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Integrated planning for blood platelet production: a robust optimization approach

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Abstract

Perishability of blood products as well as uncertainty in their demands complicates the management of blood supply for blood centers. This paper addresses a mixed-integer linear programming model for blood platelets production planning while integrating the processes of blood collection as well as production/testing, inventory control and distribution. Whole blood-derived production methods for blood platelets (i.e., Buffy Coat and platelet-rich plasma methods) are particularly focused in our research. The problem is tackled with the aim of minimizing the supply chain total cost. To capture inherent uncertainty of input data, a robust programming approach is devised. A set of numerical experiments is carried out to evaluate the performance of the proposed model and the solution technique. Thereto, in this paper we employ two criteria. These criteria are the mean and standard deviation of constraint violations under a number of random realizations to measure the quality of solutions achieved by both the proposed deterministic and robust models. Several sensitivity analyses are accomplished to provide valuable managerial insights. The results show that the robust approach dominates the deterministic one.

Keywords: Blood supply chains, healthcare, platelet-rich plasma, Buffy Coat, robust optimization.

1- Introduction

The world has witnessed a remarkable increase in health spending over the last fifty years. Health systems, especially in developing countries, are struggling with rapid cost increase, which seriously prevents them from getting improved (Riahi, Hosseini-Motlagh and Teimourpour, 2013). To be more specific, according to the World Bank (2015), healthcare costs comprised about 18% of GDP in the US in 2010, and it will grow over 20% by the year 2021 (Kaiser Health News, 2015).However, in Iran, the spending on healthcare was estimated around 6% of GDP up to 2010 while it is expected to increase more in the years ahead.

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Among all, increasing growth of aging population besides the developments in healthcare technologies can exacerbate the costs of healthcare service (Brandeau et al., 2004).

Thus, the necessity of having an efficient system for healthcare service supply and delivery, which can be practically influenced by social network analysis (Rastegar-Panah et al., 2013), arises since public resources cannot bear the pressure of healthcare costs in the future.

A considerable portion of healthcare costs belongs to healthcare supply chains. Baring this in mind, any improvement in the healthcare supply chain efficiency can result in increased cost savings as well as customer's satisfaction. This paper seeks to optimize the blood supply chain (BSC) as a critical part of a healthcare supply chain.

BSCs differ substantially from other perishable supply chains. One of the most significant differences between them lays on both supply and demand sides. In other words, the (primary) suppliers of BSCs are humans, being the only and scarce source of blood donation, and the final customers are humans as well. Blood donation rate is varied from one country to another. In the US for example, blood donation rate does not exceed 5% of the population. Although this rate will not climb to more than 6% in the UK, it is even worse in low-income countries. However, unbelievable or not, some developed countries like Japan demand the import of blood (Drackley et al., 2012; Beliën and Forcé, 2012). Indeed, BSC is a human-to-human supply chain and any deficiency or disruption in blood supply may even lead to humans' death. Additionally, the most noticeable of all, is that blood products preparation and storage have major differences, which are discussed in continue, comparing to other perishable supply chains.

Blood is a life-saving product for which there is an endless demand with almost no substitution. Red blood cells (RBC), platelets (PLT) and plasma (PLS) can be mentioned as the main products fractionated from whole blood, and each product is applicable for a special need. The most required blood component (i.e., RBC) is widely used in surgeries, etc. As the vessels are damaged, PLTs, which are normally counted to 270,000 per cubic microliter on average, are the components in charge of ending bleeding through the function of blood coagulation. In emergency operations, PLS, by which nearly 55% of total blood volume in human's body is made, plays a critical role (Schreiber et al., 2006).

Each blood product has certain shelf life under a special storage condition. Blood PLT, which is known as the most perishable component can live for maximum 7 days, but it will keep its storage quality up to 15 days by using additive solutions if it is fractionated by Buffy Coat production method (Vassallo and Murphy, 2006). RBC will not be outdated before 42 days of production date if it is stored at 1-6 ℃ and lastly, PLS is known as almost non-perishable blood component since it can remain for about one year.

Thus, blood supply chain management (BSCM) is not a straightforward process since it is incurred complexity due to the special features of blood products including their perishability, uncertain and irregular pattern of blood supply (donation), and demand and inventory shortage. Therefore, these conditions must be taken into account while planning for BSCs.

A typical BSC (see Fig.1) consists of four main echelons; collection, production/screening, inventory control and distribution.

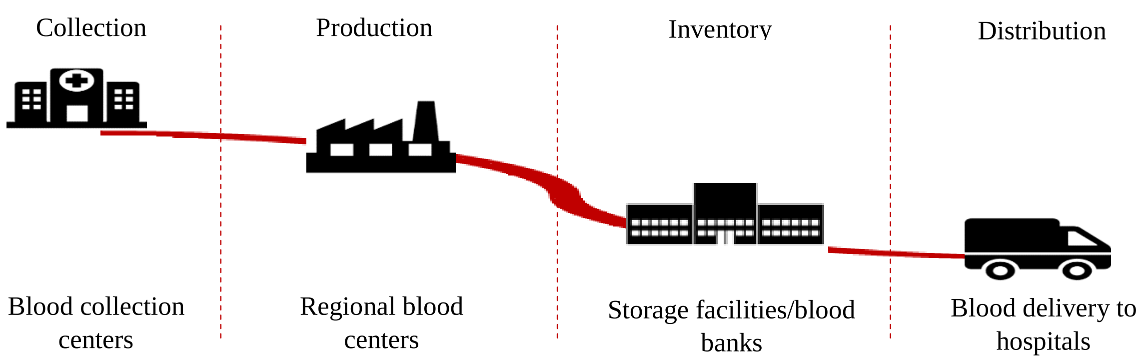

Fig.1. A typical blood supply chain

Firstly, donors refer to blood collection centers and blood units are drawn after the donors are checked up. Afterwards, the blood units are transported to regional blood centers within a certain length of time to be screened and decomposed into products. Each product can possibly be fractionated via different processes. PLTs, for example, are drawn in two main types; apheresis-derived platelet concentrates (AP-PCs) and whole blood-derived PLTs (Vassallo and Murphy, 2006). The latter case can be yielded by two different methods; Platelet-Rich Plasma (PRP) production method and Buffy Coat (BC) production method (Levin et al., 2008), both of which have their own features in terms of cost, function, etc. and the PLTs produced by each method is affected by these features. AP-PC is prepared by passing donor's blood through the apheresis devise (automatic equipment), by which only blood platelets are separated and the rest is returned to the donor's body. Although the process of AP-PCs benefits from less wastage, inventory and polling, easier cross-matching and less possibility of transferring infection, it is more costly and more time consuming in comparison to whole blood-derived PLTs since the former requires special equipment, specialized staff, etc. Even though in-vitro properties for all three types of PCs (i.e., BC-PCs, PRP-PCs and AP-PCs) are almost similar by day 5 or day 7 of storage, investigating the extant literature reveals that different platelet preparation methods end up with different storage characteristics (Vassallo and Murphy, 2006), which will be discussed in Section 2.1.Blood products are then stored in storage facilities and eventually, they are distributed to demand zones to be transfused into patients.

Planning for BSCs requires to make several strategic decisions (e.g. facility location-allocation, determining the production mechanism) along with a set of tactical and operational decisions accounting for inventory management and blood distribution. Accordingly the main inspiration of this research is improving BSCs while regarding their special characteristics besides the inevitable uncertainty in input data by means of efficient planning.

Uncertainty in blood demand, supply or any other parameters is generally derived from two sources: randomness and fuzziness. Randomness, which is caused by random nature of input data for an event which happens regularly and is repeated several times during the planning horizon, is handled by applying stochastic programming approach if the distribution function of the random data is accessible. Robust programming approach is also applicable when the distribution function of random parameter is not available. Fuzziness lends itself to events not repeated over the planning horizon and of which enough historical data is not on hand. Fuzzy parameters are usually estimated based on the professional opinions or subjective knowledge of the field experts (Tofighi, Torabi & Mansouri, 2016).

In this paper, we employ an efficient robust programming approach to deal with the random uncertainty in the demand data. More details about the adopted robust programming approach have been provided in Section 3.1. Now, we first have a brief review of the related papers to blood production planning. Afterwards, the works on integrated planning for BSCs are investigated.

1-1- Blood production planning

Deuermeyer & Pierskalla (1978) addressed an optimization problem conceptualized as a dynamic programming model for a by-product blood production system. Their model aimed to minimize inventory costs along with production costs corresponding to production processes of RBC and PLT over a multi-period horizon. However, their model does not account for donors as the system suppliers. A production and inventory problem for a Dutch blood bank was put forward by Haijema et al. (2007) with the aim of minimizing costs, shortages and outdates. Demands and production are both periodic in their work. Two types of demands are taken into account; one for young PLTs and another for PLTs of any age and order-up-to policies are regarded to satisfy them. Notably, they could reach near optimal solutions by hybridizing Markov dynamic programming (MDP) with simulation approach. In another effort, Haijema et al. (2009) presented an optimization problem for PLT production with breaks in special periods (e.g. Christmas and Easter). Arrivals of donors are tainted with uncertainty in their paper. They provided a new approach in the form of combining simulation and stochastic dynamic programming (SDP) to present theoretical support as well as nearly optimal and practical order-up-to policies. Their research succeeded in decreasing PLT shortages and spill considerably. Van Dijk et al. (2009) considered a mathematical formulation for PLT production and inventory management under supply uncertainty. A five-step combined method based on simulation and SDP was devised to solve the problem. They utilized real data to evaluate the performance of their research. Their work resulted in a nearly optimal policy of PLT production by which they came up with a main reduction in the level of outdating with negligible shortage. A mixed-integer non-linear programming (MINLP) model was strived by Ghandforoush and Sen (2010) to minimize platelets production costs and schedule regional blood centers. Applying a two-step conversion process, their model was then converted to a linear binary problem to assure optimality since the initial formulation carried a non-convex objective function with no convergence to optimal solutions.

