



Available online at www.sciencedirect.com

ScienceDirect

Fuzzy Sets and Systems 434 (2022) 48-72



www.elsevier.com/locate/fss

A fuzzy bi-level programming approach to scarce drugs supply and ration planning problem under risk

Bahareh Aghababaei, Mir Saman Pishvaee*, Farnaz Barzinpour

Received 20 May 2019; received in revised form 16 January 2021; accepted 27 February 2021 Available online 5 March 2021

Abstract

In this paper, a possibilistic bi-objective bi-level programming model is proposed to optimize the management of scarce drugs supply and rationing under difficult situations such as COVID-19 outbreak. Multiple followers and single leader exist in the proposed Stackelberg model in which the followers are divided into two groups, manufacturers and suppliers. The first group has priority over the latter. The competition between these two groups is addressed using a lexicographical procedure. Moreover, the interaction between the individuals in each group is incorporated through a normalized Nash equilibrium. To avoid the discriminative allocations, the disability-adjusted life years (DALY) index is employed to improve the rationing process. Due to the significance of uncertainty in such a problem, a novel risk-based possibilistic expected value approach is devised to control the mean and risk values of the objective functions. Finally, to validate the proposed solution method, the model is solved by applying Karush–Kuhn–Tucker (KKT) conditions and using the data extracted from a real case study. The results reveal the applicability and usefulness of the proposed possibilistic model compared to the conventional possibilistic approach © 2021 Elsevier B.V. All rights reserved.

Keywords: Fuzzy mathematical programming; Scarce resources allocation; Bi-level programming; Pricing; Possibilistic programming; Multi-objective optimization; COVID-19

1. Introduction

From past up to now, the growth of healthcare expenditures have been increasing dramatically even faster than GDP in the most countries, which the majority of these costs belongs to the pharmaceutical sector [1]. The outbreak of COVID-19 disease, the global public health crisis, has been deteriorating this situation to a large extent. In this regard, drug shortages costs are one of the most significant ones imposing on the healthcare system [2]. In fact, drug shortage is a situation in which the total supply of all substitutable versions of a given drug is not capable of satisfying the current or estimated demands of patients [3]. Drug shortage crisis is a serious threat as it poses unrecoverable losses on both patients and the healthcare system. In the most cases, shortages result in either postponing or discontinuation of the needed care of patients and in other ones, it leads to prescribing the alternative drugs which may be less effective along with additional risks for patients [4].

E-mail address: pishvaee@iust.ac.ir (M.S. Pishvaee).

^{*} Corresponding author.

Since in epidemic outbreaks, most of the healthcare resources are scarce and the health organizations cannot meet all the patients' needs, they have no choice to allocate these resources efficiently. To deal with this issue, scarce resources rationing, rational allocation of the restricted resources, is adopted by the government [5]. In this regard, government and healthcare administrators are pressured by contradictory aspects in the PSC. On the one hand, they should consider the public benefits by providing affordable and accessible resources. On the other hand, since the economics forces often prevent suppliers to produce more profitable resources, addressing the suppliers' benefits is vital in the heathcare supply chain [6]. Providing both cost-efficient resources and their equitable distribution among demand zones could be realized through applying the mathematical programming approaches and operation research principles.

Moreover, the uncertainty is an inseparable part of the healthcare scarce resources rationing problem as most of the critical parameters are estimated (e.g., demand) because of the unavailability of accurate data. Thus, by considering the uncertainty, the problem gets closer to the reality and the results will be more practical. In this regard, because of the lack of knowledge about the parameters' exact values, the fuzzy mathematical programming [7] is the best approach to deal with the uncertain and imprecise nature of the parameters.

As a result, this paper is motivated by the need to optimize the supply and allocation of the scarce drugs effectively through a fuzzy bi-objective bi-level programming model (single leader-multiple followers) in a multi-period planning horizon. In the proposed model, the government is assumed to be the leader who pursues to minimize the providing costs of medicines and shortage in the demand zones simultaneously, and the providers are assumed to be the followers who seek to maximize their own profit based on the leader's decisions. At the first level, the leader makes the decisions related to pricing and quota of each demand zone, and at the lower level, the provided quantities are determined by followers. Moreover, the competition among followers is formulated by generalized Nash equilibrium. Due to the imprecise nature of some parameters, a possibilistic programming approach is applied to handle the epistemic uncertainty in input parameters. In addition, to overcome the possibilistic programming shortcomings, a fuzzy semi-variance measure along with the mean value of objective function are augmented to curb the considered objective functions risk.

This rest of this paper is organized as follows. The next section gives a brief overview of related works. In Sections 3 and 4, the concerned problem is defined and formulated, respectively. The proposed method to deal with uncertain parameters is illustrated in Section 5. In Section 6, the solution method for integrating the model into a single-level, linearization approaches and the method for dealing with bi-objective are elaborated. The application of the model to the real studied case as well as the acquired results are presented in Section 7. Finally, Section 8 presents concluding remarks and future research directions.

2. Literature review

The situation in which demand outstrips supply, rationing becomes an indisputable component in the healthcare system [8]. The comprehensive survey of literature indicates that scarce resource rationing issue has had a long history in healthcare settings and it has been addressing a serious dilemma for health authorities from a long time ago [9]. By this way, a growing body of literature has been dedicated to propose the explicit guidelines and ethical considerations for allocating of scarce medicines, effectively [10]. Nevertheless, despite urgent necessity in order to optimize scarce resources allocation, utilizing the mathematical programming approaches have received little attention in the body of scarce resource allocation literature. Table 1 indicates the synopsis of the most relevant papers in the domain of rationing of healthcare scarce resources.

Perusing the reviewed papers leads us to conclude that all of the researchers have considered some simplifying assumptions in their mathematical modeling which result in being inapplicable in the real world. One of these assumptions is considering a single-period planning horizon [11–15]. To eliminate the imbalance between supply and demand, a multi-period planning model should be taken into account, in which, unsatisfied demands of each period are postponed to the subsequent periods (i.e., considering unsatisfied demand as backlog) [16].

One remarkable point is that prior investigations in this area have been used a wide variety of need-based indicators such as mortality rate, population, and socio-economics. In this regard, the regional burden of disease is a suitable tool for estimating the diseases prevalence and quantifying heath loss in each given region calculated in terms of disability-adjusted life years (DALYs) [17,18]. This measure could be an influential index in order to allocate medicines equitably [19,20]. No prior research paper has incorporated this indicator in the scarce drugs rationing

Table 1 Classification of the related existing papers in the healthcare scarce resources allocation area.

Reference	Model T	ype				Criterion		Time Per	riod
	Linear	Non-Linear	Integer Linear	Mixed-Integer Non-Linear	Mixed-Integer Linear	Health Status	Population	Single	Multiple
Feng et al. (2017)			X					X	
Sung (2016)					X				X
Schniederjans et al. (2017)			X				X	X	
Anparasan (2017)			X			X		X	
Aghababaei et.al (2019)	X					X	X		X
Kargar et al. (2020)				X		X		X	
This paper				X		X			X

Reference	Objecti	ve Function	Function			Solution Method			Uncertainty		Perspective	
	Single	Multiple			Exact	Heuristic	Meta-Heuristic	Stochastic	Fuzzy	Single	Multiple	
		Goal Programming	Augmented ε -constraint	Evolutionary Algorithm								
Feng et al. (2017)				X			X	X		X		
Sung (2016)	X					X				X		
Schniederjans et al. (2017)	X				X					X		
Anparasan (2017)	X				X					X		
Aghababaei et.al (2019)	X				X				X		X	
Kargar et al. (2020)		X			X				X	X		
This paper			X		X				X		X	

process. Therefore, one contribution of our model is that it prioritizes demand zones based on the shortages quantities and their respective burden of diseases.

Moreover, in the current literature, almost all studies have been developed rationing models under deterministic conditions while uncertainty is an inherent property of the rationing process. Schniederjans et al. [14] proposed an integer linear programming model for rationing medical antiviral drugs intending to minimize inequity for the Nebraska state. Sung [21] developed a mixed-integer linear programming model for the resource allocation management in the event of mass casualty incidents which aimed to maximize the number of expected survivals. For some other relevant works, it can be referred to [11,12,15,22]. On the other hand, other researchers applied stochastic programming to deal with the uncertain parameters. For instance, in the work that has been done by Feng et al. [13] the patient arrival interval times and service times were assumed as the uncertain parameters. Besides that, in another work by Feng et al. [23], a simulation-based multi-objective genetic algorithm has been developed to cope with the random nature of both demand and supply in the liver allocation system. It stands to reason that stochastic programming approaches have serious drawbacks as it increases the computational complexity of the problem as well as it requires dependable historical data. In this regard, the fuzzy set theory is applied as an alternative approach to handle the epistemic uncertainty in input parameters [7]. To the best our knowledge, in the domain of scarce resources allocation, the paper by Aghababei et al. [21] was the first paper which tackled the epistemic uncertainty through possibilistic programming approach. They developed a two-stage fuzzy mathematical programming model for supply and ration planning of scarce drugs in Iran. In another paper, Ahmadvand [24] applied fuzzy common weights DEA approach to evaluate the efficiency of eligible patient-kidney pairs in order to prioritize candidates and allocate scarce kidney organs. Moreover, in a recently published paper, Kargar et al. [23] developed a multi-objective possibilistic programming model for a liver allocation problem considering three basics health concepts such as equity, efficiency and accessibility. The model aimed to maximize the survival rate of patients and minimizes the transportation cost and time.

Nearly all related papers in the domain of scarce resource allocation have considered the problem from the single perspective (government's viewpoint) while in the real situation, the government's decisions are influenced by the decisions of the other participants of the PSC. It means that, since the government has not full control over all decisions in such supply chain, formulating the problem into a monolithic model does not make sense [25]. It is due to the fact that different participants involving in the PSC have conflict benefits and act non-cooperatively against each other [26]. In other words, suppliers strive to maximize their own profit function in the supply chain while providing equity is the policymakers' main goal. This issue has been accounted in a paper by Aghababaei et al. [27] in which utilizes from a bi-perspective approach. They developed a two stage mathematical programming model which solved by means of an iterative algorithm in which the impact of new information in each iteration is accounted by rolling planning horizon. The first and second stages were formulated by the government and suppliers' perspective, respectively. That being said, since suppliers' decisions directly influence the government's decisions and vice versa, the best approach to deal with the hierarchical nature of such problems is utilizing a bi-level programming approach [28].

A Stackelberg game is a kind of sequential game which consists of two players: a leader and a follower. The leader takes the first step, then the follower reacts to the leader's action. The leader dominates the activity of follower. Having considered the best response of the follower, the leader selects its own optimal strategy. In fact, the model is solved by backward induction technique [29,30]. On the contrary, another non-cooperative game, Nash equilibrium, exists in which several players determine their decisions simultaneously. In some cases, an action taken by one player restricts the pay-off and strategy set of other players [31]. This leads to the development of the concept of generalized Nash equilibrium which is an extension of Nash equilibrium. In fact, the concept of generalized Nash equilibrium results from a situation that players compete for a restricted and shared resource or constraint [32]. In this respect, in a work by Yue [33], the concept of generalized Nash equilibrium was applied for designing a competitive multi-echelon supply chain network.

It is needless to say that, manufacturers play a pivotal role in the medicine scarcity issue in the pharmaceutical supply chain, as the main reason for medicine shortages chiefly results from failures in producing a drug e.g. discontinuing in manufacturing a fruitless drug and producing an alternative drug [4]. In this situation, government through proposing incentive stimuli for them could resolve this problem. By this way, an appropriate pricing strategy would be a motivation to encourage manufacturers to offer the required medicines for patients. Therefore, one of the contributions of this paper is considering price as a decision variable. Several studies on pricing applied bi-level modeling in different domains (e.g. [34,35]). In the present study, the government as the leader, makes decisions for pricing and allocation policies while the providers as the followers, determine the manufacturing and purchasing's planning.

Last but not least, suppliers not only seek to maximize their profit but also prefer to consider risk in their decision-making process, even though risk-based approaches have been received very little attention in the literature of scarce resource rationing. Gaivoronski et al. [36] extended the multi-stage stochastic programming model by including the risk measures for the management of scarce resources. Among the numerous works in other areas which have dealt with risk by using stochastic programming methods, we could mention to [37,38].

