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Blood Supply Chain Network Design Considering Responsiveness and Reliability in Conditions of Uncertainty Using the Lagrangian Relaxation Algorithm

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Abstract

The growing need for adequate and safe blood and the high costs of health systems have prompted governments to improve the functioning of health systems. One of the most critical parts of a health system is the blood supply chain, which accounts for a significant share of the health system's costs. In the present study, with an operational approach, the total network costs are minimized along with the minimization of transportation time and lead time of delivery of blood products. Also, determining the optimal routing decisions is improved the level of responsiveness and reliability of the network. In this research, a multi-objective stochastic nonlinear mixed-integer model has been developed for Tehran's blood supply chain network. Robust scenario-based programming is capable of effectively controlling parametric uncertainty and the level of risk aversion of network decisions. Also, the proposed reliability approach controls the adverse effects of disturbances and creates an adequate confidence level in the capacity of the network blood bank. Lastly, the model is solved through the Lagrangian relaxation algorithm. Comparison of the results shows the high convergence rate of the solutions in the Lagrangian relaxation algorithm.

Keywords: Blood supply chain, Stochastic programming, Robust, Reliablility, Lagrangian relaxation.

1 | Introduction

Providing healthy and adequate blood for hospitals is a vital issue that governments' health systems are constantly facing. There is always a need for blood donors and their products; while the supply from donors is somewhat erratic, and the demand for blood products is often an uncertain trend. Disasters are natural or artificial disasters that occur suddenly and cause a great deal of damage. Earthquakes, floods, tornadoes, wars, etc. are examples of disasters that exacerbate the uncertainty of supply and demand for this vital product [1]. When a crisis occurs, there is a significant increase in demand and a shortage of blood supply. In addition, the amount of blood expected to help the injured is highly erratic and highly volatile, and demand from blood centers is unclear [2]. On the other hand, Blood is a perishable substance that in critical situations, its collection and transfer rate is a serious challenge to the health system [3]. Despite all efforts to find alternatives to blood, no

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similar specimen has been found for this vital and valuable element, which means that the only way to supply blood to applicants is to receive it from a donor and inject it into the patient's body. After receiving blood and at the beginning of the work, the donor goes to blood donation centers. Subsequently, the whole blood received is sent to the relevant laboratories for health testing and to be tested and converted into blood products and can be consumed. The blood supply chain begins when blood donors volunteer at donation centers. Blood collection can be done in mobile centers or fixed collection centers. The collected blood units are transferred to blood banks and processed to be ready for recipients. Blood banks perform bacterial tests and several mandatory tests necessary for the health of blood units, and additional tests can be requested as needed. Blood units that have been tested are stored in blood banks to be distributed in hospitals and health centers [4]. A Crisis can affect many aspects of the blood supply chain. Blood collection centers and blood banks may be easily disrupted and inaccessible due to road disruptions, traffic, or other reasons, in which case blood products become inaccessible. When a facility in the supply chain fails, a replacement must be considered, otherwise, it will affect all echelons of the network [5]. Therefore, it is crucial to use a reliable design to ensure the correct operation of blood supply chains in crises [6]. Because disasters and incidents are not always predictable, decision-makers must consider possible crisis scenarios to determine the optimal number of service centers to assist in before a crisis occurs [7].

In the current study, a stochastic multi-objective non-linear mathematical programming model for developing a reliable blood supply chain network under uncertain conditions is presented. Robust scenario-based programming is proposed for robustness against existing uncertainties and mitigation of crisis effects. The Lagrangian relaxation algorithm is used to accelerate the solution time. The remainder of this paper is organized as follows reviewing the literature and examining the remarkable contribution the present paper with other researches in Section 2 and defining and formulating the problem in Section 3 is presented. The research approach in single-objective modeling, implementation of robust programming and application of Lagrangian relaxation algorithm are given in Sections 4, 5 and 6, respectively. In Section 7, the results and some management implications are reported. Finally, the conclusions and some guidelines for future research are set out in Section 8.

2 | Literature Review

Since blood is a rare and perishable product, articles on the collection, production, distribution, storage, and perishability of blood products have been presented based on modeling approaches with several solution methods. In this section, some articles are reviewed, and lastly, the difference between the present study and other researches is highlighted. Arvan et al. [8] a mathematical optimization model for the network for multi-product blood supply chains consisting of collection units, laboratory facilities, storage facilities, distribution centers, and demand locations in definite conditions with a precise solution approach in software GAMS software provided. Chaiwuttisak et al. [9] designed a blood supply chain network to improve the blood supply situation of the Thai Red Crescent Society, to encourage donors and facilitate their access to blood donation centers. Ramezanian and Behboodi [10] presented a mixed-integer mathematical programming model for designing a blood supply chain considering various social factors such as distance, advertising costs, and experimental factors that influence blood donor decision-making processes. Zahiri et al. [11] expanded a two-objective mixed-integer model for the collection, production/screening, distribution, and routing of blood products that simultaneously optimize the total cost and health of blood products transferred to Hospitals. Ghorashi et al. [12] developed a mathematical model for optimizing a reliable network of blood supply chains in critical situations concering blood compatibility using the MOGWO approach.

Hosseinifard and Abbasi [13] examined the importance of concentrating inventory in the second tier of the two-tier blood supply chain. The first floor includes a single blood bank with uncertain supply, while the second floor includes hospitals with external demand. Dutta and Nagurney [14] presented a US-focused, multi-purpose competitive supply chain network model for the blood banking industry that depicts economic interactions between three rows of stakeholders: blood service organizations, hospitals, or health centers that bleed and the payment groups to which patients belong. Haghjoo et al. [15] in a case study of the actual crisis, presented a robust dynamic location model to design a blood supply chain network under conditions of uncertainty with the risk of disruption of facilities in a crisis. For further review of the literature, the papers in *Table 1* are reviewed.

Table 1. Review of some existing models.