1-2- Integrated planning for blood supply chains

Research on perishable supply chain management particularly BSCM was commenced in 1960. Later on, Nagurney et al. (2012) introduced a bi-objective linear programming (LP) model for localization of blood bank systems. The location of collection facilities and laboratories besides distribution centers and hospitals were to be determined through the model in a way that the optimal allocation, supply risks and waste cost were obtained. Minimizing total costs including the operating cost, route waste cost, penalty and unsatisfied demands costs besides total risks of each route are considered as the objectives. An integer non-linear programming model (INLP) formulation along with new simulation optimization was outlined by Duan and Liao (2014) for modelling inventory management of blood supply chain with ABO blood group compatibility with respect to their shelf lives. The model looked for minimizing the expected outdating under a predetermined maximum shortage level. A dynamic programming (DP) model was utilized by Abdulwahab and Wahab (2014) for blood platelets inventory problem. In their model, platelets supply and demand amounts are assumed to be stochastic. They evaluated the model by regarding four measures of effectiveness including platelets shortage and outdating as well as inventory level and reward gained in the concerned stochastic model. Jokar and Hosseini-Motlagh (2015) developed an MILP model for blood supply chain in emergency situations to reduce the total cost of considered network including blood shortage and wastage costs. The optimal number as well as service areas of blood facilities are determined under several disaster scenarios while the capacity of mobile blood facilities is assumed as a variable. Their findings imply that the optimal number of both permanent and mobile facilities is remarkably influenced by changes in the capacity of mobile blood facilities. A bi-objective mixed-integer non-linear programming (MINLP) model was put forward by Arvan et al. (2015) for the blood supply chain network design considering laboratories, blood bank centers, hospitals and donation zones. Minimizing operating costs and transportation costs as well as blood products expiration were considered as the objectives. They applied ε-constraint approach to solve the proposed model in which all parameters are regarded to be deterministic. A stochastic MINLP model was presented by Gunpinar & Centeno (2015) with the sole objective seeking to minimize costs including blood products wastage and shortage costs. C/T ratio and release period of cross match along with two types of patients (i.e., the ones who demand for fresh blood and the rest with the need of blood of any age) are taken into consideration in their study. To handle demand uncertainty, a stochastic programming approach is utilized. Fahimnia et al. (2015) suggested a bi-objective two-stage stochastic programming (TSSP) model while regarding a set of disaster scenarios. Total cost of the concerned network is minimized through the first objective function. Determining the optimal way of blood distribution to hospitals by minimizing the average delivery time from local and regional blood centers to demand points in disasters was also taken into account as another objective. They applied the ε-constraint and Lagrangian relaxation methods to solve the proposed bi-objective model. An MINLP model for blood collection management was proposed by Zahiri et al. (2015). They employed a robust possibilistic approach to handle the data uncertainty, and applied a case study of Babol city. The location of mobile blood facilities as well as permanent blood centers was to be determined in the strategic level, and donors' allocation to blood facilities besides the quantity of blood, transported from blood facilities to demand zones in each period, was then decided in the tactical level.

In Table 1, the papers are categorized while mainly considering integrated models and focusing on their special characteristics including planning horizon, Type of blood product, modeling approach, etc.

To the best of our knowledge, research on designing blood supply chain particularly accounting for blood platelet production methods in the context of integrated planning is non-existent. To fill this gap, this paper puts forward an integrated approach toward blood supply chain planning while concentrating on blood platelet production methods. To this aim, the following contributions differentiate our work from other existing papers in the literature of BSCs.

1) Integrated planning for blood PLTs production under uncertainty

2) Jointly consideration of different production methods while accounting for the respective product quantity

3) Regarding blood PLTs life time after fractionation through the production methods

4) Applying robust programming (RP) approach to cope with the data uncertainty

The rest of the paper is organized on these trials: The problem description and mathematical formulation of the proposed model are brought together in Section 2. Section 3 is dedicated to define the solution technique. A number of numerical examples along with several sensitivity analyses are performed in Section 4. Lastly, Section 5 provides concluding remarks and possible future research.

Table 1. A taxonomic structure of the studied papers

Authors	planning horizon			Type of blood product				Modeling approach									Type of uncertainty		Solution method		Time period	
	Strategic	Tactical	Operational	Whole blood	Red blood cell	Platelet	Plasma	MILP	D P	MINLP	LP	INLP	SDP	Simulation	TSSP	Deterministic	Stochastic/ Robust	Fuzzy	Exact	(Meta) heuristic	Single-period	Multi-period
Haijema et al. (2007)			●			●			●					●			●		●		●	
Van Dijk et al. (2009)		●				●							●	●			●		●		●	
Haijema et al. (2009)			●			●							●	●			●			●		
Ghandforoush and Sen (2010)			●			●				●						●			●		●	
Nagurney et al. (2012)	●				●	●					●						●			●	●	
Duan and Liao (2014)			●	●								●					●			●		●
Abdulwahab and Wahab (2014)			●			●							●				●			●		●
Jokar and Hosseini-Motlagh (2015)	●	●		●				●									●		●		●	
Arvan et al. (2015)	●			●	●	●	●	●								●			●		●	
Gunpinar & Centeno (2015)			●		●	●		●									●		●			●
Fahimnia et al. (2015)	●			●											●		●		●			●
Zahiri et al. (2015)	●	●		●						●								●	●			●
This article	●	●	●	●		●		●									●		●			●

2- Problem description

In this research, we address a blood supply chain network which is home to mobile blood facilities and local blood centers as collection sites, regional blood centers which are responsible for testing whole blood units and preparing blood platelets, and hospitals as demand points. Blood donation can take place in both mobile and local collection sites. The whole blood units are collected at the end of each period and transported from mobile blood facilities to local blood centers and from local blood centers to regional blood centers. After being tested to assure their health (i.e., no infectious disease, etc.) blood units are broken down into several products such as PLT, the most significant one considered in this research, by using the production methods of whole blood-derived PLTs (i.e., PRP and BC production methods). PLT units are then stored in the regional centers blood banks under specific conditions. Lastly, the units will be distributed to hospitals based on their demands. The model is presented with the aim of minimizing total cost of the network such as opening cost of local collection facilities (i.e., local blood centers), repositioning cost of mobile blood facilities, blood transportation cost from mobile sites to local ones and from local sites to regional centers, blood PLTs production cost, PLTs outdating cost as well as inventory holding cost and transportation cost from regional blood centers to hospitals. Noteworthy, the candidate locations for both mobile blood facilities and local blood centers are assumed to be given. Each group of donors represents a given blood supplier's point as it is practically impossible to plan for every single donor, and the center of each point is considered for calculating the Euclidean distance between donors and blood collection sites. In addition, the locations of regional blood centers are assumed to be predetermined. The scheme of concerned network is presented in Fig.2. Solving the proposed model, we obtain the following values:

- The optimal number and location of mobile blood facilities as well as local blood centers.
- Donors' allocation to each mobile blood facility or local blood center in each period.
- The quantity of whole blood, collected by each mobile blood facility or local blood center in each period.
- The quantity of whole blood, transported from mobile blood facilities to local blood centers in each period.
- The quantity of whole blood, transported from local blood centers to regional blood centers in each period.
- The quantity of blood PLTs produced by each method at each regional blood center in each period.
- PLTs inventory level in regional blood centers at the end of each period.
- The quantity of blood PLTs transported from regional blood centers to hospitals in each period.
- PLTs outdates in regional blood centers in each period.

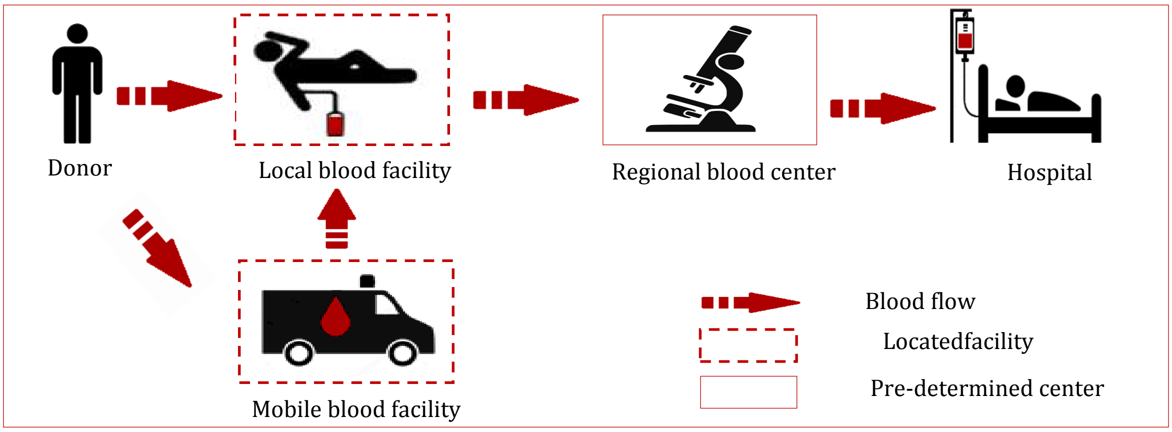

Fig.2. The scheme of concerned BSC

2-1- BC method versus PRP method

The aforementioned production methods differ in some aspects mainly pointed out as follows:

- BC method is the least expensive method among the others (i.e., PRP method and apheresis) for PLTs production (Vassallo and Murphy, 2006).
- Whole blood units must be decomposed within 8 hours if PRP method is supposed to be used while this time length will be extended up to 24 hours lending itself to BC method privilege.

