SIMULATION-OPTIMIZATION MODEL FOR PRODUCTION PLANNING IN THE BLOOD SUPPLY CHAIN

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ABSTRACT

Production planning in the blood supply chain is a challenging task. Many complex factors such as uncertain supply and demand, blood group proportions, shelf life constraints and different collection and production methods have to be taken into account, and thus advanced methodologies are required for decision making. This paper presents an integrated simulation-optimization model to support both strategic and operational decisions in production planning. Discrete-event simulation is used to represent the flows through the supply chain, incorporating collection, production, storing and distribution. On the other hand, an integer linear optimization model running over a rolling planning horizon is used to support daily decisions, such as the required number of donors, collection methods and production planning. This approach is evaluated using real data from a blood center in Colombia. The results show that, using the proposed model, key indicators such as shortages, outdated units, donors required and cost are improved.

Keywords: production planning, blood supply chain, blood collection, simulation, optimization

1 INTRODUCTION

The blood supply chain involves the collection, production, storing and distribution of blood and its components. Special features make the blood supply chain different from typical industrial supply chains and render it a very challenging study area. In many countries, blood is considered a highly scarce resource since only a small percentage of the eligible population actually donates blood. In the US this percentage is about 10%; however, in medium- and low-income countries this rate is much

lower [1]. A recent review by Osorio et al. [2] includes 110 papers containing quantitative models that study different aspects of the blood supply chain, and identifies several gaps in this literature. In particular, only eight of the 110 papers focus on the production stage. In this paper we address this research gap and present an integrated simulation-optimization model to support strategic and operational decisions in production planning in the blood supply chain.

The most common collection method is called whole blood donation, which consists of extracting approximately 450 ml of blood from a donor into a collection bag. There are different types of collection bag, each yielding different blood products. The whole blood is centrifuged and, depending on the type of bag used for collection, is *fractionated* (split up) into different components such as red blood cells (RBCs), platelets, cryoprecipitate and plasma. An alternative collection method is apheresis, which directly withdraws a single blood component from a donor. Apheresis is considerably more efficient than fractionation, but has the disadvantages of higher costs and longer collection times. The chosen collection method largely determines the production method, with the exception of blood units collected using a quadruple bag. In this case there are two alternative fractionation methods, and a decision is normally made after the unit has arrived at the blood center.

Given the range of production alternatives, uncertainty in supply and demand throughout the year, and special features such as perishability, it is essential to develop efficient methods for production planning which consider the different collection methods, fractionation alternatives and donation rates. There is a trade-off between the indicators for outdates and stockouts in the blood supply chain: very large inventories of blood products can generate outdated units, but low inventories can cause stockouts, decreasing the service level (and potentially putting patients at risk). Furthermore, blood supply chain planning tools need to consider not only inventory policies that take into account uncertainty and seasonality, but also the trade-off between efficiency and cost for the different collection/production alternatives.

In this paper we present a model that combines discrete-event simulation (DES) with integer linear programming (ILP) to support decision making in the blood supply chain. The model includes several characteristics that have not been taken into account in previous research, for example multiple products and different collection/production methods, and the impact of variability. The model can be used in two modes: firstly at a strategic level, to enable blood center managers to evaluate different resource allocation policies, and secondly at an operational level, to set daily collection and production targets. The model outputs in both cases are the standard key performance indicators for blood supply chains: stockouts, outdates, number of donors, and production costs. In both modes, the ILP calculates the optimal required number of donors each day by blood group and collection/production method, whereas the DES represents the daily operations of the blood center, incorporating uncertainty in supply and demand, based on probability distributions fitted from historical data routinely collected in all blood centers.

The DES does not depict the detailed minute-by-minute operations of the center, but aggregates these at a daily level. The ILP is run every day over a 7-day planning horizon: thus for example the ILP is run at the start of day 5 and produces collection/production targets for days 5 to 11. The DES then simulates the center's operations on day 5, based on a) the system state at the end of day 4 (i.e. the numbers of units of each blood product in stock, by age and blood type) and b) the optimal donor and production targets for day 5. At the start of day 6, the process repeats: the ILP is run for days 6 to 12, and the DES simulates the center's operations on day 6, based on the system state at the end of day 5 and the optimal targets for day 6.

In strategic mode, the combined DES/ILP model can be run for many months in order to evaluate different collection and production policies: the model is initialized by running the DES for a month to obtain the system state at the start of day 1. However in operational mode, the simulated system state information passed to the DES at the start of day t is replaced by "live" data from the blood

center for day *t* -1. In this case no warm-up is required since real data will be used to initialize the system state at the start of day 1. Moreover, in operational mode only the collection/production plan for Day *t* will actually be implemented, since the ILP will be run again on Day *t*+1, potentially resulting in a different collection/production plan for that day depending on the real system state at the end of day *t*. The model is tested for three different scenarios which make increasingly realistic assumptions about a blood center's ability to achieve the desired optimum values. The results are compared with a baseline scenario which uses observed data and the collection/production rules used by a real blood center in Colombia.

Our computational results are obtained using data from the Hemocentro Distrital blood center in Bogota, Colombia. The blood supply chain in Colombia is decentralized and there are many public and private blood centers; in addition, some large public and private hospitals also operate their own internal blood banks. The Hemocentro Distrital is the second largest blood center in Colombia. Annually, it collects about 40,000 blood units and supplies over 70,000 blood products to more than 18 hospitals. In our study period (July 2013 - June 2014), the total number of stockouts of RBCs was 9,490 units; however, in the same period, the outdated number of units was 1,989 for RBCs and 1,736 for platelets. This means that some of the collected units were not used while at the same time some hospital requests were not met. Hence, collection and production planning can be improved in order to make better use of resources, reducing both shortages and outdating. Our model addresses these problems.

This paper is structured as follows. Section 2 describes the literature related to the collection and production stages as well as integrated models. Section 3 presents the detail of our framework, as well as a description of the simulation model and the mathematical formulation of the optimization model. Sections 4, 5 and 6 present some of the features of the case study, the description of the scenarios analyzed and the model results, respectively. Finally, Section 7 presents the main conclusions of this research, including modeling issues, as well as further extensions to this work.

2 LITERATURE REVIEW

In recent years the literature related to the blood supply chain has been increasing. However, some areas have received less attention than others. The blood supply chain can be split into four echelons or stages: collection, production, inventory and distribution. Traditionally, most research interest has focused on inventory policies, and the least-studied stage is production. Some papers have considered several echelons, so-called integrated models. In this section, the literature on the collection and production stages is presented, as well as integrated models for these stages.

2.1 Collection Stage

The literature in the collection stage covers various aspects such as the configuration of collection points, collection policies and collection methods, and special situations such as disasters and emergencies. In Pratt and Grindon [3] and Brennan et al. [4], different configurations of collection points for different donor arrival rates are evaluated. Brennan et al. [4] extend this work, considering staff allocation and working place policies. Both articles use simulation as the main methodology to measure the impact of changes in conditions through indicators such as the time taken in different stages of the collection process. In Michaels et al. [5] different strategies of donor scheduling are studied. Other researchers have studied collection policies and collection methods and their impact on the performance indicators of the blood supply chain. Lowalekar and Ravichandran [6] develop a simulation model to evaluate different collection policies. One of the main conclusions of this work is that it is not necessarily beneficial to collect as much blood as possible. Alfonso et al. [7,8] also

develop a simulation model aimed at determining the capacity and staff required. Two recent papers, Alfonso and Xie [9] and Alfonso et al. [10] present mathematical models for collection planning. The aim of the first model is to minimize products obtained from external suppliers. Madden et al. [11] evaluate the impact of two different collection methods for RBCs, using fractionation and double red blood cells donation by apheresis (2RBC) (fractionation produces just one unit of RBCs while 2RBC produces two units). Ghandforoush and Sen [12] use a nonlinear integer program to support the daily process of platelet production planning. Finally, Gunpinar [13] minimizes the distance of collecting blood units from remote donors. Other papers such as Glynn et al. [14], Sonmezoglu et al. [15], Boppana and Chalasani [16] and Jabbarzadeh et al. [17] present quantitative models aimed at studying blood collection aspects of disaster and emergency situations. However, none of these studies have considered the multiple alternatives available for collecting blood and blood products, which is one of the key features of the proposed models.