	Objective Functions			Problem Coverage			Network Structure		Planning Horizon		Problem Modeling		
Papers	Cost	Time	Reliability	Transportation	Routing	Location	Reliable	Unreliable	Single-Period	Multi-Period	Linear	Non-linear	Optimization approach
[16]	✔					✔		✔		✔		✔	LGR
[17]		✔				✔				✔	✔		RO
[8]	✔	✔				✔		✔	✔			✔	EPS
[18]	✔				✔	✔		✔		✔		✔	FZ
[19]	✔	✔		✔		✔		✔		✔	✔		EPS-LGR
[20]	✔			✔		✔		✔		✔	✔		FZ
[21]	✔			✔		✔		✔		✔	✔		RO
[10]	✔			✔		✔		✔		✔	✔		RO
[22]	✔					✔		✔		✔	✔		RO
[11]	✔		✔		✔			✔		✔		✔	MH
[23]	✔			✔		✔	✔			✔	✔		RO
[12]	✔	✔	✔	✔	✔	✔		✔		✔	✔		MH
[24]	✔	✔		✔	✔	✔		✔		✔		✔	LGR
[25]	✔			✔			✔			✔	✔		ST
[26]	✔			✔		✔		✔	✔		✔		MH
Current research	✔	✔	✔	✔	✔	✔	✔			✔		✔	EPS-RO-LGR

Abbreviation: Epsilon constraint: EPS, Lagrangian relaxation algorithm: LGR, Robust optimization: RO, Fuzzy programming: FZ, Meta heuristic: MH, Stochastic programming: ST

Accordingly, the main focus of the present study will be the transfer of blood products with maximum responsiveness and optimal routing. An essential feature of this network is ensuring the transfer of blood products from the blood bank to hospitals in the face of demand uncertainty and disruptions. In addition, a novel and operational concept of reliability have been developed to assess the accuracy of blood products according to their expiration period, which raises the level of satisfaction of the target community, including hospitals and medical centers. Another property illustrated for the extended model is its use as a decision guide for all subgroups and the complete disruption. Robust scenario-based programming covers the stochastic nature of uncertain demand for blood products. The developed model is defined as large-scale operational problems, which use the efficient Lagrangian relaxation algorithm to reduce problem-solving time and allocate accurate solutions. The notable innovation and distinction of this research compared to other related papers in the literature are the following:

- *Introducing a novel reliable multi-period blood supply chain network design model that integrates tactical and strategic level decisions and addressing partial disruptions of blood banks.*
- *Applying the optimal routing approach with the feature of transverse transmission to ensure the satisfaction of the demand of medical centers.*
- *Applying a multi-objective model to design a robust blood supply chain network by considering two remarkable aspects of responsiveness including delivery time and accelerating the transfer of blood products according to their lifespan.*
- *Designing an operational model based on actual data can be generalized in various critical situations.*

- *Applying the Lagrange release algorithm is designed for a large-scale nonlinear programming model that with an iterative approach reduces the complex constraints of the problem and finds the upper and lower bounds on the optimal solution of the problem with a reasonable convergence rate.*

3 | Problem Description and Formulation

This research is one of the applied development researches which is exploratory. The mathematical model of a blood supply chain in the event of random uncertainty has been developed by blood banks with maximum reliability in mind to meet the needs of hospitals and medical centers. Reliability is the probability of optimal performance along with the satisfaction of a system under specific working conditions in a certain period [27]. If in the *Eq. (1)*, T a non-negative continuous random variable is assumed to represent the lifetime before failure (useful life) of a system, a product or a component, and its reliability function is shown as $R(t)$, the expression Is the probability of an event in a system, a product or a part under study that lasts longer than time t and is shown in *Eq. (1)* [28].

$$R(t) = R(T > t) = \int_{t}^{+\infty} f(x)dx. \tag{1}$$

One of the most critical points in designing blood supply chain networks is the reliability of blood products according to their longevity. Delays in the delivery of blood products can affect the performance of the network since blood products have an expiration time, and can reduce the time to respond to the needs of hospitals and medical centers and increase their satisfaction. Objective function three models have been developed to evaluate the reliability of blood products according to the lifespan and expiration date of the products. It should be noted that product failure is an exponential probability distribution used to model the failure of blood products in each blood bank and their corresponding responses. The parameter λ_{pa} is the average lifespan of blood product p in blood bank a. The q parameter indicates the time allotted for sending the blood product in each period. The probability of survival of blood products for each blood bank during the period can be calculated in *Eq. (2)*.

$$P(t \geq q) = \int_{q}^{+\infty} \lambda_{pa} \cdot e^{-\lambda_{pa} \cdot q} = e^{-\lambda_{pa} \cdot q}. \tag{2}$$

In the above relation, multiplying the number of products sent from the blood bank of hospitals and medical centers shows the number of expected products delivered to the customer promptly. This can be used as a criterion for assessing network responsiveness and the level of satisfaction of hospitals and medical centers. According to *Fig. 1* in the present study, blood supply chain is four tiers consisting of blood donors, collection centers, blood banks and hospitals and medical centers, and collection centers are considered as fixed and mobile.

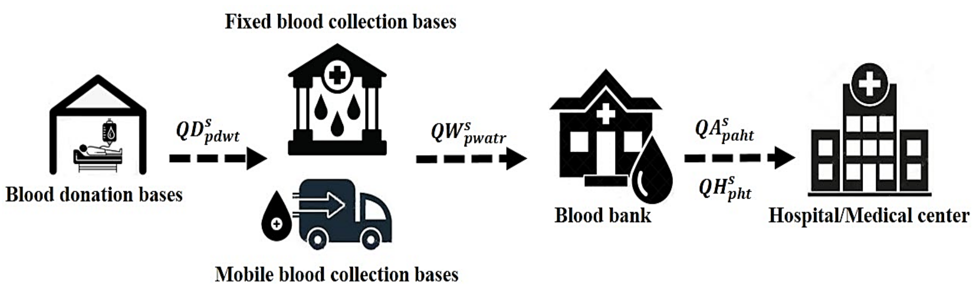

Fig. 1. Graphical representation of proposed reliable blood supply chain network.

This model, based on robust optimization techniques and two-stage stochastic uncertainty to reduce the effects of crises and disasters, with the aim of minimizing the expected costs of the system, minimizing the delivery time of purified blood to hospitals and medical centers and maximizing response to hospitals. It has been developed by minimizing the delay in the delivery of blood packages after a crisis, while taking into account possible disruptions in blood facilities and transportation routes. It is essential to minimize the total time expected in crisis, requiring immediate blood transfusions. Blood reserves are stored in blood banks to offset some of the effects of the disorder. These disruption scenarios are considered in the model through Stage two decisions in which the path between supply chain levels is not available in the event of a disruption. In each of the scenarios, a disturbance is assumed. If there is a disruption in the facilities of the blood banks, that blood bank will provide services if the undamaged parts are recovered. This model is designed to prioritize the supply of blood demand from the same area. However, in the absence of local supply, if necessary, it has a transverse transfer due to the variable of maximum demand that receives services from blood banks in neighboring areas to compensate for this shortage.