The above advantage lets the product be perfectly manufactured until the day after collection. Furthermore, it is logistically cost-effective in the sense that it avoids multiple trips from local blood centers to the regional blood centers (Vassallo and Murphy, 2006).

- BC-derived PLTs perform better in terms of storage quality in comparison to PRP-derived PLTs. In other words, the quality of BC-derived PLTs will be kept up to 15 days of storage by using a platelet additive solution. Interestingly, an in-vitro study by Bertolini et al. (1992) compared the viability factors of Buffy Coat-platelet concentrates (BC-PCs) stored for 15 days in a platelet additive solution with those of platelet-rich plasma-platelet concentrates (PRP-PCs) stored in plasma. The result was intriguing, showing improvement in the quality of BC-PCs even after 15 days of storage, being favorably comparable with that of PRP-PCs stored for 7 days.
- PLT counts in PRP-derived PLTs outperform the ones in BC-derived PLTs (Levin et al, 2008; Soleimany Ferizhandy, 2011).Due to the differences in BC and PRP methods, PLTs produced by PRP benefit from somewhat more concentrated solution, which means high levels of PLT concentration in the mixture, in comparison with the more dilute BC-PCs (Levin et al, 2008).

However, no final and settled research exists to back evidence-based decisions considering a specific source of platelets (i.e., whole blood-derived platelets and apheresis-derived platelets (platelet pheresis)) as the preferred one (Vassallo and Murphy, 2006). Accordingly, in this paper, we discuss the harvest of PLTs from whole blood since the considered blood collection system only accounts for whole blood donation not for apheresis technology, which requires different collection considerations. The proposed mixed-integer linear programming model can be formulated while applying the following components.

2-2- Notations

Sets:

I	Set of donors groups; $(i = 1, 2, \dots, I)$
J	Set of candidate locations of mobile blood facilities; $(j = 1, 2, \dots, J)$
K	Set of candidate locations of local blood centers; $(k = 1, 2, \dots, K)$
R	Set of regional blood centers; $(r = 1, 2, \dots, R)$
P	Set of platelet production methods; $(p = 1, 2)$
H	Set of hospitals; $(h = 1,2, \dots, H)$
T	Set of time periods; $(t = 1,2, \dots, T)$
T'	Set of time periods; $(t = 1,2, \dots, T')$

Cost parameters:

c_k	Opening cost of local blood center k
c_{j_1,j_2}	Unit cost of moving a mobile blood facility from locationj_1 to locationj_2
Tc'_{jk}	Unit cost of transporting whole blood from mobile blood facility j to local blood center k
Tc_{kr}	Unit cost of transporting whole blood from local blood center k to regional blood center r
Td_{rh}	Unit cost of transporting blood platelets from regional blood center $r$to hospital h
Pc_p	Unit cost of producing blood platelets by production method p in regional blood centers
hc_p	Unit cost of holding blood platelets produced by production method p in regional blood centers
ex_p	Unit cost of expiring blood platelets produced by production method $p$in hospitals

Technical parameters:

v	Maximum capacity of each mobile blood facility
v'_k	Maximum capacity of local blood center k
v''_r	Maximum capacity of regional blood center $r$for receiving whole blood
p'_{prt}	Production capacity of platelets by method $p$in blood center r in period t
o_{rt}	Maximum inventory of PLTs for regional blood center $r$in period t
d_{it}	Quantity of whole blood donated by donors group i in period t
r_{ij}	Distance between donors group i and mobile blood facility j
r_0	Coverage radius of each mobile blood facility by which donors group i is served if $r_{ij} \leq r_0$
q_{jk}	Distance between mobile blood facility j and local blood center k
q_0	Coverage radius of each local blood center by which mobile blood facility $j$is served if $q_{jk} \leq q_0$
w'_{ik}	Distance between donors group i and local blood center k
w_0	Coverage radius of each local blood center by which donors group i is served if $w'_{ik} \leq w_0$
$de_{hpt'}$	Total demand of hospital h for blood plateletproduced by production method p in period t'
q'_p	Blood platelet counts produced by production method $p$in regional blood centers
l_p	Blood platelet life time produced by method $p$in regional blood centers
l'_p	Lead time for testing and producing platelets from whole blood by production method p
α	Usable blood rate
ω	Minimum demand satisfaction rate
M	A reasonably large number

Binary variables:

z_k	Is equal to 1 if local blood center k is set up; 0, otherwise
x_{ikt}	Is equal to 1 if donors group$i$ is assigned to local blood center k in period t; 0, otherwise
x'_{ijt}	Is equal to 1 if donors group$i$ is assigned to mobile blood facility j in period t; 0, otherwise
x''_{jkt}	Is equal to 1 if mobile blood facility j is assigned to local blood center k in period t; 0, otherwise
$y_{j_1,j_2,t}$	Is equal to 1 if a mobile blood facility is located at site $j_1$in period $t-1$, and moves to site j_2 in period t; 0, otherwise

Integer variables:

N	number of mobile blood facilities required in each period

Positive variables:

u_{ijt}	Quantity of whole blood donated by donors group i in mobile blood facility j in period t
u'_{jkt}	Quantity of whole blood transported from mobile blood facility j to regional blood center k in period t
s_{ikt}	Quantity of whole blood donated by donors group i in local blood center k in period t
s'_{krt}	Quantity of whole blood transported from local blood center k to regional blood center r in period t
Q'_{prt}	Quantity of blood platelet produced by method p in regional blood center r in period t
I_{prt}	Inventory of blood platelet which is produced by method p in regional blood center r in period t
$Q_{prh}^{tt'}$	Quantity of blood platelet produced by method p in regional blood center r in period t and distributed to hospital h in period t'

$E_{prt'}$ Quantity of blood platelet produced by method p and expired in regional blood center$r$ in period t'

2-3- Mathematical formulation

Total cost of the concerned network including establishment cost of local blood centers, cost of repositioning mobile blood facilities in successive periods, (whole) blood transportation cost from mobile sites to local ones and from local blood centers to regional blood centers, platelets production cost, inventory holding cost and outdating cost in regional blood centers and transportation cost from regional centers to hospitals, is to be minimized through objective function (1).

2-3-1-Objective function

$$Min\, Z = \sum_{k} c_k z_k + \sum_{j_1,j_2,t} c_{j_1,j_2} y_{j_1,j_2,t} + \sum_{j,k,t} Tc'_{jk} u'_{jkt} + \sum_{k,r,t} Tc_{kr} s'_{krt} + \sum_{r,p,t} Pc_p Q'_{prt} + \sum_{r,p,t,t'} hc_p I^{tt'}_{pr} + \sum_{p,r,t'} ex_p E_{prt'} + \sum_{r,h,p,t,t'} Td_{rh} Q^{tt'}_{prh} \tag{1}$$

2-3-2-Model constraints

$$\sum_{j_1} y_{j_1,j_2,t} \leq 1 \qquad \forall j_2, t \tag{2}$$

Constraint (2) assures that no more than one mobile blood facility can move to a specific candidate location from other locations in each period.

$$\sum_{j_1 \neq j_2} y_{j_1,j_2,t} = N \qquad \forall t \tag{3}$$

Constraint (3) determines the number of mobile blood facilities opened in each period.

$$\sum_{j_2} y_{j_1,j_2,t} \leq \sum_{j} y_{j,j_1,t-1} \qquad \forall j_1, t \geq 2 \tag{4}$$

Each mobile facility can move to another location in the next period only if it has been founded before, as presented in constraint (4).

$$\sum_{k} x_{ikt} + \sum_{j} x'_{ijt} \leq 1 \qquad \forall i, t \tag{5}$$

Constraint (5) guarantees that each group of donors can be assigned to no more than either one local blood center or a mobile blood facility in each period.

$$x'_{ijt} r_{ij} \leq r_0 \sum_{j_1} y_{j_1,j,t} \qquad \forall i, j, t \tag{6}$$

Constraint (6) determines the coverage restriction of each mobile blood facility such that each group of donors can be served by a mobile blood facility only if located within coverage radius of the mobile blood facility.

$$x''_{jkt} q_{jk} \leq q_0 z_k \qquad \forall j, k, t \tag{7}$$

Each mobile blood facility can be served by a local blood center only if located within coverage radius of the local blood center, as defined in constraint (7).

$$x''_{jkt} \leq \sum_{j_1} y_{j_1,j,t} \qquad \forall j, k, t \tag{8}$$

Constraint (8) assures that blood units can only be delivered from a mobile collection site to a local center provided that it has been established before.

$$u_{ijt} \leq M x'_{ijt} \qquad \forall i, j, t \tag{9}$$

$$s_{ikt} \leq M x_{ikt} \qquad \forall i,k,t \qquad (10)$$

Constraints (9) and (10) denote that blood donation may occur in both mobile and local blood sites only if these centers have been opened before.

$$u'_{jkt} \leq M x''_{jkt} \qquad \forall j,k,t \qquad (11)$$

Constraint (11) makes sure the blood flow from mobile blood facilities to local blood centers only if the local centers exist.

