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RESEARCH PAPER

Optimizing Adequacy, Effectiveness and Efficiency Measures in a Robust Blood Supply Chain

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ABSTRACT
In this research paper, we present a comprehensive and innovative approach to improving the performance of blood supply chain (BSC) networks under uncertain conditions. Firstly, we provide a brief review of the most recent BSC management studies to set the context for our study. Subsequently, we propose a first-ever multi-objective robust BSC model that incorporates three key objectives: network efficiency through cost minimization, adequacy by ensuring reliable and sufficient blood supply, and effectiveness by controlling blood freshness. To effectively address uncertainty in parameters, we devise a two-phase approach that combines robust programming and an augmented epsilon-constraint method. This method provides a single-objective counterpart of the original multi-objective robust model, making it more practical for real-world applications. To illustrate the applicability of our model, we present a case study and perform sensitivity analyses on critical parameters. Our results demonstrate the model's capability to effectively manage BSC networks while accounting for uncertain parameters. Overall, our research contributes to the BSC literature by providing an integrated approach that considers multiple objectives and uncertainties, paving the way for future studies in this field. The proposed model and its solution technique have practical applications for healthcare organizations, policymakers, and blood banks in developing effective BSC management strategies.

KEYWORDS: *Blood supply chain; Adequacy; Effectiveness; Efficiency; Multi-objective optimization; Robust optimization.*

1. Introduction and Background

Comprising around 7% of humans' total weight, blood is a crucial and life-saving product. Additionally, there is an eternal demand since every second one on the planet of all races and at any age needs a blood transfusion [1]. On the other hand, BSC as a critical part of the healthcare network is typically a set of processes including collection, production/testing, inventory control, and distribution, each of which requires their considerations and imposes different costs on the supply chain [2]. Fig. 1 presents a schematic view of the portion of these costs related to each part of the BSC. Regarding the different parts of the illustrated figure, as well as being a substantial part of the healthcare supply chain, an appropriately designed BSC network as well as making improvement in it can bring about considerable cost savings for health systems. To this aim, supply chain network design (SCND) emerges as a strategy on which the performance of a supply chain is highly dependent [3].

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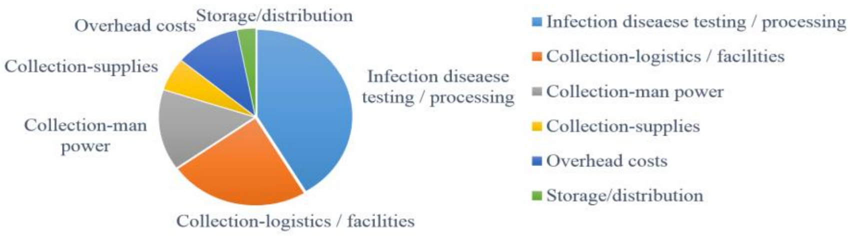

Fig. 1. Cost spending partitioned according to BSC echelons

Three critical factors are of great importance in BSC network design and eventually stimulated us to develop this research:

- Cost-effective accessibility to healthy blood (i.e., efficiency);
- Appropriate use of blood products at the best possible time (i.e., effectiveness);
- A sufficient supply of required blood (i.e., adequacy).

One of the most noticeable properties of BSC networks is the uncertainty of parameters coming to importance, especially while making strategic decisions. This characteristic, originating from either the fuzzy or random nature of data, can be tackled using uncertainty modeling approaches, including robust optimization, fuzzy programming, stochastic programming approaches, etc. In this paper, regarding the nature of data in our case study, we devise the robust optimization approach which yields the appropriate solution by making a trade-off between optimality and feasibility robustness. Indeed, this approach undertakes near-optimal solutions and maintains its feasibility while trying to improve the worst case. The main properties of the similar studies investigated in this paper ([3], [6]–[35]) have been provided in Table 1. Based on the aforementioned explanations, this study aims to address the following key questions:

1. What policies and strategies should be employed for the design and operation of the BSC network, including the collection of blood?
2. How can the performance of the BSC network be enhanced by considering the critical factors of efficiency, effectiveness, and adequacy? What trade-offs should be made between these factors?
3. How can the inherent uncertainty in the BSC network be incorporated into the mathematical model, and what is the optimal approach for managing this uncertainty?

In a nutshell, the main novelties of the present paper are as follows:

- Proposing an integrated novel multi-objective robust BSC model to design a high-performance network as an essential part of healthcare systems;
- Joint consideration of cost efficiency, blood freshness as the measure of efficacy, and reliability and sufficiency of blood supply as the objectives;
- Employing an efficient mixed solution approach by hybridizing multi-objective programming and robust optimization techniques to deal with uncertainties;
- Illustrating the real case application of the proposed model by investigating a case study.

2. Problem Statement and Mathematical Modeling

As shown in Fig. 2, the concerned BSC is composed of four main parts, namely collection, production and inventory management, distribution, and disposal.

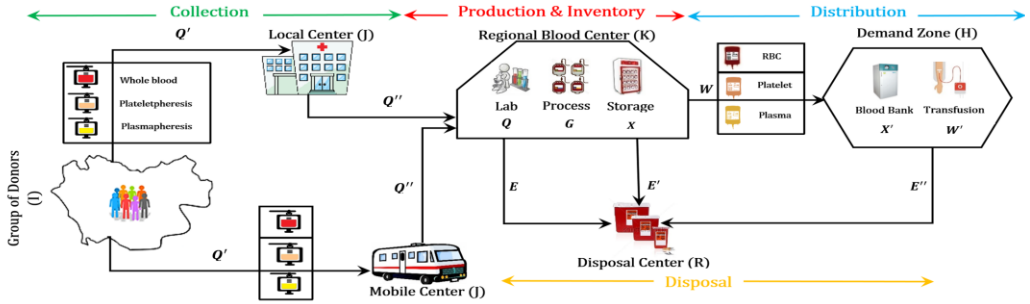

Fig. 2. An overview of the BSC

Tab. 1. Classification of the reviewed papers

References	Hierarchical level					Planning horizon			Type of blood product				Modeling*	Objective function		Performance measure								Time period		Uncertainty approach				Solution method	
	Integrated	Collection	Production	Inventory	Distribution	Strategic	Tactical	Operational	Whole blood	Platelets	Plasma	Red blood cell		Single-objective	Multi-objective	Cost	Distance	Shortage	Outdate	Freshness	Time	Risk	Blood supply	Single-period	Multi-period	Fuzzy	Stochastic	Robust	Hybrid uncertainty	Exact	
[3]		•				•	•		•				MILP	•		•													•	•	
[6]			•					•		•			INLP	•		•								•			•				
[7]	•						•		•				MINLP	•		•									•						•
[8]	•					•			•				TSSP		•	•					•				•		•			•	
[9]				•				•				•	INLP, S	•					•						•		•				•
[10]				•				•		•		•	ILP	•		•									•		•			•	
[11]		•					•		•				IP		•	•							•		•						•
[12]		•					•	•	•			•	MILP	•							•		•		•					•	
[13]	•					•			•		•	•	LP	•		•			•			•		•			•			•	
[14]	•								•	•	•	•	MIN		•	•		•							•				•	•	