The model assumptions are as follows:

- *This blood supply chain includes five facilities related to blood and its products, which include blood donation bases, fixed blood collection bases, mobile blood collection bases, blood banks, and hospitals/medical centers.*
- *Blood products including plasma, platelets and blood cells are considered in 8 blood groups.*
- *Blood products have a certain lifespan.*
- *Expired blood products are considered in this blood supply chain.*
- *The cost of maintaining the cost of expired blood products is considered in this blood supply chain.*
- *Blood products are sent from specific blood banks in each region and blood banks in other provinces to hospitals and medical centers.*
- *Blood banks can store blood products.*
- *The cost of maintaining the inventory of blood products in blood banks is considered.*
- *The maximum storage capacity of blood products in blood banks is limited.*
- *Maximum blood supply capacity in blood donation centers is limited. The maximum amount of blood donated is based on the population of each region and the ratio of blood groups to the total population.*
- *Blood donation with a specific capacity is made by staff and donation stations next to the collection center.*
- *Maximum blood collection capacity in fixed and mobile blood collection bases is limited.*
- *Supply chain network planning horizon is defined as multi-period.*
- *In this chain, transportation costs between different levels are considered.*
- *Inventory maintenance costs are considered at the level of blood banks.*
- *The capacity level is considered in suppliers, manufacturers, primary distribution centers, collection bases, repair centers, secondary distribution centers and limited recycling centers.*
- *Fixed construction costs for mobile blood collection bases.*
- *Fixed costs for equipping fixed blood collection bases.*
- *Only one mobile or fixed collection base can be located in each area.*
- *Travel time between chain levels from collection bases to blood banks, from regional blood banks to hospitals and treatment centers, and from regional blood banks in other provinces to hospitals and treatment centers is considered.*
- *There are specific routes for sending blood products from collection bases to blood banks.*
- *The total probability of occurrence of different scenarios is considered.*
- *In each of the disruption scenarios, access to pathways is determined, which allows the model to select only the accessible pathways for blood transfusion.*
- *The location of each of the mobile collection facility bases can be changed in any period.*
- *Demand is considered in a scenario-oriented situation with uncertainty and random approach.*
- *If a disturbance occurs in a collection base, the undisturbed capacity of that center may be restored. Otherwise, the capacity of that collection base will be zero.*

3.1 | Sets, Parameters and Variables

The sets, parameters, decision variables, constraints and objectives used in the mathematical model are as follows:

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Set	
p	Set of different blood products ($p = 1,2, \dots, P$).
d	Set of blood donation locations ($d = 1,2, \dots, D$).
f	Set of fixed blood collection bases ($f = 1,2, \dots, F$).
m	The total number of representative sites for the facilities of mobile collection bases, which N is the total number of fixed and mobile collection bases $M = \{n+1, \dots, N\} \in W$.
w	Set of possible locations in fixed or mobile blood collection bases $w \in W = F \cup MW$.
a	Set of blood banks ($a = 1,2, \dots, A$).
h	Set of hospitals/medical centers ($h = 1,2, \dots, H$).
s	Set of crisis scenarios ($s = 1,2, \dots, S$).
t , e	Set of periods ($t = 1,2, \dots, T$), ($e = 1,2, \dots, E$).
r	Set of paths between nodes in the supply chain network ($r = 1,2, \dots, R$).
Parameters	
CM	Fixed cost of setting up a mobile blood collection center.
CF	The cost of equipping a fixed blood collection center is the same for all fixed centers.
TN	Total number of fixed blood collection locations and candidate locations for mobile collection base facilities. The number of locations of the fixed blood collection base is n. While the number of candidate locations in the facilities of $TN - n$ mobile collection base.
LT_p	Lifespan of blood product p.
CAP_a	Blood bank capacity a.
$CAPF_w$	Capacity of fixed blood collection base.
$CAPM_w$	Capacity of Mobile blood collection base.
BDE^s_{pht}	Demand of hospital h for blood product type p in period t under scenario s.
MAX^s_{pdt}	Maximum storage of blood product p at location d at period t under scenario s.
BBD^s_{at}	If blood bank a at period t under scenario s recovers the remaining capacity in case of disruption and continues to provide services, 1 otherwise 0.
FBD^s_{wt}	If the fixed blood collection base w is not disturbed at period t under scenario s, 1 otherwise 0.
RBD^s_{wart}	If the path r between the blood collection base w and the blood bank a is not disrupted under scenario s at period t, 1 otherwise 0.
PS^s	Probability of scenario s.
TT_{ht}	Travel time from blood banks in other provinces to hospital h at period t.
TTW_{war}	Travel time from blood collection base w to blood bank a using route r.
TTA_{ah}	Travel time from blood bank a to hospital h.
λ_p	Average lifespan of blood product p.
q	The time allotted for sending blood products in each period.
$UA^s{}_a$	Percentage of impaired capacity of blood bank a under scenario s.
TC	Cost per transport unit between chain facilities.
IC	Cost of each blood inventory maintenance unit.
IE_p	Cost of each blood product storage unit applied p.
Positive decision variables	
BV^s_{pat}	The amount Blood inventory level of product p in blood bank a at the end of period t under scenario s.
QW^s_{pwatr}	The amount of blood product that is delivered from the blood collection base w to the blood bank a using the path r at period t under scenario s.
$QA^s{}_{paht}$	The amount of blood product p delivered from the blood bank a to the hospital at period t under scenario s.
$QD^s{}_{pdwt}$	The amount of blood product p donated from donor d to the blood collection center w is transferred at period t under scenario s.
QH^s_{pht}	The amount of blood product p transferred from blood banks in other areas is transferred to hospital h at period t under scenario s.
QB^s_{pat}	The amount of obsolete blood product p in the blood bank a at period t under scenario s.
Binary decision variables	
OW_w	If the fixed blood collection base w is equipped 1 otherwise 0.
OM^s_{wt}	If the mobile blood collection base w is activated at period t under scenario s 1 otherwise 0.
OR^s_{watr}	If the blood collection base w is assigned to blood bank a using route r at period t under scenario s, 1 otherwise 0.
OP^s_{dwt}	If the blood donor in location d is assigned to the blood collection base w under scenario s at period t, 1 is otherwise 0.