2.2 Production Stage

As mentioned previously, the production stage has received little attention from researchers. Some articles have studied aspects such as production alternatives, single product production and platelet production as well as production capacity and internal processes. The first studies that consider multiple products are presented by Deuermeyer and Pierskalla [18] and Deuermeyer [19] who develop an analytical model to minimize the production costs of RBCs and platelets. In this paper, production decisions are associated with different production processes and are defined according to the initial inventories of each product. Some of the production models have focused exclusively on single products. Sirelson and Brodheim [20] use simulation to develop profile graphs, where inventory levels are associated with accepted shortage and outdating rates. Katz et al. [21] propose an equation to define a platelets production function. This function is based on historical demand and deviations for each day as well as planned inventory and service levels. Finally, Ledman and Groh [22] develop production planning rules considering demand mean, variability and collection schemes. This paper introduces concepts that had not been previously considered, such as different collection policies. Special attention has been paid to platelets in the past decade. Haijema et al. [23], Haijema et al. [24] and van Dijk et al. [25] develop a Markovian model to represent decisions on production and inventories of platelets. Multiple periods, special periods such as weekends and different types of demand are included in the model. Dynamic programming and local search algorithms are used as solution methods, depending on the problem size. Finally, Baesler et al. [26] present a simulation model to study capacity and support decisions on capacity expansion, in terms of resource utilization and internal waiting times and queues. Most of these studies consider only red blood cells or platelets. Our model considers the four main blood products as well as different fractionation alternatives and collection methods to obtain them.

2.3 Integrated Models

Most literature in the blood supply chain is focused on individual echelons and does not consider relationships between the different stages. For example, models for collection rarely consider production and distribution policies. A few, more recent, publications have aimed to connect donors with recipients by considering flows of blood and blood products throughout the supply chain. Different methodologies have been used, such as simulation, optimization and hybrid approaches to study and improve the blood supply chain. One of the main approaches to represent and study the blood supply chain is discrete event simulation (DES). Page [27], Rytilä and Spens [28], Katsaliaki and Brailsford [29], Yegül [30] and Baesler et al. [31] use DES to evaluate and improve different aspects of the blood supply chain such as inventory allocation, recycling blood, crossmatching and

mismatching rules, collection targets, and transshipments. The standard performance indicators used to measure improvements are the numbers of outdated units, stockouts and emergency orders, and of course cost. Another simulation paradigm used to study the blood supply chain is Monte Carlo simulation. Using this methodology, Lowalekar and Ravichandran [32] consider different strategies, including fixed and variable collection quantities. In the production stages, the authors evaluate different fractionation rates. On the other hand, Simonetti et al. [33] combine DES and Monte Carlo simulation to study different issuing policies, evaluating availability and shortage indicators. Mathematical programming is used by Nagurney et al. [34] to optimize the whole blood supply chain. This model considers the blood supply chain as a network problem, defining different nodes, arcs and flows to represent the stages in the supply chain. An extension of this work is presented in Nagurney and Masoumi [35], including discard rates and arc capacities. In addition, Abdulwahab and Wahab [36] propose a combination of methodologies such as the newsvendor problem, linear programming and approximate dynamic programming to address the platelets inventory problem. Finally, multi-objective approaches and simulation optimization methodologies have been used: Lang [37] uses a combination of simulation and heuristic methodologies to evaluate the impact of both transshipment and substitution.

3 METHODOLOGY

The combination of simulation and optimization is a powerful approach for capturing the complex features of supply chain systems. This approach can be implemented in various ways, depending on the simulation paradigms chosen. Examples can be found in Nikolopoulou and Ierapetritou [38], Santoso et al. [39] and Almeder et al. [40] for agent-based simulation, Monte Carlo simulation and DES, respectively. In the blood supply chain, optimization models have been used less frequently than in industrial supply chains. Approaches such as dynamic programming have been used in the blood supply chain to study the case of platelets, as seen in Haijema et al. [23], Haijema et al. [24] and more recently in Abdulwahab and Wahab [36]. The shelf life of platelets is only five days, making it possible to apply analytical techniques. However, the shelf life of red blood cells is 42 days, and thus the problem size is too large for exact solution, since the age of the products must be tracked throughout the planning horizon, greatly increasing the number of decision variables in the model. In addition, the combination of integrality constraints (since the decision variables include donors and blood units), uncertainty, multiple time periods and multiple products make it even more challenging to apply exact solution methods. On the other hand, DES models are ideally suited to representing complex stochastic systems of this nature, although of course there is no guarantee of finding an optimal solution with DES. The combination of simulation and optimization offers a practical way to handle complex decisions in the blood supply chain.

The simulation model was developed using the Anylogic® simulation software package, probability distributions were fitted using @RiskTM and the optimization models were solved using the Java interface of the Gurobi Solver

3.1 Simulation-Optimization Framework

In our framework, as outlined in Section 1, simulation is used to represent the daily behavior of the real-world system, incorporating variability in donation and demand. Features such as perishability, blood type proportions and multiple products are included in the DES model. Mismatching and crossmatching are not included, since they only become relevant in the hospital when a specific request is made by a physician, and are thus outside the scope of this model. Optimization is used to support decisions concerning the required number of donors (either in total or broken down by blood

group) and the associated collection and production methods, in order to minimize the production cost. The proposed methodology can be classified as an "Iterative Optimization-based Simulation (IOS)" according to the taxonomy proposed in Figueira and Almada-Lobo [41]. In our case, the ILP is run at the start of every day, and the DES then implements the resulting solution for that day. The sole purpose of the DES is to generate the "system state" at the start of the following day: this then becomes part of the input required by the ILP for the next day.

3.2 Assumptions

The model presented in this paper includes many assumptions. Firstly, some general assumptions:

- All the required data will be available on a daily basis.
- The collection teams will follow the collection goals obtained from the optimization model.
- Special cases such as natural disasters or epidemics that decrease historical donation rates are excluded.
- Demand follows historical patterns and can be predicted using standard forecasting techniques.

Secondly, some reasonable assumptions are made about donor arrivals and demand, as follows:

- Donor arrivals are distributed throughout the day, and follow historical rates by day of week.
- Donor blood types follow historical proportions.
- There is always sufficient capacity to process the target number of donors.
- Donors can be deferred, depending on the scenario analyzed.
- Donors from specific blood groups can be targeted and will donate.
- No additional donor campaigns are run other than normal daily collection.
- Demand can be partially satisfied. Hospitals always accept the products dispatched by the blood center.
- Demand follows historical behavior throughout the year, taking seasonality into account.
- Substitution of products is made at the hospitals.
- Returns of blood products to the blood center are not allowed.