On the other hand, some works have used possibilistic programming as a risk-based method to handle the uncertain parameters. Babazadeh et al. [39] presented a reformulation of possibilistic programming method by introducing possibilistic mean value and absolute deviation of fuzzy numbers for designing a second generation biodiesel supply chain under risk. In another work, Ghaderi et al. [40] enhanced the work by Babazadeh et al. [39] by proposing a novel possibilistic programming model through introducing three separate objective functions to control average performance, optimality and feasibility robustness of objective function.

In this study, in order to cope with the epistemic uncertainty of parameters and curb the performance risk of suppliers' objective functions, a fuzzy semi-variance measure along with the mean value of objective function are augmented to control the considered objective functions' risk. The main contributions of this paper, which distinguishes it from the existing studies summarize as follows:

- 1. Proposing a multi-period bi-objective bi-level programming model for supply and rationing the scarce drugs using a single leader multi followers Stackelberg game and the generalized Nash equilibrium.
- 2. Considering priority between two groups of followers through the lexicographic procedure.
- 3. Proposing a novel possibilistic programming approach based on mean value and semi-variance to control of followers' objective functions' risk.
- 4. Employing the burden disease of each demand zone as the need-based indicator for rationing medicines.
- 5. Analyzing the proposed model in a real case study.

3. Problem description

In this paper, the concerned problem is inspired by a real case study. Iranian food and drug administration (IFDA) is aimed to promote public health through supervising the members of the PSC in the country, including manufacturers, suppliers and distributor firms. Based on the IFDA's policies, two groups of domestic manufacturers and importers companies (which we call them suppliers) are responsible for the supply of the healthcare resources. In order to decrease the amount of the imported medications and encourage the manufacturers to enhance their production capacity, based on the IFDA policies, the manufactures have priority to the suppliers in Iran pharmaceutical supply chain.

The reports on the medicine shortages are announced to IFDA by the medical science universities of each demand zone. Then, IFDA transfers the information associated with the aggregated amount of the shortages of all the demand zones to the medicine provider firms e.g. manufacturers and suppliers to satisfy the required demands. To maintain the market equilibrium, IFDA uses an appropriate pricing strategy as a stimulus to motivate the provider firms to fulfill the demands. The higher the IFDA-offer price to the provider firms, the more amounts of demands will be met. As a non-profit organization, IFDA, however, should consider an affordable price. As a result, IFDA should choose the optimal price through a reasonable trade-off between the total providing costs and shortages. Thus, minimizing the total cost and shortage are considered as the objective functions of IFDA's problem.

In the problem under study, two separate pricing processes are carried out by IFDA. Since the manufacturing firms take the first priority for satisfying the demand, IFDA first offers a price to the first group of providers. Considering the offered price and with the aim of maximizing their own profit, manufacturers decide on the number of products to be delivered to the demand zones, based on the limited production capacity and Constraints (10)–(14). The remained shortages which could not be provided by manufacturers are then asked from the second group of providers and another price is determined for the suppliers. They also seek to maximize their own profit function through purchasing and transferring the medicines to the demand zones. Based on the total amounts stated by both manufacturers and suppliers, IFDA will then decide on allocating of the scarce medicines among the demand zones; and the providers should transport the medicines to each demand zone by their distribution centers in accordance with the ration specified by IFDA. The structure of the mentioned scarce drugs supply chain is briefly illustrated in Fig. 1.

Accordingly, as it is shown in Fig. 2, this problem is formulated as a bi-objective, bi-level framework in which the IFDA is considered as the leader in the first level while the manufacturers and suppliers play the role of followers in the

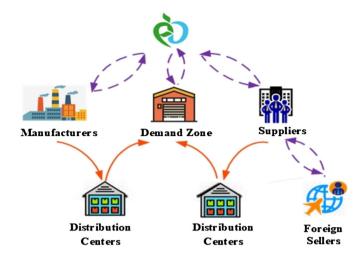


Fig. 1. The structure of the scarce medicines management network used in this study.

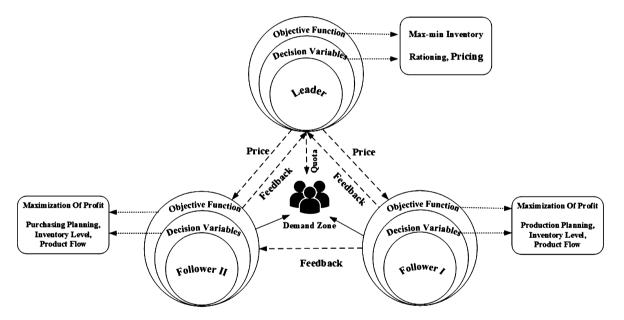


Fig. 2. The hierarchical structure of the concerned supply chain.

second level. Leader is in charge of pricing the domestic and foreign medicines and their rationing; while the production, purchase quantities, and material flow among the distribution centers will be decided by the followers. It is noteworthy that the concept of normalized Nash equilibrium has been applied to model the simultaneous competition on the restricted resource (demand) among the followers (manufacturers with each other and suppliers with each other).

Other main assumptions used for formulating the aforementioned problem are:

- The relationship between IFDA and providers is modeled as the Stackelberg game and relationship between the individuals in each group provider is assumed under normalized Nash equilibrium
- The competition between the two groups of followers, manufacturers, and suppliers is addressed by a lexicographical procedure in which the first stage, the individuals of the first group struggle to meet the demands, then the remainders are fulfilled by the second ones.
- It is possible that both providers fail to satisfy the total shortages, hence, the remained shortages will be transferred to the next period as the backlogged.

- To improve the effectiveness of the proposed model, DALYs' index is incorporated in the first objective function of the first level model.
- To deal with the uncertainty of some input data, a new fuzzy programming approach is applied to control the risk of the objective functions by the aid of semi-variance measure.

4. Problem formulation

In this subsection, to formulate the concerned fuzzy bi-level programming model, indices, parameters, and decision variables are defined as follows: Notably, parameters with a tilde on are tainted with epistemic uncertainty.

Indices		w_{pjt}^{max}	Upper bound of production capacity of manufacturer j for medicine p in period t
i	Index of demand zones (provinces)	w_{pjt}^{min}	Lower bound of production capacity of manufacture j for medicine p in period t
j	Index of manufacturing firms	φ_{pvt}	Maximum capacity of foreign seller v for medicine p in period t
k	Index of supplier firms	$b_{pkt}^{max} \ b_{pkt}^{min}$	The upper limit of available budget of supplier k in period t
v	Index of the foreign sellers	b_{nkt}^{min}	The lower limit of available budget of supplier k in period t
l	Index of distribution centers (DC)	ϑ_t	Customs duty rate in period t
p	Index of scarce medicines	\tilde{e}_{vt}	Exchange rate from the currency of foreign seller v to the standard currency in period t
t	Index of time periods	$tr_{pt}^{j \to l}$	Unit transportation cost of medicine p from manufacturing center j to local DC m in period t
Paramo	eters	$r_{pt}^{k \to l}$	Unit transportation cost of medicine p from supplier center k to local DC l in period t
σ_{pi}	The penalty of unsatisfied demands of medicine p at demand zone i	$g_{pt}^{l o i}$	Unit transportation cost of medicine p from distribution center l to demand zone i in period t
\tilde{d}_{pit}	The demand of province i for medicine p in period t	∂_{pj}	Unit inventory holding cost of medicine p at manufacturing center j
$\overline{v}'_{pkt}^{max}$	Maximum desired price of supplier k for selling medicine p in period t	\tilde{c}_{pjt}	The unit production cost of medicine p in manufacturing center j in period t
$a_{pt}^{v \to k}$	Unit purchasing cost of medicine p from foreign seller v by supplier k in period t	x_{pjt}	quantity of medicine p produced by manufacturer j in period t
$h_{pt}^{v \to k}$	Unit transportation cost of medicine p from foreign seller v to importing center k in period t	$s_{pt}^{v \to k}$	quantity of medicine p purchased from foreign seller v by supplier k in period t
v_{pjt}^{max}	Maximum desired price of manufacturer j for selling medicine p in period t	$y_{pt}^{k \to l}$	quantity of medicine p transferred from supplier center k to distribution center l in period t
π_{pkt}	Unit insurance cost of medicine p by supplier k in period t	$z_{pt}^{j \to l}$	quantity of medicine p transferred from manufacturing cente j to distribution center l in period t
∂'_{pk}	Unit inventory holding cost of medicine p at supplier center k	IM_{pjt}	Inventory level of medicine p at manufacturing center j in period t
\overline{mc}_{pkt}	Unit marginal costs of supplied medicine p by supplier k in period t	IS_{pkt}	Inventory level of medicine p at supplier center k in period t
ss_{pi}	safety stock of product p in demand zone i	ID_{pit}	Inventory level of medicine p at demand zone i in period t
$\frac{ss_{pi}}{q_{pkt}^{l o i}}$	The optimal quantities of medicine p provided by manufacturer k and shifted to demand zone i in period t	$ID_{pit} \ q_{pjt}^{l o i}$	quantity of medicine p produced by manufacturing center j and transferred from distribution center l to demand zone i in period t
Decisio	n variables	$o_{pkt}^{l o i}$	quantity of medicine p purchased by supplier k and transferred from distribution center l to demand zone i in period t
$v'_{pt} \ v_{pt} \ u_{pit}$	Unit Selling price of imported medicines p in period t Unit Selling price of manufactured medicine p in period t Quota of medicine p dedicated to demand zone i in period t	$\overline{\omega}$	An auxiliary variable for the first objective function

4.1. The upper-level optimization problem

As it was mentioned before, the first level problem contains two objective functions. The first objective function is to maximize distributive equity among demand zones. In other words, the leader seeks to maximize the minimization

of inventory level of all demand zones and in all periods. Notably, to enhance the equity among provinces, the parameter σ_{pi} is utilized as a shortage penalty of drug p in each demand zone which is calculated based on burden disease of provinces, i.e., DALY index. Simultaneously, to minimize the summation of the drugs supply cost is addressed as the second objective function of the first level which is obtained by multiplying the quantity provided via followers by their corresponding selling price.

$$\max LF_1 = \min_{n,i,t} \left\{ \sigma_{ni} \left(ID_{nit} - \varpi \right) \right\} \tag{1}$$

$$\min LF_2 = \sum_{p,j,l,t} z_{pt}^{j \to l} v_{pt} + \sum_{p,k,l,t} y_{pt}^{k \to l} v'_{pt}$$
(2)

$$ID_{pit} = ID_{pi,t-1} + u_{pit} - \tilde{d}_{pit} \quad \forall i, p, t$$
(3)

$$u_{pit} = \sum_{i,l} z_{pt}^{j \to l} + \sum_{k,l} y_{pt}^{k \to l} \quad \forall p, i, t$$

$$\tag{4}$$

$$\tilde{c}_{pjt} \le v_{pt} \le \overline{v}_{pjt}^{max} \quad \forall p, j, t \tag{5}$$

$$\sum_{v} \left(\tilde{e}_{vt} \left(a_{pt}^{k \to v} + h_{pt}^{k \to v} \right) + \pi_{pkt} \right) \le v_{pt}' \le \overline{v}_{pkt}'^{max} \quad \forall p, k, t$$
 (6)

$$ID_{pit} - \varpi \le ss_{pi} \quad \forall p, i, t \tag{7}$$

$$u_{pit}, v_{pt}, \overline{\omega} \ge 0 \quad \forall p, i, t$$
 (8)

Constraint (3) illustrates the inventory balance equation at each demand zone. Constraint (4) states that the quota assigned to each demand zone in each period should be equal to the summation of the quantities procured by two group providers. Constraint (5) binds the lower and upper bond for per unit selling price of drugs produced by manufacturers. Lower bond is considered based on manufacturers' production cost and an upper bond is also considered as the determined price could not be deviated from the maximum considered price by manufacturers. Constraint (6) is doing the same for foreign medicines. The lower bond is associated with drugs importing costs imposed to suppliers. Constraint (7) is an auxiliary constraint related to objective function (1). This inequality guarantees that the inventory levels of demand zones do not exceed their safety stock. Accordingly, if the inventory level of a given demand zone was less than its corresponding safety stock, its respective auxiliary variable's value in the objective function (ϖ) would be equal to zero. Otherwise, the value of ϖ would be equal to $(ID_{pit} - ss_{pi})$. In either case, the inventory level of each province would be not more than its safety stock value. Constraint (8) is related to non-negativity of decision variables in the first level.