3.2 | Equations

The objectives of this model are three objectives: minimization of cost, delivery time and delivery time of products for reliability in response to demand points.

$$\text{minimize F1} = \sum_{s,t,m\in w} PS^s * CM * OM^s_{wt} + \sum_{f\in w} CF * OW_w$$

$$+\left(TC * \left(\begin{aligned} &\sum_{p,w,a,t,r,s} PS^s * QW^s_{pwatr} + \sum_{p,a,h,t,s} PS^s * QA^s_{paht} \\ &+ \sum_{p,h,t,s} PS^s * QH^s_{pht} + \sum_{p,d,w,t,s} PS^s * QD^s_{pdwt} \end{aligned}\right)\right) \quad (3)$$

$$+\left(IC * \sum_{p,a,t,s} PS^s * BV^s_{pat}\right) + \left(\sum_{p,a,t,s} IE_p * PS^s * QB^s_{pat}\right).$$

The second objective function- Minimization is the sum of three terms, the first of which refers to the time of transport from blood collection centers to blood banks. The second term is the time of transfer from blood banks to hospitals, and the third term is the time of transfer from blood banks to hospitals in other provinces.

$$\begin{aligned}\text{minimize F2} = &\sum_{p,w,a,t,r,s} PS^s * QW^s_{pwatr} * TTW_{war} + \sum_{p,a,h,t,s} PS^s * QA^s_{paht} * TTA_{ah} \\ &+ \sum_{p,h,t,s} PS^s * QH^s_{pht} * TT_{ht}.\end{aligned} \quad (4)$$

Third Objective Function- Minimizes the delay in delivering blood packages according to the lifespan of blood products to hospitals. Alternatively, maximizes the response to the needs of hospitals and treatment centers by blood banks.

$$\text{minimize F3} = \sum_{p,a,h,t,s} PS^s * \left(1 - e^{-\lambda_p * q}\right) * \left(QA^s_{paht} + QH^s_{pht}\right). \quad (5)$$

Restrictions (4) and *(5)* limit the amount of blood donated from each urban area to not exceed the maximum amount of donor blood for each blood product.

$$QD^s_{pdwt} \leq MAX^s_{pdt} * OP^s_{dwt}. \quad \forall\ p,d,w,t,s \quad (6)$$

$$\sum_{w} QD^s_{pdwt} \leq MAX^s_{pdt}. \quad \forall\ p,d,t,s \quad (7)$$

Restriction (6) ensures that donors' blood levels do not exceed the capacity to collect blood at any fixed or mobile facility.

$$\sum_{d,p} QD^s_{pdwt} \leq CAPF_w * OW_w + CAPM_w * OM^s_{wt}. \quad \forall\ w,t,s \quad (8)$$

Restriction (7) ensures that a maximum of one fixed or mobile blood collection center is established at each location.

$$OW_w + OM^s_{wt} \leq 1. \quad \forall\ w,t,s \quad (9)$$

Restriction (8) ensures that blood donation centers are dedicated only to reopened mobile units or fixed blood collection centers that have not been disrupted.

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$$OP^{s}_{dwt} \leq FBD^{s}_{wt} * OW_{w} + OM^{s}_{wt}. \qquad \forall d, w,t,s \qquad (10)$$

Restriction (9) ensures that the amount sent from blood collection centers to blood banks is less than the amount of blood sent from blood donation centers to blood collection centers.

$$\sum_{a,r} QW^{s}_{pwatr} \leq \sum_{d} QD^{s}_{pdwt}. \qquad \forall p, w,t,s \qquad (11)$$

Restriction 10 guarantees that the amount of blood sent from blood collection centers to blood banks is less than the remaining capacity of the disorder in each blood bank, if the capacity of those centers is not entirely disrupted.

$$\sum_{w,r,p} QW^{s}_{pwatr} \leq (1 - UA^{s}{}_{a}) * CAP_{a} * BBD^{s}_{at}. \qquad \forall a,t,s \qquad (12)$$

Restriction (11) ensures that fixed blood collection centers are reserved for blood banks only if the routes and facilities between these centers are not disrupted and the capacity of active blood banks is not wholly disrupted after disruption.

$$OR^{s}_{watr} \leq FBD^{s}_{wt} * BBD^{s}_{at} * RBD^{s}_{wart} * OW_{w}. \qquad \forall\ w \in F,a,t,r,s \qquad (13)$$

Restriction (12) guarantees that if a mobile blood collection center is assigned to a specific blood bank, then the path between the mobile blood collection center to the blood bank is not disrupted and the blood bank is not entirely disrupted after the disruption.

$$OR^{s}_{watr} \leq OM^{s}_{wt} * BBD^{s}_{at} * RBD^{s}_{wart}. \qquad \forall\ w \in M,a,t,r,s \qquad (14)$$

Restriction (13), there is only one route between each blood collection center and the blood bank.

$$\sum_{r} OR^{s}_{watr} \leq 1. \qquad \forall\ w \in M,a,t,s \qquad (15)$$

Restrictions (16) to *(18)* ensure that blood products are not transferred from a fixed or mobile blood collection center to a blood bank unless a route is provided between them.

$$QD^{s}_{pdwt} \leq MAX^{s}_{pdt} * OP^{s}_{dwt}. \qquad \forall\ w \in F,a,t,s \qquad (16)$$

$$\sum_{p} QW^{s}_{pwatr} \leq CAPF_{w} * OR^{s}_{watr}. \qquad \forall\ w \in F,a,t,s \qquad (17)$$

Restriction (16) guarantees that the blood bank can only be allocated to the hospital if it is not completely disrupted, and that the amount sent from the blood bank to the hospital is less than the amount of capacity left after the disruption in each blood bank.

$$\sum_{p} QW^{s}_{pwatr} \leq CAPM_{w} * OR^{s}_{watr}. \qquad \forall\ w \in M,a,t,r,s \qquad (18)$$

$$\sum_{p,h} QA^{s}{}_{paht} \leq (1 - UA^{s}{}_{a}) * CAP_{a} * BBD^{s}_{ht}. \qquad \forall a,t,s \qquad (19)$$

Restriction (17) indicates the number of blood products delivered to each hospital from blood banks in other regions and provinces.