3.3 Simulation – Optimization Interaction

Figure 1 depicts the interaction between the DES and the ILP. After initialization, the model runs interactively in one-day time steps with a 7-day planning horizon. This rolling horizon scheme helps to reduce the impact of uncertainty in the ILP model. The reason for a seven day period is to account for the fact that collection rates vary by day of week and other factors. In addition to the system state at the start of day t, the ILP also receives external information: whether collection is possible on days $t,...,t+6$ (for example, whether these days are working days or holidays), minimum inventory targets, proportions of donations by day of week and the predicted demand for days $t,...,t+6$. Based on this information, the ILP is run and the results (the optimum number of donors required by blood group and collection method) are sent to the simulation model. The DES model then simulates day t and passes the results (the system state at the end of day t) back to the ILP model ready for the start of day $t+1$. In strategic mode, the cycle then repeats until the end of the analysis period (one year in our experiments).

The optimal donor information from the ILP is treated in three different ways in the DES, depending on the scenario analyzed. In the first scenario, the required number of donors is broken down by blood group and collection method. In the second scenario we only consider the total number of donors, and the proportion of these donors allocated to each collection method. Finally, in the third

scenario we only consider the donor proportions for each collection method. This is explained in detail in Section 5.

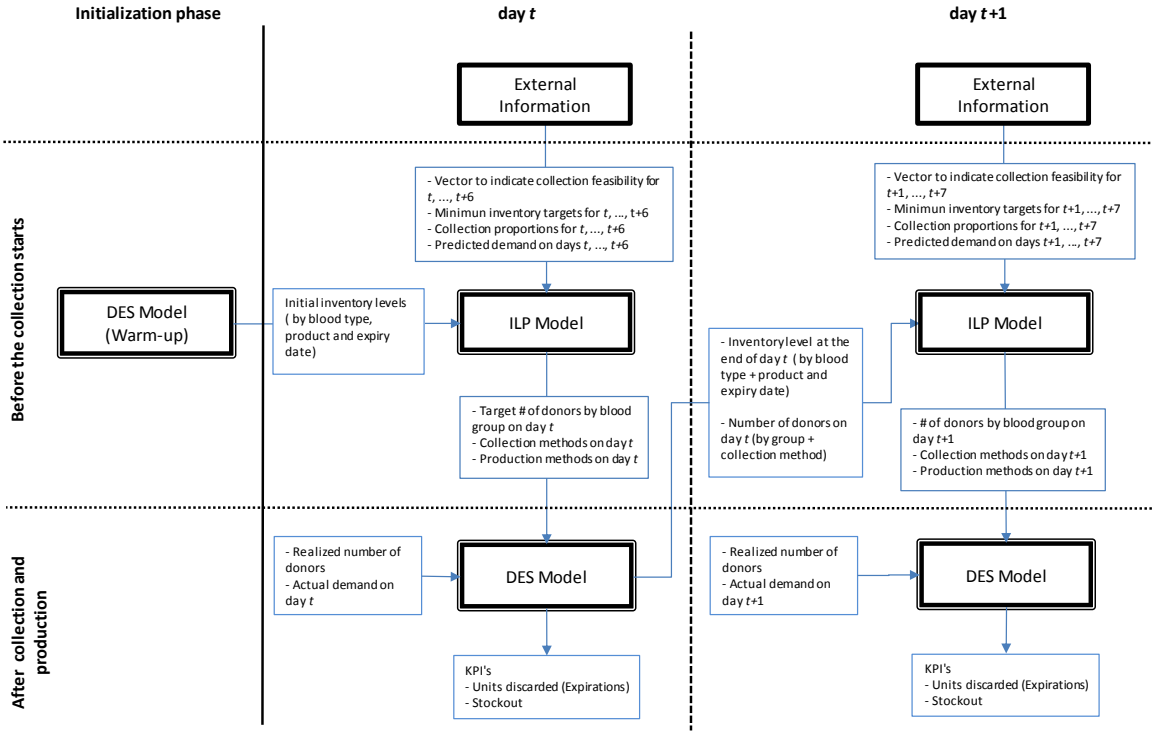

Figure 1: Simulation-optimization framework proposed for strategic level production planning in the blood supply chain.

In a real application used in operational mode, as previously stated, the simulation output at the end of day *t* is replaced by the live data from the real system. The ILP model must be run every day by the decision-maker responsible for collection before the collection starts. The results of the optimization model determine the collection goals for the teams and need to be shared with the production section of the blood center. For practical implementation, the optimization model would need to be integrated into the central information system of the blood bank in order to receive up-to-date information every time it is run. All the information required by the model is normally available in blood bank information systems and the routine periodic reports produced by blood centers.

3.4 Incorporating variability

The sources of uncertainty, in the real system and in the model, relate mainly to demand for blood products and the arrival of donors at the collection stage. However, in our first set of experiments (see Section 5) both demand and donor arrivals are replaced by empirical data, in order to compare the actual performance of the Hemocentro Distrital in the study period with the results that could have been achieved if our model had been applied. In the our second set of experiments, probability distributions are fitted to historical data on donor arrivals and the realized values are obtained by sampling.

3.5 DES Model

Figure 2 presents the flow diagram of the different stages in the DES model. The blood supply chain is highly complex, and each stage involves several interacting processes. Since this study focuses on daily collection and production policies, all transactions are aggregated on a daily basis. The simulation model represents a typical blood center that provides blood products for several demand points. The collection, production, inventory and distribution processes are included in varying levels of detail. As mentioned earlier, processes carried out in hospitals are not included, so the distribution stage in particular is modeled at a very high level.

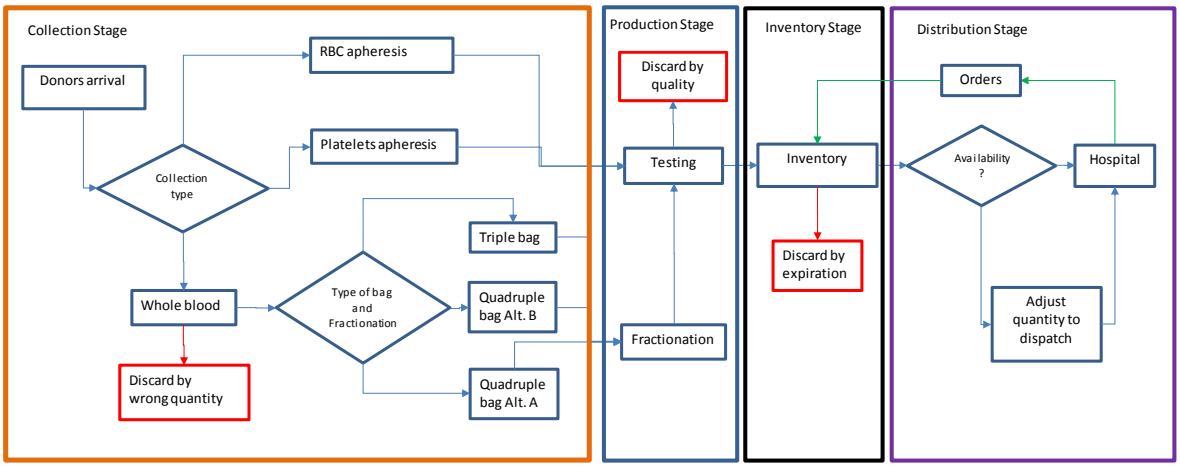

Figure 2: Flow diagram of the blood supply chain

3.5.1 Collection Stage

Donors arrive and are assigned to a collection method according to the chosen scenario. The donor arrival rate corresponds to the historical data from the studied blood center. The collection alternatives are whole blood donation, RBC apheresis and platelets apheresis. For whole blood donations, the type of bag to be used is also considered, since (with the exception of quadruple bags) the production processes depend entirely on the type of bag. Since whole blood collected in quadruple bags can be fractionated in two different ways, in our model this fractionation decision, alternative A or B, is made at the collection stage, as shown in Table 1. This is a very minor assumption in practice, and avoids the need for another index set which would greatly increase the problem size. Donor blood groups are defined according to historical donation rates in the blood center. A discard rate for whole blood units, based on historical data, is included before fractionation, since errors during collection can result in blood units that do not meet the volume requirements. The total number of units collected is proportionally reduced by this discard rate in order to obtain the final number of units that will proceed to the production stage.