4.2. The lower-level optimization problem

4.2.1. The manufacturers' Nash equilibrium game model

In the lower level optimization problem, every follower strives to maximize its own benefit function as each of them is considered to be an independent player. As a result, each manufacturer optimizes its decisions given to the decisions adopted by the leader and anticipating the decisions of other competitors.

Profit function of each player includes the difference between revenue resulting from selling drugs and the costs of production, inventory holding, and transportation in distribution centers and demand zones.

$$\max MF_{j} = \sum_{p,l,t} \left(v_{pt} - tr_{pt}^{j \to l} \right) z_{pt}^{j \to l} - \sum_{p,t} \tilde{c}_{pjt} x_{pjt} - \sum_{p,t} \partial_{pj} IM_{pjt} - \sum_{p,l,i,t} g_{pt}^{l \to i} q_{pjt}^{l \to i} \quad \forall j$$

$$\tag{9}$$

$$x_{pjt} \le w^{min}_{pjt} + \left(\frac{v_{pt} - \tilde{c}_{pjt}}{v_{pit}^{max} - \tilde{c}_{pjt}}\right) \left(w^{max}_{pjt} - w^{min}_{pjt}\right) \quad \forall p, j, t$$

$$(10)$$

$$\sum_{l} q_{pjt}^{l \to i} + \sum_{j' \neq j, l} q_{pj't}^{l \to i} \leq \left(\tilde{d}_{pit} + ss_i - ID_{pi, t-1} \right) \quad \forall p, j, i, t$$

$$\tag{11}$$

$$IM_{pjt} = IM_{pj,t-1} + x_{pjt} - \sum_{l} z_{pt}^{j \to l} \quad \forall p, j, t$$
 (12)

$$z_{pt}^{j \to l} = \sum_{i} q_{pjt}^{l \to i} \quad \forall p, j, l, i, t$$
 (13)

$$x_{pjt}, z_{pt}^{j \to l}, IM_{pjt}, q_{pit}^{l \to i} \ge 0 \quad \forall p, j, i, t$$

$$\tag{14}$$

Constraints (10) demonstrates the relationship between determinate selling price by the leader and drug quantities produced by each manufacturer. In fact, the production quantities by the manufacturers are dependent on the price offered by the leader. If the higher price is offered by the leader, the manufacturer will utilize the greater share of its production capacity and the more drug quantities could be produced by manufacturers. Thus, as the selling price moves toward to the manufacturers desired price, the quantities produced by them will approach the upper bound of production capacity. Note that, offered prices and the manufactured quantities are decision variables. Hence, determination of the variable (v_{pt}) plays an pivotal role in the problem as it affects both manufacturers' profit and the leader's objective function (i.e., inventory levels of provinces). Constraints (11) ensures that the total transferred by all manufacturers to each demand zone could not be more than the summation of shortages and safety stock level in that demand zone. It is noteworthy that this constraint is shared by all manufacturers. Thus, under the assumption of generalized Nash equilibrium, the decisions of other competitors $(q_{pj't}^{l\rightarrow i} \ for \ j' \neq j)$ are treated as constants from manufacturer j's viewpoint. Constraints (12) and (13) indicate the flow balance equations of each medicine at each manufacturing and distribution center in each period, respectively. Constraint (14) enforces non-negativity constraints on the corresponding decision variables of the model.

4.2.2. The suppliers' Nash equilibrium game model

The suppliers' objective function is almost identical to the manufactures one. Since each supplier is taken into account as an independent player, we formulate an optimization problem for each one. Therefore, given the drug selling price determined in the leader's problem and quantities arranged by all manufacturers in the first set follower's problem, each supplier attempts to maximize its own profit, after anticipating other competitors' decisions as follows:

$$\max SF_{k} = \sum_{p,l,t} \left(v'_{pt} - r^{k \to l}_{pt} \right) y^{k \to l}_{pt} - \sum_{p,v,t} \tilde{e}_{vt} \left(a^{v \to k}_{pt} + h^{v \to k}_{pt} \right) s^{v \to k}_{pt} - \sum_{p,v,t} \pi_{pkt} s^{v \to k}_{pt}$$

$$- \vartheta_{t} \sum_{p,v,t} \left(\tilde{e}_{vt} \left(a^{v \to k}_{pt} + h^{v \to k}_{pt} \right) + \pi_{pkt} \right) s^{v \to k}_{pt} - \sum_{p,t} \vartheta'_{pk} I S_{pkt}$$

$$- \sum_{p,l,i} g^{l \to i}_{pt} o^{l \to i}_{pkt} \quad \forall k$$

$$(15)$$

The profit function consists of the difference between revenue derived from selling drugs and total costs of purchasing drugs from foreign sellers, international transportations, insurance, importing and custom duties and finally transportation among distribution centers and demand zones.

$$\sum_{v} \left(\tilde{e}_{vt} \left(a_{pt}^{v \to k} + h_{pt}^{v \to k} \right) + \pi_{pkt} \right) s_{pt}^{v \to k} \le b^{min}_{pkt} + \left(\frac{v_{pt}' - \overline{mc}_{pkt}}{\overline{v_{nit}''} - \overline{mc}_{pkt}} \right) \left(b^{max}_{pkt} - b^{min}_{pkt} \right) \quad \forall p, k, t \quad (16)$$

$$s_{pt}^{v \to k} + \sum_{k' \neq k} s_{pt}^{v \to k'} \le \varphi_{pvt} \quad \forall p, k, v, t \tag{17}$$

$$IS_{pkt} = IS_{pk,t-1} + \sum_{v} s_{pt}^{v \to k} - \sum_{l} y_{pt}^{k \to l} \quad \forall p, k, t$$
 (18)

$$y_{pt}^{k \to l} = \sum_{i} o_{pkt}^{l \to i} \quad \forall p, k, l, t \tag{19}$$

$$o_{pkt}^{l \to i} + \sum_{k' \neq k} o_{pk't}^{l \to i} \le \left(\tilde{d}_{pit} + ss_i - ID_{pi,t-1} \right) - \sum_{i,l} \overline{q}_{pjt}^{l \to i} \quad \forall p, i, t$$
 (20)

$$s_{pt}^{v \to k}, y_{pt}^{k \to l}, IS_{pkt}, o_{pt}^{l \to i} \ge 0 \quad \forall p, k, v, i, t$$

$$\tag{21}$$

Constraint (16) indicates the relationship between the price selected for selling the foreign medicines by the leader and the quantity of purchased by suppliers. Similar to Constraint (10), the purchased quantities by the suppliers are

dependent on the price offered by the leader. If the higher price is offered by the leader, the supplier will be encouraged to dedicate the greater share of its budget for purchasing medicines. Thus, as the leader offers a higher price which is closer to the upper bound, more number of medicines will be purchased by the supplier. Therefore, the upper bound of constraint (16) depends on the variable (v'_{pt}) . Constraint (17) states that the total quantities purchased by suppliers from each foreign seller should not exceeded its available capacity. Also, this constraint is shared between suppliers, thus, from the supplier k's perspective, decisions related to other suppliers $(s_{pt}^{k'\to v})$ are treated as parameters. Constraint (18) and (19) show flow balance equations in the supplier and distribution centers, respectively. Constraint (20) guarantees that the quantities transferred by all suppliers to a given demand zone should be Less than or equal to the difference between its needed quantities (i.e., aggregation of the shortage and safety stock) and the total quantities transferred by manufacturers to that province. It should be noted that, in the suppliers' problem, the amount of $\overline{q}_{pjt}^{l\to i}$ is regarded as a parameter. This originates from the proposed lexicographical procedure. Accordingly, the results of Equations (1)–(14) under sequential and simultaneous competitions between players determine the $\overline{q}_{pjt}^{l\to i}$ value, then, it is incorporated as a parameter in suppliers' problem. Constraint (21) shows the type of decision variables.

5. Proposed possibilistic semi variance model

Due to fluctuating nature of macroeconomic factors such as inflation rate, escalating the costs of raw materials, labors, etc., the precise estimation of some parameters included in the mathematical programming model (e.g., production cost, exchange rate, and provinces demand) is impossible for the IFDA. After the several interviews with the experts, these three parameters not only have been recognized as the most significant and influential parameters but also they have high variations not following their historical pattern. While the parameters such as safety stock, custom duty, inventory holding cost, etc. usually have been conforming their historical trend, and their deviations are insignificant. Therefore, considering uncertainty for these parameters does not have significant impacts on the results, so, they have been assumed as deterministic in the model.

Generally speaking, uncertainty of data is divided into two separate categories [41]: (1) randomness and (2) epistemic uncertainty. The first one arises from the random nature of input parameters for which stochastic programming approaches [37,42] is usually applied when there are available, adequate and dependable historical data for extracting the probability distribution. Epistemic uncertainty is related to lack of knowledge about the exact value of the imprecise parameters and modeled by possibilistic programming approaches [43,44]. Due to fluctuating nature of some input parameters over the planning horizon as well as unavailability of historical data, the present model is classified as the latter category.

It is worth mentioning that various factors affect the amount of these critical parameters such as an outbreak of a new disease which directly influences the rate of demand for a specific medicine in a period of time or political and economic conditions which have a direct impact on the exchange rate and production cost values. Thus, the foreseen based on historical data is not applicable. Accordingly, the suitable possibility distributions of these imprecise parameters are estimated by some available objective data and experts' opinions. Some kinds of possibilistic programming models such as necessity fractile and modality models are regarded as the risk-centered approaches [45,46]; based on α -necessity fractile, the model seeks to find the smallest value of u that the minimum possibility of the event that the objective function is not smaller than u is at least α . Hence, we have

Maximize u

S.t
$$Nes(\tilde{c}x \ge u) \ge \alpha$$
 (22)

where the certainty degree α is a predetermined value.

In contrast to fractile model, in the modality optimization approach, the decision maker pays more attention to the certainty degree of the event and aims to maximize the necessity of the event that the objective function is not smaller than a predetermined value z_0 in this model:

Maximize
$$Nes(\tilde{c}x \ge z_0)$$
. (23)

However, the expected value-based models have no control over the objective function's risk. In order to decrease the probability of failures in such models, most investors prefer to consider risk-based approaches in their model formulation. In the domain of scarce resources allocation, Gaivoronski et al. [36] applied variance as a risk measure in

the stochastic environment. On the contrary, in other areas, some researchers such as Babazadeh et al. [39] and Ghaderi et al. [40] employed the fuzzy absolute standard deviation measure for controlling the risk of the objective function. Nevertheless, most investors, based on the type of their objective function, pay highly attention to either extent of losses (negative deviations) or the extent of gains (positive deviations). For instance, in the case of minimizing the objective function, DM attempts to minimize the positive deviations and vice versa. Accordingly, if the distributions of uncertain parameters are non-symmetrical, applying the risk measures such as variance, the absolute standard deviation would put a potential risk on the investors through excessive reduction of expected profit for eliminating both positive and negative deviations [47].

In this situation, semi-variance measure [48] as a single-sided risk measure, is superior to the absolute standard deviation [49] and variance measures which consider both upside and downside risks [50]. In this regard, Zhang et al. [47] presented a possibilistic mean semi-variance model for multi-period portfolio selection. However, in their proposed model, minimizing the risk of portfolio and maximizing the diversification degree of the portfolio are assigned as the objective functions while the mean value is considered as a constraint whose upper bound is determined by decision maker's preferences. Hence, in this paper, we integrate the risk measure in the objective function to be optimized beside possibilistic mean value. This enables DM to make a trade-off between possibilistic mean value and semi-variance. Moreover, since semi-variance like variance leads to nonlinearity of model, Zhang et al. [47] combined two meta-heuristic algorithms of GA and SA for solving the problem. In our model, nonlinearity results from using semi-variance in objective functions does not interfere with the convexity of the problem. Thus, we could use the exact solution method for finding optimal solutions. Notably, our data uncertainty is in the form of a triangular fuzzy number. All required procedures and prerequisite definitions for developing the structure of the possibilistic mean-semi variance model as well as converting the proposed model to its corresponding crisp counterpart are stated in Appendix A.