$$\sum_i u_{ijt} \leq v \qquad \forall j,t \qquad (12)$$

The capacity of each mobile blood facility is restricted via constraint (12).

$$\sum_i u_{ijt} = \sum_k u'_{jkt} \qquad \forall j,t \qquad (13)$$

Constraint (13) guarantees that total quantity of blood collected by mobile blood facilities are transported to local blood centers at the end of each period.

$$x_{ikt} w'_{ik} \leq w_0 z_k \qquad \forall i,k,t \qquad (14)$$

Constraint (14) defines the coverage restriction of each local blood facility in the sense that each group of donors can be served by a local blood center only if located within coverage radius of the local blood center.

$$\sum_k S_{ikt} + \sum_j u_{ijt} \leq d_{it} \qquad \forall i,t \qquad (15)$$

Constraint (15) restricts blood donation from each group of donors in each period.

$$\sum_i S_{ikt} + \sum_j u'_{jkt} \leq v'_k \qquad \forall k,t \qquad (16)$$

Constraint (16) limits the capacity of each local blood center in each period.

$$\sum_i S_{ikt} + \sum_j u'_{jkt} = \sum_r S'_{krt} \qquad \forall k,t \qquad (17)$$

Constraint (17) makes sure that total (whole) blood units collected by each local blood center are transported to regional blood centers at the end of each period.

$$\sum_{k,t} S'_{krt} \leq v''_r \qquad \forall r \qquad (18)$$

Constraint (18) limits the capacity of each regional blood center for receiving whole blood.

$$\alpha(\sum_k S'_{krt}) q'_p = Q'_{p,r,t+l'_p} \qquad \forall r,p,t \qquad (19)$$

Constraint (19) determines the volume of PLTs produced by each production method in each period.

$$Q'_{p,r,t+l'_p} \leq p'_{prt} \qquad \forall r,p,t \qquad (20)$$

Constraint (20)confines the production capacity of PLTs in each regional blood center in each period.

$$Q'_{p,r,t+l'_p} + I_{p,r,t+l'_p-1} = I_{p,r,t+l'_p} + \sum_{h,t'} Q^{t+l'_p,t'}_{p,r,h} \qquad \forall r,p,t \qquad (21)$$

Constraint (21) is known as inventory conservation equation for each regional blood center in each period.

$$\sum_p I_{p,r,t} \leq o_{rt} \qquad \forall r,t \qquad (22)$$

Constraint (22) restricts the inventory of PLTs for each regional blood center in each period.

$$\sum_{t' \leq t+l_p-l'_p} \sum_r Q_{p,r,h}^{t+l'_p,t'} \geq \omega(de_{hpt'}) \qquad \forall h,p,t' \qquad (23)$$

Constraint (23) forces the model to satisfy total demand of each hospital for PLTs at least at ω percent in each period.

$$\sum_{h,t'>t+l_{p-l'_p}} Q_{p,r,h}^{t+l'_p,t'} \geq E_{rpt'} \qquad \forall r,p,t' \qquad (24)$$

Constraint (24) restricts blood PLTs expiration in regional blood centers in each period.

$$z_k, x_{ikt}, x'_{ijt}, x''_{jkt}, y_{j_1,j_2,t} \in \{0,1\} \qquad (25)$$

$$u_{ijt}, u'_{jkt}, s_{ikt}, s'_{krt}, Q'_{prt}, I_{prt}, Q_{prh}^{tt'}, E_{prt'} \geq 0 \qquad (26)$$

Constraints (25) and (26) define the domain of decision variables.

3- The robust programming approach

Robust programming synchronizes optimality and feasibility robustness required to an optimization problem. The feasibility of solutions for any possible values of uncertain parameters lends itself to the feasibility robustness while finding (near) optimal solutions under a set of realizations is guaranteed by the optimality robustness (Zahiri et al., 2015). In this research, an RP approach is employed to capture the random nature of data. Several robust approaches can be addressed in the literature, applied to a number of optimization models; e.g., the one introduced by Soyster (1982) to handle data uncertainty by means of mathematical models, however, it used to hand rather poor solutions in terms of optimality due to its over-conservative models, which are not appropriate in terms of cost, in most cases. Later on, Ben-Tal and Nemirovski (1999), Ben-Tal and Nemirovski (2000), and Ben-Tal and Nemirovski (2002) put forward less conservative models while accounting for ellipsoidal uncertainties. A new approach arose resulting from the works of Bertsimas and Sim (BS) (2003) and Bertsimas and Sim (BS) (2004) to make up for the previous deficiencies in the sense that, as observed, all coefficients will not concurrently possess their worst-case values.

3-1- The light robust (LR) heuristic

Light Robustness, an efficient approach to cope with uncertainty, is somehow the combination of a lightened two-stage stochastic programming approach and robust optimization, which carries simplicity as well as flexibility as its privileges. Applying LR, we can sometimes come up with comparable solutions in terms of quality with the ones acquired by either robust models or stochastic programming individually while benefiting from simpler model formulation along with less computing time (Fischetti and Monaci, 2009). To tackle infeasibility, LR employs slack variables having a role like what second-stage recourse variables have in stochastic programming models. These slacks let local violations of constraints, better to say, define solution robustness while absorbing variations of uncertain parameters. The slacks are then minimized via an auxiliary objective function. Thereto, the optimality of solutions is accounted for in the form of a constraint through the LR model.

This approach will be accomplished by solving three linear programming (LP) models (i.e., the nominal problem and the two following models of LR).

Step 1: Consider nominal problem (26)–(29) for which x^* represents an optimal solution.

$$\min \sum_{j \in N} c_j \, x_j \qquad (27)$$

$$\sum_{j \in N} a_{ij}\, x_j \ \geq d_i \qquad i \in M \qquad (28)$$

$$\sum_{j \in N} b_{ij}\, x_j \ \leq h_i \qquad i \in M \qquad (29)$$

$$x_j \ \geq 0 \qquad j \in N \qquad (30)$$

In which the number of constraints and variables are defined by $|M|$and$|N|$, respectively.

Step 2: Assume matrices$D$and Htakevalues, say$\tilde{d}_i \in [d_i, d_i + \hat{d}_i]$ and$\tilde{h}_i \in [h_i - \hat{h}_i, h_i]$, respectively. Thus, the maximum violations of uncertain constraints$i$aredetermined by equations (31) and (32):

$$L_i^* = \left(d_i + \hat{d}_i\right) - \sum_{j \in N} a_{ij} x_j{}^* \qquad (31)$$

$$L_i^* = \sum_{j \in N} b_{ij} x_j{}^* - \left(h_i - \hat{h}_i\right) \qquad (32)$$

In addition, the constraints for which sufficient slacks should be considered are introduced in the set U, say$U = \{i \in M : L_i^* > 0\}$ and $|U| \geq 1$ since the slack variable is required for at least one constraint, otherwise x^* would be feasible, thereby optimal in any realization of the uncertain parameter.

The first model of LR in the form of the following LP model is solved:

$$max\ \sigma \qquad (33)$$

$$\sum_{j \in N} a_{ij} x_j - s_i = d_i \qquad i \in M \qquad (34)$$

$$\sum_{j \in N} b_{ij} x_j + s_i = h_i \qquad i \in M \qquad (35)$$

$$\sigma \leq \frac{s_i}{L_i^*} \qquad i \in U \qquad (36)$$

$$\sum_{j \in N} c_j\, x_j \leq (1 + \delta) z^* \qquad (37)$$

$$x_j \geq 0 \qquad j \in N \qquad (38)$$

$$s_i \geq 0 \qquad i \in M \qquad (39)$$

That maximizes the minimum slack considered for any uncertain constraint. The uncertainty in constraints i can be taken into account individually by dividing the slack variable s_i by L_i^* such that $i \in U$ (i.e., normalization) as can be observed in constraint (36).

The max-min nature of the above LP model results in several equivalent optimal solutions. Indeed, since only the minimum normalized slack is accounted for by the objective function, no force will be imposed to assign a large slack, however important to improve robustness, to the remaining constraints. Thus, LR presents its second LP model (41)-(49) with the aim of balancing the slacks among uncertain constraints.

Step 3: The model (33)–(39) is assumed to have an optimal solution, say (x^*,s^*,σ^*). Therefore, we can define the average of the normalized slacks as below:

$$s_{avg} = \frac{\sum_{i \in U} s_i^* / L_i^*}{|U|} \qquad (40)$$

Additionally, the normalized slacks have the minimum value as defined in relationship (41).

$$s_{min} = min\{s_i^*/L_i^* : i \in U\} \tag{41}$$

The second model of LR is presented as follows:

$$min \sum_{i \in U} t_i \tag{42}$$

$$\sum_{j \in N} a_{ij} x_j - s_i = d_i \qquad i \in U \tag{43}$$

$$\sum_{j \in N} b_{ij} x_j + s_i = h_i \qquad i \in U \tag{44}$$

$$\sum_{j \in N} c_j x_j \leq (1 + \delta) z^* \tag{45}$$

$$\frac{s_i}{L_i^*} + t_i \geq s_{avg} \qquad i \in U \tag{46}$$

$$x_j \geq 0 \qquad j \in N \tag{47}$$

$$\frac{s_i}{L_i^*} \geq s_{min} \qquad i \in U \tag{48}$$

$$s_i \geq 0 \, , t_i \geq 0 \qquad i \in U \tag{49}$$

In which variables$t_i$take positive values in case $s_{avg}$is bigger than the corresponding normalized slack. Also, the sum of t_i is to be penalized through objective function (42) to balance the normalized slacks among all rows.