$$BDE^{s}_{pht} - \sum_{h} QA^{s}{}_{paht} = QH^{s}_{pht}. \qquad \forall\ p,h,t,s \qquad (20)$$

Restriction (18) indicates the balance of blood in the blood bank.

$$BV^s_{pa,t-1} + \sum_{w.r} QW^s_{pwatr} = BV^s_{pa,t} + \sum_{h} QA^s_{paht} + QB^s_{pat}. \qquad \forall\ t \geq 2, \forall\ p,a,s \tag{21}$$

Restriction (19) determines the number of units of obsolete blood products in each period.

$$QB^s_{pat} = \max\left\{0, BV^s_{pa,t-LT_p} - \sum_{h} \sum_{e=t-LT_p}^{t} QA^s_{pahe} - \sum_{e=t-LT_p}^{t} QB^s_{pae}\right\}. \tag{22}$$

$\forall\ t \geq 2, \forall\ p,a,s$

Restriction (20) indicates the number of mobile blood collection centers.

$$\sum_{w \in F} OM^s_{wt} \leq N - n. \qquad \forall\ t,s \tag{23}$$

Restriction (21) limits the level of blood storage according to the remaining capacity of each blood bank after the disorder.

$$\sum_{h} BV^s_{pat} \leq (1 - UA^s_a) * CAP_a. \qquad \forall\ a,t,s \tag{24}$$

Constraint (22) shows the positive and binary variables of the model.

$$BV^s_{pat}, QW^s_{pwatr} QA^s_{paht}, QD^s_{pdwt}, QH^s_{pht}, QB^s_{pat} \geq 0, \\ OW_w, OM^s_{wt}, OR^s_{watr}, OP^s_{dwt} \in \{0,1\}. \qquad \forall\ p,d,w,a,h,t,r,s \tag{25}$$

3.3 | Constraint of Linearization

Constraint (19) is a nonlinear "maximum" function, it must be linear to solve the model as a hybrid programming model. This constraint is replaced by *Constraint (23)* as follows:

$$QB^s_{pat} \geq BV^s_{pat} - \sum_{h} \sum_{e=t-LT_p}^{t} QA^s_{pahe} - \sum_{e=t-LT_p}^{t} QB^s_{pae}. \qquad \forall\ t \geq 2, \forall\ p,a,s \tag{26}$$

4 | Single-Objective Modeling

Although the Epsilon constraint method had an advantage over other methods, it had significant weaknesses such as the multiplicity of optimal solutions in the model objectives, the inefficiency of the obtained solutions, and the increase in the solution time multi-objective models. To solve the above cases, a lexicographic method model was proposed to calculate the efficiency table, and the generalized constraint epsilon method was developed according to *Eqs. (27)-(30)*. Mentioned approach has been used in the present study [29].

$$\text{Min}\left(f_1(x) + eps \times (s_2 + s_3)\right), \tag{27}$$

s. t.

$$f_2(x) + s_2 \leq e_2, \tag{28}$$

$$f_3(x) + s_3 \leq e_3, \tag{29}$$

$$x \in N, s_i \in R^+. \tag{30}$$

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It is worth noting, the value of eps is generally a minimal number in the range 10^{-3} to10^{-6}, for maximization objectives, the s_i coefficients should be negative and the *eps* coefficient should be positive.

5 | Robust Optimization

Considering that the demand of hospitals and medical centers fluctuates in the short term or other words, is accompanied by uncertainty, a robust scenario-based formulation has been used to robustness the model. Which has three parts: expected cost and feasibility robustness for changing scenarios and optimality robustness for unmet demand. Also, for each scenario, a constraint has been added to minimize the instability caused by the scenarios [21].

$$\text{Min} \sum_{s\in S} P_s \xi_s + \lambda \sum_{s\in S} P_s \left[\left(\xi_S - \sum_{s'\in S} P_{s'} \xi_{s'}\right) + 2\theta_s\right] + \omega \sum_{s\in S} P_s \delta_{s'} \quad (31)$$

s. t.

$$Ax = b, \quad (32)$$

$$B_s x + C_s y_s + \delta_s = e_s, \quad (33)$$

$$\xi_s - \sum_{s'\in S} P_{s'} \xi_{s'} + \theta_s \geq 0, \quad (34)$$

$$x, y_s, \theta_s, \delta_s \geq 0, \forall s \in \Omega. \quad (35)$$

The expression $\{\delta_1, \delta_2, \dots, \delta_s\}$ in the objective function is a penalty function to justify the model, which in some scenarios is considered for fines, violations and violations of control restrictions. The balance and exchange between the stability of the answer and the model with the help of ω weight can be modeled by a multi-criteria decision-making process. The balance between the feasibility robustness and optimality robustness of the model is done by the control coefficient λ. θ_s is the linearization coefficient of the objective function in each scenario [30].

6 | Lagrangian Relaxation Algorithm

The Lagrangian relaxation algorithm was first developed by Held and Karp to solve the Travelling salesman problem. One of the methods that solve a constrained and complex optimization problem with a simpler problem [31] and [32]. The main idea of the Lagrangian relaxation method is to release complex constraints and multiply them by a coefficient called the Lagrangian coefficients and add them to the objective function of the problem. Removing complex and hard constraints and adding them to the objective function of the problem as a penalty considering Lagrangian coefficients is the main idea of this approach to reduce the model solution time. Lagrangian coefficients are fines that are added to a model that has not been violated and met when solving a particular constraint [33]. Consider following the compact model:

$$\text{Min } c^T, \quad (36)$$

s. t. (37)

$$Ax \geq b, \quad (38)$$

$$x \epsilon X. \quad (39)$$

The above model is transformed by applying the Lagrangian relaxation method as follows, μ^T is the Lagrangian coefficient in the second part of the objective function.