												LP																	
[15]	●					●	●	●			●	S/ST	●		●	●	●								●			●	
[16]		●						●				S	●					●							●				●
[17]	●							●				ST	●					●				●							
[18]	●						●		●		●	S	●		●	●	●	●				●			●				●
[19]		●							●			SDP	●			●	●						●		●				●
[20]		●					●		●			S/SDP	●			●	●					●			●				●
[21]			●			●					●	DP, S	●		●								●						
[22]	●		●			●		●				S	●		●	●	●	●					●		●			●	
[23]		●					●	●	●	●	●	S	●		●	●	●						●						
[24]	●				●	●			●	●	●	MILP		●	●	●		●					●	●				●	
[25]	●				●	●		●				MILP	●		●							●					●	●	
[26]	●				●	●	●		●	●	●	MILP		●	●				●				●				●	●	
[27]	●				●	●			●	●	●	MILP		●	●			●		●			●			●		●	
[28]	●				●	●					●	MILP		●	●				●				●		●			●	
[29]	●				●	●		●				MILP	●		●								●			●		●	
[30]			●			●	●				●	MILP	●		●								●		●			●	
[31]		●		●		●		●				MILP	●		●	●							●	●				●	
[32]		●			●	●			●	●	●	MILP	●		●								●		●			●	
[33]		●				●	●	●				MILP	●		●								●				●	●	
[34]	●					●			●			MILP		●	●						●		●						●
[35]			●			●	●	●				MILP		●	●								●				●		●
Our research	●				●	●		●	●	●	●	MILP		●	●	●	●	●		●			●			●		●	

* MILP: mixed integer linear programing; (M) INLP: (mixed) integer non-linear programming; S: simulation; (S) DP: (stochastic) dynamic programming; ST: statistical analysis; TSSP: two-stage stochastic

The problem concerned can be formulated in the light of the following main assumptions:

- The maximum donation of blood from each donor group (DG) is considered to be the supply amount of each DG as it is impossible to have a collection plan separately for each donor.
- There is limited capacity for demand zones (DZs), including mobile blood collection facilities (MBCFs) and local blood collection facilities (LBCFs).
- Blood products have limited shelf lives, and their perishability starts from the time when they are produced.
- Blood units are transported directly from regional blood facilities (RBFs) to DZs.
- We consider the environment where the concerned network operates while all input parameters are known to be fixed except for supply, demands, production time, and network costs and weights, which are tainted with uncertainty.

Notations

Sets

I	Set of DGs; $i, i' = 1, \dots, I''$
J	Set of candidate location of blood collection facilities (LBCF or MBCFs); $j = 1, \dots, J'$
K	Set of RBFs; $k = 1, \dots, K'$
R	Set of disposal centers; $r = 1, \dots, R'$
P	Set of blood products; $p = 1, \dots, P'$
H	Set of DZs; $h = 1, \dots, H'$
M	Set of blood donation methods; $m = 1, \dots, M'$
T	Set of periods; $t, t' = 1, \dots, T''$

Parameters

S_j	The capacity of blood collection facility (BCF) *j*.
S'_{pk}	The capacity of RBF k to store blood product p.
S''_{ph}	The capacity of DZ *h* for storing product *p*.
L_p	The blood product *p*'s maximum shelf life.
O_{kt}	The maximum production time during period *t* in RBF *k*.
N	The maximum distance between each DG and a BCF.
O'_p	The production time of blood product *p*.
F_j	The establishment cost of BCF *j*.
F'_m	The operating cost of blood donation by method *m*.
F''_{pm}	The unit production cost of blood product *p* by method *m*.
U_{pkt}	The unit holding cost of product *p* in RBF *k* in period *t*.
U'_{pht}	The unit holding cost of product *p* in Dz *h* in period *t*.
C_{jk}	The unit transportation cost of blood units from BCF *j* to RBF *k*.
C'_{kh}	The unit transportation cost of blood product units from RBF *k* to DZ *h*.
D_{kr}	The unit cost of transportation of unusable blood units from RBF *k* to disposal center *r*.
D'_{kr}	The unit cost of transportation from RBF *k* to disposal center *r* for expired units.
D''_{hr}	The unit cost of transportation for expired blood units from Dz *h* to disposal center *r*.
V	The average speed of vehicles carrying blood to RBFs.
A	The maximum allowable time for vehicles arriving in RBFs.
B'_{it}	The maximum amount of blood supplied by DG i in period *t*.
$B''_{pht'}$	The total demand of DZ *h* for blood product *p* in the period *t'*.
δ_{pm}	The production rate of product *p* by method *m*.
φ_m	The percentage of usable blood donated by method *m*.
∂_{ij}	The distance between DG i and BCF *j*.
∂'_{jk}	The distance between BCF *j* and RBF *k*.
ϑ_{mjkt}	The weight of each unit of whole blood collected by method *m* and transported from BCF *j* to RBF *k* in period *t*.
θ_{khpt}	The weight of each unit of blood product *p* remaining in RBF *k* and transported to DZ *h* in period *t*.

Ψ The maximum allowable violation in the ratio of blood collection.
ω A very large number

Binary Variables

Z'_{jk} The allocation variable of BCF *j* to RBF *k*; is equal to 1 if BCF *j* is assigned to RBF *k*, and 0 otherwise.
Y_j The location variable of BCF *j*; is equal to 1 if BCF *j* is established, and 0 otherwise.
Z_{ij} The allocation variable of DG *i* to BCF *j*; is equal to 1 if DG *i* is assigned to BCF *j*, and 0 otherwise.

Positive Variables

Q'_{mijt} The amount of blood donated by DG *i* via method *m* in BCF *j* in period *t.*
Q''_{mjkt} The amount of blood donated by method *m* and transported from BCF *j* to RBF *k* in period *t.*
Q_{pmkt} The amount of blood product *p* donated by method *m* and produced in RBF *k* in period *t.*
G_{pkt} The quantity of blood product *p* produced during time *t* in the RBF *k*.
$W_{khptt'}$ The amount of blood product *p* transported in time period *t'* from RBF *k* to Dz *h*, provided it is produced in period *t*.
$W'_{khptt'}$ The amount of blood product *p* transported from RBF *k* to DZ *h* in period *t* to be used in time period *t'*.
E_{pkrt} The quantity of unusable product *p* transported from RBF *k* to disposal center *r* in period *t.*
$E'_{pkrt'}$ The quantity of expired product *p* transported from RBF *k* to disposal center *r* in period *t'*.
$E''_{phrt'}$ The quantity of expired product *p* transported from DZ *h* to disposal center *r* in period *t'*.
$X_{pktt'}$ The inventory level of product p is processed in period t and remains in RBF *k* until period *t'*.
$X'_{phtt'}$ The inventory level of product *p*, which is processed in period *t*, and remains in DZ *h* until period *t'*.

2.1. Objective functions (OFs)

In this section, a multi-objective formulation is presented. The objectives are: (1) minimizing the total cost of the network, (2) minimizing the time interval between blood production in RBFs and consumption in DZs, and (3) minimizing the average amount of blood distributed from unreliable Blood Collection Facilities (BCFs) to RBFs.