3-2- The robust equivalent of our original model

After solving the nominal model (1) - (26), the robust counterpart of our basic model would be introduced as follows with respect to the aforementioned steps. It is worth mentioning that, we have considered the amount of blood PLT demand as an uncertain (random) parameter (i.e.,$\widetilde{de}_{hpt'}$) such that$\widetilde{de}_{hpt'} \in \left[de_{hpt'}, \; de_{hpt'} + \widehat{de}_{hpt'}\right]$, in which$\widehat{de}_{hpt'}$ represents the worst-case (maximum violation) of the nominal value of blood PLT demand (i.e., $de_{hpt'}$).

Thus, by defining $L_{hpt'}^*$ as equation (50) and the set U,the first LR counterpart for our original formulation would be presented as model (51)-(55) and (1)-(26).

$$L_{hpt'}^* = \omega\left(de_{hpt'} + \widehat{de}_{hpt'}\right) - \sum_{t' \leq t + l_p - l_p'} \sum_r Q_{p,r,h}^{t+l_p',t'} \qquad \forall h, p, t' \tag{50}$$

The set$U$ is also considered as:

$$U = \{(h, p, t') \in M : L_{hpt'}^* > 0\}$$

Therefore, we have the first LR counterpart formulated as:

$$max \; \sigma \tag{51}$$

$$\sum_{t' \leq t + l_p - l_p'} \sum_r Q_{p,r,h}^{t+l_p',t'} = \omega(de_{hpt'}) + s_{hpt'} \qquad \forall h, p, t' \tag{52}$$

$$\sigma \leq \frac{s_{hpt'}}{L_{hpt'}^*} \qquad \forall h, p, t' \tag{53}$$

$$(54)$$

$$s_{hpt'} \geq 0 \qquad \forall h, p, t' \in U \qquad (55)$$

In which Z^* states the objective function value of the nominal formulation (1) – (26) and δ denotes deterioration degree in the objective function value, or better to say, conservative level decided by the DM.

plus relationships (1) – (26).

Thereto, we have the average of normalized slacks defined as:

$$s_{avg} = \frac{\sum_{\forall (h,p,t') \in U} s^*_{hpt'} / L^*_{hpt'}}{|U|} \qquad (56)$$

Then, the second LR counterpart (i.e., third LP model) could be modeled as follows:

$$min \sum_{h,p,t \in U} t_{hpt'} \qquad (57)$$

$$\frac{s_{hpt'}}{L^*_{hpt'}} + t_{hpt'} \geq s_{avg} \qquad \forall h, p, t' \in U \qquad (58)$$

$$\frac{s_{hpt'}}{L^*_{hpt'}} \geq s_{min} \qquad \forall h, p, t' \in U \qquad (59)$$

$$t_{hpt'} \geq 0 \qquad (60)$$

In which s_{min} denotes the objective function value of the first LR counterpart (i.e., σ^*).

4- Computational experiments

In this section, the efficiency of the proposed model besides its solution method is evaluated by carrying out a series of numerical examples. To do so, both deterministic and robust models are firstly implemented on test problems, specified in Tab.2, under different uncertainty levels (δ) while using nominal data which are generated randomly by applying the uniform distributions presented in Tab. 3.The value of parameters is logically determined with respect to the paper presented by Zahiri et al. (2015). Additionally, some parameters such as PLT lifetime and PLT counts from either production method are considered based on the objective data and the sources such as Vassallo and Murphy (2006), Levin et al. (2008) and Soleimany Ferizhandy (2011).

Table 2. The size of test problems

Problem no.	$\lvert I\rvert$	$\lvert J\rvert$	$\lvert K\rvert$	$\lvert R\rvert$	$\lvert P\rvert$	$\lvert H\rvert$	$\lvert T\rvert$
#TP 1	3	3	3	2	2	3	4
#TP 2	5	5	5	4	2	5	6
#TP 3	10	7	7	6	2	10	8
#TP 4	15	10	10	8	2	15	10

Table 3. Random generation of nominal parameters

parameters	Corresponding random distribution	parameters	Corresponding random distribution
c_k	$\sim uniform$ (1500,3000)	d_{it}	$\sim uniform$ (1400,1600)
c_{j_1,j_2}	$\sim uniform$ (0.1,0.6)	r_{ij}	$\sim uniform$ (20,40)
Tc'_{jk}	$\sim uniform$ (0.35,3.5)	r_0	100
Tc_{kr}	$\sim uniform$ (0.35,3.5)	q_{jk}	$\sim uniform$ (20,30)
Td_{rh}	$\sim uniform$ (0.75,1)	q_0	180
Pc_p	$\sim uniform$ (0.1,0.3)	w'_{ik}	$\sim uniform$ (100,200)
q'_p	$\sim uniform$ (0.25,0.35)	w_0	100
v	$\sim uniform$ (500,700)	q_0	180
v'_k	$\sim uniform$ (1000,2100)	p'_{prt}	$\sim uniform$ (2000,2500)
v''_r	$\sim uniform$ (2000,2500)	o_{rt}	$\sim uniform$ (600,800)
$de_{hpt'}$	$\sim uniform$ (300,600)		

Then, the performance of deterministic and robust models are compared under a number of realizations of the uncertain parameter (i.e., demand) in continue. Realizations are generated randomly in the corresponding uncertainty set, as expressed in Section 5.2. Using GAMS software, the experiments are carried out on a laptop computer with Intel Core i5, CPU 2.5GHz and 6GB of RAM.

4-1- Sensitivity analysis on demand satisfaction level (ω)and uncertainty level (δ)

In this section, we determine how the changes in the value of ω and δ affect the performance of proposed deterministic (D) and robust (R) models. To do so, each test problem is performed while varying the values of ω and δaccording to Tab. 4. As can be understood from the results, for test problems 1 and 4, increasing demand satisfaction level from 0.6 to 0.8 makes an increase in the number of blood collection facilities, mobile (N) and local (Z) facilities, in both deterministic and robust models while test problems 2 and 3 remain almost indifferent to this change. It can be justified that when the value of ω increases, in test problems 1 and 4, we need to add the number of collection facilities, since their capacities are limited, to cover the additional service. However, test problems 2 and 3 can still respond to the increased demand satisfaction level by the current capacity, thus they require no tangible changes in the number of collection facilities.

Table 4. Summary of results (robust approach versus deterministic approach)

$\alpha = 0.8$	ω	δ	|Z|		|N|		Total network cost under nominal data ($)		Constraint violation cost under nominal data ($)	CPU time (s)
Problem no.			D	R	D	R	D	R	R	
1	0.6	0.04	1	1	1	0	9162.372	9528.867	6625.032	0:1.524
		0.08	1	1	1	0		9895.362	3760.916	0:1.375
		0.12	1	1	1	0		10261.857	896.8	0:1.329
		0.2	1	1	1	0		10994.846	0	0:1.273
	0.8	0.04	2	2	2	2	14965.322	15563.934	8006.213	0:1.818
		0.08	2	2	2	2		16162.547	3248.398	0:2.402
		0.12	2	2	2	2		16761.160	0	0:1.803
		0.2	2	2	2	2		17958.386	0	0:1.721
2	0.6	0.04	1	1	2	2	22141.788	23027.459	15100.436	0:7.964
		0.08	1	1	2	2		23913.131	6548.878	0:12.321
		0.12	1	1	2	2		24798.802	0	0:10.901
		0.2	1	1	2	2		26570.145	0	0:7.974
	0.8	0.04	1	1	1	0	30271.456	31482.314	20164.912	0:8.449
		0.08	1	2	2	2		32693.172	6348.536	0:13.154
		0.12	1	2	2	2		33904.031	0	0:8.115
		0.2	1	2	0	2		36325.747	0	0:6.67
3	0.6	0.04	2	2	3	3	37647.123	39153.008	31428.644	1:14.861
		0.08	2	2	3	3		40658.893	12054.465	1:01.32
		0.12	2	2	3	3		42164.778	4020	0:57.120
		0.2	2	2	3	3		45176.548	0	1:13.359
	0.8	0.04	2	2	3	3	49877.839	51872.953	42946.734	0:59.646
		0.08	2	2	3	3		53868.066	13925.964	1:10.776
		0.12	2	2	3	3		55863.18	0	0:56.705
		0.2	2	2	3	3		59853.407	0	1:20.487
4	0.6	0.04	2	2	4	4	70961.217	73798.824	65207.112	8:14.736
		0.08	2	2	4	5		76821.618	24131.415	8:06:24
		0.12	2	2	4	5		80137.22	0	7:47.215
		0.2	2	3	4	5		85144.275	0	7:31.12
	0.8	0.04	3	3	5	5	94780.13	98571.335	86459.177	8:29.066
		0.08	3	3	5	6		102416	31878.104	8:31.274
		0.12	3	3	5	6		106270	0	7:55.414
		0.2	3	4	5	7		113740	0	7:16.118

Thereto, the normalized values (i.e., dividing each value by the sum of respective column) of objective function of both robust and deterministic models and robust constraint violation cost are compared schematically in Figs. 3-6. As can be observed in the following figures, on one hand, the objective function (total network cost) of robust model takes higher values as the uncertainty level increases and it gets intensified when ω reaches 0.8 while the objective function value of deterministic model remains constant. On the other hand, we witness a considerable decrease in constraint violation cost in all test problems when the value of δ goes up, and it comes to zero as δ gets the value 0.12 for all test problems 1-4 at $\omega = 0.8$.