$$\text{Min } c^T x + \mu^T (Ax - b), \quad (40)$$

s. t. (41)

$$x \epsilon X. \quad (42)$$

In most cases, the answer obtained after relaxation is not feasible for the primary mathematical model. This infeasible answer is considered in models with a lower bound minimization objective function and models with an upper bound maximization function for the primary model. The Lagrangian relaxation approach, based on the heuristic process, make feasible the initial result obtained. Given that the optimal solution of the primary mathematical model is obtained between these upper and lower bounds, the Lagrangian relaxation algorithm seeks to reduce the limits and thus achieve an answer close to the optimal solution. An essential part of the Lagrange algorithm is the correct choice of complex constraints for release, which will have a direct effect on the performance of this algorithm. In the present study, the fifth constraint has been released. Thus, the relaxed blood supply chain model is as follows:

$$\text{Min } Z_2 + \mu_1 \times \left(\sum_{W} QD^{s}_{pdwt} - MAX^{s}_{pdt} \right), \tag{43}$$

$$\text{s. t.} \tag{44}$$

$$LB_1 \leq Z_1 \leq LB_1, \tag{45}$$

$$LB_3 \leq Z_3 \leq LB_3. \tag{46}$$

Also other *Constraints (4)* to *(23)* except *Constraint (5)* are added to the model. In *Relation (42)*, μ_1 is the Lagrangian coefficient and non-negative. At the beginning of this algorithm, the Lagrangian coefficient value is considered a constant value. Therefore, this value must be updated each time the algorithm is replicated. Several approaches have been proposed to update the value of these coefficients, the sub-gradient method being the most commonly used in this research [23]. The Lagrangian coefficient, based on the sub-gradient method, in the $C + 1$ iteration of the algorithm can be calculated as follows:

$$\mu_1^{c+1} = \max\left[0, \left\{\mu_1^{c} + \pi_1^{c} \dots \dots . \right\}\right]. \tag{47}$$

In the above relation, μ_1^{c+1} is the step size of the algorithm and can be calculated as follows:

$$\pi_1^{c} = \frac{v^{c}.\,(UB^{c} - BUB)}{\left(\sum_{W} QD^{s}_{pdwt} - MAX^{s}_{pdt}\right)^{2}}. \tag{48}$$

In the above relation, *BUB* is calculated to be the lowest limit up to the cth iteration, the upper bound of the UB problem is in the cth iteration, and the coefficient v^c is usually a value between 0 and 2.

7 | Problem-Solving Process

In GAMS software, problem-solving with small and medium sizes is done efficiently and at the right time, but the speed of problem-solving will decrease as they increase in size. However, solving large-size software is time-consuming and challenging. In general, large-scale algorithms such as Lagrange are used to reduce problem-solving time. The Lagrange algorithm reduces CPU solution time by modifying the structure of problems. To evaluate the Lagrangian algorithm, the proposed model is solved in small, medium, and large sizes and compared with a reference value of the exact solution for GAMS software, intended for small and medium sizes. The choice of complex constraints is vital in the Lagrangian release solution approach. In most cases, after relaxing the answer obtained for the original mathematical model, it is not feasible. This infeasible solution is considered a lower bound in models with a minimization objective function and an upper bound in models with a maximization objective function. In other words, each solution to the relaxed problem provides a boundary for the solution to the main problem. Due to the removal of some constraints and the enlargement of the feasible area, solving the relaxed sub problem will be easier than solving the main problem. In this regard, the heuristic algorithm is proposed for generating a feasible solution (upper bound) from a lower bound solution. As a result, by maximizing the minimum obtained from the relaxed problem, a better lower bound is produced for the main problem, and in an iterative process, the resulting answer can be directed to the solution to the main problem. Hence, the sub gradient method is used to solve the Lagrangian double problem. The problem of maximizing the Lagrangian function with dual variables (Lagrangian coefficients) is called the Lagrangian dual problem, where the best boundary is obtained from the optimal value of the Lagrangian double and the lower bound is determined to the optimal value of the problem. The results of model solving are presented in *Tables 1* and *2*.

To select a complex constraint, all constraints are first released separately, and then the model is executed to determine the CPU time. Then, the released constraints that have a significant effect on CPU time in solving the model are determined. Decision-makers choose one or more relaxed constraints that reduce the resolution time more than the other constraints. Fifteen numerical examples in small, medium, and large sizes have been used to evaluate and test the exact Epsilon method of generalized constraint and Lagrangian release solution numerical value of target functions and CPU time. In this section, 15 numerical problems designed in different sizes are solved and the results are examined. These 15 issues are designed with the different number of donors, fixed collection centers, mobile collection centers, blood bank, hospital and treatment centers, and the periods in 4 scenarios and three blood products.

These 15 issues are designed in GAMS 2.3 software and run on a GHs 3.6 computer with 8 GB of RAM. A time limit of 3600 seconds is provided for solving in GAMS software. Due to this time constraint, GAMS in the generalized constraint method without the Lagrangian release solution approach can solve ten problems of small and medium-size, but for problems 11 to 15 could not find the optimal solution. The results of solving the problems are shown in *Tables 1* and *2*. Objective function 2 of the model Due to its preference for decision-makers, the objective function of the generalized Epsilon constraint method is placed and objectives 1 and 3 are added to the constraints of the model. The cut of the lower bound of Objectives 1 and 3 have been used for single-objective construction and solution in 15 examples. The related parameters of algorithms such as Lagrange in a maximum of 40 iterations are as follows.

v^c	The coefficient is usually between 0 and 2.
π^c	The size of the algorithm steps.
u_1	Lagrange coefficient.
ε	Reaching the limit of boundary differences to a certain level.
γ	Reaching the value of v ^ c to the specified γ.

The initial values of the parameters are $\pi^0 = 2$, $v^0 = 1.5$, $u_1 = 1.5$, $\varepsilon = 0.1$. If at the assumed value v ^ 0 after ten iterations of the Lagrangian algorithm, the lower limit does not improve, this value is halved and this process continues until the condition γ reaches 0.05. The exact results obtained from Gomez software are compared with the results of the Lagrangian Relaxation algorithm. For comparison, 15 different numerical examples in small, medium, and large sizes are shown in *Table 1* and *2*. CPU time and the difference between the values of the Gomez solution and the Lagrange algorithm are considered for comparison. As shown in *Table 1*, the average percentage difference between the GAMS method and the Lagrange algorithm based on $\frac{f_{LR}-f_{GAMS}}{f_{GAMS}} \times 100\%$ in small sizes is 0.098 and in medium, sizes is 0.478. The highest percentage difference between the GAMS method and the Lagrange algorithm is 0.17 in small sizes and 1.08 in medium sizes. In addition, the average solving time of the GAMS method and Lagrange algorithm is 50.912 and 13.85 in small sizes and 1478.40 and 157.22 in medium sizes. A small percentage difference between the GAMS method and Lagrange algorithm indicates the effectiveness of the Lagrangian relaxation algorithm. Examination of the results shows that the Lagrangian algorithm works better than the exact method in terms of CPU time and amount of solution. The performance of the epsilon method is compared with that of the Lagrange algorithm in solving large problems, five numerical examples have been implemented for this task. The difference between the upper and lower bounds of the algorithm is used as a measure to evaluate the performance of the Lagrange algorithm. As shown in *Table 2*, the average difference between the upper and lower bounds of the algorithm basis on $\frac{UB-LB}{LB} \times 100\%$ is 1.67. Although the exact method can achieve the optimal solution in the predetermined time up to 3600, with the help of the Lagrangian relaxation algorithm in a reasonable time with an average of 767.326 seconds, the optimal value is obtained.

