine transferred from the IFDO 1 to the pharmacy

QOP_{opntc}																
$IFDO = 1 \quad Customer = 4$																
Vaccine type	**period**	**Pharmacy**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	2	245			613											
1	3									408						
2	2											265				
2	3	163														
3	3					408		490								
3	5											142				
4	3			163							408					408
4	5		82												408	
5	4												408			

Table 19. The amount of vaccine transferred from the IFDO 2 to the pharmacy

QOP_{opntc}																
$IFDO = 2 \quad Customer = 4$																
Vaccine type	**period**	**Pharmacy**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	2						612									
3	3								408							

Table 20. The amount of vaccine transferred from the IFDO 1 to the pharmacy

QOP_{opntc}																
$IFDO = 1 \quad Customer = 5$																
Vaccine type	**period**	**Pharmacy**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	3										408					
2	2									408						
2	3		408												408	
3	3												408			
3	5				347											

Table 21. The amount of vaccine transferred from the IFDO 2 to the pharmacy

QOP_{opntc}																
$IFDO = 2 \quad Customer = 5$																
Vaccine type	**period**	**pharmacy**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
4	4						612		408							

Table 22. The amount of vaccine transferred from the IFDO 1 to the pharmacy

QOP_{opntc}																
$IFDO = 1 \quad Customer = 6$																
Vaccine type	**period**	**Pharmacy**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
6	4	408	408							368					408	
6	5				612	408					408	408	164			

Table 23. The amount of vaccine transferred from the IFDO 2 to the pharmacy

QOP_{opntc}																
$IFDO = 2 \quad Customer = 6$																
Vaccine type	**period**	**Pharmacy**														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
6	4								408							

Mehdi Alizadeh is a Ph.D. student at the Iran University of Science and Technology, in Tehran, Iran. He also received his master's degree in Industrial Engineering from Iran University of Science and Technology in 2019. His research interests include health supply chain, supply chain network design and redesign, multi-objective optimization, and stochastic programming. He has published some papers in international journals and conferences including Computers & Industrial Engineering, Applied Soft Computing, etc.

Mohammad Mahdi Paydar is an Associate Professor in the Department of Industrial Engineering at the Babol Noshirvani University of Technology, in Babol, Iran. He received his Ph.D. in Industrial Engineering from Iran University of Science and Technology in 2014. His research interests include supply chain design, applied operations research, multi-objective optimization, and cellular manufacturing. He has published more than 90 papers in international journals and conferences including Tourism Management, Expert Systems with Applications, Computers & Operations Research, Journal of Cleaner Production, Computers & Industrial Engineering, Knowledge-Based Systems, Scientia Iranica, Applied Mathematical Modelling, etc.

Seyyed Mehdi Hosseini received his MSc in Industrial Engineering from the Babol Noshirvani University of Technology, in Babol, Iran. His research interests include ecotourism supply chain and sustainability in the supply chain.

Ahmad Makui received the bachelor’s, MBA, and doctoral degrees in industrial engineering from the Iran University of Science and Technology (IUST), Tehran, Iran, in 1985, 1991, and 1994, respectively. He is a Professor at the Department of Industrial Engineering, Iran University of Science and Technology, Tehran, Iran. He has published four books in the field of operations research, production planning, and MCDM. His research interests include operation research, production planning, multi-criteria decision-making, and technology transfer. Prof. Makui is the Editor-in-Chief of the Journal of Industrial and Systems Engineering.