3.5.2 Production Stage

The simulation of the production stage represents the testing and fractionation processes. Products obtained by apheresis do not need fractionation, but still go through the production stage for testing and quality control purposes. Historical discard rates are applied here too, to represent the different reasons for discarding collected blood units during production, such as reactive tests and substandard quality. This stage also includes a period called quarantine, where the products are isolated while samples are tested in order to identify diseases and other defects. One unit of whole blood collected

in a triple bag yields one unit of RBCs and one unit of plasma. For quadruple bags, Alternative A yields one unit of RBCs, one unit of plasma and one unit of platelets, whereas Alternative B generates one unit of RBCs and one unit of cryoprecipitate. Apheresis generates only one type of product. The production alternatives and the resulting number of units of each product are presented in Table 1. We note that, in general, apheresis for platelets can yield up to 12 standard units, but in the Hemocentro Distrital, normally only six units are collected.

Table 1: Blood products obtained in each process

Process	RBCs	Plasma	Platelets	Cryoprecipitate
Triplex bag	1	1		
Quadruple bag – Alternative A	1	1	1	
Quadruple bag – Alternative B	1			1
RBC by apheresis	2			
Platelets by apheresis			6	

3.5.3 Inventory

In the inventory stage, the daily operation of the inventory levels for each product is represented. After quarantine is complete (in our case study, at approximately 5:00 pm each day), products are added to the inventory and are available to be used. At the beginning of each working day, all outdated units of each product are removed from the inventory to be incinerated. In our case study, orders are normally received by 10:00 am and are dispatched throughout the day. However this level of detail is not captured in the model, which is concerned only with total transactions per day. Thus, for the purposes of production planning, demand is defined for each day as the sum of all individual orders, both normal and emergency. The products are dispatched based on a first-in-first-out rule. The inventory system is defined as periodic where the review period is one day. Inventory levels are checked daily and a replenishment order up to a level S is placed. The optimization model operates on a daily basis. It is possible to operate a periodic inventory system with a different review time period, but it is of course necessary to adhere to the shelf life constraints. Some hospitals use continuous inventory systems. In the case of blood centers, the most widely used system is periodical with one-day period [2], probably because this synchronizes with collection, discarding, and distribution, which all usually operate on a daily basis. Thus our model is generally applicable to most blood centers.

3.5.4 Distribution

Finally, distribution is represented at a high level: only the dispatching rules are simulated, since the allocation of blood to individual patients is performed within hospitals and is outside the scope of our model. Given the critical importance of having some inventory on hand at all times in the blood center, a minimal safety stock is defined for each product. The dispatching rule states that, for every day, the maximum quantity that can be dispatched is the difference between the available quantity and the minimum stock (S) for each product. The choice of the values of S for different blood products is a managerial decision and is an external parameter in our model.

3.5.5 Data Required by the Model

The information required to run the model consists of both historical and current data relating to the analyzed system. At the collection stage, the model needs information related to the structure and

capacity of the collection points, historical data of donor arrivals for each day, by blood group, the collection methods used, and the discard rates. At the production stage, the model requires information on the capacity of the production centers, the efficiency of the production processes, the production costs and inventory policies. At the inventory and distribution stages, it is necessary to know daily historical demand for each blood product by blood group and current inventory levels of each product. Historical data on donor arrivals by blood group and demand for blood productions allow patterns to be identified over time, and probability distributions to be fitted to represent the uncertain aspects of the system. On the other hand, discard rates, shelf life information and inventory policies define some of the model parameters which represent a specific blood center. Finally, in order to compare the performance of the proposed models, knowledge of current costs, outdate and shortage rates, and number of donors required is needed. We note that all these data are normally routinely recorded and stored by blood centers, and would be readily available (as they were in our case study).

3.6 ILP Model

The optimization model supports decisions on collection and production. The model considers blood group proportions, demand, inventory, capacity and shelf life constraints, and seeks to optimize a cost function composed of production costs, penalties for expired units, number of stockout units and violation of the blood group proportionality constraint. The decision variables are the number of donors required per day, by blood group and production method. Auxiliary variables are defined to calculate production and inventories to ensure the correct balance of products throughout production planning.

Definition of Sets

K = Collection alternatives – indexed by *k*.
J = Products required – indexed by *j*.
T = Planning horizon – indexed by *t*.
I = Blood types – indexed by *i*.
S = Set of values for the shelf life alternatives of platelets – indexed by *s*.
P = Set of types of platelets – indexed by *p*.

The indexed elements for each set can be found in Appendix B.

Model Data (Information Provided)

A_{ik} = Number of donors of blood type *i* served by process *k* on the previous day, $i \in I, k \in K$.
B_{jt} = Predicted demand for product *j* in period *t*, $j \in J, t \in T$, [Units of product]. This parameter is obtained from the actual forecast demand B'_{jt} after taking into account the discard rate α_j, and is calculated as $B_{jt} = B'_{jt}\ (1+\alpha_j),\ \forall j \in J, \forall t \in T$.
C_{ikj} = Number of units of product type *j* obtained from applying process *k* to a unit of blood type *i*, $i \in I, j \in J, k \in K$.
D_i = Proportion of blood type *i* in the population studied, $i \in I$.
E_k = Collection cost for one donor assigned to collection method *k*, $k \in K$ [US$].
F = Daily capacity for serving whole blood donors, on days when collection is possible.
G = Daily capacity for serving RBC apheresis donors (as above).
H = Daily capacity for serving platelets apheresis donors (as above).
α_j = Historical discard rate of product $j, j \in J$.

L = Penalty cost for each unit of product not available [US$].

M_j = Minimum inventory of product j, $j \in J$. (This parameter is equivalent to S, as defined in Section 3.5.3.)

N_j = Initial inventory of product j, $j \in J$ [Units].

O_t = Observed proportion of donations in period t, $t \in T$. Each day of the week has a different behavior, but the order varies since it is a rolling horizon model.

Q = Penalty cost for each unit of platelet expired [US$].

R_t = 1 if it is possible to collect blood in period t, 0 otherwise, $t \in T$. This parameter represents the possibility of collecting blood for each day of the planning horizon, given public holidays and special days where collection is not carried out.

X_{ps} = Initial inventory of type p platelets with s remaining days of shelf life, $p \in P$, $s \in S$. [Units]. Shelf life constraints are only considered for platelets.

V = Maximum daily number of donors.

W = Maximum weekly number of donors.

Z = Penalty for violating the soft constraint on proportionality (Constraint (15)) [US$].

Decision Variables

x_{ikt} = Required number of donors of blood type i, for collection using process k in period t, $i \in I, k \in K, t \in T$.

Auxiliary Variables

q_{jt} = Number of units of product j produced in period t (and available in period t+1), $j \in J, t \in T$.

i_{jt} = Number of units of product j in inventory at the end of period t (and available in period t+1), $j \in J, t \in T$.

y_{jt} = Estimated stockout of product j in period t, $j \in J, t \in T$ [Units].