The possibilistic mean-semi variance model is characterized as follows:

$$\max z = \overline{M} \left(\tilde{d}x \right) - \rho V a r^{-} \left(\tilde{d}x \right)$$
s.t. $\tilde{a}x \ge \tilde{b}$

$$\tilde{a}x = \tilde{b}$$

$$x > 0$$
(24)

In the above-mentioned model, the first and second term seek to minimize the possibilistic mean value and semi-variance of the objective function, respectively. In this objective function, ρ (risk coefficient) represents the importance of risk to the decision maker which provides a trade-off between the possibilistic mean value and semi-variance of the objective function. Therefore, the novel proposed possibilistic model covers the weakness of the conventional possibilistic programming model which considers only expected value and ignores the objective function deviations [51]. According to the information presented in Appendix A, the crisp equivalent model is indicated as follows:

$$\max z = \left(\frac{d_{(1)} + 4d_{(2)} + d_{(3)}}{6}\right) x - \rho \left(\frac{d_{(3)}^2 - 2d_{(1)}d_{(3)} + 2d_{(2)}^2 - 4d_{(1)}d_{(2)} + 3d_{(1)}^2}{36}\right) x^2$$
s.t. $(1 - \alpha) M_2^{a_i} + \alpha M_1^{a_i} \ge \alpha M_2^{b_i} + (1 - \alpha) M_1^{b_i}$

$$\left(\left(1 - \frac{\alpha}{2}\right) M_2^a + \frac{\alpha}{2} M_1^a\right) x \ge \left(\frac{\alpha}{2} M_2^b + \left(1 - \frac{\alpha}{2}\right) M_1^b\right)$$

$$\left(\frac{\alpha}{2} M_2^a + \left(1 - \frac{\alpha}{2}\right) M_1^a\right) x \le \left(\left(1 - \frac{\alpha}{2}\right) M_2^b + \frac{\alpha}{2} M_1^b\right)$$

$$x \ge 0$$
(25)

It is worth mentioning that among existing approaches to deal with the constraints containing uncertain parameters such as Parra et al. [52], the ranking method of Jimenez et al. [53] is applied as the defuzzification approach to convert constraints into the equivalent auxiliary crisp one. Accordingly, based on the aforementioned formulation, the possibilistic objective functions (9) and (15) and constraints (3), (5), (6), (10), (11), (16) and (20) of the proposed model can be transformed into their equivalent crisp model. The detailed formulation is calculated in Appendix A.

6. Solution approach

As it was mentioned previously, the proposed model is a bi-objective, bi-level and non-linear programming model. Due to the non-convexity of the bi-level problem, the exact solution approach, i.e., K.K.T approach is used to integrate the model in to a single-level. Owing to the presence of some non-linear expressions in the model, the McCormick Envelope is applied in order to linearize and convex the model. Finally, to deal with the bi-objective nature of the model, we have applied the augmented ε -constraint as a posteriori method to generate the only efficient solutions. All of these methods are discussed in this section in detail.

6.1. K.K.T transformation method

Bi-level programming is an appropriate technique for modeling hierarchical decisions structures which involve non-cooperative and independent participants. Bi-level programming models are known as the non-convex and NP-hard problems even their simplest and linear forms [54]. Indeed, since these optimization problems contain a set of optimization problems in the constraints, they cannot be directly resolved by the conventional mathematical programming solvers [33]. Hence, a considerable number of solution approaches are developed to address this sort of mathematical programming models including vertex enumeration techniques, reformulation methods, and penalty function methods, to name but a few [55]. Among them, the Kuhn-Tucker (KKT) method is the most prevalent reformulation technique for solving non-linear bi-level problems provided that the lower level is a continues and convex problem. In this case, KKT conditions are necessary and sufficient conditions for optimality and guarantee the global optimal solution to the lower level problem [56]. Based on the KKT optimality conditions, the bi-level problem is converted into a single-level one in which the follower level problem is added as a set of constraints into the upper level problem [34,35].

In the problem under study, solution region of the both followers' levels, manufacturers and suppliers' level problems, are linear and continuous as well as their both objective functions (9 and 15) are concave. Hence, we can employ the Kuhn-Tucker (KKT) conditions for integrating the proposed model. The proof of the concavity of both objective functions is represented in Appendix B.

The KKT optimality conditions for a maximization problem is stated as follows:

$$\nabla f(x) = \sum_{i=1}^{m} \lambda_i \nabla g_i(x)$$

$$\lambda_i g_i(x) = 0 \qquad i = 1, \dots, m$$

$$g_i(x) \le 0 \qquad i = 1, \dots, m$$

$$\lambda_i \ge 0 \qquad i = 1, \dots, m$$
(26)

 λ_i is the Lagrange coefficient that should be identical for constraints are mutual between players e.g. Constraints (11), (17) and (20) because of the assumption of normalized Nash equilibrium. Due to space limitation, the KKT conditions for the proposed problem have been not provided here.

6.2. Linearization of the non-linear expressions

6.2.1. Linearization of the first objective function

The first objective function, Eq. (1) in the leader problem is non-linear because of its max-min form. Thus, we can define a free variable, to convert the model into its exact counterpart as follows:

$$\max LF_1 = \tau$$

$$\min LF_2$$

$$\tau \le \sigma_{pi} \left(ID_{pit} - \varpi \right) \quad \forall p, i, t$$
(27)

plus, Constraints (3)–(23).

6.2.2. Linearization of the second objective function

The second objective function in the upper level problem is non-linear and non-convex because of multiplying two continues variables, $z_{pt}^{j\rightarrow l}*v_{pt}$ and $y_{pt}^{k\rightarrow l}*v_{pt}'$. Solving non-convex problems is complex and they should be transformed into a convex one by relaxing the parameters on the problem. On the other hand, this convex relaxed problem does not always guarantee the optimal solution. Hence, choosing a convex relaxation with the tighter bounds offers a lower bound that is closer to the optimal solution [57]. To this purpose, McCormick Envelope is used to linearize the model that not only ensures convexity but also it provides constricted bound. In this approach, by defining an upper bound (UB) and lower bound (LB) for both continues variables and using the formulation proposed by Castro [57], the model is converted into a liner convex problem.

$$\varrho_{pt}^{j\to l} = z_{pt}^{j\to l} * v_{pt} \qquad \qquad \varsigma_{pt}^{k\to l} = y_{pt}^{k\to l} * v_{pt}' \\
LB(v_{pt}) = L^{v_{pt}} \qquad UB(v_{pt}) = U^{v_{pt}} \qquad LB(v_{pt}) = L^{v_{pt}} \qquad UB(v_{pt}) = U^{v_{pt}} \\
LB(z_{pt}^{j\to l}) = L^{z_{pt}^{j\to l}} \qquad UB(z_{pt}^{j\to l}) = U^{z_{pt}^{j\to l}} \qquad LB(y_{pt}^{k\to l}) = L^{y_{pt}^{k\to l}} \qquad UB(y_{pt}^{k\to l}) = U^{y_{pt}^{k\to l}} \\
\varrho_{pt}^{j\to l} \geq z_{pt}^{j\to l} L^{v_{pt}} \qquad \qquad \varsigma_{pt}^{k\to l} L^{v_{pt}} \qquad \qquad \varsigma_{pt}^{k\to l} L^{v_{pt}} \\
\varrho_{pt}^{j\to l} \geq U^{z_{pt}^{j\to l}} v_{pt} + z_{pt}^{j\to l} U^{v_{pt}} - U^{z_{pt}^{j\to l}} L^{v_{pt}} \qquad \qquad \varsigma_{pt}^{k\to l} \geq U^{y_{pt}^{k\to l}} v_{pt}^{l} + y_{pt}^{k\to l} U^{v_{pt}} - U^{y_{pt}^{k\to l}} U^{v_{pt}} \\
\varrho_{pt}^{j\to l} \leq U^{z_{pt}^{j\to l}} v_{pt} + z_{pt}^{j\to l} L^{v_{pt}} - U^{z_{pt}^{j\to l}} L^{v_{pt}} \qquad \qquad \varsigma_{pt}^{k\to l} \leq U^{y_{pt}^{k\to l}} v_{pt}^{l} + y_{pt}^{k\to l} L^{v_{pt}^{l}} - U^{y_{pt}^{k\to l}} L^{v_{pt}^{l}} \\
\varrho_{pt}^{j\to l} \leq z_{pt}^{j\to l} U^{v_{pt}} \qquad \qquad \varsigma_{pt}^{k\to l} \leq y_{pt}^{k\to l} U^{v_{pt}^{l}} - U^{y_{pt}^{k\to l}} L^{v_{pt}^{l}} \\
\varrho_{pt}^{k\to l} \leq z_{pt}^{k\to l} U^{v_{pt}^{l}} \qquad \qquad \varsigma_{pt}^{k\to l} \leq y_{pt}^{k\to l} U^{v_{pt}^{l}} - U^{y_{pt}^{k\to l}} L^{v_{pt}^{l}} \\
\varrho_{pt}^{k\to l} \leq z_{pt}^{k\to l} U^{v_{pt}^{l}} \qquad \qquad \varsigma_{pt}^{k\to l} \leq y_{pt}^{k\to l} U^{v_{pt}^{l}} - U^{y_{pt}^{k\to l}} L^{v_{pt}^{l}} \\
\varrho_{pt}^{k\to l} \leq z_{pt}^{k\to l} U^{v_{pt}^{l}} \qquad \qquad \varsigma_{pt}^{k\to l} \leq y_{pt}^{k\to l} U^{v_{pt}^{l}} \qquad \qquad \varsigma_{pt}^{k\to l} L^{v_{pt}^{l}} \qquad \qquad \varsigma_{pt}^{k\to l} L^{v_{pt}^{l}} + V^{v_{pt}^{l}} L^{v_{pt}^{l}} + V^{v_{pt}^$$

6.2.3. Linearization of the complementary slackness constraints

The complementary slackness constraints contained in KKT conditions are non-linear and non-convex which can be linearized by the aid of two sets of inequality constraints and by introducing a set of binary variables as follows [58]:

$$\lambda_i \le M * \omega_i \quad \forall i$$

$$-g_i(x) \le M(1 - \omega_i) \quad \forall i$$
(29)

6.3. Coping with multiple objective functions

Multi-objective programming is a part of mathematical programming which consists of multiple conflicting objective functions, i.e., improving one objective function results in deteriorating the results for other ones [59]. In these problems, no single optimal solution simultaneously optimizes all the objective functions; hence, decision makers explore the efficient (or non-dominated, Pareto-optimal) solutions. In other words, the solutions that cannot be improved in one objective, without worsening its performance in other objective functions are named Pareto-optimal solutions [60]. There are a plethora of methods for transforming a multi-objective programming model into single-objective such as weighted sum, lexicographic, goal programming (as priori methods), ε -constraint (as a posteriori method) and interactive methods [61]. In this paper, we apply the augmented ε -constraint method to convert the proposed model into a single one. Augmented ε -constraint is categorized as a posteriori method that produces only efficient solutions, in contrast to the conventional ε -constraint method that does not guarantee the efficiency of obtained solutions [39,44,62]. In fact, the Pareto optimal solutions produced by the ε -constraint method may be dominated or inefficient solutions while augmented ε -constraint resolves this deficiency as follows:

$$Min \ f_1(x) - eps\left(\sum_{i=2}^k \frac{s_i}{r_i}\right)$$

$$f_i(x) + s_i = e_i \quad \forall i = 1, 2, \dots, k$$

$$(30)$$

where $f_i(x)$ is the *i*th objective functions of the problem. s_1, s_2, \ldots, s_k are slack variables. Also, the parameters r_1, r_2, \ldots, r_k are the ranges of objective function *i*th as calculated from the payoff table and *eps* is an adequately small number (usually between 10^{-3} and 10^{-6}).

Table 2
Unit preferred sale price and capacity data for manufacturers.

period	Manufacturer I		Manufacture	r II	Manufacture	r III	Manufacture	r IV	Manufacture	r V
	Suggested sale price (Rial)	Maximum capacity								
1	7,300	-	7,310	-	7,315	9,680,912	7,312	4,855,912	7,314	4,855,912
2	7,405	-	7,407	8,837,736	7,709	7,950,000	7,403	2,550,000	7,400	2,550,000
3	7,560	77,736	7,570	7,125,000	7,565	6,375,000	7,575	2,550,000	7,555	2,550,000
4	7,705	212,736	7,710	11,250,000	7,715	1,0125,000	7,710	2,550,000	7,700	2,550,000

Table 3
Unit preferred sale price, transportation and purchasing cost and budget data for suppliers.