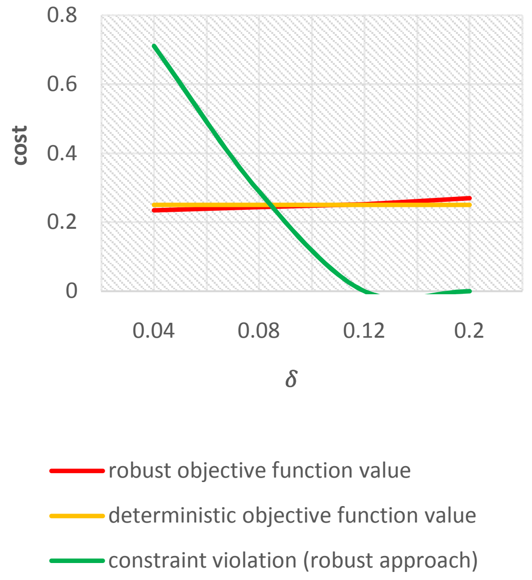

Fig. 3 Objective function value versus constraint violation for test problem 1 under $\omega = 0.8$

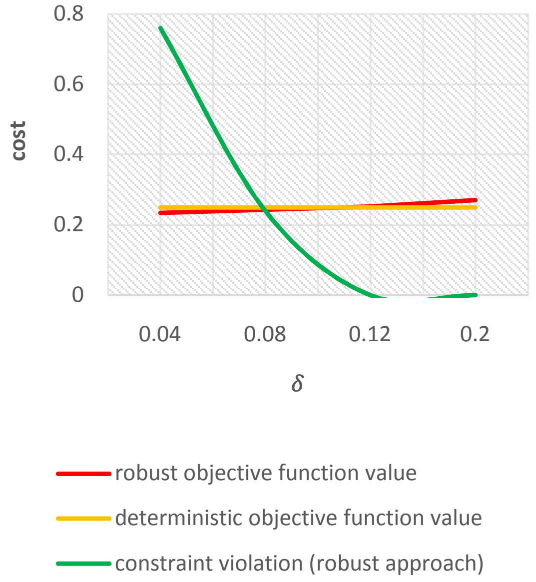

Fig. 4 Objective function value versus constraint violation for test problem 2 under $\omega = 0.8$

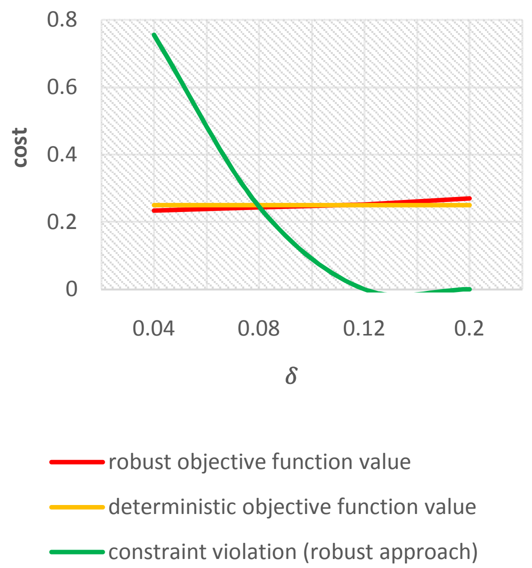

Fig. 5 Objective function value versus constraint violation for test problem 3 under $\omega = 0.8$

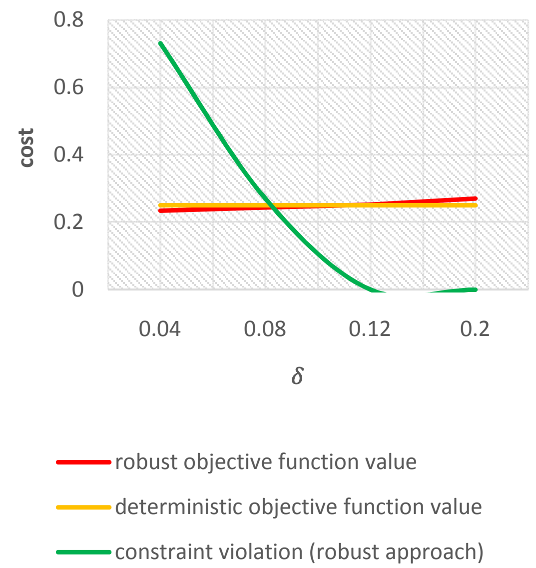

Fig. 6 Objective function value versus constraint violation for test problem 4 under $\omega = 0.8$

As mentioned before, increasing the value of δ leads to an increase in total network cost, but simultaneously leads to the reduction of violation cost. For test problem one, for instance, constraint violation cost comes to zero at $\delta = 0.12$ and $\omega = 0.8$ while it imposes a total cost about $16,761. As the problem gets larger, this cost expectedly increases until it reaches the value of $106,270 for test problem 4.

Accordingly, the DM needs to make a tradeoff between these two costs to decide on an appropriate conservative level (δ). Depending on the DM's professional point of view, the value of δ might be increased or lessen. In more critical situations, constraint violation cost might be even more highlighted and assigned higher weight by the DM, which may push the value of δ to the right (i.e., to increaseδ) in favor of reducing violation cost rather than the objective function value.

In this article, we suggest basic levels forδ, determined by the intersection between the curves of robust constraint violation cost and robust total network cost. These levels are 0.085 for test problems 1, 4 and 0.08 for test problems 2 and 3 which are being used in Section 4.3.

4-2- Sensitivity analysis on different realization values and uncertainty levels

In this section, we put the proposed robust and deterministic models into analysis via uniformly generating random realizations of the uncertain parameter (i.e., demand) and under different uncertainty levels. The realizations are generated randomly in the respective uncertainty set, say$\left[de_{hpt'},\ de_{hpt'}+\widehat{de}_{hpt'}\right]$, in which $\widehat{de}_{hpt'}$ represents maximum violation in demand defined as: $\widehat{de}_{h,t}=0.1de_{hpt'}$, and then are sorted ascendingly. The models are implemented while varying the uncertainty level and generating five realizations for each test problem, as presented in Tab. 5. As the results show, for all test problems, larger realization values result in increasing constraint violation costs. Having the value of δ increased, we observe a decrease in robust violation cost, but an increase in the value of robust objective function while the deterministic model shows no changes in the values.

A general observation from Figures 7-10 is that although robust constraint violation cost (Cv_R) increases as the result of increasing realization values, it can be remarkably lessen by taking larger uncertainty levels. For test problem No1 in Figure 7, Cv_R decreases from \$7371.813 to zero as the value of δ changes from 0.04 to 0.12 under realization 5. In Fig. 8, we will have the minimum value of Cv_R by spending \$33904.031under the fifth realization and $\delta=0.12$. In Fig. 9, we will come up with no constraint violation cost of robust model when taking $\delta=0.12$ and spending \$55863.18 under realization 5. Eventually, for test problem 4, Fig. 10,Cv_Rcomes to its minimum value by imposing a cost of \$106270 under realization 5 and $\delta=0.12$.

Table 5. Objective function values (Z) and constraint violation (Cv) costs under different realizations and uncertainty levels (robust approach versus deterministic approach)

$\alpha = 0.8$ / $\omega = 0.8$			Realization					Avg. CPU time (s)
Problem no.	δ		1	2	3	4	5	
1		Z_D	14965.322					0:2.384
		Cv_D	2537.6	4440.8	6344	10150.4	12053.6	
	0.04	Z_R	15563.934					0:3.213
		Cv_R	0	0	1662.213	5468.613	7371.813	
	0.08	Z_R	16162.547					0:4.213
		Cv_R	0	0	0	787.38	2690.58	
	0.12	Z_R	16761.16					0:4.407
		Cv_R	0	0	0	0	0	
	0.2	Z_R	17958.386					0:2.643
		Cv_R	0	0	0	0	0	
2		Z_D	30271.456					0:7.491
		Cv_D	6385.6	11270.8	16156	25926.4	30811.6	
	0.04	Z_R	31482.314					0:10.76
		Cv_R	0	0	3928.105	13651.312	18536.512	
	0.08	Z_R	32693.172					0:10.54
		Cv_R	0	0	0	385.146	4850.346	
	0.12	Z_R	33904.031					0:9.619
		Cv_R	0	0	0	0	0	
	0.2	Z_R	36325.747					0:10. 3
		Cv_R	0	0	0	0	0	
3		Z_D	49877.839					1:17.54
		Cv_D	14424.32	25242.56	36060.8	57697.28	68515.52	
	0.04	Z_R	51872.953					1:04.73
		Cv_R	0	0	6885.934	28522.414	39340.654	
	0.08	Z_R	53868.066					1:00.51
		Cv_R	0	0	0	0	10373.644	
	0.12	Z_R	55863.18					1:15.74
		Cv_R	0	0	0	0	0	
	0.2	Z_R	59853.407					1:16.69
		Cv_R	0	0	0	0	0	
4		Z_D	94780.13					8:41.21
		Cv_D	9883.721	32171.116	55815.23	74741.62	117921	
	0.04	Z_R	98571.335					8:46.3
		Cv_R	0	0	1821.312	20115.06	61276.4	
	0.08	Z_R	102416					9:04.15
		Cv_R	0	0	0	0	8713.521	
	0.12	Z_R	106270					9:23.61
		Cv_R	0	0	0	0	0	
	0.2	Z_R	113740					9:32.04
		Cv_R	0	0	0	0	0	