2.1.1. The first OF (F_1)

The design of a network configuration and planning of its activities incur various costs. The cost of establishing a facility, the cost of producing various products, the cost of transporting products to DZs, etc., are parts of the costs imposed. In this subsection, we formulate the total cost of the concerned BSC network as Equation (1). One of the goals of the BSC is to minimize the total cost (F_1) of design and planning. The total cost includes the fixed opening cost of facilities (Equation (2)), i.e., $F_{1\{\mathrm{FC}\}}$, the operating cost of blood collection (Equation (3)), i.e., $F_{1\{\mathrm{OC}\}}$, production cost (Equation (4)), i.e., $F_{1\{\mathrm{PC}\}}$, transportation cost (Equation (5)), i.e., $F_{1\{\mathrm{TC}\}}$, and inventory holding cost (Equation (6)), i.e., $F_{1\{\mathrm{IC}\}}$.

$$Min\, F_1 = F_{1\{\mathrm{FC}\}} + F_{1\{\mathrm{OC}\}} + F_{1\{\mathrm{PC}\}} + F_{1\{\mathrm{TC}\}} + F_{1\{\mathrm{IC}\}} \tag{1}$$

$$\text{Fixed opening cost: } F_{1\{\mathrm{FC}\}} = \sum_j F_j * Y_j \tag{2}$$

$$\text{Operating cost: } F_{1\{\mathrm{OC}\}} = \sum_m \sum_i \sum_j \sum_t F'_m * Q'_{mijt} \tag{3}$$

$$\text{Production cost: } F_{1\{\mathrm{PC}\}} = \sum_p \sum_m \sum_k \sum_t F''_{pm} * Q_{pmkt} \tag{4}$$

$$\text{Transportation costs: } F_{1\{TC\}} = \sum_m \sum_j \sum_k \sum_t C_{jk} * Q''_{mjkt} + \sum_k \sum_h \sum_p \sum_t \sum_{t'} C'_{kh} * W_{khptt'} + \sum_p \sum_k \sum_r \sum_t D_{kr} * E_{pkrt} + \sum_p \sum_k \sum_r \sum_{t'} D'_{kr} * E'_{pkrt'} + \sum_p \sum_h \sum_r \sum_{t'} D''_{hr} * E''_{phrt'} \quad (5)$$

$$\text{Inventory costs: } F_{1\{IC\}} = \sum_p \sum_k \sum_t \sum_{t'} U_{pkt} * X_{pktt'} + \sum_p \sum_h \sum_t \sum_{t'} U'_{pht} * X'_{phtt'} \quad (6)$$

2.1.2. The second OF (F_2)

The model aims to preserve the freshness of blood products by increasing their remaining shelf lives. Indeed, the word "preserve" refers to the optimal storage time of blood products. For doing so, the time interval between blood consumption in DZs and blood production in RBFs is to be minimized through Equation (7).

$$\min F_2 = \sum_k \sum_h \sum_p \sum_t \sum_{t'} \theta_{khpt} * \frac{|t' - t|}{L_p} * (X_{pktt'} + X'_{phtt'}) \quad (7)$$

In Equation (7), θ_{khpt} denotes the importance of product p, which is delivered from RBF k to DZ h in period t [36].

2.1.3. The third OF (F_3)

Another factor to account for is the adequate and reliable provision of blood. Various reasons such as weather conditions, human factors, natural events, and so on, can negatively affect the blood supply's reliability. One crucial issue is to consider the reliability of BCFs in charge of distributing the collected blood units to RBFs. Equation (8) defines the reliability of facility j (R_j) which may not fail to perform until period τ. Based on this probability equation, the time required until facility j will fail follows an exponential distribution with a mean of ρ_{jt}. Thus, BCF j is reliable for dispatching blood units to the RBFs in period T_j [37].

$$R_j = P(T_j > \tau) = e^{-\rho_{jt}\tau} \quad \forall j = 1,2,\ldots \quad (8)$$

It is worth noting that, after a failure, BCF j is not able to return to the functional state. Without loss of generality, Equation (8) can be replaced with the following relationship:

$$R'_j = 1 - R_j; \quad R'_j = 1 - P(T_j > \tau) = 1 - e^{-\rho_{jt}\tau} \quad \forall j = 1,2,\ldots \quad (9)$$

In Equation (9), R'_j is defined as the unreliability of BCF j in blood supply to RBFs, which must be minimized as an unfavorable factor. Therefore, to respect the adequacy and reliability of blood collection facilities, the average number of blood units distributed from unreliable BCFs to RBFs ($\vartheta_{mjkt} \times Q''_{mjkt} \times (1 - e^{-\rho_{jt}\tau})$) must be minimized via the third OF through Equation (10).

$$\min F_3 = \sum_m \sum_j \sum_k \sum_t \vartheta_{mjkt} * Q''_{mjkt} * (1 - e^{-\rho_{jt}\tau}) \quad (10)$$

2.2. Constraints

$$Z_{ij} \le Y_j \quad \forall i, j \quad (11)$$

$$\sum_m \sum_i Q'_{mijt} \le S_j \quad \forall j, t \quad (12)$$

$$\sum_m \sum_j Q'_{mijt} \le B'_{it} \quad \forall i, t \quad (13)$$

$$\partial_{ij} * Z_{ij} \le N \quad \forall i, j \quad (14)$$

$$Z'_{jk}\left(\frac{\partial'_{jk}}{V}\right) \le A \qquad \forall j,k \qquad (15)$$
$$Q'_{mijt} \le \omega * Z_{ij} \qquad \forall m,i,j,t \qquad (16)$$
$$Z'_{jk} \le \omega * Y_j \qquad \forall j,k \qquad (17)$$
$$Q''_{mjkt} \le \omega * Z'_{jk} \qquad \forall m,j,k,t \qquad (18)$$
$$\sum_i Q'_{mijt} = \sum_k Q''_{mjkt} \qquad \forall m,j,t \qquad (19)$$
$$-\Psi \le \sum_m \sum_j Q'_{mijt} / B'_{it} - \sum_m \sum_j Q''_{mjkt} / B'_{i't} \le \Psi \qquad \forall i,i',t \qquad (20)$$
$$\varphi_m * \delta_{pm} * \sum_j Q''_{mjkt} = Q_{pmkt} \qquad \forall p,m,k,t \qquad (21)$$
$$\sum_m Q_{pmkt} = G_{pkt} \qquad \forall p,k,t \qquad (22)$$
$$G_{pkt} = X_{pktt'} + \sum_h W_{khptt'} \qquad \forall p,k,t=t' \qquad (23)$$
$$X_{pktt'} = X_{pkt,t'-1} - \sum_h W_{khptt'} \qquad \forall p,k,t<t' \qquad (24)$$
$$\sum_k W_{khptt'} = X'_{phtt'} + \sum_k W'_{khptt'} \qquad \forall p,h,t=t' \qquad (25)$$
$$X'_{phtt'} = X_{pkt,t'-1} + \sum_k W_{khptt'} - \sum_k W'_{khptt'} \qquad \forall p,h,t<t' \qquad (26)$$
$$\sum_{t' \le t+l_p} \sum_k W'_{khptt'} \ge B''_{pht'} \qquad \forall h,p,t' \qquad (27)$$
$$\sum_p O'_p * G_{pkt} \le O_{kt} \qquad \forall k,t \qquad (28)$$
$$(1-\varphi_m) * \sum_j Q''_{mjkt} = \sum_r E_{pkrt} \qquad \forall p,m,k,t \qquad (29)$$
$$\sum_{t' > t+l_p} X'_{phtt'} = \sum_r E''_{phrt'} \qquad \forall p,h,t' \qquad (30)$$
$$\sum_{t' > t+l_p} X_{pktt'} = \sum_r E'_{pkrt'} \qquad \forall p,k,t' \qquad (31)$$
$$\sum_{t' \le t+l_p} X_{pktt'} \le S'_{pk} \qquad \forall k,p,t' \qquad (32)$$
$$\sum_{t' \le t+l_p} X'_{phtt'} \le S''_{ph} \qquad \forall h,p,t' \qquad (33)$$
$$Y_j \; Z_{ij} \;\; Z'_{jk} \in \{0,1\} \qquad \forall i,k,j \qquad (34)$$
$$Q'_{mijt} \; Q''_{mjkt} \; Q_{pmkt} \; G_{pkt} \; W_{khptt'} \; W'_{khptt'} \; E_{pkrt} \; E'_{pkrt'} \; E''_{phrt'} \; X_{pktt'} \; X'_{phtt'} \ge 0 \qquad \forall i,j,m,k,p,r,h,t,t' \qquad (35)$$