Period	Supplier I			Supplier II	Supplier II			Supplier III		
	Suggested Sale Price (Rial)	Transporta- tion and Purchasing cost (Euro)	Maximum Budget (Rial)	Suggested Sale Price	Transporta- tion and Purchasing cost (Euro)	Maximum Budget (Rial)	Suggested Sale Price (Rial)	Transporta- tion and Purchasing cost (Euro)	Maximum Budget (Rial)	
1	7,305	0.055	4*10 ⁹	7,300	0.059	20*10 ⁹	7,310	0.064	40*10 ¹⁰	
2	7,356	0.051	4*10 ⁹	7,370	0.059	$20*10^{10}$	7,320	0.064	$40*10^{10}$	
3	7,513	0.051	4*10 ⁹	7,500	0.059	$30*10^{10}$	7,525	0.064	$40*10^{10}$	
4	7,570	0.051	4*10 ⁹	7,575	0.059	$10*10^{10}$	7,600	0.064	$40*10^{10}$	

7. Implementation and evaluation

In this section, the efficiency and performance of the proposed possibilistic bi-level programming model are assessed through a real case study. As previously demonstrated, the proposed model in this research was formulated based on the structure and characteristics of Iran scarce drugs rationing management. Thus, the model was implemented and the results were evaluated using sodium valproate data extracted from a case study of Iran food and drug organization. Sodium valproate is employed for treatment of epilepsy patients, bipolar disorders and migraine headaches [63]. This medication is produced by five manufacturers and imported by three suppliers purchasing them from two seller firms. In this paper, it was assumed that provinces were deficient in sodium valproate. The upper bound production capacity for manufacturers and their desired selling price in each period are presented in Table 2; while Table 3 shows the maximum budget, the preferred selling price, purchasing and transportation costs of foreign sellers for each supplier. The foreign seller firms were located in Germany and France with limited capacities, as shown in Table 4. It should be noted that all of the monetary data presented in the Iranian currency (Rial) and Euro were considered as the foreign currency. The considered planning horizon was 1 year and 4 three-month periods.

It should be mentioned that the production cost, exchange rate and demand were assumed as the uncertain parameters. To estimate their corresponding possibility distributions and determine three prominent values (i.e. the most pessimistic, the most possible and the most optimistic), it was first assumed that the corresponding crisp value is equal to the most possible value for all parameters; then, the other two extreme points were estimated based on the available data and the opinion of a group experts in this field. In this regard, the deterministic parameters were transformed into the triangular fuzzy numbers. The values of the fuzzy parameters used in the studied case are presented in Table 5 and Table 6. For calculating the regional burden of disease (DALYs), first, the population affected with the neurological disorders (i.e. epilepsy and migraine) and mental disorder (i.e., bipolar) were calculated. Then multiplied them to their corresponding indicator which are respectively 294.9 and 1336.3 [64]. Finally, considering two DALYs indicators, the average of disability-adjusted life years for each province was calculated. The regional DALYs values are listed in Table 6.

There are 8,408 constraints and 6,100 constant and discrete variables in the proposed model. The proposed model was solved under the feasibility degree of 0.8 ($\alpha = 0.8$) for all computations by GAMS optimization software and CPLEX solver. All the tests were implemented on a 7-core 4 GB RAM computer.

Table 4 Maximum capacity of foreign sellers.

Period	Foreign Seller I	Foreign Seller II
	Maximum Capacity	Maximum Capacity
1	6,500,000	5,500,000
2	8,800,000	7,000,000
3	5,500,000	5,700,000
4	6,900,000	4,400,000

Table 5
Values of exchange rate and production cost per unit.

Period	Exchange rate (Rial)	Production cost (Rial) (c_1, c_2, c_3)						
	(e_1, e_2, e_3)	Manufacturer I	Manufacturer II	Manufacturer III	Manufacturer IV	Manufacturer V		
1	(39326,43326,51326)	(1250,1450,1750)	(1240,1440,1740)	(1255,1460,1755)	(1235,1445,1650)	(1270,1560,1800)		
2	(40195,44196,52196)	(1260,1460,1760)	(1245,1455,1660)	(1262,1452,1762)	(1250,1450,1750)	(1260,1460,1760)		
3	(41165,45165,53165)	(1265,1465,1765)	(1255,1465,1765)	(1260,1460,1735)	(1255,1455,1755)	(1265,1570,1780)		
4	(42134,46134,54134)	(1270, 1470, 1770)	(1260, 1460, 1760)	(1280, 1475, 1780)	(1260, 1460, 1760)	(1270,1575,1785)		

Table 6 Values of demand and DALY of each demand zone.

Provinces	Monthly demand (d_1, d_2, d_3) (1000)	DALYs value (1000)
(1) Tehran	(1000,1500,2000)	263.6
(2) Esfahan	(850,900,950)	104.2
(3) Fars	(650,700,750)	70.9
(4) Razavi Khorasan	(700,750,800)	79.0
(5) East Azerbaijan	(700,750,800)	85.4
(6) Khuzestan	(500,550,600)	55.0
(7) Mazandaran	(450,500,550)	55.3
(8) Guilan	(350,400,450)	43.2
(9) West Azerbaijan	(250,300,350)	12.4
(10) Kerman	(300,350,400)	20.5
(11) North Khorasan	(300,350,400)	17.5
(12) Sistan & Baluchistan	(100,200,300)	8.4

Table 7
Lexicographic pay-off table of the first stage bi-level problem.

Objectives	Provinces' Inventory Levels (max)	Supply Cost Of Domestic Medications (min)
Provinces' Inventory Levels (max)	-5/16E+08	-4.65E+10
Supply Cost Of Domestic Medications (min)	1.39E+11	0

7.1. Results and discussions

To deal with the multiple-objective nature of the proposed model, the augmented ε -constraint method was applied via a lexicographic approach [60]. Accordingly, to construct the lexicographic pay-off matrix for the objectives with only Pareto optimal solutions, two respective single-objective models were first separately optimized; the achieved optimal values were assigned to the main diagonal of the pay-off table. Then, in order to find the efficient upper bound of the second objective function, in the first column, the second objective function was optimized (i.e. $\min w_2$) by preserving the optimality of the first objective function through adding the constraint $w_1 = z_1^*$. The same process was repeated for the second column to achieve the efficient lower bound of the first objective function (i.e. the first objective was solved by adding $w_2 = z_2^*$ constraint). The pay-off table of the first stage bi-level programming model is provided in Table 7.

Table 8
Pareto optimal solutions of the first stage bi-level programming model.

ID	Provinces'	Supply Cost Of	Selling Price				Quantity	Followers'
ID	Inventory Levels	Domestic Medications	First Period	Second Period	Third Period	Fourth Period	Supplied	Profits
1	-5.16E+08	1.39E+11	6355	6188	5551	6028	6.89E+07	3.33E+10
2	-5.26E+08	1.33E+11	6283	6179	5563	6028	6.87E+07	3.34E+10
3	-5.38E+08	1.27E+11	6211	6171	5572	6028	6.84E+07	3.36E+10
4	-5.51E+08	1.21E+11	6140	6166	5579	6028	6.81E+07	3.40E+10
5	-5.64E+08	1.16E+11	6069	6160	5586	6028	6.78E+07	3.42E+10
6	-5.77E+08	1.10E+11	5997	6154	5593	6028	6.75E+07	3.45E+10
7	-5.95E+08	1.04E+11	5892	6188	5551	6028	6.71E+07	3.42E+10
8	-6.62E+08	9.83E+10	6013	5914	5355	6006	6.57E+07	2.94E+10
9	-8.89E+08	9.25E+10	6314	5835	4806	5075	6.20E+07	9.56E+09

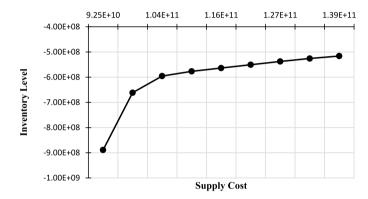


Fig. 3. Pareto front found by the augmented ε -constraint.

In the next step, since the first objective function (minimization of shortage) had the first priority followed by the second one (minimization of domestic drugs supply cost), it remained as the main objective function and the second one was shifted to the constraints. Then, the range of the second objective function was divided into 24 equal intervals. Accordingly, the model was solved for 25 grid points. After solving the model, 9 desirable efficient solutions were obtained as listed in Table 8. Also, the first and second objective function values are depicted in Fig. 3. As the figure indicates, the supply costs and shortage minimizations are in conflict with each other.

The numerical results provided in Table 8 indicates that as the supply cost of domestic medications' values increased, the higher sale price in average was offered to the first followers, i.e. manufacturers; hence the manufacturers were motivated to produce more which resulted in diminishing shortage among the demand zones. On the contrary, by declining the supply cost value (i.e., the pareto solutions 8 and 9), the lower sale price was offered to the followers leading to a reduction in the manufacturers' profits and deterioration of the inventory level in the demand zones. However, the relationship between the sale price and the followers' profit is not necessarily linear. For instance, in some solutions, by decreasing the average sale price up to 5,915 Rial and reduction in provided quantities, the followers could receive higher profit through managing their systems costs. When reducing the price exceeds from the threshold (e.g., the solution 8 and 9), the profit is significantly plummeting. It should be noted that in both cases, the reduction in supply by producers leads to worsening the first objective function.

In other words, since the sale price was considered as a decision variable in the concerned problem, the followers manufactured and supplied quantities were regulated according to this price which means that the model offered higher prices for receiving larger drug quantities from the followers. Accordingly, this pricing strategy could be a constructive motivation to encourage the manufacturers to diminish the shortage in the demand zones.

On the other hand, fulfilling the patients' demands is the main goal of the leader. To put it another way, IFDA seeks to meet the largest portion of the patients' demands by the help of the manufacturers. Accordingly, among the Pareto optimal set, the leader prefers to select the first Pareto solution to take advantage of the maximum capacity of producers although this solution does not generate the maximum profit for the manufacturers. This decision is

Table 9
Lexicographic pay-off table of the second stage bi-level problem.

Objectives	Provinces' Inventory Level (max)	Supply Cost Of Foreign Medications (min)
Provinces' Inventory Level (max)	-4.38E+07	-2.06E+09
Supply Cost Of Foreign Medications (min)	1.44658E+11	0

Table 10 Pareto optimal solutions of the second stage bi-level programming model.

ID	Provinces'	Supply Cost Of	Selling Price				Followers'
	Inventory Levels	Foreign Medications	First Period	Second Period	Third Period	Fourth Period	Profits
1	-4.38E+07	1.447E+11	7245	7221	7047	3653	4.50E+10
2	-8.93E+07	1.386E+11	7245	7221	7047	3653	4.88E+10
3	-1.35E+08	1.326E+11	7245	7209	7059	3653	5.11E+10
4	-1.80E+08	1.266E+11	7245	7209	6338	4391	5.12E+10
5	-2.26E+08	1.205E+11	7245	7122	5284	5563	4.52E+10
6	-2.72E+08	1.145E+11	7245	7221	4310	6454	3.71E+10
7	-3.18E+08	1.085E+11	7245	7165	4369	6454	4.13E+10
8	-3.65E+08	1.025E+11	7245	7118	4418	6454	4.39E+10
9	-4.12E+08	9.644E+10	7245	7175	4358	6454	4.42E+10
10	-4.58E+08	9.041E+10	7175	7158	4451	6454	4.44E+10
11	-5.10E+08	8.438E+10	6801	6481	5558	6454	4.37E+10
12	-5.77E+08	7.836E+10	6386	6099	6400	6454	4.03E+10
13	-6.45E+08	7.233E+10	6516	5967	6400	6454	3.75E+10
14	-7.15E+08	6.630E+10	6516	5967	6400	6454	3.51E+10
15	-7.84E+08	6.027E+10	6516	5967	6400	6454	3.11E+10
16	-8.55E+08	5.425E+10	6516	5967	6400	6454	2.84E+10
17	-9.26E+08	4.822E+10	6516	5967	6400	6454	2.44E+10
18	-9.98E+08	4.219E+10	6538	5944	6400	6454	2.42E+10
19	-1.07E+09	3.616E+10	6629	5851	6400	6454	8.02E+08
20	-1.26E+09	2.411E+10	6405	6081	6400	6454	1.73E+10
21	-1.36E+09	1.808E+10	6221	6269	6400	6454	1.45E+10
22	-1.47E+09	1.205E+10	6221	6269	6400	5967	9.66E+09

reasonable in aspects. First; it can be considered as a support for domestic production since the manufacturers will be motivated to increase their production level to achieve the possible profit. Moreover, it is financial advantageous for the patients as well, since the price of domestic medications is more reasonable compared to their foreign counterparts.