δ_{it}^{-} = Slack variable for the soft constraint of blood type i in period t, $i \in I, t \in T$.

δ_{it}^{+} = Surplus variable for the soft constraint of blood type i in period t, $i \in I, t \in T$.

p_{pt} = Estimated stockout of platelets of type p in period t, $p \in P, t \in T$ [Units].

r_{pst} = Number of platelets of type p with shelf life s in the inventory in period t, $p \in P, s \in S, t \in T$.

u_{pst} = Number of platelets of type p with shelf life s in period t used to meet demand, $p \in P, s \in S, t \in T$.

e_{pt} = Number of platelets of type p expired in period t, $p \in P, t \in T$.

Objective Function:

$$\text{Minimise } W = \sum_{i \in I} \sum_{k \in K} \sum_{t \in T} E_k \, x_{ikt} + Q \sum_{t \in T} \sum_{p \in P} e_{pt} + L \sum_{t \in T} \sum_{j \in J} y_{jt} + Z \sum_{t \in T} \sum_{i \in I} \delta_{it}^{+} \quad (1)$$

The first term in equation (1) computes the production cost while the second and third terms contain the penalties for outdated units and stockouts, respectively. The last term penalizes the violation of the proportionality constraint.

Constraints

$$\sum_{i \in I} \sum_{k=0,1,2} x_{ikt} \leq FR_t, \qquad \forall\, t \in T \tag{2}$$

Constraints (2) guarantee that the collection of whole blood donations does not exceed the capacity available. For RBCs and platelets obtained from apheresis, the constraints become $X_{i3t} \leq GR_t, \forall\, i \in I, \forall\, t \in T$ and $X_{i4t} \leq HR_t, \forall\, i \in I, \forall\, t \in T$, respectively.

$$q_{j0} = \sum_{i \in I} \sum_{k \in K} A_{ik} C_{ikj}, \qquad \forall\, j \in J \tag{3}$$

$$q_{jt} = \sum_{i \in I} \sum_{k \in K} x_{ikt-1}\, C_{ikj}, \qquad t \geq 1, \forall\, j \in J \tag{4}$$

Constraints (3) and (4) represent the production balance constraints for $t = 0$ and $t > 0$ respectively. The actual number of donors on the previous day is multiplied by the parameter C_{ikj} that defines the quantity of each product to be obtained from the different alternatives. For $t = 0$, actual information about the collection on the previous day is assumed to be available. For $t > 0$, the production is a function of the collection target of the previous day. Products produced in period t will only become available in period t+1, because of the production and testing processes.

$$i_{j0} - y_{j0} = N_j - B_{j0}, \qquad t = 0, j \neq 16, 17 \tag{5}$$

$$i_{jt} = i_{jt-1} + q_{jt-1} + y_{jt} - B_{jt}, \qquad t > 0, j \neq 16, 17 \tag{6}$$

In Constraints (5) and (6) the initial inventory is decreased by the quantity used (demand – stockout) and this is equal to the number of units in inventory at the end of the period (which will be available at the beginning of the next period). In periods where $t > 0$ the constraint balance is modified by the addition of the number of units produced on the previous day. Platelets (indexed by k = 16 and k = 17) are excluded from this balance constraint since additional features such as remaining shelf life must be considered.

$$e_{p0} = X_{p0} - u_{p00}, \qquad \forall\, p \in P, s = 0, t = 0 \tag{7}$$

$$r_{ps-1,0} = X_{ps} - u_{ps0}, \qquad \forall\, p \in P, s > 0, t = 0 \tag{8}$$

$$e_{pt} = r_{p0t-1} - u_{p0t}, \qquad \forall\, p \in P, s = 0, t > 0, t \in T \tag{9}$$

$$r_{ps-1,t} = r_{pst-1} - u_{pst}, \qquad \forall\, p \in P, s \neq 0, 4, t > 0, t \in T \tag{10}$$

$$r_{0s-1,t} = r_{0s,t-1} + q_{16t-1} - u_{0st}, \qquad s = 4, t > 0, t \in T, j = 16, p = 0 \tag{11}$$

$$r_{1s-1,t} = r_{1s,t-1} + q_{17t-1} - u_{1st}, \qquad s = 4, t > 0, t \in T, j = 17, p = 1 \tag{12}$$

Constraints (7) – (12) define the balance of platelets considering inventory, production, expiration and use. In Constraints (7) and (9) ($s = 0$) the number of units available at the beginning of the period is decreased by the number of platelets used with a shelf life of zero; the remaining quantity will be outdated and will not be available in the next period. In Constraints (8) and (10), the number of units available is also decreased by the quantity used; however, in this case, the remaining quantity will be the initial inventory in the next period. The shelf life of the platelets in Constraints (8), (10), (11) and (12) is updated at the end of the period; the new shelf life will be s-1. Finally, for the shelf life index s = 4 (Constraints (11) and (12)), the constraint is slightly different, since a new value q_{lt-1} is incorporated into the balance constraint. This value corresponds to the quantity of platelets produced in the previous period.

$$\sum_{s \in S} u_{0st} - p_{0t} = B_{16t}, \qquad \forall\, t \in T, j = 16, p = 0 \tag{13}$$

$$\sum_{s \in S} u_{1st} - p_{1t} = B_{17t}, \qquad \forall\, t \in T, j = 17, p = 1 \tag{14}$$

Since platelets have different shelf lives, we include an auxiliary variable u_{pst} to specify the number of units of platelets of different ages. This allows the inventory to be updated while tracking the age of platelets. Constraints (13) and (14) define the number of units used as demand minus stockout.

$$\sum_{k \in K} x_{ikt} - \sum_{i' \in I} \sum_{k \in K} x_{i'kt}\, D_i + \delta_{it}^{-} - \delta_{it}^{+} = 0, \qquad \forall\, i \in I, \forall\, t \in T \tag{15}$$

$$\sum_{k \in K} x_{ikt} \leq D_i V, \qquad \forall\, i \in I, \forall\, t \in T \tag{16}$$

$$\sum_{i \in I} \sum_{k \in K} x_{ikt} \leq WO_t, \qquad \forall\, t \in T \tag{17}$$

$$i_{jt} \geq M_j, \qquad \forall\, j \in J, \forall\, t \in T \tag{18}$$

$$x_{ikt}, y_{jt}, p_{pt}, r_{pst}, u_{pst}, e_{pt}, q_{jt}, i_{jt} \in \mathbb{Z}^{+}, \delta_{it}^{-}, \delta_{it}^{+} \in \mathbb{R}^{+} \tag{19}$$

Constraints (15) and (16) guarantee one of the most important features of the blood supply chain: blood group proportionalities need to be met when production planning is considered. Constraints (15) guarantee the proportionality for each blood type for every day of the 7-day planning period. In order to keep the integrality of the variables, the constraint is relaxed by adding slack and surplus variables. The surplus variable is penalized in the objective function to try to maintain the proportionality conditions. Constraints (16) are introduced in order to control the quantity collected daily for each type. In addition, Constraints (17) limit the collection for each day according to historical rates. These constraints are necessary since, historically, days might have different behaviors. For instance, in the data obtained for the case study, the collection is higher on Wednesdays and Thursdays, while weekends are the lower collection days and the collection planning must to consider this feature. Finally, the minimum inventory is defined by Constraints (18) and domains are given in Constraints (19).