A BCF can be assigned to each DG only if the facility has been established. This limitation can be formulated by Constraint (11). Constraint (12) shows a limited capacity of the BCF j. Each DG can supply blood no more than its potential capacity. Thus, the total quantity of blood collected by each facility cannot exceed the potential capacity of DG i in each period. This constraint is bounded by Constraint (13). Each DG is allowed to be assigned to a BCF within its coverage area. This limitation is imposed by Constraint (14). The delivery of vehicles carrying blood from collection facilities to RBFs must be assured within the maximum possible arrival time (A). The limitation, as mentioned above, is bound by Constraint (15). Blood can be transported between two nodes only if the assignment between that pair of nodes holds. Such a limitation can be imposed by a binary variable and a very large number (ω) as defined in Constraints (16)-(18). The quantity of blood collected from all DGs by facility j must be distributed among RBFs [38]. This restriction of inflow and outflow can be formulated as an Equation (19). According to Constraint (20), the difference between blood quantity collected from DG (region) i and that from the DG (region) i' must not exceed an admissible value (Ψ). The amount of products obtained by all methods will represent the total supply of blood products. These are expressed by Constraints (21) and (22). As formulated in Constraints (23) and (24), the quantity of products kept at each RBF in each period is composed of the quantity remaining from the previous period and/or the quantity produced in the current period minus the quantity dispatched to DZs. In addition, according to Constraints (25) and (26), The quantity held in each DZ shall be determined by the quantity remaining from the preceding period plus the quantity obtained from RBFs minus the quantity consumed in the DZ. Constraint (27) guarantees demand satisfaction for each DZ. Besides, the time duration for producing blood products at each RBF cannot exceed the maximum available time. This limitation can be imposed by Constraint (28). The discarded (unusable or outdated) blood units must be transported from RBFs and DZs toward disposal centers. This is binding through Constraints (29)- (31). At each RBF, each product's inventory level must not surpass the center's storage capacity for that item. Constraint (32) represents this limitation. Similarly, the level of inventory at each DZ must not exceed its storage capacity for that product. This limitation can be formulated as a Constraint (33). The domain of decision variables is specified by Constraints (34) and (35).

3. Uncertainty and Solution Approaches

Adopting an appropriate approach that favorably enables the network to handle uncertainty in parameters is of great significance. Thus, in this paper, a robust approach developed by Ben-Tal and Nemirovski [39], which is conservative enough to save the network against uncertainty, is applied. Assume a nominal linear optimization compact model as a relationship (36). In the model mentioned below, y is the vector of binary decision variables, and x is the vector of continuous decision variables. Additionally, A, H, N, M, B and C are the matrices of coefficients, f and c represent the OF coefficients, d and r are the RHS parameters.

$$\begin{aligned}
&\min z\\
&\text{Subject to}\\
&z \geq fy + cx\\
&Ax \geq d\\
&Hx = r\\
&Nx = 0\\
&Mx \leq 0\\
&Bx \leq Cy\\
&y \in \{0,1\}, x \in R^{+}
\end{aligned} \tag{36}$$

Where c, d, r may take the values from box uncertainty set Q, which is a bounded-interval set and defined as a relationship (37).

$$Q_{Box} = \{\gamma \in R^n : |\gamma_a - \overline{\gamma_a}| \leq \rho G_a\} \tag{37}$$

In which $\gamma \in R^n$ represents an n-dimensional vector, γ_a, the a^{th} parameter of vector γ has the nominal value $\overline{\gamma_a}$, ρ, a positive number, denotes the uncertainty level, and finally $G_a > 0$ states the uncertainty scale. According to Ben-Tal et al. [40], if $G_a = \overline{\gamma_a}$, we will come across a specific case where in the above uncertainty set the deviation of γ_a from its nominal value $\overline{\gamma_a}$ is of size up to ρ. Accordingly, the robust formulation of the compact model can be equivalent to the following tractable form [41, 42]:

$$\begin{aligned}
&\min z\\
&\text{Subject to}
\end{aligned} \tag{38}$$

$$
\begin{aligned}
&\sum_{t}(\overline{c_a}x_a+\theta_a)\leq z-fy && \\
&\rho_c G_a^c x_a \leq \theta_a && \forall a\in\{1,\dots,n_c\}\\
&\rho_c G_a^c x_a \geq -\theta_a && \forall a\in\{1,\dots,n_c\}\\
&a_i x \geq \overline{d_i}+\rho_d G_i^d && \forall i\in\{1,\dots,n_d\}\\
&h_j x_j \geq \overline{r_j}-\rho_r G_j^r && \forall j\in\{1,\dots,n_r\}\\
&h_j x_j \leq \overline{r_j}+\rho_r G_j^r && \forall j\in\{1,\dots,n_r\}\\
&Nx=0\\
&Mx\leq 0\\
&Bx\leq Cy\\
&y\in\{0,1\}, x,\theta\in R^+
\end{aligned}
$$

Several techniques have been addressed in the literature to solve the multi-objective mathematical models, including the weighted sum method, ε-constraint method, fuzzy programming approaches, the goal programming method, and so on [43-45]. In the former method (i.e., the ε-constraint method), which obtains a Pareto-optimal set of solutions, one of the objectives (that of the highest priority) is set as the OF while the others are set as constraints in addition to the ones existing in the original model. Model (39) defines the basic ε-constraint formulation of the nominal compact model.

$$
\begin{aligned}
&\min Z_1(x)\\
&\text{Subject to}\\
&Z_2(x)\leq e_2\\
&Z_3(x)\leq e_3\\
&\dots\\
&Z_b(x)\leq e_b\\
&x\in R
\end{aligned}
\tag{39}
$$

In this paper, the augmented ε-constraint method, which is an improved version of the ε-constraint method is tailored to convert the proposed multi-objective robust BSC formulation to the equivalent single-objective one. The formulation of the original augmented ε-constraint method can be presented as follows:

$$
\begin{aligned}
&\min Z_1(x)+\varepsilon\ \times\{\left({}^{s_2}/_{r_2}\right)+\left({}^{s_3}/_{r_3}\right)+\cdots+\left({}^{s_b}/_{r_b}\right)\}\\
&\text{Subject to}\\
&Z_2(x)+s_2=e_2\\
&Z_3(x)+s_3=e_3\\
&\dots\\
&Z_b(x)+s_b=e_b\\
&x\in R; s_j\geq 0
\end{aligned}
\tag{40}
$$

Where in the model (40), s_j for $j=2\ \dots\ b$ indicate the slack variables of the corresponding constraints, and ε is a small value between 10^{-3} and 10^{-6}. The above model is solved iteratively for each value of e_j and only an efficient solution for each vector e is thus guaranteed by the second term of the above model (i.e., $\varepsilon\times\{\frac{s_j}{r_j}\}$), called the augmented term, where r_j for $j=2\ \dots\ b$ is defined as the difference between the ideal and nadir values of Z_i for $i=2\ \dots\ b$ the pay-off table [46, 47].