Table 1. Lagrange objective function values in small and medium-size problems.

Run Time Value Lagrange	GAMS	Objective Function Values Difference Percentage	Lagrange	GAMS	Issue NO	Problem Size
4.514	8.32	0	3769	3769	1	Small-size
8.97	23.48	0.14	4850	4857	2	
11.46	37.99	0.04	4531	4533	3	
21.04	95.38	0.17	5148	5157	4	
23.27	89.39	0.14	5373	5381	5	
13.85	50.912	0.09	Average			
51.67	416.38	0.13	5781	5789	6	Medium-size
81.04	923.47	0.49	6180	6211	7	
69.43	724.91	0.42	6743	6772	8	
173.92	1854.27	0.27	7274	7294	9	
410.05	3472.98	1.08	7098	7176	10	
157.22	1478.40	0.478	Average			

Table 2. Lagrange objective function values in Large-size problems.

Run Time Value Lagrange	GAMS	The Value of The Objective Function Percentage Difference	Upper Bound	Lower Bound	Issue Number	Problem Size
541.31	4978.14	2.71	7796	7584	11	Large-size
754.02	....	2.58	8639	8416	12	
696.35	....	1.49	9083	8947	13	
968.54	....	0.62	9945	9883	14	
876.41	....	0.95	9703	9610	15	
767.326	....	1.67	Average			

Tables 1 and *2* show that the Lagrangian relaxation algorithm has the appropriate answer for the 15 designed problems. *Fig. 1* shows the upper and lower bound convergence of the Lagrange relaxation algorithm for the designed *Problem 11* with constraint *Release 4*. If the number of release restrictions increases to 3 with the release of *Restrictions 6* and *10*. According to the results, the execution time will be reduced to 458.67 and the percentage difference to 1.79. These results show the appropriate velocity of the Lagrangian relaxation algorithm in the convergence of the answers. *Fig. 2* shows the upper and lower bound convergence of the Lagrangian relaxation algorithm for the designed *Problem 11* with the release of three constraints. The horizontal axis represents the iteration of the solution and the vertical axis the objective function.

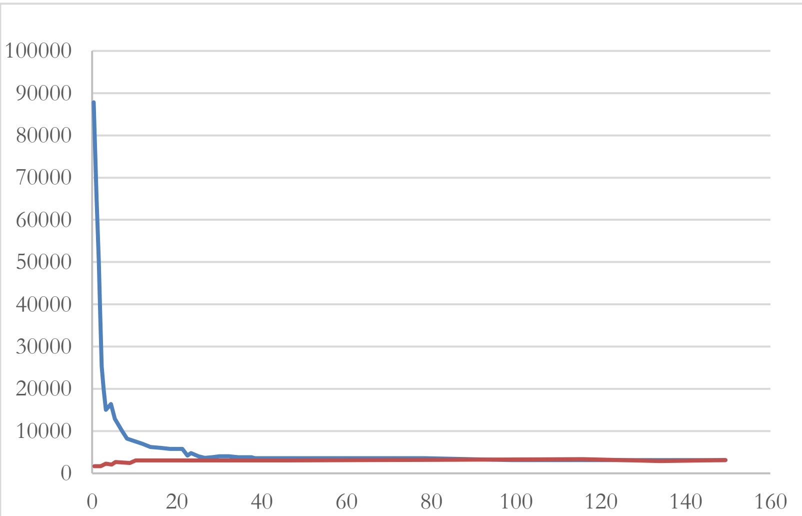

Fig. 1. Upper and lower bound convergence of the Lagrangian relaxation algorithm with the release of one constraint.

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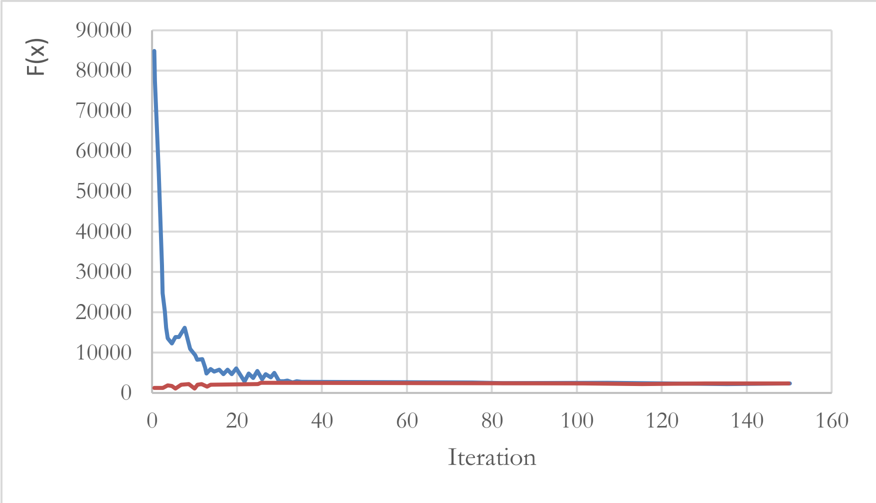

Fig. 2. Upper and lower bound convergence of the Lagrange release algorithm with the release of three constraints.

The gap between this lower bound and the cost of the best solution obtained via the heuristic is an upper bound to errors of the heuristic solutions. According to the performed iterations and error analysis in *Fig. 3*, at the upper bounds and taking u = 1.5, shows boundary errors between 1% and 5% for the release of the first constraint. Also the mean error obtained is 0.17%. The results of the upper and lower bounds analysis demonstrate that the closer the upper and lower boundaries are to each other, the less error is generated. *Fig. 4* shows that at upper bounds the errors is between 5% and 9% in the period u = 2 and the mean error is 1.08%. u = 2 has increased the objective function compared to the period u = 1. In *Fig. 5*, the upper bounds of error are between 6 and 9% with the release of the third constraint, and the mean error is 1.67. Therefore, at u = 3, it shows the worst solution relative to the first and second constraints. Hence, as the number of points increases, the average error percentage decreases.