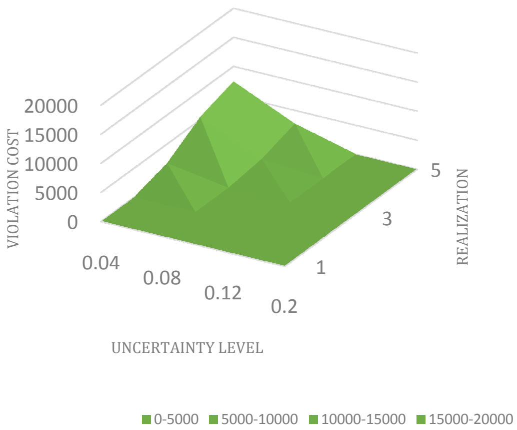

Fig. 7 Constraint violation for test problem 1 under different realizations and uncertainty levels; $\omega = 0.8$

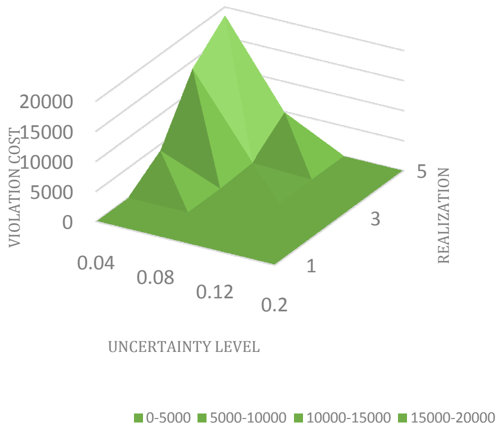

Fig. 8 Constraint violation for test problem 2 under different realizations and uncertainty levels; $\omega = 0.8$

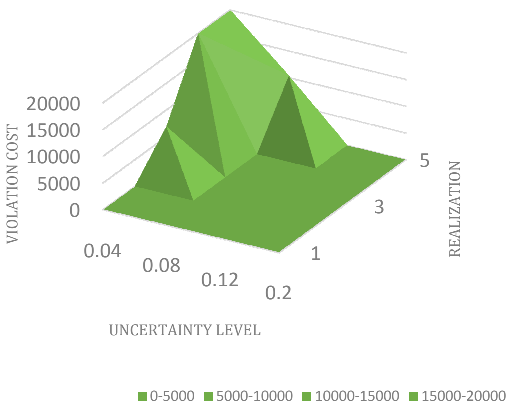

Fig. 9 Constraint violation for test problem 3 under different realizations and uncertainty levels; $\omega = 0.8$

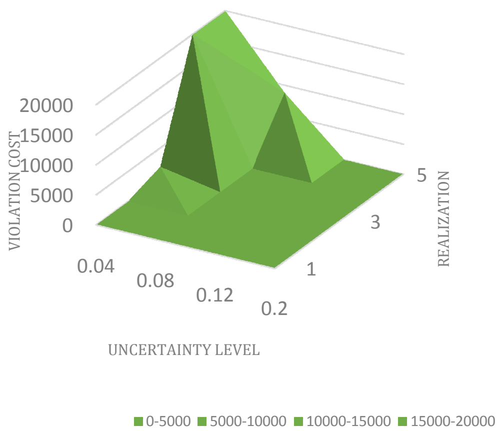

Fig. 10 Constraint violation for test problem 4 under different realizations and uncertainty levels; $\omega = 0.8$

4-3- A sensitivity analysis for the performance of robust model versus deterministic model

To evaluate the robustness of solutions obtained by the proposed robust model as well as the ones achieved by the deterministic MILP model, the models are solved under a set of realizations, sorted ascendingly. Then, the quality of solutions obtained by both models is compared by employing two criteria: the average and standard deviation of constraint violation cost. To be more specific, as mentioned earlier in Section 4.1, we carry out each test problem under a specific uncertainty level (i.e., the intersection between robust objective function and constraint violation curves). Accordingly, as reported in Tab. 6, we set the value of δ to 0.085, 0.08, 0.08 and 0.085 for test problems 1, 2, 3 and 4, respectively.

Table 6. Objective function values and constraint violation costs under a number of realizations (robust strategy versus deterministic approach)

$\alpha = 0.8$ / $\omega = 0.8$	δ	Realization	Total network cost under realizations		Constraint violation cost		CPU time (s)
Problem no.			Robust	Deterministic	Robust	Deterministic	
1	0.085	1	16237.374	18137.322	0	3172	2.516
		2	16237.374	19786.762	0	4821.44	2.023
		3	16237.374	21943.722	0	6978.4	1.915
		4	16237.374	23212.522	0	8247.2	1.931
		5	16237.374	24861.962	0	9896.64	2.541
		6	16439.6	25115.72	202.226	10150.4	2.164
		7	17074	25750.12	836.626	10784.8	3.5
		8	17962.16	26638.28	1724.786	11672.96	2.114
		9	18469.68	27145.8	2232.306	12180.48	2.289
		10	18723.43	27399.56	2486.06	12434.24	2.257
Average			16985.57	23999.18	748.2004	9033.856	
Standard deviation			1015.511	3169.912	1015.511	3169.913	
2	0.08	1	32693.17	38285.46	0	8014	8.48
		2	32693.17	42519.3	0	12247.84	8.015
		3	32693.17	48055.86	0	17784.4	7.504
		4	32693.17	51312.66	0	21041.2	10.187
		5	32693.17	55546.5	0	25275.04	7.913
		6	33078.32	56197.86	385.146	25926.4	8.067
		7	34566.72	57826.26	1873.546	27554.8	9.01
		8	36650.48	60106.02	3957.306	29834.56	8.904
		9	37841.2	61408.74	5148.026	31137.28	9.244
		10	38432.46	62066.11	5739.288	31794.656	8.405
Average			34403.5	53332.47	1710.331	23061.02	
Standard deviation			2345.399	8137.36	2345.399	8137.36	
3	0.08	1	53868.07	67908.24	0	18030.4	1:47.118
		2	53868.07	77284.05	0	27406.208	1:06.708
		3	53868.07	89544.72	0	39666.88	1:22.055
		4	53868.07	96756.88	0	46879.04	1:15.616
		5	53868.07	106132.7	0	56254.848	1:13.328
		6	53868.07	107575.1	0	57697.28	59.177
		7	57186.13	111181.2	3318.062	61303.36	59.853
		8	62110.32	116229.7	8242.252	66351.872	1:34.98
		9	64952.18	119114.6	11084.11	69236.736	1:49.38
		10	66373.1	120557	12505.036	70679.168	1:20.97
Average			57383.01	101228.4	3514.946	51350.58	
Standard deviation			5105.87	18018.54	5105.87	18018.54	
4	0.085	1	127308.4	115233.2	0	20453.1	8:21.04
		2	127308.4	125475.1	0	30694.95	8:38.17
		3	127308.4	139207	0	44426.91	8:16.3
		4	127308.4	147284.7	0	52504.52	9:24.61
		5	127308.4	157785.6	0	63005.43	9:34.23
		6	127308.4	159401.1	0	64620.95	10:16.1
		7	127308.4	163439.9	0	68659.76	10:32.4
		8	137023.6	169094.2	9715.2	74314.1	11:10.37
		9	141323.6	172325.3	14015.203	77545.14	11:42.1
		10	143451.5	173940.8	16143.12	79160.67	10:37.25

Table 6. Continued (Results)

	Deterministic	Robust	Deterministic	Robust
Average	57538.55	3987.352	152318.7	131295.8
Standard deviation	20127.63	6603.211	20127.63	6603.211

As the results show, for all four test problems, the proposed robust model dominates over the deterministic one in terms of both the average and standard deviation of constraint violation cost, and this could happen for any other test problems without loss of generality. For the first test problem for instance, the average constraint violation cost of robust model is about $748which represents a high gap with that of the deterministic model ($9034). Moreover, it is obvious from Figs. 11-14 that for realizations 1-6, the robust model ends in no constraint violation cost while the deterministic model carries this cost under all 10 realizations for all test problems. Additionally, test problem four holds this pattern till realization 7, and it terminates the analysis while imposing an average robust violation cost about $3987, which is too little in comparison to $57538.55 caused by the deterministic model. Test problem 2 ends in an average robust violation cost of $1710.331 with a high difference from that of the deterministic model ($23061.02). Lastly, test problem three imposes an average robust violation cost about $3515 with considerably less standard deviation than the deterministic approach with an average violation cost about $51350 and remarkably large standard deviation. To sum up, in all test problems robust approach overcomes the deterministic one as it burdens lower total network cost in comparison to that of the deterministic approach.