4. Case Description

In this section, the BSC network of Esfahan, one of the most populated cities in Iran, is considered as the case study to implement the design of the proposed BSC network problem and improve the efficiency and responsiveness of Esfahan BSC network, which provides about 12% of blood supply for the country. Based on a field investigation and the interviews held with the head of Esfahan Blood Transfusion Organization (EBTO), the city suffers from inefficiencies in the BSC. Esfahan City consists of 14 districts, as depicted in Fig. 5, each of which represents a blood donation point and is assumed to participate in the blood collection process. In addition, Table 2 presents the geographic coordinates, i.e., longitude (LONG) and latitude (LAT) of each blood donation point *i* and the maximum amount of blood supplied by each donation point in each period according to EBTO.

Tab. 2. The properties of each district

Distinct	Supply	$(LONG_i, LAT_i)$
1	152	(32.642621, 51.644619)
2	171	(32.672591, 51.638637)
3	158	(32.669548, 51.693438)
4	241	(32.642613, 51.707759)
5	209	(32.548344, 51.678606)
6	223	(32.621526, 51.667376)
7	182	(32.694546, 51.676402)
8	195	(32.704260, 51.666390)
9	172	(32.649222, 51.619120)
10	217	(32.688192, 51.711012)
11	152	(32.689343, 51.605573)
12	223	(32.752577, 51.604743)
13	202	(32.614448, 51.616126)
14	178	(32.728228, 51.704234)

The geographic coordinates of BCFs (MBCF or LBCFs *j*), RBF *k*, and disposal center *r* are provided in Tables 3 and 4, respectively.

Tab. 3. The properties of each facility for blood collection

Row	Facility	Type of facility	$(LONG_i, LAT_i)$
1	Khajoo Center	Existing LBCF	(32.640902, 51.683623)
2	Shariati Center	Existing LBCF	(32.631361, 51.658855)
3	Ashegh Esfahani Center	Existing LBCF	(32.706916, 51.732621)
4	Mosala Center	Candidate LBCF	(32.679220, 51.697553)
5	Jahad Center	Candidate LBCF	(32.655686, 51.644533)
6	Kazemi Center	Candidate MBCF	(32.699414, 51.638611)
7	Hatef Center	Candidate MBCF	(32.662664, 51.684507)
8	Eshragh Center	Candidate MBCF	(32.701551, 51.679946)
9	Foroghi Center	Candidate MBCF	(32.674390, 51.653558)
10	Mardavich Center	Candidate MBCF	(32.614424, 51.664349)

Tab. 4. The properties of the RBF and disposal center

Row	Facility	Type of facility	$(LONG_i, LAT_i)$
1	Moshtagh Center	RBF	(32.653012,

2	Moshtagh Center	Disposal Center	51.739842) (32.652888, 51.748279)

Similarly, the traveling distance between blood collection facilities and the RBF, between the RBF, the disposal center, and DZs can be calculated according to the relationship (41). The blood products are stored in the Moshtagh blood bank to be distributed between DZs in need, as featured in Table 5.

Tab. 5. The properties of each DZ

Row	Demand Zone	Number of Beds	$(LONG_i, LAT_i)$
1	Hazrat-e Zahra Hospital	122	(32.715170, 51.728390)
2	Feiz Medical Clinic	172	(32.679097, 51.686407)
3	Zahraye Marzie Charity Hospital	96	(32.676454, 51.688269)
4	Askarieh Hospital	100	(32.674555, 51.701120)
5	Amin Hospital	152	(32.670674, 51.676303)
6	Amir-Al-Momenin Hospital	100	(32.660848, 51.687191)
7	Kashani Hospital	394	(32.660683, 51.652074)
8	Sina Hospital	60	(32.654653, 51.666885)
9	Khorshid Hospital	275	(32.654406, 51.675321)
10	Isa ben Maryam Hospital	261	(32.649781, 51.665610)
11	Sadooghi Hospital	217	(32.651020, 51.696706)
12	Omid Hospital	90	(32.645981, 51.644030)
13	Shahid Beheshti Hospital	180	(32.644413, 51.653348)
14	Saadi Hospital	120	(32.640034, 51.652074)
15	Shariati Hospital	850	(32.628295, 51.663550)
16	Hojjatieh Hospital	130	(32.628873, 51.700728)
17	Farabi Hospital	288	(32.626476, 51.764978)
18	Khanevadeh Hospital	250	(32.612680, 51.650505)
19	Milad Hospital	365	(32.610449, 51.619606)
20	Alzahra Hospital	950	(32.609374, 51.652172)

According to the WHO report [48], the estimation of the blood demand is provided with respect to the population of patients in each DZ. Based on this report, an average of 10 units of platelets per DZ's bed are consumed annually. The required data is collected by the interviews conducted with officials of BCFs and real data from EBTO. Also, data of some parameters in common is adopted from the related papers existing in the literature [49]–[63]. In line with the data collected, on average, establishing LBCFs costs about 1500$, and the setup cost of MBCFs is estimated to be 200$. The unit holding cost of products in the RBF and DZs is set at 0.3$ [64]. It is estimated that vehicles' average speed for transporting blood units in the city area is 20 km / h. Unit transport costs are proportional to the travel distance between each pair of facilities and centers, which is calculated to be $1 per kilometer. Blood collection also imposes an operational expense of about $10 for the whole blood collection [65]. Capacities of BCFs are considered to be 250 and 100 units for LBCFs and MBCFs, respectively. Also, the blood collected by collection facilities is allowed to arrive at the RBF within 4 hours [3]. Noteworthy, an estimation of technical parameters of blood products, including lifetime, processing time, production rate and cost, and so on, is provided based on the information about the properties of blood products [5], [66]–[68] and data from EBTO. Fig. 3 traces the locations of collection facilities (both existing and candidate), the RBF, and DZs which are featured in Tables 3-5. Besides, the distance between each pair of nodes i and j can be estimated based on the following great circle distance formula:

$$d_{ij} = 6.3711 * \arccos\left[\sin(LAT_i) * \sin\left(LAT_j\right) + \cos(LAT_i) * \cos\left(LAT_j\right) * \cos\left(LONG_j - LONG_i\right)\right] \tag{41}$$

It should be noted that LAT_i and $LONG_i$ are the latitude and longitude of node i. In the above equation, the geographic coordinates of i and j are in radians. Thus, the geographic coordinates presented in Tables (2)-(5) must be converted to radians by multiplying them by $\frac{\pi}{180}$.