After determining the quantity provided by manufacturers for the demand zones, the unmet demands of provinces were entered as an input parameter to the second stage bi-level model which was solved by a process similar to the previous one. The results associated with the lexicographic pay-off table and the optimal Pareto solutions are reported in Table 9 and Table 10, respectively.

As Table 10 suggests, compared to the second and third point, the first solution is more suitable because for the same price average (i.e. about 6,291 Rial), the first objective function value (Provinces' Inventory Level) worked better. However, to find more precise and better solutions, the gap between the first and second solution was split into much more points. Finally, among the provided efficient solutions, one solution could satisfy the DM for which the values of the first and second objective function were obtained as -5.89E+07 and 1.43E+11, respectively. Also, the sale prices for the four periods were 7245, 7254, 7012 and 3653, respectively.

Fig. 4 graphically represents the drugs allocation among the provinces. The density of colors corresponds to the number of drugs received by the demand zones. The violet outer circles indicate that the drugs were provided by the manufacturers while the pink color stands for the suppliers. According to the figure, in the first stage when the manufacturers supplied the drug, the provinces including Tehran and Esfahan received the maximum quantity due to their higher demand and DALY's value. On the other hand, the provinces such as Sistan & Baluchistan and West Azerbaijan were allocated with the minimum quantity due to possessing minimum demand and DALY's value. Sistan & Baluchistan province did not receive any drug from the manufacturers. Moreover, the usefulness and effectiveness of the DALY's values are clearly indicated in the cases with the same demands, e.g., Razavi Khorasan and East

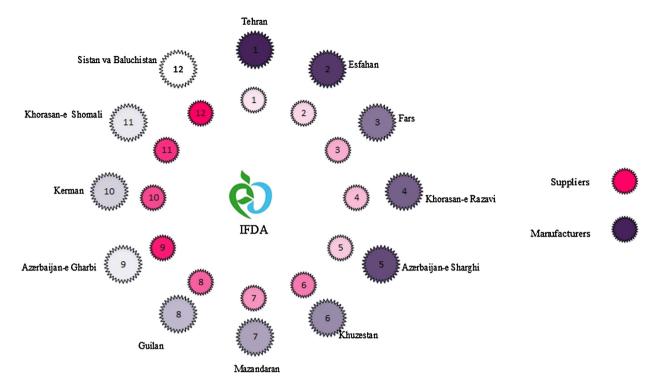


Fig. 4. Graphical representation of medication allocation among the demand zones. (For interpretation of the colors in the figure(s), the reader is referred to the web version of this article.)

Azerbaijan. In this case, East Azerbaijan received higher amounts of medications as it had higher DALY's value compared to Razavi Khorasan

In the next stage, the remaining demands were provided by suppliers. Sistan & Baluchistan which had not been allocated in the previous stage got the first priority followed by West Azerbaijan. Finally, Tehran and Esfahan which had already received the maximum portion by manufacturers, took the lowest quantity.

Accordingly, the DALY value can be used as a quantitative and transparent index by policymakers, IFDA, to equitably ration the medications among the demand zones.

7.2. Performance assessment of the proposed risk-based possibilistic approach

To compare the performance of the possibilistic mean-semi variance model with the expected value approach, the given models (the first and second stage bi-level programming models) were surveyed under different risk coefficient values (Figs. 5 and 6). According to the information reported in Table 11, the following results can be derived.

- Our observations showed that although in the expected value model, the possibilistic mean value of followers' profit is maximal (i.e., $\rho = 0$), the possibilistic semi-variance had the highest value. Thus, the expected value model puts the most downside risk on the DMs and the robustness of the model is not guaranteed.
- By increasing the risk coefficient values, the followers' possibilistic mean value and the objective function deviations were simultaneously reduced in both models, resulting in deterioration of the first objective function value.
- Regarding the result represented in Table 11, it can be concluded that the semi-variance risk measure is a very sensitive measure; even very trivial values can cause a dramatic reduction in the DM's profit function. Hence, decision makers should be so cautious in selecting the risk coefficient value as paying too much attention to the objective functions fluctuations i.e., risk value, can negatively affect the DMs' total profitability. As a result, the DMs should make a suitable trade-off between the average profit and risk value.

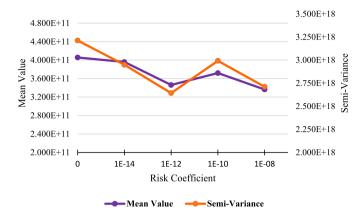


Fig. 5. Performance of the possibilistic Mean value and possibilistic semi-variance under different values of risk coefficient for the first stage model. (For interpretation of the colors in the figure(s), the reader is referred to the web version of this article.)

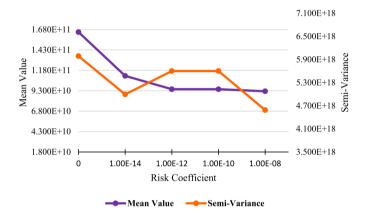


Fig. 6. Performance of the possibilistic Mean value and possibilistic semi-variance under different values of risk coefficient for the second stage model. (For interpretation of the colors in the figure(s), the reader is referred to the web version of this article.)

Table 11
The performance of the proposed risk-based possibilistic approach under different risk coefficient.

The first stage bi-level model				The second stage bi-level model			
Risk Coefficient	Obj 1	Follower's Profit		Risk Coefficient	Obj 1	Follower's Profit	
		Mean Value	Semi Variance			Mean Value	Semi Variance
0	-5.2E+08	4.057E+11	3.212E+18	0	-4.38E+07	1.648E+11	5.988E+18
1E-14	-5.2E+08	3.959E+11	2.949E+18	1E-14	-4.38E+07	1.112E+11	4.994E+18
1E-12	-5.2E+08	3.461E+11	2.643E+18	1E-12	-4.38E+07	9.490E+10	5.600E+18
1E-10	-5.2E+08	3.719E+11	2.992E+18	1E-10	-4.38E+07	9.490E+10	5.600E+18
1E-08	-8.3E+08	3.364E+11	2.711E+18	1E-08	-1.03E+08	9.241E+10	4.587E+18

Moreover, the objective functions of deterministic and the proposed models consist of different terms which make it impossible to compare. In order to assess the superiority of the solutions obtained by possibilistic mean-semi variance model over deterministic, the results of the both models under nominal data were measured using a deterministic linear programming model. This model which is a simulation of reality is called 'realization model'. To be more specific, in the realization model, which is a deterministic equivalent model, the uncertain parameters are generated as the random numbers uniformly between minimum and maximum points of variations interval of the corresponding possibility distribution function. For example if $\tilde{a} = (a_1, a_2, a_3)$ is an imprecise parameter with triangular possibility distribution function, the realization is produced by generating a random number uniformly between the two extreme points of the corresponding possibility distribution function (i.e. $[a_1, a_3]$). Afterward, by substituting the solutions

Table 12
The results of the realization models for the deterministic and proposed possibilistic model.

No. of realization	Deterministic	Possibilistic Semi-Variance Model $\alpha = 0.6$	Possibilistic Semi-Variance Model $\alpha = 0.7$	Possibilistic Semi-Variance Model $\alpha = 0.8$	Possibilistic Semi-Variance Model $\alpha = 0.9$
1	-4/38E+09	-2/95E+09	-2/77E+09	-1/03E+10	-1/81E+11
2	-2/35E+11	-4/60E+09	-1/93E+09	-3/69E+09	-3/98E+09
3	-6/58E+10	-3/53E+09	-1/68E+10	-7/44E+09	-5/79E+09
4	-2/51E+10	-3/85E+09	-6/68E+09	-4/52E+09	-5/66E+09
5	-2/97E+09	-3/04E+09	-3/00E+09	-3/33E+09	-5/22E+09
6	-2/00E+11	-6/01E+09	-7/03E+09	-4/32E+09	-7/94E+09
7	-1/06E+10	-3/07E+09	-8/66E+10	-1/10E+11	-6/51E+09
8	-2/87E+09	-1/61E+09	-1/72E+09	-5/10E+09	-4/57E+10
9	-1/73E+09	-1/95E+09	-1/87E+09	-7/13E+09	-1/10E+11
10	-4/73E+09	-4/42E+09	-4/37E+09	-4/77E+09	-6/31E+09
Average	-5/53E+10	-3/50E+09	-1/33E+10	-1/60E+10	-3/78E+10
Standard deviation	8/35E+10	1/23E+09	2/48E+10	3/13E+10	57412916771

obtained by both models under nominal data (X^*, LF_1^*) , the realization model was solved using several experiments, and finally, the objective functions' values are compared with each other in terms of the average and standard deviation measures.

Consider the compact form of the realization model as follows:

$$\begin{aligned} & \text{Max } LF_1^* - \pi_1 Slack_1 - \sigma_1^+ Slack_2^+ - \sigma_2^- Slack_2^- - \delta_3 Slack_3 \\ & \text{s.t.} \quad LF_2 + s_2 = e_2 \\ & \quad AX^* + Slack_1 \geq \tilde{C} \\ & \quad TX^* - \tilde{D} = Slack_2^+ - Slack_2^- \\ & \quad GX^* - Slack_3 \leq \tilde{D} \\ & \quad Slack_1, Slack_2^+, Slack_2^-, Slack_3 \geq 0 \end{aligned}$$

where A, T and G are coefficient matrices of the constraints and \tilde{C} and \tilde{D} are fuzzy numbers. It should be noted that $Slack_1$, $Slack_2^+$, $Slack_2^-$ and $Slack_3$ are the violation variables for chance constraints under random realization. Besides, the parameter π_1 , σ_1^+ , σ_2^- and δ_3 were assigned as the corresponding values of violation penalty. The results of realization model for 10 experiments were reported in Table 12.

As it can be seen, considering the average and standard deviation of objective functions as the two performance measures, the possibilistic semi-variance model outperformed the deterministic model under different values of confidence levels (i.e., $\alpha = 0.6, 0.7, 0.8$ and 0.9). In addition, based on our observation the performance of the proposed possibilistic programming model was closely dependent on the violation penalty values of the chance constraints (i.e., $\pi_1, \sigma_1^+, \sigma_2^-$ and δ_3). To put it simply, the superiority of the proposed model would be more justifiable as the violation penalty goes up.

8. Conclusions

The scarcity of health resources is inescapable, particularly in epidemic outbreaks e.g., Corona virus. Due to the lack of sufficient resources to allocate the vulnerable people and high expenditures imposed on the government and patients, it is essential for policymakers in the healthcare area to adopt effective strategies to cope with this dilemma. In this paper, the supply and allocation of the healthcare scarce resources were addressed for the first time through a possibilistic bi-objective bi-level programming model over a multi-period planning horizon. To present a more realistic model, the roles of the government and provider firms (i.e., manufacturers and suppliers) were modeled using the Stackelberg game. Moreover, the competition among individuals of the followers was incorporated through a normalized Nash equilibrium. In the proposed model, two groups of followers were considered and their priority was included in the model formulation through a lexicographical procedure. The disability-adjusted life years (DALY)

indicator was used as a quantitative index to measure the actual needs of different demand zones assisting the government in the impartial allocation of the medications. Due to the importance of risk and uncertainty in the pharmaceutical supply chain, an appropriate risk management tool using the possibilistic mean and semi variance of fuzzy numbers was developed to effectively curb the fluctuations of objective functions values. Since the model included two obiective functions, the augmented ε -constraint method was applied to find efficient solutions from the Pareto-optimal set. Finally, a real case study was provided to validate the applicability of the proposed model and the performance of the novel possibilistic approach. According to the results, the pricing policy adopted by the government can positively affect both the followers' profitability and shortage minimization in the demand zones. Another conclusion is that the risk-neutral possibilistic approaches are not a reliable tool for optimizing the concerned supply chain under uncertainty while the novel possibilistic approach is capable of effective control of the objective functions variations. However, to reduce the risk arisen from uncertain parameters, the less profit is achieved for DMs. Accordingly, the DM preferences and the nature of the problem should be taken into account for determining the degree of conservatism or risk coefficient value. The future research could extend the proposed possibilistic programming model into the robust possibilistic programming ones to control the mean value and optimality robustness of objective functions along with feasibility robustness. It would be also interesting to consider the effect of the supply disruptions risks on the followers' problem in the proposed model and develop the heuristic or meta-heuristic solution methods for solving the mix-integer programming model.