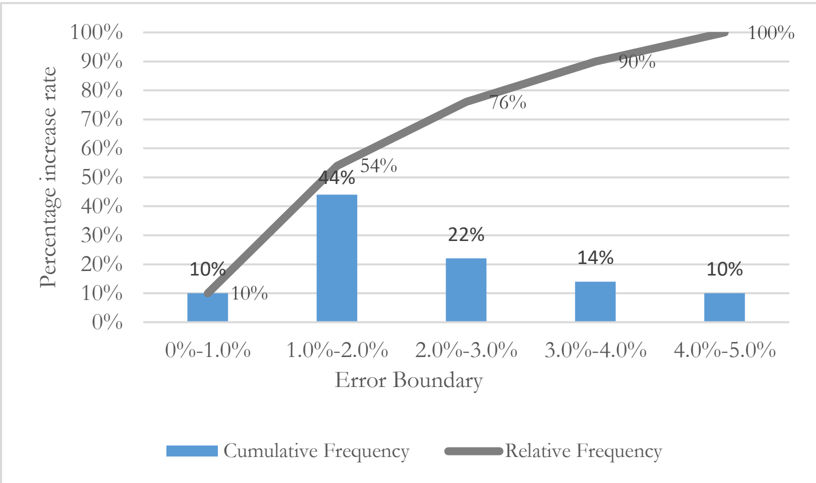

Fig. 3. Reviewed upper bounds of solution errors for the relaxation of the first constraint (u=1).

It is worth noting that according to *Tables 1* and *2*, first the problem was solved with the GAMS solver and then using the Lagrangian relaxation algorithm. The values of the objective function, the run time, and the values of the upper and lower bounds are presented. The problem dimensions and the solving time without using the Lagrangian relaxation method have been greatly increased; while using the Lagrangian relaxation algorithm, the run time is very short and shows the efficiency of the algorithm in solving the model. On the other hand, the upper and lower boundary convergence after the release of the first constraint and all the constraints are presented in *Figs. 1* and *2*, which show the appropriate speed of the convergence solution algorithm toward the optimal solution of the problem.

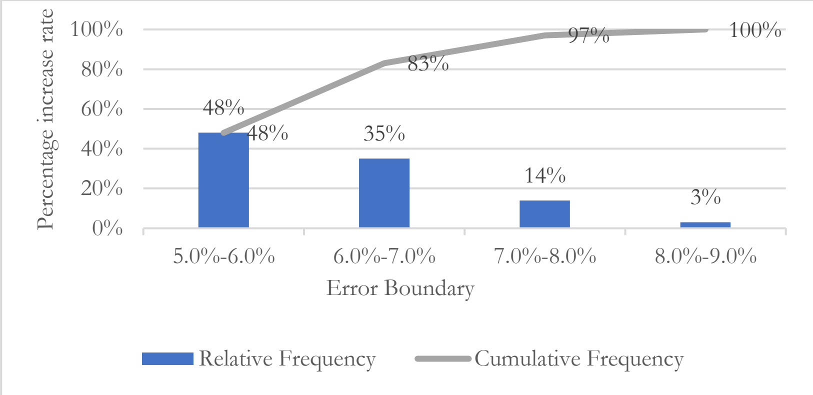

Fig. 4. Reviewed upper bounds of solution errors for the relaxation of the second constraint (u=2).

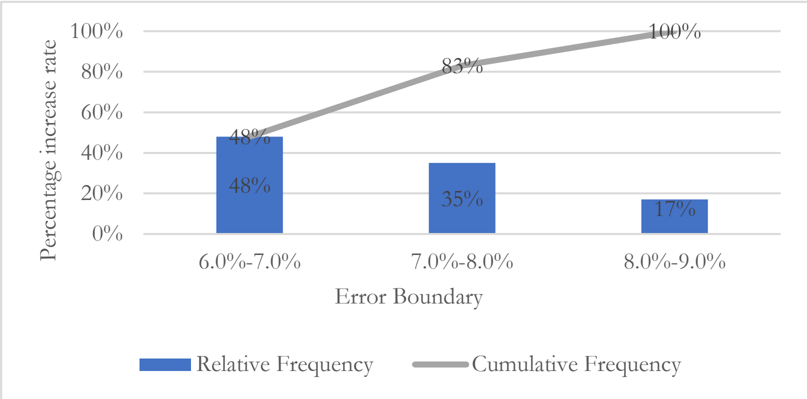

Fig. 5. Reviewed upper bounds of solution errors for the relaxation of the third constraint (u=3).

Based on the enumerated matters, GAMS cannot solve large-size problems. The results of the proposed heuristic method in large-size samples that are the upper bound of the Lagrangian algorithm are compared with the lower bound of the above method. And the extent of the gap between them is considered a criterion for analysis. The performance of the proposed Lagrangian relaxation algorithm shows the mean percentage of gaps between upper and lower bounds results are less than 2%. Since the optimal results of the problems are between the lower and upper boundaries, the lower the gap percentage, the closer the result is to the optimal solution.

8 | Conclusion

The blood supply chain is one of the most critical areas in health. In this study, the blood supply chain consists of blood donors, fixed and mobile collection centers, blood banks and hospitals, and medical centers. A mathematical model with a robust optimization approach in case of random uncertainty in 2 steps to reduce the effects of the crisis, to minimize the expected costs of the system, minimize the delivery time of purified blood to hospitals and treatment centers, and maximize response to hospitals with Possible disturbances in blood establishments and transport routes have been developed accordingly. The capacity of blood collection centers and banks is limited according to real-world conditions. Due to the immediate demand in times of crisis and blood corruption, the products are immediately sent to the demand points or stored in the blood bank after performing the necessary tests. Due to the complexity of the constraints, the mathematical model is solved by the Lagrangian relaxation algorithm. Based on the results, large-scale problems can be solved promptly using the Lagrangian relaxation algorithm. For future research, it is suggested to prioritize hospitals along with the possibility of cross-transfer of products.

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