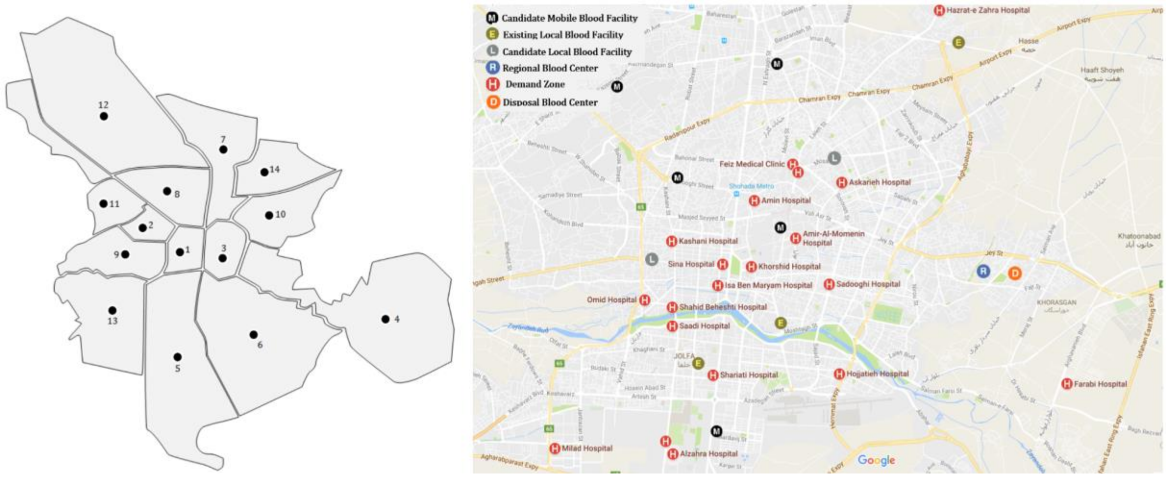

Fig. 3. Geographic dispersion and locations of collection facilities, the RBF, and DZs in Esfahan

5. Implementation

In this section, we first investigate the performance of the proposed multi-objective model and make a pairwise comparison of the conflicting behavior of objectives. Then, computational efforts are made to evaluate the model's performance and analyze its sensitivity to changes in the value of critical parameters. In this section, the validity of the proposed model and its solution approach is illustrated by solving the problem according to both deterministic and robust approaches and implementing several sensitivity analyses on the critical parameters. The computations are carried out by GAMS optimization software (refer to https://www.gams.com) on a personal computer with Intel Core i7, CPU 2.2GHz, and 16GB of RAM.

5.1. The robust model versus the deterministic model: evaluation of the performance

As presented in Table 6, five Pareto-optimal solutions are chosen to calculate the values of each OF while $\rho = 0$, i.e., deterministic model. A general trend, understood from columns 3-5, is that as the first OF improves, the other two objectives get worse, which shows the conflicts between the objectives clearly. The proposed model is then put into evaluation under different uncertainty levels, as shown in column 6, for both robust and deterministic models. Columns 8-11 represent the mean of each OF value and total standard deviation under various realizations. A general comparison of the results indicates that the robust model outperforms the deterministic model in terms of the mean and standard deviation of OF values in most realizations for different uncertainty levels. In other words, the robust model provides solutions with lower standard deviation and better value for OFs in comparison to the solutions obtained under the deterministic model. Moreover, by increasing the uncertainty level for uncertain parameters, the value of each OF gets worth due to applying a higher conservatism level. In other words, to make the BSC network more robust with respect to uncertain parameters such as supply, demand, and production time, the system should incur more costs to better respond to the environment's irregular behavior. It is interesting to note that the gaps of obtained results are 0.00%, which denotes that the obtained results under both deterministic and robust models are exact.

Tab. 6. Results summary under uncertain parameters and different realizations

Uncertainty level (ρ)	Pareto solution	The first OF values under nominal data	The second OF values under nominal data	The third OF value under nominal data	Uncertainty level (ρ)	Pareto solution	The mean of first OF values under realizations: Deterministic	The mean of first OF values under realizations: Robust	The mean of the second OF values	The mean of third OF values	The total standard deviation of OF values under realizations: Deterministic	The total standard deviation of OF values under realizations: Robust	Gap%
					ρ =0.1	ε^1	261856.4	224573.3	18181.8	3107.4	7227.6	5588.3	0.00%
	ε^1	194687.1	4329.0	1561.2		ε^2	261855.2	224547.3	19047.6	3204.0	7227.6	5592.0	0.00%
						ε^3	261854.1	223014.7	19913.4	3300.7	7227.6	5605.7	0.00%
						ε^4	261853.4	223229.2	20779.2	3397.3	7227.6	5607.8	0.00%
	ε^2	193716.3	8658.0	2044.4		ε^5	261853.4	223381.4	21645.0	3494.0	7227.6	5610.4	0.00%
						Average	261854.5	223749.2	19913.4	3300.68	7227.6	5600.8	0.00%
					ρ =0.3	ε^1	585693.6	398274.8	5268.4	3444.8	480635.5	21710.7	0.00%
						ε^2	599164.7	398222.0	10536.9	3672.7	501315.8	21710.1	0.00%
ρ = 0	ε^3	193673.0	12987.0	2527.6		ε^3	624319.1	398295.3	15805.4	3900.6	540327.1	21683.2	0.00%
						ε^4	590137.0	398285.4	21073.9	4128.5	487075.7	21682.9	0.00%
						ε^5	572082.0	398285.4	26342.4	4356.4	460321.7	21682.9	0.00%
	ε^4	193641.6	17316.0	3010.8		Average	594279.3	398272.6	15805.4	3900.6	493935.2	21693.9	0.00%
					ρ =0.5	ε^1	2265459.8	747878.8	6331.2	5222.7	2301254.3	187500.4	0.00%
						ε^2	2293967.7	747815.3	12662.4	5578.5	2329384.8	187498.3	0.00%
						ε^3	2272577.8	747984.0	18993.7	18993.7	2307295.3	187443.8	0.00%
	ε^5	193637.5	21645.0	3494.0		ε^4	2265964.7	747982.2	25324.9	6290.0	2299723.1	187443.5	0.00%
						ε^5	2264640.6	747981.9	31656.2	6645.8	2299874.2	187443.5	0.00%
						Average	2272522.1	747928.4	18993.6	8546.14	2307506.3	187465.9	0.00%

As can be seen in Table 6, the superiority and robustness of obtained results, in terms of average and standard deviation, from the robust model is clearly evident over the deterministic one. Therefore, it can be said the performance of the proposed robust model in multi-objective robust BSC is higher than the model with deterministic parameters. For example, when the uncertainty level is 10%, i.e., $\rho = 0.1$, the mean of network cost under deterministic and robust approaches are 261854.5 and 223749.2, respectively. It implies that the performance of the robust model in obtaining efficient solutions is 14.5% higher than the deterministic one. Moreover, when the uncertainty level is raised to 30% and 50%, the robust model outperforms the deterministic one, which shows the great performance of the proposed approach to cope with the inherent uncertainty of multi-objective robust BSC. That is to say, when the uncertainty level is equal to 0.3, the mean of network costs under deterministic and robust approaches are 594279.3 and 398272.6, respectively. It shows the value of cost OF under the deterministic model is surpassed by a robust approach of about %22.5. Similarly, this matter also holds for the standard deviation that in uncertainty levels of 0.1,0.3, and 0.5, the obtained results from the proposed robust model remarkably outperform those of the deterministic one.