4 CASE STUDY

The Colombian National Blood Bank Network is comprised of 87 blood banks and 414 points for transfusion services [42]. Blood banks differ in size and types of services offered. Large public and private blood centers supplying products for several hospitals can be found in the large cities. Blood banks are also located within hospitals. The distribution centers are usually co-located with the blood banks. The Colombian system is highly decentralized, compared, for example, with the UK National Blood Service network, which consists of five large production centers and 15 stock holding units across the country [43]. Another feature of the Colombian system is the range of collection strategies across the country; each region defines the collection goals for blood and blood products using local decision rules. The highest proportion of platelets collected by apheresis in 2012 is represented by the Valle del Cauca region with 93%, followed by Antioquia with 42%. However, most regions collect platelets from whole blood donations. On the other hand, the highest proportion of RBCs produced

using apheresis processes is represented by the Tolima region with 8.24%, followed by 6.26% from Bogota. Again, most regions obtain RBCs exclusively from whole blood donations.

The Hemocentro Distrital comprises three main service areas: blood bank, tissue bank and cord blood bank. It is the second largest blood center and the unique multipurpose tissue bank in Colombia. The blood bank section is responsible for supplying blood products to more than 33 institutions, both public and private; however, priority is given to public hospitals in Bogota. During the analysis period (June 2013 to June 2014), 77,309 units of products were ordered, of which 56.6% were RBCs, 22.2% platelets, 19.2% plasma and 1.87% cryoprecipitate. The months of January and February are atypical: donations in these months are usually lower and the blood center can only meet part of the total demand. Therefore, the hospitals increase the quantity ordered, creating a distortion in real demand. The blood group proportionality in the observed data at the collection stage is as follows: O+ 60.9%, A+ 23%, B+ 7.92%, O- 4.22%, A- 1.72%, AB+ 1.54%, B- 0.51%, AB- 0.11%. In the case study system, hospitals can choose between products obtained by apheresis and those obtained from fractionation, and hence demand for these products is independent. During the study period, although apheresis collection processes were in use, information about demand for products obtained by apheresis was not available. Nevertheless, apheresis collection methods are included in the model for the sake of generality. In other blood service systems, it is possible to meet demand using products obtained from either fractionation or apheresis processes.

Quantitative information for modeling purposes was obtained from the information systems of the blood center as well as monthly indicator reports. Interviews conducted with the staff of the blood center were used to validate and to adjust the simulation model. Daily information about collection, including blood groups, demand and shipments for each product was obtained for the period June 2013 to June 2014. Monthly information about discard rates, shortage and outdating rates were also obtained. In order to generate a realistic initial inventory considering the age of the products, the model used a one-month warm-up period, without including demand. The results obtained from this warming-up period were validated with the staff. The collection behavior is different for each day of the week. In order to represent this feature, probability distributions were fitted for each day (Appendix A). A monthly adjustment factor was also applied to the values generated in order to represent the monthly seasonal behavior in the collection stage. In addition, a probability distribution was fitted for each product for each day, with the exception of cryoprecipitate where actual information was used in all the scenarios. In the case of blood groups, proportionality rates were applied for both collection and demand. The indicators presented in the results section were generated using 100 iterations of one year for each scenario; the values presented were calculated using 95% confidence intervals.

5 SCENARIOS

The model was tested for three different scenarios which make increasingly realistic assumptions about a blood center's ability to achieve the desired optimum values generated by the ILP:

- Scenario 1A: The blood center is able to recruit the optimal number of donors, by blood type and collection method
- Scenario 2A: The blood center can recruit the optimal number of donors but by collection method only
- Scenario 3A: The blood center can only control the optimal proportions for each collection method

The results obtained from these three scenarios are compared with the KPIs from a baseline scenario which uses the observed empirical data and the real decision rules in operation at the time in the Hemocentro Distrital. Table 2 presents the data used in the simulation of each scenario. With the exception of scenarios 1A and 2A, daily donor arrivals are obtained from the historical data from the blood center. The demand in all four scenarios is the actual observed demand for each product type, by blood group.

Table 2: Summary of scenarios: data used in simulation

Scenario	**Total number of donors**	**Donors by blood group**	**Collection method**	**Demand**
Baseline	Observed data	Observed data	Observed data	Observed data
1A	Determined by the ILP model	Determined by the ILP model	Determined by the ILP model	Observed data
2A	Determined by the ILP model	Proportions in the observed data	Determined by the ILP model	Observed data
3A	Observed data	Observed data	Determined by the ILP model	Observed data

Scenario 1A represents an idealized situation, since it assumes that each day, a blood center is able to recruit the precise number of donors by blood group specified by the ILP model. In practice it is impossible to have total control over the number of donors by blood group. However, this scenario helps decision-makers understand the importance of taking blood groups into account, and there are practical steps that blood centers can take to get closer to these ideal collection targets. They can target advertising at specific blood groups; they can defer donors whose blood type is not required at the time; and they can offer non-financial rewards for donation, e.g. gifts and souvenirs. Moreover, in countries where donors are paid, these incentives can be straightforward cash payments. We shall see that system performance improves considerably when collection is close to the results determined by the ILP model.

Scenarios 2A and 3A test the robustness of the ILP model in more realistic settings, since scenario 1A is almost certainly unachievable in practice. In scenario 2A, we only consider the total number of donors for each collection method, irrespective of blood group; this implies that no action is carried out to target the blood groups specified by the ILP. In this scenario, simulated donors are assigned blood groups sampled at random, following the observed proportions in the data. Finally, in scenario 3A the ILP results are used exclusively to define the proportion of donors assigned to each collection method; this means that no action is carried out to recruit even a target number of donors, let alone by blood group. In this scenario the numbers of simulated donors are simply the observed numbers in the data, and they are assigned blood groups in the same way as for scenario 2A. The results from these three scenarios show what would have happened if the ILP model had been fully or partially applied in the Hemocentro Distrital during the study period.

In order to test whether the model can be generalized to other time periods, the results for three new scenarios (1B, 2B and 3B) are presented in Section 6.5. In this case, the observed data for donor arrivals are replaced by samples from probability distributions fitted to the data. The results obtained using the distributions are very similar to those using actual data. This means that the analysis presented for scenarios 1A, 2A and 3A also applies for scenarios 1B, 2B and 3B respectively.

6 RESULTS AND DISCUSSION

6.1 Stockouts

Given the life-critical nature of blood products, stockouts are probably the most important indicator to measure blood supply chain performance. In the Hemocentro Distrital, demand for RBCs is considerably greater than supply. One of the reasons for this is that hospitals are risk-averse and overestimate requirements when they place orders. Table 3 shows the magnitude of stockouts in each scenario and the percentage improvement over the baseline, with 95% confidence intervals. The optimization model improves this indicator for all products in every scenario (shown by the green shading). The best results are obtained in the "ideal" scenario 1A. The percentage improvement for RBCs and platelets are slightly higher in scenario 3A than in 2A, since in scenario 2A the ILP specifies a lower number of donors than in reality (see Section 6.3). In all three scenarios a larger number of donors are assigned to platelet collection methods, and thus more platelets are produced and the number of stockouts is lower. However, this also causes deterioration in the outdating indicator, as we shall see in Section 6.2. Finally, use of the ILP totally eliminated stockouts of plasma and cryoprecipitate.