Declaration of competing interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Appendix A

Assume that ξ^{\sim} is a triangular fuzzy number. The following statement can be defined as the membership function of ξ^{\sim} :

$$\mu_{\xi^{\sim}}(X) = \begin{cases} 0 & if \ x \ge \xi_{(3)}, x \le \xi_{(1)} \\ f_{\xi}(x) = \frac{x - \xi_{(1)}}{\xi_{(2)} - \xi_{(1)}} & if \ \xi_{(1)} \le x \le \xi_{(2)} \\ g_{\xi}(x) = \frac{\xi_{(3)} - x}{\xi_{(3)} - \xi_{(2)}} & if \ \xi_{(2)} \le x \le \xi_{(3)} \end{cases}$$
(A.1)

According to [65], the possibilistic mean value of the triangular fuzzy number ξ^{\sim} can be expressed as follows:

$$M\left(\tilde{\xi}\right) = \left[M_1^{\tilde{\xi}}, M_2^{\tilde{\xi}}\right] = \left[2\int_0^1 \alpha f_{\xi}^{-1}(\alpha) d\alpha, 2\int_0^1 \alpha g_{\xi}^{-1}(\alpha) d\alpha\right] = \left[\frac{2}{3}\xi_{(2)} + \frac{1}{3}\xi_{(1)}, \frac{2}{3}\xi_{(2)} + \frac{1}{3}\xi_{(3)}\right] \tag{A.2}$$

$$\overline{M}\left(\tilde{\xi}\right) = \frac{\xi_{(1)} + 4\xi_{(2)} + \xi_{(3)}}{6} \tag{A.3}$$

Let \tilde{a} and \tilde{b} be two fuzzy triangular numbers, λ and γ be two real numbers [66], then

$$\left[f_{\lambda \tilde{a} + \gamma \tilde{b}}^{-1}(x), g_{\lambda \tilde{a} + \gamma \tilde{b}}^{-1}(x) \right] = \left[\lambda f_{\tilde{a}}^{-1}(x) + \gamma f_{\tilde{b}}^{-1}(x), \lambda g_{\tilde{a}}^{-1}(x) + \gamma g_{\tilde{b}}^{-1}(x) \right]$$
(A.4)

Accordingly, the following conclusion can be derived for any real number λ and γ [65], then

$$\overline{M}\left(\lambda \tilde{a} + \gamma \tilde{b}\right) = \lambda \overline{M}\left(\tilde{a}\right) + \gamma \overline{M}\left(\tilde{b}\right) \tag{A.5}$$

The crisp upper and lower possibilistic semi variances of fuzzy number of ξ^{\sim} is calculated as follows [67]:

$$Var^{-}\left(\tilde{\xi}\right) = \int_{0}^{1} 2\alpha \left(\overline{M}\left(\tilde{\xi}\right) - f_{\xi}^{-1}\left(\alpha\right)\right)^{2} d\alpha = \left(\frac{\xi_{(3)}^{2} - 2\xi_{(1)}\xi_{(3)} + 2\xi_{(2)}^{2} - 4\xi_{(1)}\xi_{(2)} + 3\xi_{(1)}^{2}}{36}\right) \tag{A.6}$$

$$Var^{+}\left(\tilde{\xi}\right) = \int_{0}^{1} 2\alpha \left(\overline{M}\left(\tilde{\xi}\right) - g_{\xi}^{-1}(\alpha)\right)^{2} d\alpha = \left(\frac{3\xi_{(3)}^{2} - 4\xi_{(2)}\xi_{(3)} + 2\xi_{(2)}^{2} - 2\xi_{(1)}\xi_{(3)} + \xi_{(1)}^{2}}{36}\right) \tag{A.7}$$

In particular, if $\tilde{\xi}$ is a symmetric fuzzy number, then we have $Var^-\left(\tilde{\xi}\right) = Var^+\left(\tilde{\xi}\right)$.

According to the ranking method of Jimenez for any pair of fuzzy triangular numbers \tilde{a} and \tilde{b} , the degree in which \tilde{a} is bigger than \tilde{b} is expressed as follows:

$$\mu_N\left(\tilde{a},\tilde{b}\right) = \begin{cases} 0 & m_2^a - M_1^b < 0\\ \frac{M_2^a - M_1^b}{M_2^a - M_1^b - (M_1^a - M_2^b)} & M_1^a - M_2^b \le 0 \le M_2^a - M_1^b\\ 1 & M_1^a - M_2^b > 0 \end{cases}$$
(A.8)

When $\mu_N\left(\tilde{a},\tilde{b}\right) \geq \alpha$, it is stated that, \tilde{a} is bigger than or equal to \tilde{b} at least in degree α and it is shown by $\tilde{a} \geq_{\alpha} \tilde{b}$.

Moreover, as mentioned by Parra et al. [52] two fuzzy numbers \tilde{a} and \tilde{b} are indifferent in degree α if the relationships mentioned below hold simultaneously:

$$\tilde{a} \ge_{\alpha/2} \tilde{b}, \qquad \tilde{a} \le_{\alpha/2} \tilde{b}$$
 (A.9)

The above inequalities can be shown as follows:

$$\frac{\alpha}{2} \le \mu_N \left(\tilde{a}, \tilde{b} \right) \le 1 - \frac{\alpha}{2} \tag{A.10}$$

Based on [53], a decision vector $x \in R$ is feasible in degree α if $min_{i=1,...,n} \left\{ \mu_N \left(\tilde{a}_i x, \tilde{b}_i \right) \right\} = \alpha$.

According to the above-mentioned relations, the equations $\tilde{a}_i x \geq \tilde{b}_i$ and $\tilde{a}_i x = \tilde{b}_i$ are converted into their crisp counterparts as follows:

$$((1 - \alpha) M_2^{a_i} + \alpha M_1^{a_i}) x \ge \alpha M_2^{b_i} + (1 - \alpha) M_1^{b_i} \quad i = 1, \dots, l$$
 (A.11)

$$\left(\left(1 - \frac{\alpha}{2} \right) M_2^{a_i} + \frac{\alpha}{2} M_1^{a_i} \right) x \ge \left(\frac{\alpha}{2} M_2^{b_i} + \left(1 - \frac{\alpha}{2} \right) M_1^{b_i} \right) \quad i = l + 1, \dots, m$$
(A.12)

$$\left(\frac{\alpha}{2}M_2^{a_i} + \left(1 - \frac{\alpha}{2}\right)M_1^{a_i}\right)x \le \left(\left(1 - \frac{\alpha}{2}\right)M_2^{b_i} + \frac{\alpha}{2}M_1^{b_i}\right) \quad i = l + 1, \dots, m$$
(A.13)

Appendix B

Proving the concavity of the objective functions:

The linearized crisp equivalent of the manufacturers and suppliers' objective functions are represented as follows, respectively:

$$\begin{aligned} \max MF_{j} &= \left[\sum_{p,l,t} \left(v_{pt} - tr_{pt}^{j \to l} \right) z_{pt}^{j \to l} - \sum_{p,t} \left(\frac{c^{(1)}_{pjt} + 4c^{(2)}_{pjt} + c^{(3)}_{pjt}}{4} \right) x_{pjt} \right. \\ &- \sum_{p,t} \partial_{pj} I M_{pjt} - \sum_{p,l,i,t} g_{pt}^{l \to i} q_{pjt}^{l \to i} \right] \\ &- \rho \left[\sum_{p,t} x_{pjt}^{2} \left(\frac{c_{pjt(3)}^{2} - 2c_{pjt(1)}c_{pjt(3)} + 2c_{pjt(2)}^{2} - 4c_{pjt(1)}c_{pjt(2)} + 3c_{pjt(1)}^{2}}{36} \right) \right] \\ \max SF_{k} &= \left[\sum_{p,l,t} \left(v'_{pt} - r_{pt}^{k \to l} \right) y_{pt}^{k \to l} - \sum_{p,v,t} \left(\frac{e_{vt}^{1} + 4e_{vt}^{2} + e_{vt}^{3}}{6} \right) \left(a_{pt}^{v \to k} + h_{pt}^{v \to k} \right) s_{pt}^{v \to k} - \sum_{p,v,t} g_{pkt} s_{pt}^{v \to k} \right. \\ &- \vartheta_{t} \sum_{p,v,t} \left(\left(\frac{e_{vt}^{1} + 4e_{vt}^{2} + e_{vt}^{3}}{6} \right) \left(a_{pt}^{v \to k} + h_{pt}^{v \to k} \right) + g_{pkt} \right) s_{pt}^{v \to k} - \sum_{p,t} \partial_{pk}^{t} I S_{pkt} - \sum_{p,l,i,t} g_{pt}^{l \to i} o_{pkt}^{l \to i} \right] \end{aligned}$$

$$-\rho \left[\sum_{p,v,t} \left(\left(a_{pt}^{v \to k} + h_{pt}^{v \to k} \right) s_{pt}^{k \to v} \right)^2 \left(\frac{e_{vt(3)}^2 - 2e_{vt(1)}e_{vt(3)} + 2e_{vt(2)}^2 - 4e_{vt(1)}e_{vt(2)} + 3e_{vt(1)}^2}{36} \right) + \vartheta_t^2 \sum_{p,v,t} \left(\left(a_{pt}^{v \to k} + h_{pt}^{v \to k} \right) s_{pt}^{v \to k} \right)^2 \left(\frac{e_{vt(3)}^2 - 2e_{vt(1)}e_{vt(3)} + 2e_{vt(2)}^2 - 4e_{vt(1)}e_{vt(2)} + 3e_{vt(1)}^2}{36} \right) \right]$$

Since the terms firth to fifth in the manufacturer's objective function are linear, to prove the concavity of the objective function, we must prove that the second derivative of the last term is negative:

$$\frac{dz_{j}}{dx_{pjt}} = -2\rho x_{pjt} \left(\frac{c_{pjt(3)}^{2} - 2c_{pjt(1)}c_{pjt(3)} + 2c_{pjt(2)}^{2} - 4c_{pjt(1)}c_{pjt(2)} + 3c_{pjt(1)}^{2}}{36} \right)$$

$$\frac{d^{2}z_{j}}{dx_{pjt}^{2}} = -2\rho \left(\frac{c_{pjt(3)}^{2} - 2c_{pjt(1)}c_{pjt(3)} + 2c_{pjt(2)}^{2} - 4c_{pjt(1)}c_{pjt(2)} + 3c_{pjt(1)}^{2}}{36} \right) < 0$$

As it can be seen, the non-linearity of the last term does not lead to non-concavity of the problem. Moreover, the calculation of the second derivative of the non-linear term of suppliers' objective function is done as follows:

$$\begin{split} \frac{dz_k'}{ds_{pt}^{k\to v}} &= -2\rho s_{pt}^{k\to v} \left(a_{pt}^{v\to k} + h_{pt}^{v\to k}\right)^2 \left(\frac{e_{vt(3)}^2 - 2e_{vt(1)}e_{vt(3)} + 2e_{vt(2)}^2 - 4e_{vt(1)}e_{vt(2)} + 3e_{vt(1)}^2}{36}\right) \left(\vartheta_t^2 + 1\right) \\ \frac{d^2z_k'}{ds_{pt}^{k\to v2}} &= -2\rho \left(a_{pt}^{v\to k} + h_{pt}^{v\to k}\right)^2 \left(\frac{e_{vt(3)}^2 - 2e_{vt(1)}e_{vt(3)} + 2e_{vt(2)}^2 - 4e_{vt(1)}e_{vt(2)} + 3e_{vt(1)}^2}{36}\right) \left(\vartheta_t^2 + 1\right) < 0 \end{split}$$

Therefore, both of the objective functions are concave and we can use the KKT conditions.