Fig. 4 and Fig. 5 show the performance of the first OF for deterministic and robust models under different uncertainty levels ($\rho = 0.1$ 0.3 0.5), and Pareto-optimal solutions ε^1 and ε^2, respectively. A general observation from Fig. 10 is that as the uncertainty level increases, the mean of the OF of cost increases. Although the cost imposed on the network in a deterministic state is less than that of a robust model, the difference between the performance of robust and deterministic models is comparable with respect to the mean and standard deviation values. As can be seen, the results obtained from the robust approach outperform the results obtained from the determinist one. Moreover, increasing the uncertainty level, the variation of optimal value means for OF under the robust approach is lower than the deterministic model to a large extent.

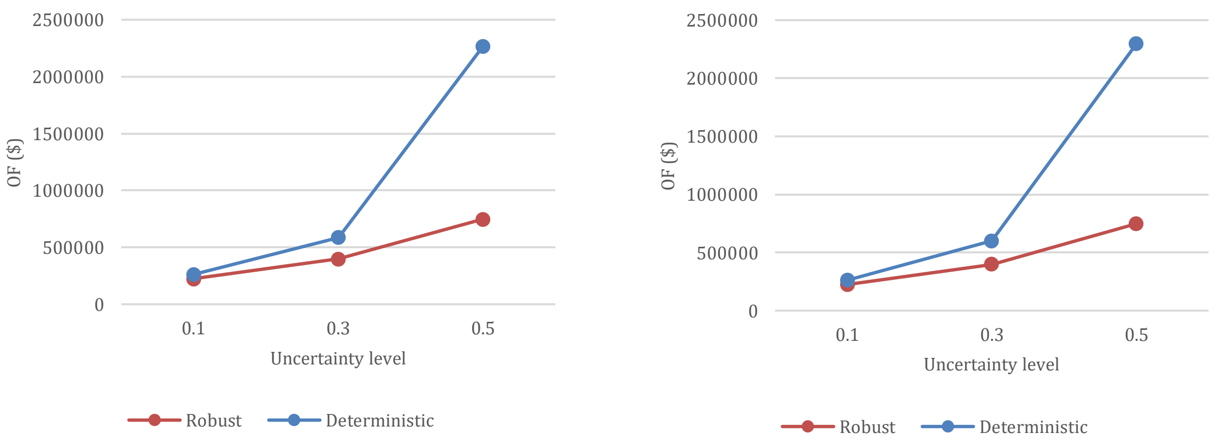

Fig. 4. Mean of the OF values for ε^1(the left side) and ε^2(the right side)

Fig. 6 shows the second and third OF values for ε^1 and ε^2. Similar to Fig. 4, the standard deviation of the robust approach outperforms that of the deterministic model regarding Fig. 5. Moreover, the variation of the deterministic model is greatly considerable by increasing the uncertainty level, while the changes in the standard deviation of results obtained from the robust approach are too slight.

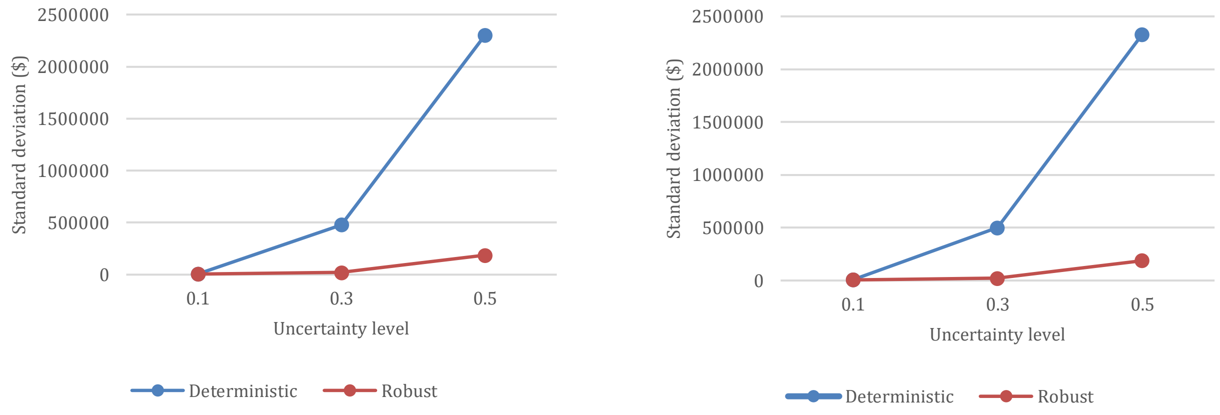

Fig. 5. Standard deviation of the OF values for ε^1(the left side) and ε^2(the right side)

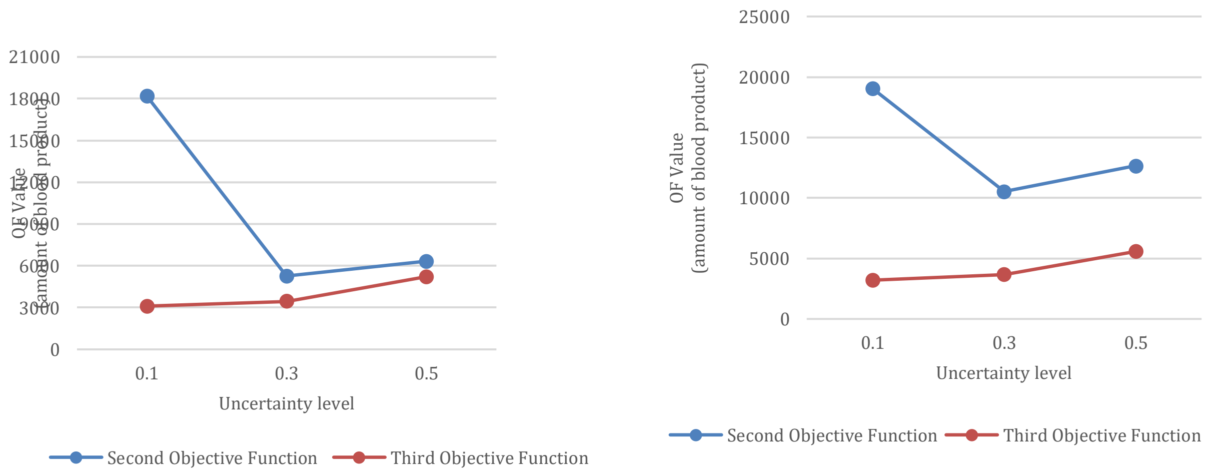

Fig. 6. Second and third OF values for ε^1(the left side) and ε^2(the right side)

Fig. 7 depicts the location of collection facilities (established and current facilities) under $\rho = 0.3$ and the Pareto-optimal solution with the least network cost. As can be observed from the following figure, 3 locations for MBCFs, namely Eshragh, Foroghi, and Mardavich, are chosen to be opened among 5 candidate locations, and one more LBCF is Mosala established in addition to the current ones.