Table 3. Results: stockouts

Scenario		Stockout (Units)			
		RBC	**Platelets**	**Plasma**	**Cryoprecipitate**
Baseline		**9490**	**185**	**74**	**292**
1A	95% CI	7948 ± 29.8	110 ± 9.3	0 ± 0	0 ± 0
	% improvement	16.3%	40.3%	100.0%	100.0%
2A	95% CI	9006 ± 24.9	60 ± 5.2	0 ± 0	0 ± 0
	% improvement	5.1%	67.6%	100.0%	100.0%
3A	95% CI	8894 ± 22.3	53 ± 5.8	0 ± 0	0 ± 0
	% improvement	6.3%	71.2%	100.0%	100.0%

6.2 Outdated Units

The number of expired units is another important KPI for blood supply chains. Collecting blood is costly, and moreover donors do not like to think that their blood is being wasted: high expiration rates can have an undesirable impact on future donations. Results obtained for the expiration indicator are presented in Table 4. The ILP improves the expiration rate for RBCs in all three scenarios: the improvement is greater in scenario 3A than in scenario 2A, since in scenario 3A the number of donors by blood group follows the real observed data, which contains implicit empirical decisions that avoid collection for blood groups that are not required at the time. In contrast, in scenario 2A the blood groups are defined by strictly applying the blood group proportions from the historical data to a target number of donors.

Expiration is more critical for platelets, given their short shelf life. Expired platelets are lower in scenarios 1A and 2A, but higher in scenario 3A, because in this scenario the quantity of collected blood is not determined by the ILP (real data are used) and just the proportions of collection methods are applied. Clearly, if the quantity collected is too large there will be a surplus of final products which is critical in the case of platelets.

Table 4. Results: outdates

Indicator (Units)	Baseline	Scenario 1A		Scenario 2A		Scenario 3A	
		95% CI	%	95% CI	%	95% CI	%
Outdated RBC	**1989**	33 ± 0.7	98.3%	1182 ± 20.7	40.6%	1064 ± 12.5	46.5%
Outdated Platelets	**1736**	1152 ± 23.7	33.6%	1349 ± 20.3	22.3%	1875 ± 28.6	-8.0%

6.3 Number of donors

Table 5 presents the average number of donors, by blood group. The results show a modest improvement in the number of donors required. We note that in systems where demand can be supplied using both apheresis and fractionation, this indicator can be improved considerably. However, in our case the Hemocentro Distrital only uses fractionation. Scenario 3A uses exactly the same number of donors as the baseline. The parameter *W* in the ILP limits the total number of donors per week, since the aim is to achieve an improvement without using additional resources. It can be seen that the model is able to reduce donor numbers slightly, in addition to improving the stockout and expiration KPIs.

Table 5. Results: number of donors

Type	**O+**	**A+**	**B+**	**O-**	**A-**	**AB+**	**B-**	**AB-**	**Total**	**Improvement**
Baseline	**23541**	**8896**	**3059**	**1629**	**663**	**593**	**197**	**41**	**38619**	
Scenario 1A	24583	8141	2780	1884	614	176	0	0	38178	1.1%
Scenario 2A	23920	9022	2084	1644	684	595	198	40	38186	1.1%
Scenario 3A	23541	8896	3059	1629	663	593	197	41	38619	0.0%

6.4 Costs

The total cost comprises the production cost, the stockout cost and the outdate cost. The results for each type of cost are presented in Table 6. In scenario 3A the production cost is slightly increased, because the number of donors is not controlled by the optimization model. The stockout and expiration costs are considerably reduced in Scenario 1A. The actual costs in the baseline scenario are not shown, for reasons of confidentiality. Again, the results depend on the extent to which the blood center is able to implement the recommendations from the ILP model. Scenario 1A achieves the greatest improvement in all the indicators, which implies that decision-makers must try to take blood groups into account when planning collection and production strategies.

Table 6. Results: costs

Type of Cost	**Scenario** (% of improvement)		
	1A	**2A**	**3A**
Production Cost	1.22%	1.06%	-0.28%
Stockout Cost	17.04%	6.14%	7.32%
Expiration Cost	68.20%	32.07%	21.11%
Total Cost	4.13%	2.05%	1.05%

6.5 Generalizing the model for other time periods

In order to evaluate the performance of the model for different time periods, probability distributions were fitted for the donor arrival rates (see Appendix A) and used to replace the observed data from the study period as used in scenarios 1A, 2A and 3A. The same three implementation levels of the ILP outputs are analyzed, in three new scenarios 1B, 2B, and 3B. The results are consistent and are very similar to those obtained in scenarios 1A, 2A and 3A. The results are summarized in Table 7, which shows mean absolute values with 95% confidence intervals and mean % improvement over the baseline scenario.

Table 7. Summary of results with stochastic donor arrivals

Indicator	Baseline	Scenario 1B		Scenario 2B		Scenario 3B	
		95% CI	%	95% CI	%	95% CI	%
Stockout RBC	9490	7874 ± 101.4	17.0%	8960 ± 116	5.6%	8868 ± 134.9	6.6%
Stockout Platelets	185	76 ± 11.5	58.8%	47 ± 8.8	74.6%	108 ± 16.9	41.7%
Stockout Plasma	74	0 ± 0	100%	0 ± 0	100%	0 ± 0	100%
Stockout Cryo	292	0 ± 0	100%	0 ± 0	100%	0 ± 0	100%
Outdated RBC	1989	125 ± 9.7	93.7%	1249 ± 34.6	37.2%	1224 ± 49.1	38.5%
Outdated Platelets	1736	941 ± 41.2	45.8%	1067 ± 47.6	38.5%	1455 ± 63	16.2%
Number of Donors	38619	38167 ± 8.2	1.2%	38160 ± 8.4	1.2%	38671 ± 131.7	-0.1%
Total Cost US$ (M)		4.2%		2.2%		0.8%	

6.6 What-if Analysis

The results presented in Sections 6.1 – 6.5 are obtained using the actual weekly capacity (based on historical data). However, there is a large gap between supply and demand. Part of this gap is explained by demand overestimation in January and February, as discussed in Section 4. The other part corresponds to stockouts in other months. In order to evaluate the impact of variability in the number of donors and collection capacity, we now present the results for a further set of scenarios in which two further modifications are introduced with the aim of better matching supply and demand. We have previously seen that the best results are obtained in scenarios 1A and 1B, which (unrealistically) assume that the number of donors in the DES is exactly equal to the optimal value of the variable x_{ikt}. Therefore we now assume the number of donors is a random sample from a uniform probability distribution with limits

$$\sum_{k \in K} x_{ikt} \pm 10\%$$

The collection method for each donor is assigned according to the original proportions in the data. Secondly, the weekly collection capacity (represented by the parameter W in the ILP problem) is also allowed to vary from –40% to +40% of the original value, in steps of 10%. Figure 3 presents the percentage improvements in all KPIs, giving the decision-maker a better overview of the impact of variation in the weekly collection capacity. The x-axis in Figure 3 is the value of W, and the y-axis is the % improvement over the baseline. The results correspond to the mean of 30 iterations of the simulation model.