References

- [1] WHO, World Health Statistics, World Healthcare Organization, 2015.
- [2] E.R. Fox, B.V. Sweet, V. Jensen, Drug Shortages: A Complex Health Care Crisis, Mayo Clinic Proceedings, vol. 89(3), Elsevier, 2014, pp. 361–373.
- [3] B.G. Jericho, Ethical Issues in Anesthesiology and Surgery, Springer, 2015.
- [4] Food and D Administration, Strategic Plan for Preventing and Mitigating Drug Shortages, Food and Drug Administration, 2013.
- [5] D. Mechanic, Muddling through elegantly: finding the proper balance in rationing, Health Aff. 16 (5) (1997) 83–92.
- [6] P.B. Hofmann, 7 factors complicate ethical resource allocation decisions: we should be more aware of the issues most likely to produce conflicts, Healthc. Exec. 26 (3) (2011) 62–63.
- [7] L.A. Zadeh, Fuzzy sets as a basis for a theory of possibility, Fuzzy Sets Syst. 100 (1) (1999) 9-34.
- [8] P.A. Ubel, S.D. Goold, Rationing health care: not all definitions are created equal, Arch. Intern. Med. 158 (3) (1998) 209-214.
- [9] S. Teutsch, B. Rechel, Ethics of resource allocation and rationing medical care in a time of fiscal restraint-US and Europe, Public Health Rev. 34 (1) (2012) 15.
- [10] J. Peppercorn, A. Armstrong, D.W. Zaas, D. George, Rationing in Urologic Oncology: Lessons from Sipuleucel-T for Advanced Prostate Cancer, Urologic Oncology: Seminars and Original Investigations, vol. 31(7), Elsevier, 2013, pp. 1079–1084.
- [11] G.J.C. Esmeria, An Application of Goal Programming in the Allocation of Anti-TB Drugs in Rural Health Centers in the Philippines Track Title: Healthcare Management.
- [12] M. Koyuncu, R. Erol, Optimal resource allocation model to mitigate the impact of pandemic influenza: a case study for Turkey, J. Med. Syst. 34 (1) (2010) 61–70.
- [13] Y-Y. Feng, I-C. Wu, T-L. Chen, Stochastic resource allocation in emergency departments with a multi-objective simulation optimization algorithm, Health Care Manage. Sci. 20 (1) (2017) 55–75.
- [14] D. Schniederjans, Q. Cao, M.J. Schniederjans, Pandemic drug rationing model: Nebraska state government case study, Int. J. Oper. Res. 29 (4) (2017) 478–494.
- [15] A. Anparasan, M. Lejeune, Resource deployment and donation allocation for epidemic outbreaks, Ann. Oper. Res. (2017) 1–24.
- [16] Z. Hu, G. Hu, A multi-stage stochastic programming for lot-sizing and scheduling under demand uncertainty, Comput. Ind. Eng. 119 (2018) 157–166.
- [17] C.J. Murray, T. Vos, R. Lozano, M. Naghavi, A.D. Flaxman, C. Michaud, M. Ezzati, K. Shibuya, J.A. Salomon, S. Abdalla, Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010, Lancet 380 (9859) (2012) 2197–2223.
- [18] C.J. Murray, A.K. Acharya, Understanding DALYs, J. Health Econ. 16 (6) (1997) 703–730.

- [19] Institute for Health Metrics and Evaluation (IHME), Protocol for the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD).
 Version 2.0, IHME, Seattle (WA), 2015, Available at: http://www.healthdata.org/sites/default/files/files/Projects/GBD/GBD_Protocol.pdf.
 (Accessed 3 March 2018).
- [20] J.E. Saunders, Z. Rankin, K.Y. Noonan, Otolaryngology and the global burden of disease, Otolaryngol. Clin. North Am. 51 (3) (2018) 515–534.
- [21] I. Sung, T. Lee, Optimal allocation of emergency medical resources in a mass casualty incident: patient prioritization by column generation, Eur. J. Oper. Res. 252 (2) (2016) 623–634.
- [22] J.M. Swaminathan, Decision support for allocating scarce drugs, Interfaces 33 (2) (2003) 1–11.
- [23] W-H. Feng, Z. Lou, N. Kong, H. Wan, A multiobjective stochastic genetic algorithm for the pareto-optimal prioritization scheme design of real-time healthcare resource allocation, Oper. Res. Health Care 15 (2017) 32–42.
- [24] S. Ahmadvand, M.S. Pishvaee, An efficient method for kidney allocation problem: a credibility-based fuzzy common weights data envelopment analysis approach, Health Care Manage. Sci. (2017) 1–17.
- [25] G.P. Cachon, S. Netessine, Game theory in supply chain analysis, in: Models, Methods, and Applications for Innovative Decision Making: INFORMS, 2006, pp. 200–233.
- [26] D.J. Garcia, F. You, Supply chain design and optimization: challenges and opportunities, Comput. Chem. Eng. 81 (2015) 153–170.
- [27] M.-s.P. Bahareh Aghababei, Barzinpour Farnaz, A Two-Stage Fuzzy Mathematical Programming Model for Scarce Drugs Supply and Ration Planning Under Uncertainty: A Case Study in Iran, Vol. 29, 2018, applied soft Computing (under review).
- [28] J. Fortuny-Amat, B. McCarl, A representation and economic interpretation of a two-level programming problem, J. Oper. Res. Soc. 32 (9) (1981) 783–792.
- [29] J.F. Gaski, The theory of power and conflict in channels of distribution, J. Mark. (1984) 9–29.
- [30] H. Von Stackelberg, Market Structure and Equilibrium, Springer Science & Business Media, 2010.
- [31] K.J. Arrow, G. Debreu, Existence of an equilibrium for a competitive economy, Econometrica (1954) 265–290.
- [32] F. Facchinei, C. Kanzow, Generalized Nash equilibrium problems, Ann. Oper. Res. 175 (1) (2010) 177-211.
- [33] D. Yue, F. You, Game-theoretic modeling and optimization of multi-echelon supply chain design and operation under Stackelberg game and market equilibrium, Comput. Chem. Eng. 71 (2014) 347–361.
- [34] N.S. Sharif, M.S. Pishvaee, A. Aliahmadi, A. Jabbarzadeh, A bi-level programming approach to joint network design and pricing problem in the municipal solid waste management system: a case study, Resour. Conserv. Recycl. 131 (2018) 17–40.
- [35] M. Ghomi-Avili, S.G.J. Naeini, R. Tavakkoli-Moghaddam, A. Jabbarzadeh, A fuzzy pricing model for a green competitive closed-loop supply chain network design in the presence of disruptions, J. Clean. Prod. 188 (2018) 425–442.
- [36] A. Gaivoronski, G.M. Sechi, P. Zuddas, Cost/risk balanced management of scarce resources using stochastic programming, Eur. J. Oper. Res. 216 (1) (2012) 214–224.
- [37] Z. Ghelichi, M. Saidi-Mehrabad, M.S. Pishvaee, A stochastic programming approach toward optimal design and planning of an integrated green biodiesel supply chain network under uncertainty: a case study, Energy 156 (2018) 661–687.
- [38] H. Ensafian, S. Yaghoubi, M.M. Yazdi, Raising quality and safety of platelet transfusion services in a patient-based integrated supply chain under uncertainty, Comput. Chem. Eng. 106 (2017) 355–372.
- [39] R. Babazadeh, J. Razmi, M.S. Pishvaee, M. Rabbani, A sustainable second-generation biodiesel supply chain network design problem under risk. Omega 66 (2017) 258–277.
- [40] H. Ghaderi, A. Moini, M.S. Pishvaee, A multi-objective robust possibilistic programming approach to sustainable switchgrass-based bioethanol supply chain network design, J. Clean. Prod. 179 (2018) 368–406.
- [41] J. Mula, R. Poler, J. Garcia, MRP with flexible constraints: a fuzzy mathematical programming approach, Fuzzy Sets Syst. 157 (1) (2006) 74–97.
- [42] M.S. Pishvaee, F. Jolai, J. Razmi, A stochastic optimization model for integrated forward/reverse logistics network design, J. Manuf. Syst. 28 (4) (2009) 107–114.
- [43] M.S. Pishvaee, M. Rabbani, S.A. Torabi, A robust optimization approach to closed-loop supply chain network design under uncertainty, Appl. Math. Model. 35 (2) (2011) 637–649.
- [44] M. Mousazadeh, S.A. Torabi, M. Pishvaee, F. Abolhassani, Accessible, stable, and equitable health service network redesign: a robust mixed possibilistic-flexible approach, Transp. Res., Part E, Logist. Transp. Rev. 111 (2018) 113–129.
- [45] M. Inuiguchi, J. Ramık, Possibilistic linear programming: a brief review of fuzzy mathematical programming and a comparison with stochastic programming in portfolio selection problem, Fuzzy Sets Syst. 111 (1) (2000) 3–28.
- [46] M. Inuiguchi, M. Sakawa, A possibilistic linear program is equivalent to a stochastic linear program in a special case, Fuzzy Sets Syst. 76 (3) (1995) 309–317.
- [47] W-G. Zhang, Y-J. Liu, W-J. Xu, A possibilistic mean-semivariance-entropy model for multi-period portfolio selection with transaction costs, Eur. J. Oper. Res. 222 (2) (2012) 341–349.
- [48] H. Markowitz, Portfolio Selection, Wiley, New York, 1959.
- [49] P. Zhang, W-G. Zhang, Multiperiod mean absolute deviation fuzzy portfolio selection model with risk control and cardinality constraints, Fuzzy Sets Syst. 255 (2014) 74–91.
- [50] L. Yang, L. Liu, Fuzzy fixed charge solid transportation problem and algorithm, Appl. Soft Comput. 7 (3) (2007) 879–889.
- [51] M.S. Pishvaee, J. Razmi, S.A. Torabi, Robust possibilistic programming for socially responsible supply chain network design: a new approach, Fuzzy Sets Syst. 206 (2012) 1–20.
- [52] M.A. Parra, A.B. Terol, B.P. Gladish, M.R.g. Uría, Solving a multiobjective possibilistic problem through compromise programming, Eur. J. Oper. Res. 164 (3) (2005) 748–759.
- [53] M. Jiménez, M. Arenas, A. Bilbao, M.V. Rodri, Linear programming with fuzzy parameters: an interactive method resolution, Eur. J. Oper. Res. 177 (3) (2007) 1599–1609.

- [54] O. Ben-Ayed, C.E. Blair, Computational difficulties of bilevel linear programming, Oper. Res. 38 (3) (1990) 556–560.
- [55] A.M.F. Fard, M. Hajaghaei-Keshteli, A tri-level location-allocation model for forward/reverse supply chain, Appl. Soft Comput. 62 (2018) 328–346
- [56] J. Bard, Practical Bilevel Optimization: Applications and Algorithms, Series: Nonconvex Optimization and Its Applications, vol. 30, Springer, 1998.
- [57] P.M. Castro, Tightening piecewise McCormick relaxations for bilinear problems, Comput. Chem. Eng. 72 (2015) 300–311.
- [58] I.E. Grossmann, C.A. Floudas, Active constraint strategy for flexibility analysis in chemical processes, Comput. Chem. Eng. 11 (6) (1987) 675–693.
- [59] M. Ehrgott, M.M. Wiecek, Mutiobjective programming, in: Multiple Criteria Decision Analysis: State of the Art Surveys, Springer, 2005, pp. 667–708.
- [60] G. Mavrotas, Effective implementation of the ε -constraint method in multi-objective mathematical programming problems, Appl. Math. Comput. 213 (2) (2009) 455–465.
- [61] C.-L. Hwang, A.S.M. Masud, Multiple Objective Decision Making—Methods and Applications: A State-of-the-Art Survey, Springer Science & Business Media. 2012.
- [62] J. Aghaei, N. Amjady, H.A. Shayanfar, Multi-objective electricity market clearing considering dynamic security by lexicographic optimization and augmented epsilon constraint method, Appl. Soft Comput. 11 (4) (2011) 3846–3858.
- [63] K. Sayehmiri, H. Tavan, F. Sayehmiri, I. Mohammadi, K.V. Carson, Prevalence of epilepsy in Iran: a meta-analysis and systematic review, Iran. J. Child Neurol. 8 (4) (2014) 9.
- [64] M.H. Forouzanfar, S.G. Sepanlou, S. Shahraz, D. Dicker, P. Naghavi, F. Pourmalek, A. Mokdad, R. Lozano, T. Vos, M. Asadi-Lari, A.-A. Sayyari, C.J.L. Murray, M. Naghavi, Evaluating causes of death and morbidity in Iran, global burden of diseases, injuries, and risk factors study 2010, Arch. Iran. Med. 17 (5) (2014) 304.
- [65] C. Carlsson, R. Fullér, Possibilistic mean value and variance of fuzzy numbers: some examples of application, in: 2009 IEEE International Conference on Fuzzy Systems, IEEE, 2009, pp. 587–592.
- [66] D.J. Dubois, Fuzzy Sets and Systems: Theory and Applications, Academic Press, 1980.
- [67] A. Saeidifar, E. Pasha, The possibilistic moments of fuzzy numbers and their applications, J. Comput. Appl. Math. 223 (2) (2009) 1028–1042.