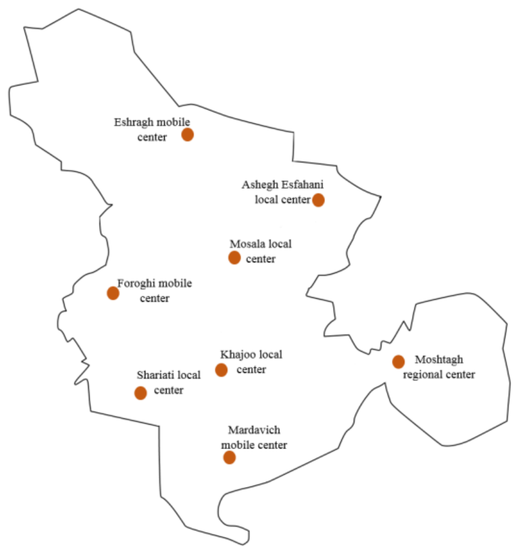

Fig. 7. Location of established and current blood facilities under $\rho = 0.3$

5.2. Sensitivity analysis

The impact of changing inventory unit costs for each product, which is stored in both RBF and DZs, on the values of the OFs, is discussed in this section. To this aim, we perform analyses for three different levels of uncertainty (i.e., $\rho = 0.1, 0.3, 0.5$). The findings show no significant change in the third OF as the inventory cost is varied. The result may arise from the fact that the third OF accounts for minimizing the blood collected and distributed by unreliable facility j and so does not remarkably respond to the changes in inventory cost. Accordingly, the third OF is laid away, and the other two OFs are investigated to know if they react to changing the inventory costs U_{pkt} and U'_{pht}. After solving the problem under the three uncertainty levels $\rho = 0.1\ \ 0.3\ \ 0.5$, and five different values of inventory cost, i.e., $U_{pkt} = U'_{pht} = 0.1\$, 0.2\$, 0.3\$, 0.4\$$, the Pareto-optimal solutions are shown in Figs. 8-10.

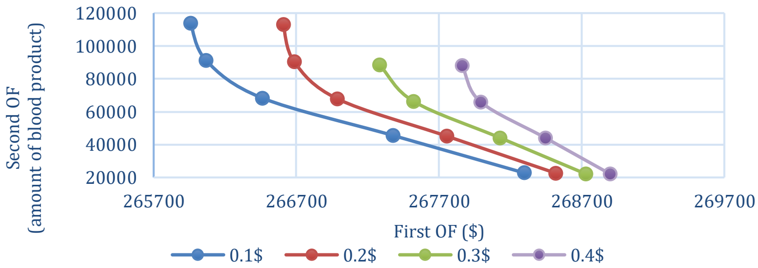

Fig. 8. Pareto optimal solutions under different levels of unit inventory cost and $\rho = 0.1$

A general interpretation of Figs. 14-16 is that, as the first OF aims to minimize the total network cost, increasing unit inventory cost can worsen the value of the first OF. On the contrary, an increase in unit inventory cost works in favor of the second OF since a lower inventory level will be kept in the RBF and DZs if unit inventory cost enhances. Keeping a lower inventory level means that the RBF tends to keep blood products for a shorter time and distribute to DZs as soon as possible, also DZs are willing to use the products soon after. Thus, this trend improves blood freshness, which is aimed at the second OF, and reduces the values of this OF. Deviating unit inventory cost up to 0.4$ or down to 0.1$ will change the behavior of the OFs. Increasing unit inventory cost to 0.4$ works for the second OF while against the first one. Decreasing unit inventory cost to 0.1$ works in favor of the first OF while against the second OF. To sum up, as unit inventory cost increases, blood freshness is improved while a higher cost can be imposed on the network.

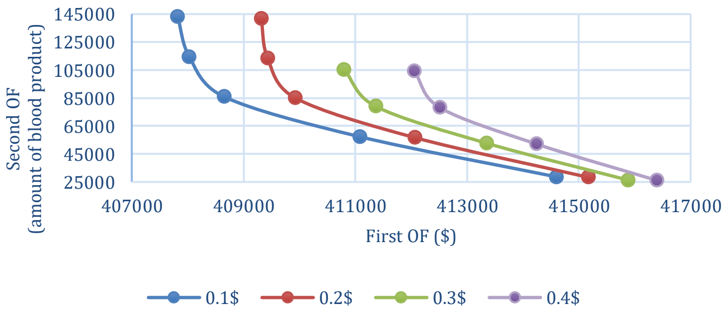

Fig. 9. Pareto optimal solutions under different levels of unit inventory cost, and ρ=0.3

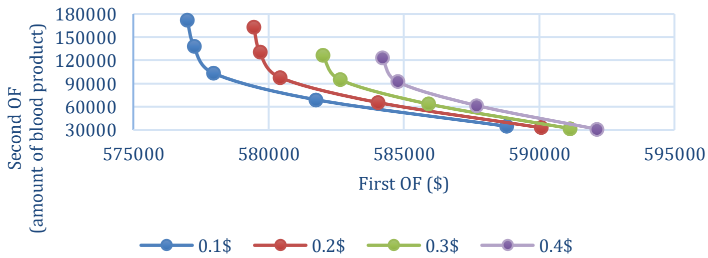

Fig. 10. Pareto optimal solutions under different levels of unit inventory cost, and ρ=0.5

6. Conclusion and Future Directions

Uncertainty in the elements of a BSC network such as blood supply, demand, processing time, and so on besides the perishability of blood is of challenge which makes planning for BSCs more demanding. Additionally, making a balance between reliability for sufficient blood supply, preserving blood freshness, and cost efficiency complicate the issue further. This paper addressed a multi-objective robust BSC problem capable of dealing with the uncertainty in data and blood perishability as a critical property of BSCs and the multiplicity of conflicting objectives concurrently. A robust programming approach captured the uncertainty, and an augmented epsilon-constraint method converted the proposed multi-objective problem into a single-objective counterpart. Then, the proposed multi-objective robust BSC problem was employed for designing a real case network of Esfahan BSC, and the results were reported. As the results indicated: (1) the robust model outperforms the deterministic model in terms of the mean and standard deviation of OF values in most realizations of uncertain parameters. The former provides robust solutions with lower standard deviation and OF values. (2) tending to keep a lower inventory level; blood freshness will improve since the RBF will distribute blood products to DZs as soon as possible and DZs are also willing to use the products soon after.

The interested researchers can extend the current work in the following directions: one can account for other uncertainty modeling approaches such as fuzzy programming, stochastic programming, robust-possibilistic programming, and so on, to compare the respective outcomes with those obtained in the current research. Future research can also address exact solution approaches or meta-heuristic techniques required for solving the proposed problem in large size to achieve optimal solutions within reasonable CPU time. Another avenue could be opened to researchers by extending the current work while considering transshipment between RBFs and also between DZs in case they face blood shortage. Additionally, one can account for the congestion in collection facilities to improve their efficiency in the blood collection process.

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