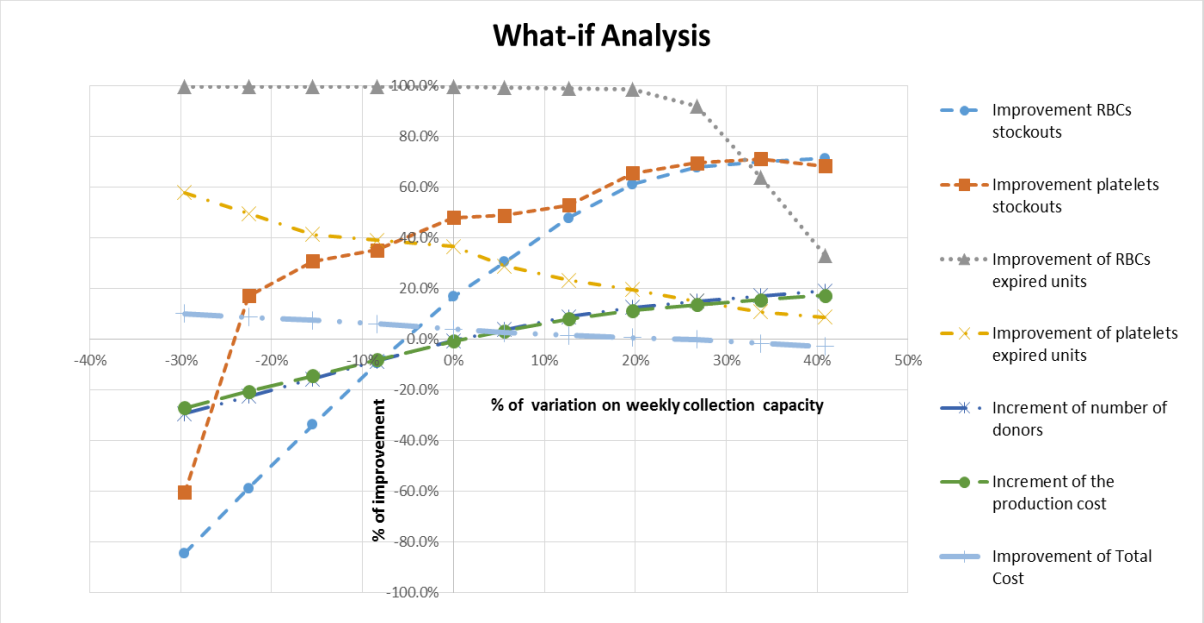

Figure 3: Performance indicators when weekly collection capacity is varied

Since in the case of the Hemocentro Distrital there is already a gap between demand and supply, those strategies in which W is decreased may be disregarded by the decision-maker. Further conclusions can be drawn from Figure 3, of which perhaps the most relevant is that the Hemocentro Distrital can considerably improve its performance indicators, without increasing the total cost, by using the proposed ILP model to plan collection and production. When the weekly collection capacity is increased, the production cost also increases since more collection and processing are carried out; however, this leads to a reduction in stockouts which compensates for the increased production cost in the total cost. Nevertheless, the improvement in the stockout KPI is not linear, since demand in some periods is overestimated and thus these stockouts are not "real" and cannot be covered even by increasing the weekly collection capacity. Increasing collection also results in a deterioration of the outdating indicator. Nevertheless, in every case where collection capacity is increased, the outdate indicators in the simulation are improved over the baseline.

7 CONCLUSIONS AND FURTHER RESEARCH

The blood supply chain continues to be an active research topic. Despite the increasing number of publications, some stages and topics, such as production and collection planning, have been studied less than others. The model presented in this paper extends the research in these areas.

The optimization model has improved supply chain performance in a range of different scenarios, with or without considering donor blood groups, and taking into account variability in donor arrivals, but including the collection/production method as a decision variable. Through the use of simulation, we have shown that the best results are obtained when the collection quantities are closest to the optimal numbers of donors, *by blood group*, determined by the optimization model.

The combination of simulation and optimization in the blood supply chain allows modeling and analysis of aspects that could be intractable using only one methodology. This integration offers a robust framework for modeling special features of the blood supply chain. In addition, the impact of uncertainty can be reduced by incorporating real-time information during the planning process. Rolling horizon models provide a means of including live information in the decision-making process.

The proposed model uses a large amount of information such as donations, demand, discard rates, costs, and inventory levels; however, this information is usually available in all blood banks. Currently blood bank information systems store very detailed information including that used here, as well as additional information regarding test results, and tracking methods for each unit of product.

The active participation of the Hemocentro Distrital throughout this project was very important: many discussions were required to understand the operational details and ensure that the models were a good representation of the real system. In view of the encouraging results, the Hemocentro Distrital is interested in starting a pilot for the proposed model, initially as a spreadsheet model and then, depending on the outcome, as an integrated module in its main information system. In terms of implementation, the most efficient way would be to integrate the optimization model into the Hemocentro Distrital's central information system. When the collection targets obtained from the model are assigned to the collection teams, the decision-maker would also need to bear in mind the specific characteristics of the chosen collection locations: the model is only a tool to support a human decision-maker, and such decisions may need to be modified in practice depending on circumstances. The optimization model solves in seconds in the commercial solver used.

Finally, the models presented in this paper can be extended in several ways. Inclusion of mismatching for internal blood banks in hospitals, multiple objective functions, prioritization of demand points and staff shift planning can all complement the model presented. This model represents a typical blood center, which operates independently from hospitals and demand points. It could be adapted for other blood supply chain topologies, but for blood banks in hospitals, the model would need to be adjusted to include compatibility of products.

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Appendix A. Probability distributions used.

Day	Donors	RBC	Plasma	Cryoprecipitate	Platelets
Sunday	Lognormal(90.725,45.635,0)	Gamma(3.6582,19.145,0)	0.5493*Weibull(1.571,43.243,0)	Actual	Weibull(2.6342,44.874,0)
Monday	Triangular(0,172.01,116)	triangular(0,132,250.37)	1.0864*Weibull(1.571,43.243,0)	Actual	Gamma(4.9766,9.2618,0)
Tuesday	Gamma(14.908,7.406, 0)	Gamma(10.466,12.198,0)	1.0327*Weibull(1.571,43.243,0)	Actual	Gamma(6.9138,8.1944,0)
Wednesday	Gamma(12.853,9.96,0)	Weibull(3.457,132.19,0)	1.2364*Weibull(1.571,43.243,0)	Actual	Gamma(4.7146,9.317,0)
Thursday	Weibull(3.3489,145.3,0)	Gamma(10.277,11.586,0)	1.1006*Weibull(1.571,43.243,0)	Actual	Gamma(5.7338,8.06,0)
Friday	Gamma(10.47,9.8342,0)	Gamma(13.781,11.601,0)	1.3835*Weibull(1.571,43.243,0)	Actual	Gamma(4.8136,8.7179,0)
Saturday	Weibull(1.8248,57.18,0)	Gamma(6.6579,10.279,0)	0.6111*Weibull(1.571,43.243,0)	Actual	Beta(1.5186,1.2625,0,68.669)

Appendix B. Values of set elements used in the example model

Index	**Collection Alternatives**	**Products required**	**Horizon planning** (days)	**Blood groups**	**Set of values for the shelf life of platelets** (days)	**Platelets production method**
	Set K	Set J	Set T	Set I	Set S	Set P
0	Triplex bag	RBCs O+ Fractionation	0	O+	0	Fractionation
1	Quadruple bag – Alt. A	RBCs A+ Fractionation	1	A+	1	Apheresis
2	Quadruple bag – Alt. B	RBCs B+ Fractionation	2	B+	2	
3	RBC by apheresis	RBCs O- Fractionation	3	O-	3	
4	Platelets by apheresis	RBCs A- Fractionation	4	A-	4	
5		RBCs B- Fractionation	5	B-	5	
6		RBCs AB+ Fractionation	6	AB+		
7		RBCs AB- Fractionation		AB-		
8		RBCs O+ Apheresis				
9		RBCs A+ Apheresis				
10		RBCs B+ Apheresis				
11		RBCs O- Apheresis				
12		RBCs A- Apheresis				
13		RBCs B- Apheresis				
14		RBCs AB+ Apheresis				
15		RBCs AB- Apheresis				
16		Platelets Fractionation				
17		Platelets Apheresis				
18		Plasma				
19		Cryoprecipitate				