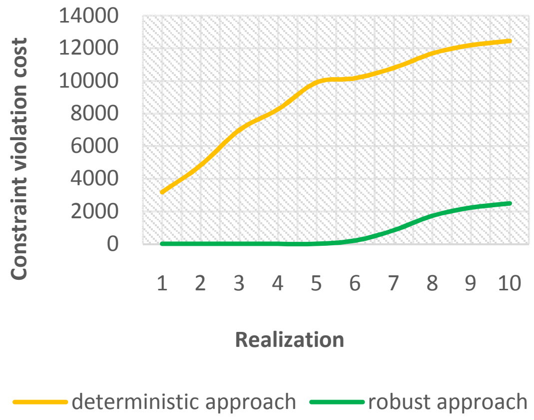

Fig. 11 Constraint violation cost for test problem1

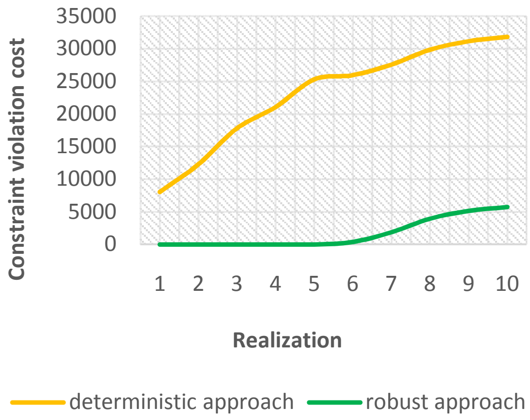

Fig. 12 Constraint violation cost for test problem2

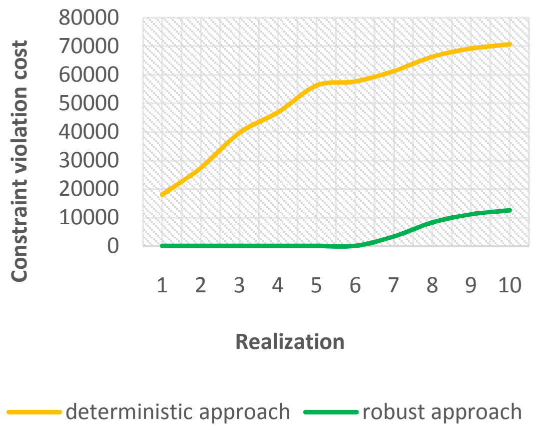

Fig. 13 Constraint violation cost for test problem3

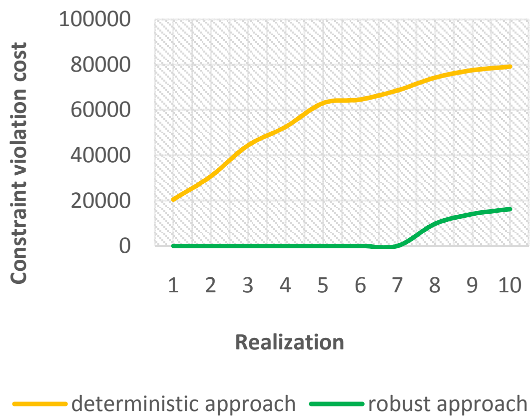

Fig. 14 Constraint violation cost for test problem4

5- Concluding remarks and future research recommendations

This paper proposed an MILP model for blood PLTs production under integrated planning. The concerned network is composed of four echelons including collection, production/screening, inventory control and distribution as well. Two types of methods for PLTs production, called BC and PRP and known as whole blood- derived production methods are taken into account in the production echelon. The proposed model seeks to minimize the network overall cost. The amount of demands from hospitals, tainted with random uncertainty, is handled by using a robust programming approach. The performance of proposed model along with its solution technique was tested into several numerical examples. Eventually, valuable insights were extracted through computational results. To be more specific, domination of robust strategy over deterministic approach is proved by comparing the results. In other words, the proposed robust model absorbs unfavorable changes resulting from demand realizations and outperforms the deterministic model in terms of mean and standard deviation of constraint violation cost and thus the total network cost.

Future investigation on this subject could be carried on in the following directions:

- Developing the presented model to an MOMILP model by accounting for objectives such as minimizing maximum unsatisfied demand and maximizing blood freshness.
- Considering uncertainty in other parameters including blood supply, etc. besides demand amounts and applying other approaches (e.g., stochastic programming, or fuzzy approach when facing fuzzy uncertainty)
- Applying (meta) heuristic algorithms in case the problem comes in larger size for which the exact solvers may not be able to obtain a solution in reasonable length of time.

References

Abdulwahab U., & Wahab, M. (2014). Approximate dynamic programming modeling for a typical blood platelet bank. *Computers & Industrial Engineering*, 78, 259-270.

Arvan, M., Tavakkoli-Moghaddam, R., & Abdollahi, M. (2015). Designing a bi-objective, multi-product supply chain network for blood supply. *Uncertain Supply Chain Management*, 3, 57–68.

Beliën, J., & Forcé, H. (2012). Supply chain management of blood products: a literature review. *European Journal of Operational Research*, 217 (1), 1–16.

Ben-Tal, A., &Nemirovski, A. (1999). Robust solutions of uncertain linear programs. *Operations research letters*, 25(1), 1-13.

Ben-Tal, A., &Nemirovski, A. (2000). Robust solutions of linear programming problems contaminated with uncertain data. *Mathematical programming*, 88(3), 411-424.

Ben-Tal, A., &Nemirovski, A. (2002). Robust optimization–methodology and applications. *Mathematical Programming*, 92(3), 453-480.

Bertolini F., Rebulla P., Porretti L.,& Murphy S. (1992). Platelet quality after 15-day storage of platelet concentrates prepared from buffy coats and stored in a glucose-free crystalloid medium. *Transfusion*, 32, 9–16.

Bertsimas, D., &Sim, M. (2003). Robust discrete optimization and network flows. *Mathematical programming*, 98(1-3), 49-71.

Bertsimas, D., &Sim, M. (2004). The price of robustness. *Operations research*, 52(1), 35-53.

Brandeau M. L., Sainfort, F., & Pierskalla, W. P. (2004). Operations research and Health Care: a

Handbook of methods and applications. *Springer Science & Business Media*, 70.

Deuermeyer, B. L., Pierskalla, W. P. (1978) .A By-Product Production System with an Alternative. *Management Science*, 24(13), 1373-1383.

Drackley, A., Newbold, K. B., Paez, A. & Heddle, N. (2012). Forecasting Ontario's blood supply and demand, *Transfusion*, 52(2), 366-374.

Duan, Q., &Liao, T. W. (2014). Optimization of blood supply chain with shortened shelf lives and ABO compatibility. *International Journal of Production Economics*, 153, 113-129.

Fischetti, M., &Monaci, M. (2009). Light robustness. In Robust and online large-scale optimization, *Springer Science & Business Media*, 61-84.

Ghandforoush, P., & Sen, T. K. (2010). A DSS to manage platelet production supply chain for regional blood centers. *Decision Support Systems*, 50(1), 32-42.

Gunpinar, S., & Centeno, G. (2015). Stochastic integer programming models for reducing wastages and shortages of blood products at hospitals. *Computers & Operations Research*, 54, 129-141.

Haijema, R., Van Der Wal, J., & Van Dijk, N. M. (2007). Blood platelet production: Optimization by dynamic programming and simulation. *Computers & Operations Research*, 34, 760-779.

Haijema, R., Van Der Wal, J., & Sibinga, C. S. (2009). Blood platelet production with breaks: Optimization by SDP and simulation. *International Journal of Production Economics*, 121,464-473.

Jokar, A., & Hosseini-Motlagh, S. M. (2015). Impact of Capacity of Mobile Units on Blood Supply Chain Performance: Results from a Robust Analysis. *International Journal of Hospital Research*, 4(3), 109-114.

Kaiser Health News, 2015. *http://www.kaiserhealthnews.org/Daily-Reports/2012/June/13/health-care-costs.aspx [accessed 01.05.16]*.

Levin, E., Culibrk,B., Gyöngyössy-Issa, M., Weiss, S., Scammell, K., LeFresne, W., Jenkins, C., & Devine, D. V. (2008). Implementation of buffy coat platelet component production: comparison to platelet-rich plasma platelet production. *Transfusion*, 48(11), 2331-2337.

Nagurney, A., Masoumi, A., & Yu, M. (2012). Supply chain network operations management of a blood banking system with cost and risk minimization. *Computational Management Science*, 9, 205-231.

Rastegar-Panah, M. M., Hosseini-Motlagh, S. M., Babaei, E., and Noughani, F. (2013). Use and usefulness of social network analysis in the primary health context. *International Journal of Hospital Research*, 2(4), 177-186.

Riahi, N., Hosseini-Motlagh, S. M., & Teimourpour, B. A. (2013). Three-phase Hybrid Times Series Modeling Framework for Improved Hospital Inventory Demand Forecast. *International Journal of Hospital Research*, 2(3), 133-142.

Schreiber, G. B., Schlumpf, K. S., Glynn, S. A., Wright, D. J. , Tu, Y., King, M. R., Higgins, M. J., Kessler, D., Gilcher, R., Nass, C. C., Guiltinan, A. M., and L. B. I. R. E. D. S. (2006). National Heart, "Convenience, the bane of our existence, and other barriers to donating," *Transfusion*, 46, 545-553.

Singh, C. (1982). Convex programming with set-inclusive constraints and its applications to generalized linear and fractional programming. *Journal of Optimization Theory and Applications*, 38(1), 33-42.

Soleimany Ferizhandy, A. (2011). Platelet activation of platelet concentrates derived from buffy coat and apheresis methods. *Transfusion and Apheresis Science*, 44, 11‑13.

The World Bank, 2015. *<http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS> [accessed 01.05.16]*.

Tofighi, S., Torabi, S. A., & Mansouri, S. A. (2016). Humanitarian logistics network design under mixed uncertainty. *European Journal of Operational Research*, 250(1), 239-250.

Van Dijk, N., Haijema, R. Van Der Wal, J., & Sibinga, C. S. (2009). Blood platelet production: a novel approach for practical optimization. *Transfusion*, 49, 411-420.

Vassallo, R. R., & Murphy, S. (2006). A critical comparison of platelet preparation methods. *Current Opinion in Hematology*, 13(5), 323-330.

Zahiri, B., Torabi, S. A., Mousazadeh, M., & Mansouri, S. A. (2015). Blood collection management: Methodology and application. *Applied Mathematical Modelling*, 39(23), 7680-7696.